INVESTIGATION OF CRITICAL MATERIAL ATTRIBUTES OF NANOCELLULOSE IN TABLETS

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ABSTRACT

Objective: The present work aims to compare powder flow properties and post-compression characteristics of acid hydrolysed nanocellulose (AH-NC) as a novel excipient with microcrystalline cellulose (MCC PH200) to demonstrate the applicability and performance of AH-NC.

Methods: I-optimal design was applied separately for both the excipient, i.e., MCC PH200 and AH-NC. Independent variables were MCC PH200 as diluent (X1), AH-NC as diluent (X1), starch as disintegrant (X2), and PVP K30 as dry binder (X3). The dependent variables in design were Carr’s index (CI) (R1), angle of repose (AR) (R2), hardness (R3), friability (R4), disintegration time (DT) (R5), and T90 (R6).

Results: Fourier-transform infrared spectroscopy (FTIR) and Differential scanning calorimetry (DSC) studies showed the compatibility of the drug with an excipient. CI was found in the range of 8%–17.84% for MCC PH200 and 5.25%–11.94% for AH-NC. AR was found in the range of 31.48–37.66 for MCC PH200 and 29.62–35.30 for AH-NC. The values of friability, DT, and T90 were almost identical in both the cases.

Conclusion: Not only does AH-NC demonstrate better flow properties but also problems of weight variation and content uniformity are not observed when compared to MCC PH200. Hence, AH-NC is more suitable as an excipient for modern high-speed rotary tablet press.

Keywords: Microcrystalline cellulose PH200, Acid hydrolysed nanocellulose, Novel excipient, I-optimal design, Powder flow properties.

INTRODUCTION

The production of nanocellulose (NC) and their application in different areas has gained increasing attention recently due to their low density, high surface area to volume ratio, higher Young’s modulus, higher tensile strength, thermal stability, and biodegradable nature [1]. Extraction of NC has been carried out by acid hydrolysed (AH), enzymatic hydrolysed, homogenization, microfluidization, grinding, cryocrushing, and ultrasonication [2,3] from algae, tunicates, bacteria, and natural plant [4]. Application of NC as a nanocomposite has been studied [5–6]. However, application of NC in the pharmaceutical field has not been reported so far which basically is the objective of this study – to evaluate the usability of NC as a novel tableting excipient produced by processing corn husk as an agricultural waste, through AH. For that purpose, AH-NC was compared to commercially available grades of microcrystalline cellulose (MCC): Avicel PH 200. MCC was chosen for comparison due to its similarity to AH-NC in chemical structure. Besides, Avicel PH 200 is the most common grade of MCC used in tabletting.

GLIBENCLAMIDE (GLB), an oral hypoglycemic agent for the treatment of non-insulin-dependent diabetes mellitus, was selected as a model drug in the present study [9–11]. Design Expert® Version 12 was used for the data treatment of I-optimal design to ensure optimum use of time and cost to obtain high quality of powder flow property using direct compression [12,13].

MATERIALS AND METHODS

Materials

GLB from Cadila Pharmaceuticals Ltd. (India), MCC PH 200 (Avicel®,PH200) from Signet Pharma (India), PVP K30 from J H Nanhang Life Sciences Co. Ltd. (China), starch, magnesium stearate, and talc from ACME Chemicals, Mumbai (India), were obtained as a gift sample. Indigenously produced AH-NC from corn husk.

Methods

Fourier-transform infrared spectroscopy (FTIR)

FTIR spectra of a drug, a physical mixture of drug and excipients, were recorded using KBr discs on a Perkin-Elmer FTIR spectrometer. Spectrum range was 4,000–400/cm [14–17].

Differential scanning calorimeter (DSC)

Thermal properties of a drug, a physical mixture of drug and excipients, were investigated by DSC on a thermal analyzer (DSC-Thermal Analysis: Shimadzu Corporation). About 20 mg of each sample was heated from room temperature to 300°C at a rate of 10°C/min under nitrogen [14–17].

Preparation of GLB tablet

All the ingredients weighed accurately and passed through sieve number 60. Tablets were prepared by direct compression using a rotary press (Rimek, Karnavati Engineering Ltd., Gujarat). The total tablet weight (GLB, starch, PVP K30, MCC PH200/AH-NC, magnesium stearate, and talc) was 160 mg each with ±0.2 mm thickness and 8 mm in diameter. Experimental runs, their factor combinations, and the translation of the coded levels to the experimental units used in the study are summarized in Table 1. Com position of all prepared batches is mentioned in Table 2.

Evaluation of GLB tablets

Pre-compression parameters

Carr’s index (CI)

Bulk density (ρb) and the tapped density (ρt) of the sample were determined with a bulk/tap density test apparatus (Elecrolab, EDT-1020). CI was calculated as 100 times; the ratio of the difference between the tapped density and bulk density to the tapped density calculated by utilizing the following equation [18–20].

\[ CI = \left( \frac{\rho_t - \rho_b}{\rho_t} \right) \times 100 \]
Friability was tested using Roche friability tester.

Friability, CI, hardness and angle of repose were recorded using Monsanto hardness tester. Hardness of three tablets was measured and mean and the standard deviation was calculated and reported and expressed in terms of kg/cm² [21-23].

Friability
Friability of the tablets was tested using Roche friability tester. Ten tablets (Fa) were placed in friabilator and operated at 5 rpm for 4 min [21-23]. Afterward, the fines were removed by sieving through a 250-μm mesh and the fraction above 250 μm mesh (Fa) was used to calculate the friability of tablets according to the following equation:

\[ \text{Friability} = \frac{\text{Fa} - \text{Fa}}{\text{Fa}} \times 100 \]

Weight variation
Twenty tablets were weighed individually and then the average weight was calculated. The weight of an individual tablet is then compared to the average. The tablet passes the test if no more than two tablets are outside the percentage limit [21].

Disintegration time (DT)
In vitro DT was performed by USP disintegration apparatus at 50 rpm. Phosphate buffer (pH 6.8), 600 ml was used as disintegration medium, the temperature was maintained at 37°C ± 2°C and one tablet was

### Table 1: Experimental runs for the glibenclamide tablet with coded values

| Independent variables | Name       | Unit | 0 (low) | 1 (high) |
|-----------------------|------------|------|---------|----------|
| X1                    | Starch     | %    | 4       | 8        |
| X2                    | PVP K30    | %    | 2       | 10       |
| X3                    | MCC PH 200 | %    | 79.87   | 87.87    |

### Table 2: Composition of all formulations of glibenclamide tablet

| Batches | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 10  | 11  | 12  | 13  | 14  | 15  | 16  |
|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|         | MCC PH 200 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Talc    | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   |
| Magnesium stearate | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |

### Table 3: Composition of all formulations of glibenclamide tablet

| Batches | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 10  | 11  | 12  | 13  | 14  | 15  | 16  |
|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| AH‑NC   |      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Talc    | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   |
| Magnesium stearate | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |

MCC: Microcrystalline cellulose, AH‑NC: Acid hydrolysed-nanocellulose, AR: Angle of repose, CI: Carr’s index

**Angle of repose (AR)**

It is defined as the angle between the free surfaces of a pile of powder to a horizontal plane. In the present study, the AR was determined using a fixed cone method [18-20]. The sample was carefully poured through the funnel until the apex of the cone, thus formed just touched the tip of the funnel. The mean radius (r) and height (h) of the heap were measured and the AR was calculated from the following equation:

\[ \tan \theta = \frac{h}{r} \]

**Post-compression parameters**

**Hardness**

Hardness is termed as the tablet crushing strength or defined as the force required breaking a tablet in a diametric compression test. It was recorded using Monsanto hardness tester. Hardness of three tablets was measured and mean and the standard deviation was calculated and reported and expressed in terms of kg/cm² [21-23].

**Friability**

Friability of the tablets was tested using Roche friability tester. Ten tablets (Fa) were placed in friabilator and operated at 5 rpm for 4 min [21-23]. Afterward, the fines were removed by sieving through a 250-μm mesh and the fraction above 250 μm mesh (Fa) was used to calculate the friability of tablets according to the following equation:

\[ \text{Friability} = \frac{\text{Fa} - \text{Fa}}{\text{Fa}} \times 100 \]

**Weight variation**

Twenty tablets were weighed individually and then the average weight was calculated. The weight of an individual tablet is then compared to the average. The tablet passes the test if no more than two tablets are outside the percentage limit [21].

**Disintegration time (DT)**

In vitro DT was performed by USP disintegration apparatus at 50 rpm. Phosphate buffer (pH 6.8), 600 ml was used as disintegration medium, the temperature was maintained at 37°C ± 2°C and one tablet was
placed in each of the six basket tubes of the apparatus and one disc was added to each tube. Time taken for the complete disintegration of the tablet was noted [21].

In vitro dissolution
GLB release was determined using a dissolution apparatus USP type II (Paddle type). Tablet was added with sinkers in a dissolution medium consisting of 900 ml 0.05 M, pH 7.5 phosphate buffer and was stirred at 50 rpm at 37°C ± 0.5°C. Five ml of sample was withdrawn at defined time intervals and was replaced with the same volume of fresh dissolution media. The samples were analyzed spectrophotometrically (UV-1700, Shimadzu Corp., Kyoto, Japan) at 231.5 nm (Cruz-Antonio 83). Dissolution tests (n = 3) were carried out for all the batches and the percentage drug released was calculated using a standard calibration curve [24].

RESULTS AND DISCUSSION

FTIR
Spectrum of GLB and physical mixture of GLB with excipients is shown in Fig. 1. GLB showed carbonyl stretching at 1712.67/cm, symmetrical and asymmetrical sulfonyl stretching at 1161.07 and 1344.29/cm, respectively, and amide stretching at 3315.41 and 3365.55/cm. Comparison of functional group peaks of GLB and physical mixture revealed that there were no major changes observed for characteristic peaks which confirm the absence of interaction between drug and the excipients [10].

DSC
DSC thermograms of GLB and physical mixture of GLB with other excipients are compared as shown in Fig. 2. A sharp endothermic peak at 175.58°C in the thermogram of GLB was observed. Characteristic peak of GLB was observed at 175.22°C in a physical mixture containing MCC PH200, whereas peak of a mixture containing AH-NC was observed at 175.23°C. This confirmed that no major changes were observed in characteristic peaks showing compatibility between drug and excipients used in the formulation [11].

Responses for GLB tablet
Experimental trials (16 batches) and their observed responses are shown in Tables 3 and 4. From the results, it is suggested that the quadratic model is the best fit model for all responses.

CI (R1)
Model F-value for MCC PH200 is 479.04 and for AH-NC is 6.01 implies that the model is significant. The results of multiple regression analysis indicate a fairly high value of correlation coefficient, i.e., 0.9979 for MCC PH200 and for AH-NC is 0.8662. It is concluded that the value of CI can be predicted within the design space, with fair accuracy. The interaction terms are statistically significant in nature as shown in Table 5.

The highest value of the coefficient was seen with starch in the mathematical model. The reason for poor fluidity is starch, due to the
The presence of moisture in it and fine particles. Curved lines in response surface plot indicate non-linear relation between independent and dependent variables as shown in Fig. 3.

AR (R2)

Model F-value for MCC PH200 is 34.99 and for AH-NC is 5.18 implies that the model is significant. The results of multiple regression analysis indicate a fairly high value of correlation coefficient, i.e., 0.972 for MCC PH200 and for AH-NC is 0.8493. It is concluded that the value of the AR can be predicted within the design space, with fair accuracy. The interaction terms are statistically significant in nature as shown in Table 6.

Starch showed an insignificant effect on the AR due to lowest coefficient value, i.e., 16.81 for MCC PH200 and 10.95 for AH-NC. As shown in Fig. 4, left corner red in color shows that AR is on the higher side. The high amount of PVP K30, MCC PH200, and AH-NC showed decline in AR.

Table 3: Observed responses of glibenclamide tablets using microcrystalline cellulose PH200

| Response     | Batches | 1     | 2     | 3     | 4     | 5     | 6     | 7     | 8     |
|--------------|---------|-------|-------|-------|-------|-------|-------|-------|-------|
| CI*          |         | 13.31±3.62 | 12.29±7.03 | 9.06±3.81 | 13.42±6.05 | 8.52±1.62 | 9.48±1.48 | 8.00±3.17 | 17.84±6.67 |
| AR*          |         | 35.27±1.44 | 31.48±5.33 | 34.67±4.53 | 33.72±0.88 | 34.34±1.38 | 34.54±3.66 | 34.07±4.45 | 32.03±0.81 |
| Hardness*    |         | 4.9±0.36 | 3.53±0.42 | 4.77±0.38 | 4.85±0.21 | 4.73±0.31 | 4.40±1.06 | 4.87±0.23 | 3.30±0.70 |
| Friability   | 0.47    | 0.92    | 0.89    | 0.56    | 0.77    | 0.56    | 0.76    | 0.75    |       |
| DT**         | 295.17±1.94 | 57.33±4.63 | 168.00±1.26 | 172.67±1.75 | 185.17±1.47 | 140.83±1.47 | 185.17±1.41 | 150.83±2.07 |       |
| T90*         | 26.72±0.13 | 22.72±0.32 | 26.68±0.33 | 41.44±0.13 | 17.16±0.10 | 20.22±0.32 | 15.43±0.33 | 21.33±0.11 |       |
| Weight variation | 160.49 | 160.06 | 159.99 | 160.3 | 160.05 | 160.23 | 161.17 | 161.2 |       |

| Response     | Batches | 9     | 10    | 11    | 12    | 13    | 14    | 15    | 16    |
|--------------|---------|-------|-------|-------|-------|-------|-------|-------|-------|
| CI*          |         | 10.84±8.15 | 9.06±3.81 | 9.06±3.81 | 16.50±4.42 | 11.83±1.82 | 13.92±1.87 | 14.33±1.70 | 9.42±1.05 |
| AR*          |         | 34.21±5.27 | 35.92±1.52 | 35.92±1.52 | 37.66±2.14 | 36.56±1.02 | 35.27±1.44 | 31.48±5.33 | 34.62±0.92 |
| Hardness*    | 4.27±0.31 | 4.80±0.20 | 4.67±0.15 | 4.53±0.06 | 4.33±0.42 | 4.47±0.23 | 3.63±0.15 | 4.60±0.20 |       |
| Friability   | 0.88    | 0.8     | 0.89   | 0.7    | 0.93    | 0.47    | 0.92    | 0.66    |       |
| DT**         | 147.00±2.07 | 168.33±1.90 | 168.3±1.63 | 42.00±2.66 | 82.33±2.42 | 294.67±2.66 | 123.67±2.42 | 140.83±1.72 |       |
| T90*         | 40.78±0.32 | 21.47±0.33 | 20.33±0.24 | 32.33±0.28 | 36.63±0.31 | 23.2±0.35 | 36.25±0.39 | 39.06±0.43 |       |
| Weight variation | 161.03 | 161.16 | 161.29 | 161.42 | 161.55 | 161.69 | 161.82 | 161.95 |       |

*Average of three determinations, **An average of six determinations. AR: Angle of repose, CI: Carr’s index, DT: Disintegration time.
Table 4: Observed responses of glibenclamide tablets using AH-NC

| Response      | Batches       |
|---------------|---------------|
|               | 1      | 2      | 3      | 4      | 5      | 6      | 7      | 8      |
| CI*           | 5.25±2.06 | 11.94±0.93 | 6.41±1.39 | 9.26±2.86 | 5.81±2.17 | 7.03±0.34 | 10.11±4.06 | 7.89±8.66 |
| AR*           | 33.72±0.88 | 31.25±0.77 | 32.03±0.81 | 31.05±1.89 | 34.62±0.92 | 32.27±3.61 | 33.45±1.31 | 31.73±3.60 |
| Hardness*     | 5.23±0.21 | 3.20±0.20 | 5.00±0.10 | 5.73±0.31 | 4.20±0.20 | 5.27±0.31 | 6.40±0.87 | 3.13±0.99 |
| Friability    | 0.81    | 0.46   | 0.86   | 1.09   | 0.65   | 0.61   | 0.65   | 0.64   |
| DT**          | 254.00±3.03 | 47.62±1.68 | 163.44±3.22 | 169.17±1.72 | 279.17±1.72 | 131.75±1.08 | 175.00±0.63 | 140.82±0.92 |
| T90*          | 26.60±0.33 | 43.84±0.48 | 35.56±0.33 | 27.77±0.13 | 35.00±0.10 | 43.53±0.32 | 35.00±0.42 | 34.77±0.11 |
| Weight variation | 161.45 | 160.91 | 163.17 | 162.87 | 161.11 | 163.05 | 164.22 | 160.65 |

Table 5: Full model in coded form for Carr’s index

| A   | B   | C   | AB  | AC  | BC  |
|-----|-----|-----|-----|-----|-----|
| MCC PH 200 |
| CI  | 47.4699 | 16.4503 | 13.5083 | −3.50830 | −3.50830 | −3.50830 |
| p   | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| AH-NC |
| CI  | 29.7483 | 6.14168 | 8.95201 | −24.7036 | −46.9373 | 2.44815 |
| p   | 0.1875 | 0.1875 | 0.1875 | 0.0429 | 0.0015 | 0.5209 |

Table 6: Full model in coded form for an angle of repose

| A   | B   | C   | AB  | AC  | BC  |
|-----|-----|-----|-----|-----|-----|
| MCC PH 200 |
| AR  | 16.8085 | 37.7675 | 33.9237 | 14.3515 | 29.0784 | −2.54291 |
| p   | <0.0001 | <0.0001 | <0.0001 | 0.0119 | 0.0001 | 0.1468 |
| AH-NC |
| AR  | 10.9593 | 29.6747 | 30.4561 | 40.5637 | 44.3385 | 9.95272 |
| p   | 0.5574 | 0.5574 | 0.5574 | 0.0031 | 0.0020 | 0.0204 |

Fig. 3: Response surface plot for Carr’s index a) MCC PH200 b) AH-NC
Hardness of tablets (R3)
Model F-value for MCC PH200 is 17.72 and for AH-NC is 7.72 implies that the model is significant. The results of multiple regression analysis indicate a fairly high value of correlation coefficient, i.e., 0.947 for MCC PH200 and for AH-NC is 0.8911. It is concluded that the value of the hardness can be predicted within the design space, with fair accuracy. The interaction terms are statistically significant in nature as shown in Table 7.

The coefficient associated with starch is negative, i.e., −3.75 for MCC PH200 and −8.25 for AH-NC. As shown in Fig. 5, if the amount of starch is increased in the powder blend, the hardness of the tablets will reduce. PVP K30, MCC PH200, and AH-NC showed positive coefficients. The hardness of the tablets should increase if PVP K30 and/or MCC PH200/AH-NC are increased in the powder blend.

Friability of tablets (R4)
Model F-value for MCC PH200 is 53.88 and for AH-NC is 160.83 implies that the model is significant. The results of multiple regression analysis indicate a fairly high value of correlation coefficient, i.e., 0.981 for MCC PH200 and for AH NC is 0.9938. It is concluded that the value of the friability can be predicted within the design space, with fair accuracy. The interaction terms are statistically significant in nature as shown in Table 8.

As shown in Fig. 6, plots show a steep change in the values of friability of the GLB tablets. It may be concluded from the contour plot of friability of GLB tablets that low concentration of PVP K30 is not favorable to keep the friability below 1%. PVP K30 played a key role in managing the mechanical strength of the tablets.

Table 7: Full model in coded form for hardness

|         | A    | B    | C    | AB   | AC   | BC    |
|---------|------|------|------|------|------|-------|
| MCC PH 200 |      |      |      |      |      |       |
| Hardness | −3.74738 | 4.42348 | 4.68266 | 12.6804 | 11.9954 | −0.425618 |
| p        | 0.0003 | 0.0003 | 0.0003 | <0.0001 | <0.0001 | 0.5231 |
| AH-NC   |      |      |      |      |      |       |
| Hardness | −8.25355 | 4.63199 | 4.93067 | 22.332 | 19.8701 | −1.1776 |
| p        | 0.0527 | 0.0527 | 0.0527 | 0.0003 | 0.0008 | 0.4251 |

MCC: Microcrystalline cellulose, AH-NC: Acid hydrolysed-nanocellulose
DT of GLB tablets (R5)
Model F-value for MCC PH200 is 212.25 and for AH-NC is 6.67 implies that the model is significant. The results of multiple regression analysis indicate a fairly high value of correlation coefficient, i.e., 0.9866 for MCC PH200 and for AH-NC is 0.8771. It is concluded that the value of the DT can be predicted within the design space, with fair accuracy. The interaction terms are statistically significant in nature as shown in Table 9.

The coefficient associated with starch is negative, i.e., −742.6 for MCC PH200 and −733.13 for AH-NC. As shown in Fig. 7, if the amount of starch is increased in the powder blend, the DT of the tablets will reduce.

T90 of GLB tablets (R6)
Model F-value for MCC PH200 is 2.05 and for AH-NC is 4.81 implies that the model is significant. The results of multiple regression analysis indicate a fairly high value of correlation coefficient, i.e., 0.9325 for MCC PH200 and for AH-NC is 0.8405. It is concluded that the value of the T90 can be predicted within the design space, with fair accuracy. The interaction terms are statistically significant in nature as shown in Table 9.

Table 8: Full model in coded form for friability

|       | A    | B    | C    | AB   | AC   | BC   |
|-------|------|------|------|------|------|------|
| MCC PH 200 | Friability | 2.57209 | 0.680256 | 0.556855 | −2.90677 | −3.3165 | 1.50394 |
|       | p    | 0.0010 | 0.0010 | 0.0010 | <0.0001 | <0.0001 | <0.0001 |
| AH-NC | Friability | 0.49526 | 0.9097 | 1.08407 | −1.04139 | −0.484124 | −0.22969 |
|       | p    | <0.0001 | <0.0001 | <0.0001 | 0.0013 | 0.0728 | 0.0186 |

MCC: Microcrystalline cellulose, AH-NC: Acid hydrolysed-nanocellulose

Table 9: Full model in coded form for disintegration time

|       | A    | B    | C    | AB   | AC   | BC   |
|-------|------|------|------|------|------|------|
| MCC PH 200 | DT  | −742.607 | 41.6313 | 177.117 | 1593.51 | 1836.66 | 10.2776 |
|       | p    | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.7028 |
| AH-NC | DT  | −733.137 | 34.7646 | 196.026 | 1588.38 | 1613.75 | 134.527 |
|       | p    | 0.0075 | 0.0075 | 0.0075 | 0.0032 | 0.0032 | 0.3661 |

MCC: Microcrystalline cellulose, AH-NC: Acid hydrolysed-nanocellulose, DT: Disintegration time

Table 10: Full model in coded form for T90

|       | A    | B    | C    | AB   | AC   | BC   |
|-------|------|------|------|------|------|------|
| MCC PH 200 | T90 | 91.6893 | 35.8989 | 44.1256 | −131.778 | −167.588 | −37.2486 |
|       | p    | 0.2715 | 0.2715 | 0.2715 | 0.0979 | 0.0459 | 0.1660 |
| AH-NC | T90 | 20.4789 | 29.811 | 28.5094 | 71.9557 | 25.4957 | 1.27329 |
|       | p    | 0.0071 | 0.0071 | 0.0071 | 0.0822 | 0.5170 | 0.9231 |

MCC: Microcrystalline cellulose, AH-NC: Acid hydrolysed-nanocellulose

Fig. 6: Response surface plot for friability a) MCC PH200 b) AH-NC
PVP K30 and MCC PH200/AH-NC have positive coefficients as shown in Fig. 8.

**Overlay plot for GLB tablet**

To check the predictive ability of all the mathematical points, two points were randomly chosen as shown in Fig. 9 for MCC PH200 and AH-NC. A composition with 7.71% starch, 3.91% PVP K30, and 82.23% MCC PH200 showed acceptable values of dependent variables (CI = 13.36, AR = 32.30, hardness = 3.73, friability = 0.84, DT = 147.69 sec, and T90 = 23.90 min). A composition with 4.28% starch, 7.60% PVP K30, and 81.97% AH-NC showed acceptable values of dependent variables (CI = 7.11, AR = 32.4, hardness = 4.77, friability = 0.86, DT = 129 sec, and T90 = 31 min).

![Fig. 7: Response surface plot for disintegration time a) MCC PH200 b) AH-NC](image)

![Fig. 8: Response surface plot for T90 a) MCC PH200 b) AH-NC](image)

![Fig. 9: Overlay plot for glibenclamide tablet using a) MCC PH200 b) AH-NC](image)
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