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EVALUATION OF EFFECT OF EXCIPIENTS, TEMPERATURE AND HUMIDITY ON THE STABILITY OF LEVOTHYROXINE SODIUM

BY

NIRAJ S. AMIN

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN PHARMACEUTICS

UNIVERSITY OF RHODE ISLAND

2000
MASTER OF SCIENCE THESIS

OF

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2000
ABSTRACT

Levothyroxine Sodium is one of the most critical drugs for a significant segment of the population. The development of HPLC method of analysis for levothyroxine sodium revealed that there were significant stability problems associated with this drug. On August 14th, 1997, FDA announced that there was evidence which shows significant stability and potency problems associated with orally administered levothyroxine sodium products. This lack of stability and potency has a potential to cause serious health consequence to the public. The literature, on determining the stable formulation of levothyroxine sodium is very little. Much of the published work on levothyroxine sodium describes the innumerable bioavailability and potency problems with this drug. However, little in the literature explored the stability of levothyroxine sodium in presence of various excipients. The portion of work in this thesis represents a series of investigations we have performed to evaluate the stability of levothyroxine sodium in presence of some of the most commonly used excipients at different temperatures and humidities. These studies indicated that levothyroxine sodium is unstable in presence of carbohydrates such as dextrose, lactose and starch. These excipients have an aldehyde group, which may be reacting with the free amino group of levothyroxine sodium leading to a Schiff-base reaction along with oxidation reaction.

In further, series of investigations, the kinetics of degradation reactions were evaluated. First order and bi-phasic first order models were evaluated for our studies. Nonlinear regression was performed using Sigma Plot and the results suggest a biphasic-first order degradation pathway in most of the cases. The shelf life for levothyroxine sodium was
determined using the k-values obtained from the best fit models. The lower $t_{90}$ values indicated that levothyroxine sodium is highly unstable in presence of moisture and higher temperatures and so the tablets should be formulated and stored at or below room temperature with 0% humidity.
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This body of work represents the series of investigations we have performed to determine the stability of levothyroxine sodium in presence of different excipients under various conditions. Section I includes the general introduction regarding the solid state stability of levothyroxine sodium. The main body of this thesis can be found in Section II and Section III. The various chapters in the second and third section can be best envisioned as the series of investigation performed to look at the stability of levothyroxine sodium. Appendix A contains the statistical output of non-linear regression (Sigma Plot, Version 4, SPSS Inc., 1997) in modeling the degradation kinetics of levothyroxine sodium. Appendix B includes the residual plots which were used in checking the adequacy of a fit. At the end of the thesis a bibliography, which sites all the sources used in this document, is included.
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| Condition | Value |
|-----------|-------|
| 75% RH    | 75    |
SOLID STATE STABILITY: AN OVERVIEW

Background

Among the different types of drug delivery systems, solid dosage forms are by far the most common due to their dose precision, low cost, easy and inexpensive packaging and shipping. In addition product identification for these dosage forms is simple when done using embossed or monogrammed punch faces; lend themselves to certain special-release profiles, such as enteric or delayed released products; having the best combined properties of chemical, mechanical and microbiological stability of all oral forms and are the lightest and most compact of all oral dosage forms. The advantages of solid dosage forms are reflected by widely accepted practice of delivering drugs in this manner during initial clinical trials [1, 2]. Solid state stability of a drug is one of the most intrinsic and vital parts in the formulation of drug substance. One of the primary concerns during product development is producing a drug substance that has consistent stability properties in the bulk form as well as when formulated [3]. Stability testing provides evidence of how the quality of the drug substance or drug product varies over time under the influence of a variety of environmental factors such as temperature, humidity and light. A systematic approach should be adopted in the testing and evaluation of stability information which should cover, as necessary, physical, chemical, biological, and microbiological quality characteristics, including unique properties of the dosage form (for example, dissolution rate for oral solid dose forms). The design of the stability study is to establish, based on testing a minimum of three batches of the drug product, shelf life and label storage instructions applicable to all future batches of the dosage form manufactured and packed under similar circumstances. The degree of variability of
individual batches establishes the confidence that a future production batch will remain within specification until the expiration date [4]. Stability testing of the drug substances and drug products is required to support the defined expiry period for the following categories of drug regulatory submissions: Investigational New Drug Applications (IND’s), New Drug Applications (NDA’s) for both the New Molecular Entities (NME’s) and non-NME’s, Abbreviated New Drug Applications (ANDA’s), Supplements and annual reports, Biologics License Application (BLA’s) and product license applications (PLA’s) [5].

The term ‘pharmaceutical stability’ encompasses a range of parameters. The most common interpretation is the chemical stability of the drug substance in a dosage form. However, the performance of a drug when given as a tablet, capsule, syrup or injection is not only dependent upon the content of the drug substance, but also on its pharmaceutical properties (dissolution, disintegration, hardness, friability, content uniformity etc.) [1]. All of these parameters must, therefore, be a part of the stability program. In 1994 International Conference on Harmonization (ICH) guidelines for stability testing were published and are as follows [4].

Information on the stability of Active Pharmaceutical Ingredient (API) under defined storage conditions is an integral part of the systematic approach to stability evaluation. Stability information from accelerated and long-term testing should be provided on at least three production batches. Long term stability should cover a minimum of 12 month’s duration on at least three production batches at the time of submission. The testing should cover especially those features susceptible to change during storage and likely to influence quality, safety and/or efficacy. Stability information should cover as
necessary the physical, chemical, biological, and microbiological test characteristics. The length of studies and storage conditions should be sufficient to cover storage, shipment, and subsequent use. The 6-month accelerated testing should then be carried out at a temperature at least 15°C above long term storage temperature (25°C ± 2°C, 60% ± 5% RH. The general guidelines for storage conditions and testing periods for bulk drugs and drug product is given in Table 1.

Table 1. Long-term/accelerated testing conditions

|                      | Conditions                        | Minimum Time Period At Submission |
|----------------------|-----------------------------------|-----------------------------------|
| **Bulk Drug**        |                                   |                                   |
| Long Term Testing    | 25°C ± 2°C, 60% ± 5% RH           | 12 months                         |
| Accelerated Testing  | 40°C ± 2°C, 75% ± 5% RH           | 6 months                          |
| Intermediate Testing | 30°C ± 2°C, 60% ± 5% RH           | 6 months                          |
| **Drug Product**     |                                   |                                   |
| Long Term Testing    | 25°C ± 2°C, 60% ± 5% RH           | 12 months                         |
| Accelerated Testing  | 40°C ± 2°C, 75% ± 5% RH           | 6 months                          |
| Intermediate Testing | 30°C ± 2°C, 60% ± 5% RH           | 6 months                          |

If 'significant change' occurs due to accelerated testing, additional testing at an intermediate condition e.g., 30°C ± 2°C, 60% ± 5% RH should be conducted. 'Significant change' at the accelerated condition is defined as [1]:

a) A 5 percent potency loss from the initial assay value of the batch;
b) Any specific degradant exceeding its specification limit;
c) The product exceeding its pH limits;
d) Dissolution exceeding the specification limits for 12 capsules or tablets;
e) Failure to meet specifications for appearance and physical properties e.g., color, phase separation, resuspendibility, delivery per actuation, caking, hardness etc.
Modes of Drug Degradation

Drug degradation occurs by four main processes [6]:

Hydrolysis due to $\text{H}_2\text{O}$, $\text{H}_3\text{O}^+$, $\text{OH}^-$, pH

Oxidation

Photolysis due to UV, visible light

Trace metal ion catalysis due to $\text{Fe}^{2+}$, $\text{Fe}^{3+}$, $\text{Cu}^{2+}$, $\text{Co}^{2+}$, etc.

The decomposition of drugs are most often classified as either hydrolysis or oxidation. Most drugs contain more than one functional group, and hence may be subjected simultaneously to oxidation as well as hydrolysis. Other reactions such as epimerization, isomerization and photolysis may also affect the stability of drugs.

Hydrolysis may be caused by reaction of water with amides or esters. Water may also react with the ions of salts of weak acids and weak bases. Molecular hydrolysis reactions proceed much more slowly then the ionic hydrolysis (protolysis) [7]. In solid dosage formulations, free moisture is contributed by various additives or excipients, as well as the drug. In tablets a small percentage, typically 2% (w/w) of moisture, is required to facilitate good compression. This free water has the ability to act as a vector for chemical reactions between the drug and the excipients [6]. Some of the most common examples are: the hydrolysis of aspirin above pH 10 and hydrolysis of chloramphenicol which is pH independent is catalyzed by general acids and bases [7].

Oxidation reactions involve the removal of electrons or loss of hydrogen (dehydrogenation) from the molecules. When the reaction involves molecular oxygen, it is called auto-oxidation. Oxidation reactions frequently involve free radicals of atoms or molecules containing one or more unpaired electrons, or free hydroxy and molecular
Oxygen (O — O). Oxidation may be catalyzed by the presence of trace amounts of heavy metals and organic peroxides [7]. The oxidation of unsaturated fats and oils proceeds in the presence of atmospheric oxygen, light and trace amounts of catalysts according to free radical chain reactions. The hydroperoxide (R’—CHOOH—CH=CH—R”) formed in the reaction may further decompose, and the reaction continues until the free radicals formed in the reactions are destroyed by inhibitors or by side reactions which will break the chain. Another classic example is the oxidation of ascorbic acid to dehydroascorbic acid in the presence of copper ions and oxygen. When the solution of ascorbic acid is freed from copper ions, the oxidation of ascorbic acid in alkaline medium will cease [7].

Oxidation and, to some extent, photolysis may be catalyzed by light. The energy of light is inversely related to wavelength (ultraviolet > visible > infrared) and is independent of temperature. When the molecules are exposed to electromagnetic radiation (EMR), they absorb light at characteristic wavelengths, which causes an increase in the energy state of the compound. This energy may cause:

decomposition

retention or transfer of energy

conversion to heat

emission of light at a new wavelength (as fluorescence, phosphorescence).

Photodegradation is dependent on both the intensity and the wavelength of light and is usually mediated by free radicals to produce dark colored substituents [6]. Some of the simple strategies for improving drug stability are given in Table 2.
Table 2. Simple strategies for improving drug stability

(Table reprinted from reference 6)

| Degradation Process | Method of Protection |
|---------------------|----------------------|
| 1) Hydrolysis       | Remove water, moisture |
|                     | e.g. Use dry desiccant |
|                     | Lower water activity |
|                     | e.g. Add humectants |
|                     | Change excipient(s) |
|                     | e.g. Compatibility studies |
|                     | Use solid dosage forms |
|                     | e.g. Tablets and capsules |
|                     | Freeze dry injections |
| 2) pH               | Identify pHmin |
|                     | e.g. Addition of buffers |
| 3) Temperature      | Refrigerate 4°C |
|                     | Cool place ≤ 15°C |
| 4) Oxidation        | Include antioxidant |
|                     | e.g. Ascorbic acid |
|                     | Sulphites |
|                     | Chelate metal ions |
|                     | e.g. EDTA |
|                     | Remove O2 |
|                     | e.g. N2, CO2 or He |
| 5) Photolysis       | Protect from light, Packaging |
Drug-Excipient Compatibility Testing

What emerges from a drug discovery program is an Active Pharmaceutical Ingredient (API) or drug substance. The API is the basis for producing the therapeutic activity expected of the drug and becomes a drug product after formulation with various excipients to produce a dosage form. Hastening the drug development process and optimization of dosage form stability are two major goals of any drug development program. The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients used to facilitate administration, promote consistent release, enhance bioavailability of the drug and protect it from degradation. Hence, excipients are the integral components of almost all pharmaceutical dosage forms. In mixtures of solids, incompatibilities or chemical interactions can occur by following mechanisms [6]:

- degradation by nucleation via the gaseous phase
- contracting surface due to nucleation with coverage by the breakdown products
- degradation mediated by surface moisture or eutectic films
- oxidation
- photolysis.

Degradation in the solid state may be affected by several factors, such as the proportion of the drug to excipient(s), method of mixing, hygroscopicity of the powder mixture, hygroscopicity of the substance involved, temperature, humidity, particle size distribution, particle packing, porosity of the powder bed, etc. Hence, in pharmaceutical preformulation drug-excipient compatibility studies are obligatory. Interestingly, with the
importance of drug-excipient compatibility studies, no general method is available for these studies.

Ahlneck et al. [8] studied the three commonly used methods for drug-excipient screening: the suspension technique, storage of powder mixtures and compacts at specified temperatures and stored at specified relative humidities; and evaluated the variables influencing drug degradation. They concluded that the suspension technique is a fast-screening method for detecting chemical stability problems but gives limited information on the stability of a drug in solid dosage forms. The solid state techniques, i.e. the powder mixtures and compacts, gave a better picture of the stability profile of a solid dosage form composition. The solid state procedure took into account a large number of variables such as powder mixing, particle size, surface area, moisture adsorption, etc.

Monkhouse et al. [9] suggested that one should eliminate drug-excipient compatibility testing and instead select excipients on the basis of the physical and chemical characteristics of the drug substance and the literature data for the excipients. They recommended that the final composition should be selected on the basis of the accelerated stability testing of one or more target formulations at high temperature and humidity.

In 1999, Serajuddin et al. [10] reported a method that may be used successfully to identify the relative influence of different excipients on the stability of the drug. They proposed a model which involved storing drug-excipient blends with 20% added water in a closed glass vials at 50°C and analyzing at one and three weeks for chemical and physical stability. The amount of the drug substance in the blend was determined on the basis of the expected drug-to-excipient ratio in the final formulation. The effect of several
key factors such as the chemical nature of the excipient, drug-to-excipient ratio, moisture, micro environmental pH of the drug-excipient mixture, temperature, and light on the dosage form stability could be identified by using this model. They suggested that selection of the dosage form composition by using this model at the outset of the drug development program would lead to a reduction of surprise problems during long term stability testing of drug products.

**Quality and Functionality of The Excipients**

Excipients are better known as promoters of degradation rather than as stabilizers of drug substances. Different functional groups or residues present in the excipients may have the propensity to interact with labile active ingredients or drugs, causing loss of molecular integrity or degradation. The quality of the final product depends not only on the active principles and production processes, but also on the performance of the excipients. Excipients have undergone an evolution from an ‘inert’ and cheap vehicle to an essential constituent of the formulation that enhances the stability and the bioavailability of the drug substance in the drug product and improves its manufacturability on a production scale. The studies of interactions between a drug and the excipients shows that complexation, hydrogen bonding, ion-dipole, dipole-dipole and van der waals attractions can modify the physicochemical, pharmacological or pharmacokinetical behavior of the final product especially in the solid dosage forms [11, 12, 13].

If excipients have to act as stabilizers they must obviate or alternate the factors that cause molecular transformation of drug substances. These factors may be environmental components such as water vapor and sunlight. Other factors include stress during the
processing of the dosage form such as size reduction, compaction or sterilization, or interactions between adjacent molecules of the drug or functional groups on the same molecule [11].

**Moisture Related Degradation**

Water is one of the major factors responsible for causing degradation in pharmaceutical formulations. It may be associated with the drug or the excipients, may be incorporated during the processing of dosage forms or may be acquired from the environment during packaging or storage. Because of its ubiquitous nature and its ability to exist as a vapour, water is virtually impossible to avoid and difficult to control. The molecular mass of water is low, and so small amounts may be significant in terms of molecular reactivity. Water is also capable of diffusing, to some extent, through packaging materials, pack seals or through compacted solid dosage forms [11].

Excipients with a greater affinity for moisture might aid in mitigating moisture sensitivity. Thus, formulation with a substance having a greater affinity for water as compared to the drug may help in sequestering moisture in the product. Perrier et al. [14] used nitrogen sorption isotherms to predict the effect of common excipients on the stability of nitrazepam. They determined that excipients with higher absorption energies caused less degradation, meaning, if the excipient has a higher binding energy for water as compared to the drug, the excipient may act as a desiccant and stabilize the drug. Along with moisture, residues of lower alcohols (methanol, ethanol, isopropanol) might be present in the final formulation, as a result of synthesis, isolation of the drug or the process used for manufacturing the dosage form. Nimry et al. [15] and Tobyn et al. [16]
showed that materials such as amorphous silica and microcrystalline cellulose may act as ‘scavengers’ of volatile residues and help in stabilizing the formulation.

**Degradation by Oxidation**

Loss of drug quality due to oxidation is usually secondary to hydrolytic breakdown. These reactions are often complex and caused by factors that are difficult to separate and clarify. Oxidation can be catalyzed by exposure to air or light, the presence of trace residues (metal ions), by other components in the formulation or the combination of all the above mentioned factors.

Formulation additives have been effective in the stabilization of vitamin preparations. The antioxidants tocopherol, butylated hydroxy anisole, butylated hydroxy toluene and propyl gallate have all be used to stabilize vitamins A and D₃ [17, 18]. Reyes [19] showed that magnesium, calcium and aluminium stearates helped in the stabilization of ascorbic acid.

**Photodegradation**

Exposure to light may precipitate a plethora of degradation reactions, such as polymerization, isomerization, addition reactions in unsaturated systems, substitution reactions and photo-oxidation [20].

Thoma and Klimek introduced the concept of spectral overlay. This approach involves formulating with an excipient whose UV absorption spectrum overlaps (or substantially overlaps) that of the compound requiring stabilization. The excipient would thus compete with the active compound for photons from a radiation source and hence the impact of damaging radiation would be attenuated. They showed that the photolabile calcium antagonist nifedipine can be stabilized by the natural food colorant, curcumin, or by riboflavin [21]. Sanderson et al. [22] showed that the stability of a β-lactam BRL42715B
can also be enhanced by addition of a ‘blocker’ such as titanium dioxide and addition of soft paraffin with a UV spectrum that provided a partial spectral cover.

The spectral overlay approach is an elegant way to stabilize a drug. However the list of potentially useful materials which are free from pharmaceutical activity and are non-toxic is very limited.

**Other Modes of Degradation**

Some degradation reactions like isomerization, dimerization, polymerization and other forms of molecular rearrangements do not involve species other than the active ingredient. These of reactions are common in drugs of large molecular mass or those of biological origin. Hence it might seem that molecules with an intrinsic ‘self-destructing’ capability would be most difficult to stabilize.

Cyclodextrins are unique compounds, due to their unique, molecular complexation capability has been shown to improve the stability of compounds such as clofibrate and isosorbide which have tendency to sublime [23]. Cyclodextrins have also been shown to stabilize labile materials such as PGE$_1$ and PGF$_2$ by forming molecular encapsulation [24].

The use of excipients to stabilize an unstable ingredient is an attractive concept. A product can be developed that will retain its quality while the drug and other formulation ingredients are in close association. However, there are few examples, as listed in Table 3, in which excipients may destabilize or decrease the efficacy of the drug.
### Table 3. Studies of interactions between API’s and excipients in pharmaceutical formulation

| Active Medicament/Excipient | Stoichiometry (molar ratios percentages) | Therapeutic activity | Pharmaceutical formulation | Results of interaction | References |
|-----------------------------|------------------------------------------|----------------------|----------------------------|------------------------|------------|
| Acetylsalicylic acid/Eudragit RS, starch, Dextrose monohydrate | Different proportions – 5, 10, 15, 25% | Analgesic antipyretic | Matrix-tablets | Poor drug release | Ref. 25 |
| Carteolol hydrochloride/ Eudragit L | 22% Carteolol | A potent β-adrenergic blocking action | Tablet | Type ammonium salt interactions (Polymeric complex) | Ref. 26 |
| Chloramphenicol stearate/ colloidal silica | | Antibiotic | Powder | In vitro higher enzymatic hydrolysis rate | Ref. 27 |
Methods for Studying Interactions between Drug and Excipients in Pharmaceutical Formulations

Presently, infra-red (IR)-spectroscopy, nuclear magnetic resonance (NMR) spectroscopy, differential scanning calorimetry (DSC) and X-ray diffraction are the most commonly used methods to investigate interactions between drugs and the excipients in pharmaceutical formulations. IR spectroscopy is sensitive to crystalline form changes. Since it is inherently based on molecular vibrations, IR has an advantage of being sensitive to functional group changes in low or non-crystalline materials. IR spectroscopy helps in looking at interactions between the drug and the excipient by following important characteristics such as the appearance of new IR absorption band(s), the broadening of band(s), and alteration in intensity. These comparisons are performed by comparing the IR spectra of the drug alone, the excipient alone, the complex and the simple physical mixture (prepared in same stoichiometry as a complex from both the drug and the excipient(s) [13]. For example, IR was used to determine which excipients participate in the salt to free base conversion of delavirdine. The spectra of delavirdine mesylate indicated that free base was formed in all the mixtures except the one where croscarmellose sodium was absent. The spectra revealed that croscarmellose sodium in the tablet matrix was necessary to prevent conversion of the delavirdine salt to a free base [27]. An electronic database is available for comparison and identification of absorption and transmission spectra for excipients and the drugs which can be used to determine functional groups or degradation products present in the mixtures. This can be done by extrapolating the spectra obtained with that present in the database.
Solid state NMR can be used to determine inter and intra-molecular interactions and crystal packing in the solids at a molecular level; and are, therefore, useful for distinguishing between closely related solid forms of the same molecular entity. Rohrs et al. [28] used solid state NMR to characterize and quantify the forms of delavirdine in the tablet form. Three crystalline forms of delavirdine mesylate have been characterized, and the distinct NMR features observed among these and other forms were used for diagnostic purposes. The identification of the drug form(s) were used to verify that no major interferences occurred from tablet excipients. It was seen that there were no interferences from the tablet excipients with the drug forms in the tablet matrix.

DSC is another important tool which is used to study changes in the melting point of compounds and hence determine polymorphic changes in the mixtures. Jain et al. [29] used DSC to evaluate the amount of moisture pickup in a drug-moisture-lactose interaction. They found that stable solid lactose exists in α-monohydrous, α-anhydrous, and β-anhydrous forms. DSC studies revealed that the α-anhydrous lactose which is present in small quantities in β-lactose is responsible for moisture uptake and hence makes the formulation unstable.

Crystalline materials in powder form exhibit highly characteristic X-ray diffraction patterns in which the positions and relative intensities of peaks are well-defined and reproducible. The diffraction pattern of a crystalline powder is characteristic for the crystal lattices of that particular polymorph. By measuring the rate of disappearance (or appearance) of a peak unique to a reactant (or product), the kinetics of a reaction or transformation can be determined. This method has been used to follow the desolvation reaction of several crystalline hydrates. Since crystals serve as unique micro-reaction
vessels, X-ray crystallography can often be used to determine the exact position of atoms as they re-orient themselves during a reaction. This can provide valuable information in predicting the path followed by atoms throughout the course of a reaction. Because of the wealth of information offered by X-ray analysis, it can be expected to play an important role in solid state stability studies [30].

LEVOTHYROXINE

INTRODUCTION

In 1891, G.R. Murray published a paper in the British Medical Journal showing the beneficial effects of using sheep thyroid extract in the treatment of hypothyroidism [31]. Kendall [32] and Harrington [33] later determined that levothyroxine was the primary active component in thyroid extracts.

Levothyroxine Sodium is a sodium salt of the levo isomer of the endogenous secretion of the thyroid gland thyroxine. Thyroid hormones affect protein, lipid, and carbohydrate metabolism; growth; and development. Thyroid hormones stimulate oxygen consumption by most of the cells in the body, resulting in an increased energy expenditure and heat production. It also possesses a cardiostimulatory effect that may result in direct stimulation of the heart [34]. Orally administered levothyroxine sodium is used as a supplemental or replacement therapy in conditions with diminished or absent thyroid function such as cretinism, myxedema, nontoxic goiter or hypothyroidism. It is also used as replacement or supplemental therapy in patients with secondary (pituitary) or tertiary (hypothalamic) hypothyroidism, making levothyroxine a life long medication [35]. In
1997, it was estimated that about 8 million Americans received thyroid replacement therapy, which makes it a drug of critical importance for a significant segment of population [36].

In 1955, Flint laboratories introduced the first orally administered synthetic levothyroxine sodium in the United States [37]. In 1982, the FDA, in conjunction with the United States Pharmacopeial Convention, took an initiative in organizing a workshop to set the standard for the use of High Pressure Liquid Chromatography (HPLC) assay for the quality control of levothyroxine sodium. The assay method initially used in the USP was based on a titrametric determination of iodine content, was deemed to be neither specific nor stability indicating and was unable to distinguish between active drug and the iodine containing decomposition products. Moreover, the iodine content method was quite insensitive, requiring 3 mg of levothyroxine sodium per assay or 120 tablets of the 25 ug dosage form which made the method unsuitable for product quality control, regulatory control, content uniformity and routine stability testing [38].

In the quest to find a stability indicating method, Smith et al. [39]. In 1981, proposed the first HPLC system for the determination of levothyroxine sodium in tablets. They used an octadecylsilane reversed phase column, with a mobile phase consisting of potassium dihydrogen phosphate, methanol, and water at 44°C and using a UV spectrophotometric response at 254 nm. Though this method exhibited accuracy and precision, it was not stability indicating, and the quantitation of levothyroxine sodium was complicated by interferences observed in aged samples. In 1984, Garnick et al. [38] proposed a HPLC system which consisted of a bonded phase cyanopropyl column with a mobile phase consisting of acetonitrile : water (40 : 60 v/v) and 0.05% phosphoric acid; and used a UV
detector at 225 nm. After several modifications to this method the USP published a stability indicating assay for levothyroxine sodium and determined that orally administered levothyroxine sodium products had significant stability problems [40].

In 1990, Gupta et al. [41] analyzed levothyroxine sodium tablets from two different manufacturers. The results indicated that one of the brands, contained excipient(s) which acted as catalyst(s) to hasten decomposition. Tablets from the same manufacturer but from different batches showed an additional long peak in the chromatogram, indicating that the excipient(s) may have been changed. In 1992, Won [42], published a most interesting paper, which indicated that the kinetics of degradation of levothyroxine in aqueous solution and in the solid state are significantly different. It appears that in aqueous solution the major degradation pathway involves deiodination while in solid state levothyroxine follows a deamidation pathway.

Between 1987 and 1994, FDA received 58 adverse drug experience reports associated with the potency of orally administered levothyroxine sodium products. Out of the 58 reports, 47 suggested that the products were sub-potent, while 9 suggested super-potency. Some of the problems reported were the result of switching products from different manufacturers. However, other adverse events occurred when a patient received a prescription refill of a product from the same manufacturer on which they had previously been stabilized, indicating a lack of consistency, potency and bioavailability between different lots of tablets from the same manufacturer. From 1991 to 1997, there had been no less than 10 firms initiating recalls of levothyroxine sodium tablets, involving 150 lots and more than 100 million tablets. In all but one case, the recalls were initiated because the tablets were found to be either sub-potent or potency could not be assured through the
expiration date. The remaining recalls were initiated on the products that were found to be superpotent. It appears that the stability problem for levothyroxine sodium is quite complex and with some products, at least, stability is batch dependent [35].

After evaluation of the above mentioned problems, on August 14th, 1997, the FDA stated that there was sufficient evidence which showed significant stability and potency problems associated with levothyroxine sodium products. Usage of such products is believed to cause potentially serious health consequences in the public. In view of the stability and potency problems associated with levothyroxine sodium products, FDA retrograded all levothyroxine products as new drugs for which approval by NDA or ANDA would be required [35].

From the literature, it can be seen that very little has been done to successfully develop a stable formulation of levothyroxine. There are limited publications exploring the stability of levothyroxine sodium in presence of excipients. Investigations to evaluate the stability of levothyroxine sodium in presence of some of the most commonly used excipients, such as dextrose, dicalcium phosphate dihydrate, calcium sulfate, mannitol, etc at various temperatures and humidities would assist in selecting formulation ingredients, and would also provide insight into the nature of degradation typical with levothyroxine sodium. Such studies were hoped to provide a better understanding of the formulation parameters to be used to optimize formulations and processing for the improvement of the drug stability.
GENERAL PROPERTIES OF LEVOTHYROXINE (Ref. 43)

i) Chemical Name:
   a) Sodium derivative of 3-[4-(4-hydroxy-3,5-diodophenoxy)-3,5-diodophenyl]-L-alanine.
   b) L-3,3',5,5'-Tetraiodothyronine, sodium salt, pentahydrate.
   c) β-[(3,5-diiodo-4-hydroxyphenoxy)-3,5-diodophenyl]-alanine, sodium salt pentahydrate.

ii) Generic Name: Sodium Levothyroxine

iii) Trade Names: Synthroid®, Levoxyl®, Eltroxin® etc.

iv) Empirical Formula and Molecular Weight:
   L-4 Sodium salt pentahydrate
   \[ \text{C}_{13}\text{H}_{10}\text{I}_{4}\text{N}_{\text{Na}}\text{O}_{4} \cdot 5\text{H}_{2}\text{O} \]
   888.96
   Anhydrous Sodium salt of L-4
   \[ \text{C}_{13}\text{H}_{10}\text{I}_{4}\text{N}_{\text{Na}}\text{O}_{4} \]
   798.86
   L-4 free acid
   \[ \text{C}_{13}\text{H}_{11}\text{I}_{4}\text{NO}_{4} \]
   776.93
v) **Structure:**

![Structure of levothyroxine sodium]

Figure 1. Structure of levothyroxine sodium

vi) **Organoleptic Properties:**

Color: White to Pale Yellow.

Odor: Odorless.

vii) **Melting Range:**

235°C – 236°C.

viii) **Stability:**

Levothyroxine is sensitive to irradiation, hydrolysis, oxidation and heat.

ix) **Solubility:**

| Solvent            | Levotroxine Solubility in gm/100ml |
|-------------------|------------------------------------|
| H₂O               | 0.14                               |
| 95% Ethanol       | 0.4                                |
| Alkali Hydroxides | Soluble                            |
| Chloroform        | Almost insoluble                    |
| Ethyl Ether       | Almost insoluble                    |
| Phosphate buffer pH 7.4 | 0.022 - 0.044         |

Table 4. Solubility profile of levothyroxine sodium in presence of different solvents
SECTION II : EXPERIMENTAL
The study of drug-decomposition kinetics, the development of a stable dosage forms, and the establishment of expiration dates for drug products should evaluate the parameters that are likely to affect the quality, safety, and/or efficacy of the drug product. The analytical procedure should be fully validated and the assays should be stability-indicating.

During pre-formulation stage, one of the objectives of the stability studies is to establish excipient-compatibility information to help the formulator design a stable and efficacious formulation. Excipients can affect the stability of drugs by: (1) acting as surface catalysts; (2) altering the pH of the moisture layer; and (3) undergoing direct chemical reaction with the drug. The above mentioned problems thus require a screening of a large number of excipients under several storage conditions such as temperature, humidity, and light. This study helps in developing analytical, physical, and chemical data that will facilitate formulation studies and manufacturing. These studies also allows the formulator to: (1) determine reactivities of the drug substances; (2) establish whether or not special handling and storage procedures are required to protect the drug substance; (3) ensure that the potency is sufficient and the level of significant degradation products may be significant throughout the life of the supplies; (4) develop supporting data for subsequent stability studies of the formulated drug; and (5) delineate any interaction between selected formulation excipients and the drug substance.

Once the initial screening of the excipients is done, the next step is to perform the stability studies on the formulated dosage form(s) under several storage conditions of temperature and humidity. In case of tablets, stability studies should also include
evaluation of characteristics such as: appearance, friability, strength, hardness, color, disintegration and dissolution.

I) STABILITY INDICATING ASSAY FOR LEVOTHYROXINE SODIUM:
The selected HPLC method was selected to provide high sensitivity for levothyroxine sodium along with its reference standard liothyronine sodium at very low concentrations, as well as to be highly reliable and simple to use within the constraint of these studies.

REAGENTS / EQUIPMENTS USED:

Equipments

Metler AE 240 Weighing balance
Ultrasonifier (Fisher Scientific)
Magnetic Stirrer (Thermix® Model 120 MR)

HPLC System consisting of:
Automated Gradient Controller (Waters®)
HPLC Pumps (Waters® Model 515)
Auto Sampler (Waters® Model 717 plus)
LC Spectrophotometer (Waters® Model 480)
Data Module (Waters® Model 746)
L-10 column (Zorbax®)

Column Temperature Controller (Fiatron Systems Inc, Model TC-50)

Reagents
Levothyroxine Sodium (Biochemie Labs, Lot# 78459003)
Liothronine Sodium (Sigma Labs, Lot # 98H11681)
Sodium Hydroxide (Fisher Scientific, Lot # S318-500)
Methanol (HPLC Grade, Fisher Scientific, Lot # A452-4)
Acetonitrile (HPLC Grade, Fisher Scientific, Lot # A998-4)
O-Phosphoric Acid (Fisher Scientific, Lot # A260-500)
Deionized water.

STANDARD PROCEDURE:
If the HPLC system has not been used for a week or more, the system should be purged and primed as described in the instruction manual.

PREPARATION OF MOBILE PHASE:
Prepare a mixture of water and acetonitrile (70 : 30) containing 1 ml of o-phosphoric acid in each 1000 ml of the mixture. While making the mobile phase water and o-phosphoric acid should be mixed prior to the addition of acetonitrile. Mix the mobile phase for 5 minutes with magnetic stirrer. Filter the mobile phase using vacuum pump. Degas the mobile phase in ultra-sonifier for 5 minutes.

PREPARATION OF HPLC SYSTEM:
Connect the L-10 column to the system and make sure that the connections are tight.

Turn on the system and set the following parameters:
The column thermostat temperature should be set to 30°C.
The absorbance of the spectrophotometer should be set to 225 nm.
The flow rate should be set to 1 ml/minute.
The run time should be set to 20 minutes.
Injection volume should be set to 25 µl.
Number of injections from each vial should be set to 5.
Allow the system to stabilize for at least 2 hours.

PREPARATION OF STANDARDS:

0.01M METHANOLIC NaOH: Approximately 400mg of NaOH was weighed and dissolved in 500ml of water in 1000ml volumetric flask. To it 500ml of methanol was added to make up the volume.

STOCK SOLUTION (500µg/ml) OF L-4: Approximately 0.025g of L-4 was weighed and transferred to 50 ml volumetric flask. The volume was made up with 0.01M methanolic NaOH.

STANDARD SOLUTION (5µg/ml) OF L-4: 1ml of above stock solution was taken in 100ml volumetric flask and the volume was made up with 0.01M methanolic NaOH.

L-4 SOLUTION (10 µg/ml): 1ml of above stock solution was taken in 50 ml volumetric flask and the volume was made up with 0.01M methanolic NaOH.

Following the above procedure, L-3 solutions were prepared.

SERIAL DILUTIONS:

L-4 (0.2 µg/ml) and L-3 (0.2 µg/ml): 2ml of L-4 (10 µg/ml) + 2ml of L-3 (10 µg/ml) in 100ml volumetric flask and volume made up with 0.01M methanolic NaOH.

L-4 (0.4 µg/ml) and L-3 (0.4 µg/ml): 4ml of L-4 (10 µg/ml) + 4ml of L-3 (10 µg/ml) in 100ml volumetric flask and volume made up with 0.01M methanolic NaOH.

L-4 (0.6 µg/ml) and L-3 (0.6 µg/ml): 60 µL of L-4 stock + 60 µL of L-3 stock in 50ml volumetric flask and volume made up with 0.01M methanolic NaOH.
L-4 (8 µg/ml) and L-3 (8 µg/ml): 80 µL of L-4 stock + 80 µL of L-3 stock in 50ml volumetric flask and volume made up with 0.01M methanolic NaOH.

L-4 (1 µg/ml) and L-3 (1 µg/ml): 100 µL of L-4 stock + 100 µL of L-3 stock in 50ml volumetric flask and volume made up with 0.01M methanolic NaOH.

L-4 (2 µg/ml) and L-3 (2 µg/ml): 200 µL of L-4 stock + 200 µL of L-3 stock in 50ml volumetric flask and volume made up with 0.01M methanolic NaOH.

L-4 (4 µg/ml) and L-3 (4 µg/ml): 400 µL of L-4 stock + 400 µL of L-3 stock in 50ml volumetric flask and volume made up with 0.01M methanolic NaOH.

L-4 (6 µg/ml) and L-3 (6 µg/ml): 600 µL of L-4 stock + 600 µL of L-3 stock in 50ml volumetric flask and volume made up with 0.01M methanolic NaOH.

L-4 (8 µg/ml) and L-3 (8 µg/ml): 800 µL of L-4 stock + 800 µL of L-3 stock in 50ml volumetric flask and volume made up with 0.01M methanolic NaOH.

L-4 (10 µg/ml) and L-3 (10 µg/ml): 1000 µL of L-4 stock + 1000 µL of L-3 stock in 50ml volumetric flask and volume made up with 0.01M methanolic NaOH.

RECOMMENDATIONS:

Confirming to the standard procedure described above, together with the following recommendations allowed the assay of levothyroxine sodium in a consistent and reproducible manner.

Prepare fresh standards everyday.

Wait for the HPLC system to stabilize.

The mobile phase should be properly degassed and the pump should be free of air bubbles. If there are erratic changes in the pump pressures, it might be due to entrapment
of air in the pump heads. The pumps should be primed to remove the entrapped air. If the problem still persists, inlet and outlet check valves of the pump should be checked.

Always mount the magnetic stirrer in the mobile phase.

Any problem with the assay may be due to pumps, column, standard, sample, technique and should be isolated by checking each in turn.

A) VALIDATION OF ASSAY:

Investigations into the validity of the method have been undertaken. Using suitable standards, all containing liothyronine, the slope, measuring range and linearity of the calibration curve were determined for levothyroxine sodium. Additional studies were also completed to determine the validity of the typical analytical parameters used in the assay such as precision, accuracy, linearity, selectivity etc. In a further series of investigations, the storage of levothroxine sodium in .01 M methanolic NaOH at room temperature over a period of 2 days was also investigated. This was performed to make sure that levothyroxine sodium does not degrade during the analysis, which takes 35 hours.

PRECISION: The precision of an analytical method is the closeness of the test results when the procedure is applied repeatedly to multiple aliquots from a single homogenous sample. Thus, it is a measure of the degree of reproducibility of the analytical method under normal operating circumstances. Precision is determined by repeatedly assaying multiple samples removed from the homogenous sample.

ACCURACY: The accuracy of an analytical method is the closeness of test results obtained by the method to the true value. It is a measure of the exactness of the analytical
method. Accuracy is determined by using the calibration curve to determine the concentration of a sample (with known concentration). The accuracy of our assay method, expressed as percent recovery was found to be greater than 95% throughout the linear range used.

**LINEARITY:** The linearity of an analytical method is its ability to elicit test results that are directly, or by a well defined mathematical transformation, proportional to the concentration of analyte in samples within a given range. Linearity expressed in terms of the variance around the slope of the regression line.

**ACCURACY SELECTIVITY / INTERFERENCES:** Placebo analysis was performed to check for interference or junk peaks due to excipients. No interfering peaks were observed with all nine excipients.

**REPRODUCIBILITY:** Reproducibility is limited by factors such as temperature, fluctuations and noise. The reproducibility was found to be independent of concentration and temperature, as the temperature of the column was controlled by a thermostat.

**LIMIT OF DETECTION (LOD):** Determination of the signal-to-noise ratio is performed by comparing measured signals from samples with known low concentrations of analyte with those of blank samples and establishing the minimum concentration at which the analyte can be readily detected. A signal-to-noise ratio between 3 or 2:1 is generally considered acceptable for estimating the detection limit. In our assay method LOD was found to be 0.4µg/ml, with a signal-to-noise ratio of 3:1.

**LIMIT OF QUANTITATION (LOQ):** Determination of the signal-to-noise ratio is performed by comparing measured signals from samples with known low concentrations of analyte with those of blank samples and establishing the minimum concentration at
which the analyte can be readily quantified. A typical signal-to-noise ratio is 10:1. In our assay method LOQ came out to be 0.6µg/ml, with a signal-to-noise ratio of 10:1.

No significant differences were found in the concentrations of the samples stored for 2 days at room temperature. Placebo analysis were performed for all excipients to be used to make sure that the excipient peaks do not interfere with the levothyroxine peaks. No additional peak were seen which confirmed that the excipients did not interfere with levothyroxine peaks. Tables 5 and 6 shows the mean values of the data generated out of five days of validation studies for ten separate and distinct samples for series of levothyroxine sodium and liothyronine sodium concentrations ranging from 0.2 to 10 µg/ml. Figures 2 and 3 illustrate the complete as well as linear portion of the calibration curve for these samples. The correlation coefficient was found to be 0.9999 and 0.9997 for levothyroxine sodium and liothyronine sodium respectively.
Table 5. Reproducibility of levothyroxine sodium from standard solutions over 5 days of validation studies

| DAY 1,2,3,4&5 | AVERAGE      | Std Dev     | %CV         |
|--------------|--------------|-------------|-------------|
| 0.2          | 23155.8      | 1692.483    | 7.30911     |
| 0.4          | 51158.36     | 2037.795    | 3.983307    |
| 0.6          | 84070.32     | 3589.236    | 4.269326    |
| 0.8          | 112283.96    | 5918.373    | 5.270898    |
| 1            | 139962.48    | 4930.562    | 3.522774    |
| 2            | 293628.6     | 6953.736    | 2.368208    |
| 4            | 600607.8     | 12771.75    | 2.126471    |
| 6            | 904545.04    | 27866.95    | 3.082981    |
| 8            | 1215639.2    | 30161.43    | 2.481117    |
| 10           | 1496429.92   | 43786.46    | 2.926062    |

Standard curve for Levothyroxine Sodium

\[ y = 151358x - 6665.3 \]
\[ R^2 = 0.9999 \]

Figure 2. Representative calibration curve from the validation study for levothyroxine sodium assay
Table 6. Reproducibility of liothyronine sodium from standard solutions over 5 days of validation studies

| DAY 1,2,3,4&5 | AVERAGE  | Std Dev   | %CV      |
|--------------|----------|-----------|----------|
| 0.2          | 22956.28 | 1132.168  | 4.931844 |
| 0.4          | 52606.12 | 3601.949  | 6.847016 |
| 0.6          | 64867.24 | 7805.121  | 12.03245 |
| 0.8          | 102057.24| 7582.398  | 7.429554 |
| 1            | 137360.4 | 7228.503  | 5.262436 |
| 2            | 302628.04| 4502.396  | 1.487766 |
| 4            | 622099.6 | 4146.621  | 0.666553 |
| 6            | 937045.56| 9922.515  | 1.058915 |
| 8            | 1241169.04| 17554.86  | 1.414381 |
| 10           | 1573166.8| 13105.93  | 0.833092 |

Standard curve for Liothyronine Sodium

\[ y = 158219x - 15026 \]

\[ R^2 = 0.9997 \]

Figure 3. Representative calibration curve from the validation study for liothyronine sodium assay
B) NORMALIZATION OF LEVOTHYROXINE SODIUM

Levothyroxine sodium obtained from Biochemie, Inc. was compared for purity with the standard levothyroxine sodium obtained from Sigma Chemical Company (Lot # 088H1318) which had a purity of 99.1% using our validated HPLC method.

Three samples each containing 5µg/ml of levothyroxine sodium obtained from Sigma Chemical Company and Biochemie, Inc. were prepared using the standard method. The samples were analyzed by HPLC and the results compared using a two sided t-test with 95% confidence interval as shown in Table 7 and Table 8. It was seen that there was no significant difference between the levothyroxine sodium obtained from Sigma Chemical Company and that obtained from Biochemie, Inc.

Table 7. Normalization data for levothyroxine sodium obtained from Sigma chemical company (Standard) and Biochemie, Inc. (Sample)

| Standard#1 (5µg/ml) | Standard#2 (5µg/ml) | Standard#3 (5µg/ml) |
|---------------------|---------------------|---------------------|
| AUC RetentionTime   | AUC RetentionTime   | AUC RetentionTime   |
| 708356 15.16        | 727869 14.96        | 744958 14.93        |
| 725036 15.12        | 742935 14.96        | 747136 14.91        |
| 734825 15.06        | 749291 14.94        | 739102 14.94        |
| 737402 15.04        | 746845 14.94        | 745375 14.96        |
| MEAN               | MEAN               | MEAN               |
| AUC 726404.75      | AUC 741645         | AUC 744142.75      |
| RT 15.095          | RT 14.95           | RT 14.935          |

| Sample#1 (5µg/ml) | Sample#2 (5µg/ml) | Sample#3 (5µg/ml) |
|-------------------|-------------------|-------------------|
| AUC RetentionTime | AUC RetentionTime | AUC RetentionTime |
| 736790 15.02      | 745838 14.94      | 716068 14.96      |
| 750280 15.01      | 754013 14.94      | 741785 14.97      |
| 742310 15         | 768462 14.94      | 748421 14.96      |
| 759268 14.96      | 746411 14.92      | 754361 14.96      |
| MEAN              | MEAN              | MEAN              |
| AUC 747162        | AUC 753681        | AUC 740158.75     |
| RT 14.9975        | RT 14.935         | RT 14.9625        |
Table 8. t-Test: two-sample assuming equal variances for Sigma and Biochemie.

|                          | **Sigma**       | **Biochemie**  |
|--------------------------|-----------------|----------------|
| Mean                     | 737397.50       | 747000.58      |
| Variance                 | 92190103.00     | 45732353.00    |
| Observations             | 3.00            | 3.00           |
| Pooled Variance          | 68961228.00     |                |
| Hypothesized Mean Difference | 0.00            |                |
| df                       | 4.00            |                |
| t Stat                   | -1.42           |                |
| P(T<=t) one-tail         | 0.11            |                |
| t Critical one-tail      | 2.13            |                |
| P(T<=t) two-tail         | 0.23            |                |
| t Critical two-tail      | 2.78            |                |
II) STABILITY STUDIES FOR LEVOTHYROXINE SODIUM

Evaluation of a stable solid dosage formulation often begins with drug-excipient compatibility studies. The present study was designed to investigate the stability of levothyroxine as a pure drug as well as in the presence of different excipients at different temperatures and humidities. From results of these investigations, excipients as well as optimal formulation and processing conditions were identified that would yield a more stable and reliable dosage form of levothyroxine. Of the many excipients available in the market, selection for this study was based on the physical and chemical properties. Nine excipients were selected for inclusion in the study. The studies were divided into four sections:

1) Use of saturated salt solutions to achieve specified relative humidities.
2) Stability testing of 900 μg of levothyroxine sodium (pure drug).
3) Drug-Excipient compatibility studies.
4) Stability studies for levothyroxine sodium tablets.

Samples were placed under different conditions in dessicators to maintain different conditions such as 25°C ± 2°C, 25°C ± 2°C and 60% ± 5%RH, 40°C ± 2°C and 75% ± 5%RH, 50°C with 20% w/w moisture and 50°C (without addition of moisture) and samples were removed at various intervals and analyzed.
METHODS AND MATERIALS:

MATERIALS:

Plastic dessicators (Fisher Scientific), HPLC System (Waters, Inc.), Magnetic Stirrer (Thermix® Model 120 MR), Weighing balance (Metler, Model # AE 240), Temperature and Humidity Logger (Dickson, Model # TL120), Sodium Chloride (AR Grade, Fisher Scientific, Lot # S640-3), Sodium Bromide (AR Grade, Sigma Labs, Lot # S45-47), Dextrose (AR Grade, Fisher Scientific, Lot # S640-3), Sodium Hydroxide (Fisher Scientific, Lot # S318-500), Methanol (HPLC Grade, Fisher Scientific, Lot # A452-4), Acetonitrile (HPLC Grade, Fisher Scientific, Lot # A998-4), O-Phosphoric Acid (Fisher Scientific, Lot # A260-500), Lactose Monohydrate (Quest International, Lot # MRP867682), Lactose Anhydrous (Quest International, Lot # M018151), Ferric Oxide (Fluka Chemicals, Lot # 44955), Mannitol (SPI Polyols, Inc. Lot # 3127G9), Starch 1500 (National Starch and Chemical Company, Lot # CB7137), Calcium Sulfate (Mendell, Lot # 8072CX), Di Calcium Sulfate Dihydrate (Mendell, Lot # X26AX), Talc (Cyprus Industrial Minerals Co., ID # ACM-189-7-03) and Deionized water.

PREPARATION OF SATURATED SALT SOLUTIONS FOR MAINTAINING SPECIFIED RELATIVE HUMIDITIES:

Saturated salt solutions are used to maintain specified relative humidities in closed chambers. Different salts are used to prepare saturated salt solutions, which can be used to obtain a wide range of relative humidities within the different temperature intervals suitable for stability studies of pharmaceuticals [44].
Saturated salt solutions of NaBr and NaCl were prepared to provide the relative humidity levels of 60% ± 5%RH and 75% ± 5%RH in storage dessicators at 25°C ± 2°C and 40°C ± 2°C respectively.

Experimental Design: To obtain the humidity of 60% ± 5%RH at 25°C ± 2°C and 75% ± 5%RH at 40°C ± 2°C, saturated salt solutions of NaBr and NaCl were prepared by dissolving the salts at 60°C. The slush of NaBr was kept at 25°C ± 2°C and that of NaCl was kept at 40°C ± 2°C in the dessicators. A dessicator with silica as a dessicant was also kept at 25°C ± 2°C and vacuum was applied to this dessicator. The dessicators were allowed to equilibrate for 48 hours. A temperature humidity logger was kept in each dessicator for two days to record the temperature and humidity. The data obtained from these studies is shown in Figures 4, 5 and 6. Measurements were repeated monthly to ensure that the conditions prevailed throughout the stability studies when samples were in the dessicators.

![Graph showing temperature and humidity data over time](image)

**Figure 4.** Showing 25°C ± 2°C and 0% humidity in the dessicator
STABILITY TESTING OF 900 µg OF LEVOTHYROXINE SODIUM (PURE DRUG)

Experimental Design: For these studies, 0.0009 gm (900 µg) of levothyroxine was carefully weighed and transferred to 4 ml HPLC vials. The vials were placed under different conditions in the dessicators. Three samples were withdrawn randomly from each dessicators at predetermined time intervals. HPLC analysis of these samples was performed to determine the percent of pure levothyroxine sodium left un-degraded. The studies were conducted for a period of 10 weeks.

Recovery Procedure: To a 4 ml HPLC vial containing 0.0009gm of a drug, 4ml of .01 M methanolic NaOH was added. The vials were shaken and kept in sonifier bath for 5 minutes, such that the drug dissolves in 4 ml of 0.01 M methanolic NaOH, to give an approximate concentration of 225 µg/ml. One ml of this solution was withdrawn and diluted in a 25 ml volumetric flask with 0.01 M methanolic NaOH, to get a concentration of 9 µg/ml. The samples were then analyzed by the HPLC method discussed earlier.

Note: The concentration of 9 µg /ml was selected to ensure that the sample concentration falls within the validated range of our HPLC method. Also, if the drug degrades over a period of time it would still be within the detection limits of the HPLC method.

RESULTS AND DISCUSSION:
The data presented in Table 9 shows the amount of drug remaining over a period of 10 weeks. Figure 7 shows a graphical presentation of the data. As can be seen from the plot, the drug appeared to be relatively stable at the different conditions evaluated except at 50°C. This is further corroborated by the fact that none of the kinetic models designed to
measure degradation fitted to the stability profiles of pure drug at the different conditions tested. It is believed that any trend in the degradation behavior of pure drug would have been accentuated and revealed by these models evaluated. Absence of any such trend within the limits of experimental variability coupled with the high values of percent drug left support this conclusion. Temperature induced degradation appeared to be significant at 50°C, as compared to the lower temperatures (see 25°C, 40°C and 50°C curves in Figure 7). These findings are supported by Won’s study indicating a threshold temperature between 50°C and 60°C where levothyroxine sodium degrades rapidly [42]. Won, studied the kinetics of degradation of levothyroxine sodium in aqueous solution and in the solid state. The author concluded that levothyroxine sodium followed simple first-order degradation by the process of deiodination in aqueous solution. In contrast to solution degradation, levothyroxine sodium did not deiodinate in the solid state. Instead, the isolated degradation products
Table 9. Percentage of drug remaining after each time period under different conditions.

| Time (Weeks) | 25°C | 25°C/60%RH | 40°C/75%RH | 50°C/20% moisture | 50°C (dry) |
|--------------|------|------------|------------|------------------|-----------|
| Day 0        | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |
| 1            | 104.01 | 97.37 | 98.00 | 121.02 | 104.00 |
| 2            | 102.72 | 95.02 | 102.57 | 105.10 | 106.54 |
| 7            | 95.04 | - | 102.63 | 90.01 | 92.96 |
| 10           | 103.48 | 114.32 | 114.04 | 102.80 | 84.26 |

Figure 7. Percent levothyroxine remaining after storage for a period of 10 weeks.
indicated a deamination reaction. Furthermore, the solid-state degradation profiles showed biphasic first order degradation profiles, indicating the possibility of additional and complex degradation pathways [42].

As stated earlier, the drug exhibited stability at the different conditions monitored in this study. Studies at rather adverse conditions might have provided more insight into the degradation pathways. However, these are outside the scope of this study considering the FDA stipulated guidelines.

While the possibility of multiple complex degradation pathways may be indicated, what becomes important in context of predicting a model are those mechanisms that contribute significantly to that degradation. First order and biphasic first order models were evaluated to find the best fit for degradation kinetics of levothyroxine sodium under various conditions.

Statistical analysis of the data was performed using a non-linear curve fitting procedure from Sigma Plot for Windows (SPSS Inc., 1997). The raw data generated following the experimental procedures described earlier was evaluated using nonlinear regression. The goodness of fit of the experimental data for first-order and biphasic first-order model was evaluated using residual plots, adjusted $r^2$ values, normality testing etc. The equations used for first order and biphasic first order are shown below:

**First-Order Equation**  \[ c = c_0 \cdot e^{-kt} \]

**Biphasic First-Order Equation**  \[ c = a_1 e^{-k_1 t} + a_2 e^{-k_2 t} \]
Attempts to fit a model to understand the nature of degradation in this regime were unrewarding considering the stable behavior of pure drug. Inherent variability in the data arising as a result of the complex sample preparation (refer to page 40) and storage conditions involved further complicated the prediction of model. While no particular trend in the degradation profile of pure drug is seen at various conditions tested, it can be stated that the drug's stability seems unaffected at these conditions for short period of testing. An understanding of the stability behavior of pure levothyroxine sodium at the FDA stipulated conditions will form a basis for later studies which are expected to involve more complex multiple interactions.

III) DRUG-EXCIPIENT COMPATIBILITY TESTING

Drug-Excipient compatibility studies were conducted to determine the formulation ingredients and conditions that might provide a stable formulation of levothyroxine sodium.

Experimental Design: For these studies, nine commonly used excipients were selected. These excipients were dextrose, dicalcium phosphate dihydrate, calcium sulfate, mannitol, lactose anhydrous, lactose monohydrate, starch 1500, talc and ferric-oxide. The maximum strength of levothyroxine sodium tablets available in the market is 300 µg. According to FDA c-GMP guidelines, the sampling from the mixture should not be more than 3 times the maximum dose concentration available. Thus, it was decided to work at three times 900 µg. The levothyroxine sodium-excipient ratio was kept at 1:10.
Levothyroxine sodium and the excipients were mixed using a Crescent Wtg-L-Bug mixer. 0.0099gm of the mixture was carefully weighed out in separate 4 ml HPLC vials and recovery analysis was performed using the method described earlier. The vials were placed in the dessicatators under the different conditions previously described. At defined time intervals, three samples for each drug-excipient mixture were analyzed. The studies were conducted for a period of 20 weeks.

RESULTS AND DISCUSSION:

The data presented in Tables 10 to 18 shows the amount of drug degraded in presence of different excipients over a period of 20 weeks. Figures 8 to 16 provide a graphical presentation of the data along with standard errors.

From the data obtained, it can be seen that levothyroxine sodium seems to be most stable in the presence of mannitol, starch 1500 and talc at 25°C, 25°C /60% RH and 40°C /75% RH. Drug degradation seems to be significant in the presence of some of the excipients containing carbohydrate. However, among this similar chemical class of excipients, wide differences in the degradation patterns were seen between dextrose and mannitol. While as little as 14% drug degradation was seen after 20 weeks in the presence of mannitol (40°C/75%RH condition), drug degradation was as large as 94% under similar experimental conditions in presence of the dextrose. In the order of increasing compatibility and stability of drug at 25°C, the various excipients evaluated can be ranked as: mannitol, starch 1500, ferric-oxide, talc, lactose hydrous, dicalcium phosphate dihydrate, dextrose, lactose anhydrous and calcium sulfate.
Table 10. Levothyroxine remaining in the presence of dextrose after each time period under different conditions.

| Time (weeks) | 25°C | 25°C/60%RH | 40°C/75%RH | 50°C/20%moisture | 50°C (dry) |
|--------------|------|------------|------------|------------------|------------|
| Day 0        | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |
| 1            | 91.80 | 86.43 | 10.07 | 9.96 | 92.06 |
| 2            | 94.24 | 85.96 | 8.03 | 10.08 | 89.45 |
| 4            | 86.31 | 62.76 | 6.51 | 6.74 | 67.54 |
| 7            | 87.38 | 45.63 | 7.70 | 7.07 | 58.04 |
| 10           | 80.90 | 68.55 | 6.13 | 8.88 | 55.48 |
| 20           | 82.42 | 62.40 | 6.16 | 7.39 | 41.64 |

Dextrose

Figure 8. Levothyroxine remaining in the presence of dextrose over a period of 20 weeks.
Table 11. Levothyroxine remaining in the presence of dicalcium phosphate dihydrate after each time period under different conditions.

| Time (weeks) | 25°C | 25°C/60%RH | 40°C/75%RH | 50°C/20%moisture | 50°C (dry) |
|--------------|------|------------|------------|------------------|-----------|
| Day 0        | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |
| 1            | 95.65 | 70.89 | 76.94 | 92.90 | 66.97 |
| 2            | 78.56 | 84.03 | 71.82 | 93.12 | 77.15 |
| 3            | 121.70 | 74.15 | 98.00 | 103.12 | 57.96 |
| 4            | 78.53 | 78.06 | 87.40 | 91.35 | 78.81 |
| 7            | 65.81 | 78.11 | 67.55 | 70.38 | 59.33 |
| 10           | 93.03 | 72.84 | 68.22 | 67.38 | 44.61 |
| 20           | 87.00 | 125.68 | 62.91 | 56.59 | 43.44 |

**Dicalcium Phosphate Dihydrate**

Figure 9. Levothyroxine remaining in the presence of dicalcium phosphate dihydrate over a period of 20 weeks.
Table 12. Levothyroxine remaining in the presence of calcium sulfate after each time period under different conditions.

| Time (weeks) | 25°C | 25°C/60%RH | 40°C/75%RH | 50°C/20%moisture | 50°C (dry) |
|--------------|------|------------|------------|------------------|------------|
| Day 0        | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |
| 1            | 91.92  | 88.39 | 86.92 | 74.72 | 84.16 |
| 2            | 90.09  | 86.84 | 84.26 | 82.37 | 83.91 |
| 3            | 91.00  | 89.35 | 87.23 | 76.19 | 81.98 |
| 4            | 83.74  | 87.87 | 85.57 | 78.41 | 72.51 |
| 7            | 83.69  | 88.73 | 78.27 | 89.02 | 60.83 |
| 10           | 82.41  | 90.89 | 85.30 | 68.50 | 60.80 |
| 20           | 74.80  | 80.26 | 83.28 | 47.34 | 54.93 |

**Calcium Sulfate**

Figure 10. Levothyroxine remaining in the presence of calcium sulfate over a period of 20 weeks.
Table 13. Levothyroxine remaining in the presence of mannitol after each time period under different conditions.

| Time (weeks) | 25°C | 25°C/60%RH | 40°C/75%RH | 50°C/20%moisture | 50°C (dry) |
|--------------|------|------------|------------|------------------|------------|
| Day 0        | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |
| 1            | 99.62  | 96.91  | 96.84  | 100.78 | 95.69 |
| 2            | 101.32 | 100.96 | 97.75  | 95.21  | 96.09 |
| 3            | 99.32  | 97.14  | 92.61  | 90.57  | 91.04 |
| 4            | 96.46  | 91.51  | 94.59  | 91.03  | 89.51 |
| 7            | 94.71  | 92.11  | 92.13  | 87.26  | 59.09 |
| 10           | 89.22  | 94.78  | 98.23  | 92.47  | 75.06 |
| 20           | 91.85  | 98.42  | 86.41  | 83.05  | 70.70 |

**Mannitol**

Figure 11. Levothyroxine remaining in the presence of mannitol over a period of 20 weeks.
Table 14. Levothyroxine remaining in the presence of lactose anhydrous after each time period under different conditions.

| Time (weeks) | 25°C | 25°C/60%RH | 40°C/75%RH | 50°C/20% moisture | 50°C (dry) |
|--------------|------|------------|------------|-------------------|-----------|
| Day 0        | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |
| 1            | 91.87  | 89.59 | 78.30 | 75.98 | 88.87 |
| 2            | 91.61  | 91.36 | 76.57 | 61.55 | 66.12 |
| 3            | 88.27  | 82.51 | 76.78 | 58.09 | 64.97 |
| 4            | 84.40  | 81.11 | 70.83 | 54.74 | 81.79 |
| 7            | 74.94  | 69.22 | 63.14 | 58.91 | 43.14 |
| 10           | 73.66  | 69.21 | 63.51 | 53.14 | 45.48 |
| 20           | 66.07  | 61.79 | 56.62 | 50.94 | 43.87 |

**Lactose Anhydrous**

Figure 12. Levothyroxine remaining in the presence of lactose anhydrous over a period of 20 weeks.
Table 15. Levothyroxine remaining in the presence of lactose hydrous after each time period under different conditions.

| Time (weeks) | 25°C | 25°C/60%RH | 40°C/75%RH | 50°C/20% moisture | 50°C (dry) |
|--------------|------|------------|------------|------------------|-----------|
| Day 0        | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |
| 1            | 96.86  | 93.86  | 83.35  | 75.17  | 96.77  |
| 2            | 98.54  | 97.16  | 79.34  | 61.08  | 85.06  |
| 3            | 101.98 | 86.79  | 77.71  | 59.80  | 75.39  |
| 4            | 84.23  | 83.68  | 80.61  | 65.94  | 67.96  |
| 7            | 86.59  | 85.21  | 69.87  | 53.29  | 65.11  |
| 10           | 83.88  | 69.05  | 71.35  | 60.15  | 56.60  |
| 20           | 76.69  | 79.65  | 67.43  | 34.35  | 37.29  |

**Lactose Hydrous**

Figure 13. Levothyroxine remaining in the presence of lactose hydrous over a period of 20 weeks.
Table 16. Levothyroxine remaining in the presence of starch 1500 after each time period under different conditions.

| Time (weeks) | 25°C | 25°C/60%RH | 40°C/75%RH | 50°C/20% moisture | 50°C (dry) |
|--------------|------|------------|------------|-------------------|------------|
| Day 0        | 100.00 | 100.00     | 100.00     | 100.00            | 100.00     |
| 1            | 100.39 | 101.70     | 100.85     | 97.26             | 94.65      |
| 2            | 99.84  | 103.89     | 103.37     | 90.47             | 89.57      |
| 3            | 95.66  | 97.61      | 99.91      | 86.07             | 87.21      |
| 4            | 96.92  | 96.50      | 101.55     | 80.36             | 76.05      |
| 6            | 95.74  | 96.69      | 98.80      | 64.39             | 63.08      |
| 8            | 92.10  | 95.93      | 102.38     | 68.50             | 59.58      |
| 10           | 96.53  | 98.30      | 100.66     | 72.19             | 53.85      |
| 20           | 88.98  | 93.90      | 99.50      | 73.78             | 41.01      |

Figure 14. Levothyroxine remaining in the presence of starch 1500 over a period of 20 weeks.
Table 17. Levothyroxine remaining in the presence of talc after each time period under different conditions.

| Time (weeks) | 25°C | 25°C/60%RH | 40°C/75%RH | 50°C/20%moisture | 50°C (dry) |
|-------------|------|------------|------------|------------------|------------|
| Day 0       | 100.00 | 100.00    | 100.00     | 100.00           | 100.00    |
| 1           | 103.49 | 102.67    | 99.12      | 87.19            | 100.14    |
| 2           | 103.05 | 99.86     | 100.06     | 79.11            | 87.20     |
| 3           | 97.36  | 98.22     | 97.43      | 66.64            | 79.61     |
| 4           | 95.07  | 101.49    | 104.43     | 73.49            | 77.79     |
| 6           | 96.59  | 101.99    | 100.10     | 64.01            | 68.88     |
| 8           | 88.43  | 98.32     | 108.48     | 68.72            | 64.40     |
| 10          | 89.71  | 94.77     | 98.60      | 58.90            | 60.01     |
| 20          | 80.15  | 94.11     | 99.70      | 59.92            | 39.45     |

**Figure 15.** Levothyroxine remaining in the presence of talc over a period of 20 weeks.
Table 18. Levothyroxine remaining in the presence of ferric-oxide after each time
Period under different conditions.

| Time(weeks) | 25°C  | 25°C/60%RH | 40°C/75%RH | 50°C/20%moisture | 50°C (dry) |
|-------------|-------|------------|------------|------------------|------------|
| Day 0       | 100.00| 100.00     | 100.00     | 100.00           | 100.00     |
| 1           | 90.09 | 93.16      | 94.61      | 85.05            | 87.89      |
| 2           | 97.45 | 96.88      | 97.73      | 91.40            | 87.90      |
| 3           | 93.80 | 91.54      | 99.21      | 97.04            | 83.48      |
| 4           | 93.10 | 89.95      | 97.38      | 88.44            | 73.69      |
| 6           | 91.25 | 94.38      | 93.34      | 84.27            | 70.19      |
| 8           | 85.47 | 88.63      | 88.69      | 84.95            | 62.02      |
| 10          | 84.21 | 89.28      | 88.46      | 85.17            | 60.72      |
| 20          | 86.16 | 91.71      | 94.17      | 85.21            | 45.03      |

Ferric Oxide

Figure 16. Levothyroxine remaining in the presence of ferric-oxide over a period of 20 weeks.
Considering that a Schiff-base reaction and an oxidation reaction may be the predominant pathways [43, 46], first-order and biphasic first-order models were evaluated to find the best fit for degradation kinetics of levothyroxine sodium in the presence of different excipients under various conditions. Significant degradation involving any single pathway is best explained by simple first order kinetics as seen with dextrose, where Schiff-Base reaction is seemingly predominant. On the other hand, degradation following two different mechanisms (Schiff-base reaction plus oxidation) that are regulated by different rate kinetics seems to be best explained by bi-phasic first order models. The majority of the drug-excipient mixtures that were evaluated exhibited dual mechanism as reflected in the number of successfully fitted biphasic first order models. A non-linear regression analysis similar to the one used for the pure drug data was performed on the experimental data obtained from drug-excipient compatibility studies. The complete output of this statistical analysis along with the model parameters and constraints are shown in detail in Appendix A. Residual plots are generated from this statistical output using suitable graphing procedure (Microsoft® Excel 97) and are shown in Appendix B. After selecting the model that fits the data following the above analysis, expiration dates \((t_{90})\) for levothyroxine sodium in the presence of different excipients were calculated. For all conditions, the \(k\)-values for first order reactions and \(a_1, a_2, k_1\) and \(k_2\) for biphasic first order reactions were calculated from the models and used to calculate \(t_{90}\) values. The summary of the various results obtained is presented in Table 19.

It was noticed that levothyroxine degraded to a higher extent at 50°C in presence of all the excipients. These findings further support the fact that 50°C- 60°C is the threshold
Table 19. T<sub>90</sub> values for different drug-excipient mixtures at different conditions.

| Excipients                  | t-90 in Weeks |
|-----------------------------|---------------|
|                            | 25 C | 25 C/60% RH | 40 C/75% RH | 50 C/20% moisture | 50 C |
| Dextrose                    | 2.77 | 0.76        | 0.001       | 5.29E-06          | 1.23 |
| Dicalcium Phosphate Dihydrate| 2.98 | <1          | 0.54        | 3.18              | 2.38 |
| Calcium Sulfate             | 1.89 | 16.4        | 0.56        | 0.023             | 0.94 |
| Mannitol                    | 24.22| 153.6       | 19.44       | 5.26              | 2.29 |
| Lactose Anhydrous           | 2.13 | 1.55        | 0.29        | 0.29              | 0.68 |
| Lactose Hydrous             | 7.29 | 5.1         | 2.38        | 0.22              | 0.45 |
| Starch                      | 18.1 | 28.37       | >20         | 1.61              | 1.67 |
| Talc                        | 9.24 | 26.92       | >20         | 0.68              | 1.67 |
| Ferric Oxide                | 14   | 153.6       | 307.2       | 2.74              | 1.26 |

temperature for the degradation of levothyroxine sodium. Among all of the different types of excipients used, degradation of levothyroxine sodium occurs most quickly in the presence of carbohydrates such as dextrose, lactose hydrous, lactose anhydrous and starch. At higher temperatures, it is theorized that the ring structure of the carbohydrates breaks to open up a free aldehyde group. This leads to a Schiff-base reaction between a
free aldehyde group of the carbohydrates and the highly reactive amino group of levothyroxine sodium. The general Schiff-base reaction is shown in Figure 17.

Figure 17. Reaction mechanism for Schiff-base reaction
The availability of the free aldehyde group varies among the carbohydrates. For example, dextrose which is composed of only one ring structure, can easily break open to give a free aldehyde group, and so by this mechanism the drug would degrade very quickly in presence of dextrose. Lactose, which is composed of a two-ring structure, would be more stable with the drug as compared to dextrose but less stable as compared to starch. Levothyroxine sodium was found to be much more stable in presence of mannitol. This could be attributed to the absence of the ring structure and the free aldehyde group in mannitol.

The literature also indicates that levothyroxine has a tendency to undergo oxidation reaction [43]. Accordingly, in the presence of various components capable of oxidizing the pure drug, the degradation can be expected to be rather severe. It was seen that the mixture of levothyroxine with carbohydrates had turned brown, and this may be attributed to the oxidation of the drug by the mechanism shown in Figure 18.

![Figure 18. Reaction mechanism for Oxidation](image)
The overall results showed that the drug was most stable at 25°C and 25°C / 60% RH. One of the most interesting findings observed was in the case of talc and starch, where levothyroxine sodium was much more stable at 25°C / 60% RH and 40°C / 75% RH in the presence of these excipients (Figure 14 and 15) than at the same temperatures with added humidity. This behavior may be due to a higher moisture uptake ability of starch and talc as compared to other excipients [47]. A higher affinity of these excipients towards moisture might have sequestered the free moisture, thereby reducing the availability of water for reaction with pure drug.

Overall for this group of excipients the lowest t-90 values of levothyroxine sodium were observed in the presence of dextrose, dicalcium phosphate dihydrate and calcium sulfate at 25°C, 25°C / 60% RH and 40°C / 75% RH (Table 19) with stability well below usable levels.

Interestingly, the stability of the mixtures of levothyroxine sodium and lactose anhydrous were much lower as compared to that of levothyroxine sodium and lactose monohydrate as seen in Table 19 (Figures 23 and 24). HPLC analysis demonstrated that at higher humidity/temperature, the mixture containing lactose anhydrous exhibited relatively greater degradation of the drug than that containing lactose monohydrate. This type of degradation was reported by Jain et al. [29], who studied the stability of a proprietary hydrophobic drug in the presence of hydrous and anhydrous lactose. The authors concluded that, lactose anhydrous becomes hydrated on exposure to high humidity/temperature condition and that the transition state of the lactose, not its stable state may be responsible for its greater interaction and subsequent degradation of the drug. They also concluded that in certain cases, lactose anhydrous may absorb a
significant amount of moisture, which can affect its inherent properties and may directly come in contact with the drug. For a moisture sensitive drug like levothyroxine sodium, this behavior may drastically affect its stability. Therefore, the general belief that lactose anhydrous, which has less than 0.5% moisture, should provide greater stability as compared to lactose hydrous needs to be properly evaluated.

The comparative effects of the different storage conditions on the stability of each of the drug-excipient mixtures are presented in Figures 19 to 27.
Figure 19. Effect of storage conditions on drug+dextrose mixture

Figure 20. Effect of storage conditions on drug+DCPD mixture

Figure 21. Effect of storage conditions on drug+calcium sulfate mixture
Figure 22. Effect of storage conditions on drug+mannitol mixture

Figure 23. Effect of storage conditions on drug+lactose anhydrous mixture

Figure 24. Effect of storage conditions on drug+lactose hydrous mixture
Figure 25. Effect of storage conditions on drug+starch 1500 mixture

Figure 26. Effect of storage conditions on drug+talc mixture

Figure 27. Effect of storage conditions on drug+ferric-oxide mixture
A) FORMULATION OF LEVOTHYROXINE SODIUM TABLETS

After the completion of drug-excipient compatibility studies, evaluation of the stability of tablet formulations proceeds in two consecutive steps; the first is the formulation of tablets that meet USP criterions and second is to monitor stability under various conditions. The present study is designed to formulate and evaluate the properties of levothyroxine tablets.

METHODS AND MATERIALS:

Materials:
Sodium Hydroxide (Fisher Scientific, Lot # S318-500), Methanol (HPLC Grade, Fisher Scientific, Lot # A452-4), Acetonitrile (HPLC Grade, Fisher Scientific, Lot # A998-4), O-Phosphoric Acid (Fisher Scientific, Lot # A260-500), Mannitol (SPI Polyols, Inc. Lot # 3127G9), Starch 1500 (National Starch and Chemical Company, Lot # CB7137), Talc (Cyprus Industrial Minerals Co., ID # ACM-189-7-03), Deionized water, pH/mv meter (model 420A, Orion Research, Inc.), Stokes Single Punch Tablet Press, Turbula mixer, Tablet Hardness Tester, USP Dissolution Apparatus, USP Disintegration Apparatus, HPLC System(Waters, Inc.), Magnetic Stirrer (Thermix® Model 120 MR), Weighing balance (Metler, Model # AE 240) and Sieve # 40.

EXPERIMENTAL PROCEDURE:

Based on the results obtained from drug-excipient compatibility studies, the more stable excipients, mannitol(diluent), starch 1500(disintegrant and binder) and talc(lubricant)
were selected for use in formulating the tablets. Due to the low concentration of the levothyroxine sodium in the tablets drug-to-excipient ratios of the excipients slightly different from those studied in the compatibility studies were used to obtain tablets of consistent weight and hardness. The total weight of the tablets was fixed at 115mg. Table 20 indicates the selected formulation.

Table 20. Composition of levothyroxine sodium tablet formulation

| Ingredients       | Composition (%) | Composition (mg/tablet) | Batch of 30,000 tablets (gms) |
|-------------------|-----------------|-------------------------|-------------------------------|
| Levothyroxine Sodium | 0.299           | 0.345                   | 0.9                           |
| Mannitol         | 93.718          | 108.1                   | 282                           |
| Starch 1500      | 4.985           | 5.75                    | 15                            |
| Talc             | 0.997           | 1.15                    | 3                             |

Tabletting Procedure

Ingredients for the batch of 30,000 tablets, each weighing 115mg and containing 345µg of levothyroxine sodium were weighed as shown in Table 20.

All the excipients as well as the drug were passed through a #40 sieve to get uniform particle size distribution. 282 gm of mannitol, 15 gm of starch 1500 and 3 gm of talc were weighed into a jar and mixed for 5 minutes using Turbula® mixer. Levothyroxine sodium was added to the remaining ingredients using geometric dilution while mixing. The overall optimum mixing time was estimated to be 20 minutes. This was determined by addition of a red dye to the excipient mixture and observation of the homogeneity of the dye dispersed in the mixture at various time intervals. Further to confirm the homogeneity of the mixture, a 100mg sample of the powder was taken from 6 different points in the container and compared with standard L-4 (6mcg/ml). Results of homogeneity testing are shown in Table 21. The amount of drug recovered expressed as
mean (% CV) of six random samples was found to be 98.6% (7.00). Accordingly, the homogeneity of the drug mixture passes the USP specified limits (85% – 115%).

Table 21. Homogeneity check for 100mg of powder mixture as compared to standard (6 ug/ml) after 20 minutes of mixing.

| Sample 1 | Sample 2 | Sample 3 | Sample 4 | Sample 5 | Sample 6 |
|----------|----------|----------|----------|----------|----------|
| Mean % Recovery | 103.78  | 96.32    | 109.03   | 98.36    | 94.51    | 89.61    |

An ANOVA was applied to the data and the p-value of .07 obtained indicated no significant difference between these samples. The mixture was considered acceptable and tablets were compressed using a Stokes® single punch tabletting machine. The following tests were performed to check the general properties of the tablets:

1) Weight Variation: Twenty tablets were selected at random and weighed. The weight of these tablets are shown in Table 22.

USP limits: For tablet weights below 130mg, percentage difference accepted is ±10% which allows weight limits for these tablets of 105mg to 125mg.

Average weight of 20 tablets = 116.05mg

Allowable deviation is 10%

Number of tablets in sample exceeding limits was 0 tablets

Result: Therefore the batch passes the weight variation test.
Table 22. Weight of 20 tablets for weight variation test

| Tablet  | Tablet Weight (gm) | Tablet  | Tablet Weight (gm) |
|---------|--------------------|---------|--------------------|
| Tablet 1 | 0.123              | Tablet 11 | 0.122              |
| Tablet 2 | 0.114              | Tablet 12 | 0.113              |
| Tablet 3 | 0.114              | Tablet 13 | 0.107              |
| Tablet 4 | 0.119              | Tablet 14 | 0.110              |
| Tablet 5 | 0.117              | Tablet 15 | 0.113              |
| Tablet 6 | 0.115              | Tablet 16 | 0.122              |
| Tablet 7 | 0.111              | Tablet 17 | 0.123              |
| Tablet 8 | 0.120              | Tablet 18 | 0.120              |
| Tablet 9 | 0.107              | Tablet 19 | 0.118              |
| Tablet 10| 0.121              | Tablet 20 | 0.112              |

2) Content Uniformity: 30 Tablets were selected at random, out of which 10 tablets were randomly chosen for the content uniformity test. The data for content uniformity test is presented in Table 23.

USP Limits: The concentration of the drug should lie in the range of 85% to 115% and the %CV should be less than or equal to 6.0%.

Results: The tablets passed the USP content uniformity test.

3) Tablet Hardness: Hardness of 10 tablets was determined using the Erweka® tablet hardness tester and the data is shown in Table 24. The average hardness of the tablets was 7.125kg.
Table 23. Data for content uniformity test for 115mg tablets

| Tablet | % of L-4  |
|--------|-----------|
| Tablet 1 | 96.03     |
| Tablet 2 | 109.3     |
| Tablet 3 | 105.82    |
| Tablet 4 | 107.07    |
| Tablet 5 | 101.21    |
| Tablet 6 | 99.89     |
| Tablet 7 | 97.87     |
| Tablet 8 | 93.28     |
| Tablet 9 | 103.04    |
| Tablet 10 | 90.95    |
| Mean % Recovery | 100.45 |
| Std. Dev | 6.02     |
| % CV    | 5.87     |

Table 24. Data for hardness test for levothyroxine tablets

| Tablet | Hardness in kg |
|--------|----------------|
| Tablet 1 | 7.00          |
| Tablet 2 | 6.50          |
| Tablet 3 | 7.50          |
| Tablet 4 | 7.00          |
| Tablet 5 | 7.50          |
| Tablet 6 | 7.25          |
| Tablet 7 | 6.75          |
| Tablet 8 | 7.50          |
| Tablet 9 | 7.50          |
| Tablet 10 | 6.75         |
| Mean   | 7.13          |
| Std. Dev | 0.38        |
| % CV   | 5.30          |
4) Friability Test:
Weight of 10 tablets = 1.161 gms
Weight of 10 tablets after 150 revolutions (5 minutes) = 1.153 gms
Percentage weight loss of 10 tablets = 0.69%.
USP Limits: A maximum weight loss of not more than 1% of the weight of tablets being tested is considered acceptable for most products.

Results: The tablets passed USP friability test.

5) Disintegration Test: The USP (Vanderkamp) disintegration tester was used for these studies. 1000 ml of distilled water was placed in a glass beaker and was kept in the water bath maintained at the temperature 37 ± 2°C. Six tablets were selected and the disintegration time noted. All tablets disintegrated within 5 minutes.

USP Limits: All six tablets should disintegrate within 30 minutes.

Results: The tablets passed the USP disintegration test.

6) Dissolution Test: USP apparatus 2 was used. The apparatus was set to 100 rpm.
The temperature of water bath was set to 37 ± 2°C.
Dissolution media: .05M phosphate buffer with pH 7.4; 500 ml.
Dissolution Studies: 500 ml of pH 7.4, .05M phosphate buffer was filled in the dissolution flasks and the system was allowed to equilibrate for 30 minutes. Six tablets weighing 105 mg were selected and placed in each of the six dissolution flasks. Sampling was performed at predetermined time points, namely 10, 20, 30, 45, 60, 80 and 100 minutes. At each time interval, 5 ml of the sample was withdrawn from the dissolution flask and 1 drop of phosphoric acid was added to
the sample. The media was not replaced because the volume of dissolution media after sampling was still adequate to maintain sink conditions (solubility of L-4 in phosphate buffer pH 7.4 is 0.022 - 0.044 gm/100ml) [43]. A correction factor was used to correct for the volume of the media not replaced, and hence to calculate the percent of drug dissolved. The samples were directly analyzed by HPLC. Table 25 shows the data obtained. Figure 28 shows the dissolution profile of levothyroxine sodium from its tablets over the 100 minutes of run time.

Results: USP limits state that not less than 55% \((Q)\) of the labeled amount of Levothyroxine sodium is dissolved in 80 minutes. Hence the tablets passed the dissolution test.

Table 25. Dissolution of levothyroxine sodium tablets

| Time (minutes) | Mean % Dissolved \(n=6\) | Standard Deviation |
|---------------|--------------------------|-------------------|
| 0             | 0                        | 0                 |
| 10            | 79.32                    | 11.05             |
| 20            | 82.22                    | 4.99              |
| 30            | 74.83                    | 2.79              |
| 45            | 79.82                    | 8.83              |
| 60            | 76.87                    | 4.1               |
| 80            | 78.58                    | 8.87              |
| 100           | 74.86                    | 6.6               |
Figure 28. Dissolution profile of levothyroxine sodium in tablet formulation
B) EVALUATION OF THE STABILITY OF LEVOTHYROXINE SODIUM TABLETS

Evaluation of the stability of formulation is an integral part of the development process. A complete understanding of the stability of the formulation can only be obtained after the underlying component interactions are studied. This also helps the formulator in selecting the tableting excipients that should offer optimum stability. The importance of such studies is exemplified by cases like the marketed levothyroxine sodium formulations where the potency could not be assured through the expiration date. The many problems and issues associated with levothyroxine sodium formulations have been discussed in the earlier section (Chapter 1).

In view of the above facts, studies were performed to evaluate the stability of pure drug and excipient compatibility. Based on these results an optimum formulation components were selected. Further tablet testing was performed on the selected formulation and the tablets produced were found to conform to the USP standards. This portion of work deals with the stability testing of these tablets.

Experimental Design:

The previously formulated and manufactured levothyroxine sodium tablets were stored in stability chambers under same conditions as excipients. The stability of the tablets was evaluated over a period of 10 weeks. Tablets were sampled at predetermined time points and drug content was determined after extraction using the previously discussed HPLC method. At the end of 10 weeks, dissolution studies were also conducted on these tablets, that had been stored at 25°C / 60%RH and at 40°C / 75%RH to determine if dissolution was affected by moisture.
RESULTS AND DISCUSSION: From the results obtained from the drug-excipient compatibility studies, it was decided to use mannitol (diluent), starch 1500 (binder and disintegrant) and talc (lubricant) as the excipients in the formulation of the levothyroxine sodium tablets. Immediately after manufacture, the tablets were characterized by good mechanical strength and a shorter disintegration time than the limits specified in the USP. Further dissolution studies indicated that 80% of levothyroxine sodium was released within 30 minutes. The data for stability studies after 10 weeks is shown in table 26 and Figure 29.

From the data (Table 26) it can be seen that the drug degraded to less than 90% in less than a week, at all conditions studied. The stability of tablets was found to be much worse than the stability of levothyroxine sodium determined in presence of individual excipients (refer to Figure 29 versus Figures 11, 14 and 15). It appears that the rate of degradation of levothyroxine sodium contained in the tablets was the synergistic effect of the individual excipients used. This is reflected in the shape of the degradation curves for the tablets when compared to those of individual excipients. A general trend showing an initial faster degradation rate followed by a relatively slower phase is apparent for all the conditions studied.

The results of the dissolution studies of the tablets stored for 10 weeks are presented in Table 27 and 28 and Figures 30 and 31. The amount of drug released was corrected basing on the percentage of drug left undegraded under respective conditions. Dissolution profiles were found to be identical when compared to the freshly manufactured tablets. Basing on these findings it could be stated that the physical stability of the formulation did not change at the end of 10 weeks. Dissolution testing of tablets is considered as a
quality-indicating tool in ensuring batch to batch uniformity [2]. For our purposes, it is therefore believed that any minor changes in the physical stability of the formulation would have been accentuated and reflected in the dissolution behavior of tablets.

Table 26. Evaluation of the stability of levothyroxine sodium tablets.

| Time (weeks) | 25°C | 25°C/60%RH | 40°C/75%RH | 50°C (dry) |
|-------------|------|------------|------------|------------|
| Day 0       | 100.00 | 100.00 | 100.00 | 100.00 |
| 1           | 83.25 | 83.46 | 91.45 | 73.73 |
| 2           | 74.83 | 82.42 | 82.64 | 75.25 |
| 7           | 81.68 | 94.57 | 72.52 | 54.66 |
| 10          | 77.50 | 79.37 | 80.88 | 52.14 |

Figure 29. Stability profile of levothyroxine sodium tablets
Table 27. Dissolution studies of levothyroxine sodium tablets after 10 weeks at 25°C / 60%RH.

| Time (minutes) | Mean % Dissolved n=6 |
|----------------|----------------------|
| 0              | 0                    |
| 10             | 87.88                |
| 20             | 97.24                |
| 40             | 90.73                |
| 60             | 95.54                |
| 80             | 93.21                |
| 100            | 92.89                |

Table 28. Dissolution studies of levothyroxine sodium tablets after 10 weeks at 40°C / 75%RH.

| Time (minutes) | Mean % Dissolved n=6 |
|----------------|----------------------|
| 0              | 0.00                 |
| 10             | 32.10                |
| 20             | 44.85                |
| 40             | 66.16                |
| 60             | 78.78                |
| 80             | 87.35                |
| 100            | 79.91                |
Figure 30. Dissolution profile of levothyroxine sodium tablets stored at 25°C / 60%RH after 10 weeks

Figure 31. Dissolution profile for levothyroxine sodium tablets stored at 40°C / 75%RH after 10 weeks
To better define the rate of degradation of the tablets as compared to the excipients, first-order and biphasic first-order models were evaluated using Sigma Plot. Details of the modeling procedure have been discussed earlier (refer to page 43). Results of the statistical analysis and goodness of fit calculations are compiled in appendices A and B. 

$T_{90}$ values at the different storage conditions studied were derived from the kinetic parameters obtained from best fit models. In few cases of excipient/conditions (DCPD and levothyroxine sodium tablets at 25°C/60%RH and starch and talc at 40°C/75%RH) limited success was seen in fitting a kinetic model for degradation. A combination of factors such as the complexity in degradation, variability in the data etc., restricted selection of the best kinetic model.

For comparative purposes, the effect of series of storage conditions on $t_{90}$ values of levothyroxine in tablets are shown together with those of single excipient mixtures in Figures 32 to 35. As can be seen from Figures 32 to 35, the $t_{90}$ values of levothyroxine sodium tablets are significantly lower when compared to those determined in the presence of individual excipients. As discussed earlier the excipients that offered the best $t_{90}$ values and those exhibiting the highest compatibility on an individual basis were selected for the final formulation. However, it can be seen that in combination, the incompatibility caused by these excipients was more seemingly complex. For example, the $t_{90}$ values of levothyroxine sodium at 25°C in tablets dropped by 98.55% when compared to that in presence of pure mannitol. As a result of the rapid degradation seen in presence of the tablet formulation at all storage conditions studied no particular trend was observed. The rapid rate of degradation is believed to mask the effect of temperature and humidity on the final formulation.
Figure 32. $T_{90}$ of levothyroxine sodium in presence of different excipients and as a tablet when stored at 25°C
Excipients

Figure 33. $T_{90}$ of levothyroxine sodium in presence of different excipients and as a tablet when stored at 25°C / 60% RH

t-90 for DCPD and L-4 tablets * is < 1 week
Figure 34. * t-90 for Starch* and Talc* is > 20 week

*Figure 34. T$_{90}$ of levothyroxine sodium in presence of different excipients and as a tablet when stored at 40°C / 75% RH*
Figure 35. T_{90} of levothyroxine sodium in presence of different excipients and as a tablet when stored at 50°C
Figure 36 shows that estimated $t_{90}$ values for the tablet formulation under all storage conditions studied were found to be less than one week. The loss of potency often observed in the marketed levothyroxine sodium formulations was confirmed by these results.

It remains to be seen why levothyroxine sodium in tablets exhibited a complex and rapid degradation as compared to pure levothyroxine sodium and levothyroxine sodium in presence of single excipients. Compatibility studies involving multiple excipients and evaluation of the effect of environmental conditions during manufacture may help in understanding this behavior. To this objective, our studies are believed to form a firm basis for future research in this direction.
$t_{90}$ for L-4 tablets at 25 C/60 %RH is < 1 week
$t_{90}$ for L-4 tablets at 50 C is 3.3 $E$-05

Figure 36. Effect of storage conditions on levothyroxine sodium tablets
V) SUMMARY AND CONCLUSIONS

The proposed testing program was designed to evaluate excipient compatibility studies with levothyroxine sodium as a pre-formulation tool. The results provided an insight on the stability of the drug in the presence of single as well as multiple excipients under the FDA stipulated conditions of temperature and humidity.

The acquired results indicated that the pure drug was relatively stable for up to 10 weeks under different conditions evaluated except at 50°C. Won CM [42] had observed rapid degradation of the pure drug above 50°C. A similar trend was observed in our studies, which indicates that there might be additional and complex degradation pathways at higher temperatures.

Nine commonly used excipients were selected for the compatibility studies. These excipients were dextrose, dicalcium phosphate dihydrate, calcium sulfate, mannitol, lactose anhydrous, lactose monohydrate, starch 1500, talc and ferric-oxide. In the presence of these excipients the stability of the drug decreased as compared to that of pure drug with the extent of degradation dependant on the chemical properties of the excipients. The lowest drug degradation of the investigated drug-excipient mixtures was observed in the drug mixtures with mannitol, starch 1500 and talc. Considerable degradation of the drug was noted in the presence of carbohydrates having an aldehyde group. This behavior of the drug in presence of carbohydrates was attributed to Schiff-base and oxidation reactions. The lowest t-90 values for the drug was observed in the presence of dextrose, dicalcium phosphate dihydrate and calcium sulfate at 25°C, 25°C / 60% RH and 40°C / 75% RH (Table 19) with stability well below usable levels.
The results of the compatibility studies led to the selection of mannitol, starch 1500 and talc for use in formulating levothyroxine sodium tablets. The formulated tablets were found to conform to USP standards. The data on the stability of tablets revealed that the drug degraded to less than 90% in less than a week at all the conditions studied. These results indicate that in the presence of multiple excipients, the stability of the drug appeared to be much less. No particular trend was observed in the degradation profile as a function of temperature and humidity on the final formulation. It appears that the rapid degradation of the drug in tablets may be due to the synergistic effect of the individual excipients used or the processing variables such as mixing techniques, compaction pressures etc.

From the overall results obtained it can be concluded that levothyroxine sodium has very little stability at 50°C. It is also recommended that dextrose, lactose hydrous, lactose anhydrous, calcium sulfate and dicalcium phosphate dihydrate should not be used as excipients along with levothyroxine due to the very low stability in presence of these excipients.

VI) RECOMMENDATIONS FOR FUTURE WORK

The future work on the stability studies of levothyroxine sodium should focus on the following:

- Increase the drug concentration and study the degradation pattern using IR, NMR or DSC for better understanding of the degradation pathways.
- Investigate the stability of the drug in presence of different formulation environments like adjusting micro-environmental pH or addition of anti-oxidants
or coating the drug particles with inert polymers and thereby reducing the contact of the drug with excipients.

- **Stability of the drug in presence of different mini-formulations (multiple excipients) consisting of different compositions and ratios.**

- **Evaluate the effect of processing conditions and equipments on the stability of the drug.**
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APPENDIX A

INTRODUCTION:

This appendix includes the statistical output of non-linear regression for first-order and biphasic first-order reactions. Sigma plot for Windows (Version 4, SPSS Inc., 1997) was used to perform the curve fitting procedures for both the models. First section gives the definition of the variables, constraints and model parameters. This is followed by tests to validate the equal variance and normality assumptions for model errors. The final section gives the residuals and other diagnostics. Salient parameters basing on which our conclusions are made, include adjusted $r^2$ values, normality tests and residual plots indicating the goodness of the fit followed by providing the validity of the assumptions.
DEXTROSE (First-order reaction)
25°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

*Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {{previous: 94.074}}
b = ln(.5)/(x50(x,y)-min(x)) "Auto {{previous: 0.00908564}}

[Equation]
f=a*exp(-b*x)

fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.79403850 Rsqr = 0.63049713 Adj Rsqr = 0.55659656

Standard Error of Estimate = 4.5081

| Coefficient | Std. Error | t    | P    |
|-------------|------------|------|------|
| a           | 94.0740    | 2.4474 | <0.0001 |
| b           | 0.0091     | 0.0032 | 0.0350  |

Analysis of Variance:

| DF    | SS     | MS   | F    | P    |
|-------|--------|------|------|------|
| Regression | 173.3889 | 173.3889 | 8.5317 | 0.0330 |
| Residual | 5     | 101.6146 | 20.3229 |      |
| Total   | 6     | 275.0034 | 45.8339 |      |

PRESS = 385.8371

Durbin-Watson Statistic = 2.1014
Normality Test: Passed (P = 0.7083)

Constant Variance Test: Passed (P = 0.7810)

Power of performed test with alpha = 0.0500: 0.5810

The power of the performed test (0.5810) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 94.0740   | 5.9260   | 1.3145    | 1.5653     | 1.9604          |
| 2   | 93.2232   | -1.1485  | -0.3147   | -0.3623    | -0.3284         |
| 3   | 92.3800   | 1.8564   | 0.4118    | 0.4625     | 0.4228          |
| 4   | 90.7165   | -4.4046  | -0.9770   | -1.0648    | -1.0830         |
| 5   | 88.2772   | -0.9019  | -0.2001   | -0.2167    | -0.1948         |
| 6   | 85.9036   | -5.0004  | -1.1092   | -1.2432    | -1.3378         |
| 7   | 78.4427   | 3.9775   | 0.8823    | 1.7381     | 2.4711          |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.5119      | 0.2947   | 1.2673 |
| 2   | 0.0214      | 0.2459   | -0.1876|
| 3   | 0.0279      | 0.2072   | 0.2161 |
| 4   | 0.1064      | 0.1580   | -0.4691|
| 5   | 0.0041      | 0.1479   | -0.0811|
| 6   | 0.1980      | 0.2040   | -0.6771|
| 7   | 4.3516      | 0.7423   | 4.1943 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 94.0740   | 87.7828  | 100.3652  | 80.8880 | 107.2600 |
| 2   | 93.2232   | 87.4765  | 98.9698   | 80.2881 | 106.1582 |
| 3   | 92.3800   | 87.1052  | 97.6548   | 79.6476 | 105.1124 |
| 4   | 90.7165   | 86.1103  | 95.3227   | 78.2462 | 103.1868 |
| 5   | 88.2772   | 83.8206  | 92.7339   | 75.8614 | 100.6931 |
| 6   | 85.9036   | 80.6701  | 91.1370   | 73.1882 | 98.6189  |
| 7   | 78.4427   | 68.4584  | 88.4271   | 63.1464 | 93.7391  |
DEXTROSE (First-order reaction)
25°C / 60 %RH

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {{previous: 85.5238}}
b = -ln(0.5)/(x50(x,y)-min(x)) "Auto {{previous: 0.0276726}}

[Equation]
f=a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.63120454 Rsqr = 0.39841917 Adj Rsqr = 0.27810301
Standard Error of Estimate = 15.7556

| Coefficient | Std. Error | t  | P   |
|-------------|------------|----|-----|
| a           | 9.0764     | 9.4226 | 0.0002 |
| b           | 0.0157     | 1.7668 | 0.1375 |

Analysis of Variance:

| DF | SS     | MS  | F     | P   |
|----|--------|-----|-------|-----|
| Regression 1 | 822.0289 | 822.0289 | 3.3114 | 0.1285 |
| Residual 5    | 1241.1974 | 248.2395   |
| Total 6       | 2063.2264 | 343.8711   |

PRESS = 3064.4031

Durbin-Watson Statistic = 1.2174

Normality Test: Passed (P = 0.0576)

Constant Variance Test: Passed (P = 0.9684)

Power of performed test with alpha = 0.0500: 0.3181

The power of the performed test (0.3181) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 85.5238   | 14.4762  | 0.9188    | 1.1241     | 1.1630          |
| 2   | 83.1896   | 3.2403   | 0.2057    | 0.2392     | 0.2151          |
| 3   | 80.9191   | 5.0445   | 0.3202    | 0.3599     | 0.3262          |
| 4   | 76.5623   | -13.8018 | -0.8760   | -0.9526    | -0.9417         |
| 5   | 70.4629   | -24.8293 | -1.5759   | -1.7223    | -2.4156         |
| 6   | 64.8494   | 3.6990   | 0.2348    | 0.2693     | 0.2426          |
| 7   | 49.1729   | 13.2297  | 0.8397    | 1.4033     | 1.6122          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.3138     | 0.3319   | 0.8197 |
| 2   | 0.0101     | 0.2605   | 0.1277 |
| 3   | 0.0171     | 0.2088   | 0.1676 |
| 4   | 0.0828     | 0.1543   | -0.4022|
| 5   | 0.2885     | 0.1628   | -1.0653|
| 6   | 0.0114     | 0.2398   | 0.1363 |
| 7   | 1.7657     | 0.6420   | 2.1589 |
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 85.5238   | 62.1921  | 108.8555  | 38.7830 | 132.2646|
| 2   | 83.1896   | 62.5191  | 103.8600  | 37.7186 | 128.6605|
| 3   | 80.9191   | 62.4128  | 99.4253   | 36.3902 | 125.4479|
| 4   | 76.5623   | 60.6541  | 92.4704   | 33.0489 | 120.9756|
| 5   | 70.4629   | 54.1204  | 86.8054   | 26.7889 | 114.1369|
| 6   | 64.8494   | 45.0165  | 84.6824   | 19.7531 | 109.9458|
| 7   | 49.1729   | 16.7218  | 81.6239   | -2.7252 | 101.0709|

### 2D Graph 3

#### DEXTROSE (First-order reaction)

**40°C / 75% RH**

Nonlinear Regression

```plaintext
[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_y^2=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
ytaxnear0(q,r)=ytaymax(q,xnear0(r))

[Parameters]
a = ytaxnear0(y,x) "Auto {{previous: 99.9044}}
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {{previous: 2.14682}}

[Equation]
f=a*exp(-b*x)
```
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^2

[Constraints]
b > 0

[Options]
Epsilon = 0.0001
Steps = 100
Iterations = 100

R = 0.98465494   Rsqr = 0.96954536   Adj Rsqr = 0.96345443

Standard Error of Estimate = 6.6937

| Coefficient | Std. Error | t     | P   |
|-------------|------------|-------|-----|
| a           | 99.9044    | 6.6931|     |
| b           | 2.1468     | 0.5596|     |

Analysis of Variance:

| DF | SS       | MS       | F      | P     |
|----|----------|----------|--------|-------|
| Regression | 7132.0364 | 7132.0364 | 159.1786 | <0.0001 |
| Residual  | 224.0263  | 44.8053  |        |       |
| Total     | 7356.0627 | 1226.0105|        |       |

PRESS = 282946.1962

Durbin-Watson Statistic = 0.3366

Normality Test: Failed (P = 0.0025)

Constant Variance Test: Passed (P = 0.2965)

Power of performed test with alpha = 0.0500: 0.9981

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 99.9044   | 0.0956   | 0.0143    | 1.0642     | 1.0823          |
| 2   | 11.6744   | -1.6080  | -0.2402   | -1.0510    | -1.0650         |
| 3   | 1.3642    | 6.6708   | 0.9966    | 1.0238     | 1.0300          |
| 4   | 0.0186    | 6.4913   | 0.9698    | 0.9698     | 0.9627          |
| 5   | 0.0000    | 7.7013   | 1.1505    | 1.1505     | 1.2001          |
| 6   | 0.0000    | 6.1283   | 0.9155    | 0.9155     | 0.8976          |
| 7   | 0.0000    | 6.1587   | 0.9201    | 0.9201     | 0.9029          |
### Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 3143.8469   | 0.9998   | 80.6421 |
| 2   | 10.0185     | 0.9478   | -4.5360 |
| 3   | 0.0290      | 0.0524   | 0.2422  |
| 4   | 0.0000      | 0.0000   | 0.0061  |
| 5   | 0.0000      | 0.0000   | 0.0000  |
| 6   | 0.0000      | 0.0000   | 0.0000  |
| 7   | 0.0000      | 0.0000   | 0.0000  |

### 95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|------------|----------|-----------|---------|----------|
| 1   | 99.9044    | 82.6993  | 117.1095  | 75.5716 | 124.2372 |
| 2   | 11.6744    | -5.0767  | 28.4255   | -12.3395| 35.6883  |
| 3   | 1.3642     | -2.5741  | 5.3025    | -16.2874| 19.0158  |
| 4   | 0.0186     | -0.0901  | 0.1274    | -17.1883| 17.2256  |
| 5   | 0.0000     | -0.0003  | 0.0003    | -17.2066| 17.2067  |
| 6   | 0.0000     | -0.0000  | 0.0000    | -17.2066| 17.2066  |
| 7   | 0.0000     | -0.0000  | 0.0000    | -17.2066| 17.2066  |

---

**DEXTROSE (First-order reaction)**

50°C / 20% moisture

Nonlinear Regression

[Variables]

\[ x = \text{col}(1) \]
\[ y = \text{col}(2) \]
\[ \text{reciprocal}_y = 1/|y| \]
\[ \text{reciprocal}_y\text{square} = 1/y^2 \]

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 99.8667}"
b = -ln(0.5)/(x50(x,y)-min(x)) "Auto {previous: 2.10922}"

[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_y^2"

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

R = 0.97845723 Rsqr = 0.95737856 Adj Rsqr = 0.94885427

Standard Error of Estimate = 7.8399

| Coefficient | Std. Error | t      | P     |
|-------------|------------|--------|-------|
| a           | 99.8667    | 7.8390 | <0.0001 |
| b           | 2.1092     | 0.6285 | 0.0202 |

Analysis of Variance:

| DF | SS          | MS     | F       | P     |
|----|-------------|--------|---------|-------|
| Regression | 1 | 6903.0535  | 6903.0535 | 112.3119 | 0.0001 |
| Residual    | 5  | 307.3163   | 61.4633  |         |       |
| Total       | 6  | 7210.3698  | 1201.7283|         |       |

PRESS = 400202.4543

Durbin-Watson Statistic = 0.4245

Normality Test: Failed (P = 0.0112)

Constant Variance Test: Passed (P = 0.0545)

Power of performed test with alpha = 0.0500: 0.9948

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|----------------|
| 1   | 99.8667   | 0.1333   | 0.0170    | 1.1699     | 1.2278         |
| 2   | 12.1171   | -2.1559  | -0.2750   | -1.1575    | -1.2100        |
| 3   | 1.4702    | 8.6146   | 1.0988    | 1.1313     | 1.1731         |
4 0.0216 6.7143 0.8564 0.8565 0.8293
5 0.0000 7.0723 0.9021 0.9021 0.8818
6 0.0000 8.8752 1.1321 1.1321 1.1741
7 0.0000 7.3872 0.9423 0.9423 0.9293

Influence Diagnostics:
Row Cook's Dist Leverage DFFITS
1 3240.5340 0.9998 84.4919
2 11.1981 0.9436 -4.9472
3 0.0384 0.0566 0.2873
4 0.0000 0.0001 0.0059
5 0.0000 0.0000 0.0000
6 0.0000 0.0000 0.0000
7 0.0000 0.0000 0.0000

95% Confidence:
Row Predicted Regr. 5% Regr. 95% Pop. 5% Pop. 95%
1 99.8667 79.7159 120.0176 71.3676 128.3658
2 12.1171 -7.4589 31.6931 -15.9785 40.2127
3 1.4702 -3.3245 6.2649 -19.2453 22.1857
4 0.0216 -0.1220 0.1653 -20.1318 20.1751
5 0.0000 -0.0004 0.0005 -20.1529 20.1530
6 0.0000 -0.0000 0.0000 -20.1530 20.1530
7 0.0000 -0.0000 0.0000 -20.1530 20.1530

2D Graph 5
DEXTROSE (First-order reaction)
50°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 95.1795}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0531936}"

[Equation]
f=a*exp(-b*x)
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.95335268   Rsqr = 0.90888134   Adj Rsqr = 0.89065761

Standard Error of Estimate = 7.2707

| Coefficient | Std. Error |   t  | P     |
|-------------|------------|------|-------|
| a           | 95.1795    | 21.1072 | <0.0001 |
| b           | 0.0532     | 5.9329  | 0.0019 |

Analysis of Variance:

|          | DF | SS        | MS        | F      | P     |
|----------|----|-----------|-----------|--------|-------|
| Regression | 1  | 2636.4745 | 2636.4745 | 49.8735 | 0.0009|
| Residual  | 5  | 264.3162  | 52.8632   |        |       |
| Total     | 6  | 2900.7906 | 483.4651  |        |       |

PRESS = 595.5611

Durbin-Watson Statistic = 1.2438

Normality Test: Passed (P = 0.6459)
Constant Variance Test: Passed (P = 0.6019)

Power of performed test with alpha = 0.0500: 0.9620

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 95.1795   | 4.8205   | 0.6630    | 0.8452     | 0.8165          |
| 2   | 90.2489   | 1.8105   | 0.2490    | 0.2926     | 0.2640          |
| 3   | 85.5737   | 3.8791   | 0.5335    | 0.5993     | 0.5564          |
| 4   | 76.9373   | -9.3995  | -1.2928   | -1.4073    | -1.6197         |
| 5   | 65.5891   | -7.5493  | -1.0383   | -1.1601    | -1.2137         |
| 6   | 55.9148   | -0.4379  | -0.0602   | -0.0716    | -0.0641         |
| 7   | 32.8480   | 8.7874   | 1.2086    | 1.6836     | 2.2881          |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.2233      | 0.6456   |        |
| 2   | 0.0163      | 0.1630   |        |
| 3   | 0.0470      | 0.2847   |        |
| 4   | 0.1831      | -0.6966  |        |
| 5   | 0.1671      | -0.6048  |        |
| 6   | 0.0011      | -0.0412  |        |
| 7   | 1.3327      | 2.2189   |        |

95% Confidence:

| Row | Predicted      | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|----------------|----------|-----------|---------|----------|
| 1   | 95.1795        | 83.5879  | 106.7712  | 73.1868 | 117.1723 |
| 2   | 90.2489        | 80.4312  | 100.0665  | 69.1373 | 111.3605 |
| 3   | 85.5737        | 77.0603  | 94.0870   | 65.0361 | 106.1112 |
| 4   | 76.9373        | 69.5534  | 84.3211   | 56.8416 | 97.0329  |
| 5   | 65.5891        | 57.2538  | 73.9244   | 45.1247 | 86.0535  |
| 6   | 55.9148        | 45.8099  | 66.0196   | 34.6680 | 77.1615  |
| 7   | 32.8480        | 19.8368  | 45.8593   | 10.0751 | 55.6210  |
DEXTROSE (Biphasic First-order reaction)

25°C

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {previous: 0.168671}
b = -ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 0.267513}
c = yatxnear0(y,x)/2 "Auto {previous: 0.819683}
d = -ln(.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 4.2155e-012}

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100
\[ R = 0.94079403 \quad \text{Rsqr} = 0.88509342 \quad \text{Adj Rsqr} = 0.77018683 \]

Standard Error of Estimate = 0.0325

| Coefficient | Std. Error | t    | P    |
|-------------|------------|------|------|
| a           | 0.1299     | 1.2984 | 0.2850 |
| b           | 0.3250     | 0.8230 | 0.4708 |
| c           | 0.1373     | 5.9708 | 0.0094 |
| d           | 0.0090     | 0.0000 | 1.0000 |

Analysis of Variance:

| DF | SS   | MS   | F    | P    |
|----|------|------|------|------|
| Regression | 0.0243 | 0.0081 | 7.7027 | 0.0638 |
| Residual   | 0.0032 | 0.0011 |      |      |
| Total      | 0.0275 | 0.0046 |      |      |

PRESS = 0.2526

Durbin-Watson Statistic = 3.5677

Normality Test: Passed (P = 0.6858)

Constant Variance Test: Passed (P = 0.4907)

Power of performed test with alpha = 0.0500: 0.9370

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 0.9884    | 0.0116   | 0.3588    | 0.9128     | 0.8770          |
| 2   | 0.9488    | -0.0307  | -0.9464   | -1.1514    | -1.2585         |
| 3   | 0.9185    | 0.0239   | 0.7363    | 0.9658     | 0.9500          |
| 4   | 0.8775    | -0.0144  | -0.4442   | -0.5757    | -0.4984         |
| 5   | 0.8456    | 0.0281   | 0.8671    | 1.1115     | 1.1833          |
| 6   | 0.8313    | -0.0223  | -0.6863   | -1.1178    | -1.1947         |
| 7   | 0.8205    | 0.0037   | 0.1146    | 1.3110     | 1.6380          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 1.1398     | 0.8455   | 2.0514 |
| 2   | 0.1591     | 0.3244   | -0.8720|
| 3   | 0.1680     | 0.4187   | 0.8063 |
| 4   | 0.0563     | 0.4046   | -0.4109|
| 5   | 0.1986     | 0.3914   | 0.9489 |
| 6   | 0.5163     | 0.6231   | -1.5360|
| 7   | 55.8124    | 0.9924   | 18.6680|
## DEXTROSE (Biphasic First-order reaction)

25°C / 60 %RH

Nonlinear Regression

[Variables]
- \( x = \text{col}(1) \)
- \( y = \text{col}(2) \)
- \( \text{reciprocal}_y = 1/\text{abs}(y) \)
- \( \text{reciprocal}_y\text{square} = 1/y^2 \)

'Automatic Initial Parameter Estimate Functions

\( x\text{near0}(q) = \max(\text{abs}(q)) - \text{abs}(q) \)
\( y\text{at}x\text{near0}(q,r) = y\text{at}x\text{max}(q,x\text{near0}(r)) \)

[Parameters]
- \( a = y\text{at}x\text{near0}(y,x)/2 \) "Auto \{previous: 0.433192\}"
- \( b = -\ln(0.5)/(0.5*(x50(x,y)-\text{min}(x))) \) "Auto \{previous: 0.421275\}"
- \( c = y\text{at}x\text{near0}(y,x)/2 \) "Auto \{previous: 0.586266\}"
- \( d = -\ln(0.5)/(1.5*(x50(x,y)-\text{min}(x))) \) "Auto \{previous: 1.86902e-010\}"

### Table

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 0.9884    | 0.8934   | 1.0833    | 0.8480  | 1.1287   |
| 2   | 0.9488    | 0.8899   | 1.0076    | 0.8299  | 1.0676   |
| 3   | 0.9185    | 0.8516   | 0.9853    | 0.7954  | 1.0415   |
| 4   | 0.8775    | 0.8118   | 0.9432    | 0.7551  | 0.9999   |
| 5   | 0.8456    | 0.7810   | 0.9102    | 0.7238  | 0.9674   |
| 6   | 0.8313    | 0.7498   | 0.9128    | 0.6997  | 0.9629   |
| 7   | 0.8205    | 0.7176   | 0.9234    | 0.6747  | 0.9663   |
Equation:
\[ f = a \cdot \exp(-b \cdot x) + c \cdot \exp(-d \cdot x) \]

fit \( f \) to \( y \) with weight reciprocal \( y \)
fit \( f \) to \( y \) with weight reciprocal \( y \) square

Constraints:
\[ b > 0 \]
\[ d > 0 \]

Options:
tolerance = 1e-6
steepsie = 0.1
iterations = 100

\[ R = 0.89024727 \quad \text{Rsqr} = 0.79254021 \quad \text{Adj Rsqr} = 0.58508042 \]

Standard Error of Estimate = 0.1194

| Coefficient | Std. Error | \( t \) | \( P \) |
|-------------|------------|--------|--------|
| a           | 0.4332     | 0.2466 | 1.7565 | 0.1773 |
| b           | 0.4213     | 0.4753 | 0.8864 | 0.4407 |
| c           | 0.5863     | 0.2447 | 2.3958 | 0.0962 |
| d           | 0.0000     | 0.0270 | 0.0000 | 1.0000 |

Analysis of Variance:

|          | DF | SS   | MS  | \( F \)   | \( P \)  |
|----------|----|------|-----|-----------|---------|
| Regression | 3  | 0.1635 | 0.0545 | 3.8202   | 0.1500  |
| Residual  | 3  | 0.0428 | 0.0143 |           |         |
| Total     | 6  | 0.2063 | 0.0344 |           |         |

PRESS = 3.5557

Durbin-Watson Statistic = 2.3563

Normality Test: Passed (\( P = 0.6032 \))

Constant Variance Test: Passed (\( P = 0.1815 \))

Power of performed test with alpha = 0.0500: 0.8123

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0195    | -0.0195  | -0.1629   | -0.5416    | -0.4656         |
| 2   | 0.8705    | -0.0062  | -0.0522   | -0.0664    | -0.0543         |
| 3   | 0.7728    | 0.0868   | 0.7269    | 0.9972     | 0.9958          |
| 4   | 0.6666    | -0.0390  | -0.3264   | -0.4020    | -0.3375         |
| 5   | 0.6090    | -0.1526  | -1.2778   | -1.6945    | -6.6847         |
| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.7373     | -1.4762  |        |
| 2   | 0.0007     | -0.0428  |        |
| 3   | 0.2192     | 0.9352   |        |
| 4   | 0.0209     | -0.2427  |        |
| 5   | 0.5447     | -5.8228  |        |
| 6   | 0.2794     | 1.1073   |        |
| 7   | 57.9123    | (+inf)   |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0195    | 0.6569   | 1.3820    | 0.4942  | 1.5448   |
| 2   | 0.8705    | 0.6353   | 1.1058    | 0.4235  | 1.3176   |
| 3   | 0.7728    | 0.5126   | 1.0330    | 0.3121  | 1.2335   |
| 4   | 0.6666    | 0.4447   | 0.8885    | 0.2264  | 1.1068   |
| 5   | 0.6090    | 0.3593   | 0.8586    | 0.1542  | 1.0638   |
| 6   | 0.5927    | 0.3274   | 0.8580    | 0.1291  | 1.0562   |
| 7   | 0.5864    | 0.2101   | 0.9626    | 0.0515  | 1.1212   |

2D Graph 2

- Col 15 v Col 18
- Time, weeks v DDo, [Dextrose, 25°C/80%RH]
DEXTROSE ( Biphasic First-order reaction)
40°C / 75 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto \{ previous: 0.912799 \}
b = -ln(0.5)/(0.5*(x50(x,y)-min(x))) "Auto \{ previous: 93.796 \}
c = yatxnear0(y,x)/2 "Auto \{ previous: 0.0872007 \}
d = -ln(0.5)/(1.5*(x50(x,y)-min(x))) "Auto \{ previous: 0.0233318 \}

[Equation]
f = a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b > 0
d > 0

[Options]
tolerance = 1e-6
stepsize = 0.1
iterations = 100

R = 0.99961260   Rsqr = 0.99922535   Adj Rsqr = 0.99845071

Standard Error of Estimate = 0.0138

| Coefficient | Std. Error | t    | P        |
|-------------|------------|------|----------|
| a           | 0.9128     | 0.0167 | 54.5026  | <0.0001 |
| b           | 93.7960    | 685683.1062 | 0.0001  | 0.9999 |
| c           | 0.0872     | 0.0095 | 9.1641   | 0.0027 |
| d           | 0.0233     | 0.0139 | 1.6780   | 0.1919 |

Analysis of Variance:

|        | SS  | MS     | F       | P       |
|--------|-----|--------|---------|---------|
| Regression | 0.7350 | 0.2450 | 1289.9098 | <0.0001 |
| Residual  | 0.0006 | 0.0002 |         |         |
| Total    | 0.7356 | 0.1226 |         |         |
PRESS = 1898897780025.0015

Durbin-Watson Statistic = 2.3452

Normality Test: Passed (P = 0.7511)

Constant Variance Test: Passed (P = 0.6019)

Power of performed test with alpha = 0.0500: 1.0000

| Regression Diagnostics: |
|-------------------------|
| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0000    | -0.0000  | -0.0000   | -1.4899    | -2.3854         |
| 2   | 0.0852    | 0.0155   | 1.1227    | 1.4238     | 2.0414          |
| 3   | 0.0832    | -0.0029  | -0.2086   | -0.2497    | -0.2060         |
| 4   | 0.0794    | -0.0143  | -1.0399   | -1.1666    | -1.2888         |
| 5   | 0.0741    | 0.0030   | 0.2142    | 0.2354     | 0.1940          |
| 6   | 0.0691    | -0.0078  | -0.5638   | -0.6430    | -0.5655         |
| 7   | 0.0547    | 0.0069   | 0.5008    | 0.9322     | 0.9031          |

| Influence Diagnostics: |
|------------------------|
| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 2499270892732516.5000 | 1.0000   | -160084122.9027 |
| 2   | 0.3082     | 0.3782   | 1.5920 |
| 3   | 0.0067     | 0.3017   | -0.1354|
| 4   | 0.0880     | 0.2055   | -0.6555|
| 5   | 0.0029     | 0.1720   | 0.0884 |
| 6   | 0.0311     | 0.2312   | -0.3101|
| 7   | 0.5354     | 0.7114   | 1.4177 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|--------|---------|
| 1   | 1.0000    | 0.9561   | 1.0439    | 0.9380 | 1.0620  |
| 2   | 0.0852    | 0.0582   | 0.1122    | 0.0337 | 0.1367  |
| 3   | 0.0832    | 0.0591   | 0.1073    | 0.0332 | 0.1333  |
| 4   | 0.0794    | 0.0595   | 0.0993    | 0.0313 | 0.1276  |
| 5   | 0.0741    | 0.0559   | 0.0923    | 0.0266 | 0.1215  |
| 6   | 0.0691    | 0.0480   | 0.0901    | 0.0204 | 0.1177  |
| 7   | 0.0547    | 0.0177   | 0.0917    | -0.0027| 0.1121  |
**DEXTROSE (Biphasic First-order reaction)**

50°C / 20% moisture

Nonlinear Regression

[Variables]
- \( x = \text{col}(1) \)
- \( y = \text{col}(2) \)
- \( \text{reciprocal}_y = 1/\text{abs}(y) \)
- \( \text{reciprocal}_y^2 = 1/y^2 \)

'Automatic Initial Parameter Estimate Functions

- \( x_{\text{near}0}(q) = \max(\text{abs}(q))-\text{abs}(q) \)
- \( y_{\text{at}x_{\text{near}0}}(q,r) = x_{\text{at}y_{\text{max}}}(q,x_{\text{near}0}(r)) \)

[Parameters]
- \( a = y_{\text{at}x_{\text{near}0}}(y,x)/2 \) "Auto {previous: 0.908409}"
- \( b = -\ln(0.5)/(0.5*(x50(y,x)-\text{min}(x))) \) "Auto {previous: 22045.5}"
- \( c = y_{\text{at}x_{\text{near}0}}(y,x)/2 \) "Auto {previous: 0.0915914}"
- \( d = -\ln(0.5)/(1.5*(x50(y,x)-\text{min}(x))) \) "Auto {previous: 0.0130566}"

[Equation]

\[ f = a\exp(-b*x) + c\exp(-d*x) \]

fit f to y

"fit f to y with weight reciprocal_y"

"fit f to y with weight reciprocal_y^2"

[Constraints]
- \( b > 0 \)
- \( d > 0 \)

[Options]
- tolerance = 1e-6
- stepsize = 0.1
- iterations = 100
R = 0.99941069  Rsqr = 0.99882173  Adj Rsqr = 0.99764346

Standard Error of Estimate = 0.0168

| Coefficient | Std. Error | t    | P   |
|-------------|------------|------|-----|
| a           | 0.9084     | 0.0201 | 45.0839  | <0.0001  | 0.9806 |
| b           | 22045.4822 |       | 837239.9928 | 0.0263  |
| c           | 0.0916     | 0.0111 | 8.2664  | 0.0037   |
| d           | 0.0131     | 0.0140 | 0.9319 | 0.4201   |

Analysis of Variance:

|      | DF | SS     | MS     | F      | P     |
|------|----|--------|--------|--------|-------|
| Regression | 3  | 0.7202 | 0.2401 | 847.7015 | <0.0001 |
| Residual   | 3  | 0.0008 | 0.0003 |
| Total      | 6  | 0.7210 | 0.1202 |

PRESS = 58309481048160.2500

Durbin-Watson Statistic = 1.8654

Normality Test: Passed (P = 0.3935)

Constant Variance Test: Passed (P = 0.8429)

Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0000    | -0.0000  | -0.0000   | -9.5623    | (+inf)          |
| 2   | 0.0904    | 0.0092   | 0.5472    | 0.6820     | 0.6058          |
| 3   | 0.0892    | 0.0116   | 0.6903    | 0.8213     | 0.7616          |
| 4   | 0.0869    | -0.0196  | -1.1630   | -1.3071    | -1.6266         |
| 5   | 0.0836    | -0.0129  | -0.7647   | -0.8383    | -0.7822         |
| 6   | 0.0804    | 0.0084   | 0.4975    | 0.5608     | 0.4840          |
| 7   | 0.0705    | 0.0033   | 0.1979    | 0.4049     | 0.3400          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | -51475181805011992.0000 | 0.4505   | 1.0000  (+inf) |
| 2   | 0.0643     | 0.3561   |        |
| 3   | 0.0700     | 0.2934   |        |
| 4   | 0.1124     | 0.2083   | -0.8344|
| 5   | 0.0355     | 0.1680   | -0.3514|
| 6   | 0.0213     | 0.2131   | 0.2519 |
| 7   | 0.1306     | 0.7611   | 0.6070 |
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|--------|---------|
| 1   | 1.0000    | 0.9464   | 1.0536    | 0.9243 | 1.0757  |
| 2   | 0.0904    | 0.0684   | 0.1224    | 0.0280 | 0.1528  |
| 3   | 0.0892    | 0.0562   | 0.1182    | 0.0283 | 0.1501  |
| 4   | 0.0869    | 0.0625   | 0.1114    | 0.0281 | 0.1458  |
| 5   | 0.0836    | 0.0616   | 0.1055    | 0.0257 | 0.1415  |
| 6   | 0.0804    | 0.0557   | 0.1051    | 0.0214 | 0.1394  |
| 7   | 0.0705    | 0.0238   | 0.1173    | -0.0005| 0.1416  |

**DEXTROSE (Biphasic First-order reaction)**

50°C

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y_square = 1/y^2

'Automatic Initial Parameter Estimate Functions'
xnear(0) = max(abs(q)) - abs(q)
yatxnear(0, r) = yatymax(q, xnear(r))

[Parameters]
a = yatxnear(0, x)/2 "Auto {previous: 0.507061}"
b = -ln(0.5)/(0.5*(x50(x, y) - min(x))) "Auto {previous: 0.198221}"
c = yatxnear(0, x)/2 "Auto {previous: 0.509762}"
d = -ln(0.5)/(1.5*(x50(x, y) - min(x))) "Auto {previous: 0.010782}"
**Equation**

\[ f = a \cdot \exp(-b \cdot x) + c \cdot \exp(-d \cdot x) \]

*fit f to y*

*fit f to y with weight reciprocal_y*

*fit f to y with weight reciprocal_y\_square*

**Constraints**

b > 0
d > 0

**Options**

tolerance = 1e-6
steps = 0.1
iterations = 100

R = 0.98931299  \quad \text{Rsqr} = 0.97874020  \quad \text{Adj Rsqr} = 0.95748039

Standard Error of Estimate = 0.0453

| Coefficient | Std. Error | t       | P     |
|-------------|------------|---------|-------|
| a           | 0.5071     | 0.1634  | 0.3288|
| b           | 0.1982     | 0.1900  | 0.3735|
| c           | 0.5098     | 0.1290  | 0.3410|
| d           | 0.0108     | 0.2619  | 0.8104|

**Analysis of Variance:**

|         | DF | SS   | MS   | F     | P     |
|---------|----|------|------|-------|-------|
| Regression | 3  | 0.2839 | 0.0946 | 46.0371 | 0.0052 |
| Residual   | 3  | 0.0062 | 0.0021 |       |       |
| Total      | 6  | 0.2901 | 0.0483 |       |       |

PRESS = 0.6980

Durbin-Watson Statistic = 2.6392

Normality Test: Passed (P = 0.4222)

Constant Variance Test: Passed (P = 0.8429)

Power of performed test with alpha = 0.0500: 0.9995

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|------------|----------|-----------|------------|-----------------|
| 1   | 1.0168     | -0.0168  | -0.3710   | -0.8581    | -0.8066         |
| 2   | 0.9202     | 0.0004   | 0.0091    | 0.0110     | 0.0090          |
| 3   | 0.8400     | 0.0545   | 1.2028    | 1.5404     | 2.7511          |
| 4   | 0.7177     | -0.0423  | -0.9337   | -1.2409    | -1.4524         |
| 5   | 0.5993     | -0.0189  | -0.4171   | -0.5293    | -0.4538         |
| Row | Cook's Dist | Leverage  | DFFITS   |
|-----|-------------|-----------|----------|
| 1   | 0.8006      | 1.6821    |          |
| 2   | 0.0000      | 0.0060    |          |
| 3   | 0.3798      | 2.2011    |          |
| 4   | 0.2951      | -1.2716   |          |
| 5   | 0.0427      | -0.3544   |          |
| 6   | 0.5911      | 1.5870    |          |
| 7   | 80.8563     | -21.8923  |          |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0168    | 0.8867   | 1.1469    | 0.8225  | 1.2111   |
| 2   | 0.9202    | 0.8397   | 1.0006    | 0.7550  | 1.0854   |
| 3   | 0.8400    | 0.7498   | 0.9301    | 0.6699  | 1.0101   |
| 4   | 0.7177    | 0.6227   | 0.8128    | 0.5449  | 0.8905   |
| 5   | 0.5993    | 0.5105   | 0.6881    | 0.4299  | 0.7687   |
| 6   | 0.5275    | 0.4087   | 0.6463    | 0.3406  | 0.7144   |
| 7   | 0.4205    | 0.2766   | 0.5644    | 0.2167  | 0.6243   |

2D Graph 5
DiCalcium Phosphate Dihydrate (First-order reaction)
25°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y2 = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxminear0(q,r) = xatymax(q,xnear0(r))

[Parameters]
a = yatxminear0(y,x) "Auto {previous: 93.5638}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.00669228}

[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_y2"

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

R = 0.22215643    Rsqr = 0.04935348  Adj Rsqr = 0.00000000

Standard Error of Estimate = 17.8133

| Coefficient | Std. Error | t     |        |
|-------------|------------|-------|--------|
| a           | 93.5638    | 8.9201| <0.0001|
| b           | 0.0067     | 0.0120| 0.5977 |

Analysis of Variance:

| DF | SS     | MS      | F     | P     |
|----|--------|---------|-------|-------|
| Regression | 1 | 98.8417 | 98.8417 | 0.3115 | 0.5970 |
| Residual   | 6  | 1903.8879 | 317.3146 |       |       |
| Total      | 7  | 2002.7295 | 286.1042 |       |       |

PRESS = 3042.9073

Durbin-Watson Statistic = 2.6111
Normality Test: Passed (P = 0.2724)

Constant Variance Test: Passed (P = 0.8849)

Power of performed test with alpha = 0.0500: 0.0729

The power of the performed test (0.0729) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 93.5638   | 6.4362   | 0.3613    | 0.4174     | 0.3867          |
| 2   | 92.9397   | 2.7105   | 0.1522    | 0.1711     | 0.1566          |
| 3   | 92.3198   | -13.7590 | -0.7724   | -0.8509    | -0.8283         |
| 4   | 91.7040   | 29.9978  | 1.6840    | 1.8281     | 2.5074          |
| 5   | 91.0924   | -12.5671 | -0.7055   | -0.7586    | -0.7283         |
| 6   | 89.2818   | -23.4710 | -1.3176   | -1.4143    | -1.5813         |
| 7   | 87.5071   | 5.5220   | 0.3100    | 0.3448     | 0.3179          |
| 8   | 81.8426   | 5.1597   | 0.2897    | 0.5839     | 0.5489          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.0292     | 0.2237   |        |
| 2   | 0.0039     | 0.0805   |        |
| 3   | 0.0773     | -0.3828  |        |
| 4   | 0.2983     | 1.0594   |        |
| 5   | 0.0450     | -0.2879  |        |
| 6   | 0.1522     | -0.6168  |        |
| 7   | 0.0141     | 0.1549   |        |
| 8   | 0.5224     | 0.9608   |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 93.5638   | 71.7371  | 115.3905  | 44.8166 | 142.3109 |
| 2   | 92.9397   | 73.0151  | 112.8643  | 45.0140 | 140.8654 |
| 3   | 92.3198   | 74.0355  | 110.6041  | 45.0525 | 139.5871 |
| 4   | 91.7040   | 74.7404  | 108.6677  | 44.9317 | 138.4763 |
| 5   | 91.0924   | 75.0696  | 107.1151  | 44.6531 | 137.5317 |
| 6   | 89.2818   | 73.4427  | 105.1208  | 42.9055 | 135.6580 |
| 7   | 87.5071   | 68.4207  | 106.5936  | 39.9238 | 135.0905 |
| 8   | 81.8426   | 43.9956  | 119.6896  | 24.1167 | 139.5685 |
DiCalcium Phosphate Dihydrate (First-order reaction)
25°C/ 60 %RH
NO OUTPUT

DiCalcium Phosphate Dihydrate (First-order reaction)
40°C/ 75 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 88.6789}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0208095}"

[Equation]
f=a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
R = 0.68153155  \quad \text{Rsqr} = 0.46448525 \quad \text{Adj Rsqr} = 0.37523279

Standard Error of Estimate = 11.3148

| Coefficient | Std. Error | t   | P     |
|-------------|------------|-----|-------|
| a           | 88.6789    | 5.9606 | 14.8776 | <0.0001 |
| b           | 0.0208     | 0.0098 | 2.1212 | 0.0782  |

Analysis of Variance:

| DF | SS   | MS   | F    | P     |
|----|------|------|------|-------|
| Regression | 1    | 666.2571 | 666.2571 | 5.2042 | 0.0627 |
| Residual   | 6    | 768.1417  | 128.0236 |       |       |
| Total      | 7    | 1434.3988 | 204.9141 |       |       |

PRESS = 1338.7404

Durbin-Watson Statistic = 2.1340

Normality Test: Passed (P = 0.5252)

Constant Variance Test: Failed (P = 0.0287)

Power of performed test with alpha = 0.0500: 0.4603

The power of the performed test (0.4603) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|------------|----------|-----------|------------|-----------------|
| 1   | 88.6789    | 11.3211  | 1.0006    | 1.1771     | 1.2254          |
| 2   | 86.8526    | -9.9140  | -0.8762   | -0.9923    | -0.9907         |
| 3   | 85.0639    | -13.2474 | -1.1708   | -1.2914    | -1.3874         |
| 4   | 83.3120    | 14.6881  | 1.2981    | 1.4075     | 1.5700          |
| 5   | 81.5963    | 5.7987   | 0.5125    | 0.5503     | 0.5156          |
| 6   | 76.6581    | -9.1053  | -0.8047   | -0.8689    | -0.8484         |
| 7   | 72.0187    | -3.7947  | -0.3354   | -0.3792    | -0.3504         |
| 8   | 58.4886    | 4.4182   | 0.3905    | 0.6921     | 0.6586          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
|     |            |          |        |
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 88.6789   | 74.0939  | 103.2638  | 57.3859 | 119.9718|
| 2   | 86.8526   | 73.8590  | 99.8461   | 56.2689 | 117.4362|
| 3   | 85.0639   | 73.3804  | 96.7473   | 55.0134 | 115.1143|
| 4   | 83.3120   | 72.6105  | 94.0136   | 53.6296 | 112.9945|
| 5   | 81.5963   | 71.5077  | 91.6849   | 52.1292 | 111.0633|
| 6   | 76.6581   | 66.2136  | 87.1025   | 47.0673 | 106.2488|
| 7   | 72.0187   | 59.0921  | 84.9453   | 41.4635 | 102.5740|
| 8   | 58.4886   | 35.6301  | 81.3470   | 22.5854 | 94.3917 |

5% Confidence:

2D Graph 2

- Col 11 v Col 12
- Time, weeks v % Drug (DCPD, 40C/75%RH)
DiCalcium Phosphate Dihydrate (First-order reaction)
50°C/20 %moisture
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_y^2=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=yxatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 100.426}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0329605}"

[Equation]
f=a*exp(-b*x)

"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_y^2"

[Constraints] b > 0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.92115552 Rsqr = 0.84852748 Adj Rsqr = 0.82328207

Standard Error of Estimate = 7.1942

| Coefficient | Std. Error | t    | P   |
|-------------|------------|------|-----|
| a           | 100.4257   | 25.3879 | <0.0001 |
|             | 0.0330     | 5.0732  | 0.0023 |

Analysis of Variance:

|     | SS    | MS     | F        | P     |
|-----|-------|--------|----------|-------|
| DF  |       |        |          |       |
| Regression | 1 | 1739.5926 | 1739.5926 | 33.6111 | 0.0012 |
| Residual  | 6 | 310.5385  | 51.7564  |        |       |
| Total     | 7 | 2050.1312 | 292.8759 |        |       |

PRESS = 556.3837

Durbin-Watson Statistic = 1.7568
Normality Test: Passed (P = 0.7068)

Constant Variance Test: Passed (P = 0.1196)

Power of performed test with alpha = 0.0500: 0.9463

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 100.4257  | -0.4257  | -0.0592   | -0.0708    | -0.0647         |
| 2   | 97.1696   | -4.2745  | -0.5942   | -0.6769    | -0.6429         |
| 3   | 94.0190   | -0.9002  | -0.1251   | -0.1381    | -0.1263         |
| 4   | 90.9706   | 12.1472  | 1.6885    | 1.8288     | 2.5095          |
| 5   | 88.0211   | 3.3287   | 0.4627    | 0.4967     | 0.4630          |
| 6   | 79.7339   | -9.3572  | -1.3007   | -1.4154    | -1.5832         |
| 7   | 72.2270   | -4.8509  | -0.6743   | -0.7750    | -0.7458         |
| 8   | 51.9462   | 4.6423   | 0.6453    | 1.0346     | 1.0419          |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.0011      | 0.3023   | -0.0426|
| 2   | 0.0682      | 0.2294   | -0.3508|
| 3   | 0.0021      | 0.1790   | -0.0590|
| 4   | 0.2895      | 0.1476   | 1.0442 |
| 5   | 0.0188      | 0.1321   | 0.1806 |
| 6   | 0.1846      | 0.1556   | -0.6796|
| 7   | 0.0964      | 0.2430   | -0.4226|
| 8   | 0.8404      | 0.6110   | 1.3057 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 100.4257  | 90.7466  | 110.1048  | 80.3367 | 120.5148|
| 2   | 97.1696   | 88.7379  | 105.6013  | 77.6509 | 116.6883|
| 3   | 94.0190   | 86.5712  | 101.4669  | 74.9048 | 113.1333|
| 4   | 90.9706   | 84.2080  | 97.7333   | 72.1128 | 109.8285|
| 5   | 88.0211   | 81.6236  | 94.4186   | 69.2911 | 106.7511|
| 6   | 79.7339   | 72.7900  | 86.6779   | 60.8103 | 98.6575 |
| 7   | 72.2270   | 63.5486  | 80.9053   | 52.6005 | 91.8535 |
| 8   | 51.9462   | 38.1866  | 65.7058   | 29.6031 | 74.2893 |
DiCalcium Phosphate Dihydrate (First-order reaction)  
50°C  
Nonlinear Regression

[Variables]
x = col(1) 
y = col(2) 
reciprocal_y=1/abs(y)  
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions  
xnear0(q)=max(abs(q))-abs(q)  
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 82.5879}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0440508}"

[Equation]
f=a*exp(-b*x)  
fit f to y  
"fit f to y with weight reciprocal_y  
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0

[Options]

tolerance=0.0001  
stepsize=100
Iterations = 100

\[ R = 0.79944607 \quad \text{Rsqr} = 0.63911401 \quad \text{Adj Rsqr} = 0.57896635 \]

Standard Error of Estimate = 12.3137

| Coefficient | Std. Error | t      | P    |
|-------------|------------|--------|------|
| a           | 82.5879    | 11.7450| <0.0001 |
| b           | 0.0441     | 2.8216 | 0.0303 |

Analysis of Variance:

|                  | DF | SS       | MS     | F       | P    |
|------------------|----|----------|--------|---------|------|
| Regression       | 1  | 1611.1606| 1611.1606| 10.6257 | 0.0173 |
| Residual         | 6  | 909.7677 | 151.6279|         |      |
| Total            | 7  | 2520.9282| 360.1326|         |      |

PRESS = 1870.5517

Durbin-Watson Statistic = 2.6031

Normality Test: Passed (P = 0.6617)

Constant Variance Test: Passed (P = 0.1196)

Power of performed test with alpha = 0.0500: 0.6891

The power of the performed test (0.6891) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 82.5879   | 17.4121  | 1.4140    | 1.7225     | 2.2116          |
| 2   | 79.0288   | -12.0604 | -0.9794   | -1.1214    | -1.1514         |
| 3   | 75.6231   | 1.5303   | 0.1243    | 0.1372     | 0.1254          |
| 4   | 72.3641   | -14.4028 | -1.1697   | -1.2658    | -1.3497         |
| 5   | 69.2456   | 9.5619   | 0.7765    | 0.8339     | 0.8096          |
| 6   | 60.6735   | -1.3395  | -0.1088   | -0.1195    | -0.1092         |
| 7   | 53.1626   | -8.5527  | -0.6946   | -0.8106    | -0.7842         |
| 8   | 34.2213   | 9.2182   | 0.7486    | 1.1062     | 1.1318          |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.7179      | 1.5385   |        |
| 2   | 0.1954      | -0.6419  |        |
| 3   | 0.0021      | 0.0586   |        |
| 4   | 0.1371      | -0.5584  |        |
DiCalcium Phosphate Dihydrate (Biphasic First-order reaction)

25°C

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = xatymax(q,xnear0(r))
[Parameters]
a = ytxnear0(y,x)/2 "Auto {previous: 0.166203}
b = -ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 0.327697}
c = ytxnear0(y,x)/2 "Auto {previous: 0.837541}
d = -ln(.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 7.31869e-011}

[Equation]
f = a*exp(-b*x)+c*exp(-d*x)

fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b > 0
d > 0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

R = 0.34643013 Rsqr = 0.12001384 Adj Rsqr = 0.00000000

Standard Error of Estimate = 0.2099

| Coefficient | Std. Error | t | P   |
|-------------|------------|---|-----|
| a           | 0.1662     | 0.6081 | 0.2733 | 0.7981 |
| b           | 0.3277     | 1.9321 | 0.1696 | 0.8736 |
| c           | 0.8375     | 0.6331 | 1.3228 | 0.2564 |
| d           | 0.0000     | 0.0440 | 0.0000 | 1.0000 |

Analysis of Variance:

| DF  | SS      | MS   | F     | P    |
|-----|---------|------|-------|------|
| Regression | 3    | 0.0240 | 0.0080 | 0.1818 | 0.9035 |
| Residual   | 4    | 0.1762 | 0.0441 |
| Total      | 7    | 0.2003 | 0.0286 |

PRESS = 8.8045

Durbin-Watson Statistic = 2.7848

Normality Test:   Passed (P = 0.6135)

Constant Variance Test:   Passed (P = 0.4979)

Power of performed test with alpha = 0.0500: 0.1247

The power of the performed test (0.1247) is below the desired power of 0.8000.
You should interpret the negative findings cautiously.
### Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|----------------|
| 2   | 1.0037    | -0.0037  | -0.0178   | -0.0466    | -0.0404        |
| 3   | 0.9573    | -0.0008  | -0.0038   | -0.0045    | -0.0039        |
| 4   | 0.9238    | -0.1382  | -0.6586   | -0.7957    | -0.7511        |
| 5   | 0.8997    | 0.3173   | 1.5116    | 1.8178     | 3.7747         |
| 6   | 0.8824    | -0.0971  | -0.4626   | -0.5427    | -0.4883        |
| 7   | 0.8543    | -0.1962  | -0.9347   | -1.2012    | -1.3011        |
| 8   | 0.8438    | 0.0865   | 0.4120    | 0.6309     | 0.5758         |
| 9   | 0.8378    | 0.0322   | 0.1536    | 1.4559     | 1.8390         |

### Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 2   | 0.0032     | -0.0974  |        |
| 3   | 0.0000     | -0.0025  |        |
| 4   | 0.0728     | -0.5092  |        |
| 5   | 0.3685     | 2.5211   |        |
| 6   | 0.0277     | -0.2996  |        |
| 7   | 0.2350     | -1.0502  |        |
| 8   | 0.1339     | 0.6678   |        |
| 9   | 47.0686    | 17.3316  |        |

### 95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 2   | 1.0037    | 0.4654   | 1.5421    | 0.2103  | 1.7971   |
| 3   | 0.9573    | 0.6420   | 1.2727    | 0.2947  | 1.6199   |
| 4   | 0.9238    | 0.5968   | 1.2509    | 0.2556  | 1.5921   |
| 5   | 0.8997    | 0.5760   | 1.2234    | 0.2331  | 1.5664   |
| 6   | 0.8824    | 0.5776   | 1.1871    | 0.2247  | 1.5400   |
| 7   | 0.8543    | 0.4883   | 1.2203    | 0.1661  | 1.5425   |
| 8   | 0.8438    | 0.4024   | 1.2852    | 0.1128  | 1.5749   |
| 9   | 0.8378    | 0.2582   | 1.4173    | 0.0159  | 1.6597   |

**Graph:**

- Col 10 vs Col 11
- Time, weeks vs D/Oo, [OCP O, 25C]
DiCalcium Phosphate Dihydrate (Biphasic First-order reaction)
25°C / 60 %RH

NO OUTPUT

DiCalcium Phosphate Dihydrate (Biphasic First-order reaction)
40°C / 75 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {previous: 0.333646}
b = -ln(0.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 0.113982}
c = yatxnear0(y,x)/2 "Auto {previous: 0.586469}
d = -ln(0.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 1.50132e-010}

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)

fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

R = 0.70718831   Rsqr = 0.50011531  Adj Rsqr = 0.12520180

Standard Error of Estimate = 0.1339

| Coefficient | Std. Error | t      | P      |
|-------------|------------|--------|--------|
| a           | 0.3336     | 3.9740 | 0.0840 | 0.9371 |
| b           | 0.1140     | 1.1744 | 0.0971 | 0.9274 |
| c           | 0.5865     | 4.0325 | 0.1454 | 0.8914 |
| d           | 0.0000     | 0.2444 | 0.0000 | 1.0000 |
### Analysis of Variance:

|    | DF | SS    | MS   | F    | P    |
|----|----|-------|------|------|------|
| Regression | 3  | 0.0717| 0.0239| 1.3339 | 0.3811 |
| Residual   | 4  | 0.0717| 0.0179|       |      |
| Total      | 7  | 0.1434| 0.0205|       |      |

$\text{PRESS} = 22.9003$

Durbin-Watson Statistic = 2.1035

Normality Test: Passed ($P = 0.7263$)

Constant Variance Test: Failed ($P = 0.0212$)

Power of performed test with alpha = 0.0500: 0.5045

The power of the performed test (0.5045) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

### Regression Diagnostics:

| Row | Predicted Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|--------------------|-----------|------------|-----------------|
| 1   | 0.9201 0.0799      | 0.5967    | 1.2068     | 1.3106          |
| 2   | 0.8842 -0.1148     | -0.8573   | -1.0046    | -1.0061         |
| 3   | 0.8521 -0.1339     | -1.0004   | -1.1552    | -1.2256         |
| 4   | 0.8235 0.1565      | 1.1690    | 1.4051     | 1.7101          |
| 5   | 0.7980 0.0760      | 0.5676    | 0.6926     | 0.6394          |
| 6   | 0.7367 -0.0612     | -0.4569   | -0.5619    | -0.5070         |
| 7   | 0.6932 -0.0110     | -0.0818   | -0.1635    | -0.1420         |
| 8   | 0.6206 0.0085      | 0.0632    | 1.4989     | 1.9606          |

### Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 1.1254      | 0.7556   | 2.3042 |
| 2   | 0.0941      | 0.2716   | -0.6144|
| 3   | 0.1113      | 0.2501   | -0.7078|
| 4   | 0.2196      | 0.3079   | 1.1405 |
| 5   | 0.0587      | 0.3284   | 0.4471 |
| 6   | 0.0404      | 0.3386   | -0.3628|
| 7   | 0.0200      | 0.7495   | -0.2457|
| 8   | 315.4957    | 0.9982   | 46.4673|

95% Confidence:

| Row | Predicted Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-------------------|-----------|---------|----------|
| 1   | 0.9201 0.5970     | 1.2432    | 0.4276  | 1.4127   |
| 2   | 0.8842 0.6904     | 1.0779    | 0.4650  | 1.3034   |
DiCalcium Phosphate Dihydrate (Biphasic First-order reaction)

50°C / 20% moisture
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y_square = 1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {{previous: 0.630224}}
b = -ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto {{previous: 0.0706267}}
c = yatxnear0(y,x)/2 "Auto {{previous: 0.393708}}
d = -ln(.5)/(1.5*(x50(x,y)-min(x))) "Auto {{previous: 6.18862e-01}}

[Equation]
f = a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b > 0
d > 0

[Options]
tolerance = 1e-6
stepsize = 0.1
iterations = 100

R = 0.92794829   Rsqr = 0.86108803   Adj Rsqr = 0.75690405

Standard Error of Estimate = 0.0844

| Coefficient | Std. Error | t   | P     |
|-------------|------------|-----|-------|
| a           | 0.6302     | 9.4315 | 0.0668 | 0.9499 |
| b           | 0.0706     | 0.7448 | 0.0948 | 0.9290 |
| c           | 0.3937     | 9.4717 | 0.0416 | 0.9688 |
| d           | 0.0000     | 0.6242 | 0.0000 | 1.0000 |

Analysis of Variance:

|                | DF | SS   | MS     | F     | P     |
|----------------|----|------|--------|-------|-------|
| Regression     | 3  | 0.1765 | 0.0588 | 8.2651 | 0.0345 |
| Residual       | 4  | 0.0285 | 0.0071 |       |       |
| Total          | 7  | 0.2050 | 0.0293 |       |       |

PRESS = 309.8853

Durbin-Watson Statistic = 1.6439

Normality Test: Passed (P = 0.5092)

Constant Variance Test: Passed (P = 0.9309)

Power of performed test with alpha = 0.0500: 0.9568

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0239    | -0.0239  | -0.2836   | -0.5485    | -0.4940         |
| 2   | 0.9810    | -0.0520  | -0.6163   | -0.7225    | -0.6711         |
| 3   | 0.9409    | -0.0097  | -0.1152   | -0.1321    | -0.1146         |
| 4   | 0.9036    | 0.1276   | 1.5120    | 1.8096     | 3.6799          |
| 5   | 0.8688    | 0.0447   | 0.5294    | 0.6503     | 0.5956          |
| 6   | 0.7781    | -0.0743  | -0.8811   | -1.0811    | -1.1128         |
| 7   | 0.7047    | -0.0310  | -0.3668   | -0.7862    | -0.7404         |
| 8   | 0.5472    | 0.0187   | 0.2216    | 6.7997     | (+inf)          |
Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.2061     | -0.8177  |        |
| 2   | 0.0489     | -0.4106  |        |
| 3   | 0.0014     | -0.0642  |        |
| 4   | 0.3539     | 2.4196   |        |
| 5   | 0.0538     | 0.4249   |        |
| 6   | 0.1477     | -0.7912  |        |
| 7   | 0.5552     | -1.4036  |        |
| 8   | 10866.7651 | 0.9989   | (+inf) |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 1.0239    | 0.8234   | 1.2245    | 0.7156  | 1.3323  |
| 2   | 0.9810    | 0.8587   | 1.1032    | 0.7167  | 1.2452  |
| 3   | 0.9409    | 0.8264   | 1.0554    | 0.6802  | 1.2017  |
| 4   | 0.9036    | 0.7749   | 1.0323    | 0.6363  | 1.1709  |
| 5   | 0.8688    | 0.7328   | 1.0049    | 0.5979  | 1.1397  |
| 6   | 0.7781    | 0.6424   | 0.9139    | 0.5073  | 1.0489  |
| 7   | 0.7047    | 0.4975   | 0.9119    | 0.3920  | 1.0175  |
| 8   | 0.5472    | 0.3130   | 0.7813    | 0.2160  | 0.8784  |

2D Graph 8

Graph showing data points and a trend line with axis labels and a legend indicating the variables, such as 'Col 20 v Col 21' and 'Time, weeks v D/D0, (DCF/0C/20% Moisture)'.
DiCalcium Phosphate Dihydrate (Biphasic First-order reaction)
50°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2
'A Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {previous: 0.257223}"
b = -ln(0.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 356066}"
c = yatxnear0(y,x)/2 "Auto {previous: 0.742777}"
d = -ln(0.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 0.0315182}"

[Equation]
f = a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b > 0
d > 0

[Options]
tolerance = 1e-6
stepsize = 0.1
iterations = 100

R = 0.90478094  Rsqr = 0.81862855  Adj Rsqr = 0.68259996

Standard Error of Estimate = 0.1069

| Coefficient | Std. Error | t     | P    |
|-------------|------------|-------|------|
|             | 0.2572 0.1277 | 2.0138 | 0.1143 |
|             | 356065.7031 | 5319171.9321 | 0.0669 | 0.9498 |
|             | 0.7428 0.0699 | 10.6286 | 0.0004 |
|             | 0.0315 0.0139 | 2.2608 | 0.0866 |

Analysis of Variance:

| DF     | SS         | MS       | F      | P    |
|--------|------------|----------|--------|------|
| Regression | 0.2064 | 0.0688  | 6.0181 | 0.0578 |
| Residual  | 0.0457 | 0.0114  |        |      |
| Total    | 0.2521  | 0.0360  |        |      |
PRESS = 12930026640575624.0000

Durbin-Watson Statistic = 3.1687

Normality Test: Passed (P = 0.7820)

Constant Variance Test: Passed (P = 0.6194)

Power of performed test with alpha = 0.0500: 0.9177

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0000    | 0.0000   | 0.0000    | 11.2065    | (inf)           |
| 2   | 0.7197    | -0.0500  | -0.4681   | -0.5694    | -1.0045         |
| 3   | 0.6974    | 0.0741   | 0.9341    | 0.7999     | 0.7558          |
| 4   | 0.6758    | -0.0961  | -0.8993   | -1.0033    | -1.0045         |
| 5   | 0.6548    | 0.1333   | 1.2466    | 1.3639     | 1.6150          |
| 6   | 0.5957    | -0.0024  | -0.0222   | -0.0243    | -0.0210         |
| 7   | 0.5420    | -0.0959  | -0.8967   | -1.0289    | -1.0391         |
| 8   | 0.3955    | 0.0389   | 0.3642    | 0.6307     | 0.5756          |

| Row | Cook'sDist | Leverage | DFFITS | DFFITS |
|-----|-------------|----------|--------|--------|
| 1   | 282793880062915520.0000 | 1.0000 | (+inf) |
| 2   | 0.0389      | 0.3242   | -0.3563|        |
| 3   | 0.0529      | 0.2486   | 0.4348 |        |
| 4   | 0.0616      | 0.1966   | -0.4969|        |
| 5   | 0.0917      | 0.1646   | 0.7169 |        |
| 6   | 0.0000      | 0.1591   | -0.0091|        |
| 7   | 0.0838      | 0.2404   | -0.5846|        |
| 8   | 0.1988      | 0.6665   | 0.8137 |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0000    | 0.7032   | 1.2968    | 0.5802  | 1.4198   |
| 2   | 0.7197    | 0.5507   | 0.8887    | 0.3781  | 1.0613   |
| 3   | 0.6974    | 0.5494   | 0.8454    | 0.3657  | 1.0291   |
| 4   | 0.6758    | 0.5441   | 0.8074    | 0.3510  | 1.0005   |
| 5   | 0.6548    | 0.5344   | 0.7752    | 0.3345  | 0.9751   |
| 6   | 0.5957    | 0.4773   | 0.7141    | 0.2761  | 0.9153   |
| 7   | 0.5420    | 0.3964   | 0.6875    | 0.2114  | 0.8726   |
| 8   | 0.3955    | 0.1531   | 0.6378    | 0.0123  | 0.7787   |
CALCIUM SULFATE (First-order reaction)

25°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q,r) = xatymax(q, xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 93.7223}"
b = -ln(.5)/(x50(x,y) - min(x)) "Auto {previous: 0.0127838}"

[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

R = 0.89831165      Rsqr = 0.80696382      Adj Rsqr = 0.77479112
Standard Error of Estimate = 3.6322

| Coefficient | Std. Error | t   | P     |
|--------------|------------|-----|-------|
| a            | 93.7223    | 1.8595 | 50.4022 | <0.0001 |
| b            | 0.0128     | 0.0027 | 4.7961  | 0.0030  |

Analysis of Variance:

|    | DF | SS   | MS   | F    | P     |
|----|----|------|------|------|-------|
| Regression | 1  | 330.9054 | 330.9054 | 25.0823 | 0.0024 |
| Residual    | 6  | 79.1569  | 13.1928 |      |       |
| Total       | 7  | 410.0623 | 58.5803 |      |       |

PRESS = 183.7898

Durbin-Watson Statistic = 1.3821

Normality Test: Passed (P = 0.6907)

Constant Variance Test: Passed (P = 0.7053)

Power of performed test with alpha = 0.0500: 0.9053

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 93.7223   | 6.2777   | 1.7284    | 2.0120     | 3.2203          |
| 2   | 92.5318   | -0.6072  | -0.1672   | -0.1886    | -0.1727         |
| 3   | 91.3564   | -1.2651  | -0.3483   | -0.3839    | -0.3549         |
| 4   | 90.1960   | 0.8058   | 0.2218    | 0.2407     | 0.2208          |
| 5   | 89.0502   | -5.3088  | -1.4616   | -1.5706    | -1.8683         |
| 6   | 85.6997   | -2.0053  | -0.5521   | -0.5939    | -0.5588         |
| 7   | 82.4752   | -0.0686  | -0.0189   | -0.0212    | -0.0193         |
| 8   | 72.5779   | 2.2181   | 0.6107    | 1.1624     | 1.2055          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.7189     | 0.2621   | 1.9192 |
| 2   | 0.0048     | 0.2139   | -0.0901 |
| 3   | 0.0159     | 0.1770   | -0.1646 |
| 4   | 0.0051     | 0.1506   | 0.0930 |
| 5   | 0.1908     | 0.1339   | -0.7348 |
| 6   | 0.0277     | 0.1358   | -0.2215 |
| 7   | 0.0001     | 0.2026   | -0.0097 |
| 8   | 1.7722     | 0.7240   | 1.9525 |

95% Confidence:
CALCIUM SULFATE (First-order reaction)

25°C / 60 %RH

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q)) - abs(q)
yatxminear0(q,r) = yatxymax(q,xnear0(r))

[Parameters]
a = yatxminear0(y,x) "Auto {previous: 92.3787}"
b = [ln(0.5)/(x50(x,y) - min(x))] "Auto {previous: 0.00639435}"

[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
**fit f to y with weight reciprocal_ysquare**

[Constraints]
- b=0

[Options]
- tolerance=0.0001
- stepsize=100
- iterations=100

R = 0.67039550  Rsqr = 0.44943012  Adj Rsqr = 0.35766848

Standard Error of Estimate = 4.3632

| Coefficient | Std. Error | t      | P     |
|-------------|------------|--------|-------|
| a 92.3787   | 2.1829     | 42.3187| <0.0001|
| b 0.0064    | 0.0030     | 2.1532 | 0.0748 |

Analysis of Variance:

| DF | SS       | MS      | F       | P     |
|----|----------|---------|---------|-------|
| Regression 1 | 93.2440 | 93.2440 | 4.8978  | 0.0688 |
| Residual      | 114.2276| 19.0379 |         |       |
| Total         | 207.4715| 29.6388 |         |       |

PRESS = 203.7636

Durbin-Watson Statistic = 1.5918

Normality Test: Passed (P = 0.2602)

Constant Variance Test: Passed (P = 0.0716)

Power of performed test with alpha = 0.0500: 0.4422

The power of the performed test (0.4422) is below the desired power of 0.8000.
You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 92.3787   | 7.6213   | 1.7467    | 2.0173     | 3.2467          |
| 2   | 91.7898   | -3.3997  | -0.7792   | -0.8759    | -0.8562         |
| 3   | 91.2048   | -4.3680  | -1.0011   | -1.1028    | -1.1274         |
| 4   | 90.6234   | -1.2764  | -0.2925   | -0.3176    | -0.2924         |
| 5   | 90.0458   | -2.1758  | -0.4987   | -0.5362    | -0.5017         |
| 6   | 88.3349   | 0.3927   | 0.0900    | 0.0966     | 0.0882          |
| 7   | 86.6565   | 4.2343   | 0.9704    | 1.0792     | 1.0974          |
| 8   | 81.2889   | -1.0288  | -0.2358   | -0.4765    | -0.4434         |
Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.6794      | 1.8760   |        |
| 2   | 0.1012      | -0.4398  |        |
| 3   | 0.1298      | -0.5209  |        |
| 4   | 0.0090      | -0.1235  |        |
| 5   | 0.0225      | -0.1983  |        |
| 6   | 0.0007      | 0.0344   |        |
| 7   | 0.1378      | 0.5338   |        |
| 8   | 0.3500      | -0.7787  |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 92.3787   | 87.0372  | 97.7201   | 80.4406 | 104.3168 |
| 2   | 91.7898   | 86.9119  | 96.6678   | 80.0518 | 103.5279 |
| 3   | 91.2048   | 86.7268  | 95.6828   | 79.6272 | 102.7823 |
| 4   | 90.6234   | 86.4679  | 94.7790   | 79.1667 | 102.0802 |
| 5   | 90.0458   | 86.1204  | 93.9712   | 78.6706 | 101.4211 |
| 6   | 88.3349   | 84.4572  | 92.2127   | 76.9760 | 99.6938  |
| 7   | 86.6565   | 81.9866  | 91.3265   | 75.0034 | 98.3097  |
| 8   | 81.2889   | 72.0113  | 90.5664   | 67.1446 | 95.4331  |

2D Graph 6

Graph 6

- Col 15 v Col 19
- Time, weeks v % Drug (Ca Sulfate, 250/60%RH)
CALCIUM SULFATE (First-order reaction)
40°C / 75 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxmin0(q,r)=yatymax(q,xnear0(r))

[Parameters]
a = yatxmin0(y,x) "Auto {previous: 89.0732}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0053762}"

[Equation]
f=a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.47385900   Rsqr = 0.22454235   Adj Rsqr = 0.09529941

Standard Error of Estimate = 5.8884

| Coefficient | Std. Error | t    | P     |
|-------------|------------|------|-------|
| a           | 89.0732    | 2.9347| 30.3520 | <0.0001 |
| b           | 0.0054     | 0.0041| 1.3127 | 0.2373  |

Analysis of Variance:

|          | SS       | MS     | F        | P      |
|----------|----------|--------|----------|--------|
| Regression| 60.2402 | 60.2402| 1.7374   | 0.2356 |
| Residual  | 208.0396| 34.6733|          |        |
| Total     | 268.2798| 38.3257|          |        |

PRESS = 505.4006

Durbin-Watson Statistic = 1.3856
Normality Test: Passed (P = 0.5123)

Constant Variance Test: Passed (P = 0.4228)

Power of performed test with alpha = 0.0500: 0.2095

The power of the performed test (0.2095) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 89.0732   | 10.9268  | 1.8557    | 2.1404     | 4.0184          |
| 2   | 88.5956   | -1.6784  | -0.2850   | -0.3203    | -0.2949         |
| 3   | 88.1206   | -3.8642  | -0.6562   | -0.7228    | -0.6906         |
| 4   | 87.6481   | -0.4213  | -0.0715   | -0.0777    | -0.0709         |
| 5   | 87.1781   | -1.6130  | -0.2739   | -0.2946    | -0.2709         |
| 6   | 85.7833   | -7.5173  | -1.2766   | -1.3698    | -1.5083         |
| 7   | 84.4109   | 0.8923   | 0.1515    | 0.1683     | 0.1540          |
| 8   | 79.9926   | 3.2879   | 0.5584    | 1.1399     | 1.1756          |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.7570      | 0.2484   | 2.3100 |
| 2   | 0.0135      | 0.2079   | -0.1511|
| 3   | 0.0557      | 0.1757   | -0.3188|
| 4   | 0.0005      | 0.1516   | -0.0300|
| 5   | 0.0068      | 0.1354   | -0.1072|
| 6   | 0.1419      | 0.1314   | -0.5866|
| 7   | 0.0033      | 0.1896   | 0.0745 |
| 8   | 2.0578      | 0.7600   | 2.0923 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 89.0732   | 81.1823  | 96.2541   | 72.9745 | 105.1718 |
| 2   | 88.5956   | 82.0263  | 95.1649   | 72.7603 | 104.4309 |
| 3   | 88.1206   | 82.0808  | 94.1603   | 72.4975 | 103.7436 |
| 4   | 87.6481   | 82.0374  | 93.2588   | 72.1858 | 103.1104 |
| 5   | 87.1781   | 81.8762  | 92.4801   | 71.8252 | 102.5311 |
| 6   | 85.7833   | 80.5607  | 91.0059   | 70.4576 | 101.1091 |
| 7   | 84.4109   | 78.1378  | 90.6840   | 68.6961 | 100.1256 |
| 8   | 79.9926   | 67.4313  | 92.5539   | 60.8775 | 99.1078 |
CALCIUM SULFATE (First-order reaction) 
50°C / 20% moisture 
Nonlinear Regression

Variables
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxmin0(q,r) = yatxmax(q,xnear0(r))

Parameters
a = yatxmin0(y,x) "Auto {previous: 89.2674}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0271455}"

Equation
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

Constraints
b > 0

Options
[ tolerance = 0.0001
    steps size = 100
    iterations = 100

R = 0.81445053  Rsqr = 0.66332967  Adj Rsqr = 0.60721794
Standard Error of Estimate = 9.6577

| Coefficient | Std. Error | t     | P     |
|-------------|------------|-------|-------|
| a           | 89.2674    | 17.1544 | <0.0001 |
| b           | 0.0271     | 2.9908  | 0.0243 |

Analysis of Variance:

|         | DF  | SS         | MS          | F      | P   |
|---------|-----|------------|-------------|--------|-----|
| Regression | 1   | 1102.6058  | 1102.6058   | 11.8216| 0.0138 |
| Residual | 6   | 559.6232   | 93.2705     |        |     |
| Total    | 7   | 1662.2290  | 237.4613    |        |     |

PRESS = 1019.5279

Durbin-Watson Statistic = 2.1187

Normality Test: Passed (P = 0.2449)

Constant Variance Test: Passed (P = 0.3207)

Power of performed test with alpha = 0.0500: 0.7222

The power of the performed test (0.7222) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 89.2674   | 10.7326  | 1.1113    | 1.3192     | 1.4292          |
| 2   | 86.8768   | -12.1566 | -1.2588   | -1.4300    | -1.6078         |
| 3   | 84.5502   | -2.1805  | -0.2258   | -0.2491    | -0.2286         |
| 4   | 82.2860   | -6.0993  | -0.6315   | -0.6844    | -0.6507         |
| 5   | 80.0823   | -1.6722  | -0.1732   | -0.1859    | -0.1702         |
| 6   | 73.8192   | 15.2045  | 1.5743    | 1.7064     | 2.1713          |
| 7   | 68.0459   | 0.4526   | 0.0469    | 0.0534     | 0.0488          |
| 8   | 51.8693   | -4.5297  | -0.4690   | -0.7877    | -0.7594         |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.3560     | 0.2903   | 0.9141 |
| 2   | 0.2971     | 0.2251   | -0.8667|
| 3   | 0.0668     | 0.1787   | -0.1066|
| 4   | 0.0408     | 0.1484   | -0.2716|
| 5   | 0.0026     | 0.1322   | -0.0664|
| 6   | 0.2545     | 0.1488   | 0.9078 |
| 7   | 0.0004     | 0.2310   | 0.0267 |
95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 89.2674   | 76.5343  | 102.0006  | 62.4239 | 116.1110 |
| 2   | 86.8768   | 75.6639  | 98.0897   | 60.7201 | 113.0336 |
| 3   | 84.5502   | 74.5615  | 94.5389   | 58.8944 | 110.2060 |
| 4   | 82.2860   | 73.1815  | 91.3904   | 56.9613 | 107.6106 |
| 5   | 80.0823   | 71.4892  | 88.6754   | 54.9370 | 105.2276 |
| 6   | 73.8192   | 64.7037  | 82.9347   | 48.4906 | 99.1478  |
| 7   | 68.0459   | 56.6884  | 79.4034   | 41.8268 | 94.2649  |
| 8   | 51.8693   | 32.8841  | 70.8545   | 21.5562 | 82.1824  |

CALCIUM SULFATE (First-order reaction)
50°C
Nonlinear Regression

[Variables]
\[ x = \text{col}(1) \]
\[ y = \text{col}(2) \]
\[ \text{reciprocal}_y = 1/|y| \]
\[ \text{reciprocal}_y\text{square} = 1/|y|^2 \]
'Automatic Initial Parameter Estimate Functions
\[ \text{xnear0}(q) = \max(|q|) - |q| \]
\[ \text{ytxnear0}(q,r) = \text{ytxmax}(q,\text{xnear0}(r)) \]
[Parameters]
\[ a = \text{ytxnear0}(y,x) \] "Auto {previous: 89.2447}"
\[ b = \text{min}(.5)/(\text{x50}(x,y) - \text{min}(x)) \] "Auto {previous: 0.0333771}"
Equation
\[ f = a \cdot e^{-b \cdot x} \]
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^2

Constraints
b > 0

Options
tolerance = 0.0001
stepsize = 100
iterations = 100

R = 0.88984785 Rsqr = 0.79182919 Adj Rsqr = 0.75713406

Standard Error of Estimate = 7.5621

| Coefficient | Std. Error | t   | P   |
|-------------|------------|-----|-----|
| a           | 89.2447    | 4.1608 | <0.0001 |
| b           | 0.0334     | 0.0077 | 0.0049 |

Analysis of Variance:

|           | SS         | MS       | F             | P   |
|-----------|------------|----------|---------------|-----|
| Regression| 1305.1093  | 1305.1093| 22.8225       | 0.0031 |
| Residual  | 343.1114   | 57.1852  |               |     |
| Total     | 1648.2207  | 235.4601 |               |     |

PRESS = 991.9402

Durbin-Watson Statistic = 1.2651

Normality Test: Passed (P = 0.5061)

Constant Variance Test: Passed (P = 0.7053)

Power of performed test with alpha = 0.0500: 0.8884

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 89.2447   | 10.7553  | 1.4223    | 1.7033     | 2.1636          |
| 2   | 86.3151   | -2.1575  | -0.2853   | -0.3250    | -0.2994         |
| 3   | 83.4817   | 0.4318   | 0.0571    | 0.0630     | 0.0575          |
| 4   | 80.7413   | 1.2402   | 0.1640    | 0.1776     | 0.1626          |
| 5   | 78.0909   | -5.5809  | -0.7380   | -0.7922    | -0.7642         |
| 6   | 70.6503   | -9.8174  | -1.2982   | -1.4130    | -1.5791         |
| 7   | 63.9186   | -3.1203  | -0.4126   | -0.4744    | -0.4414         |
| 8   | 45.7797   | 9.1538   | 1.2105    | 1.9377     | 2.8914          |
**Influence Diagnostics:**

| Row | Cook'sDist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.6298      | 1.4257   |        |
| 2   | 0.0157      | -0.1634  |        |
| 3   | 0.0004      | 0.0269   |        |
| 4   | 0.0027      | 0.0676   |        |
| 5   | 0.0477      | -0.2981  |        |
| 6   | 0.1843      | -0.6785  |        |
| 7   | 0.0362      | -0.2504  |        |
| 8   | 2.9330      | 3.6141   |        |

**95% Confidence:**

| Row | Predicted | Regr.5% | Regr.95% | Pop.5% | Pop.95% |
|-----|-----------|---------|----------|--------|---------|
| 1   | 89.2447   | 79.0635 | 99.4259  | 68.1249| 110.3645|
| 2   | 86.3151   | 77.4494 | 95.1809  | 65.7971| 106.8332|
| 3   | 83.4817   | 75.6528 | 91.3107  | 63.3899| 103.5736|
| 4   | 80.7413   | 73.6336 | 87.8491  | 60.9194| 100.5633|
| 5   | 78.0909   | 71.3662 | 84.8156  | 58.4031| 97.7787 |
| 6   | 70.6503   | 63.3453 | 77.9553  | 50.7568| 90.5438 |
| 7   | 63.9186   | 54.7886 | 73.0487  | 43.2850| 84.5523 |
| 8   | 45.7797   | 31.3309 | 60.2285  | 22.3029| 69.2564 |

**2D Graph 9**

![Graph showing y vs x, with data points and trend line.](image-url)
CALCIUM SULFATE (Biphasic First-order reaction)

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
ymax0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxmin0(y,x)/2 "Auto {previous: 0.10396}
b = -ln(0.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 0.831913}
c = yatxmin0(y,x)/2 "Auto {previous: 0.893294}
d = -ln(0.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 0.0088255}

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
steps=0.1
iterations=100

R = 0.97516606  Rsqr = 0.95094885  Adj Rsqr = 0.91416049

Standard Error of Estimate = 0.0224

| Coefficient | Std. Error | t | P |
|-------------|------------|---|---|
| a           | 0.1040     | 3.1144 | 0.0357 |
| b           | 0.8319     | 1.3798 | 0.2398 |
| c           | 0.8933     | 32.6200 | <0.0001 |
| d           | 0.0088     | 3.4236 | 0.0267 |

Analysis of Variance:

| DF | SS    | MS    | F    | P    |
|----|-------|-------|------|------|
| Regression | 3  | 0.0390 | 0.0130 | 25.8492 | 0.0044 |
| Residual    | 4  | 0.0020 | 0.0005 |      |      |
| Total       | 7  | 0.0410 | 0.0059 |      |      |
PRESS = 0.0191

Durbin-Watson Statistic = 2.7875

Normality Test: Passed (P = 0.2261)

Constant Variance Test: Passed (P = 0.6194)

Power of performed test with alpha = 0.0500: 0.9983

| Regression Diagnostics: | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-------------------------|-----------|----------|-----------|------------|-----------------|
| Row                     |           |          |           |            |                 |
| 1                       | 0.9973    | 0.0027   | 0.1224    | 0.8138     | 0.7716          |
| 2                       | 0.9307    | -0.0114  | -0.5104   | -0.7925    | -0.7475         |
| 3                       | 0.8974    | 0.0036   | 0.1586    | 0.1970     | 0.1715          |
| 4                       | 0.8785    | 0.0315   | 1.4044    | 1.6131     | 2.3632          |
| 5                       | 0.8660    | -0.0286  | -1.2765   | -1.5233    | -2.0360         |
| 6                       | 0.8401    | -0.0031  | -0.1401   | -0.1744    | -0.1516         |
| 7                       | 0.8179    | 0.0062   | 0.2767    | 0.3262     | 0.2863          |
| 8                       | 0.7488    | -0.0008  | -0.0353   | -0.1181    | -0.1025         |

| Influence Diagnostics: |          |          | Leverage | DFFITS    |
|------------------------|----------|----------|----------|-----------|
| Row                    | Cook'sDist |          |          |           |
| 1                      | 7.1494   | 0.9774   | 5.0700   |           |
| 2                      | 0.2215   | 0.5852   | -0.8879  |           |
| 3                      | 0.0053   | 0.3520   | 0.1264   |           |
| 4                      | 0.2077   | 0.2420   | 1.3353   |           |
| 5                      | 0.2461   | 0.2978   | -1.3260  |           |
| 6                      | 0.0042   | 0.3546   | -0.1123  |           |
| 7                      | 0.0104   | 0.2804   | 0.1788   |           |
| 8                      | 0.0355   | 0.9107   | -0.3271  |           |

| 95% Confidence:        |          |          |          |          |          |
|------------------------|----------|----------|----------|----------|----------|
| Row                    | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
| 1                      | 0.9973    | 0.9357   | 1.0588   | 0.9097   | 1.0848   |
| 2                      | 0.9307    | 0.8831   | 0.9783   | 0.8523   | 1.0091   |
| 3                      | 0.8974    | 0.8604   | 0.9343   | 0.8250   | 0.9697   |
| 4                      | 0.8785    | 0.8479   | 0.9092   | 0.8091   | 0.9479   |
| 5                      | 0.8660    | 0.8321   | 0.9000   | 0.7951   | 0.9370   |
| 6                      | 0.8401    | 0.8030   | 0.8772   | 0.7676   | 0.9125   |
| 7                      | 0.8179    | 0.7849   | 0.8508   | 0.7474   | 0.8883   |
| 8                      | 0.7488    | 0.6893   | 0.8082   | 0.6627   | 0.8348   |
CALCIUM SULFATE (Biphasic First-order reaction)  
$25^\circ$C / 60%RH  
Nonlinear Regression

[Variables]  
$x = \text{col}(1)$  
$y = \text{col}(2)$  
$\text{reciprocal}\_y = \frac{1}{\text{abs}(y)}$  
$\text{reciprocal}\_ysquare = \frac{1}{y^2}$

'Automatic Initial Parameter Estimate Functions'  
$x\text{near}0(q) = \text{max}(\text{abs}(q)) - \text{abs}(q)$  
$y\text{atxmax}(q,x\text{near}0(r)) = x\text{atymax}(q,x\text{near}0(r))$

[Parameters]  
$a = y\text{atxmax}(y,x)/2$  
$b = \frac{\ln(0.5)}{(0.5*\text{y}50(x,y) - \text{min}(x))}$  
$c = y\text{atxmax}(y,x)/2$  
$d = -\frac{\ln(0.5)}{(1.5*\text{y}50(x,y) - \text{min}(x))}$

[Equation]  
$f = a*\exp(-b*x) + c*\exp(-d*x)$  
fit f to y  
"fit f to y with weight reciprocal\_y"  
"fit f to y with weight reciprocal\_ysquare"

[Constraints]  
$b > 0$  
$d > 0$

[Options]  
tolerance = 1e-6
\text{stepsize}=0.1 \\
\text{iterations}=100 \\
R = 0.67039549 \quad \text{Rsqr} = 0.44943012 \quad \text{Adj Rsqr} = 0.03650270 \\
\text{Standard Error of Estimate} = 0.0534 \\
\begin{array}{cccc}
\text{Coefficient} & \text{Std. Error} & t & P \\
a & 0.4093 & 2.7704 & 0.1477 & 0.8897 \\
b & 0.0064 & 0.8393 & 0.0077 & 0.9943 \\
c & 0.5145 & 2.7704 & 0.1857 & 0.8617 \\
d & 0.0064 & 0.6629 & 0.0096 & 0.9928 \\
\end{array} \\
\text{Analysis of Variance:} \\
\begin{array}{cccc}
\text{DF} & \text{SS} & \text{MS} & \text{F} & \text{P} \\
\text{Regression} & 3 & 0.0093 & 0.0031 & 1.0884 & 0.4499 \\
\text{Residual} & 4 & 0.0114 & 0.0029 & \\
\text{Total} & 7 & 0.0207 & 0.0030 & \\
\end{array} \\
PRESS = 0.0223 \\
\text{Durbin-Watson Statistic} = 1.5918 \\
\text{Normality Test:} \quad \text{Passed (P} = 0.2601) \\
\text{Constant Variance Test:} \quad \text{Passed (P} = 0.0716) \\
\text{Power of performed test with alpha} = 0.0500: 0.4422 \\
\text{The power of the performed test (0.4422) is below the desired power of 0.8000.} \\
\text{You should interpret the negative findings cautiously.} \\
\text{Regression Diagnostics:} \\
\begin{array}{cccc}
\text{Row} & \text{Predicted} & \text{Residual} & \text{Std. Res.} & \text{Std. Res.} & \text{Std. Del. Res.} \\
1 & 0.9238 & 0.0762 & 1.4262 & 1.6587 & 2.5712 \\
2 & 0.9179 & -0.0340 & -0.6362 & -0.7167 & -0.6648 \\
3 & 0.9120 & -0.0437 & -0.8174 & -0.9011 & -0.8741 \\
4 & 0.9062 & -0.0128 & -0.2389 & -0.2599 & -0.2270 \\
5 & 0.9005 & -0.0218 & -0.4072 & -0.4405 & -0.3911 \\
6 & 0.8834 & 0.0039 & 0.0735 & 0.0814 & 0.0705 \\
7 & 0.8666 & 0.0423 & 0.7923 & 0.9560 & 0.9426 \\
8 & 0.8129 & -0.0103 & -0.1926 & -0.4148 & -0.3672 \\
\end{array} \\
\text{Influence Diagnostics:} \\
\begin{array}{cccc}
\text{Row} & \text{Cook'sDist} & \text{Leverage} & \text{DFFITS} \\
1 & 0.2426 & 0.2607 & 1.5270 \\
\end{array}
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|----------|---------|---------|
| 1   | 0.9238    | 0.8480   | 0.9995   | 0.7572  | 1.0904  |
| 2   | 0.9179    | 0.8496   | 0.9862   | 0.7546  | 1.0812  |
| 3   | 0.9120    | 0.8496   | 0.9745   | 0.7511  | 1.0730  |
| 4   | 0.9062    | 0.8478   | 0.9647   | 0.7468  | 1.0657  |
| 5   | 0.9005    | 0.8439   | 0.9571   | 0.7417  | 1.0593  |
| 6   | 0.8834    | 0.8196   | 0.9471   | 0.7219  | 1.0448  |
| 7   | 0.8666    | 0.7835   | 0.9496   | 0.6966  | 1.0366  |
| 8   | 0.8129    | 0.6493   | 0.9765   | 0.5920  | 1.0337  |

2D Graph 11

CALCIUM SULFATE (Biphasic First-order reaction)
40°C / 75%RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y

Automatic Initial Parameter Estimate Functions

\[ x_{\text{near0}}(q) = \max(\text{abs}(q)) - \text{abs}(q) \]

\[ x_{\text{atxmin}}(q, r) = \max(\text{abs}(q), x_{\text{near0}}(r)) \]

[Parameters]
\[ a = \frac{\ln(0.5)}{0.5(\text{min}(x50(x, y)) - \text{min}(x))} \quad \text{Auto} \quad \{\text{previous: 0.15346}\} \]
\[ b = \frac{-\ln(0.5)}{0.5(\text{min}(x50(x, y)) - \text{min}(x))} \quad \text{Auto} \quad \{\text{previous: 1.84686}\} \]
\[ c = \frac{\ln(0.5)}{0.5(\text{min}(x50(x, y)) - \text{min}(x))} \quad \text{Auto} \quad \{\text{previous: 0.846437}\} \]
\[ d = \frac{-\ln(0.5)}{0.5(\text{min}(x50(x, y)) - \text{min}(x))} \quad \text{Auto} \quad \{\text{previous: 0.00115251}\} \]

[Equation]
\[ f = a \exp(-b \times x) + c \exp(-d \times x) \]

fit f to y

"fit f to y with weight reciprocal_y"

"fit f to y with weight reciprocal_y^2"

[Constraints]
b > 0
d > 0

[Options]
tolerance = 1e-6
stepsize = 0.1
iterations = 100

R = 0.91149456 \quad \text{Rsqr} = 0.83082234 \quad \text{Adj Rsqr} = 0.70393910

Standard Error of Estimate = 0.0337

| Coefficient | Std. Error | t   | P   |
|-------------|------------|-----|-----|
| a           | 0.1535     | 3.6682 | 0.0214 |
| b           | 1.8469     | 1.0931 | 0.3358 |
| c           | 0.8464     | 33.4390 | <0.0001 |
| d           | 0.0012     | 0.3996 | 0.7099 |

Analysis of Variance:

| DF | SS   | MS   | F    | P    |
|----|------|------|------|------|
| Regression | 3  | 0.0223 | 0.0074 | 6.5479 | 0.0505 |
| Residual    | 4  | 0.0045 | 0.0011 |      |      |
| Total       | 7  | 0.0268 | 0.0038 |      |      |

PRESS = 0.0727

Durbin-Watson Statistic = 2.5967

Normality Test: Passed (P = 0.0534)

Constant Variance Test: Passed (P = 0.1597)
Power of performed test with alpha = 0.0500: 0.9299

| Regression Diagnostics: |   |   | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-------------------------|---|---|-----------|------------|-----------------|
| **Row** | **Predicted** | **Residual** |   |   |   |
| 1 | 0.9999 | 0.0001 | 0.0031 | 0.1511 | 0.1313 |
| 2 | 0.8697 | -0.0005 | -0.0147 | -0.0569 | -0.0493 |
| 3 | 0.8483 | -0.0057 | -0.1705 | -0.1954 | -0.1700 |
| 4 | 0.8441 | 0.0282 | 0.8357 | 0.9882 | 0.9843 |
| 5 | 0.8426 | 0.0130 | 0.3863 | 0.4554 | 0.4050 |
| 6 | 0.8396 | -0.0570 | -1.6914 | -1.8922 | -5.0595 |
| 7 | 0.8367 | 0.0163 | 0.4837 | 0.5417 | 0.4874 |
| 8 | 0.8271 | 0.0057 | 0.1679 | 0.4485 | 0.3986 |

| Influence Diagnostics: | Cook'sDist | Leverage | DFFITS |
|------------------------|------------|----------|--------|
| **Row** |   |   |   |
| 1 | 14.0117 | 0.9996 | 6.5020 |
| 2 | 0.0113 | 0.9330 | -0.1840 |
| 3 | 0.0030 | 0.2387 | -0.0952 |
| 4 | 0.0972 | 0.2848 | 0.6212 |
| 5 | 0.0202 | 0.2804 | 0.2529 |
| 6 | 0.2251 | 0.2010 | -2.5373 |
| 7 | 0.0186 | 0.2026 | 0.2457 |
| 8 | 0.3086 | 0.8599 | 0.9873 |

| 95% Confidence: | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|----------------|-----------|----------|-----------|---------|---------|
| **Row** |   |   |   |   |   |
| 1 | 0.9999 | 0.9064 | 1.0934 | 0.8676 | 1.1321 |
| 2 | 0.8697 | 0.7793 | 0.9600 | 0.7396 | 0.9997 |
| 3 | 0.8483 | 0.8026 | 0.8940 | 0.7442 | 0.9524 |
| 4 | 0.8441 | 0.7942 | 0.8940 | 0.7381 | 0.9501 |
| 5 | 0.8426 | 0.7931 | 0.8922 | 0.7368 | 0.9485 |
| 6 | 0.8396 | 0.7977 | 0.8816 | 0.7371 | 0.9421 |
| 7 | 0.8367 | 0.7946 | 0.8788 | 0.7342 | 0.9393 |
| 8 | 0.8271 | 0.7404 | 0.9139 | 0.6996 | 0.9547 |
CALCIUM SULFATE (Biphasic First-order reaction)
50°C / 20% moisture
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxminq(r) = yatymax(q,xnear0(r))

[Parameters]
a = yatxminq(y,x)/2 "Auto {previous: 0.148785}"
b = -ln(0.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 46.9667}"
c = yatxminq(y,x)/2 "Auto {previous: 0.851214}"
d = -ln(0.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 0.0225145}"

[Equation]
f = a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b > 0
d > 0

[Options]
tolerance = 1e-6
stepsize = 0.1
iterations = 100
\[ R = 0.87160383 \quad \text{Rsqr} = 0.75969324 \quad \text{Adj Rsqr} = 0.57946318 \]

Standard Error of Estimate = 0.0999

| Coefficient | Std. Error | t     | P     |
|-------------|------------|-------|-------|
| a           | 0.1488     | 1.2625| 0.2754|
| b           | 46.9667    | 497.1732, 3.006    | 0.0000| 1.0000|
| c           | 0.8512     | 13.6268 | 0.0002|
| d           | 0.0225     | 2.2500 | 0.0876|

Analysis of Variance:

| DF | SS   | MS   | F   | P    |
|----|------|------|-----|------|
| 3  | 0.1263 | 0.0421 | 4.2151 | 0.0992|
| 4  | 0.0399 | 0.0100 |       |      |
| 7  | 0.1662 | 0.0237 |       |      |

PRESS = 0.0000

Durbin-Watson Statistic = 1.8740

Normality Test: Failed \( (P = 0.0154) \)

Constant Variance Test: Passed \( (P = 0.5373) \)

Power of performed test with alpha = 0.0500: 0.8498

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|----------------|
| 1   | 1.0000    | 0.0000   | 0.0000    | (+inf)     | (+inf)         |
| 2   | 0.8323    | -0.0851  | -0.8512   | -1.0224    | -1.0303        |
| 3   | 0.8137    | 0.0100   | 0.0997    | 0.1146     | 0.0994         |
| 4   | 0.7956    | -0.0338  | -0.3378   | -0.3769    | -0.3323        |
| 5   | 0.7779    | 0.0062   | 0.0620    | 0.0679     | 0.0588         |
| 6   | 0.7271    | 0.1631   | 1.6325    | 1.7725     | 3.3137         |
| 7   | 0.6796    | 0.0054   | 0.0538    | 0.0610     | 0.0528         |
| 8   | 0.5426    | -0.0692  | -0.6925   | -1.2949    | -1.4714        |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | (+inf)      | 1.0000   | (+inf) |
| 2   | 0.1157      | 0.3069   | -0.6856|
| 3   | 0.0001      | 0.2430   | 0.0563 |
| 4   | 0.0087      | 0.1967   | -0.1645|
| 5   | 0.0002      | 0.1663   | 0.0263 |
| 6   | 0.1404      | 0.1517   | 1.4012 |
CALCIUM SULFATE (Biphasic First-order reaction)

50°C

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {{previous: 0.437725}}"
b = \ln(0.5)/(0.5*(x50(x,y)-\min(x))) \ "Auto \{\text{previous: 0.211931}\} \\
c = yatxnear0(y,x)/2 \ "Auto \{\text{previous: 0.54193}\} \\
d = \ln(0.5)/(1.5*(x50(x,y)-\min(x))) \ "Auto \{\text{previous: 2.18758e-011}\} \\

[Equation] 
\[ f = a \exp(-b*x) + c \exp(-d*x) \]

[Options] 
tolerance=1e-6  
stepsize=0.1  
iterations=100

R = 0.97882582  
Rsqr = 0.95809999  
Adj Rsqr = 0.92667497

Standard Error of Estimate = 0.0416

| Coefficient | Std. Error | t | P  |
|-------------|------------|---|----|
| a 0.4377    | 0.2591     | 1.6896 | 0.1664 |
| b 0.2119    | 0.1610     | 1.3161 | 0.2585 |
| c 0.5419    | 0.2714     | 1.9965 | 0.1166 |
| d 0.0000    | 0.0245     | 0.0000 | 1.0000 |

Analysis of Variance:

|       | DF | SS   | MS   | F     | P     |
|-------|----|------|------|-------|-------|
| Regression | 3  | 0.1579 | 0.0526 | 30.4885 | 0.0032 |
| Residual  | 4  | 0.0069 | 0.0017 |
| Total    | 7  | 0.1648 | 0.0235 |

PRESS = 0.0772

Durbin-Watson Statistic = 2.4276

Normality Test:   Passed (P = 0.4467)

Constant Variance Test:   Passed (P = 0.1597)

Power of performed test with alpha = 0.0500: 0.9991

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Student's Res. | Student's Del. Res. |
|-----|-----------|----------|-----------|----------------|---------------------|
| 1   | 0.9797    | 0.0203   | 0.4896    | 1.1091         | 1.1543              |
| 2   | 0.8961    | -0.0545  | -1.3112   | -1.5403        | -2.0912             |
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 0.9797    | 0.8761   | 1.0832    | 0.8247  | 1.1347   |
| 2   | 0.8961    | 0.8355   | 0.9566    | 0.7658  | 1.0263   |
| 3   | 0.8284    | 0.7674   | 0.8895    | 0.6979  | 0.9589   |
| 4   | 0.7737    | 0.7090   | 0.8384    | 0.6415  | 0.9060   |
| 5   | 0.7294    | 0.6660   | 0.7929    | 0.5978  | 0.8611   |
| 6   | 0.6412    | 0.5720   | 0.7105    | 0.5067  | 0.7758   |
| 7   | 0.5945    | 0.5002   | 0.6888    | 0.4455  | 0.7435   |
| 8   | 0.5482    | 0.4332   | 0.6633    | 0.3853  | 0.7112   |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 1.2704      | 2.3460   |        |
| 2   | 0.2253      | -1.2890  |        |
| 3   | 0.0090      | 0.1659   |        |
| 4   | 0.2057      | 1.0582   |        |
| 5   | 0.0017      | -0.0716  |        |
| 6   | 0.1378      | -0.7399  |        |
| 7   | 0.1589      | 0.7195   |        |
| 8   | 7.4290      | 4.8078   |        |

95% Confidence:

In Graph 15, the relationship between Y Data and X Data is shown with a trend line indicating a negative correlation. The data points are scattered along the curve, suggesting variability in the relationship over the range of X Data values. The confidence intervals are depicted with shaded areas around the curve, highlighting the uncertainty in the predicted values at the 5% and 95% confidence levels.
ANNITOL (First-order reaction)

25°C
Nonlinear Regression

[Variables]
\(x = \text{col}(1)\)
\(y = \text{col}(2)\)
\(\text{reciprocal}_y = 1/\text{abs}(y)\)
\(\text{reciprocal}_y^2 = 1/y^2\)

[Automatic Initial Parameter Estimate Functions]
\(\text{xnear}_0(q) = \max(\text{abs}(q))-\text{abs}(q)\)
\(\text{yatxnear}_0(q,r) = \text{yatymax}(q, \text{xnear}_0(r))\)

[Parameters]
\(a = \text{yatxnear}_0(y,x) \text{ Auto } \{\text{previous: 99.7941}\}\)
\(b = -\ln(0.5)/(x_{50}(x,y)-\text{min}(x)) \text{ Auto } \{\text{previous: 0.00571098}\}\)

[Equation]
\(f = a \exp(-b \cdot x)\)
fit f to y
*fit f to y with weight reciprocal_y
*fit f to y with weight reciprocal_y^2

[Options]
\(\text{tolerance} = 0.0001\)
\(\text{stepsize} = 100\)
\(\text{iterations} = 100\)

\(R = 0.81183641\quad \text{Rsqr} = 0.65907835\quad \text{Adj Rsqr} = 0.60225808\)

Standard Error of Estimate = 2.7275

| Coefficient | Std. Error | t   | P   |
|-------------|------------|-----|-----|
| \(a\)       | 99.7941    | 1.3611 | <0.0001 |
| \(b\)       | 0.0057     | 0.0017 | 0.0153   |

Analysis of Variance:

|                | DF | SS     | MS     | F      | P   |
|----------------|----|--------|--------|--------|-----|
| Regression     | 1  | 86.2916| 86.2916| 11.5994| 0.0144|
| Residual       | 6  | 44.6361| 7.4393 |        |     |
| Total          | 7  | 130.9276| 18.7039|        |     |

\(\text{PRESS} = 191.7129\)

Durbin-Watson Statistic = 2.0012

Normality Test: Passed \((P = 0.4365)\)
Constant Variance Test: Failed (P = 0.0212)

Power of performed test with alpha = 0.0500: 0.7164

The power of the performed test (0.7164) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|----------------|
| 1   | 99.7941   | 0.2059   | 0.0755    | 0.0871     | 0.0796         |
| 2   | 99.2258   | 0.3929   | 0.1441    | 0.1619     | 0.1481         |
| 3   | 98.6608   | 2.6544   | 0.9732    | 1.0720     | 1.0883         |
| 4   | 98.0989   | 1.2187   | 0.4468    | 0.4851     | 0.4518         |
| 5   | 97.5403   | -1.0840  | -0.3974   | -0.4274    | -0.3962        |
| 6   | 95.8833   | -1.1694  | -0.4287   | -0.4601    | -0.4276        |
| 7   | 94.2546   | -5.0372  | -1.8468   | -2.0522    | -3.4314        |
| 8   | 89.0225   | 2.8270   | 1.0365    | 2.1085     | 3.7821         |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.0013     | 0.0458   |        |
| 2   | 0.0034     | 0.0759   |        |
| 3   | 0.1225     | 0.5026   |        |
| 4   | 0.0210     | 0.1910   |        |
| 5   | 0.0143     | -0.1568  |        |
| 6   | 0.0160     | -0.1664  |        |
| 7   | 0.4944     | -1.6627  |        |
| 8   | 6.9770     | 6.7004   |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 99.7941   | 96.4636  | 103.1247  | 92.3352 | 107.2530 |
| 2   | 99.2258   | 96.1807  | 102.2709  | 91.8900 | 106.5617 |
| 3   | 98.6608   | 95.8626  | 101.4589  | 91.4239 | 105.8976 |
| 4   | 98.0989   | 95.5004  | 100.6974  | 90.9369 | 105.2609 |
| 5   | 97.5403   | 95.0851  | 99.9954   | 90.4290 | 104.6515 |
| 6   | 95.8833   | 93.4626  | 98.3041   | 88.7839 | 102.9828 |
| 7   | 94.2546   | 91.3443  | 97.1649   | 86.9736 | 101.5355 |
| 8   | 89.0225   | 83.2105  | 94.8346   | 80.1726 | 97.8725  |
MANNITOL (First-order reaction)
25°C / 60 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q,r) = yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {{previous: 96.8219}}
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {{previous: 0.000606115}}

[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100
\[ R = 0.10972658 \quad \text{Rsqr} = 0.01203992 \quad \text{Adj Rsqr} = 0.00000000 \]

Standard Error of Estimate = 3.7103

**Coefficient** | **Std. Error** | **t** | **P**
---|---|---|---
a | 96.8219 | 1.8177 | 53.2664 | <0.0001
b | 0.0006 | 0.0022 | 0.2729 | 0.7941

**Analysis of Variance:**

| DF | SS | MS | F | P |
|---|---|---|---|---|
| Regression | 1 | 1.0066 | 1.0066 | 0.0731 | 0.7959 |
| Residual | 6 | 82.5959 | 13.7660 | |
| Total | 7 | 83.6025 | 11.9432 | |

PRESS = 266.4003

Durbin-Watson Statistic = 1.1848

Normality Test: Passed (P = 0.6426)

Constant Variance Test: Passed (P = 0.7053)

Power of performed test with alpha = 0.0500: 0.0433

The power of the performed test (0.0433) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|---|---|---|---|---|---|
| 1 | 96.8219 | 3.1781 | 0.8566 | 0.9826 | 0.9792 |
| 2 | 96.7632 | 0.1484 | 0.0400 | 0.0448 | 0.0409 |
| 3 | 96.7046 | 4.2603 | 1.1482 | 1.2640 | 1.3470 |
| 4 | 96.6460 | 0.4894 | 0.1319 | 0.1433 | 0.1310 |
| 5 | 96.5874 | -5.0795 | -1.3691 | -1.4733 | -1.6834 |
| 6 | 96.4119 | -4.3008 | -1.1592 | -1.2423 | -1.3159 |
| 7 | 96.2368 | -1.4615 | -0.3939 | -0.4356 | -0.4040 |
| 8 | 95.6553 | 2.7657 | 0.7454 | 1.5934 | 1.9152 |

**Influence Diagnostics:**

| Row | Cook'sDist | Leverage | DFFITS |
|---|---|---|---|
| 1 | 0.1524 | 0.5503 |
| 2 | 0.0003 | 0.0207 |
| 3 | 0.1691 | 0.6198 |
| 4 | 0.0018 | 0.0555 |
| 5 | 0.1715 | -0.6692 |
| 6 | 0.1147 | -0.5073 |
95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 96.8219   | 92.3741  | 101.2696  | 86.7123 | 106.9315|
| 2   | 96.7632   | 92.6630  | 100.8634  | 86.8016 | 106.7248|
| 3   | 96.7046   | 92.9098  | 100.4993  | 86.8647 | 106.5444|
| 4   | 96.6460   | 93.1039  | 100.1881  | 86.9008 | 106.3912|
| 5   | 96.5874   | 93.2336  | 99.9412   | 86.9091 | 106.2657|
| 6   | 96.4119   | 93.1463  | 99.6776   | 86.7638 | 106.0601|
| 7   | 96.2368   | 92.3628  | 100.1108  | 86.3661 | 106.1075|
| 8   | 95.6553   | 87.6313  | 103.6792  | 83.5389 | 107.7716|

MANNITOL (First-order reaction)

40°C / 75 %RH

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_y_square=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 97.8276}"
\[ b = -\ln(0.5)/(x_{50}(x,y) - \min(x)) \]  
"Auto \{\text{previous: 0.00540918}\} \]

**Equation**

\[ f = a \cdot \exp(-b \cdot x) \]

fit f to y

fit f to y with weight reciprocal_y

fit f to y with weight reciprocal_ysquare

**Constraints**

b > 0

**Options**

tolerance = 0.0001

stepsize = 100

iterations = 100

R = 0.75578351 \quad \text{Rsqr} = 0.57120871 \quad \text{Adj Rsqr} = 0.49974349

Standard Error of Estimate = 3.0952

| Coefficient | Std. Error | t | P |
|-------------|------------|---|---|
| a           | 97.8276    | 63.4009 | <0.0001 |
| b           | 0.0054     | 0.0020  | 0.0330  |

**Analysis of Variance:**

\[
\begin{array}{ccc}
\text{DF} & \text{SS} & \text{MS} \\
\text{Regression} & 76.5729 & 76.5729 \\
\text{Residual} & 57.4812 & 9.5802 \\
\text{Total} & 134.0541 & 19.1506 \\
\end{array}
\]

PRESS = 116.2583

Durbin-Watson Statistic = 2.4989

Normality Test: Passed (P = 0.4876)

Constant Variance Test: Passed (P = 0.4228)

Power of performed test with alpha = 0.0500: 0.5970

The power of the performed test (0.5970) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 97.8276   | 2.1724   | 0.7019    | 0.8096     | 0.7831          |
| 2   | 97.2999   | -0.4606  | -0.1488   | -0.1672    | -0.1530         |
| 3   | 96.7750   | 0.9734   | 0.3145    | 0.3464     | 0.3194          |
| 4   | 96.2529   | -3.6432  | -1.1770   | -1.2779    | -1.3674         |

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|     | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 97.8276   | 94.0520  | 101.6032  | 89.3650 | 106.2902 |
| 2   | 97.2999   | 93.8463  | 100.7535  | 88.9759 | 105.6238 |
| 3   | 96.7750   | 93.6001  | 99.9498   | 88.5628 | 104.9872 |
| 4   | 96.2529   | 93.3038  | 99.2021   | 88.1253 | 104.3805 |
| 5   | 95.7337   | 92.9469  | 98.5204   | 87.6636 | 103.8038 |
| 6   | 94.1927   | 91.4471  | 96.9383   | 86.1367 | 102.2487 |
| 7   | 92.6765   | 89.3780  | 95.9750   | 84.4157 | 100.9373 |
| 8   | 87.7966   | 81.1954  | 94.3979   | 77.7499 | 97.8434  |
MANNITOL (First-order reaction)
50°C / 20 % moisture
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y^2 = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q, r) = yatymax(q, xnear0(r))

[Parameters]
a = yatxnear0(y, x) "Auto {previous: 97.1413}"
b = -ln(.5)/(x50(x, y) - min(x)) "Auto {previous: 0.00848034}

[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^2

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

R = 0.82013595   Rsqr = 0.67262297   Adj Rsqr = 0.61806013

Standard Error of Estimate = 3.7282

| Coefficient | Std. Error | t    | P     |
|-------------|------------|------|-------|
a | 97.1413 | 1.8792 | 51.6935 | <0.0001 |
b | 0.0085  | 0.0025 | 3.4134  | 0.0143  |

Analysis of Variance:

| DF | SS   | MS   | F     | P     |
|----|------|------|-------|-------|
| Regression | 1 | 171.3449 | 171.3449 | 12.3275 | 0.0127 |
| Residual | 6 | 83.3965  | 13.8994  | | |
| Total | 7 | 254.7413 | 36.3916  | | |

PRESS = 139.4052

Durbin-Watson Statistic = 1.2545

Normality Test: Passed (P = 0.5928)
**Constant Variance Test:** Passed ($P = 0.8393$)

Power of performed test with alpha = 0.0500: 0.7349

The power of the performed test (0.7349) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 97.1413   | 2.8587   | 0.7668    | 0.8878     | 0.8696          |
| 2   | 96.3210   | 4.4557   | 1.1951    | 1.3450     | 1.4691          |
| 3   | 95.5076   | -0.3017  | -0.0809   | -0.0892    | -0.0814         |
| 4   | 94.7011   | -4.1309  | -1.1080   | -1.2027    | -1.2603         |
| 5   | 93.9014   | -2.8757  | -0.7714   | -0.8292    | -0.8045         |
| 6   | 91.5426   | -4.2865  | -1.1498   | -1.2348    | -1.3052         |
| 7   | 89.2430   | 3.2310   | 0.8666    | 0.9658     | 0.9594          |
| 8   | 81.9869   | 1.0640   | 0.2854    | 0.5655     | 0.5306          |

**Influence Diagnostics:**

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.1342      | 0.5075   |        |
| 2   | 0.2411      | 0.7584   |        |
| 3   | 0.0009      | -0.0377  |        |
| 4   | 0.1288      | -0.5319  |        |
| 5   | 0.0535      | -0.3175  |        |
| 6   | 0.1170      | -0.5113  |        |
| 7   | 0.1129      | 0.4720   |        |
| 8   | 0.4680      | 0.9077   |        |

**95% Confidence:**

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 97.1413   | 92.5431  | 101.7395  | 86.9234 | 107.3572 |
| 2   | 96.3210   | 92.1362  | 100.5058  | 86.2844 | 106.3576 |
| 3   | 95.5076   | 91.6772  | 99.3380   | 85.6135 | 105.4017 |
| 4   | 94.7011   | 91.1536  | 98.2486   | 84.9131 | 104.4891 |
| 5   | 93.9014   | 90.5526  | 97.2502   | 84.1836 | 103.6192 |
| 6   | 91.5426   | 88.2151  | 94.8701   | 81.8321 | 101.2531 |
| 7   | 89.2430   | 85.2161  | 93.2699   | 79.2712 | 99.2148  |
| 8   | 81.9869   | 74.1112  | 89.8626   | 69.9350 | 94.0388  |
MANNITOL (First-order reaction)
50°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2
*Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 95.6578}"
b = -ln(0.5)/(x50(x,y) - min(x)) "Auto {previous: 0.0224532}"

[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

R = 0.74699016   Rsqr = 0.55799429   Adj Rsqr = 0.48432668
Standard Error of Estimate = 10.4869

| Coefficient | Std. Error | t   | P     |
|--------------|------------|-----|-------|
| a            | 95.6578    | 17.2206 | <0.0001 |
| b            | 0.0225     | 2.6065 | 0.0403 |

Analysis of Variance:

| DF | SS    | MS   | F    | P     |
|----|-------|------|------|-------|
| Regression | 1 | 833.0008 | 833.0008 | 7.5745 | 0.0332 |
| Residual    | 6 | 659.8475  | 109.9746  |       |       |
| Total       | 7 | 1492.8483 | 213.2640  |       |       |

PRESS = 1658.5926

Durbin-Watson Statistic = 1.8270

Normality Test: Failed (P = 0.0176)

Constant Variance Test: Passed (P = 0.8393)

Power of performed test with alpha = 0.0500: 0.5794

The power of the performed test (0.5794) is below the desired power of 0.8000.
You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 95.6578   | 4.3422   | 0.4141    | 0.4882     | 0.4548          |
| 2   | 93.5339   | 2.1604   | 0.2060    | 0.2335     | 0.2141          |
| 3   | 91.4572   | 4.6360   | 0.4421    | 0.4877     | 0.4543          |
| 4   | 89.4266   | 1.6171   | 0.1542    | 0.1672     | 0.1530          |
| 5   | 87.4410   | 2.0683   | 0.1972    | 0.2118     | 0.1940          |
| 6   | 81.7450   | -22.6505 | -2.1599   | -2.3342    | -7.0284         |
| 7   | 76.4201   | -1.3635  | -0.1300   | -0.1473    | -0.1347         |
| 8   | 61.0513   | 9.6455   | 0.9198    | 1.6086     | 1.9472          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.0465     | 0.2806   | 0.2840 |
| 2   | 0.0078     | 0.2215   | 0.1142 |
| 3   | 0.0258     | 0.1782   | 0.2116 |
| 4   | 0.0024     | 0.1492   | 0.0640 |
| 5   | 0.0034     | 0.1326   | 0.0759 |
| 6   | 0.4575     | 0.1438   | -2.8801|
| 7   | 0.0031     | 0.2211   | -0.0718|
MANNITOL (BiPhasic First-order reaction)
25°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y_square = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {[previous: 0.121814]}
b = ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto {[previous: 0.133524]}

---

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 95.6578   | 82.0656  | 109.2500  | 66.6198 | 124.6958 |
| 2   | 93.5339   | 81.4584  | 105.6095  | 65.1741 | 121.8937 |
| 3   | 91.4572   | 80.6237  | 102.2907  | 63.6036 | 119.3108 |
| 4   | 89.4266   | 79.5159  | 99.3373   | 61.9187 | 116.9344 |
| 5   | 87.4410   | 78.0965  | 96.7856   | 60.1321 | 114.7500 |
| 6   | 81.7450   | 72.0150  | 91.4751   | 54.3018 | 109.1883 |
| 7   | 76.4201   | 64.3544  | 88.4858   | 48.0645 | 104.7757 |
| 8   | 61.0513   | 39.9992  | 82.1034   | 27.8601 | 94.2424  |

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2D Graph 15

---
\( c = \text{atan2near0}(y, x)/2 \)  
\( d = -\ln(0.5)/(1.5*(x50(x,y)-\text{min}(x))) \)

**Equation**

\[ f = a\exp(-b*x) + c\exp(-d*x) \]

fit \( f \) to \( y \)

"fit \( f \) to \( y \) with weight reciprocal_y"

"fit \( f \) to \( y \) with weight reciprocal_ysquare"

**Constraints**

\( b > 0 \)

\( d > 0 \)

**Options**

\( \text{tolerance} = 1\times10^{-6} \)

\( \text{stepsize} = 0.1 \)

\( \text{iterations} = 100 \)

\[ R = 0.89221155 \quad \text{Rsqr} = 0.79604144 \quad \text{Adj Rsqr} = 0.64307252 \]

**Standard Error of Estimate** = 0.0258

| Coefficient | Std. Error | \( t \) | \( P \) |
|-------------|------------|--------|--------|
| \( a \) | 0.1218 | 0.5065 | 0.2405 | 0.8218 |
| \( b \) | 0.1335 | 0.5219 | 0.2558 | 0.8107 |
| \( c \) | 0.8952 | 0.5172 | 1.7310 | 0.1585 |
| \( d \) | 0.0000 | 0.0224 | 0.0000 | 1.0000 |

**Analysis of Variance:**

| DF | SS | MS | \( F \) | \( P \) |
|----|----|----|--------|--------|
| Regression | 3 | 0.0104 | 0.0035 | 5.2039 | 0.0725 |
| Residual | 4 | 0.0027 | 0.0007 | | |
| Total | 7 | 0.0131 | 0.0019 | | |

\( \text{PRESS} = 45.5486 \)

**Durbin-Watson Statistic** = 2.0680

**Normality Test:** Passed (\( P = 0.7148 \))

**Constant Variance Test:** Passed (\( P = 0.7941 \))

**Power of performed test with alpha** = 0.0500: 0.8932

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0170    | -0.0170  | -0.6599   | -1.3628    | -1.6125         |
| 2   | 1.0018    | -0.0056  | -0.2181   | -0.2556    | -0.2232         |
| 3   | 0.9885    | 0.0247   | 0.9541    | 1.1057     | 1.1492          |

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### Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 1.5161     | 0.7655   | -2.9139|
| 2   | 0.0061     | 0.2717   | -0.1363|
| 3   | 0.1049     | 0.2555   | 0.6733 |
| 4   | 0.0650     | 0.3100   | 0.4776 |
| 5   | 0.0011     | 0.3239   | -0.0588|
| 6   | 0.0049     | 0.3414   | 0.1215 |
| 7   | 4.7995     | 0.7342   | (+inf) |
| 8   | 17010.3237 | 0.9978   | (+inf) |

### 95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0170    | 0.9543   | 1.0798    | 0.9217  | 1.1124   |
| 2   | 1.0018    | 0.9644   | 1.0392    | 0.9209  | 1.0827   |
| 3   | 0.9885    | 0.9522   | 1.0248    | 0.9081  | 1.0689   |
| 4   | 0.9768    | 0.9369   | 1.0168    | 0.8947  | 1.0589   |
| 5   | 0.9666    | 0.9258   | 1.0075    | 0.8841  | 1.0492   |
| 6   | 0.9431    | 0.9012   | 0.9850    | 0.8600  | 1.0262   |
| 7   | 0.9273    | 0.8658   | 0.9888    | 0.8328  | 1.0218   |
| 8   | 0.9037    | 0.8320   | 0.9753    | 0.8023  | 1.0051   |
MANITOL (BiPhasic First-order reaction)
25°C / 60 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_y^square=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto (previous: 0.0547482})
b = -ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto (previous: 0.487789})
c = yatxnear0(y,x)/2 "Auto (previous: 0.948324})
d = -ln(.5)/(1.5*(x50(x,y)-min(x))) "Auto (previous: 1.26353e-011})

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^square

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

R = 0.55878062    Rsqr = 0.31223578    Adj Rsqr = 0.00000000

Standard Error of Estimate = 0.0379

| Coefficient | Std. Error | t | P |
|-------------|------------|---|---|
| a | 0.0547 | 0.0695 | 0.7882 | 0.4746 |
| b | 0.4878 | 1.2185 | 0.4003 | 0.7094 |
| c | 0.9483 | 0.0662 | 14.3342 | 0.0001 |
| d | 0.0000 | 0.0048 | 0.0000 | 1.0000 |

Analysis of Variance:

| DF  | SS   | MS   | F    | P    |
|-----|------|------|------|------|
| Regression | 3   | 0.0026 | 0.0009 | 0.6053 | 0.6455 |
| Residual   | 4   | 0.0057 | 0.0014 |      |      |
| Total      | 7   | 0.0084 | 0.0012 |      |      |
PRESS = 1.6045

Durbin-Watson Statistic = 1.5317

Normality Test: Passed (P = 0.7430)

Constant Variance Test: Passed (P = 0.7053)

Power of performed test with alpha = 0.0500: 0.2915

The power of the performed test (0.2915) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0031    | -0.0031  | -0.0810   | -0.2768    | -0.2420         |
| 2   | 0.9819    | -0.0128  | -0.3382   | -0.4224    | -0.3742         |
| 3   | 0.9690    | 0.0407   | 1.0731    | 1.3410     | 1.5653          |
| 4   | 0.9610    | 0.0104   | 0.2732    | 0.3218     | 0.2824          |
| 5   | 0.9561    | -0.0410  | -1.0821   | -1.2497    | -1.3862         |
| 6   | 0.9501    | -0.0290  | -0.7652   | -1.0112    | -1.0151         |
| 7   | 0.9487    | -0.0010  | -0.0261   | -0.0348    | -0.0301         |
| 8   | 0.9483    | 0.0359   | 0.9464    | 5.6130     | (+inf)          |

**Influence Diagnostics:**

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.2043     | -0.7905  |        |
| 2   | 0.0250     | -0.2800  |        |
| 3   | 0.2525     | 1.1731   |        |
| 4   | 0.0100     | 0.1757   |        |
| 5   | 0.1303     | -0.8009  |        |
| 6   | 0.1908     | -0.8769  |        |
| 7   | 0.0002     | -0.0266  |        |
| 8   | 269.1707   | (+inf)   |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0031    | 0.9024   | 1.1037    | 0.8574  | 1.1487   |
| 2   | 0.9819    | 0.9189   | 1.0450    | 0.8592  | 1.1047   |
| 3   | 0.9690    | 0.9058   | 1.0321    | 0.8462  | 1.0917   |
| 4   | 0.9610    | 0.9054   | 1.0166    | 0.8419  | 1.0801   |
| 5   | 0.9561    | 0.9034   | 1.0088    | 0.8384  | 1.0738   |
| 6   | 0.9501    | 0.8813   | 1.0189    | 0.8244  | 1.0759   |
| 7   | 0.9487    | 0.8790   | 1.0185    | 0.8225  | 1.0750   |
| 8   | 0.9483    | 0.8446   | 1.0521    | 0.8005  | 1.0961   |

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MANNITOL (BiPhasic First-order reaction)
40°C / 75 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {previous: 0.323691}
b = -ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 0.00543067}
c = yatxnear0(y,x)/2 "Auto {previous: 0.654584}
d = -ln(.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 0.00539824}

[Equation]
f = a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
\( \text{Stepsize} = 0.1 \)
\( \text{Iterations} = 100 \)

\[ R = 0.75578349 \quad \text{Rsqr} = 0.57120869 \quad \text{Adj Rsqr} = 0.24961521 \]

\[ \text{Standard Error of Estimate} = 0.0379 \]

| Coefficient | Std. Error | \( t \) | \( P \) |
|-------------|------------|--------|--------|
| a 0.3237    | 753959.2906 | 0.0000 | 1.0000 |
| b 0.0054    | 215.4067   | 0.0000 | 1.0000 |
| c 0.6546    | 753959.2906 | 0.0000 | 1.0000 |
| d 0.0054    | 106.9689   | 0.0001 | 1.0000 |

\[ \text{Analysis of Variance:} \]

| DF | SS  | MS  | \( F \) | \( P \) |
|----|-----|-----|--------|--------|
| Regression | 3   | 0.0077 | 0.0026 | 1.7762 | 0.2906 |
| Residual   | 4   | 0.0057 | 0.0014 |        |        |
| Total      | 7   | 0.0134 | 0.0019 |        |        |

\[ \text{PRESS} = 0.0572 \]

\[ \text{Durbin-Watson Statistic} = 2.4989 \]

\[ \text{Normality Test: Passed (} P = 0.4877 \) \]

\[ \text{Constant Variance Test: Passed (} P = 0.4228 \) \]

\[ \text{Power of performed test with } \alpha = 0.0500: 0.5970 \]

The power of the performed test (0.5970) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

\[ \text{Regression Diagnostics:} \]

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 0.9783    | 0.0217   | 0.5731    | 0.7641     | 0.7161          |
| 2   | 0.9730    | -0.0046  | -0.1215   | -0.1376    | -0.1194         |
| 3   | 0.9677    | 0.0097   | 0.2568    | 0.2581     | 0.2254          |
| 4   | 0.9625    | -0.0364  | -0.9610   | -1.0366    | -1.0497         |
| 5   | 0.9573    | -0.0114  | -0.3011   | -0.3345    | -0.2938         |
| 6   | 0.9419    | -0.0207  | -0.5452   | -0.6668    | -0.6125         |
| 7   | 0.9268    | 0.0555   | 1.4647    | 1.8386     | 4.0451          |
| 8   | 0.8780    | -0.0139  | -0.3663   | -1.4318    | -1.7760         |

\[ \text{Influence Diagnostics:} \]

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.1135     | 0.4375   | 0.6315 |
MANNITOL (BiPhasic First-order reaction)

50°C / 20% moisture

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
$x_{\text{near0}}(q) = \max(\text{abs}(q)) - \text{abs}(q)$

$y_{\text{atxmax}}(q, x_{\text{near0}}(r))$

**Parameters**

- $a = y_{\text{atxmax}}(y, x)/2$ "Auto {previous: 0.093512}
- $b = \ln(5)/(0.5*(x50(x,y)-\text{min}(x)))$ "Auto {previous: 0.488568}
- $c = y_{\text{atxmax}}(y, x)/2$ "Auto {previous: 0.921222}
- $d = \ln(5)/(1.5*(x50(x,y)-\text{min}(x)))$ "Auto {previous: 0.00453147}

**Equation**

$$f = a*\exp(-b*x) + c*\exp(-d*x)$$

*[fit f to y]*

"[fit f to y with weight reciprocal_y]

"[fit f to y with weight reciprocal_y_square]

**Constraints**

- $b > 0$
- $d > 0$

**Options**

- `tolerance=1e-6`
- `stepsize=0.1`
- `iterations=100`

$R = 0.90606896$ \hspace{1cm} $Rsqr = 0.82096096$ \hspace{1cm} $\text{Adj Rsqr} = 0.68668169$

Standard Error of Estimate = 0.0338

| Coefficient | Std. Error | t       | P    |
|-------------|------------|---------|------|
| $a$         | 0.0935     | 0.0647  | 1.4451 | 0.2219 |
| $b$         | 0.4886     | 0.6485  | 0.7534 | 0.4932 |
| $c$         | 0.9212     | 0.0623  | 14.7985 | 0.0001 |
| $d$         | 0.0045     | 0.0047  | 0.9683 | 0.3877 |

**Analysis of Variance:**

| DF | SS     | MS     | F     | P    |
|----|--------|--------|-------|------|
| Regression | 3 | 0.0209 | 0.0070 | 6.1138 | 0.0564 |
| Residual  | 4 | 0.0046 | 0.0011 |       |       |
| Total    | 7 | 0.0255 | 0.0036 |       |       |

PRESS = 0.1631

Durbin-Watson Statistic = 2.6143

Normality Test: Passed (P = 0.1765)

Constant Variance Test: Passed (P = 0.8393)

Power of performed test with alpha = 0.0500: 0.9201
### Regression Diagnostics:

| Row | Predicted Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|---------------------|-----------|------------|-----------------|
| 1   | 1.0147              | -0.0147   | -0.4363    | -1.4949         | -1.9487         |
| 2   | 0.9744              | 0.0333    | 0.9873     | 1.2347          | 1.3593          |
| 3   | 0.9481              | 0.0040    | 0.1170     | 0.1463          | 0.1270          |
| 4   | 0.9304              | -0.0247   | -0.7307    | -0.8608         | -0.8259         |
| 5   | 0.9179              | -0.0077   | -0.2270    | -0.2625         | -0.2293         |
| 6   | 0.8955              | -0.0230   | -0.6799    | -0.9062         | -0.8730         |
| 7   | 0.8811              | 0.0436    | 1.2919     | 1.7180          | 2.9059          |
| 8   | 0.8414              | -0.0109   | -0.3228    | -1.8256         | -3.8717         |

### Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 5.9980     | -6.3851  |        |
| 2   | 0.2149     | 1.0208   |        |
| 3   | 0.0030     | 0.0953   |        |
| 4   | 0.0718     | -0.5143  |        |
| 5   | 0.0058     | -0.1332  |        |
| 6   | 0.1525     | -0.7576  |        |
| 7   | 0.5668     | 2.5470   |        |
| 8   | 25.8207    | -21.5526 |        |

### 95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0147    | 0.9251   | 1.1044    | 0.8850  | 1.1445   |
| 2   | 0.9744    | 0.9181   | 1.0307    | 0.8651  | 1.0838   |
| 3   | 0.9481    | 0.8918   | 1.0044    | 0.8388  | 1.0574   |
| 4   | 0.9304    | 0.8808   | 0.9799    | 0.8243  | 1.0364   |
| 5   | 0.9179    | 0.8708   | 0.9650    | 0.8130  | 1.0228   |
| 6   | 0.8955    | 0.8341   | 0.9570    | 0.7834  | 1.0076   |
| 7   | 0.8811    | 0.8193   | 0.9429    | 0.7688  | 0.9934   |
| 8   | 0.8414    | 0.7491   | 0.9337    | 0.7099  | 0.9730   |

![Graph 19](image-url)
MANNITOL (BiPhasic First-order reaction)  
50°C  
Nonlinear Regression

[Variables]  
\[ x = \text{col}(1) \]  
\[ y = \text{col}(2) \]  
reciprocal_y = 1/abs(y)  
reciprocal_y^2 = 1/y^2

'Automatic Initial Parameter Estimate Functions
\[ x\text{near0}(q) = \max(\text{abs}(q)) - \text{abs}(q) \]  
\[ y\text{atxnear0}(q,r) = \text{yatymax}(q, x\text{near0}(r)) \]

[Parameters]  
\[ a = y\text{atxnear0}(y,x)/2 \text{ Auto } \{ \text{previous: 0.367652} \} \]  
\[ b = -\ln(0.5)/(0.5\times(x50(x,y)-\text{min}(x))) \text{ Auto } \{ \text{previous: 0.200456} \} \]  
\[ c = y\text{atxnear0}(y,x)/2 \text{ Auto } \{ \text{previous: 0.668022} \} \]  
\[ d = -\ln(0.5)/(1.5\times(x50(x,y)-\text{min}(x))) \text{ Auto } \{ \text{previous: 3.69366e-010} \} \]

[Equation]  
\[ f = a \times \exp(-b\times x) + c \times \exp(-d\times x) \]  
fit f to y  
"fit f to y with weight reciprocal_y"  
"fit f to y with weight reciprocal_y^2"  

[Constraints]  
\[ b > 0 \]  
\[ d > 0 \]

[Options]  
\[ \text{tolerance} = 1\times10^{-6} \]  
\[ \text{stepsize} = 0.1 \]  
\[ \text{iterations} = 100 \]

\[ R = 0.85831342 \quad \text{Rsr} = 0.73670192 \quad \text{Adj Rsr} = 0.53922836 \]

Standard Error of Estimate = 0.0991

| Coefficient | Std. Error | t  | P    |
|-------------|------------|----|------|
| a           | 0.3677     | 0.6963 | 0.5280 | 0.6254 |
| b           | 0.2005     | 0.4714 | 0.4253 | 0.6925 |
| c           | 0.6680     | 0.7276 | 0.9181 | 0.4105 |
| d           | 0.0000     | 0.0520 | 0.0000 | 1.0000 |

Analysis of Variance:  
| DF   | SS     | MS  | F   | P   |
|------|--------|-----|-----|-----|
| Regression | 3 | 0.1100 | 0.0367 | 3.7306 | 0.1179 |
| Residual  | 4 | 0.0393 | 0.0098 |       |       |
| Total    | 7 | 0.1493 | 0.0213 |       |       |
PRESS = 55.3088

Durbin-Watson Statistic = 2.4780

Normality Test: Failed (P = 0.0438)

Constant Variance Test: Passed (P = 0.8849)

Power of performed test with alpha = 0.0500: 0.8206

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Std. Res. | Std. Del. Res. |
|-----|-----------|----------|-----------|-----------|----------------|
| 1   | 1.0357    | -0.0357  | -0.3599   | -0.8043   | -0.7608       |
| 2   | 0.9689    | -0.0119  | -0.1205   | -0.1415   | -0.1229       |
| 3   | 0.9142    | 0.0467   | 0.4710    | 0.5537    | 0.4990        |
| 4   | 0.8695    | 0.0409   | 0.4128    | 0.4984    | 0.4457        |
| 5   | 0.8329    | 0.0622   | 0.6272    | 0.7527    | 0.7036        |
| 6   | 0.7584    | -0.1674  | -1.6892   | -2.1065   | (+inf)        |
| 7   | 0.7176    | 0.0330   | 0.3330    | 0.5861    | 0.5309        |
| 8   | 0.6747    | 0.0323   | 0.3256    | 4.9393    | (+inf)        |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.6462      | -1.5207  |        |
| 2   | 0.0019      | -0.0756  |        |
| 3   | 0.0293      | 0.3083   |        |
| 4   | 0.0284      | 0.3016   |        |
| 5   | 0.0623      | 0.4668   |        |
| 6   | 0.6158      | (+inf)   |        |
| 7   | 0.1801      | 0.7687   |        |
| 8   | 1397.8128   | (+inf)   |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0357    | 0.7895   | 1.2818    | 0.6664  | 1.4049   |
| 2   | 0.9689    | 0.8247   | 1.1131    | 0.6582  | 1.2796   |
| 3   | 0.9142    | 0.7696   | 1.0589    | 0.6033  | 1.2252   |
| 4   | 0.8695    | 0.7153   | 1.0238    | 0.5540  | 1.1850   |
| 5   | 0.8329    | 0.6808   | 0.9851    | 0.5184  | 1.1474   |
| 6   | 0.7584    | 0.5940   | 0.9228    | 0.4378  | 1.0790   |
| 7   | 0.7176    | 0.4911   | 0.9440    | 0.3611  | 1.0740   |
| 8   | 0.6747    | 0.4001   | 0.9493    | 0.2859  | 1.0635   |
LACTOSE HYDROUS (First-order reaction)

25°C

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {{previous: 98.7481}}
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {{previous: 0.0143815}}

[Equation]
f=a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100
R = 0.85870060  Rsqr = 0.73736673  Adj Rsqr = 0.69359452

Standard Error of Estimate = 5.1813

| Coefficient | Std. Error | t     | P       |
|-------------|------------|-------|---------|
| a           | 2.6669     | 37.0274 | <0.0001 |
| b           | 0.0037     | 3.9608 | 0.0080  |

Analysis of Variance:

| DF | SS        | MS    | F     | P       |
|----|-----------|-------|-------|---------|
| Regression | 1 | 452.2358 | 452.2358 | 16.8455 | 0.0063 |
| Residual    | 6 | 161.0761 | 26.8460 |
| Total       | 7 | 613.3120 | 87.6160 |

PRESS = 296.5965

Durbin-Watson Statistic = 2.2560

Normality Test: Passed (P = 0.6251)

Constant Variance Test: Passed (P = 0.2327)

Power of performed test with alpha = 0.0500: 0.8215

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 98.7481   | 1.2519   | 0.2416    | 0.2818     | 0.2590          |
| 2   | 97.3382   | -0.4754  | -0.0918   | -0.1036    | -0.0946         |
| 3   | 95.9483   | 2.5909   | 0.5000    | 0.5513     | 0.5165          |
| 4   | 94.5783   | 7.3974   | 1.4277    | 1.5489     | 1.8252          |
| 5   | 93.2279   | -8.9998  | -1.7370   | -1.8662    | -2.6301         |
| 6   | 89.2911   | -2.6968  | -0.5205   | -0.5602    | -0.5254         |
| 7   | 85.5206   | -1.6393  | -0.3164   | -0.3549    | -0.3275         |
| 8   | 74.0650   | 2.6254   | 0.5067    | 0.9514     | 0.9425          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.0143     | 0.2649   | 0.1555 |
| 2   | 0.0015     | 0.2151   | -0.0495 |
| 3   | 0.0327     | 0.1773   | 0.2397 |
| 4   | 0.2123     | 0.1504   | 0.7679 |
| 5   | 0.2687     | 0.1337   | -1.0332 |
| 6   | 0.0249     | 0.1369   | -0.2092 |
| 7   | 0.0163     | 0.2054   | -0.1665 |
| 8   | 1.1429     | 0.7163   | 1.4977 |
LACTOSE HYDROUS (First-order reaction)
25°C / 60 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 93.9494}"
b = -ln(.5)/(x50(y,x)-min(x)) "Auto {previous: 0.0138593}"

[Equation]
f = a*exp(-b*x)
"fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
\[ b > 0 \]

[Options]
\[ \text{tolerance}=0.0001 \]
\[ \text{stepsize}=100 \]
\[ \text{iterations}=100 \]

\[ R = 0.71848585 \quad \text{Rsqr} = 0.51622191 \quad \text{Adj Rsqr} = 0.43559223 \]

Standard Error of Estimate = 7.5634

| Coefficient | Std. Error | t   | P   |
|--------------|------------|-----|-----|
| a            | 93.9494    | 3.8869 | <0.0001 |
| b            | 0.0139     | 0.0056 | 0.0487 |

Analysis of Variance:

|            | DF | SS    | MS    | F     | P    |
|------------|----|-------|-------|-------|------|
| Regression | 1  | 366.2527 | 366.2527 | 6.4024 | 0.0447 |
| Residual   | 6  | 343.2342 | 57.2057 |       |      |
| Total      | 7  | 709.4869 | 101.3553 |       |      |

PRESS = 1328.3486

Durbin-Watson Statistic = 2.2353

Normality Test: Passed (P = 0.6128)

Constant Variance Test: Passed (P = 0.4228)

Power of performed test with alpha = 0.0500: 0.5249

The power of the performed test (0.5249) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 93.9494   | 6.0506   | 0.8000    | 0.9325     | 0.9206 |
| 2   | 92.6563   | 1.2016   | 0.1589    | 0.1793     | 0.1641 |
| 3   | 91.3810   | 5.7777   | 0.7639    | 0.8421     | 0.8187 |
| 4   | 90.1233   | -3.3359  | -0.4411   | -0.4785    | -0.4454 |
| 5   | 88.8528   | -5.2034  | -0.6880   | -0.7392    | -0.7078 |
| 6   | 85.2630   | -0.0518  | -0.0069   | -0.0074    | -0.0067 |
| 7   | 81.7907   | -12.7367 | -1.6840   | -1.8881    | -2.7057 |
Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.1560     | 0.5515   |        |
| 2   | 0.0044     | 0.0858   |        |
| 3   | 0.0764     | 0.3799   |        |
| 4   | 0.0203     | -0.1874  |        |
| 5   | 0.0422     | -0.2781  |        |
| 6   | 0.0000     | -0.0027  |        |
| 7   | 0.4584     | -1.3721  |        |
| 8   | 5.6602     | 6.0107   |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 93.9494   | 84.4385  | 103.4603  | 73.1415 | 114.7573 |
| 2   | 92.6563   | 84.0793  | 101.2334  | 72.2583 | 113.0543 |
| 3   | 91.3810   | 83.5908  | 99.1713   | 71.3012 | 111.4609 |
| 4   | 90.1233   | 82.9448  | 97.3018   | 70.2728 | 109.9738 |
| 5   | 88.8828   | 82.1140  | 95.6517   | 69.1768 | 108.5889 |
| 6   | 85.2630   | 78.4238  | 92.1022   | 65.5327 | 104.9934 |
| 7   | 81.7907   | 73.4201  | 90.1612   | 61.4786 | 102.1027 |
| 8   | 71.2055   | 55.5171  | 86.8938   | 46.9436 | 95.4673  |

2D Graph 22

![Graph showing data points and trend line]

- Col 15 vs Col 19
- Time, weeks vs Drug [Lactose hydrous, 250/60%RH]
LACTOSE HYDROUS (First-order reaction)
40°C / 75 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,x) = yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 86.3848}
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0167549}

[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

R = 0.76339834    Rsqr = 0.58277703   Adj Rsqr = 0.51323986

Standard Error of Estimate = 7.1704

| Coefficient | Std. Error | t     | P     |
|--------------|------------|-------|-------|
| a            | 86.3848    | 3.7229| <0.0001 |
| b            | 0.0168     | 0.0060| 0.0321 |

Analysis of Variance:

|       | DF  | SS     | MS    | F      | P     |
|-------|-----|--------|-------|--------|-------|
| Regression | 1   | 430.8915 | 430.8915 | 8.3808 | 0.0275 |
| Residual  | 6   | 308.4848 | 51.4141 |        |       |
| Total    | 7   | 739.3762 | 105.6252 |        |       |

PRESS = 837.5987

Durbin-Watson Statistic = 1.2449

Normality Test: Passed (P = 0.1090)
Constant Variance Test: Passed (P = 0.8849)

Power of performed test with alpha = 0.0500: 0.6125

The power of the performed test (0.6125) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 86.3848   | 13.6152  | 1.8988    | 2.2217     | 4.8166          |
| 2   | 84.9495   | -1.5968  | -0.2227   | -0.2517    | -0.2310         |
| 3   | 83.5380   | -4.2025  | -0.5861   | -0.6463    | -0.6116         |
| 4   | 82.1500   | -4.4393  | -0.6191   | -0.6715    | -0.6375         |
| 5   | 80.7851   | -0.1747  | -0.0244   | -0.0262    | -0.0239         |
| 6   | 76.8248   | -6.9567  | -0.9702   | -1.0455    | -1.0553         |
| 7   | 73.0587   | -1.7090  | -0.2383   | -0.2682    | -0.2463         |
| 8   | 61.7883   | 5.6432   | 0.7870    | 1.4457     | 1.6349          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.9109     | 0.2696   | 2.9261 |
| 2   | 0.0088     | 0.2171   | -0.1216|
| 3   | 0.0451     | 0.1776   | -0.2842|
| 4   | 0.0398     | 0.1500   | -0.2678|
| 5   | 0.0001     | 0.1333   | -0.0094|
| 6   | 0.0881     | 0.1388   | -0.4236|
| 7   | 0.0096     | 0.2100   | -0.1270|
| 8   | 2.4815     | 0.7037   | 2.5193 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 86.3848   | 77.2752  | 95.4944   | 66.6156 | 106.1540 |
| 2   | 84.9495   | 76.7752  | 93.1238   | 65.5935 | 104.3055 |
| 3   | 83.5380   | 76.1443  | 90.9318   | 64.4985 | 102.5776 |
| 4   | 82.1500   | 75.3543  | 88.9458   | 63.3347 | 100.9654 |
| 5   | 80.7851   | 74.3789  | 87.1913   | 62.1069 | 99.4633  |
| 6   | 76.8248   | 70.2888  | 83.3608   | 58.1017 | 95.5479  |
| 7   | 73.0587   | 65.0184  | 81.0990   | 53.7589 | 92.3585  |
| 8   | 61.7883   | 47.0707  | 76.5060   | 38.8876 | 84.6891  |
LACTOSE HYDROUS (First-order reaction)

50°C / 20 %moisture

Nonlinear Regression

[Variables]
\( x = \text{col}(1) \)
\( y = \text{col}(2) \)
reciprocal\_y = 1/abs(y)
reciprocal\_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions

xnear0(q) = \text{max}(abs(q)) - abs(q)
yatxnear0(q,r) = xatymax(q, xnear0(r))

[Parameters]
\( a = \text{yatxnear0}(y,x) \) "Auto \{previous: 80.5994\}
\( b = -\ln(0.5)/(x50(x,y) - \text{min}(x)) \) "Auto \{previous: 0.0464301\}

[Equation]
\[ f = a \exp(-b \cdot x) \]

"fit f to y with weight reciprocal\_y
"fit f to y with weight reciprocal\_ysquare

[Constraints]
b > 0

[Options]
\$\text{tolerance} = 0.0001
\$\text{stepsize} = 100
\$\text{iterations} = 100
\[ R = 0.83098356 \quad \text{Rsqr} = 0.69053367 \quad \text{Adj Rsqr} = 0.63895595 \]

Standard Error of Estimate = 11.2615

| Coefficient | \text{Std. Error} | \text{t} | \text{P} |
|-------------|-------------------|---------|--------|
| a           | 80.5994           | 12.4362 | <0.0001|
| b           | 0.0464            | 3.0818  | 0.0216 |

Analysis of Variance:

|                  | \text{DF} | \text{SS}    | \text{MS}    | \text{F}  | \text{P}  |
|------------------|----------|-------------|-------------|---------|---------|
| Regression       | 1        | 1697.9183   | 1697.9183   | 13.3882 | 0.0106  |
| Residual         | 6        | 760.9311    | 126.8218    |         |         |
| Total            | 7        | 2458.8494   | 351.2642    |         |         |

PRESS = 1454.5475

Durbin-Watson Statistic = 1.2147

Normality Test: Passed (\( P = 0.6231 \))

Constant Variance Test: Passed (\( P = 0.2897 \))

Power of performed test with alpha = 0.0500: 0.7592

The power of the performed test (0.7592) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | \text{Std. Res.} | \text{Stud. Res.} | \text{Stud. Del. Res.} |
|-----|-----------|----------|------------------|-------------------|-----------------------|
| 1   | 80.5994   | 19.4006  | 1.7227           | 2.1065            | 3.7683                |
| 2   | 76.9427   | -1.7701  | -0.1572          | -0.1801           | -0.1649               |
| 3   | 73.4519   | -12.3742 | -1.0988          | -1.2128           | -1.2743               |
| 4   | 70.1195   | -10.3242 | -0.9168          | -0.9920           | -0.9904               |
| 5   | 66.9383   | -1.0011  | -0.0889          | -0.0955           | -0.0872               |
| 6   | 58.2347   | -4.9448  | -0.4391          | -0.4832           | -0.4499               |
| 7   | 50.6627   | 9.4856   | 0.8423           | 0.9861            | 0.9834                |
| 8   | 31.8453   | 2.5046   | 0.2224           | 0.3235            | 0.2979                |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 1.0988     | 0.3312   | 2.6518 |
| 2   | 0.0051     | 0.2386   | -0.0923|
| 3   | 0.1605     | 0.1792   | -0.5953|
| 4   | 0.0841     | 0.1459   | -0.4094|
| 5   | 0.0007     | 0.1332   | -0.0342|
| 6   | 0.0246     | 0.1742   | -0.2067|
### LACTOSE HYDROUS (First-order reaction)
### 50°C

#### Nonlinear Regression

**Variables**
- \( x = \text{col}(1) \)
- \( y = \text{col}(2) \)
- \( \text{reciprocal}_y = 1/\text{abs}(y) \)
- \( \text{reciprocal}_y^{\text{square}} = 1/y^2 \)

'Automatic Initial Parameter Estimate Functions
- \( \text{xnear0}(q) = \max(\text{abs}(q))-\text{abs}(q) \)
- \( \text{yatxnear0}(q,r) = \text{yatymax}(q,\text{xnear0}(r)) \)

**Parameters**
- \( a = \text{yatxnear0}(y,x) \) "Auto {previous: 95.4743}"
\[ b = -\ln(.5)/(x50(x,y)-\text{min}(x)) \]  "Auto \{\text{previous: 0.0541414}\}

[Equation]
f = a*\exp(-b*x)

"fit f to y" with weight reciprocal_y
"fit f to y with weight reciprocal_y square"

[Constraints]
b > 0

[Options]
\textit{t}olerance = 0.0001
\textit{ste}psize = 100
\textit{i}terations = 100

\[ R = 0.9670 \quad \text{Rsq}r = 0.9352 \quad \text{Adj Rsqr} = 0.9244 \]

Standard Error of Estimate = 5.7663

| Coefficient | Std. Error | t     | P  |
|-------------|------------|-------|----|
| a           | 95.4743    | 3.4038| <0.0001|
| b           | 0.0541     | 0.0072| 0.0003|

Analysis of Variance:

|            | DF | SS       | MS      | F       | P         |
|------------|----|----------|---------|---------|-----------|
| Regression | 1  | 2878.0139| 2878.0139| 86.5556 | <0.0001   |
| Residual   | 6  | 199.5029 | 33.2505 |         |           |
| Total      | 7  | 3077.5168| 439.6453|         |           |

PRESS = 362.9285

Durbin-Watson Statistic = 0.9032

Normality Test: Passed (P = 0.4645)

Constant Variance Test: Passed (P = 0.6620)

Power of performed test with alpha = 0.0500: 0.9955

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 95.4743   | 4.5257   | 0.7848    | 0.9723     | 0.9670          |
| 2   | 90.4427   | 6.3309   | 1.0979    | 1.2623     | 1.3446          |
| 3   | 85.6762   | -0.6116  | -0.1061   | -0.1171    | -0.1070         |
| 4   | 81.1609   | -5.7712  | -1.0009   | -1.0826    | -1.1017         |
| 5   | 76.8836   | -8.9200  | -1.5469   | -1.6632    | -2.0681         |
| 6   | 65.3572   | -0.2466  | -0.0428   | -0.0474    | -0.0433         |
| 7   | 55.5589   | 1.0417   | 0.1807    | 0.2136     | 0.1958          |
### Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.2528     | 0.7072   |        |
| 2   | 0.2564     | 0.7627   |        |
| 3   | 0.0015     | -0.0499  |        |
| 4   | 0.0996     | -0.4542  |        |
| 5   | 0.2157     | -0.8167  |        |
| 6   | 0.0003     | -0.0207  |        |
| 7   | 0.0091     | 0.1236   |        |
| 8   | 0.6463     | 1.1871   |        |

### 95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 95.4743   | 87.1455  | 103.8032  | 79.0898 | 111.8589 |
| 2   | 90.4427   | 83.4808  | 97.4046   | 74.7089 | 106.1764 |
| 3   | 85.6762   | 79.7983  | 91.6441   | 70.3563 | 100.9961 |
| 4   | 81.1609   | 75.7826  | 86.5391   | 66.0609 | 96.2608  |
| 5   | 76.8836   | 71.7011  | 82.0660   | 61.8522 | 91.9149  |
| 6   | 65.3572   | 59.2656  | 71.4489   | 49.9887 | 80.7257  |
| 7   | 55.5589   | 48.0275  | 63.0903   | 39.5650 | 71.5528  |
| 8   | 32.3311   | 22.5792  | 42.0830   | 15.1794 | 49.4828  |

#### 2D Graph 26

![Graph showing Y Data vs Time, weeks v % Drug (Lactose hydrous, 50C/Day)]
LACTOSE HYDROUS (BiPhasic First-order reaction)
25°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {previous: 0.288768}"
b = -ln(0.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 0.0957106}"
c = yatxnear0(y,x)/2 "Auto {previous: 0.722904}"
d = -ln(0.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 7.91853e-011}"

[Equation]
f = a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

R = 0.88330073  Rsqr = 0.78022017  Adj Rsqr = 0.61538530

Standard Error of Estimate = 0.0581

| Coefficient | Std. Error | t     | P   |
|-------------|------------|-------|-----|
| a           | 0.2888     | 2.7836| 0.1037| 0.9224|
| b           | 0.0957     | 0.7316| 0.1308| 0.9022|
| c           | 0.7229     | 2.8101| 0.2573| 0.8097|
| d           | 0.0000     | 0.1240| 0.0000| 1.0000|

Analysis of Variance:

|         | DF | SS  | MS  | F    | P    |
|---------|----|-----|-----|------|------|
| Regression | 3  | 0.0479 | 0.0160 | 4.7333 | 0.0836 |
| Residual  | 4  | 0.0135 | 0.0034 |      |      |
| Total     | 7  | 0.0613 | 0.0088 |      |      |
PRESS $= 1.0056$

Durbin-Watson Statistic $= 2.6048$

Normality Test: Passed ($P = 0.2530$)

Constant Variance Test: Passed ($P = 0.1597$)

Power of performed test with alpha $= 0.0500$: 0.8748

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0117    | -0.0117  | -0.2011   | -0.3989    | -0.3525         |
| 2   | 0.9853    | -0.0167  | -0.2875   | -0.3369    | -0.2960         |
| 3   | 0.9614    | 0.0240   | 1.3808    | 0.4764     | 2.5624          |
| 4   | 0.9396    | 0.0802   | 1.6570    |            |                 |
| 5   | 0.9198    | -0.0775  | 1.6348    |            |                 |
| 6   | 0.8707    | -0.0047  | -0.0815   | -0.1000    | -0.0867         |
| 7   | 0.8338    | 0.0050   | 0.0865    | 0.1780     | 0.1547          |
| 8   | 0.7655    | 0.0014   | 0.0244    | 0.6448     | 0.5899          |

**Influence Diagnostics:**

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.1168     | -0.6040  |        |
| 2   | 0.0106     | -0.1808  |        |
| 3   | 0.0184     | 0.2421   |        |
| 4   | 0.3020     | 1.6996   |        |
| 5   | 0.3328     | -1.7345  |        |
| 6   | 0.0013     | -0.0618  |        |
| 7   | 0.0256     | 0.2782   |        |
| 8   | 72.2003    | 15.5475  |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|--------|---------|
| 1   | 1.0117    | 0.8725   | 1.1509    | 0.7987 | 1.2246  |
| 2   | 0.9853    | 0.9013   | 1.0693    | 0.8036 | 1.1671  |
| 3   | 0.9614    | 0.8816   | 1.0412    | 0.7815 | 1.1412  |
| 4   | 0.9396    | 0.8505   | 1.0287    | 0.7554 | 1.1238  |
| 5   | 0.9198    | 0.8269   | 1.0127    | 0.7338 | 1.1059  |
| 6   | 0.8707    | 0.7771   | 0.9642    | 0.6843 | 1.0570  |
| 7   | 0.8338    | 0.6929   | 0.9746    | 0.6197 | 1.0478  |
| 8   | 0.7655    | 0.6044   | 0.9265    | 0.5376 | 0.9933  |
**LACTOSE HYDROUS (BiPhasic First-order reaction)**

25°C / 60%RH

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)

reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions

xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q,r) = xatymax(q, xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {previous: 0.255963}"
b = -ln(0.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 0.234103}"
c = yatxnear0(y,x)/2 "Auto {previous: 0.753922}"
d = -ln(0.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 2.42093e-010}"

[Equation]
f = a*exp(-b*x) + c*exp(-d*x)

fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b > 0
d > 0

[Options]
tolerance = 1e-6
stepsize=0.1
iterations=100

\( R = 0.88085926 \quad Rsqr = 0.77591304 \quad Adj \ Rsqr = 0.60784783 \)

Standard Error of Estimate = 0.0630

| Coefficient | Std. Error | t  | P   |
|-------------|------------|----|-----|
| a           | 0.2560     | 0.8102 | 0.4633 |
| b           | 0.2341     | 0.5873 | 0.5886 |
| c           | 0.7539     | 2.2689 | 0.0858 |
| d           | 0.0000     | 0.0000 | 1.0000 |

Analysis of Variance:

| DF   | SS      | MS      | F     | P     |
|------|---------|---------|-------|-------|
| Regression | 3   | 0.0551  | 0.0184 | 4.6167 | 0.0868 |
| Residual | 4   | 0.0159  | 0.0040 |       |       |
| Total  | 7   | 0.0709  | 0.0101 |       |       |

PRESS = 47.4032

Durbin-Watson Statistic = 3.1523

Normality Test: Passed (P = 0.2432)

Constant Variance Test: Passed (P = 0.1388)

Power of performed test with alpha = 0.0500: 0.8697

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stid. Res. | Std. Def. Res. |
|-----|-----------|----------|-----------|------------|---------------|
| 1   | 1.0099    | -0.0099  | -0.1568   | -0.3655    | -0.3219       |
| 2   | 0.9565    | -0.0179  | -0.2836   | -0.3337    | -0.2931       |
| 3   | 0.9142    | 0.0574   | 0.9105    | 1.0784     | 1.1090        |
| 4   | 0.8807    | -0.0129  | -0.2040   | -0.2464    | -0.2150       |
| 5   | 0.8543    | -0.0175  | -0.2772   | -0.3303    | -0.2901       |
| 6   | 0.8036    | 0.0485   | 0.7689    | 0.9665     | 0.9560        |
| 7   | 0.7786    | -0.0880  | -1.3960   | -2.3521    | (+inf)        |
| 8   | 0.7563    | 0.0402   | 0.6383    | 8.3457     | (+inf)        |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.1480      | 0.8159   | -0.6777 |
| 2   | 0.0107      | 0.2777   | -0.1817 |
| 3   | 0.1172      | 0.2872   | 0.7040  |
| 4   | 0.0070      | 0.3142   | -0.1455 |
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|----------|---------|---------|
| 1   | 1.0099    | 0.8518   | 1.1680   | 0.7740  | 1.2458  |
| 2   | 0.9565    | 0.8642   | 1.0487   | 0.7586  | 1.1543  |
| 3   | 0.9142    | 0.8204   | 1.0080   | 0.7156  | 1.1128  |
| 4   | 0.8807    | 0.7826   | 0.9788   | 0.6801  | 1.0814  |
| 5   | 0.8543    | 0.7590   | 0.9495   | 0.6550  | 1.0535  |
| 6   | 0.8036    | 0.6976   | 0.9097   | 0.5990  | 1.0083  |
| 7   | 0.7786    | 0.6377   | 0.9194   | 0.5539  | 1.0032  |
| 8   | 0.7563    | 0.5818   | 0.9308   | 0.5091  | 1.0035  |

**LACTOSE HYDROUS (BiPhasic First-order reaction)**

40°C / 75 %RH

Nonlinear Regression

- **Variables**
  - \( x = \text{col}(1) \)
  - \( y = \text{col}(2) \)
  - \( \text{reciprocal}_y = 1/\text{abs}(y) \)
  - \( \text{reciprocal}_y^\text{square} = 1/y^2 \)

- **Automatic Initial Parameter Estimate Functions**
  - \( x\text{near0}(q) = \max(\text{abs}(q))-\text{abs}(q) \)
  - \( y\text{at}x\text{near0}(q,r) = x\text{at}y\text{max}(q,x\text{near0}(r)) \)
Parameters
\[ a = \frac{y}{x} \] \text{Auto \{previous: 0.206606\}}
\[ b = -\frac{\ln(0.5)}{0.5(x(x) - \text{min}(x))} \] \text{Auto \{previous: 1.381\}}
\[ c = \frac{y}{x} \] \text{Auto \{previous: 0.792722\}}
\[ d = -\frac{\ln(0.5)}{1.5(x(x) - \text{min}(x))} \] \text{Auto \{previous: 0.00910134\}}

Equation
\[ f = a \cdot e^{-b \cdot x} + c \cdot e^{-d \cdot x} \]

fit \( f \) to \( y \)
- fit \( f \) to \( y \) with weight reciprocal \( y \)
- fit \( f \) to \( y \) with weight reciprocal \( y^2 \)

Constraints
\[ b > 0 \]
\[ d > 0 \]

Options
- tolerance = 1e-6
- stepsize = 0.1
- iterations = 100

\[ R = 0.97241729 \quad \text{Rsq} = 0.94559538 \quad \text{Adj Rsq} = 0.90479192 \]

Standard Error of Estimate = 0.0317

| Coefficient | Std. Error | t     | P       |
|-------------|------------|-------|---------|
| a           | 0.2066     | 0.0416| 4.9619  | 0.0077  |
| b           | 1.3810     | 0.7609| 1.8149  | 0.1437  |
| c           | 0.7927     | 0.0283| 28.0546 | <0.0001 |
| d           | 0.0091     | 0.0035| 2.6313  | 0.0581  |

Analysis of Variance:

| DF    | SS     | MS     | F      | P       |
|-------|--------|--------|--------|---------|
| Regression | 3 | 0.0699 | 0.0233 | 23.1744 | 0.0054  |
| Residual | 4 | 0.0040 | 0.0010 |         |         |
| Total  | 7 | 0.0739 | 0.0106 |         |         |

PRESS = 0.0895

Durbin-Watson Statistic = 2.6635

Normality Test: Passed (P = 0.3537)

Constant Variance Test: Failed (P = 0.0287)

Power of performed test with alpha = 0.0500: 0.9976

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|------------|----------|-----------|------------|-----------------|

200
| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 18.0943     | 0.9975   | 7.5397 |
| 2   | 0.1286      | 0.8412   | -0.6288|
| 3   | 0.0004      | 0.2636   | 0.0359 |
| 4   | 0.0008      | 0.2764   | 0.0488 |
| 5   | 0.2734      | 0.3116   | 1.4391 |
| 6   | 0.2012      | 0.2335   | -1.3332|
| 7   | 0.0095      | 0.2208   | -0.1719|
| 8   | 1.8580      | 0.8554   | 2.8508 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 0.9993    | 0.9114   | 1.0873    | 0.8749  | 1.1238   |
| 2   | 0.8375    | 0.7567   | 0.9182    | 0.7180  | 0.9569   |
| 3   | 0.7915    | 0.7463   | 0.8367    | 0.6925  | 0.8904   |
| 4   | 0.7747    | 0.7284   | 0.8209    | 0.6752  | 0.8741   |
| 5   | 0.7652    | 0.7161   | 0.8144    | 0.6644  | 0.8660   |
| 6   | 0.7438    | 0.7013   | 0.7864    | 0.6460  | 0.8416   |
| 7   | 0.7238    | 0.6824   | 0.7651    | 0.6265  | 0.8210   |
| 8   | 0.6608    | 0.5794   | 0.7422    | 0.5409  | 0.7807   |

20 Graph: 

![Graph with data points and regression line](image-url)
LACTOSE HYDROUS (BiPhasic First-order reaction)

50°C / 20 % moisture
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {previous: 0.315899}"
b = -ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 1.61813}"
c = yatxnear0(y,x)/2 "Auto {previous: 0.686347}"
d = -ln(.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 0.0286976}"

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)

"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

R = 0.96591365   Rsqr = 0.93298917   Adj Rsqr = 0.88273105

Standard Error of Estimate = 0.0642

| Coefficient | Std. Error | t     | P     |
|-------------|------------|-------|-------|
| a           | 0.3159     | 0.0878| 3.5962| 0.0228|
| b           | 1.6181     | 1.3311| 1.2157| 0.2910|
| c           | 0.6863     | 0.0616| 11.1483| 0.0004|
| d           | 0.0287     | 0.0105| 2.7444| 0.0517|

Analysis of Variance:

|             | DF | SS   | MS    | F     | P     |
|-------------|----|------|-------|-------|-------|
| Regression  | 3  | 0.2294| 0.0765| 18.5639| 0.0082|
| Residual    | 4  | 0.0165| 0.0041| 1.0000| 1.0000|
Total  7  0.2459  0.0351
PRESS = 6.4486
Durbin-Watson Statistic = 2.9292
Normality Test: Passed (P = 0.2917)
Constant Variance Test: Passed (P = 0.1196)
Power of performed test with alpha = 0.0500: 0.9950

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Std. Res. | Std. Del. Res. |
|-----|-----------|----------|-----------|-----------|----------------|
| 1   | 1.0022    | -0.0022  | -0.0350   | -1.1714   | -1.2516        |
| 2   | 0.7296    | 0.0222   | 0.3453    | 1.1166    | 1.1656         |
| 3   | 0.6605    | -0.0497  | -0.7744   | -0.9027   | -0.8761        |
| 4   | 0.6322    | -0.0342  | -0.5335   | -0.6421   | -0.5872        |
| 5   | 0.6124    | 0.0470   | 0.7318    | 0.8779    | 0.8462         |
| 6   | 0.5614    | -0.0285  | -0.4447   | -0.4996   | -0.4468        |
| 7   | 0.5151    | 0.0864   | 1.3456    | 1.5426    | 2.0991         |
| 8   | 0.3866    | -0.0431  | -0.6718   | -1.4034   | -1.7058        |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 384.0570   | -41.8789 |        |
| 2   | 2.9478     | 3.5845   |        |
| 3   | 0.0731     | -0.5247  |        |
| 4   | 0.0463     | -0.3933  |        |
| 5   | 0.0846     | 0.5607   |        |
| 6   | 0.0163     | -0.2287  |        |
| 7   | 0.1870     | 1.1770   |        |
| 8   | 1.6562     | -3.1285  |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0022    | 0.8241   | 1.1804    | 0.7503  | 1.2542   |
| 2   | 0.7296    | 0.5601   | 0.8990    | 0.4837  | 0.9755   |
| 3   | 0.6605    | 0.5689   | 0.7520    | 0.4601  | 0.8608   |
| 4   | 0.6322    | 0.5330   | 0.7314    | 0.4283  | 0.8361   |
| 5   | 0.6124    | 0.5140   | 0.7108    | 0.4088  | 0.8160   |
| 6   | 0.5614    | 0.4803   | 0.6426    | 0.3656  | 0.7573   |
| 7   | 0.5151    | 0.4280   | 0.6023    | 0.3168  | 0.7135   |
| 8   | 0.3866    | 0.2302   | 0.5431    | 0.1495  | 0.6237   |
LACTOSE HYDROUS (BiPhasic First-order reaction)
50°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y^2 = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yhatxnear0(q,x) = xatymax(q,xnear0(r))

[Parameters]
a = yhatxnear0(y,x)/2 "Auto {previous: 0.241149}"
b = -ln(0.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 0.398833}"
c = yhatxnear0(y,x)/2 "Auto {previous: 0.783533}"
d = -ln(0.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 0.0358982}"

[Equation]
f = a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^2

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

\[ R = 0.98839567 \quad Rsqr = 0.97692600 \quad Adj Rsqr = 0.95962050 \]

Standard Error of Estimate = 0.0421

| Coefficient | Std. Error | t    | P    |
|-------------|------------|------|------|
| a           | 0.1465     | 1.6466 | 0.1750 |
| b           | 0.3448     | 1.1566 | 0.3118 |
| c           | 0.1501     | 5.2208 | 0.0064 |
| d           | 0.0134     | 2.6705 | 0.0558 |

Analysis of Variance:

|        | DF | SS    | MS   | F      | P     |
|--------|----|-------|------|--------|-------|
| Regression | 3  | 0.3007 | 0.1002 | 56.4518 | 0.0010 |
| Residual  | 4  | 0.0071 | 0.0018 |        |       |
| Total    | 7  | 0.3078 | 0.0440 |        |       |

PRESS = 0.1257

Durbin-Watson Statistic = 2.1388

Normality Test: Passed (P = 0.6862)

Constant Variance Test: Passed (P = 0.2327)

Power of performed test with alpha = 0.0500: 0.9999

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0247    | -0.0247  | -0.5858   | -1.7854    | -3.4311         |
| 2   | 0.9177    | 0.0500   | 1.1866    | 1.4512     | 1.8264          |
| 3   | 0.8379    | 0.0128   | 0.3035    | 0.3755     | 0.3311          |
| 4   | 0.7764    | -0.0225  | -0.5346   | -0.6368    | -0.5818         |
| 5   | 0.7276    | -0.0480  | -1.1394   | -1.3299    | -1.5420         |
| 6   | 0.6242    | 0.0269   | 0.6382    | 0.8509     | 0.8143          |
| 7   | 0.5517    | 0.0143   | 0.3401    | 0.4669     | 0.4158          |
| 8   | 0.3822    | -0.0094  | -0.2229   | -1.1328    | -1.1903         |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 6.6056     | -9.8753  |        |
| 2   | 0.2610     | 1.2860   |        |
| 3   | 0.0187     | 0.2414   |        |
| 4   | 0.0424     | -0.3764  |        |
| 5   | 0.1602     | -0.9281  |        |
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0247    | 0.9142   | 1.1352    | 0.8638  | 1.1856   |
| 2   | 0.9177    | 0.8504   | 0.9851    | 0.7828  | 1.0527   |
| 3   | 0.8379    | 0.7690   | 0.9068    | 0.7021  | 0.9736   |
| 4   | 0.7764    | 0.7129   | 0.8400    | 0.6433  | 0.9096   |
| 5   | 0.7276    | 0.6673   | 0.7880    | 0.5960  | 0.8593   |
| 6   | 0.6242    | 0.5468   | 0.7016    | 0.4840  | 0.7645   |
| 7   | 0.5517    | 0.4715   | 0.6318    | 0.4099  | 0.6935   |
| 8   | 0.3822    | 0.2676   | 0.4969    | 0.2184  | 0.5461   |

**LACTOSE ANHYDROUS (First-order reaction)**

25°C

Nonlinear Regression

[Variables]

\[
x = \text{col}(1)
\]

\[
y = \text{col}(2)
\]

\[
\text{reciprocal}_y = \frac{1}{\text{abs}(y)}
\]

\[
\text{reciprocal}_y\text{square} = \frac{1}{y^2}
\]

'Automatic Initial Parameter Estimate Functions

\[
x\text{near0}(q) = \max(\text{abs}(q)) - \text{abs}(q)
\]

\[
y\text{atmax}(q,r) = x\text{atmax}(q,x\text{near0}(r))
\]
[Parameters]
a = yatxnear0(y,x) "Auto {previous: 94.4043}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0216548}"

[Equation]
f=axexp(-bx)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.94008231    Rsqr = 0.88375476   Adj Rsqr = 0.86438055

Standard Error of Estimate = 4.1858

| Coefficient | Std. Error | t   | P   |
|-------------|------------|-----|-----|
| a           | 94.4043    | 2.2117 | 42.6834 | <0.0001 |
| b           | 0.0217     | 0.0034 | 6.2780  | 0.0008  |

Analysis of Variance:

|     | SS       | MS     | F        | P    |
|-----|----------|--------|----------|------|
| DF  |          |        |          |      |
| Regression | 799.2164 | 799.2164 | 45.6150 | 0.0005 |
| Residual   | 105.1254 | 17.5209 |          |      |
| Total      | 904.3419 | 129.1917|          |      |

PRESS = 355.8653

Durbin-Watson Statistic = 1.2262

Normality Test: Passed (P = 0.7290)

Constant Variance Test: Passed (P = 0.4228)

Power of performed test with alpha = 0.0500: 0.9731

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|------------|-----------------|
| 1   | 94.4043   | 5.5957   | 1.3368    | 1.5746     | -0.1277    | 1.8765          |
| 2   | 92.3820   | -0.5158  | -0.1232   | -0.1396    | 0.2923     | -0.0463         |
| 3   | 90.4030   | 1.2047   | 0.2878    | 0.3175     | -0.0507    | -0.5219         |
| 4   | 88.4664   | -0.1959  | -0.0468   | -0.5568    | -0.0463    | -0.5219         |
| 5   | 86.5712   | -2.1704  | -0.5185   | -0.5568    | -0.5219    |                 |
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|----------|---------|---------|
| 1   | 94.4043   | 88.9924  | 99.8162  | 82.8201 | 105.9885|
| 2   | 92.3820   | 87.5679  | 97.1960  | 81.0648 | 103.6992|
| 3   | 90.4030   | 86.0797  | 94.7263  | 79.2856 | 101.5203|
| 4   | 88.4664   | 84.5091  | 92.4236  | 77.4862 | 99.4465 |
| 5   | 86.5712   | 82.8404  | 90.3021  | 75.6706 | 97.4719 |
| 6   | 81.1260   | 77.2513  | 85.0007  | 70.1753 | 92.0767 |
| 7   | 76.0232   | 71.2225  | 80.8240  | 64.7117 | 87.3348 |
| 8   | 61.2211   | 52.7941  | 69.6481  | 47.9576 | 74.4845 |

**Influence Diagnostics:**

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.4802     | 0.2792   | 1.1678 |
| 2   | 0.0028     | 0.2209   | -0.0680|
| 3   | 0.0109     | 0.1782   | 0.1361 |
| 4   | 0.0002     | 0.1493   | -0.0194|
| 5   | 0.0237     | 0.1327   | -0.2041|
| 6   | 0.2127     | 0.1431   | -0.7848|
| 7   | 0.0575     | 0.2197   | -0.3206|
| 8   | 4.3554     | 0.6769   | 4.8612 |

**95% Confidence:**

**Graph 16**

2D Graph 15

![Graph](image-url)
LACTOSE ANHYDROUS (First-order reaction)
25°C / 60 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_y^2=1/y^2

'Automatic Initial Parameter Estimate Functions
near0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {{previous: 92.638}}
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {{previous: 0.0258057}}

[Equation]
f=a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^2

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.91391868   Rsqr = 0.83524736   Adj Rsqr = 0.80778859

Standard Error of Estimate = 5.7165

| Coefficient | Std. Error | t       | P         |
|-------------|------------|---------|-----------|
| a           | 92.6380    | 3.0648  | <0.0001   |
| b           | 0.0258     | 0.0051  | 0.0023    |

Analysis of Variance:

| DF | SS     | MS     | F       | P       |
|----|--------|--------|---------|---------|
| Regression | 1 | 994.0183 | 994.0183 | 30.4182 | 0.0015 |
| Residual   | 6 | 196.0702  | 32.6784  |         |        |
| Total      | 7 | 1190.0885 | 170.0126 |         |        |

PRESS = 598.5089

Durbin-Watson Statistic = 1.3746
Normality Test: Passed (P = 0.5403)

Constant Variance Test: Passed (P = 0.8393)

Power of performed test with alpha = 0.0500: 0.9342

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 92.6380   | 7.3620   | 1.2878    | 1.5256     | 1.7802          |
| 2   | 90.2780   | -0.6919  | -0.1210   | -0.1374    | -0.1256         |
| 3   | 87.9782   | 3.3852   | 0.5922    | 0.6534     | 0.6189          |
| 4   | 85.7369   | -3.2285  | -0.5648   | -0.6121    | -0.5771         |
| 5   | 83.5527   | -2.4399  | -0.4268   | -0.4582    | -0.4258         |
| 6   | 77.3283   | -8.1106  | -1.4188   | -1.5364    | -1.8009         |
| 7   | 71.5676   | -2.3579  | -0.4125   | -0.4695    | -0.4367         |
| 8   | 55.2897   | 6.4973   | 1.1366    | 1.9313     | 2.8661          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.4695     | 0.2874   | 1.1307 |
| 2   | 0.0027     | 0.2241   | -0.0675|
| 3   | 0.0464     | 0.1786   | 0.2885 |
| 4   | 0.0327     | 0.1486   | -0.2411|
| 5   | 0.0160     | 0.1323   | -0.1663|
| 6   | 0.2038     | 0.1473   | -0.7484|
| 7   | 0.0326     | 0.2281   | -0.2373|
| 8   | 3.5194     | 0.6536   | 3.9374 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 92.6380   | 85.1386  | 100.1374  | 76.7667 | 108.5094|
| 2   | 90.2780   | 83.6568  | 96.8993   | 74.8023 | 105.7538|
| 3   | 87.9782   | 82.0675  | 93.8888   | 72.7929 | 103.1634|
| 4   | 85.7369   | 80.3439  | 91.1298   | 70.7455 | 100.7283|
| 5   | 83.5527   | 78.4646  | 88.6408   | 68.6682 | 98.4371 |
| 6   | 77.3283   | 71.9606  | 82.6960   | 62.3460 | 92.3106 |
| 7   | 71.5676   | 64.8876  | 78.2477   | 56.0667 | 87.0686 |
| 8   | 55.2897   | 43.9808  | 66.5985   | 37.3022 | 73.2771 |
LACTOSE ANHYDROUS (First-order reaction)
40°C / 75 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=yamax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 84.4599}"
b = -ln(.5)/((x50(x,y)-min(x))) "Auto {previous: 0.0265749}"

[Equation]
f=a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100
\[ R = 0.82549980 \quad \text{Rsqr} = 0.68144992 \quad \text{Adj Rsqr} = 0.62835824 \]

Standard Error of Estimate = 8.1258

| Coefficient | Std. Error | t       | P       |
|-------------|------------|---------|---------|
| a           | 84.4599    | 19.3422 | <0.0001 |
| b           | 0.0266     | 3.3241  | 0.0159  |

Analysis of Variance:

| DF | SS     | MS     | F      | P     |
|----|--------|--------|--------|-------|
| Regression | 1 | 847.4934 | 847.4934 | 12.8353 | 0.0116 |
| Residual    | 6 | 396.1686 | 66.0281 |
| Total       | 7 | 1243.6620 | 177.6660 |

PRESS = 1026.1832

Durbin-Watson Statistic = 1.2736

Normality Test: Failed (P = 0.0173)

Constant Variance Test: Passed (P = 0.8849)

Power of performed test with alpha = 0.0500: 0.7469

The power of the performed test (0.7469) is below the desired power of 0.8000.
You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 84.4599   | 15.5401  | 1.9124    | 2.2677     | 5.4759          |
| 2   | 82.2449   | -3.9467  | -0.4857   | -0.5516    | -0.5168         |
| 3   | 80.0881   | -3.5230  | -0.4336   | -0.4784    | -0.4453         |
| 4   | 77.9878   | -1.2118  | -0.1491   | -0.1616    | -0.1479         |
| 5   | 75.9425   | -5.1174  | -0.6298   | -0.6761    | -0.6421         |
| 6   | 70.1231   | -6.9791  | -0.8589   | -0.9305    | -0.9182         |
| 7   | 64.7496   | -1.2352  | -0.1520   | -0.1732    | -0.1585         |
| 8   | 49.6391   | 6.9853   | 0.8597    | 1.4528     | 1.6472          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 1.0440     | 3.4892   |        |
| 2   | 0.0441     | -0.2781  |        |
| 3   | 0.0249     | -0.2076  |        |
| 4   | 0.0023     | -0.0618  |        |
| 5   | 0.0348     | -0.2507  |        |
| 6   | 0.0752     | -0.3826  |        |
LACTOSE ANHYDROUS (First-order reaction)
50°C / 20 % moisture
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=yatymax(q,xnear0(r))
[Parameters]
a = yatxnear0(y,x) "Auto {{previous: 75.7282}}"
\[ b = -\ln(0.5)/(x50(x,y) - \min(x)) \]

[Equation]
\[ f = a \cdot \exp(-b \cdot x) \]

fit f to y
*fit f to y with weight reciprocal_y
*fit f to y with weight reciprocal_y^2

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

\[ R = 0.65684694 \quad \text{Rsq} = 0.43144790 \quad \text{Adj Rsq} = 0.33668922 \]

Standard Error of Estimate = 13.3489

| Coefficient | Std. Error | t   | P   |
|-------------|------------|-----|-----|
| a           | 75.7282    | 7.2998 | 10.3740 | <0.0001 |
| b           | 0.0315     | 0.0157 | 2.0110 | 0.0910  |

Analysis of Variance:

|            | DF | SS      | MS      | F     | P     |
|------------|----|---------|---------|-------|-------|
| Regression | 1  | 811.3322 | 811.3322 | 4.5531 | 0.0768 |
| Residual   | 6  | 1069.1549 | 178.1925 |
| Total      | 7  | 1880.4871 | 268.6410 |

PRESS = 2492.0799

Durbin-Watson Statistic = 0.8292

Normality Test: Passed (P = 0.4898)

Constant Variance Test: Passed (P = 0.2897)

Power of performed test with alpha = 0.0500: 0.4209

The power of the performed test (0.4209) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 75.7282   | 24.2718  | 1.8183    | 2.1718     | 4.2865          |
| 2   | 73.3801   | 2.5987   | 0.1947    | 0.2216     | 0.2031          |
| 3   | 71.1049   | -9.5538  | -0.7157   | -0.7898    | -0.7617         |
| 4   | 68.9002   | -10.8148 | -0.8102   | -0.8776    | -0.8581         |
| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 1.0061     | 2.7998   |        |
| 2   | 0.0073     | 0.1105   |        |
| 3   | 0.0680     | -0.3556  |        |
| 4   | 0.0668     | -0.3574  |        |
| 5   | 0.0712     | -0.3749  |        |
| 6   | 0.0020     | -0.0582  |        |
| 7   | 0.0053     | -0.0939  |        |
| 8   | 1.3591     | 1.7703   |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 75.7282   | 57.8662  | 93.5902   | 38.4997 | 112.9566|
| 2   | 73.3801   | 57.7740  | 88.9863   | 37.1799 | 109.5804|
| 3   | 71.1049   | 57.2882  | 84.9215   | 35.6393 | 106.5704|
| 4   | 68.9002   | 56.3425  | 81.4578   | 33.9059 | 103.8945|
| 5   | 66.7638   | 54.8930  | 78.6347   | 32.0101 | 101.5176|
| 6   | 60.7441   | 47.9395  | 73.5486   | 25.6604 | 95.8277 |
| 7   | 55.2671   | 39.2731  | 71.2611   | 18.8979 | 91.6362 |
| 8   | 40.3344   | 14.6064  | 66.0624   | -1.2449 | 81.9136 |

2D Graph 19

- Col 25 v Col 26
- Time, weeks x % Drug [Lactose Anhydrous, 50C/20% MoistureRH]
LACTOSE ANHYDROUS (First-order reaction)
50°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 87.9779}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.057004}"

[Equation]
f=a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.82517354       Rsqr = 0.68091137   Adj Rsqr = 0.62772993

Standard Error of Estimate = 13.3636

| Coefficient | Std. Error | t    | P       |
|-------------|------------|------|---------|
| a           | 87.9779    | 7.9557 | 11.0585 | <0.0001 |
| b           | 0.0570     | 0.0186 | 3.0672  | 0.0220  |

Analysis of Variance:

|             | DF | SS          | MS     | F       | P       |
|-------------|----|-------------|--------|---------|---------|
| Regression  | 1  | 2286.5353   | 2286.5353 | 12.8036 | 0.0117  |
| Residual    | 6  | 1071.5160   | 178.5860 |         |         |
| Total       | 7  | 3358.0512   | 479.7216 |         |         |

PRESS = 2205.0436

Durbin-Watson Statistic = 1.9746

Normality Test: Passed (P = 0.4475)
Constant Variance Test: Passed ($P = 0.6194$)

Power of performed test with alpha $= 0.0500$: 0.7462

The power of the performed test (0.7462) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 87.9779   | 12.0221  | 0.8996    | 1.1196     | 1.1492          |
| 2   | 83.1031   | 5.7646   | 0.4314    | 0.4964     | 0.4628          |
| 3   | 78.4984   | -12.3779 | -0.9262   | -1.0221    | -1.0267         |
| 4   | 74.1488   | -9.1772  | -0.6867   | -0.7427    | -0.7115         |
| 5   | 70.0402   | 11.7537  | 0.8795    | 0.9460     | 0.9363          |
| 6   | 59.0307   | -15.8898 | -1.1890   | -1.3217    | -1.4331         |
| 7   | 49.7518   | -4.2700  | -0.3195   | -0.3791    | -0.3503         |
| 8   | 28.1347   | 15.7308  | 1.1771    | 1.6030     | 1.9353          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.3441     | 0.3544   | 0.8514 |
| 2   | 0.0400     | 0.2450   | 0.2636 |
| 3   | 0.1137     | 0.1788   | -0.4790|
| 4   | 0.0468     | 0.1452   | -0.2932|
| 5   | 0.0792     | 0.1357   | 0.3709 |
| 6   | 0.2058     | 0.1907   | -0.6957|
| 7   | 0.0293     | 0.2895   | -0.2236|
| 8   | 1.0978     | 0.4608   | 1.7889 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 87.9779   | 68.5111  | 107.4447  | 49.9225 | 126.0334 |
| 2   | 83.1031   | 66.9174  | 99.2888   | 46.6169 | 119.5892 |
| 3   | 78.4984   | 64.6728  | 92.3239   | 42.9961 | 114.0066 |
| 4   | 74.1488   | 61.6906  | 86.6070   | 39.1564 | 109.1412 |
| 5   | 70.0402   | 57.9956  | 82.0848   | 35.1929 | 104.8875 |
| 6   | 59.0307   | 44.7509  | 73.3105   | 23.3491 | 94.7123  |
| 7   | 49.7518   | 32.1569  | 67.3466   | 12.6190 | 86.8845  |
| 8   | 28.1347   | 5.9385   | 50.3310   | -11.3866| 67.6561  |
LACTOSE ANHYDROUS (BiPhasic First-order reaction)
25°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxmin0(q,r)=yatxmax(q,xnear0(r))

[Parameters]
a = yatxmin0(y,x)/2 "Auto {previous: 0.350559}"
b = -ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 0.141782}"
c = yatxmin0(y,x)/2 "Auto {previous: 0.640758}"
d = -ln(.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 1.12922e-012}"

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)

fit f to y
*fit f to y with weight reciprocal_y
*fit f to y with weight reciprocal_ysquare

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
Iterations = 100

R = 0.99082047  Rsqr = 0.98172520  Adj Rsqr = 0.96801910

Standard Error of Estimate = 0.0203

| Coefficient | Std. Error | t   | P   |
|-------------|------------|-----|-----|
| a           | 0.3506     | 1.0349 | 0.3592 |
| b           | 0.1418     | 1.0577 | 0.3498 |
| c           | 0.6408     | 1.8469 | 0.1385 |
| d           | 0.0000     | 0.0000 | 1.0000 |

Analysis of Variance:

| DF | SS    | MS    | F     | P     |
|----|-------|-------|-------|-------|
| Regression | 3 | 0.0888 | 0.0296 | 71.6269 | 0.0006 |
| Residual    | 4 | 0.0017 | 0.0004 |       |       |
| Total       | 7 | 0.0904 | 0.0129 |       |       |

PRESS = 0.0704

Durbin-Watson Statistic = 2.7497

Normality Test: Passed (P = 0.1963)

Constant Variance Test: Passed (P = 0.3207)

Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|------------|----------|-----------|------------|-----------------|
| 1   | 0.9913     | 0.0087   | 0.4272    | 0.8906     | 0.8614          |
| 2   | 0.9450     | -0.0263  | -1.2946   | -1.5171    | -2.0163         |
| 3   | 0.9048     | 0.0113   | 0.5567    | 0.6462     | 0.5914          |
| 4   | 0.8699     | 0.0128   | 0.6318    | 0.7610     | 0.7126          |
| 5   | 0.8396     | 0.0044   | 0.2180    | 0.2647     | 0.2312          |
| 6   | 0.7707     | -0.0213  | -1.0464   | -1.2909    | -1.4636         |
| 7   | 0.7257     | 0.0109   | 0.5376    | 1.0295     | 1.0400          |
| 8   | 0.6613     | -0.0006  | -0.0301   | -0.6127    | -0.5574         |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.6637      | 1.5759   |        |
| 2   | 0.2147      | -1.2318  |        |
| 3   | 0.0363      | 0.3487   |        |
| 4   | 0.0653      | 0.4785   |        |
| 5   | 0.0083      | 0.1593   |        |
### LACTOSE ANHYDROUS (BiPhasic First-order reaction) 
25°C / 60%RH  
Nonlinear Regression

[Variables]

\[ x = \text{col}(1) \]
\[ y = \text{col}(2) \]
\[ \text{reciprocal}_y = 1/\text{abs}(y) \]
\[ \text{reciprocal}_y\text{square} = 1/y^2 \]

'Automatic Initial Parameter Estimate Functions

\[ x\text{near}_0(q) = \text{max}(\text{abs}(q)) - \text{abs}(q) \]
\[ y\text{at}x\text{near}_0(q,r) = x\text{at}y\text{max}(q,x\text{near}_0(r)) \]

### 95% Confidence: Predicted vs. Regressed

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 0.9913    | 0.9418   | 1.0408    | 0.9162  | 1.0664   |
| 2   | 0.9450    | 0.9156   | 0.9744    | 0.8813  | 1.0086   |
| 3   | 0.9048    | 0.8761   | 0.9334    | 0.8415  | 0.9681   |
| 4   | 0.8699    | 0.8384   | 0.9013    | 0.8053  | 0.9345   |
| 5   | 0.8396    | 0.8076   | 0.8716    | 0.7747  | 0.9045   |
| 6   | 0.7707    | 0.7377   | 0.8037    | 0.7053  | 0.8361   |
| 7   | 0.7257    | 0.6775   | 0.7738    | 0.6515  | 0.7998   |
| 8   | 0.6613    | 0.6050   | 0.7177    | 0.5816  | 0.7411   |
[Parameters]
a = \frac{y}{x+y} \quad \text{"Auto \{previous: 0.376037\}}
b = -\frac{\ln(0.5)}{(0.5*(x50(x,y)-\text{min}(x)))} \quad \text{"Auto \{previous: 0.178844\}}
c = \frac{y}{x+y} \quad \text{"Auto \{previous: 0.615759\}}
d = -\frac{\ln(0.5)}{(1.5*(x50(x,y)-\text{min}(x)))} \quad \text{"Auto \{previous: 0.000567885\}}

[Equation]
f = a*\exp(-b*x)+c*\exp(-d*x)

fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^2

[Constraints]
b > 0
d > 0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

R = 0.98365048 \quad \text{Rsq} = 0.96756827 \quad \text{Adj Rsq} = 0.94324447

Standard Error of Estimate = 0.0311

| Coefficient | Std. Error | t    | P     |
|-------------|------------|------|-------|
| a           | 0.3760     | 0.2924 | 1.2861 | 0.2678 |
| b           | 0.1788     | 0.1569 | 1.1400 | 0.3179 |
| c           | 0.6158     | 0.3033 | 2.0301 | 0.1122 |
| d           | 0.0006     | 0.0222 | 0.0255 | 0.9809 |

Analysis of Variance:

| DF  | SS     | MS      | F        | P     |
|-----|--------|---------|----------|-------|
| Regression | 3 | 0.1151 | 0.0384 | 39.7787 | 0.0020 |
| Residual | 4 | 0.0039 | 0.0010 |
| Total | 7 | 0.1190 | 0.0170 |

PRESS = 0.1794

Durbin-Watson Statistic = 3.4492

Normality Test: Passed (P = 0.7641)

Constant Variance Test: Passed (P = 0.4979)

Power of performed test with alpha = 0.0500: 0.9997

Regression Diagnostics:

| Row | Predicted Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.3084      | 0.7888   | 1.0042 |
| 2   | 0.1548      | 0.2730   | -0.8887|
| 3   | 0.1657      | 0.2693   | 0.9506 |
| 4   | 0.0156      | 0.3134   | -0.2202|
| 5   | 0.0283      | 0.3119   | 0.3010 |
| 6   | 0.1776      | 0.3511   | -0.8905|
| 7   | 0.5606      | 0.6961   | 1.4923 |
| 8   | 43.3147     | 0.9965   | -12.3919|

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 0.9918    | 0.9152   | 1.0684    | 0.8764  | 1.1071   |
| 2   | 0.9299    | 0.8848   | 0.9749    | 0.8326  | 1.0272   |
| 3   | 0.8780    | 0.8333   | 0.9228    | 0.7809  | 0.9752   |
| 4   | 0.8346    | 0.7863   | 0.8829    | 0.7358  | 0.9334   |
| 5   | 0.7982    | 0.7501   | 0.8464    | 0.6995  | 0.8970   |
| 6   | 0.7208    | 0.6697   | 0.7719    | 0.6206  | 0.8211   |
| 7   | 0.6752    | 0.6032   | 0.7471    | 0.5628  | 0.7875   |
| 8   | 0.6193    | 0.5332   | 0.7054    | 0.4975  | 0.7412   |

2D Graph 22

- Dotted line: Data points
- Solid line: Trend line
- X-axis: Time, weeks
- Y-axis: Y data
- Legend: Data categories

---

Influence Diagnostics:

```
1 0.9918  0.0082  0.2641  0.5747  0.5196
2 0.9299 -0.0340 -1.0947 -1.2839 -1.4501
3 0.8780  0.0356  1.1465  1.3412  1.5658
4 0.8346 -0.0095 -0.3066 -0.3700 -0.3260
5 0.7982  0.0129  0.4147  0.4999  0.4471
6 0.7208 -0.0287 -0.9229 -1.1457 -1.2106
7 0.6752  0.0169  0.5455  0.9895  0.9860
8 0.6193 -0.0014 -0.0467 -0.7843 -0.7384
```
LACTOSE ANHYDROUS (BiPhasic First-order reaction)
40°C / 75%RH
Nonlinear Regression

[Variables]
\( x = \text{col}(1) \)
\( y = \text{col}(2) \)
\( \text{reciprocal}_y = 1/\text{abs}(y) \)
\( \text{reciprocal}_y\text{square} = 1/y^2 \)

'Automatic Initial Parameter Estimate Functions
\( x_{\text{near}0}(q) = \max(\text{abs}(q)) - \text{abs}(q) \)
\( y_{\text{at}x_{\text{near}0}(q,r)} = x_{\text{at}x_{\text{max}}(q,x_{\text{near}0}(r))} \)

[Parameters]
\( a = y_{\text{at}x_{\text{near}0}(y,x)}/2 \) "Auto \{previous: 0.232507\}
\( b = -\ln(0.5)/(0.5*(x_{50}(x,y)-\text{min}(x))) \) "Auto \{previous: 1.80374\}
\( c = y_{\text{at}x_{\text{near}0}(y,x)}/2 \) "Auto \{previous: 0.766668\}
\( d = -\ln(0.5)/(1.5*(x_{50}(x,y)-\text{min}(x))) \) "Auto \{previous: 0.0170271\}

[Equation]
\( f = a*\exp(-b*x)+c*\exp(-d*x) \)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y\text{square}

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

R = 0.98001052  
Rsqr = 0.96042061  
Adj Rsqr = 0.93073607

Standard Error of Estimate = 0.0351

| Coefficient | Std. Error | t    | P   |
|-------------|------------|------|-----|
| a           | 0.2325     | 5.1038 | 0.0070 |
| b           | 1.8037     | 1.5753 | 0.1903 |
| c           | 0.7667     | 25.8543 | <0.0001 |
| d           | 0.0170     | 4.0412 | 0.0156 |

Analysis of Variance:

| DF | SS    | MS   | F    | P    |
|----|-------|------|------|------|
| Regression | 3 | 0.1194 | 0.0398 | 32.3542 | 0.0029 |
| Residual   | 4 | 0.0049 | 0.0012 |      |      |
| Total      | 7 | 0.1244 | 0.0178 |      |      |
PRESS = 3.2448

Durbin-Watson Statistic = 1.5293

Normality Test: Passed (P = 0.3720)

Constant Variance Test: Passed (P = 0.1597)

Power of performed test with alpha = 0.0500: 0.9993

| Regression Diagnostics: |
|------------------------|
| **Row** | **Predicted** | **Residual** | **Std. Res.** | **Stud. Res.** | **Stud. Del. Res.** |
| 1 | 0.9992 | 0.0008 | 0.0235 | 1.0960 | 1.1347 |
| 2 | 0.7920 | -0.0090 | -0.2575 | -0.9725 | -0.9639 |
| 3 | 0.7473 | 0.0183 | 0.5230 | 0.6052 | 0.5499 |
| 4 | 0.7295 | 0.0382 | 1.0899 | 1.3036 | 1.4887 |
| 5 | 0.7164 | -0.0081 | -0.2312 | -0.2741 | -0.2396 |
| 6 | 0.6805 | -0.0491 | -1.3992 | -1.5632 | -2.1704 |
| 7 | 0.6466 | -0.0115 | -0.3276 | -0.3708 | -0.3268 |
| 8 | 0.5454 | 0.0208 | 0.5943 | 1.3600 | 1.6063 |

| Influence Diagnostics: |
|------------------------|
| **Row** | **Cook'sDist** | **Leverage** | **DFFITS** |
| 1 | 651.5372 | 0.9995 | 52.8535 |
| 2 | 3.1371 | 0.9299 | -3.5108 |
| 3 | 0.0311 | 0.2533 | 0.3203 |
| 4 | 0.1830 | 0.3011 | 0.9770 |
| 5 | 0.0076 | 0.2887 | -0.1527 |
| 6 | 0.1516 | 0.1988 | -1.0811 |
| 7 | 0.0097 | 0.2196 | -0.1733 |
| 8 | 1.9589 | 0.8090 | 3.3063 |

| 95% Confidence: |
|----------------|
| **Row** | **Predicted** | **Regr. 5%** | **Regr. 95%** | **Pop. 5%** | **Pop. 95%** |
| 1 | 0.9992 | 0.9018 | 1.0965 | 0.8615 | 1.1369 |
| 2 | 0.7920 | 0.6981 | 0.8859 | 0.6567 | 0.9273 |
| 3 | 0.7473 | 0.6983 | 0.7963 | 0.6383 | 0.8563 |
| 4 | 0.7295 | 0.6761 | 0.7830 | 0.6184 | 0.8406 |
| 5 | 0.7164 | 0.6640 | 0.7687 | 0.6058 | 0.8269 |
| 6 | 0.6805 | 0.6371 | 0.7240 | 0.5739 | 0.7872 |
| 7 | 0.6466 | 0.6010 | 0.6923 | 0.5391 | 0.7542 |
| 8 | 0.5454 | 0.4578 | 0.6336 | 0.4144 | 0.6764 |
LACTOSE ANHYDROUS (BiPhasic First-order reaction)

50°C / 20% moisture
Nonlinear Regression

[Variables]
\( x = \text{col}(1) \)
\( y = \text{col}(2) \)
\( \text{reciprocal}_y = 1/\text{abs}(y) \)
\( \text{reciprocal}_y^{\text{square}} = 1/y^2 \)

'Automatic Initial Parameter Estimate Functions
\( x_{\text{near}}(q) = \text{max}(|q|) - |q| \)
\( y_{\text{at max}}(q, x_{\text{near}}(r,)) \)

[Parameters]
\( a = y_{\text{at max}}(y, x)/2 \) "Auto \{previous: 0.437135\}"
\( b = -\ln(0.5)/(0.5*(x_{50}(x, y) - \text{min}(x))) \) "Auto \{previous: 0.915575\}"
\( c = y_{\text{at max}}(y, x)/2 \) "Auto \{previous: 0.567457\}"
\( d = -\ln(0.5)/(1.5*(x_{50}(x, y) - \text{min}(x))) \) "Auto \{previous: 0.00496292\}"

[Equation]
\( f = a*\exp(-b*x) + c*\exp(-d*x) \)

\( \text{fit } f \text{ to } y \)
\( \text{fit } f \text{ to } y \text{ with weight reciprocal}_y \)
\( \text{fit } f \text{ to } y \text{ with weight reciprocal}_y^{\text{square}} \)

[Constraints]
\( b > 0 \)
\( d > 0 \)

[Options]
\( \text{tolerance} = 1e-6 \)
stepsize=0.1  
iterations=100

R = 0.99237002  Rsqr = 0.98479826  Adj Rsqr = 0.97339695

Standard Error of Estimate = 0.0267

| Coefficient | Std. Error | t    | P    |
|-------------|------------|------|------|
| a           | 0.371      | 0.0378 | 11.5746 | 0.0003 |
| b           | 0.9156     | 0.1858 | 4.9281  | 0.0079 |
| c           | 0.5675     | 0.0294 | 19.3051 | <0.0001 |
| d           | 0.0050     | 0.0044 | 1.1327  | 0.3206 |

Analysis of Variance:

|             | DF | SS   | MS   | F    | P    |
|-------------|----|------|------|------|------|
| Regression  | 3  | 0.1852 | 0.0617 | 86.3759 | 0.0004 |
| Residual    | 4  | 0.0029 | 0.0007 |       |      |
| Total       | 7  | 0.1880 | 0.0269 |       |      |

PRESS = 0.0903

Durbin-Watson Statistic = 2.9064

Normality Test: Failed (P = 0.0080)

Constant Variance Test: Passed (P = 0.8849)

Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0046    | -0.0046  | -0.1718   | -1.3469    | -1.5779         |
| 2   | 0.7396    | 0.0202   | 0.7542    | 1.2487     | 1.3843          |
| 3   | 0.6319    | -0.0164  | -0.6129   | -0.7524    | -0.7033         |
| 4   | 0.5871    | -0.0063  | -0.2340   | -0.2685    | -0.2347         |
| 5   | 0.5675    | -0.0202  | -0.7543   | -0.9040    | -0.8776         |
| 6   | 0.5488    | 0.0403   | 1.5069    | 1.8406     | 4.0744          |
| 7   | 0.5400    | -0.0086  | -0.3227   | -0.3760    | -0.3315         |
| 8   | 0.5138    | -0.0044  | -0.1659   | -0.5439    | -0.4895         |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 27.4338    | -12.2720 |        |
| 2   | 0.6787     | 1.8266   |        |
| 3   | 0.0718     | -0.5008  |        |
| 4   | 0.0057     | -0.1322  |        |
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 1.0046    | 0.9310   | 1.0782    | 0.9001  | 1.1091  |
| 2   | 0.7396    | 0.6805   | 0.7988    | 0.6447  | 0.8345  |
| 3   | 0.6319    | 0.5888   | 0.6750    | 0.5461  | 0.7177  |
| 4   | 0.5871    | 0.5507   | 0.6235    | 0.5044  | 0.6698  |
| 5   | 0.5675    | 0.5266   | 0.6084    | 0.4828  | 0.6523  |
| 6   | 0.5488    | 0.5062   | 0.5914    | 0.4632  | 0.6344  |
| 7   | 0.5400    | 0.5019   | 0.5781    | 0.4566  | 0.6235  |
| 8   | 0.5138    | 0.4432   | 0.5845    | 0.4113  | 0.6163  |

LACTOSE ANHYDROUS (BiPhasic First-order reaction)
50°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxmin0(q,r)=xatymax(q,xnear0(r))
[Parameters]
a = yaxtnear0(y,x)/2  "Auto {previous: 0.574083}
b = -ln(.5)/(0.5*(x50(x,y)-min(x)))  "Auto {previous: 0.246131}
c = yaxtnear0(y,x)/2  "Auto {previous: 0.415514}
d = -ln(.5)/(1.5*(x50(x,y)-min(x)))  "Auto {previous: 1.41089e-010}

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^2

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

R = 0.91174814  Rsqr = 0.83128468  Adj Rsqr = 0.70474819

Standard Error of Estimate = 0.1190

| Coefficient | Std. Error | t | P |
|-------------|------------|---|---|
| a           | 0.5741     | 1.0635 | 0.3475 |
| b           | 0.2461     | 0.7469 | 0.4966 |
| c           | 0.4155     | 0.7312 | 0.5052 |
| d           | 0.0000     | 0.0000 | 1.0000 |

Analysis of Variance:

| DF | SS   | MS   | F    | P    |
|----|------|------|------|------|
| Regression | 3 | 0.2791 | 0.0930 | 6.5695 | 0.0503 |
| Residual   | 4 | 0.0567 | 0.0142 |      |      |
| Total      | 7 | 0.3358 | 0.0480 |      |      |

PRESS = 8.7426

Durbin-Watson Statistic = 2.7419

Normality Test: Passed (P = 0.0932)

Constant Variance Test: Passed (P = 0.7941)

Power of performed test with alpha = 0.0500: 0.9304

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
|     |           |          |           |            |                 |

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| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 0.9896    | 0.6901   | 1.2891    | 0.5436  | 1.4355   |
| 2   | 0.8643    | 0.6898   | 1.0389    | 0.4906  | 1.2381   |
| 3   | 0.7664    | 0.5881   | 0.9447    | 0.3910  | 1.1419   |
| 4   | 0.6899    | 0.5047   | 0.8750    | 0.3111  | 1.0686   |
| 5   | 0.6300    | 0.4512   | 0.8088    | 0.2543  | 1.0057   |
| 6   | 0.5180    | 0.3168   | 0.7192    | 0.1311  | 0.9049   |
| 7   | 0.4645    | 0.2007   | 0.7283    | 0.0417  | 0.8873   |
| 8   | 0.4197    | 0.0903   | 0.7491    | -0.0469 | 0.8862   |

95% Confidence:

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.0492      | 0.3863   |        |
| 2   | 0.0056      | 0.1307   |        |
| 3   | 0.1132      | -0.6847  |        |
| 4   | 0.0190      | -0.2436  |        |
| 5   | 0.3647      | 3.0372   |        |
| 6   | 0.1241      | -0.6865  |        |
| 7   | 0.0080      | -0.1554  |        |
| 8   | 151.2061    | 162.1749 |        |

Graph 25

Col 30 v Col 31

Time, weeks v D/Do [Lactose anhydrous, 50C/Dry]
STARCH (First-order reaction)
25°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic initial Parameter Estimate Functions
xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q, r) = yatymax(q, xnear0(r))

[Parameters]
a = yatxnear0(y, x) "Auto \{previous: 99.589\}"
b = -ln(0.5)/(x50(x, y) - min(x)) "Auto \{previous: 0.0057966\}"

[Equation]
f = a * exp(-b * x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b > 0

[Options]
tolerance = 0.0001
step size = 100
iterations = 100

R = 0.88627805  Rsqr = 0.78548878  Adj Rsqr = 0.75484432

Standard Error of Estimate = 1.8803

| Coefficient | Std. Error | t     | P     |
|-------------|------------|-------|-------|
a  | 99.5890    | 0.9211| <0.0001|
b  | 0.0058     | 0.0012| 0.0016|

Analysis of Variance:

|                | DF | SS     | MS     | F     | P     |
|----------------|----|--------|--------|-------|-------|
| Regression     | 1  | 90.6282| 90.6282| 25.6323| 0.0015|
| Residual       | 7  | 24.7499| 3.5357 |       |       |
| Total          | 8  | 115.3781| 14.4223|       |       |

PRESS = 35.3794

Durbin-Watson Statistic = 2.4030
Normality Test: Passed \( (P = 0.5111) \)

Constant Variance Test: Passed \( (P = 0.8437) \)

Power of performed test with alpha = 0.0500: 0.9305

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Std. Res. | Std. Del. Res. |
|-----|-----------|----------|-----------|-----------|---------------|
| 1   | 99.5890   | 0.4110   | 0.2186    | 0.2507    | 0.2332        |
| 2   | 99.0134   | 1.3790   | 0.7334    | 0.8191    | 0.7975        |
| 3   | 98.4411   | 1.3947   | 0.7417    | 0.8118    | 0.7897        |
| 4   | 97.8722   | -2.2145  | -1.1777   | -1.2701   | -1.3405       |
| 5   | 97.3065   | -0.3822  | -0.2032   | -0.2170   | -0.2016       |
| 6   | 96.1849   | -0.4487  | -0.2386   | -0.2531   | -0.2354       |
| 7   | 95.0762   | -2.9799  | -1.5848   | -1.6971   | -2.0481       |
| 8   | 93.9804   | 2.5533   | 1.3579    | 1.4916    | 1.6719        |
| 9   | 88.6876   | 0.2894   | 0.1539    | 0.2922    | 0.2721        |

**Influence Diagnostics:**

| Row | Cook’sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.0099     | 0.2400   | 0.1310 |
| 2   | 0.0830     | 0.1984   | 0.3968 |
| 3   | 0.0652     | 0.1653   | 0.3514 |
| 4   | 0.1316     | 0.1403   | -0.5414|
| 5   | 0.0033     | 0.1231   | -0.0755|
| 6   | 0.0040     | 0.1114   | -0.0833|
| 7   | 0.2115     | 0.1280   | -0.7848|
| 8   | 0.2297     | 0.1712   | 0.7598 |
| 9   | 0.1111     | 0.7224   | 0.4390 |

**95% Confidence:**

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 99.5890   | 97.4109  | 101.7671  | 94.6379 | 104.5402 |
| 2   | 99.0134   | 97.0329  | 100.9940  | 94.1459 | 103.8809 |
| 3   | 98.4411   | 96.6336  | 100.2487  | 93.6415 | 103.2408 |
| 4   | 97.8722   | 96.2070  | 99.5373   | 93.1243 | 102.6201 |
| 5   | 97.3065   | 95.7464  | 98.8665   | 92.5944 | 102.0185 |
| 6   | 96.1849   | 94.7011  | 97.6687   | 91.4975 | 100.8723 |
| 7   | 95.0762   | 93.4853  | 96.6672   | 90.3539 | 99.7986  |
| 8   | 93.9804   | 92.1408  | 95.8200   | 89.1685 | 98.7922  |
| 9   | 88.6876   | 84.9085  | 92.4667   | 82.8522 | 94.5229  |
STARCH (First-order reaction)
25°C / 60 %RH
Nonlinear Regression

[Variables]
\( x = \text{col}(1) \)
\( y = \text{col}(2) \)
\( \text{reciprocal}_y = 1/\text{abs}(y) \)
\( \text{reciprocal}_y^2 = 1/y^2 \)

'Automatic Initial Parameter Estimate Functions
\( x_{\text{near0}}(q) = \max(\text{abs}(q))-\text{abs}(q) \)
\( y_{\text{atxmax0}}(q,r) = y_{\text{atxmax0}}(q,x_{\text{near0}}(r)) \)

[Parameters]
\( a = y_{\text{atxmax0}}(y,x) \)
\( b = -\ln(.5)/(x_{50}(x,y)-\text{min}(x)) \)

[Equation]
\( f = a \exp(-b \cdot x) \)

fit f to y
"fit f to y with weight \text{reciprocal}_y"
"fit f to y with weight \text{reciprocal}_y^2"

[Constraints]
\( b > 0 \)

[Options]
tolerance=0.0001
stepsize=100
iterations=100
\[ R = 0.72053762 \quad \text{Rsqr} = 0.51917447 \quad \text{Adj Rsqr} = 0.45048510 \]

**Standard Error of Estimate** = 2.3001

| Coefficient | Std. Error | \( t \) | \( P \) |
|-------------|------------|--------|--------|
| a | 100.4908 | 1.1173 | 89.9384 | <0.0001 |
| b | 0.0037 | 0.0014 | 2.7187 | 0.0298 |

**Analysis of Variance:**

| DF | SS   | MS     | F     | P     |
|----|------|--------|-------|-------|
| Regression | 1 | 39.9875 | 39.9875 | 7.5583 | 0.0285 |
| Residual   | 7 | 37.0338 | 5.2905 |       |       |
| Total      | 8 | 77.0213 | 9.6277 |       |       |

PRESS = 57.1891

Durbin-Watson Statistic = 1.5556

Normality Test: Passed (\( P = 0.2828 \))

Constant Variance Test: Passed (\( P = 0.6116 \))

Power of performed test with alpha = 0.0500: 0.6049

The power of the performed test (0.6049) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 106.4908  | -0.4908  | -0.2134   | -0.2441    | -0.2270         |
| 2   | 100.1152  | 1.5850   | 0.6891    | 0.7687     | 0.7438          |
| 3   | 99.7410   | 4.1537   | 1.8059    | 1.9758     | 2.7505          |
| 4   | 99.3681   | -1.7579  | -0.7643   | -0.8243    | -0.8031         |
| 5   | 98.9967   | -2.4960  | -1.0852   | -1.1591    | -1.1937         |
| 6   | 98.2579   | -1.5653  | -0.6805   | -0.7218    | -0.6946         |
| 7   | 97.5247   | -1.5963  | -0.6940   | -0.7426    | -0.7163         |
| 8   | 96.7970   | 1.5069   | 0.6552    | 0.7184     | 0.6911          |
| 9   | 93.2389   | 0.6621   | 0.2878    | 0.5570     | 0.5275          |

**Influence Diagnostics:**

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.0092      | 0.2360   | -0.1262 |
| 2   | 0.0722      | 0.1964   | 0.3678  |
| 3   | 0.3847      | 0.1646   | 1.2210  |
| 4   | 0.0555      | 0.1404   | -0.3245 |
| 5   | 0.0946      | 0.1235   | -0.4481 |
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|----------|---------|---------|
| 1   | 100.4908  | 97.8488  | 103.1329 | 94.4442 | 106.5375 |
| 2   | 100.1152  | 97.7045  | 102.5259 | 94.1660 | 106.0644 |
| 3   | 99.7410   | 97.5341  | 101.9478 | 93.8714 | 105.6105 |
| 4   | 99.3681   | 97.3304  | 101.4058 | 93.5600 | 105.1762 |
| 5   | 98.9967   | 97.0854  | 100.9079 | 93.2317 | 104.7616 |
| 6   | 98.2579   | 96.4441  | 100.0718 | 92.5245 | 103.9913 |
| 7   | 97.5247   | 95.5896  | 99.4598  | 91.7518 | 103.2976 |
| 8   | 96.7970   | 94.5653  | 99.0286  | 90.9180 | 102.6759 |
| 9   | 93.2389   | 88.5825  | 97.8952  | 86.0790 | 100.3987 |

95% Confidence:

**STARCH (First-order reaction)**

40°C / 75 %RH Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y_square = 1/y^2
😊Automatic Initial Parameter Estimate Functions😊
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = xatymax(q,xnear0(r))

[Parameters]
\[ a = \text{exp}(y, x) \quad \text{"Auto \{previous: 101.175\}} \]
\[ b = -\text{ln}(0.5)/(x50(x,y)-\text{min}(x)) \quad \text{"Auto \{previous: 0.000653841\}} \]

**Equation**

\[ f = a \cdot \text{exp}(-b \cdot x) \]

**fit f to y**

"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^2

**Constraints**

\[ b > 0 \]

**Options**

tolerance = 0.0001
stepsize = 100
iterations = 100

\[ R = 0.28113767 \quad \text{R}^2 = 0.07903839 \quad \text{Adj R}^2 = 0.0000000 \]

**Standard Error of Estimate = 1.4853**

| Coefficient | Std. Error | \( t \) | \( P \) |
|-------------|------------|---------|--------|
| \( a \)     | 101.1749   | 0.7123  |       |
| \( b \)     | 0.0007     | 0.0008  | 0.4653 |

**Analysis of Variance:**

|              | DF | SS    | MS   | \( F \) | \( P \) |
|--------------|----|-------|------|---------|--------|
| Regression   | 1  | 1.3254| 1.3254| 0.6008  | 0.4637 |
| Residual     | 7  | 15.4434| 2.2062|         |        |
| Total        | 8  | 16.7688| 2.0961|         |        |

PRESS = 23.1707

Durbin-Watson Statistic = 2.9328

Normality Test: Passed (\( P = 0.7798 \))

Constant Variance Test: Passed (\( P = 0.4620 \))

Power of performed test with alpha = 0.0500: 0.1052

The power of the performed test (0.1052) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 101.1749  | -1.1749  | -0.7910   | -0.9014    | -0.8877         |
| 2   | 101.1088  | -0.2626  | -0.1768   | -0.1968    | -0.1827         |
| 3   | 101.0427  | 2.3228   | 1.5639    | 1.7100     | 2.0747          |
| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.1214     | 0.2300   | -0.4852|
| 2   | 0.0046     | 0.1934   | -0.0895|
| 3   | 0.2860     | 0.1636   | 0.9177 |
| 4   | 0.0490     | 0.1405   | -0.3031|
| 5   | 0.0152     | 0.1241   | 0.1639 |
| 6   | 0.1243     | 0.1111   | -0.5455|
| 7   | 0.1104     | 0.1246   | 0.4931 |
| 8   | 0.0011     | 0.1642   | 0.0432 |
| 9   | 0.3511     | 0.7484   | -0.7893|

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 101.1749  | 99.4905  | 102.8593  | 97.2796 | 105.0702 |
| 2   | 101.1088  | 99.5640  | 102.6536  | 97.2718 | 104.9457 |
| 3   | 101.0427  | 99.6220  | 102.4634  | 97.2540 | 104.8314 |
| 4   | 100.9766  | 99.6601  | 102.2932  | 97.2258 | 104.7275 |
| 5   | 100.9106  | 99.6736  | 102.1477  | 97.1869 | 104.6344 |
| 6   | 100.7788  | 99.6080  | 101.9495  | 97.0765 | 104.4810 |
| 7   | 100.6471  | 99.4074  | 101.8867  | 96.9225 | 104.3717 |
| 8   | 100.5155  | 99.0921  | 101.9389  | 96.7258 | 104.3053 |
| 9   | 99.8605   | 96.8220  | 102.8990  | 95.2163 | 104.5047 |

2D Graph 29
STARCH (First-order reaction)
50°C / 20 % moisture
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {}{previous: 91.2028}"
b = -ln(0.5)/(x50(x,y)-min(x)) "Auto {}{previous: 0.0200502}"

[Equation]
f = a*exp(-b*x)
fit f to y
“fit f to y with weight reciprocal_y
“fit f to y with weight reciprocal_ysquare

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

R = 0.68798381    Rsqr = 0.47332173    Adj Rsqr = 0.39808197

Standard Error of Estimate = 9.8936

| Coefficient | Std. Error | t    | P     |
|-------------|------------|------|-------|
| a           | 91.2028    | 17.7715 | <0.0001 |
| b           | 0.0201     | 2.4673    | 0.0430   |

Analysis of Variance:

|            | DF | SS    | MS    | F      | P    |
|------------|----|-------|-------|--------|------|
| Regression | 1  | 615.7738 | 615.7738 | 6.2908 | 0.0405 |
| Residual   | 7  | 685.1887 | 97.8841 |        |      |
| Total      | 8  | 1300.9624 | 162.6203 |        |      |

PRESS = 2008.9507

Durbin-Watson Statistic = 0.7846
Normality Test: Passed (P = 0.7679)

Constant Variance Test: Passed (P = 0.4905)

Power of performed test with alpha = 0.0500: 0.5429

The power of the performed test (0.5429) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 91.2028   | 8.7972   | 0.8892    | 1.0400     | 1.0472          |
| 2   | 89.3924   | 7.8634   | 0.7948    | 0.8952     | 0.8808          |
| 3   | 87.6179   | 2.8554   | 0.2886    | 0.3166     | 0.2952          |
| 4   | 85.8786   | 0.1941   | 0.0196    | 0.0211     | 0.0196          |
| 5   | 84.1739   | -3.8098  | -0.3851   | -0.4107    | -0.3849         |
| 6   | 80.8653   | -16.4729 | -1.6650   | -1.7692    | -2.2030         |
| 7   | 77.6867   | -9.1857  | -0.9284   | -1.0016    | -1.0019         |
| 8   | 74.6331   | -2.4393  | -0.2466   | -0.2744    | -0.2554         |
| 9   | 61.0737   | 12.7112  | 1.2848    | 2.1489     | 3.4105          |

**Influence Diagnostics:**

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.1991      | 0.2691   | 0.6354 |
| 2   | 0.1077      | 0.2118   | 0.4566 |
| 3   | 0.0102      | 0.1689   | 0.1331 |
| 4   | 0.0000      | 0.1391   | 0.0079 |
| 5   | 0.0116      | 0.1208   | -0.1427|
| 6   | 0.2021      | 0.1144   | -0.7917|
| 7   | 0.0822      | 0.1408   | -0.4056|
| 8   | 0.0090      | 0.1926   | -0.1248|
| 9   | 4.1505      | 0.6425   | 4.5725 |

**95% Confidence:**

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|--------|---------|
| 1   | 91.2028   | 79.0676  | 103.3379  | 64.8480| 117.5576|
| 2   | 89.3924   | 78.6258  | 100.1589  | 63.6390| 115.1457|
| 3   | 87.6179   | 78.0020  | 97.2337   | 62.3240| 112.9117|
| 4   | 85.8786   | 77.1545  | 94.6027   | 60.9102| 110.8471|
| 5   | 84.1739   | 76.0423  | 92.3055   | 59.4062| 108.9415|
| 6   | 80.8653   | 72.9535  | 88.7770   | 56.1689| 105.5616|
| 7   | 77.6867   | 68.9082  | 86.4651   | 52.6992| 102.6742|
| 8   | 74.6331   | 64.3657  | 84.9004   | 49.0844| 100.1817|
| 9   | 61.0737   | 42.3208  | 79.8267   | 31.0906| 91.0569 |
STARCH (First-order reaction)  
50°C  
Nonlinear Regression  

[Variables]  
x = col(1)  
y = col(2)  
reciprocal_y=1/abs(y)  
reciprocal_ysquare=1/y^2  

'Automatic Initial Parameter Estimate Functions  
xnear0(q)=max(abs(q))-abs(q)  
yatxnear0(q,r)=yatymax(q,xnear0(r))  

[Parameters]  
a = yatxnear0(y,x) "Auto {previous: 98.2956}"  
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0556155}"  

[Equation]  
f=a*exp(-b*x)  
fit f to y  
"fit f to y with weight reciprocal_y  
"fit f to y with weight reciprocal_ysquare  

[Constraints]  
b>0  

[Options]  
tolerance=0.0001  
stepsize=100  
iterations=100  

R = 0.97292605  
Rsqr = 0.94658509  
Adj Rsqr = 0.93895439
Standard Error of Estimate = 5.0520

| Coefficient | Std. Error | t     | P     |
|--------------|------------|-------|-------|
| a 98.2956    | 32.9031    | <0.0001 |       |
| b 0.0556     | 9.3630     | <0.0001 |       |

Analysis of Variance:

| DF | SS      | MS     | F     | P     |
|----|---------|--------|-------|-------|
| Regression | 1      | 3166.0193 | 3166.0193 | 124.0496 | <0.0001 |
| Residual    | 7      | 178.6555   | 25.5222   |       |       |
| Total       | 8      | 3344.6748   | 418.0844   |       |       |

PRESS = 366.1160

Durbin-Watson Statistic = 1.1962

Normality Test: Passed (P = 0.5334)

Constant Variance Test: Failed (P = 0.0361)

Power of performed test with alpha = 0.0500: 0.9995

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 98.2956   | 1.7044   | 0.3374    | 0.4184     | 0.3923          |
| 2   | 92.9781   | 1.6679   | 0.3302    | 0.3789     | 0.3545          |
| 3   | 87.9482   | 1.6226   | 0.3212    | 0.3531     | 0.3298          |
| 4   | 83.1905   | 4.0165   | 0.7950    | 0.8548     | 0.8362          |
| 5   | 78.6901   | -2.6386  | -0.5223   | -0.5569    | -0.5274         |
| 6   | 70.4066   | -7.3276  | -1.4504   | -1.5614    | -1.7907         |
| 7   | 62.9950   | -3.4158  | -0.6761   | -0.7495    | -0.7236         |
| 8   | 56.3637   | -2.5136  | -0.4975   | -0.5728    | -0.5432         |
| 9   | 32.3195   | 8.6927   | 1.7207    | 2.2455     | 3.9314          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.0471     | 0.2876   |        |
| 2   | 0.0228     | 0.1997   |        |
| 3   | 0.0130     | 0.1505   |        |
| 4   | 0.0569     | 0.3301   |        |
| 5   | 0.0212     | -0.1951  |        |
| 6   | 0.1937     | -0.7138  |        |
| 7   | 0.0643     | -0.3462  |        |
| 8   | 0.0534     | -0.3099  |        |
| 9   | 1.7729     | 3.2967   |        |
95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|--------|---------|
| 1   | 98.2956   | 91.2315  | 105.3598  | 84.4173| 112.1740|
| 2   | 92.9781   | 87.1155  | 98.8407   | 79.6711| 106.2851|
| 3   | 87.9482   | 82.9879  | 92.9086   | 75.0134| 100.8831|
| 4   | 83.1905   | 78.8036  | 87.5774   | 70.4645| 95.9165 |
| 5   | 78.6901   | 74.5448  | 82.8354   | 66.0454| 91.3348 |
| 6   | 70.4066   | 65.9831  | 74.8300   | 57.6679| 83.1452 |
| 7   | 62.9950   | 57.8392  | 68.1509   | 49.9839| 76.0961 |
| 8   | 56.3637   | 50.4442  | 62.2831   | 43.0315| 69.6958 |
| 9   | 32.3195   | 24.6437  | 39.9952   | 18.1200| 46.5189 |

STARCH (BiPhasic First-order reaction)

25°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y_square = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {{previous: 0.0275784}}
b = -ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto {{previous: 0.361565}}
c = yatxnear0(y,x)/2 "Auto {previous: 0.979507}
d = -ln(.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 0.00457035}

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)

fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y'square

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
iterations=100

R = 0.90054905    Rsqr = 0.81098859   Adj Rsqr = 0.69758174

Standard Error of Estimate = 0.0209

| Coefficient | Std. Error | t    | P     |
|-------------|------------|------|-------|
| a           | 0.0276     | 0.5682 | 0.5945 |
| b           | 0.3616     | 0.3156 | 0.7651 |
| c           | 0.9795     | 19.6638| <0.0001|
| d           | 0.0046     | 1.4037 | 0.2194 |

Analysis of Variance:

| DF | SS     | MS   | F    | P     |
|----|--------|------|------|-------|
| Regression | 3  | 0.0094 | 0.0031 | 7.1511 | 0.0294 |
| Residual    | 5  | 0.0022 | 0.0004 |       |       |
| Total       | 8  | 0.0115 | 0.0014 |       |       |

PRESS = 0.0580

Durbin-Watson Statistic = 2.9669

Normality Test: Passed (P = 0.7524)

Constant Variance Test: Passed (P = 0.7418)

Power of performed test with alpha = 0.0500: 0.9509

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0071    | -0.0071  | -0.3393   | -0.9380    | -0.9243         |
| 2   | 0.9943    | 0.0097   | 0.4631    | 0.5547     | 0.5121          |
| 3   | 0.9840    | 0.0144   | 0.6886    | 0.8374     | 0.8078          |
Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 1.4614      | 0.8692   | -2.3823|
| 2   | 0.0334      | 0.3028   | 0.3375 |
| 3   | 0.0839      | 0.3237   | 0.5589 |
| 4   | 0.1181      | 0.2902   | -0.7012|
| 5   | 0.0002      | 0.2344   | 0.0267 |
| 6   | 0.0004      | 0.2471   | 0.0339 |
| 7   | 0.2945      | 0.3500   | -1.2945|
| 8   | 0.5340      | 0.4013   | 2.1707 |
| 9   | 28.0975     | 0.9812   | -12.5570|

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0071    | 0.9570   | 1.0571    | 0.9337  | 1.0805   |
| 2   | 0.9943    | 0.9647   | 1.0238    | 0.9330  | 1.0555   |
| 3   | 0.9840    | 0.9534   | 1.0145    | 0.9222  | 1.0457   |
| 4   | 0.9755    | 0.9466   | 1.0044    | 0.9145  | 1.0365   |
| 5   | 0.9683    | 0.9423   | 0.9942    | 0.9086  | 1.0279   |
| 6   | 0.9562    | 0.9295   | 0.9829    | 0.8962  | 1.0161   |
| 7   | 0.9459    | 0.9141   | 0.9776    | 0.8835  | 1.0082   |
| 8   | 0.9365    | 0.9025   | 0.9705    | 0.8729  | 1.0000   |
| 9   | 0.8940    | 0.8408   | 0.9471    | 0.8184  | 0.9695   |
STARCH (BiPhasic First-order reaction)
25°C / 60%RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y^2 = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q,r) = yatxmax(q, xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {previous: 0.0463895"
b = -ln(0.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 0.200272"
c = yatxnear0(y,x)/2 "Auto {previous: 0.970291"
d = -ln(0.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 0.00152882"

[Equation]
f = a*exp(-b*x) + c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^2

[Constraints]
b > 0
d > 0

[Options]
tolerance = 1e-6
stepsize = 0.1
iterations = 100

R = 0.75880383     Rsqr = 0.57578325     Adj Rsqr = 0.32125321

Standard Error of Estimate = 0.0256

Coefficient          Std. Error  t      P
a  0.0464             0.1746     0.2657  0.8011
b  0.2003             0.9406     0.2129  0.8398
c  0.9703             0.1830     5.3014  0.0032
d  0.0015             0.0090     0.1694  0.8722

Analysis of Variance:

DF  SS    MS   F    P
Regression 3  0.0044 0.0015  2.2621  0.1989
Residual  5   0.0033 0.0007
Total     8   0.0077 0.0010

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PRESS = 20.5658

Durbin-Watson Statistic = 1.9522

Normality Test: Passed (P = 0.2124)

Constant Variance Test: Passed (P = 0.2852)

Power of performed test with alpha = 0.0500: 0.6820

The power of the performed test (0.6820) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0167    | -0.0167  | -0.6525   | -1.4311    | -1.6659         |
| 2   | 1.0068    | 0.0102   | 0.3999    | 0.4694     | 0.4294          |
| 3   | 0.9984    | 0.0405   | 1.5858    | 1.8609     | 3.0017          |
| 4   | 0.9913    | -0.0152  | -0.5941   | -0.7130    | -0.6728         |
| 5   | 0.9852    | -0.0202  | -0.7898   | -0.9341    | -0.9196         |
| 6   | 0.9754    | -0.0085  | -0.3307   | -0.3770    | -0.3421         |
| 7   | 0.9678    | -0.0086  | -0.3348   | -0.4081    | -0.3712         |
| 8   | 0.9618    | 0.0212   | 0.8296    | 1.1842     | 1.2486          |
| 9   | 0.9419    | -0.0029  | -0.1137   | -4.4912    | (+inf)          |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 1.9509      | 0.7921   | -3.2518|
| 2   | 0.0208      | 0.2742   | 0.2639 |
| 3   | 0.3263      | 0.2737   | 1.8429 |
| 4   | 0.0560      | 0.3057   | -0.4464|
| 5   | 0.0870      | 0.2851   | -0.5807|
| 6   | 0.0107      | 0.2306   | -0.1873|
| 7   | 0.0202      | 0.3270   | -0.2588|
| 8   | 0.3636      | 0.5092   | 1.2717 |
| 9   | 7857.7743   | 0.9994   | (+inf) |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 1.0167    | 0.9582   | 1.0752    | 0.9287  | 1.1046  |
| 2   | 1.0068    | 0.9724   | 1.0412    | 0.9326  | 1.0810  |
| 3   | 0.9984    | 0.9640   | 1.0328    | 0.9242  | 1.0726  |
| 4   | 0.9913    | 0.9550   | 1.0276    | 0.9162  | 1.0664  |
| 5   | 0.9852    | 0.9501   | 1.0203    | 0.9107  | 1.0597  |
| 6   | 0.9754    | 0.9438   | 1.0069    | 0.9025  | 1.0483  |
STARCH (BiPhasic First-order reaction)
40°C / 75%RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yxnear0(q,r)=yxmax(q,xnear0(r))

[Parameters]
a = yxnear0(y,x)/2 "Auto {{previous: 0.284321}}
b = -ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto {{previous: 0.000676696}}
c = yxnear0(y,x)/2 "Auto {{previous: 0.727428}}
d = -ln(.5)/(1.5*(x50(x,y)-min(x))) "Auto {{previous: 0.000644927}}

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0
d=0
[Options]
tolerance=1e-6
steplsize=0.1
iterations=100

R = 0.28113749  Rsqr = 0.07903829  Adj Rsqr = 0.00000000

Standard Error of Estimate = 0.0176

| Coefficient | Std. Error | t | P   |
|--------------|------------|---|-----|
| a 0.2843     | 285635.0184| 0.0000 | 1.0000 |
| b 0.0007     | 23.9808    | 0.0000 | 1.0000 |
| c 0.7274     | 285635.0184| 0.0000 | 1.0000 |
| d 0.0006     | 9.3552     | 0.0001 | 0.9999 |

Analysis of Variance:

|      | DF | SS    | MS    | F     | P   |
|------|----|-------|-------|-------|-----|
| Regression | 3  | 0.0001| 0.0000| 0.1430| 0.9298|
| Residual   | 5  | 0.0015| 0.0003|       |     |
| Total      | 8  | 0.0017| 0.0002|       |     |

PRESS = 0.0057

Durbin-Watson Statistic = 2.9328

Normality Test: Passed (P = 0.7798)

Constant Variance Test: Passed (P = 0.4620)

Power of performed test with alpha = 0.0500: 0.1052

The power of the performed test (0.1052) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0117    | -0.0117  | -0.6685   | -0.8456    | -0.8170         |
| 2   | 1.0111    | -0.0026  | -0.1494   | -0.1742    | -0.1563         |
| 3   | 1.0164    | 0.0232   | 1.3217    | 1.3850     | 1.5779          |
| 4   | 1.0098    | -0.0107  | -0.6066   | -0.6344    | -0.5918         |
| 5   | 1.0091    | 0.0064   | 0.3663    | 0.3854     | 0.3499          |
| 6   | 1.0078    | -0.0197  | -1.1236   | -1.2081    | -1.2841         |
| 7   | 1.0065    | 0.0173   | 0.9849    | 1.0946     | 1.1228          |
| 8   | 1.0052    | 0.0014   | 0.0812    | 0.1021     | 0.0914          |
| 9   | 0.9986    | -0.0036  | -0.2059   | -0.8329    | -0.8027         |
Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.1073      | 0.3750   | -0.6329|
| 2   | 0.0027      | 0.2647   | -0.0938|
| 3   | 0.0470      | 0.0893   | 0.4940 |
| 4   | 0.0094      | 0.0857   | -0.1812|
| 5   | 0.0040      | 0.0967   | 0.1145 |
| 6   | 0.0569      | 0.1349   | -0.5070|
| 7   | 0.0704      | 0.1904   | 0.5445 |
| 8   | 0.0015      | 0.3667   | 0.0696 |
| 9   | 2.6632      | 0.9389   | -3.1456|

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0117    | 0.9841   | 1.0394    | 0.9588  | 1.0647   |
| 2   | 1.0111    | 0.9878   | 1.0343    | 0.9603  | 1.0619   |
| 3   | 1.0104    | 0.9969   | 1.0239    | 0.9633  | 1.0576   |
| 4   | 1.0098    | 0.9965   | 1.0230    | 0.9627  | 1.0568   |
| 5   | 1.0091    | 0.9951   | 1.0232    | 0.9618  | 1.0564   |
| 6   | 1.0078    | 0.9912   | 1.0244    | 0.9597  | 1.0559   |
| 7   | 1.0065    | 0.9868   | 1.0262    | 0.9572  | 1.0558   |
| 8   | 1.0052    | 0.9778   | 1.0325    | 0.9523  | 1.0580   |
| 9   | 0.9986    | 0.9548   | 1.0424    | 0.9357  | 1.0615   |

2D Graph 33

![2D Graph: Y Data vs. Time, weeks v CO2, [Starch, 400/75% RH]]
STARCH (BiPhasic First-order reaction)
50°C / 20 % moisture
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysq = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0 = max(abs(q))-abs(q)
yatxnear0 = y-max(abs(y),-abs(q))

[Parameters]
a = yatxnear0(y,x)/2 'Auto {previous: 0.346976}
b = ln(0.5)/0.5*(x50(x,y)-min(x)) 'Auto {previous: 0.307337}
c = yatxnear0(y,x)/2 'Auto {previous: 0.68886}
d = ln(0.5)/0.5*(x50(x,y)-min(x)) 'Auto {previous: 2.12148e-010}

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysq

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

R = 0.92855729       Rsqr = 0.86221864       Adj Rsqr = 0.77954983

Standard Error of Estimate = 0.0599

| Coefficient | Std. Error | t    | P    |
|-------------|------------|------|------|
a           | 0.3470     | 0.1666 | 2.0828 | 0.0917 |
b           | 0.3073     | 0.2517 | 1.2208 | 0.2766 |
c           | 0.6889     | 0.1751 | 3.9336 | 0.0110 |
d           | 0.0000     | 0.0149 | 0.0000 | 1.0000 |

Analysis of Variance:

|        | DF | SS     | MS      | F       | P    |
|--------|----|--------|---------|---------|------|
| Regression | 3  | 0.1122 | 0.0374  | 10.4298 | 0.0136 |
| Residual  | 5  | 0.0179 | 0.0036  |         |      |
| Total    | 8  | 0.1301 | 0.0163  |         |      |
PRESS = 16.6152

Durbin-Watson Statistic = 1.4125

Normality Test: Failed (P = 0.0446)

Constant Variance Test: Passed (P = 0.8094)

Power of performed test with alpha = 0.0500: 0.9811

Regression Diagnostics:

| Row | Predicted | Residual  | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|-----------|-----------|------------|-----------------|
| 1   | 1.0358    | -0.0358   | -0.5985   | -1.5159    | -1.8443         |
| 2   | 0.9440    | 0.0285    | 0.4765    | 0.5644     | 0.5217          |
| 3   | 0.8765    | 0.0282    | 0.4714    | 0.5648     | 0.5221          |
| 4   | 0.8269    | 0.0339    | 0.5657    | 0.6739     | 0.6322          |
| 5   | 0.7903    | 0.0133    | 0.2221    | 0.2560     | 0.2305          |
| 6   | 0.7437    | -0.0998   | -1.6672   | -1.9075    | -3.2699         |
| 7   | 0.7185    | -0.0335   | -0.5600   | -0.6951    | -0.6542         |
| 8   | 0.7049    | 0.0170    | 0.2843    | 0.3823     | 0.3470          |
| 9   | 0.6896    | 0.0482    | 0.8058    | 7.3977     | (+inf)          |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 3.1104      | -4.2915  |        |
| 2   | 0.0321      | 0.3311   |        |
| 3   | 0.0348      | 0.3447   |        |
| 4   | 0.0476      | 0.4094   |        |
| 5   | 0.0054      | 0.1323   |        |
| 6   | 0.2512      | -1.8181  |        |
| 7   | 0.0653      | -0.4810  |        |
| 8   | 0.0295      | 0.3119   |        |
| 9   | 1139.4517   | (+inf)   |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|--------|---------|
| 1   | 1.0358    | 0.8944   | 1.1772    | 0.8268 | 1.2448  |
| 2   | 0.9440    | 0.8615   | 1.0265    | 0.7694 | 1.1186  |
| 3   | 0.8765    | 0.7917   | 0.9613    | 0.7008 | 1.0522  |
| 4   | 0.8269    | 0.7432   | 0.9105    | 0.6517 | 1.0020  |
| 5   | 0.7903    | 0.7137   | 0.8669    | 0.6184 | 0.9623  |
| 6   | 0.7437    | 0.6690   | 0.8185    | 0.5726 | 0.9149  |
| 7   | 0.7185    | 0.6274   | 0.8097    | 0.5397 | 0.8974  |
| 8   | 0.7049    | 0.6020   | 0.8078    | 0.5198 | 0.8900  |
| 9   | 0.6896    | 0.5366   | 0.8426    | 0.4726 | 0.9066  |
STARCH (BiPhasic First-order reaction)
50°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
\text{reciprocal}_y = 1/\text{abs}(y)
\text{reciprocal}_y\text{square} = 1/\text{y}^2

'Automatic Initial Parameter Estimate Functions
\text{xnear0}(q) = \text{max}(\text{abs}(q))-\text{abs}(q)
\text{yatxnear0}(q,r) = \text{xatymax}(q,\text{xnear0}(r))

[Parameters]
a = \text{yatxnear0}(y,x)/2 "Auto \{\text{previous: 0.687449}\}
b = -\ln(0.5)/(0.5*(x50(x,y)-\text{min}(x))) "Auto \{\text{previous: 0.12064}\}
c = \text{yatxnear0}(y,x)/2 "Auto \{\text{previous: 0.338624}\}
d = -\ln(0.5)/(1.5*(x50(x,y)-\text{min}(x))) "Auto \{\text{previous: 6.66952e-010}\}

[Equation]
f = a*\exp(-b*x)+c*\exp(-d*x)
fit f to y
"fit f to y with weight \text{reciprocal}_y"
"fit f to y with weight \text{reciprocal}_y\text{square}

[Constraints]
b > 0
d > 0

[Options]
tolerance = 1e-6
\text{stepsize} = 0.1
iterations=100
R = 0.99125473    Rsqr = 0.98258593    Adj Rsqr = 0.97213749

Standard Error of Estimate = 0.0341

| Coefficient | Std. Error | t       | P     |
|-------------|------------|---------|-------|
| a           | 0.6874     | 0.8228  | 0.4481|
| b           | 0.1206     | 0.9178  | 0.4008|
| c           | 0.3386     | 0.3982  | 0.7069|
| d           | 0.0000     | 0.0000  | 1.0000|

Analysis of Variance:

|            | DF | SS   | MS    | F      | P     |
|------------|----|------|-------|--------|-------|
| Regression | 3  | 0.3286 | 0.1095 | 94.0414 | <0.0001|
| Residual   | 5  | 0.0058 | 0.0012 |
| Total      | 8  | 0.3345 | 0.0418 |

PRESS = 19.8656

Durbin-Watson Statistic = 1.4971

Normality Test: Passed (P = 0.4066)

Constant Variance Test: Passed (P = 0.7755)

Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|----------------|
| 1   | 1.0261    | -0.0261  | -0.7639   | -1.5218    | -1.8577        |
| 2   | 0.9479    | -0.0015  | -0.0435   | -0.0509    | -0.0456        |
| 3   | 0.8787    | 0.0170   | 0.4984    | 0.5719     | 0.5291         |
| 4   | 0.8173    | 0.0548   | 1.6042    | 1.8955     | 3.1957         |
| 5   | 0.7629    | -0.0024  | -0.0704   | -0.0835    | -0.0747        |
| 6   | 0.6720    | -0.0412  | -1.2062   | -1.3829    | -1.5741        |
| 7   | 0.6005    | -0.0047  | -0.1379   | -0.1682    | -0.1509        |
| 8   | 0.5444    | -0.0059  | -0.1716   | -0.2721    | -0.2452        |
| 9   | 0.4002    | 0.0099   | 0.2909    | 6.1616     | (+inf)         |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 1.7186     | 0.7480   | -3.2006|
| 2   | 0.0002     | 0.2706   | -0.0278|
| 3   | 0.0259     | 0.2405   | 0.2977 |
| 4   | 0.3559     | 0.2838   | 2.0115 |
95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 1.0261    | 0.9502   | 1.1020    | 0.9101  | 1.1421  |
| 2   | 0.9479    | 0.9023   | 0.9936    | 0.8491  | 1.0468  |
| 3   | 0.8787    | 0.8357   | 0.9217    | 0.7810  | 0.9764  |
| 4   | 0.8173    | 0.7706   | 0.8641    | 0.7179  | 0.9167  |
| 5   | 0.7629    | 0.7157   | 0.8101    | 0.6633  | 0.8625  |
| 6   | 0.6720    | 0.6290   | 0.7149    | 0.5743  | 0.7696  |
| 7   | 0.6005    | 0.5502   | 0.6508    | 0.4994  | 0.7016  |
| 8   | 0.5444    | 0.4763   | 0.6125    | 0.4333  | 0.6554  |
| 9   | 0.4002    | 0.3126   | 0.4878    | 0.2762  | 0.5242  |

**TALC (First-order reaction)**

25°C

Nonlinear Regression

[Variables]

\[ x = \text{col}(1) \]
\[ y = \text{col}(2) \]
\[ \text{reciprocal}_y = 1/\text{abs}(y) \]
\[ \text{reciprocal}_y^{\text{square}} = 1/y^2 \]
Automatic Initial Parameter Estimate Functions

\[ x_{\text{near}}(q) = \max(\abs{q}) - \abs{q} \]

\[ y_{\text{at} x_{\text{near}}}(q, r) = \text{atymax}(q, x_{\text{near}}(r)) \]

[Parameters]

\[ a = y_{\text{at} x_{\text{near}}}(y, x) \quad \text{"Auto \{previous: 102.241\}} \]

\[ b = -\ln(.5)/(x_{50}(x, y) - \min(x)) \quad \text{"Auto \{previous: 0.0129317\}} \]

[Equation]

\[ f = a \times \exp(-b \times x) \]

fit f to y

"fit f to y with weight reciprocal_y

"fit f to y with weight reciprocal_ysquare

[Constraints]

b > 0

[Options]

tolerance = 0.0001

stepsize = 100

iterations = 100

R = 0.94669224 \quad \text{Rsqr} = 0.89622621 \quad \text{Adj Rsqr} = 0.88140138

Standard Error of Estimate = 2.6157

| Coefficient | Std. Error | t     | P     |
|-------------|------------|-------|-------|
| a           | 102.2411   | 1.3191| <0.0001 |
| b           | 0.0129     | 0.0017| 0.0001 |

Analysis of Variance:

| DF  | SS     | MS     | F      | P     |
|-----|--------|--------|--------|-------|
| Regression | 1 | 413.6188 | 413.6188 | 60.4544 | 0.0001 |
| Residual    | 7 | 47.8928  | 6.8418  |        |      |
| Total       | 8 | 461.5116 | 57.6890 |        |      |

PRESS = 81.3825

Durbin-Watson Statistic = 2.2603

Normality Test: Passed (P = 0.7689)

Constant Variance Test: Passed (P = 0.2230)

Power of performed test with alpha = 0.0500: 0.9928

Regression Diagnostics:

| Row | Predicted Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|--------------------|-----------|------------|-----------------|
| 1   | 102.2411           | -2.2411   | -0.8568    | -0.9922         | -0.9909         |
| 2   | 100.9275           | 2.5643    | 0.9804     | 1.0997          | 1.1194          |
Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.1679      |          | -0.5787|
| 2   | 0.1561      | 0.2052   | 0.5688 |
| 3   | 0.2057      | 0.1673   | 0.7060 |
| 4   | 0.0136      | 0.1397   | -0.1547|
| 5   | 0.0469      | 0.1219   | -0.2985|
| 6   | 0.0408      | 0.1124   | 0.2774 |
| 7   | 0.1851      | 0.1339   | -0.6944|
| 8   | 0.0003      | 0.1816   | -0.0241|
| 9   | 0.7298      | 0.6836   | 1.1767 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 102.2411  | 99.1219  | 105.3604  | 95.3140 | 109.1683 |
| 2   | 100.9275  | 98.1255  | 103.7295  | 94.1373 | 107.7177 |
| 3   | 99.6308   | 97.1010  | 102.1605  | 92.9483 | 106.3132 |
| 4   | 98.3507   | 96.0386  | 100.6628  | 91.7475 | 104.9538 |
| 5   | 97.0870   | 94.9278  | 99.2462   | 90.5358 | 103.6382 |
| 6   | 94.6082   | 92.5342  | 96.6822   | 88.0846 | 101.1318 |
| 7   | 92.1927   | 89.9295  | 94.4559   | 85.6065 | 98.7789  |
| 8   | 89.8389   | 87.2029  | 92.4748   | 83.1155 | 96.5622  |
| 9   | 78.9410   | 73.8272  | 84.0549   | 70.9156 | 86.9664  |

2D Graph 32

![Graph](image-url)
TALC (First-order reaction)
25°C / 60%RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 101.384}
b = -ln(0.5)/(x50(x,y)-min(x)) "Auto {previous: 0.00392561}

[Equation]
f=a*exp(-b*x)

fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.78307565      Rsqr = 0.61320747    Adj Rsqr = 0.55795139

Standard Error of Estimate = 2.0110

| Coefficient | Std. Error | t        | P       |
|-------------|------------|----------|---------|
| a           | 101.3838   | 0.9776   | <0.0001 |
| b           | 0.0039     | 0.0012   | 0.0135  |

Analysis of Variance:

|            | DF | SS      | MS       | F         | P       |
|-------------|----|---------|----------|-----------|---------|
| Regression  | 1  | 44.8811 | 44.8811  | 11.0976   | 0.0126  |
| Residual    | 7  | 28.3096 | 4.0442   |           |         |
| Total       | 8  | 73.1907 | 9.1488   |           |         |

PRESS = 41.1859

Durbin-Watson Statistic = 2.0292
Normality Test: Passed ($P = 0.7028$)

Constant Variance Test: Passed ($P = 0.9477$)

Power of performed test with $\alpha = 0.0500$: 0.7324

The power of the performed test (0.7324) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Def. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 101.3838  | -1.3838  | -0.6881   | -0.7874    | -0.7636         |
| 2   | 100.9866  | 1.6822   | 0.8365    | 0.9332     | 0.9234          |
| 3   | 100.5909  | -0.7303  | -0.3631   | -0.3973    | -0.3721         |
| 4   | 100.1968  | -1.9726  | -0.9809   | -1.0579    | -1.0686         |
| 5   | 99.8042   | 1.6896   | 0.8401    | 0.8974     | 0.8831          |
| 6   | 99.9237   | 2.9685   | 1.4761    | 1.5657     | 1.7983          |
| 7   | 98.2493   | 0.0724   | 0.0360    | 0.0385     | 0.0357          |
| 8   | 97.4810   | -2.7063  | -1.3457   | -1.4759    | -1.6464         |
| 9   | 93.7284   | 0.3804   | 0.1891    | 0.3654     | 0.3415          |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.0959      | -0.4248  |        |
| 2   | 0.1066      | 0.4568   |        |
| 3   | 0.0156      | -0.1652  |        |
| 4   | 0.0914      | -0.4318  |        |
| 5   | 0.0567      | 0.3314   |        |
| 6   | 0.1534      | 0.6362   |        |
| 7   | 0.0001      | 0.0136   |        |
| 8   | 0.2209      | -0.7414  |        |
| 9   | 0.1823      | 0.5645   |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 101.3838  | 99.0720  | 103.6955  | 96.0963 | 106.6712 |
| 2   | 100.9866  | 98.8779  | 103.0952  | 95.7847 | 106.1884 |
| 3   | 100.5909  | 98.6611  | 102.5207  | 95.4589 | 105.7229 |
| 4   | 100.1968  | 98.4153  | 101.9783  | 95.1187 | 105.2749 |
| 5   | 99.8042   | 98.1334  | 101.4750  | 94.7639 | 104.8445 |
| 6   | 99.9237   | 97.4378  | 100.6097  | 94.0109 | 104.0365 |
| 7   | 98.2493   | 96.5566  | 99.420   | 93.2017 | 103.2969 |
| 8   | 97.4810   | 95.5284  | 99.4336  | 92.3404 | 102.6216 |
| 9   | 93.7284   | 99.6598  | 97.7969  | 87.4701 | 99.9867 |
TALC (First-order reaction)
40°C / 75%RH

NO OUTPUT

TALC (First-order reaction)
50°C / 20%moisture
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q,r) = yatymax(q, xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 84.9833}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0272392}"

[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b > 0

[Options]
tolerance=0.0001  
stepsize=100  
iterations=100

\[ R = 0.7685 \quad R^2 = 0.5906 \quad Adj R^2 = 0.5321 \]

Standard Error of Estimate = 9.2954

| Coefficient | Std. Error | t     | P       |
|--------------|------------|-------|---------|
| a            | 84.9833    | 4.9568| <0.0001 |
| b            | 0.0272     | 0.0090| 0.0191  |

Analysis of Variance:

|            | DF | SS  | MS   | F      | P       |
|------------|----|-----|------|--------|---------|
| Regression | 1  | 872.5961 | 872.5961 | 10.0989 | 0.0155  |
| Residual   | 7  | 604.8367 | 86.4052 |         |         |
| Total      | 8  | 1477.4328 | 184.6791 |         |         |

PRESS = 1511.2094

Durbin-Watson Statistic = 1.2288

Normality Test: Passed (P = 0.6711)

Constant Variance Test: Passed (P = 0.6758)

Power of performed test with alpha = 0.0500: 0.7021

The power of the performed test (0.7021) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 84.9833   | 15.0167  | 1.6155    | 1.9097     | 2.5545          |
| 2   | 82.6997   | 4.4898   | 0.4830    | 0.5463     | 0.5169          |
| 3   | 80.4774   | -1.3672  | -0.1457   | -0.1615    | -0.1498         |
| 4   | 78.3149   | -11.6707 | -1.2555   | -1.3525    | -1.4569         |
| 5   | 76.2105   | -2.7199  | -0.2926   | -0.3119    | -0.2908         |
| 6   | 72.1697   | -8.1631  | -0.8782   | -0.9347    | -0.9250         |
| 7   | 68.3432   | 0.3788   | 0.0408    | 0.0442     | 0.0409          |
| 8   | 64.7196   | -5.8232  | -0.6265   | -0.7021    | -0.6742         |
| 9   | 49.2876   | 10.6308  | 1.1437    | 1.8062     | 2.2884          |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.7245      | 0.2844   | 1.6102 |
2  0.0416  0.2182  0.2731
3  0.0027  0.1703  -0.0679
4  0.1467  0.1383  -0.5836
5  0.0002  0.1487  0.0171
6  0.0632  0.2040  -0.3413
7  2.4371  0.5991  2.7971
8  0.0066  0.1200  -0.1074
9  0.0580  0.1172  -0.3370

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 84.9833   | 73.2623  | 96.7044   | 60.0733 | 109.8934|
| 2   | 82.6997   | 72.4326  | 92.9668   | 58.4398 | 106.9596|
| 3   | 80.4774   | 71.4074  | 86.4878   | 54.8644 | 101.7654|
| 4   | 78.3149   | 70.1420  | 83.2843   | 52.9489 | 99.4720 |
| 5   | 76.2105   | 68.5966  | 79.6943   | 48.9372 | 95.4022 |
| 6   | 72.1697   | 64.6451  | 76.8194   | 44.7853 | 91.9011 |
| 7   | 68.3432   | 59.8670  | 74.6465   | 40.6017 | 88.8375 |
| 8   | 64.7196   | 54.7927  | 70.9592   | 30.9152 | 76.0633 |
| 9   | 49.2876   | 32.2752  | 66.3000   | 21.4927 | 77.0824 |

2D Graph 35

TALC (First-order reaction)
50°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)  
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q,r) = yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x) "Auto {previous: 98.224}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0510482}"

[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

R = 0.98210601    Rsqr = 0.96453222    Adj Rsqr = 0.95946539

Standard Error of Estimate = 3.9457

| Coefficient | Std. Error | t      | P     |
|-------------|------------|--------|-------|
| a           | 98.2240    | 2.2977 | <0.0001|
| b           | 0.0510     | 0.0044 | <0.0001|

Analysis of Variance:

| DF  | SS     | MS      | F       | P       |
|-----|--------|---------|---------|---------|
| Regression | 1 | 2963.6243 | 2963.6243 | 190.3622 | <0.0001 |
| Residual   | 7 | 108.9784  | 15.5683  |         |
| Total      | 8 | 3072.6027 | 384.0753 |         |

PRESS = 198.1004

Durbin-Watson Statistic = 1.1975

Normality Test: Passed (P = 0.6137)

Constant Variance Test: Passed (P = 0.4905)

Power of performed test with alpha = 0.0500: 0.9999

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
|   |         |         |         |         |         |
|---|---------|---------|---------|---------|---------|
| 1 | 98.2240 | 1.7760 | 0.4501  | 0.5537  | 0.5242  |
| 2 | 93.3357 | 6.8087 | 1.7256  | 1.9764  | 2.7523  |
| 3 | 88.6906 | -1.4945| -0.3788 | -0.4163 | -0.3903 |
| 4 | 84.2768 | -4.6651| -1.1823 | -1.2715 | -1.3423 |
| 5 | 80.0826 | -2.2969| -0.5821 | -0.6205 | -0.5909 |
| 6 | 72.3099 | -3.4261| -0.8683 | -0.9326 | -0.9227 |
| 7 | 65.2917 | -0.8959| -0.2271 | -0.2508 | -0.2332 |
| 8 | 58.9547 | 1.0517 | 0.2666  | 0.3058  | 0.2850  |
| 9 | 35.3850 | 4.0678 | 1.0310  | 1.3805  | 1.4982  |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.0787     | 0.3391   | 0.3755 |
| 2   | 0.6089     | 0.2377   | 1.5368 |
| 3   | 0.0181     | 0.1724   | -0.1781|
| 4   | 0.1265     | 0.1353   | -0.5310|
| 5   | 0.0262     | 0.1199   | -0.2181|
| 6   | 0.0668     | 0.1332   | -0.3617|
| 7   | 0.0069     | 0.1801   | -0.1093|
| 8   | 0.0148     | 0.2400   | 0.1602 |
| 9   | 0.7556     | 0.4423   | 1.3342 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 98.2240   | 92.7907  | 103.6573  | 87.4272 | 109.0208 |
| 2   | 93.3357   | 88.7871  | 97.8843   | 82.9559 | 103.7154 |
| 3   | 88.6906   | 84.8167  | 92.5646   | 78.5883 | 98.7930  |
| 4   | 84.2768   | 80.8446  | 87.7089   | 74.3355 | 94.2181  |
| 5   | 80.0826   | 76.8524  | 83.3127   | 70.2092 | 89.9559  |
| 6   | 72.3099   | 68.9051  | 75.7148   | 62.3781 | 82.2418  |
| 7   | 65.2917   | 61.3317  | 69.2518   | 55.1561 | 75.4274  |
| 8   | 58.9547   | 54.3837  | 63.5256   | 48.5651 | 69.3442  |
| 9   | 35.3850   | 29.1801  | 41.5898   | 24.1801 | 46.5899  |
TALC (BiPhasic First-order reaction)

25°C

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y_square = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q,r) = xatymax(q, xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2  "Auto {previous: 0.411743}"
b = -ln(.5)/(0.5*(x50(x,y)-min(x)))  "Auto {previous: 0.0412329}"
c = yatxnear0(y,x)/2  "Auto {previous: 0.618745}"
d = -ln(.5)/(1.5*(x50(x,y)-min(x)))  "Auto {previous: 2.52176e-011}"

[Equation]
f = a*exp(-b*x) + c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y_square

[Constraints]
b > 0

d > 0

[Options]
tolerance = 1e-6
\text{Stepsize} = 0.1 \\
\text{Iterations} = 100 \\
\text{R} = 0.9507298 \quad \text{Rsq} = 0.90388369 \quad \text{Adj Rsq} = 0.84621390 \\
\text{Standard Error of Estimate} = 0.0298 \\

\begin{tabular}{lcccc}
\text{Coefficient} & \text{Std. Error} & \text{t} & \text{P} \\
\hline
a & 0.4117 & 15.0848 & 0.0273 & 0.9793 \\
b & 0.0412 & 0.9213 & 0.0448 & 0.9660 \\
c & 0.6187 & 15.0995 & 0.0410 & 0.9689 \\
d & 0.0000 & 0.4174 & 0.0000 & 1.0000 \\
\end{tabular}

\text{Analysis of Variance:} \\
\begin{tabular}{lcccc}
\text{DF} & \text{SS} & \text{MS} & \text{F} & \text{P} \\
\hline
\text{Regression} & 3 & 0.0417 & 0.0139 & 15.6734 & 0.0056 \\
\text{Residual} & 5 & 0.0044 & 0.0009 & \\
\text{Total} & 8 & 0.0462 & 0.0058 & \\
\end{tabular}

\text{PRESS} = 6.9041 \\
\text{Durbin-Watson Statistic} = 2.4558 \\
\text{Normality Test: Passed (P = 0.7024)} \\
\text{Constant Variance Test: Passed (P = 0.1243)} \\
\text{Power of performed test with alpha = 0.0500: 0.9945} \\

\text{Regression Diagnostics:} \\
\begin{tabular}{llllll}
\text{Row} & \text{Predicted} & \text{Residual} & \text{Std. Res.} & \text{Stud. Res.} & \text{Stud. Del. Res.} \\
\hline
2 & 1.0305 & -0.0305 & -1.0236 & -1.8784 & -3.0970 \\
3 & 1.0139 & 0.0211 & 0.7071 & 0.8292 & 0.7986 \\
4 & 0.9979 & 0.0326 & 1.0934 & 1.2382 & 1.3300 \\
5 & 0.9826 & -0.0090 & -0.3025 & -0.3535 & -0.3202 \\
6 & 0.9679 & -0.0172 & -0.5766 & -0.6879 & -0.6466 \\
7 & 0.9402 & 0.0256 & 0.8596 & 0.9980 & 0.9975 \\
8 & 0.9148 & -0.0305 & -1.0253 & -1.3301 & \\
9 & 0.8914 & 0.0057 & 0.1920 & 0.3328 & 0.3010 \\
10 & 0.7992 & 0.0023 & 0.0758 & 2.5836 & (+inf) \\
\end{tabular}

\text{Influence Diagnostics:} \\
\begin{tabular}{llll}
\text{Row} & \text{Cook's Dist} & \text{Leverage} & \text{DFFITS} \\
\hline
2 & 2.0886 & 0.7031 & -4.7655 \\
3 & 0.0645 & 0.2728 & 0.4892 \\
4 & 0.1083 & 0.2202 & 0.7069 \\
\end{tabular}
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 2   | 1.0305    | 0.9663   | 1.0947    | 0.9306  | 1.1304  |
| 3   | 1.0139    | 0.9739   | 1.0538    | 0.9275  | 1.1002  |
| 4   | 0.9979    | 0.9620   | 1.0338    | 0.9133  | 1.0825  |
| 5   | 0.9826    | 0.9430   | 1.0222    | 0.8964  | 1.0688  |
| 6   | 0.9679    | 0.9261   | 1.0096    | 0.8807  | 1.0551  |
| 7   | 0.9402    | 0.9013   | 0.9791    | 0.8544  | 1.0261  |
| 8   | 0.9148    | 0.8719   | 0.9577    | 0.8270  | 1.0026  |
| 9   | 0.8914    | 0.8288   | 0.9339    | 0.7925  | 0.9902  |
| 10  | 0.7992    | 0.7227   | 0.8758    | 0.6910  | 0.9075  |

95% Confidence:

TALC (BiPhasic First-order reaction)
25°C / 66%RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_y_square=1/y^2
Automatic Initial Parameter Estimate Functions

\[ x_{\text{near}O(q)} = \max(\text{abs}(q)) - \text{abs}(q) \]
\[ y_{at\text{near}O(q, r)} = \max(\text{max}(q, x_{\text{near}O(r)}) \]

[Parameters]

\[ a = \frac{y_{at\text{near}O(y, x)}}{2} \quad \text{Auto \{previous: 0.45219\}} \]
\[ b = -\ln(0.5)/\left(0.5*(x_{50}(x, y) - \min(x))\right) \quad \text{Auto \{previous: 0.00453869\}} \]
\[ c = \frac{y_{at\text{near}O(y, x)}}{2} \quad \text{Auto \{previous: 0.561641\}} \]
\[ d = -\ln(0.5)/\left(1.5*(x_{50}(x, y) - \min(x))\right) \quad \text{Auto \{previous: 0.00342691\}} \]

[Equation]

\[ f = a*\exp(-b*x) + c*\exp(-d*x) \]

fit f to y

"fit f to y with weight reciprocal_y

"fit f to y with weight reciprocal_ysquare

[Constraints]

\[ b > 0 \]
\[ d > 0 \]

[Options]

tolerance=1e-6

stepsize=0.1

iterations=100

R = 0.78307374 \quad \text{Rsq} = 0.61320448 \quad \text{Adj Rsq} = 0.38112716

Standard Error of Estimate = 0.0238

| Coefficient | Std. Error | t     | P     |
|-------------|------------|-------|-------|
| a           | 0.4522     | 736579.2042 | 0.0000 | 1.0000 |
| b           | 0.0045     | 358.6938   | 0.0000 | 1.0000 |
| c           | 0.5616     | 736579.2032 | 0.0000 | 1.0000 |
| d           | 0.0034     | 289.4781   | 0.0000 | 1.0000 |

Analysis of Variance:

| DF  | SS     | MS    | F     | P     |
|-----|--------|-------|-------|-------|
| Regression | 3 | 0.0045 | 0.0015 | 2.6422 | 0.1610 |
| Residual  | 5 | 0.0028 | 0.0006 |       |       |
| Total    | 8 | 0.0073 | 0.0009 |       |       |

PRESS = 0.0134

Durbin-Watson Statistic = 2.0280

Normality Test: Passed (P = 0.7009)

Constant Variance Test: Passed (P = 0.9477)

Power of performed test with alpha = 0.0500: 0.7324
The power of the performed test (0.7324) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

### Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0138    | -0.0138  | -0.5813   | -0.7352    | -0.6963         |
| 2   | 1.0099    | 0.0168   | 0.7071    | 0.8204     | 0.7888          |
| 3   | 1.0059    | -0.0073  | -0.3069   | -0.3128    | -0.2825         |
| 4   | 1.0020    | -0.0197  | -0.8291   | -0.9171    | -0.8994         |
| 5   | 0.9980    | 0.0169   | 0.7098    | 0.6890     | 0.6477          |
| 6   | 0.9903    | 0.0297   | 1.2469    | 1.3606     | 1.5335          |
| 7   | 0.9825    | 0.0007   | 0.0294    | 0.0341     | 0.0305          |
| 8   | 0.9748    | -0.0271  | -1.1389   | -1.3111    | -1.4476         |
| 9   | 0.9374    | 0.0037   | 0.1555    | 0.7867     | 0.7517          |

### Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.0811     | -0.5394  |        |
| 2   | 0.0582     | 0.4641   |        |
| 3   | 0.0009     | -0.0557  |        |
| 4   | 0.0470     | -0.4250  |        |
| 5   | -0.0069    | (+inf)   |        |
| 6   | 0.0883     | 0.6697   |        |
| 7   | 0.0001     | 0.0179   |        |
| 8   | 0.1398     | -0.8257  |        |
| 9   | 3.8057     | 3.7251   |        |

### 95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0138    | 0.9764   | 1.0513    | 0.9421  | 1.0856   |
| 2   | 1.0099    | 0.9788   | 1.0409    | 0.9413  | 1.0784   |
| 3   | 1.0059    | 0.9941   | 1.0177    | 0.9436  | 1.0682   |
| 4   | 1.0020    | 0.9758   | 1.0281    | 0.9355  | 1.0685   |
| 5   | 0.9980    | 0.9980   | 0.9980    | 0.9980  | 0.9980   |
| 6   | 0.9903    | 0.9658   | 1.0147    | 0.9244  | 1.0561   |
| 7   | 0.9825    | 0.9515   | 1.0135    | 0.9139  | 1.0511   |
| 8   | 0.9748    | 0.9445   | 1.0052    | 0.9066  | 1.0431   |
| 9   | 0.9374    | 0.8774   | 0.9973    | 0.8517  | 1.0230   |
TALC (BiPhasic First-order reaction)
40°C / 75%RH

NO OUTPUT

TALC (BiPhasic First-order reaction)
50°C / 20%moisture
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_y^2=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=yatxmin(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2  "Auto {previous: 0.341123}"
b = -ln(.5)/(0.5*(x50(x,y)-min(x)))  "Auto {previous: 0.516044}"
c = yatxnear0(y,x)/2  "Auto {previous: 0.66249}"
d = -ln(.5)/(1.5*(x50(x,y)-min(x)))  "Auto {previous: 0.00541061}"

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_y^2"

[Constraints]
b=0  
d=0  
[Options]  
tolerance=1e-6  
stepsize=0.1  
iterations=100  

R = 0.9666  Rsqr = 0.9342  Adj Rsqr = 0.8948  

Standard Error of Estimate = 0.0441  

| Coefficient | Std. Error | t  | P  |
|--------------|------------|----|----|
| a  | 0.3411 | 0.0746 | 4.5705 | 0.0060   |
| b  | 0.5160 | 0.2261 | 2.2820 | 0.0714   |
| c  | 0.6625 | 0.0694 | 9.5400 | 0.0002   |
| d  | 0.0054 | 0.0078 | 0.6896 | 0.5211   |

Analysis of Variance:  

| DF   | SS    | MS    | F     | P     |
|------|-------|-------|-------|-------|
| Regression | 3     | 0.1380 | 0.0460 | 23.6729 | 0.0022 |
| Residual  | 5     | 0.0097 | 0.0019 |       |       |
| Total    | 8     | 0.1477 | 0.0185 |       |       |

PRESS = 0.0343  

Durbin-Watson Statistic = 3.4066  

Normality Test: Passed (P = 0.7948)  

Constant Variance Test: Passed (P = 0.4342)  

Power of performed test with alpha = 0.0500: 0.9988  

Regression Diagnostics:  

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|------------|----------|-----------|------------|-----------------|
| 1   | 1.0036     | -0.0036  | -0.0819   | -0.2906    | -0.2621         |
| 2   | 0.8625     | 0.0094   | 0.2126    | 0.2673     | 0.2408          |
| 3   | 0.7769     | 0.0142   | 0.3224    | 0.4034     | 0.3668          |
| 4   | 0.7244     | -0.0579  | -1.3138   | -1.5306    | -1.8780         |
| 5   | 0.6916     | 0.0433   | 0.9823    | 1.1077     | 1.1405          |
| 6   | 0.6568     | -0.0167  | -0.3785   | -0.4448    | -0.4060         |
| 7   | 0.6399     | 0.0473   | 1.0729    | 1.3067     | 1.4403          |
| 8   | 0.6296     | -0.0406  | -0.9208   | -1.1104    | -1.1443         |
| 9   | 0.5946     | 0.0046   | 0.1050    | 0.5247     | 0.4828          |

Influence Diagnostics:  

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| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.2443      | 0.9205   | -0.8917|
| 2   | 0.0104      | 0.3673   | 0.1835 |
| 3   | 0.0230      | 0.3612   | 0.2758 |
| 4   | 0.2093      | 0.2632   | -1.1226|
| 5   | 0.0833      | 0.2136   | 0.5944 |
| 6   | 0.0188      | 0.2759   | -0.2506|
| 7   | 0.2063      | 0.3259   | 1.0013 |
| 8   | 0.1401      | 0.3125   | -0.7714|
| 9   | 1.6491      | 0.9599   | 2.3632 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|------------|----------|-----------|---------|----------|
| 1   | 1.0036     | 0.8949   | 1.1123    | 0.8466  | 1.1607   |
| 2   | 0.8625     | 0.7938   | 0.9312    | 0.7300  | 0.9950   |
| 3   | 0.7769     | 0.7088   | 0.8450    | 0.6447  | 0.9091   |
| 4   | 0.7244     | 0.6662   | 0.7825    | 0.5970  | 0.8517   |
| 5   | 0.6916     | 0.6392   | 0.7440    | 0.5668  | 0.8164   |
| 6   | 0.6568     | 0.5972   | 0.7163    | 0.5287  | 0.7848   |
| 7   | 0.6399     | 0.5752   | 0.7046    | 0.5094  | 0.7704   |
| 8   | 0.6296     | 0.5662   | 0.6929    | 0.4997  | 0.7594   |
| 9   | 0.5946     | 0.4835   | 0.7056    | 0.4359  | 0.7532   |

2D Graph 39

[Graph showing data points and trend line]
**TALC (BiPhasic First-order reaction)**

50°C

Nonlinear Regression

[Variables]

\[ x = \text{col}(1) \]
\[ y = \text{col}(2) \]
\[ \text{reciprocal}_y = 1/\text{abs}(y) \]
\[ \text{reciprocal}_y^{\text{square}} = 1/\text{y}^2 \]

'Automatic Initial Parameter Estimate Functions

\[ \text{xnear0}(q) = \text{max}(\text{abs}(q))-\text{abs}(q) \]
\[ \text{yatxnear0}(q,r) = \text{xtymax}(q,\text{xnear0}(r)) \]

[Parameters]

\[ a = \text{yatxnear0}(y,x)/2 \text{ Auto \{previous: 0.194689\}} \]
\[ b = -\ln(.5)/(0.5*(\text{x50}(x,y)-\text{min}(x))) \text{ Auto \{previous: 0.296141\}} \]
\[ c = \text{yatxnear0}(y,x)/2 \text{ Auto \{previous: 0.83071\}} \]
\[ d = -\ln(.5)/(1.5*(\text{x50}(x,y)-\text{min}(x))) \text{ Auto \{previous: 0.0366477\}} \]

[Equation]

\[ f = a*\exp(-b*x)+c*\exp(-d*x) \]

"fit f to y"

"fit f to y with weight reciprocal_y"

"fit f to y with weight reciprocal_y^{\text{square}}"

[Constraints]

\[ b > 0 \]
\[ d > 0 \]

[Options]

tolerance = 1e-6

stepsize = 0.1

iterations = 100

\[ R = 0.99183104 \quad \text{Rsqr} = 0.98372882 \quad \text{Adj Rsqr} = 0.97396611 \]

Standard Error of Estimate = 0.0316

| Coefficient | Std. Error | t     | P     |
|-------------|------------|-------|-------|
| a           | 0.1947     | 0.1710| 1.1384| 0.3065 |
| b           | 0.2961     | 0.3061| 0.9675| 0.3777 |
| c           | 0.8307     | 0.1778| 4.6722| 0.0055 |
| d           | 0.0366     | 0.0129| 2.8352| 0.0365 |

Analysis of Variance:

| DF | SS   | MS   | F     | P     |
|----|------|------|-------|-------|
| Regression | 3 | 0.3023 | 0.1008 | 100.7639 | <0.0001 |
| Residual   | 5 | 0.0050 | 0.0010 |
| Total      | 8 | 0.3073 | 0.0384 |
PRESS = 0.0905

Durbin-Watson Statistic = 2.5529

Normality Test: Passed (P = 0.4865)

Constant Variance Test: Passed (P = 0.0988)

Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0254    | -0.0254  | -0.8032   | -2.0608    | -4.7497         |
| 2   | 0.9456    | 0.0558   | 1.7659    | 2.0983     | 5.4311          |
| 3   | 0.8797    | -0.0077  | -0.2440   | -0.2935    | -0.2648         |
| 4   | 0.8243    | -0.0282  | -0.8912   | -1.0622    | -1.0796         |
| 5   | 0.7770    | 0.0009   | 0.0274    | 0.0316     | 0.0282          |
| 6   | 0.6997    | -0.0108  | -0.3426   | -0.3951    | -0.3591         |
| 7   | 0.6378    | 0.0061   | 0.1938    | 0.2412     | 0.2170          |
| 8   | 0.5859    | 0.0142   | 0.4480    | 0.5911     | 0.5482          |
| 9   | 0.3997    | -0.0051  | -0.1625   | -1.0915    | -1.1186         |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 5.9275     | -11.2226 |        |
| 2   | 0.4534     | 3.4858   |        |
| 3   | 0.0096     | -0.1771  |        |
| 4   | 0.1186     | -0.7001  |        |
| 5   | 0.0001     | 0.0162   |        |
| 6   | 0.0129     | -0.2063  |        |
| 7   | 0.0080     | 0.1609   |        |
| 8   | 0.0648     | 0.4721   |        |
| 9   | 13.1347    | -7.4283  |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0254    | 0.9508   | 1.1003    | 0.9149  | 1.1359   |
| 2   | 0.9456    | 0.9017   | 0.9895    | 0.8532  | 1.0380   |
| 3   | 0.8797    | 0.8345   | 0.9249    | 0.7867  | 0.9727   |
| 4   | 0.8243    | 0.7801   | 0.8685    | 0.7318  | 0.9168   |
| 5   | 0.7770    | 0.7365   | 0.8175    | 0.6862  | 0.8678   |
| 6   | 0.6997    | 0.6592   | 0.7402    | 0.6089  | 0.7905   |
| 7   | 0.6378    | 0.5894   | 0.6862    | 0.5432  | 0.7324   |
| 8   | 0.5859    | 0.5329   | 0.6389    | 0.4888  | 0.6830   |
| 9   | 0.3997    | 0.3193   | 0.4800    | 0.2854  | 0.5140   |
FERRIC-OXIDE (First-order reaction)
25°C
Nonlinear Regression

Variables

x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_y^square = 1/y^2

'Automatic Initial Parameter Estimate Functions

xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q,r) = yatymax(q, xnear0(r))

Parameters

a = yatxnear0(y, x) "Auto \{previous: 95.3049}\}
b = -ln(.5)/(x50(x,y) - min(x)) "Auto \{previous: 0.00734397}\}

Equation

f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^square

Constraints

b > 0

Options

tolerance = 0.0001
step size = 100
iterations = 100

R = 0.73300110 Rsqr = 0.53729062 Adj Rsqr = 0.47118928
Standard Error of Estimate = 3.9417

| Coefficient | Std. Error | t     | P     |
|-------------|------------|-------|-------|
| a           | 95.3049    | 49.0490 | <0.0001 |
| b           | 0.0073     | 2.8097 | 0.0262 |

Analysis of Variance:

|       | DF | SS    | MS   | F    | P     |
|-------|----|-------|------|------|-------|
| Regression | 1  | 126.2918 | 126.2918 | 8.1283 | 0.0247 |
| Residual   | 7  | 108.7613 | 15.5373 |       |       |
| Total      | 8  | 235.0531 | 29.3816 |       |       |

PRESS = 326.1659

Durbin-Watson Statistic = 2.2618

Normality Test: Passed (P = 0.2642)

Constant Variance Test: Passed (P = 0.4072)

Power of performed test with alpha = 0.0500: 0.6296

The power of the performed test (0.6296) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|------------------|
| 1   | 95.3049   | 4.6951   | 1.1911    | 1.3690     | 1.4812           |
| 2   | 94.6075   | -4.5163  | -1.1458   | -1.2809    | -1.3553          |
| 3   | 93.9153   | 3.5307   | 0.8957    | 0.9807     | 0.9775           |
| 4   | 93.2281   | 0.5700   | 0.1446    | 0.1559     | 0.1446           |
| 5   | 92.5459   | 0.5543   | 0.1406    | 0.1501     | 0.1392           |
| 6   | 91.1966   | 0.0533   | 0.0135    | 0.0143     | 0.0133           |
| 7   | 89.8669   | -4.3953  | -1.1151   | -1.1949    | -1.2399          |
| 8   | 88.5565   | -4.3463  | -1.1026   | -1.2127    | -1.2633          |
| 9   | 82.2861   | 3.8744   | 0.9829    | 1.8391     | 2.3684           |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS  |
|-----|------------|----------|---------|
| 1   | 0.3608     | 0.8392   |         |
| 2   | 0.2049     | -0.6774  |         |
| 3   | 0.0955     | 0.4357   |         |
| 4   | 0.0020     | 0.0584   |         |
| 5   | 0.0016     | 0.0521   |         |
| 6   | 0.0000     | 0.0047   |         |
95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 95.3049   | 90.7103  | 99.8995   | 84.9132 | 105.6965 |
| 2   | 94.6075   | 90.4404  | 98.7747   | 84.3977 | 104.8174 |
| 3   | 93.9153   | 90.1208  | 97.7097   | 83.8518 | 103.9788 |
| 4   | 93.2281   | 89.7386  | 96.7176   | 83.2756 | 103.1806 |
| 5   | 92.5459   | 89.2793  | 95.8126   | 82.6693 | 102.4225 |
| 6   | 91.1966   | 88.0838  | 94.3093   | 81.3698 | 101.0233 |
| 7   | 89.8669   | 86.5167  | 93.2170   | 79.9623 | 99.7714  |
| 8   | 88.5565   | 84.6759  | 92.4371   | 78.4603 | 98.6528  |
| 9   | 82.2861   | 74.4083  | 90.1638   | 70.0821 | 94.4900  |

**FERRIC-OXIDE (First-order reaction)**

25°C / 60 %RH

Nonlinear Regression

[Variables]
\[
\begin{align*}
x &= \text{col}(1) \\
y &= \text{col}(2) \\
\text{reciprocal}_{y} &= 1/\text{abs}(y) \\
\text{reciprocal}_{y^2} &= 1/y^2 \\
'\text{Automatic Initial Parameter Estimate Functions} \\
x_{\text{near}(q)} &= \max(\text{abs}(q)) - \text{abs}(q) \\
y_{\text{at}(x_{\text{near}(q)}, r)} &= x_{\text{at}(x_{\text{max}(q, x_{\text{near}(r)})})}
\end{align*}
\]
[Parameters]
a = ytxnear0(y,x) "Auto {previous: 94.6625}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.00327568}"

[Equation]
f=a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.49034996     Rsqr = 0.24044308     Adj Rsqr = 0.13193495

Standard Error of Estimate = 3.4837

| Coefficient | Std. Error | t  | P  |
|-------------|------------|----|----|
| a           | 94.6625    | 1.6859 | 56.0487 | <0.0001 |
| b           | 0.0033     | 0.0022 | 1.4886   | 0.1802 |

Analysis of Variance:

|         | DF | SS   | MS   | F    | P    |
|---------|----|------|------|------|------|
| Regression | 1  | 26.8925 | 26.8925 | 2.2159 | 0.1802 |
| Residual  | 7  | 84.9533 | 12.1362 |      |      |
| Total     | 8  | 111.8458 | 13.9807 |      |      |

PRESS = 245.4569

Durbin-Watson Statistic = 1.9811

Normality Test:  Passed (P = 0.3652)

Constant Variance Test:  Passed (P = 0.9129)

Power of performed test with alpha = 0.0500: 0.2592

The power of the performed test (0.2592) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 94.6625   | 5.3375   | 1.5321    | 1.7518     | 2.1641          |
| 2   | 94.3530   | -1.1887  | -0.3412   | -0.3805    | -0.3560         |
|   | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|---|-----------|----------|-----------|---------|----------|
| 1 | 94.6625   | 90.6688  | 98.6562   | 85.5078 | 103.8172 |
| 2 | 94.3530   | 90.7062  | 97.9998   | 85.3442 | 103.3617 |
| 3 | 94.0444   | 90.7035  | 97.3853   | 85.1551 | 102.9337 |
| 4 | 93.7368   | 90.6503  | 96.8234   | 84.9399 | 102.5337 |
| 5 | 93.4303   | 90.5346  | 96.3260   | 84.6985 | 102.1621 |
| 6 | 92.8202   | 90.0733  | 95.5671   | 84.1366 | 101.5038 |
| 7 | 92.2141   | 89.2870  | 95.1412   | 83.4719 | 100.9563 |
| 8 | 91.6119   | 88.2385  | 94.9854   | 82.7103 | 100.5136 |
| 9 | 88.6596   | 81.5955  | 95.7238   | 77.8079 | 99.5114 |

**Influence Diagnostics:**

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.4714     | 0.2350   | 1.1996 |
| 2   | 0.0176     | 0.1960   | -0.1758|
| 3   | 0.0782     | 0.1645   | 0.3889 |
| 4   | 0.0377     | 0.1404   | -0.2631|
| 5   | 0.0802     | 0.1236   | -0.4052|
| 6   | 0.0141     | 0.1112   | 0.1583 |
| 7   | 0.0878     | 0.1263   | -0.4267|
| 8   | 0.0543     | 0.1677   | -0.3176|
| 9   | 4.0280     | 0.7354   | 3.4331 |
FERRIC-OXIDE (First-order reaction)
40°C / 75 %RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_y^square=1/y^2

'Automatic Initial Parameter Estimate Functions
xmin0(q)=max(abs(q))-abs(q)
yatxmin0(q,r)=xatymax(q,xmin0(r))

[Parameters]
a = yatxmin0(y,x) "Auto {previous: 97.0328}"
b = ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.00384635}"

[Equation]
f=a*exp(-b*x)

fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^square

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.52010303      Rsqr = 0.27050716    Adj Rsqr = 0.16629390

Standard Error of Estimate = 3.8442

| Coefficient | Std. Error | t    | P     |
|-------------|------------|------|-------|
| a           | 97.0328    | 1.8682 | 51.9404 | <0.0001 |
| b           | 0.0038     | 0.0024 | 1.6110  | 0.1512  |

Analysis of Variance:

|                   | DF | SS     | MS   | F     | P     |
|-------------------|----|--------|------|-------|-------|
| Regression        | 1  | 38.3596| 38.3596| 2.5957| 0.1512|
| Residual          | 7  | 103.4468| 14.7781|       |       |
| Total             | 8  | 141.8064| 17.7258|       |       |

PRESS = 380.7332

Durbin-Watson Statistic = 1.4961
Normality Test: Passed (P = 0.2819)

Constant Variance Test: Passed (P = 0.1243)

Power of performed test with alpha = 0.0500: 0.2919

The power of the performed test (0.2919) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 97.0328   | 2.9672   | 0.7719    | 0.8832     | 0.8674          |
| 2   | 96.6603   | -2.0478  | -0.5327   | -0.5943    | -0.5646         |
| 3   | 96.2892   | 1.4408   | 0.3748    | 0.4101     | 0.3843          |
| 4   | 95.9196   | 3.2910   | 0.8561    | 0.9233     | 0.9122          |
| 5   | 95.5514   | 1.8261   | 0.4750    | 0.5074     | 0.4786          |
| 6   | 94.8191   | -1.4809  | -0.3852   | -0.4086    | -0.3829         |
| 7   | 94.0925   | -5.4011  | -1.4050   | -1.5034    | -1.6915         |
| 8   | 93.3715   | -4.9135  | -1.2782   | -1.4017    | -1.5301         |
| 9   | 89.8483   | 4.3244   | 1.1249    | 2.1748     | 3.5354          |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.1206      | 0.4823   |        |
| 2   | 0.0432      | -0.2793  |        |
| 3   | 0.0166      | 0.1706   |        |
| 4   | 0.0696      | 0.3686   |        |
| 5   | 0.0181      | 0.1796   |        |
| 6   | 0.0104      | -0.1355  |        |
| 7   | 0.1639      | -0.6441  |        |
| 8   | 0.1991      | -0.6887  |        |
| 9   | 6.4738      | 5.8495   |        |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 97.0328   | 92.6153  | 101.4503  | 86.9261 | 107.1395|
| 2   | 96.6603   | 92.6304  | 100.6902  | 86.7169 | 106.6037|
| 3   | 96.2892   | 92.6006  | 99.9779   | 86.4792 | 106.0993|
| 4   | 95.9196   | 92.5140  | 99.3252   | 86.2124 | 105.6268|
| 5   | 95.5514   | 92.3573  | 98.7454   | 85.9164 | 105.1863|
| 6   | 94.8191   | 91.7875  | 97.8507   | 85.2368 | 104.4015|
| 7   | 94.0925   | 90.8575  | 97.3275   | 84.4439 | 103.7412|
| 8   | 93.3715   | 89.6402  | 97.1027   | 83.5453 | 103.1976|
| 9   | 89.8483   | 82.0686  | 97.6279   | 77.8836 | 101.8130|
FERRIC-OXIDE (First-order reaction)
50°C / 20% moisture
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxmin(q,r) = xatymax(q,xnear0(r))

[Parameters]
a = yatxmin(y,x)  "Auto {previous: 92.2681}"
b = -ln(.5)/((x50(x,y)-min(x))  "Auto {previous: 0.0060028}"

[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

R = 0.54301341      Rsqr = 0.29486356      Adj Rsqr = 0.19412978
Standard Error of Estimate = 5.2637

| Coefficient | Std. Error | t    | P    |
|--------------|------------|------|------|
| a            | 92.2681    | 35.7592 | <0.0001 |
| b            | 0.0060     | 0.0035 | 0.1337 |

Analysis of Variance:

| DF | SS    | MS    | F      | P    |
|----|-------|-------|--------|------|
| Regression | 1   | 81.1015 | 81.1015 | 2.9272 | 0.1308 |
| Residual  | 7   | 193.9459 | 27.7066 |        |      |
| Total     | 8   | 275.0474 | 34.3809 |        |      |

PRESS = 424.2674

Durbin-Watson Statistic = 2.0540

Normality Test: Passed (P = 0.4458)

Constant Variance Test: Passed (P = 0.2230)

Power of performed test with alpha = 0.0500: 0.3193

The power of the performed test (0.3193) is below the desired power of 0.8000.
You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 92.2681   | 7.7319   | 1.4689    | 1.6853     | 2.0240          |
| 2   | 91.7159   | -6.6647  | -1.2662   | -1.4143    | -1.5494         |
| 3   | 91.1669   | 0.2321   | 0.0441    | 0.0483     | 0.0447          |
| 4   | 90.6213   | 6.4185   | 1.2194    | 1.3151     | 1.4031          |
| 5   | 90.0790   | -1.6415  | -0.3119   | -0.3330    | -0.3108         |
| 6   | 89.0040   | -4.7380  | -0.9001   | -0.9549    | -0.9479         |
| 7   | 87.9418   | -2.9907  | -0.5682   | -0.6085    | -0.5789         |
| 8   | 86.8924   | -1.7186  | -0.3265   | -0.3587    | -0.3352         |
| 9   | 81.8298   | 3.3844   | 0.6430    | 1.2184     | 1.2709          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.4492     | 1.1383   |        |
| 2   | 0.2478     | -0.7712  |        |
| 3   | 0.0002     | 0.0199   |        |
| 4   | 0.1411     | 0.5667   |        |
| 5   | 0.0078     | -0.1164  |        |
| 6   | 0.0571     | -0.3356  |        |
| Row | Predicted | Regr. 5%  | Regr. 95%  | Pop. 5%  | Pop. 95%  |
|-----|-----------|-----------|-----------|---------|---------|
| 1   | 92.2681   | 86.1667   | 98.3694   | 78.4064 | 106.1297|
| 2   | 91.7159   | 86.1694   | 97.2623   | 78.0893 | 105.3424|
| 3   | 91.1669   | 86.1062   | 96.2277   | 77.7308 | 104.6031|
| 4   | 90.6213   | 85.9601   | 95.2825   | 77.3305 | 103.9122|
| 5   | 90.0790   | 85.7124   | 94.4456   | 76.8886 | 103.2694|
| 6   | 89.0040   | 84.8500   | 93.1580   | 75.8824 | 102.1256|
| 7   | 87.9418   | 83.4860   | 92.3976   | 74.7216 | 101.1620|
| 8   | 86.8924   | 81.7393   | 92.0454   | 73.4211 | 100.3636|
| 9   | 81.8298   | 71.2572   | 92.4025   | 65.4989 | 95.1608  |

**FERRIC-OXIDE (First-order reaction)**

50°C

Nonlinear Regression

[Variables]

\[ x = \text{col}(1) \]
\[ y = \text{col}(2) \]
\[ \text{reciprocal}_y = 1/|y| \]
\[ \text{reciprocal}_y\text{square} = 1/|y|^2 \]

'Automatic Initial Parameter Estimate Functions

\[ x_{\text{near}0}(q) = \max(|q|) - |q| \]
\[ y_{\text{at}x\text{near}0}(q,r) = x_{\text{at}y\text{max}}(q, x_{\text{near}0}(r)) \]

[Parameters]
\[
a = y \approx 0(y, x) \text{ } \text{Auto } \{ \text{previous: } 93.9272 \}
\]
\[
b = -\ln(0.5)/(x50(x, y) - \text{min}(x)) \text{ } \text{Auto } \{ \text{previous: } 0.0435405 \}
\]

**Equation**

\[
f = a \cdot \exp(-b \cdot x)
\]

"fit f to y"

"fit f to y with weight reciprocal_y"

"fit f to y with weight reciprocal_y square"

**Constraints**

\[b > 0\]

**Options**

- tolerance = 0.0001
- stepsize = 100
- iterations = 100

\[R = 0.97200797 \quad \text{Rsqr} = 0.94479949 \quad \text{Adj Rsqr} = 0.93691370\]

**Standard Error of Estimate = 4.2800**

| Coefficient | Std. Error | t | P |
|-------------|------------|---|---|
| a           | 93.9272    | 2.4277 | <0.0001 |
| b           | 0.0435     | 0.0046 | <0.0001 |

**Analysis of Variance:**

|                | DF | SS   | MS   | F    | P    |
|----------------|----|------|------|------|------|
| Regression     | 1  | 2194.7751 | 2194.7751 | 119.8104 | <0.0001 |
| Residual       | 7  | 128.2311    | 18.3187    |       |      |
| Total          | 8  | 2323.0062   | 290.3758   |       |      |

**PRESS = 287.4305**

**Durbin-Watson Statistic = 1.4476**

**Normality Test:** Passed (P = 0.7036)

**Constant Variance Test:** Passed (P = 0.8437)

**Power of performed test with alpha = 0.0500:** 0.9994

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 93.9272   | 6.0728   | 1.4189    | 1.7228     | 2.1017          |
| 2   | 89.9254   | -2.0340  | -0.4752   | -0.5423    | -0.5130         |
| 3   | 86.0940   | 1.8044   | 0.4216    | 0.4634     | 0.4357          |
| 4   | 82.4258   | 1.0546   | 0.2464    | 0.2651     | 0.2467          |
| 5   | 78.9140   | -5.2288  | -1.2217   | -1.3019    | -1.3845         |
| 6   | 72.3328   | -2.1438  | -0.5009   | -0.5362    | -0.5069         |
|   |   |   |   |   |   |
|---|---|---|---|---|---|
| 7 | 66.3004 | -4.2779 | -0.9995 | -1.0971 | -1.1162 |
| 8 | 60.7712 | -0.0489 | -0.0114 | -0.0130 | -0.0121 |
| 9 | 39.3191 | 5.7103 | 1.3342 | 1.8711 | 2.4503 |

**Influence Diagnostics:**

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.7040      | 0.3217   | 1.4475 |
| 2   | 0.0444      | 0.2320   | -0.2820|
| 3   | 0.0223      | 0.1721   | 0.1987 |
| 4   | 0.0055      | 0.1362   | 0.0980 |
| 5   | 0.1149      | 0.1194   | -0.5098|
| 6   | 0.0210      | 0.1272   | -0.1935|
| 7   | 0.1232      | 0.1700   | -0.5051|
| 8   | 0.0000      | 0.2297   | -0.0066|
| 9   | 1.6927      | 0.4916   | 2.4095 |

**95% Confidence:**

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 93.9272   | 88.1865  | 99.6679   | 82.2918 | 105.5627|
| 2   | 89.9254   | 85.0501  | 94.8006   | 78.6916 | 101.1591|
| 3   | 86.0940   | 81.8952  | 90.2928   | 75.1369 | 97.0511 |
| 4   | 82.4258   | 78.6909  | 86.1608   | 71.6380 | 93.2137 |
| 5   | 78.9140   | 75.4171  | 82.4108   | 68.2062 | 89.6217 |
| 6   | 72.3328   | 68.7228  | 75.9427   | 61.5876 | 83.0780 |
| 7   | 66.3004   | 62.1282  | 70.4727   | 55.3535 | 77.2474 |
| 8   | 60.7712   | 55.9201  | 65.6222   | 49.5479 | 71.9944 |
| 9   | 39.3191   | 32.2231  | 46.4151   | 26.9586 | 51.6796 |

![Graph 41](image)
FERRIC-OXIDE (BiPhasic First-order reaction)

25°C  
Nonlinear Regression

[Variables]
x = col(1)  
y = col(2)  
reciprocal_y = 1/abs(y)  
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions

xnear0(q) = max(abs(q)) - abs(q)  
yatxnear0(q,r) = yatymax(q, xnear0(r))

[Parameters]
a = yatxnear0(y, x)/2  "Auto {{previous: 0.141982}}
b = -ln(.5)/(0.5*(x50(x, y) - min(x)))  "Auto {{previous: 0.164601}}
c = yatxnear0(y, x)/2  "Auto {{previous: 0.840774}}
d = -ln(.5)/(1.5*(x50(x, y) - min(x)))  "Auto {{previous: 1.87663e-010}}

[Equation]
f = a*exp(-b*x) + c*exp(-d*x)

fit f to y

"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b > 0

d > 0

[Options]
tolerance = 1e-6

stepsize = 0.1

iterations = 100

R = 0.83352356    Rsqr = 0.69476153    Adj Rsqr = 0.51161844

Standard Error of Estimate = 0.0379

| Coefficient | Std. Error | t   | P   |
|-------------|------------|-----|-----|
| a           | 0.1420     | 0.4079 | 0.3480 | 0.7420 |
| b           | 0.1646     | 0.5184 | 0.3175 | 0.7637 |
| c           | 0.8408     | 0.4224 | 1.9905 | 0.1032 |
| d           | 0.0000     | 0.0218 | 0.0000 | 1.0000 |

Analysis of Variance:

| DF   | SS     | MS    | F      | P    |
|------|--------|-------|--------|------|
| Regression | 3 | 0.0163 | 0.0054 | 3.7935 | 0.0927 |
| Residual  | 5 | 0.0072 | 0.0014 |       |      |
| Total    | 8 | 0.0235 | 0.0029 |       |      |
PRESS = 19.2427

Durbin-Watson Statistic = 2.5793

Normality Test: Failed (P = 0.0160)

Constant Variance Test: Passed (P = 0.5198)

Power of performed test with alpha = 0.0500: 0.8361

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|----------------|
| 1   | 0.9828    | 0.0172   | 0.4552    | 0.9542     | 0.9437         |
| 2   | 0.9612    | -0.0603  | -1.5917   | -1.8642    | -3.0196        |
| 3   | 0.9429    | 0.0315   | 0.8324    | 0.9637     | 0.9552         |
| 4   | 0.9274    | 0.0106   | 0.2786    | 0.3308     | 0.2991         |
| 5   | 0.9143    | 0.0167   | 0.4416    | 0.5211     | 0.4792         |
| 6   | 0.8937    | 0.0188   | 0.4974    | 0.5679     | 0.5252         |
| 7   | 0.8788    | -0.0241  | -0.6364   | -0.7809    | -0.7454        |
| 8   | 0.8682    | -0.0260  | -0.6876   | -1.0426    | -1.0542        |
| 9   | 0.8461    | 0.0156   | 0.4106    | 6.8933     | (+inf)         |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 0.7725      | 0.7724   | 1.7385 |
| 2   | 0.3230      | 0.2710   | -1.8411|
| 3   | 0.0790      | 0.2540   | 0.5574 |
| 4   | 0.0112      | 0.2903   | 0.1913 |
| 5   | 0.0266      | 0.2818   | 0.3002 |
| 6   | 0.0245      | 0.2330   | 0.2895 |
| 7   | 0.0771      | 0.3359   | -0.5302|
| 8   | 0.3531      | 0.5650   | -1.2015|
| 9   | 3337.0459   | 0.9965   | (+inf) |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 0.9828    | 0.8972   | 1.0683    | 0.8531  | 1.1124  |
| 2   | 0.9612    | 0.9105   | 1.0119    | 0.8514  | 1.0710  |
| 3   | 0.9429    | 0.8939   | 0.9920    | 0.8339  | 1.0520  |
| 4   | 0.9274    | 0.8750   | 0.9799    | 0.8168  | 1.0380  |
| 5   | 0.9143    | 0.8626   | 0.9660    | 0.8040  | 1.0245  |
| 6   | 0.8937    | 0.8466   | 0.9407    | 0.7855  | 1.0018  |
| 7   | 0.8788    | 0.8224   | 0.9353    | 0.7663  | 0.9914  |
| 8   | 0.8682    | 0.7950   | 0.9413    | 0.7463  | 0.9900  |
| 9   | 0.8461    | 0.7489   | 0.9433    | 0.7085  | 0.9836  |
**FERRIC-OXIDE (BiPhasic First-order reaction)**

25°C / 60 %RH

Nonlinear Regression

*Variables*

\[ x = \text{col}(1) \]
\[ y = \text{col}(2) \]
\[ \text{reciprocal}_y = \frac{1}{\text{abs}(y)} \]
\[ \text{reciprocal}_y\text{square} = \frac{1}{y^2} \]

'Automatic Initial Parameter Estimate Functions

\[ x_{\text{near}0}(q) = \max(\text{abs}(q)) - \text{abs}(q) \]
\[ y_{x_{\text{near}0}}(q,r) = \text{yatymax}(q, x_{\text{near}0}(r)) \]

*Parameters*

\[ a = y_{x_{\text{near}0}}(y,x)/2 \] Auto \{previous: 0.087789\}
\[ b = -\ln(0.5)/(0.5*(x_{\text{50}}(x,y)-\text{min}(x))) \] Auto \{previous: 0.531831\}
\[ c = y_{x_{\text{near}0}}(y,x)/2 \] Auto \{previous: 0.905793\}
\[ d = -\ln(0.5)/(1.5*(x_{\text{50}}(x,y)-\text{min}(x))) \] Auto \{previous: 9.84071e-012\}

*Equation*

\[ f = a*\exp(-b*x) + c*\exp(-d*x) \]

"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

*Constraints*

\[ b > 0 \]
\[ d > 0 \]

*Options*

tolerance=1e-6
stepsize=0.1

---

287
iterations=100

R = 0.79886257   Rsqr = 0.63818141   Adj Rsqr = 0.42109026

Standard Error of Estimate = 0.0284

| Coefficient | Std. Error | t  | P   |
|--------------|------------|----|-----|
| a            | 0.0878     | 1.9503 | 0.1086 |
| b            | 0.5318     | 0.9400 | 0.3904 |
| c            | 0.9058     | 22.2519 | <0.0001 |
| d            | 0.0000     | 0.0000 | 1.0000 |

Analysis of Variance:

| DF | SS    | MS    | F   | P    |
|----|-------|-------|-----|------|
| Regression | 3 | 0.0071 | 0.0024 | 2.9397 | 0.1380 |
| Residual | 5 | 0.0040 | 0.0008 |
| Total | 8 | 0.0112 | 0.0014 |

PRESS = 0.1041

Durbin-Watson Statistic = 3.0961

Normality Test: Passed (P = 0.3683)

Constant Variance Test: Passed (P = 0.9129)

Power of performed test with alpha = 0.0500: 0.7653

The power of the performed test (0.7653) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 0.9936    | 0.0064   | 0.2256    | 0.8197     | 0.7880          |
| 2   | 0.9574    | -0.0257  | -0.9044   | -1.1430    | -1.1895         |
| 3   | 0.9361    | 0.0327   | 1.1505    | 1.4414     | 1.6864          |
| 4   | 0.9236    | -0.0082  | -0.2875   | -0.3341    | -0.3022         |
| 5   | 0.9163    | -0.0167  | -0.5885   | -0.6624    | -0.6204         |
| 6   | 0.9094    | 0.0344   | 1.2097    | 1.4209     | 1.6458          |
| 7   | 0.9070    | -0.0208  | -0.7308   | -0.8881    | -0.8656         |
| 8   | 0.9062    | -0.0134  | -0.4723   | -0.5678    | -0.5251         |
| 9   | 0.9058    | 0.0113   | 0.3976    | 2.0390     | 4.4425          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 2.0496     | 0.9243   | 2.7526 |
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 0.9936    | 0.9233   | 1.0639    | 0.8921  | 1.0950  |
| 2   | 0.9574    | 0.9126   | 1.0021    | 0.8716  | 1.0431  |
| 3   | 0.9361    | 0.8920   | 0.9802    | 0.8507  | 1.0215  |
| 4   | 0.9236    | 0.8863   | 0.9609    | 0.8415  | 1.0057  |
| 5   | 0.9163    | 0.8827   | 0.9498    | 0.8358  | 0.9967  |
| 6   | 0.9094    | 0.8710   | 0.9478    | 0.8268  | 0.9920  |
| 7   | 0.9070    | 0.8655   | 0.9486    | 0.8229  | 0.9912  |
| 8   | 0.9062    | 0.8656   | 0.9468    | 0.8226  | 0.9899  |
| 9   | 0.9058    | 0.8341   | 0.9775    | 0.8034  | 1.0082  |

**95% Confidence:**

**FERRIC-OXIDE (BiPhasic First-order reaction)**

40°C / 75 %RH

Nonlinear Regression

[Variables]

\[ x = \text{col}(1) \]

\[ y = \text{col}(2) \]
reciprocal_y= 1/abs(y)
reciprocal_ysquare= 1/y^2

Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q, r) = yatymax(q, xnear0(r))

[Parameters]
a = yatxnear0(y, x)/2 "Auto {previous: 0.0903676}"
b = -ln(.5)/(0.5*(x50(x, y)-min(x))) "Auto {previous: 0.210639}"
c = yatxnear0(y, x)/2 "Auto {previous: 0.907939}"
d = -ln(.5)/(1.5*(x50(x, y)-min(x))) "Auto {previous: 3.32243e-011}"

[Equation]
f = a*exp(-b*x) + c*exp(-d*x)

fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b > 0
d > 0

[Options]
tolerance= 1e-6
stepsize=0.1
iterations=100

R = 0.71054287    Rsqr = 0.50487117    Adj Rsqr = 0.20779387

Standard Error of Estimate = 0.0375

| Coefficient | Std. Error | t     | P     |
|-------------|------------|-------|-------|
| a           | 0.0904     | 0.4001| 0.7056|
| b           | 0.2106     | 0.3094| 0.7695|
| c           | 0.9079     | 3.8203| 0.0124|
| d           | 0.0000     | 0.0000| 1.0000|

Analysis of Variance:

|                | SS | MS  | F     | P     |
|----------------|----|-----|-------|-------|
| Regression     | 0.0072 | 0.0024 | 1.6995 | 0.2816 |
| Residual       | 0.0070 | 0.0014 |
| Total          | 0.0142 | 0.0018 |

PRESS = 36.0903

Durbin-Watson Statistic = 1.5338

Normality Test:    Passed (P = 0.2873)

Constant Variance Test:    Passed (P = 0.5198)
The power of the performed test (0.5855) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

**Regression Diagnostics:**

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 0.9983    | 0.0017   | 0.0452    | 0.1000     | 0.0896          |
| 2   | 0.9811    | -0.0350  | -0.9345   | -1.0962    | -1.1249         |
| 3   | 0.9672    | 0.0101   | 0.2685    | 0.3140     | 0.2836          |
| 4   | 0.9560    | 0.0361   | 0.9642    | 1.1481     | 1.1967          |
| 5   | 0.9469    | 0.0269   | 0.7185    | 0.8422     | 0.8131          |
| 6   | 0.9335    | -0.0001  | -0.0024   | -0.0028    | -0.0025         |
| 7   | 0.9247    | -0.0378  | -1.0082   | -1.2436    | -1.3384         |
| 8   | 0.9189    | -0.0344  | -0.9168   | -1.3336    | -1.4860         |
| 9   | 0.9093    | 0.0324   | 0.8659    | 11.7811    | (+inf)          |

**Influence Diagnostics:**

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.0098     | 0.7960   | 0.1769 |
| 2   | 0.1129     | 0.2732   | -0.6897|
| 3   | 0.0091     | 0.2687   | 0.1719 |
| 4   | 0.1377     | 0.2948   | 0.7736 |
| 5   | 0.0663     | 0.2722   | 0.4973 |
| 6   | 0.0000     | 0.2303   | -0.0014|
| 7   | 0.2016     | 0.3427   | -0.9665|
| 8   | 0.4962     | 0.5274   | -1.5699|
| 9   | 6387.8017  | 0.9946   | (+inf) |

**95% Confidence:**

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 0.9983    | 0.9124   | 1.0842    | 0.8692  | 1.1274   |
| 2   | 0.9811    | 0.9308   | 1.0315    | 0.8724  | 1.0898   |
| 3   | 0.9672    | 0.9173   | 1.0172    | 0.8587  | 1.0757   |
| 4   | 0.9560    | 0.9037   | 1.0083    | 0.8464  | 1.0656   |
| 5   | 0.9469    | 0.8966   | 0.9971    | 0.8382  | 1.0555   |
| 6   | 0.9335    | 0.8872   | 0.9797    | 0.8266  | 1.0403   |
| 7   | 0.9247    | 0.8683   | 0.9811    | 0.8131  | 1.0363   |
| 8   | 0.9189    | 0.8490   | 0.9889    | 0.7999  | 1.0380   |
| 9   | 0.9093    | 0.8132   | 1.0053    | 0.7732  | 1.0453   |
**FERRIC-OXIDE (BiPhasic First-order reaction)**

50°C / 20 % moisture

Nonlinear Regression

[Variables]
\( x = \text{col}(1) \)
\( y = \text{col}(2) \)
\( \text{reciprocal}_y = 1/\text{abs}(y) \)
\( \text{reciprocal}_y^{\text{square}} = 1/y^2 \)

'Automatic Initial Parameter Estimate Functions
\( \text{xnear0}(q) = \max(\text{abs}(q)) - \text{abs}(q) \)
\( y_{atxnear0}(q,r) = \text{yatxmax}(q,x_{\text{near0}}(r)) \)

[Parameters]
\( a = y_{atxnear0}(y,x)/2 \) "Auto \{previous: 0.118032\}"
\( b = -\ln(0.5)/(0.5*(x_{50}(x,y)-\text{min}(x))) \) "Auto \{previous: 0.284503\}"
\( c = y_{atxnear0}(y,x)/2 \) "Auto \{previous: 0.845865\}"
\( d = -\ln(0.5)/(1.5*(x_{50}(x,y)-\text{min}(x))) \) "Auto \{previous: 1.2391e-011\}"

[Equation]
\( f = a*\exp(-b*x)+c*\exp(-d*x) \)

"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_y^{square}"

[Constraints]
\( b > 0 \)
\( d > 0 \)

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

R = 0.68453483     Rsqr = 0.46858793     Adj Rsqr = 0.14974069

Standard Error of Estimate = 0.0541

| Coefficient | Std. Error | t   | P   |
|-------------|------------|-----|-----|
| a           | 0.1180     | 0.6841 | 0.5243 |
| b           | 0.2845     | 0.4224 | 0.6903 |
| c           | 0.8459     | 4.6351 | 0.0057 |
| d           | 0.0000     | 0.0000 | 1.0000 |

Analysis of Variance:

| DF    | SS    | MS    | F      | P    |
|-------|-------|-------|--------|------|
| Regression | 3 | 0.0129 | 0.0043 | 1.4696 | 0.3290 |
| Residual | 5 | 0.0146 | 0.0029 |       |      |
| Total    | 8 | 0.0275 | 0.0034 |       |      |

PRESS = 0.4189

Durbin-Watson Statistic = 2.2924

Normality Test: Passed (P = 0.2163)

Constant Variance Test: Passed (P = 0.1384)

Power of performed test with alpha = 0.0500: 0.5365

The power of the performed test (0.5365) is below the desired power of 0.8000.
You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 0.9639    | 0.0361   | 0.6677    | 1.6347     | 2.1430          |
| 2   | 0.9347    | -0.0842  | -1.5566   | -1.8376    | -2.8849         |
| 3   | 0.9127    | 0.0013   | 0.0242    | 0.0288     | 0.0258          |
| 4   | 0.8961    | 0.0743   | 1.3735    | 1.6375     | 2.1509          |
| 5   | 0.8837    | 0.0007   | 0.0127    | 0.0147     | 0.0131          |
| 6   | 0.8673    | -0.0246  | -0.4553   | -0.5200    | -0.4782         |
| 7   | 0.8580    | -0.0085  | -0.1567   | -0.1944    | -0.1745         |
| 8   | 0.8527    | -0.0010  | -0.0183   | -0.0250    | -0.0224         |
| 9   | 0.8463    | 0.0059   | 0.1087    | 1.0876     | 1.1133          |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 3.3361      | 0.8332   | 4.7888 |
| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|---------|
| 1   | 0.9639    | 0.8370   | 1.0908    | 0.7757  | 1.1521  |
| 2   | 0.9347    | 0.8608   | 1.0085    | 0.7773  | 1.0921  |
| 3   | 0.9127    | 0.8372   | 0.9882    | 0.7545  | 1.0709  |
| 4   | 0.8961    | 0.8205   | 0.9718    | 0.7379  | 1.0544  |
| 5   | 0.8837    | 0.8137   | 0.9537    | 0.7281  | 1.0393  |
| 6   | 0.8673    | 0.8001   | 0.9344    | 0.7129  | 1.0216  |
| 7   | 0.8580    | 0.7758   | 0.9402    | 0.6965  | 1.0195  |
| 8   | 0.8527    | 0.7579   | 0.9476    | 0.6845  | 1.0210  |
| 9   | 0.8463    | 0.7080   | 0.9846    | 0.6502  | 1.0423  |

95% Confidence:

**FERRIC-OXIDE** (BiPhasic First-order reaction)

50°C
Nonlinear Regression

[Variables]

\[ x = \text{col}(1) \]
\[ y = \text{col}(2) \]
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2

'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q)) - abs(q)
yatxnear0(q,r) = xatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2  "Auto {previous: 0.278258}"
b = -ln(.5)/(0.5*(x50(x,y)-min(x)))  "Auto {previous: 0.21828}"
c = yatxnear0(y,x)/2  "Auto {previous: 0.709415}"
d = -ln(.5)/(1.5*(x50(x,y)-min(x)))  "Auto {previous: 0.0230322}"

[Equation]
f = a*exp(-b*x) + c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b > 0
d > 0

[Options]
tolerance = 1e-6
stepsize = 0.1
iterations = 100

R = 0.99107522    Rsqr = 0.98223009    Adj Rsqr = 0.97156814

Standard Error of Estimate = 0.0287

| Coefficient | Std. Error | t     | P    |
|-------------|------------|-------|------|
| a           | 0.2783     | 1.1260| 0.3113|
| b           | 0.2183     | 1.0802| 0.3294|
| c           | 0.7094     | 2.7681| 0.0395|
| d           | 0.0230     | 1.2934| 0.2524|

Analysis of Variance:

| DF | SS   | MS   | F     | P          |
|----|------|------|-------|------------|
| Regression | 3   | 0.2282| 0.0761| 92.1248    | <0.0001    |
| Residual  | 5   | 0.0041| 0.0008|            |            |
| Total     | 8   | 0.2323| 0.0290|            |            |

PRESS = 0.0203

Durbin-Watson Statistic = 2.9617

Normality Test: Passed (P = 0.2977)

Constant Variance Test: Passed (P = 0.1384)
Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|----------------|
| 1   | 0.9877    | 0.0123   | 0.4290    | 0.9777     | 0.9724         |
| 2   | 0.9170    | -0.0380  | -1.3239   | -1.5562    | 1.9382         |
| 3   | 0.8573    | 0.0217   | 0.7546    | 0.8879     | 0.8653         |
| 4   | 0.8066    | 0.0282   | 0.9811    | 1.1699     | 1.2279         |
| 5   | 0.7632    | -0.0263  | -0.9167   | -1.0712    | -1.0915        |
| 6   | 0.6930    | 0.0089   | 0.3109    | 0.3553     | 0.3219         |
| 7   | 0.6386    | -0.0183  | -0.6385   | -0.7911    | -0.7565        |
| 8   | 0.5948    | 0.0124   | 0.4310    | 0.6098     | 0.5669         |
| 9   | 0.4511    | -0.0008  | -0.0277   | -0.2942    | -0.2654        |

Influence Diagnostics:

| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | 1.0023      | 0.8075   | 1.9914 |
| 2   | 0.2310      | 0.2762   | -1.1973|
| 3   | 0.0758      | 0.2778   | 0.5366 |
| 4   | 0.1444      | 0.2967   | 0.7976 |
| 5   | 0.1048      | 0.2676   | -0.6597|
| 6   | 0.0096      | 0.2340   | 0.1779 |
| 7   | 0.0837      | 0.3485   | -0.5532|
| 8   | 0.0932      | 0.5006   | 0.5676 |
| 9   | 2.4198      | 0.9911   | -2.8071|

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 0.9877    | 0.9213   | 1.0540    | 0.8884  | 1.0870   |
| 2   | 0.9170    | 0.8781   | 0.9558    | 0.8335  | 1.0004   |
| 3   | 0.8573    | 0.8184   | 0.8962    | 0.7738  | 0.9408   |
| 4   | 0.8066    | 0.7664   | 0.8468    | 0.7225  | 0.8907   |
| 5   | 0.7632    | 0.7250   | 0.8014    | 0.6800  | 0.8463   |
| 6   | 0.6930    | 0.6572   | 0.7287    | 0.6109  | 0.7750   |
| 7   | 0.6386    | 0.5950   | 0.6822    | 0.5528  | 0.7243   |
| 8   | 0.5948    | 0.5426   | 0.6471    | 0.5044  | 0.6853   |
| 9   | 0.4511    | 0.3776   | 0.5246    | 0.3469  | 0.5553   |
L-4 Tablets (First-order reaction)
25°C
Nonlinear Regression

[Variables]
\( x = \text{col}(1) \)
\( y = \text{col}(2) \)
\( \text{reciprocal}_y = 1/|y| \)
\( \text{reciprocal}_y^2 = 1/y^2 \)

'Automatic Initial Parameter Estimate Functions
\( x_{\text{near0}}(q) = \max(|q|) - |q| \)
\( y_{\text{at} x_{\text{near0}}}(q,r) = \text{at} y_{\text{max}}(q,x_{\text{near0}}(r)) \)

[Parameters]
\( a = y_{\text{at} x_{\text{near0}}}(y,x) \) "Auto {previous: 88.5058}"
\( b = -\ln(0.5)/(\text{x50}(x,y)-\text{min}(x)) \) "Auto {previous: 0.0151329}"

[Equation]
\( f = a \times \exp(-b \times x) \)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_y^2"

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

\( R = 0.53591830 \quad \text{Rsq} = 0.28720842 \quad \text{Adj Rsqr} = 0.04961123 \)
Standard Error of Estimate = 9.5871

| Coefficient | Std. Error | \( t \) | \( P \) |
|-------------|------------|--------|--------|
| a           | 88.5058    | 14.0651| 0.0008 |
| b           | 0.0151     | 1.0965 | 0.3530 |

Analysis of Variance:

|         | DF | SS    | MS    | \( F \)  | \( P \)     |
|---------|----|-------|-------|----------|-------------|
| Regression | 1  | 111.1047 | 111.1047 | 1.2088 | 0.3519 |
| Residual  | 3  | 275.7389 | 91.9130  |        |            |
| Total     | 4  | 386.8436 | 96.7109  |        |            |

PRESS = 684.7905

Durbin-Watson Statistic = 1.6705

Normality Test: Passed (\( P = 0.5885 \))

Constant Variance Test: Passed (\( P = 0.0500 \))

Power of performed test with alpha = 0.0500: 0.1327

The power of the performed test (0.1327) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 88.5058   | 11.4942  | 1.1989    | 1.5891     | 3.2620          |
| 2   | 87.1765   | -3.9248  | -0.4094   | -0.4970    | -0.4236         |
| 3   | 85.8672   | -11.0416 | -1.1517   | -1.3287    | -1.6912         |
| 4   | 79.6098   | 2.0661   | 0.2155    | 0.2645     | 0.2185          |
| 5   | 76.0764   | 1.4259   | 0.1487    | 0.2561     | 0.2115          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.9557     | 0.4308   | 2.8379 |
| 2   | 0.0585     | 0.3214   | -0.2915|
| 3   | 0.2921     | 0.2487   | -0.9729|
| 4   | 0.0177     | 0.3363   | 0.1556 |
| 5   | 0.0645     | 0.6628   | 0.2965 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 88.5058   | 68.4800  | 108.5316  | 52.0104 | 125.0012 |
| 2   | 87.1765   | 69.8791  | 104.4740  | 52.1039 | 122.2491 |
| 3   | 85.8672   | 70.6529  | 101.0816  | 51.7738 | 119.9606 |
L-4 Tablets (First-order reaction)

25°C / 60 % RH

Nonlinear Regression

[Variables]
\( x = \text{col}(1) \)
\( y = \text{col}(2) \)
\( \text{reciprocal}_y = \frac{1}{\mid y \mid} \)
\( \text{reciprocal}_y^2 = \frac{1}{y^2} \)

'Automatic Initial Parameter Estimate Functions
\( x\text{near}(q) = \max(\mid q \mid) - \mid q \mid \)
\( y\text{at}x\text{near}(q,r) = x\text{at}y\text{max}(q, x\text{near}(r)) \)

[Parameters]
\( a = y\text{at}x\text{near}(y,x) \) "Auto \{ previous: 90.9752 \}"
\( b = -\ln(0.5)/(x50(x,y)-\min(x)) \) "Auto \{ previous: 0.00855306 \}"

[Equation]
\( f = a \cdot \exp(-b \cdot x) \)

'fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_y^2

[Constraints]
b > 0

[Options]
tolerance = 0.0001
stepsize = 100
iterations=100

R = 0.36269390     Rsqr = 0.13154686     Adj Rsqr = 0.00000000

Standard Error of Estimate = 9.5249

| Coefficient | Std. Error | t    | P    |
|-------------|------------|------|------|
| a           | 90.9752    | 14.6590 | 0.0007 |
| b           | 0.0086     | 0.6674 | 0.5523 |

Analysis of Variance:

| DF | SS     | MS     | F     | P     |
|----|--------|--------|-------|-------|
| Regression 1 | 41.2269 | 41.2269 | 0.4544 | 0.5485 |
| Residual 3   | 272.1737 | 90.7246 |
| Total 4      | 313.4006 | 78.3502 |

PRESS = 768.9416

Durbin-Watson Statistic = 2.4655

Normality Test: Passed (P = 0.1734)

Constant Variance Test: Passed (P = 0.0500)

Power of performed test with alpha = 0.0500: 0.0774

The power of the performed test (0.0774) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 90.9752   | 9.0248   | 0.9475    | 1.2490     | 1.4720          |
| 2   | 90.2004   | -6.7429  | -0.7079   | -0.8595    | -0.8083         |
| 3   | 89.4322   | -7.0152  | -0.7365   | -0.8510    | -0.7977         |
| 4   | 85.6883   | 8.8798   | 0.9323    | 1.1388     | 1.2341          |
| 5   | 83.5175   | -4.1468  | -0.4354   | -0.7615    | -0.6922         |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.5754     | 1.2643   | 1.4720 |
| 2   | 0.1751     | -0.5565  | 1.2341 |
| 3   | 0.1213     | -0.4617  |        |
| 4   | 0.3192     | 0.8659   |        |
| 5   | 0.5970     | -0.9933  |        |

95% Confidence:
| Row | Predicted  | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|------------|----------|-----------|---------|---------|
| 1   | 90.9752    | 71.2248  | 110.7257  | 54.7961 | 127.1544|
| 2   | 90.2004    | 73.0112  | 107.3896  | 55.3534 | 125.0475|
| 3   | 89.4322    | 74.2480  | 104.6164  | 55.5293 | 123.3352|
| 4   | 85.6883    | 68.2786  | 103.0979  | 50.7319 | 120.6446|
| 5   | 83.5175    | 58.6480  | 108.3870  | 44.3086 | 122.7265|

**2D Graph 47**

**L-4 Tablets (First-order reaction)**

40°C / 75 % RH
Nonlinear Regression

[Variables]
- \( x = \text{col}(1) \)
- \( y = \text{col}(2) \)
- \( \text{reciprocal}_y = 1/\text{abs}(y) \)
- \( \text{reciprocal}_y\text{square} = 1/y^2 \)

'Automatic Initial Parameter Estimate Functions
- \( x\text{near}0(q) = \max(\text{abs}(q)) - \text{abs}(q) \)
- \( y\text{at}x\text{near}0(q,r) = \text{at}y\text{max}(q,x\text{near}0(r)) \)

[Parameters]
- \( a = y\text{at}x\text{near}0(y,x) \) "Auto \{\{\text{previous: 93.395}\}\}
- \( b = -\ln(.5)/(x50(x,y) - \text{min}(x)) \) "Auto \{\{\text{previous: 0.0231032}\}\}

[Equation]
- \( f = a \times \exp(-b \times x) \)
- \( \text{fit} f \text{ to } y \)
- \( \text{`fit f to y with weight reciprocal}_y \)
- \( \text{`fit f to y with weight reciprocal}_y\text{square} \)

[Constraints]
b > 0
[Options]
tolerance = 0.0001
stepsize = 100
iterations = 100

R = 0.77076136   Rsqr = 0.59407308   Adj Rsqr = 0.45876410

Standard Error of Estimate = 7.7486

| Coefficient | Std. Error | t   | p    |
|-------------|------------|-----|------|
| a           | 93.3950    | 5.1325 | 18.1968 | 0.0004 |
| b           | 0.0231     | 0.0111 | 2.0775  | 0.1293 |

Analysis of Variance:

|       | DF | SS    | MS     | F      | P       |
|-------|----|-------|--------|--------|---------|
| Regression | 1 | 263.6055 | 263.6055 | 4.3905 | 0.1271  |
| Residual  | 3 | 180.1202 | 60.0401 |        |         |
| Total     | 4 | 443.7258 | 110.9314|        |         |

PRESS = 697.1267

Durbin-Watson Statistic = 1.5207

Normality Test: Passed (P = 0.4144)

Constant Variance Test: Passed (P = 0.0500)

Power of performed test with alpha = 0.0500: 0.3035

The power of the performed test (0.3035) is below the desired power of 0.8000.
You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 93.3950   | 6.6050   | 0.8524    | 1.1378     | 1.2322          |
| 2   | 91.2621   | 0.1846   | 0.0238    | 0.0289     | 0.0236          |
| 3   | 89.1778   | -6.5428  | -0.8444   | -0.9724    | -0.9594         |
| 4   | 79.4491   | -6.9326  | -0.8947   | -1.1051    | -1.1718         |
| 5   | 74.1290   | 6.7522   | 0.8714    | 1.4722     | 2.2816          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 0.5060     | 1.0894   |        |
| 2   | 0.0002     | 0.0162   |        |
| 3   | 0.1542     | -0.5480  |        |
L-4 Tablets (First-order reaction)

50°C

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_y^2=1/y^2

'Automatic Initial Parameter Estimate Functions
xnear(q)=max(abs(q))-abs(q)
yatxnear(q,r)=yatymax(q,xnear(r))

[Parameters]
a = yatxnear(y,x) "Auto {previous: 88.9987}"
b = -ln(.5)/(x50(x,y)-min(x)) "Auto {previous: 0.0633019}"

[Equation]
f=a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0

[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.90949854  Rsqr = 0.82718759  Adj Rsqr = 0.76958346

Standard Error of Estimate = 9.2619

| Coefficient | Std. Error | t   | P    |
|--------------|------------|-----|------|
| a            | 88.9987    | 6.4103 | 13.8836 | 0.0008 |
| b            | 0.0633     | 0.0182 | 3.4759  | 0.0402 |

Analysis of Variance:

|     | DF | SS      | MS       | F      | P    |
|-----|----|---------|----------|--------|------|
| Regression | 1  | 1231.8276 | 1231.8276  | 14.3599 | 0.0322 |
| Residual   | 3  | 257.3480  | 85.7827  |        |      |
| Total      | 4  | 1489.1757 | 372.2939 |        |      |

PRESS = 821.6253

Durbin-Watson Statistic = 2.0680

Normality Test: Passed (P = 0.4730)

Constant Variance Test: Passed (P = 0.0500)

Power of performed test with alpha = 0.0500: 0.5778

The power of the performed test (0.5778) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-------------------|-----------|------------|-----------------|
| 1   | 88.9987           | 11.0013   | 1.1878     | 1.6456          | 4.3080          |
| 2   | 83.5396           | -9.8140   | -1.0596    | -1.2831         | -1.5596         |
| 3   | 78.4152           | -3.1642   | -0.3416    | -0.3909         | -0.3276         |
| 4   | 57.1402           | -2.4821   | -0.2680    | -0.3423         | -0.2851         |
| 5   | 47.2571           | 4.8819    | 0.5271     | 0.8133          | 0.7521          |

Influence Diagnostics:
| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 1.2451     | 0.4790   | 4.1309 |
| 2   | 0.3838     | 0.3180   | -1.0650|
| 3   | 0.0236     | 0.2360   | -0.1821|
| 4   | 0.0370     | 0.3870   | -0.2265|
| 5   | 0.4566     | 0.5799   | 0.8837 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 88.9987   | 68.5982  | 109.3992  | 53.1521 | 124.8453 |
| 2   | 83.5396   | 66.9176  | 100.1615  | 49.7004 | 117.3787 |
| 3   | 78.4152   | 64.0957  | 92.7347   | 45.6457 | 111.1848 |
| 4   | 57.1402   | 38.8039  | 75.4766   | 22.4268 | 91.8536  |
| 5   | 47.2571   | 24.8103  | 69.7038   | 10.2077 | 84.3064  |

L-4 Tablets (BiPhasic First-order reaction)

25°C

Nonlinear Regression

[Variables]
\[ x = \text{col}(1) \]
\[ y = \text{col}(2) \]
\[ \text{reciprocal}_y = 1/\text{abs}(y) \]
\[ \text{reciprocal}_y^{\text{square}} = 1/y^2 \]

'Automatic Initial Parameter Estimate Functions

\[ \text{xnear0}(q) = \max(\text{abs}(q)) - \text{abs}(q) \]
\[ \text{yatxnear0}(q,r) = \text{xatymax}(q, \text{xnear0}(r)) \]

[Parameters]
\( a = \text{yatxnear0}(y,x)/2 \) "Auto \{\text{previous: 0.219076}\}"
\( b = -\ln(0.5)/(0.5*(x50(x,y)-\text{min}(x))) \) "Auto \{\text{previous: 1.7807}\}"
\( c = \text{yatxnear0}(y,x)/2 \) "Auto \{\text{previous: 0.782068}\}"
\( d = -\ln(0.5)/(1.5*(x50(x,y)-\text{min}(x))) \) "Auto \{\text{previous: 7.60564e-011}\}"

[Equation]
\[ f = a \cdot \exp(-b \cdot x) + c \cdot \exp(-d \cdot x) \]

fit \( f \) to \( y \)
"fit \( f \) to \( y \) with weight reciprocal_\( y \)
"fit \( f \) to \( y \) with weight reciprocal_\( y^2 \)

[Constraints]
b > 0
d > 0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

\[ R = 0.95990266 \quad \text{Rsqr} = 0.92141311 \quad \text{Adj Rsqr} = 0.68565244 \]

Standard Error of Estimate = 0.0551!

| Coefficient | Std. Error | t | P |
|-------------|------------|---|---|
| a           | 0.2191     | 1.8812 | 0.3110 |
| b           | 1.7807     | 0.6318 | 0.6413 |
| c           | 0.7821     | 7.5271 | 0.0841 |
| d           | 0.0000     | 1.0000 | 0.0000 |

Analysis of Variance:

| DF | SS    | MS    | F    | P    |
|----|-------|-------|------|------|
| Regression | 0.0356 | 0.0119 | 3.9083 | 0.3522 |
| Residual    | 0.0030 | 0.0030 | 0.0097 | 0.0097 |
| Total       | 0.0387 | 0.0097 | 0.3522 | 0.3522 |

PRESS = 55.5621

Durbin-Watson Statistic = 3.4242

Normality Test: Passed \( (P = 0.6010) \)

Constant Variance Test: Passed \( (P = 0.0500) \)

Power of performed test with alpha = 0.0500: 0.7853

The power of the performed test (0.7853) is below the desired power of 0.8000.
You should interpret the negative findings cautiously.
Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|----------------|
| 1   | 1.0011    | -0.0011  | -0.0207   | -1.6711    | (+inf)         |
| 2   | 0.8190    | 0.0135   | 0.2454    | 1.6706     | (+inf)         |
| 3   | 0.7883    | -0.0400  | -0.7261   | -1.6699    | (+inf)         |
| 4   | 0.7821    | 0.0347   | 0.6292    | 0.8277     | 0.0000         |
| 5   | 0.7821    | -0.0070  | -0.1278   | -0.2779    | 0.0000         |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 4532.0189  | 0.9998   | (+inf) |
| 2   | 31.6346    | 0.9784   | (+inf) |
| 3   | 2.9906     | 0.8110   | (+inf) |
| 4   | 0.1252     | 0.4222   | 0.0000 |
| 5   | 0.0720     | 0.7886   | 0.0000 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0011    | 0.3006   | 1.7017    | 0.0104  | 1.9919   |
| 2   | 0.8190    | 0.1260   | 1.5120    | -0.1664 | 1.8044   |
| 3   | 0.7883    | 0.1574   | 1.4192    | -0.1545 | 1.7311   |
| 4   | 0.7821    | 0.3268   | 1.2373    | -0.0534 | 1.6176   |
| 5   | 0.7821    | 0.1599   | 1.4042    | -0.1549 | 1.7190   |

2D Graph 9

![Graph 9](image-url)
**L-4 Tablets (BiPhasic First-order reaction)**

**25°C / 60 %RH**

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2

'A Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2 "Auto {previous: 0.408332}"
b = -ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 0.00882357}"
c = yatxnear0(y,x)/2 "Auto {previous: 0.501416}"
d = -ln(.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 0.00832282}"

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

R = 0.36269364    Rsqr = 0.13154668    Adj Rsqr = 0.00000000

Standard Error of Estimate = 0.1650

| Coefficient | Std. Error | t     | P     |
|-------------|------------|-------|-------|
| a           | 0.4083     | 6871896.7094 | 0.0000 | 1.0000 |
| b           | 0.0088     | 14244.6038  | 0.0000 | 1.0000 |
| c           | 0.5014     | 6871896.6285 | 0.0000 | 1.0000 |
| d           | 0.0083     | 11689.2197  | 0.0000 | 1.0000 |

Analysis of Variance:

| DF | SS   | MS    | F     | P     |
|----|------|-------|-------|-------|
| Regression | 3   | 0.0041 | 0.0014 | 0.0505 | 0.9789 |
| Residual   | 1   | 0.0272 | 0.0272 |       |       |
| Total      | 4   | 0.0313 | 0.0078 |       |       |
PRESS = 0.7549

Durbin-Watson Statistic = 2.4654

Normality Test: Passed (P = 0.1730)

Constant Variance Test: Passed (P = 0.0500)

Power of performed test with alpha = 0.0500: 0.0774

The power of the performed test (0.0774) is below the desired power of 0.8000.
You should interpret the negative findings cautiously.

| Regression Diagnostics: |                     |                      |                      |                      |                      |
|-------------------------|---------------------|----------------------|----------------------|----------------------|----------------------|
| **Row** | **Predicted Residual** | **Std. Res.** | **Stud. Res.** | **Stud. Del. Res.** |
| 1     | 0.9097   | 0.0903    | 0.5471     | 0.7737     | 0.0000    |
| 2     | 0.9020   | -0.0674   | -0.4087    | -1.4294    | (+inf)    |
| 3     | 0.8943   | -0.0702   | -0.4253    | -0.6540    | 0.0000    |
| 4     | 0.8569   | 0.0888    | 0.5381     | 0.5649     | 0.0000    |
| 5     | 0.8352   | -0.0415   | -0.2516    | -0.3298    | 0.0000    |

| Influence Diagnostics: | **Cook'sDist** | **Leverage** | **DFFITS** |
|------------------------|----------------|--------------|------------|
| **Row** |                     | (+inf)       | (+inf)     |
| 1     | -0.4489   | 1.5000      | (+inf)     |
| 2     | -6.7584   | 1.0818      | (+inf)     |
| 3     | -0.3598   | 1.4229      | (+inf)     |
| 4     | -0.1677   | 1.9072      | (+inf)     |
| 5     | -0.0739   | 1.5822      | (+inf)     |

| 95% Confidence: | **Predicted** | **Regr. 5%** | **Regr. 95%** | **Pop. 5%** | **Pop. 95%** |
|----------------|---------------|--------------|---------------|-------------|-------------|
| **Row** |                     |              |              |             |             |
| 1     | 0.9097   | -1.6576     | 3.4771       | -2.4047     | 4.2242      |
| 2     | 0.9020   | -1.2782     | 3.0822       | -2.1225     | 3.9265      |
| 3     | 0.8943   | -1.6061     | 3.3948       | -2.3686     | 4.1572      |
| 4     | 0.8569   | -2.0380     | 3.7518       | -2.7173     | 4.4311      |
| 5     | 0.8352   | -1.8015     | 3.4719       | -2.5332     | 4.2037      |
L-4 Tablets (BiPhasic First-order reaction)
40°C / 75%RH
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_ysquare=1/y^2
'A Automatic Initial Parameter Estimate Functions
xnear0(q)=max(abs(q))-abs(q)
yatxnear0(q,r)=yatymax(q,xnear0(r))

[Parameters]
a = yatxnear0(y,x)/2  "Auto {previous: 0.24046}"
b = -ln(.5)/(0.5*(x50(x,y)-min(x)))  "Auto {previous: 0.606988}"
c = yatxnear0(y,x)/2  "Auto {previous: 0.765575}"
d = -ln(.5)/(1.5*(x50(x,y)-min(x)))  "Auto {previous: 4.32791e-010}"

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y"
"fit f to y with weight reciprocal_ysquare"

[Constraints]
b>0
d>0

[Options]
tolerance=1e-6
stepsize=0.1
iterations=100

\[ R = 0.95135409 \quad R^2 = 0.90507461 \quad \text{Adj } R^2 = 0.62029845 \]

Standard Error of Estimate = 0.0649

| Coefficient | Std. Error | t     | P   |
|-------------|------------|-------|-----|
| a           | 0.2405     | 0.7317| 0.5978|
| b           | 0.6070     | 0.5396| 0.6850|
| c           | 0.7656     | 2.3246| 0.2586|
| d           | 0.0000     | 0.0000| 1.0000|

Analysis of Variance:

| DF | SS    | MS   | F     | P     |
|----|-------|------|-------|-------|
| Regression | 3 | 0.0402 | 0.0134 | 3.1782 | 0.3860 |
| Residual   | 1  | 0.0042 | 0.0042 |       |       |
| Total      | 4  | 0.0444 | 0.0111 |       |       |

PRESS = 2.7170

Durbin-Watson Statistic = 2.3671

Normality Test: Passed (P = 0.6964)

Constant Variance Test: Passed (P = 0.0500)

Power of performed test with alpha = 0.0500: 0.7423

The power of the performed test (0.7423) is below the desired power of 0.8000. You should interpret the negative findings cautiously.

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0060    | -0.0060  | -0.0930   | -0.5566    | 0.0000          |
| 2   | 0.8966    | 0.0178   | 0.2749    | 0.4228     | 0.0000          |
| 3   | 0.8370    | -0.0106  | -0.1640   | -0.2543    | 0.0000          |
| 4   | 0.7690    | -0.0438  | -0.6756   | -2.0714    | (+inf)          |
| 5   | 0.7661    | 0.0427   | 0.6576    | 4.0019     | (+inf)          |

Influence Diagnostics:

| Row | Cook'sDist | Leverage | DFFITS |
|-----|------------|----------|--------|
| 1   | 2.6970     | 0.9721   | 0.0000 |
| 2   | 0.0610     | 0.5772   | 0.0000 |
| 3   | 0.0227     | 0.5841   | 0.0000 |
| 4   | 9.0114     | 0.8936   | (+inf) |
| 5   | 144.2554   | 0.9730   | (+inf) |
L-4 Tablets (BiPhasic First-order reaction)
50°C
Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
reciprocal_y=1/abs(y)
reciprocal_y_square=1/y^2

'Automatic Initial Parameter Estimate Functions
x_near0(q)=max(abs(q))-abs(q)
y_at_x_max=q,x_near0(r)

[Parameters]
a = y_at_x_max(y,x)/2 "Auto {previous: 0.209693}
b = -ln(.5)/(0.5*(x50(x,y)-min(x))) "Auto {previous: 19542.4}
c = y_at_x_max(y,x)/2 "Auto {previous: 0.790307}
d = -ln(.5)/(1.5*(x50(x,y)-min(x))) "Auto {previous: 0.0450895}

[Equation]
f=a*exp(-b*x)+c*exp(-d*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare

[Constraints]
b > 0
d > 0

[Options]
tolerance = 1e-6
stepsize = 0.1
iterations = 100

R = 0.99169616   Rsqr = 0.98346127   Adj Rsqr = 0.93384507

Standard Error of Estimate = 0.0496

| Coefficient | Std. Error | t    | P    |
|-------------|------------|------|------|
| a           | 0.2097     | 0.0676| 3.1032| 0.1985|
| b           | 19542.4191 |       | 2469070.0313| 0.0079| 0.9950|
| c           | 0.7903     | 0.0459| 17.2332| 0.0369|
| d           | 0.0451     | 0.0113| 3.9918 | 0.1563|

Analysis of Variance:

| DF   | SS       | MS   | F      | P    |
|------|----------|------|--------|------|
| Regression | 3     | 0.1465| 0.0488| 19.8214| 0.1633|
| Residual  | 1      | 0.0025| 0.0025|        |
| Total    | 4      | 0.1489| 0.0372|        |

PRESS = 0.0000

Durbin-Watson Statistic = 3.4872

Normality Test: Passed (P = 0.7092)

Constant Variance Test: Passed (P = 0.0500)

Power of performed test with alpha = 0.0500: 0.9723

Regression Diagnostics:

| Row | Predicted | Residual | Std. Res. | Stud. Res. | Stud. Del. Res. |
|-----|-----------|----------|-----------|------------|-----------------|
| 1   | 1.0000    | 0.0000   | 0.0000    | (+inf)     |                 |
| 2   | 0.7555    | -0.0182  | -0.3669   | -0.5673    | 0.0000          |
| 3   | 0.7222    | 0.0304   | 0.6116    | 0.7923     | 0.0000          |
| 4   | 0.5764    | -0.0298  | -0.6008   | -0.7556    | 0.0000          |
| 5   | 0.5035    | 0.0179   | 0.3611    | 0.6071     | 0.0000          |

Influence Diagnostics:
| Row | Cook's Dist | Leverage | DFFITS |
|-----|-------------|----------|--------|
| 1   | (+inf)      | 1.0000   | (+inf) |
| 2   | 0.1119      | 0.5817   | 0.0000 |
| 3   | 0.1064      | 0.4041   | 0.0000 |
| 4   | 0.0831      | 0.3679   | 0.0000 |
| 5   | 0.1684      | 0.6463   | 0.0000 |

95% Confidence:

| Row | Predicted | Regr. 5% | Regr. 95% | Pop. 5% | Pop. 95% |
|-----|-----------|----------|-----------|---------|----------|
| 1   | 1.0000    | 0.3694   | 1.6306    | 0.1082  | 1.8918   |
| 2   | 0.7555    | 0.2745   | 1.2364    | -0.0376 | 1.5485   |
| 3   | 0.7222    | 0.3213   | 1.1230    | -0.0250 | 1.4694   |
| 4   | 0.5764    | 0.1939   | 0.9589    | -0.1611 | 1.3139   |
| 5   | 0.5035    | -0.0035  | 1.0104    | -0.3056 | 1.3126   |

2D Graph 12
APPENDIX B

INTRODUCTION:
This appendix includes the residual plots for the output generated in Appendix A. Using a suitable graphical procedure (Microsoft® Excel 97), residual plots are drawn for the degradation data to fit first order and biphasic first order reactions. This was done for all the drug-excipient mixtures for all conditions. Residuals are plotted against experimentally determined values (observed) and model fitted values (predicted values). Essentially what is considered important while looking at residual plots is a random scatter around the baseline with no significant trend in the plot.
1) Drug + Dextrose

![Graphs showing residuals for different conditions of dextrose and dextrose biphasic first order reactions.](Image)
2) Drug + DiCalcium Phosphate Dihydrate

- **DCPD, first order (25°C)**
  - Actual Value

- **DCPD, first order (40°C/75%RH)**
  - Actual Value

- **DCPD, first order (50°C/20% moisture)**
  - Actual Value

- **DCPD, Biphasic First Order (25°C)**
  - Actual Values

- **DCPD, Biphasic First Order (40°C/75%RH)**
  - Actual Values

- **DCPD, Biphasic First Order (50°C/20% moisture)**
  - Actual Values

- **DCPD, Biphasic First Order (50°C)**
  - Actual Values
DCPD, first order (25°C)

Predicted Values

DCPD, first order (40°C/75%RH)

Predicted Values

DCPD, first order (50°C/20%moisture)

Predicted Values

DCPD, first order (50°C)

Predicted Values

DCPD, Biphasic First Order (25°C)

Predicted Values

DCPD, Biphasic First Order (40°C/75%RH)

Predicted Values

DCPD, Biphasic First Order (50°C/20%RH)

Predicted Values

DCPD, Biphasic First Order (50°C)

Predicted Values
3) Drug + Calcium Sulfate

![Graphs showing residual plots for Calcium Sulfate in various conditions](image-url)
4) Drug + Mannitol
Mannitol, first order (25°C)

Predicted Values

Mannitol, first order (25°C/60%RH)

Predicted Values

Mannitol, first order (40°C/75%RH)

Predicted Values

Mannitol, first order (50°C/20% moisture)

Predicted Values

Mannitol, first order (50°C)

Predicted Values

Mannitol, Biphasic first order (25°C)

Predicted Values

Mannitol, Biphasic first order (25°C/60%RH)

Predicted Values

Mannitol, Biphasic first order (40°C/75%RH)

Predicted Values

Mannitol, Biphasic first order (50°C/20% moisture)

Predicted Values

Mannitol, Biphasic first order (50°C)

Predicted Values
5) Drug + Lactose Anhydrous
Lactose Anhydrous, First Order (25 C)

Predicted Values

Lactose Anhydrous, First Order (25 C/60 %RH)

Predicted Values

Lactose Anhydrous, First Order (40 C/75 %RH)

Predicted Values

Lactose Anhydrous, First Order (50 C/20 %moisture)

Predicted Values

Lactose Anhydrous, First Order (50 C)

Predicted Values

Lactose Anhydrous, Biphasic First Order (25 C)

Predicted Values

Lactose Anhydrous, Biphasic First Order (25 C/60 %RH)

Predicted Values

Lactose Anhydrous, Biphasic First Order (40 C/75 %RH)

Predicted Values

Lactose Anhydrous, Biphasic First Order (50 C/20 %moisture)

Predicted Values

Lactose Anhydrous, Biphasic First Order (50 C)

Predicted Values
6) Lactose Hydrous

Lactose Hydrous, First Order (25 C)

Lactose Hydrous, Biphasic first order (25 C)

Lactose Hydrous, First Order (25C/60%RH)

Lactose Hydrous, Biphasic first order (25 C/60 %RH)

Lactose Hydrous, First Order (40C/75%RH)

Lactose Hydrous, Biphasic first order (40 C/75 %RH)

Lactose Hydrous, First Order (50C/20%moisture)

Lactose Hydrous, Biphasic first order (50 C/20 % moisture)

Lactose Hydrous, First Order (50C)

Lactose Hydrous, Biphasic first order (50 C)
Lactose Hydrous, First Order (25C)

Lactose Hydrous, Biphasic first order (25C)

Lactose Hydrous, First Order (25C/60%RH)

Lactose Hydrous, Biphasic first order (25C/60%RH)

Lactose Hydrous, First Order (40C/75%RH)

Lactose Hydrous, Biphasic first order (40C/75%RH)

Lactose Hydrous, First Order (50C/20%moisture)

Lactose Hydrous, Biphasic first order (50C/20%moisture)

Lactose Hydrous, First Order (50C)

Lactose Hydrous, Biphasic First Order (50C)
7) Drug + Starch

- Starch, First Order (25 C)
- Starch, Biphasic First Order (25 C)
- Starch, First Order (25 C/60 %RH)
- Starch, Biphasic First Order (25 C/60 %RH)
- Starch, First Order (40 C/75 %RH)
- Starch, Biphasic First Order (40 C/75 %RH)
- Starch, First Order (50 C/20 % moisture)
- Starch, Biphasic First Order (50 C/20 % moisture)
- Starch, First Order (50 C)
- Starch, Biphasic First Order (50 C)

Actual Values

Residuals

Series 1

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8) Drug + Talc

- Talc, First Order (25 C)
- Talc, Biphasic First Order (25 C)
- Talc, First Order (25 C/60 %RH)
- Talc, Biphasic First Order (25 C/60 %RH)
- Talc, First Order (50 C/20 %moisture)
- Talc, Biphasic First Order (50 C/20 %moisture)
- Talc, First Order (50 C)
- Talc, Biphasic First Order (50 C)
9) Ferric Oxide

Ferric Oxide, First Order (25 C)

Ferric Oxide, Biphasic First Order (25 C)

Ferric Oxide, First Order (25 C/60 %RH)

Ferric Oxide, Biphasic First Order (25 C/60 %RH)

Ferric Oxide, First Order (40 C/75 %RH)

Ferric Oxide, Biphasic First Order (40 C/75 %RH)

Ferric Oxide, First Order (50 C/20 %moisture)

Ferric Oxide, Biphasic First Order (50 C/20 %moisture)

Ferric Oxide, First Order (50 C)

Ferric Oxide, Biphasic First Order (50 C)
10) Levothyroxine Sodium Tablets

![Graphs showing residuals for different conditions](image-url)
L-4 Tablets, First Order (25°C)

L-4 Tablets, Biphasic First Order (25°C)

L-4 Tablets, First Order (25°C/60%RH)

L-4 Tablets, Biphasic First Order (25°C/60%RH)

L-4 Tablets, First Order (40°C/75%RH)

L-4 Tablets, Biphasic First Order (40°C/75%RH)

L-4 Tablets, First Order (50°C)

L-4 Tablets, Biphasic First Order (50°C)
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