Batch and flow injection spectrophotometric methods for determination of Ceftazidime in pharmaceutical formulations

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Received 6/3/2022, Revised 22/5/2022, Accepted 24/5/2022, Published Online First 20/11/2022
Published 1/6/2023

Abstract:
It is generally accepted that there are two spectrophotometric techniques for quantifying ceftazidime (CFT) in bulk medications and pharmaceutical formulations. The methods are described as simple, sensitive, selective, accurate and efficient techniques. The first method used an alkaline medium to convert ceftazidime to its diazonium salt, which is then combined with the 1-Naphthol (1-NPT) and 2-Naphthol (2-NPT) reagents. The azo dye that was produced brown and red in color with absorption intensities of $\lambda_{\text{max}}$ 585 and 545 nm respectively. Beer's law was followed in terms of concentration ranging from (3-40) $\mu$g.ml$^{-1}$ For (CFT-1-NPT) and (CFT-2-NPT), the detection limits were 1.0096 and 0.8017 $\mu$g.ml$^{-1}$, respectively, and the molar absorptivity was 0.7926 $\times$ 10$^4$ and 0.5466 $\times$ 10$^4$ L.mol$^{-1}$.cm$^{-1}$. The Flow Injection Analysis (FIA) method is used to estimate ceftazidime and in the second procedure record measurements using the UV-Visible approach. The Flow injection allows for exact drug estimation under ideal experimental conditions. The concentrations were in the range of (3-50) $\mu$g.ml$^{-1}$ For (CFT-1-NPT) and (CFT-2-NPT), the detection limits were 0.8102, 1. 2809 $\mu$g.ml$^{-1}$, and the molar absorptivity was 0.9565 $\times$ 10$^4$, 0.7106 $\times$ 10$^4$ L.mol$^{-1}.cm^{-1}$, respectively. The proposed two methods for determination Ceftazidime in Pharmaceutical formulation were successfully applied, as these methods were characterized by simplicity, speed, accuracy, and low cost.

Keywords: 1-Naphthol, 2-Naphthol Spectrophotometric, Azo – aye, Batch, Ceftazidime, Diazotization, Flow injection.

Introduction
Antibiotics are substances or compounds that kill or inhibit the growth of bacteria. And the antibiotics are antimicrobial substances used to treat infections caused by bacteria, fungus, and parasites. Ceftazidime is a third-generation semi-synthetic cephalosporin that inhibits Gram-negative and Gram-positive bacteria, including pseudomonas aeruginosa. Chemically, Ceftazidime (CFT) is [7-(2-(2-aminothiazol-4-yl) -2-(6R,7R,Z) carboxypropan -2-yloxyiminino ) acetamido )-8-oxo-3-(pyridinium -1-ylmethyl ) -5-thia-1-aza-bicyclo[4.2.0]oct-ene-2-carboxylate .Fig.1

Figure 1. Structural formula for ceftazidime
(Fortaz,Tazicef) is the trade name. • It is used to treat infections caused by Pseudomonas aeruginosa,
which include infections of the bones and joints, cystic fibrosis (respiratory tract infections), and cystic fibrosis gastroenteritis (intestinal infections) 5,6.

Many researches have been conducted to estimate the presence of this medication in pharmaceutical formulations such as: Two Oxidative Visible Spectrophotometric Methods 7 RP-UPLC Method 8 Poly Diphenylamine Partially Oxidized for Sensitive Electrochemical Applications 9 Using resorcinol and 2-methyl phenol, spectrophotometric detection of ceftazidime in pharmaceuticals 10 The utility of a fluorescamine-based technique for very sensitive spectrofluorimetric measurement of Ceftazidime and Vancomycin in pharmaceuticals and real human plasma was investigated using flow injection analysis (FIA). 11 Flow injection analysis is one of many analytical chemistry techniques that have been widely embraced and adopted in a variety of analytical fields. Diazotization and coupling processes have been widely used to determine a wide range of pharmaceuticals and pharmaceutical preparations, including the determination of the ceftazidime compound employing the reaction between the diazotized drug and the coupling reagent 4-tert-butylphenol 12. Many papers have been written about diazotization reactions and their connection to the flow injection system 13-17 . The proliferation of these domains is owing to the ease with which they can be linked or coupled with a variety of techniques such as chromatic Flame atomic absorption 18,19, electrochemical detection 20, chemical fluorescence 21. Through the (FIA) technology, which was characterized by high repetition and conformity, as well as its simplicity, speed, and low cost, the (FIA) technology has demonstrated its high efficiency. 22,23. (FIA) is a quantitative method for assessing or estimating minerals and materials using injection flow such as Manganese in plants 24, cholesterol 25 and Mebeverine Hydrochloride 26. In this paper, new methods for determining ceftazidime in its pure and pharmaceutical formulations have been developed using diazotization and coupling reactions with 1-naphthol and 2-naphthol reagents, and then using these reactions with the flow injection technique in the presence of a visible and ultraviolet detector, and their applications in the scientific field to estimate these drugs in their pure and pharmaceutical formulations have been developed.

Flow injection configuration a three-channels manifold was employed with, Peristaltic pump (AlLITEA, C4, made in Sweden) with polyvinyl chloride tube (0.8) internal diameter as in fig.2.

Materials and Methods
Apparatus;
All spectral and absorbance measurements were executed on an Advanced microprocessor UV-VIS spectrophotometer single beam LI-295 recording spectrophotometer using 1 cm quartz cells.

Figure 2. System of the employed flow system, P :peristaltic pump, R.C: reaction coil, S: sample injection,W: waste, FC: flow ce:
Reagents:
Pharmaceutical preparations: Ceftazidime
Pharmaceutical preparations were purchased from commercial sources, and Reagents were all analytical reagent grade chemicals.

Ceftazidime (CFT) (1000 μg/ml) ; ( Laboratorios TORLAN Barcelona - Spain ) A stock solution (1000 μg/ml) 9.1478×10⁻⁵ M of ceftazidime was prepared by dissolving 0.1 gm of CFT in distilled water. Then transfer it to a conical flask 100 ml and complete the volume to the mark.

1-Naphthol (1-NPT);1-Naphthol (50μg/ml ) 3.471×10⁻⁴ M was prepared by dissolving 0.1 g (BDH) distilled water with a small amount of 25% NaOH were added to ensue complete dissolution . Then transfer it to a conical flask 50ml and complete the volume to the mark.

2-Naphthol (2-NPT): 2-Naphthol (50μg/ml ) 3.471×10⁻⁴ M was prepared by dissolving 0.1 g (AR) distilled water with a small amount of 25% NaOH were added to ensue complete dissolution . Then transfer it to a conical flask 50ml and complete the volume to the mark.

Different concentrations of reagents from (0.0694×10⁻³ to 0.832×10⁻³) M (300 -1200) μg/ml used in the injection method were prepared by drawing different volume (1-12) ml from 2000μg/ml for reagents completing the volume of the marker in a 20 ml conical flask .

Sodium nitrite NaNO₂ 1% (0.1449 M) lg sodium nitrite (BDH) was dissolved in distilled water and diluted to the desired concentration in a 100 mL conical flask.

HCl Solution 1:1 (36.46 M ) In a 100 ml conical flask, 50 mL of 11.64 M concentrated hydrochloric acid (ADR) was diluted with distilled water

NaOH 25% solution ( 6.2505 M) 25 g sodium hydroxide (BDH) was dissolved in distilled water and diluted to the desired concentration in a 100 mL conical flask.

Pharmaceutical Ceftazidime;
Commerially available pharmaceutical preparations were used Ceftazidime Roth ( Pharma Roth GmbH 65189 Wiesbaden Germany) , YENIZidime (yeni-pharma company Turkey –Ankara) and TOTTIZIM (Made in ITALY) ( 1000μg/ml ) 0.1 g dissolved in distilled water and fill to the mark in a 100 ml conical flask

General procedure of diazotization reaction;
An aliquot of a sample solution containing CFT (1ml ) from 1000μg/ml was transferred into 20.0 mL of conical flasks and then cooled in an ice bath maintained at -5.0 °C to this solution, 1ml of HCl followed by 1.0 mL from NaNO₂ 1%(w/v), were added to the mixture and left to stand for 10 min . Then, 1 mL of 1-naphthol and 2-naphthol was added to flask, then 1ml of NaOH 25% solution was added to the mixture, and diluted to the mark with double distilled water(D.W). The azo dye that formed was monitored at λmax 585 and 545nm respectively

General procedure of Flow Injection method;
Using a three-channels peristaltic pump, the first channel contains a mixture of hydrochloric acid and sodium nitrite This mixture is passed through the injection valve, containing 100 μL of ceftazidime, to form the diazonium ion, which is passed into a 100 cm reaction coil. the second channel contains the reagent (1-NPT or 2-NPT ) that coupled with diazonium ion to form diazonium salt, the third channel contains 5% of NaOH which is added to the product, her the colored product (Brown and red respectively ) appears which will pass to the UV-Visible reagent for absorption and is measured the resulting brown and red colors were measured at λmax 585 and 545 nm for the two detectors, respectively.

Result and discussion
Absorption spectra
Diazotized CFT was coupled with 1-Naphthol and 2-Naphthol in an alkaline solution to produce brown and red colored chromophore. The absorbance of the azo dyes were recorded at wavelengths of 585 and 545nm against a blank solution that which is prepared in the same way as sample – the same additions - except for drugs , and were obtained with a maximum absorbance under optimal conditions. Figs. 3, 4.
Part 1: Optimization of experimental conditions
To achieve the optimum detection limit and highest sensitivity, the many aspects impacting the spectrum characteristics of the dyes generated by coupling nitrogenous drug with organic reagent were examined. All of these tests were carried out in 20ml volumetric flasks with (1000µg/ml) 9.1478×10⁻⁵M of CFT standard solution.

Figure 3. Absorption spectrum of 40ppm of CFT-1-NPT against reagent blank.

Figure 4. Absorption spectrum for 70ppm of CFT-2-NPT against reagent blank.
The effect of the acid type on the diazonium salt:
Acids such as HCl, H3PO4, HNO3, and H2SO4 diluted (1:1) have been examined. The results demonstrate that HCl (1:1) is the best acid for this procedure because it offers the maximum absorbance signal for both dyes. Although H2SO4 in reagent 2-NPT gave the highest absorbance, the solution was turbid, thus HCl was employed, as shown in Table 1.

Table 1 Effect of acid type on absorbance signal of CFT.

| Type of acid (1:1) | Abs of CFT-1-NPT at 585nm | Abs of CFT-2-NPT at 545nm |
|-------------------|---------------------------|---------------------------|
| HCl               | 0.864                     | 0.984                     |
| HNO3              | 0.180                     | 1.198                     |
| H2SO4             | 0.089                     | 0.339                     |
| H3PO4             | 0.220                     | 0.284                     |

Effect of the hydrochloric acid volume on diazonium salt reaction:
Various volumes of HCl ranging from 0.5ml to 2ml were used to investigate the effect of acidity on the colored solution. Although 1.5 and 2ml in reagent 2-NPT had the maximum absorbance, the solution was unstable and contained a precipitate, thus 1ml was chosen instead, Fig.5.

![Figure 5. Effect volume of (1:1) HCL](image)

Effect of the NaNO2 1% volume
The effect of the volume of the NaNO2 solution was investigated by using various volumes of NaNO2 ranging from 0.5 to 2ml, with the result that 0.5 showed better absorption for both reagents Fig.6.
Effect of reaction time after addition of NaNO₂

The effect of reaction time was investigated by utilizing different intervals ranging from 5 to 30 minutes, 15 min gave highest absorption for CFT-1-NPT and CFT-2-NPT Fig.7.

The impact of different types of bases on absorption;

The effect of different bases, 25 percent w/v [KOH, NaOH, Na₂CO₃], on the absorption of azo dye has been tested, and it was found that the KOH solution showed the highest absorption for both the reagent and the CFT-2-NPT, but the solution was unstable and continuation of bubbles, therefore NaOH was used. as shown in Table 2.

Table 2. Effect type of base on the diazonium salt reaction

| Type of base 25% | Absorbance of CFT with |
|-----------------|-----------------------|
|                 | 1-NPT at 585nm         | 2-NPT at 545nm         |
| NaOH            | 1.496                  | 1.010                  |
| KOH             | 1.487                  | 1.428                  |
| Na₂CO₃          | 0.047                  | 1.318                  |
Effect of the sodium hydroxide volume;
The effect of varied sodium hydroxide volumes on absorbance were tested for the volume range (0.5-2ml), with 1.0ml gave the maximum absorption for CFT-1-NPT and CFT-2-NPT, respectively, Fig.8.

The Effect of reagent volume on diazonium salt:
With 1 ml of 1000µg/ml ceftazidime solution, several quantities of (50µg/ml) 3.4710-4 M of reagents 1-NPT and 2-NPT were examined (0.5-1.00ml). The reagent with the highest absorbance was 0.5ml. The absorbance signal remained steady after that. Fig.9.

The possible reaction mechanism can be written as in the Fig.10.
Figure 10. The Diazotize salt reaction's proposed mechanism

**Data analysis**

The absorption signals were measured against a series of ceftazidime concentrations to plot a calibration curve. Fig 11 and Table 3 exhibit the developed method's calibration curve and analytical figures.

Figure 11. Calibration curve of CFT-1-NPT and CFT-2-NPT
Table 3. The proposed diazonium salt techniques’ distinctive parameters.

| Parameter                      | CFT-1-NPT   | CFT-2-NPT   |
|--------------------------------|-------------|-------------|
| Color of product               | Brown       | Red         |
| \( \lambda \max \) (nm)       | 585         | 545         |
| Linear range (\( \mu g.mL^{-1} \)) | (3-40)      | (3-40)      |
| Molar absorptivity, \( E \) (L.mol-1.cm-1) | \( 0.7926 \times 10^4 \) | \( 0.5466 \times 10^4 \) |
| Regression equation            | y=0.011x+.0301 | y=0.0108x-.0088 |
| Sandell sensitivity, S (\( \mu g .cm^{-2} \)/0.001A.U) | 0.0689 | 0.0952 |
| Intercept (a)                  | +0.0301     | -0.0088     |
| Slope (b) (L.mg-1.cm-1)        | 0.011       | 0.0108      |
| Coefficient of determination % | 99.96       | 99.97       |
| Correlation coefficient (r)    | 0.9997      | 0.9998      |
| Limit of detection (\( \mu g.mL^{-1} \)) | 1.2809 | 0.8017   |
| Limit of quantification (\( \mu g.mL^{-1} \)) | 4.293 | 2.6722 |
| Standard error for regression line (Sy/x) | 0.004722 | 0.002886 |

Part 2: optimization reaction of FIA for CFT

The effect of HCl concentration

The effect of the concentration of HCl was studied in the range (1.16 to 5.8) M with constant CFT concentration of (100µg/ml). The concentration (5.8 and 4.64) M gave highest absorbance for reagent (1-NPT ,2-NPT) respectively Fig.12.

![Figure 12. Effect concentration of HCl](image-url)
The effect of NaNO₂ 1% volume:
The effect of the volume of the sodium nitrite on the absorbance of the colored products Fig. 13. The effect of different volumes of sodium nitrite was studied that range from 25 to 5 ml, 20 and 15 ml that was gave the highest absorption for reagents respectively.

![Figure 13. Effect volume of NaNO2](image)

The effect of reagents concentration:
At constant CFT concentrations, the effects of 1-NPT and 2-NPT concentrations on absorbance were investigated. CFT was injected into the HCl stream in fixed volumes (100 mL) at 1000 µg/mL. Fig. 14 shows the effect of changing the reagent concentrations in the range from 0.0694×10⁻³ to 0.832×10⁻³ M (300 -1200) µg/ml on the absorption peak. The figure shows that when the reagent concentration reached 0.832×10⁻³ M, a maximum analytical signal was obtained, and it was chosen for further use.

![Figure 14. Effect concentration of reagents.](image)

The effect of different concentration of NaOH:
The effect of different concentration of NaOH was studied, the range from (5 to 25%), with a fixed concentration of acid and drug, and it 5% showed the highest absorption intensity to both of reagents. Fig. 15.
Figure 15. Effect concentration of NaOH%.

Analytical data for Flow injection. After determining the optimal experimental conditions, the calibration curve was plotted as it is shown in Fig. 16 and Table 4 calibration curve and analytical information, respectively.

Figure 16. Calibration curve of the FLA method.

Table 4. Characteristic parameters of proposed Flow injection methods.

| Parameter                             | CFT-1-NPT         | CFT-2-NPT         |
|---------------------------------------|-------------------|-------------------|
| Color of product                      | Brown             | Red               |
| λ max (nm)                            |                   |                   |
| Dynamic range (µg.ml⁻¹)               | (3-50)            | (3-50)            |
| Molar absorptivity, Ε (L.mol⁻¹.cm⁻¹)  | 0.957×10⁴         | 0.7106×10⁴        |
| Regression equation                   |                   |                   |
| Sandell sensitivity, S (µg .cm⁻²)/0.001A.U | 0.05714           | 0.07692           |
| Intercept (a)                         | +0.0034           | -0.0206           |
| Slope (b) (L.mg⁻¹.cm⁻¹)               | 0.0177            | 0.0143            |
| Coefficient of determination %        | 99.98             | 99.95             |
R^2
Correlation coefficient (r)
Limit of detection (µg.mL^-1)
Limit of quantification (µg.mL^-1)
Standard error for regression line (Sy/x)

Analytical Application: Three types of pharmaceuticals were used to examine the proposed procedures (Diazotization, Flow injection) for the analysis of pharmaceutical formulations. Table of contents (5, 6) provides all of the results that were obtained, as both approaches were accurate and precise.

Table 5. Application of the proposed Batch method for the determination of Ceftazidime in different brands of drugs.

| Ceftazidime made in | Amount of CFT(µg/ml) | E% | Recovery % | Average% | RSD (n=5) |
|---------------------|-----------------------|----|------------|----------|-----------|
| YENIZIM made in Turkey Ankara |                        |    |            |          |           |
| 1-NPT               | Taken                 | Found |
| 5                   | 4.99                  | -0.18 | 99.81 | 100.05 | 2.48 |
| 20                  | 19.81                 | -0.95 | 99.05 | 99.67 | 0.737 |
| 40                  | 40.53                 | 1.34  | 101.3 | 99.49 | 0.495 |
| 5                   | 4.88                  | -2.22 | 97.77 | 97.77 | 0.495 |
| 20                  | 20.35                 | 1.76  | 101.76 | 99.67 | 0.495 |
| 40                  | 39.79                 | -0.5  | 99.49 | 99.49 | 0.495 |
| 2-NPT               | Taken                 | Found |
| 5                   | 4.88                  | -2.22 | 97.77 | 97.77 | 0.495 |
| 20                  | 20.35                 | 1.76  | 101.76 | 99.67 | 0.495 |
| 40                  | 39.79                 | -0.5  | 99.49 | 99.49 | 0.495 |
| Ceftazidime made in ITALY | Amount of CFT(µg/ml) | E% | Recovery % | Average% | RSD (n=5) |
| TOTTIZIM made in ITALY |                        |    |            |          |           |
| 1-NPT               | Taken                 | Found |
| 5                   | 4.9                   | -2   | 98       | 99.16   | 1.57 |
| 20                  | 19.72                 | -1.41 | 98.59 | 99.16 | 0.813 |
| 40                  | 40.35                 | 0.88  | 100.88 | 99.16 | 0.472 |
| 5                   | 4.79                  | -4.07 | 95.93 | 95.93 | 0.598 |
| 20                  | 20.37                 | 1.85  | 101.85 | 99.17 | 0.699 |
| 40                  | 39.88                 | -0.28 | 99.72 | 99.72 | 0.374 |
| Ceftazidime made in Wiesbaden Germany | Amount of CFT(µg/ml) | E% | Recovery % | Average% | RSD (n=5) |
| ROTH made in Wiesbaden Germany |                        |    |            |          |           |
| 1-NPT               | Taken                 | Found |
| 5                   | 4.81                  | -3.82 | 96.18 | 98.32 | 1.367 |
| 20                  | 19.63                 | -1.86 | 98.13 | 98.32 | 0.533 |
| 40                  | 40.26                 | 0.66  | 100.66 | 98.32 | 0.495 |
| 5                   | 5.03                  | 5.03  | 100.56 | 100.56 | 0.504 |
| 20                  | 20.44                 | 2.22  | 102.22 | 100.76 | 0.613 |
| 40                  | 39.79                 | -0.51 | 99.49 | 99.49 | 0.456 |
Table 6. Application of the proposed Flow injection method for the determination of Ceftazidime in different brands of drugs.

| Ceftazidime       | Amount of CFT(µg/ml) | E%   | Recovery%  | Average% | RSD (n=5) |
|-------------------|----------------------|------|------------|----------|-----------|
| YENIZIM made in   |                      |      |            |          |           |
| Turkish Ankara    |                      |      |            |          |           |
| Taken             | Found                |      |            |          |           |
| 1-NPT             | 10 9.75              | -2.49| 97.5       | 99.05    | 1.027     |
|                   | 30 29.98             | -0.08| 99.92      |          | 0.431     |
|                   | 50 49.86             | -0.27| 99.73      |          | 0.343     |
|                   | 10 9.97              | -0.28| 99.72      |          | 0.932     |
| 2-NPT             | 30 30.25             | 0.839| 100.84     | 99.93    | 0.276     |
|                   | 50 49.62             | -0.76| 99.24      |          | 0.4889    |
| Ceftazidime       |                      |      |            |          |           |
| TOTTIZIM made in  |                      |      |            |          |           |
| ITALY             |                      |      |            |          |           |
| Taken             | Found                |      |            |          |           |
| 1-NPT             | 10 9.81              | -1.92| 98.08      |          | 1.189     |
|                   | 30 30.03             | 0.113| 100.11     | 99.34    | 0.339     |
|                   | 50 49.92             | -0.16| 99.84      |          | 0.375     |
|                   | 10 9.90              | -0.98| 99.02      |          | 1.067     |
| 2-NPT             | 30 30.32             | 1.072| 101.07     | 99.73    | 2.011     |
|                   | 50 49.55             | -0.89| 98.10      |          | 0.455     |
| Ceftazidime       |                      |      |            |          |           |
| ROTH made in      |                      |      |            |          |           |
| Wiesbaden Germany |                      |      |            |          |           |
| Taken             | Found                |      |            |          |           |
| 1-NPT             | 10 9.86              | -1.4 | 98.6       |          | 1.782     |
|                   | 30 30.09             | 0.301| 100.30     | 99.62    | 0.431     |
|                   | 50 49.98             | -0.05| 99.95      |          | 0.375     |
|                   | 10 10.04             | 0.419| 100.42     |          | 1.296     |
| 2-NPT             | 30 30.39             | 1.305| 101.3      | 100.23   | 0.216     |
|                   | 50 49.48             | -1.04| 98.96      |          | 0.457     |

Conclusion:
Because the 1-NPT and 2-NPT reagents are methods that are available and inexpensive, the research includes two simple, sensitive, fast, and inexpensive methods for estimating ceftazidime. The first (diazoization-coupling) entails converting ceftazidime into a colored dye that can be measured using a UV-method Vis spectrophotometer. The second step involves using flow injection to pre-concentrate colored dye. This is the first method for extracting CFT from a flow injection. These methods have been used to estimate ceftazidime in pharmaceuticals with great success.

Author's declaration:
- Conflicts of Interest: None.
- We hereby confirm that all the Figures and Tables in the manuscript are ours. Besides, the Figures and images, which are not ours, have been given the permission for re-publication attached with the manuscript
- Ethical Clearance: The project was approved by the local ethical committee in University of Mustansiriyah.

Authors Contribution:
M J M H: Suggesting a research project, preparing a research plan, providing all laboratory supplies and chemicals
H Ab : Executing and conducting all laboratory experiments and obtaining the results and presenting them to the supervisor.

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طريق القياس الطيفي للحقن الدفعي والتدفق لتحديد السيفتازيديم في التركيبات الصيدلانية
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الخلاصة:
تم وصف تقنيتين طيفيتين لقياس كمية السيتفتازيديم (CFT) في الأدوية والتركيبات الصيدلانية. فهي بسيطة وحساسة وانتقائية ودقيقة وفعالة. يستخدم الأسلاوب الأول وسبطاً قلباً لتحول السيتفتازيديم إلى محل الديازونيوم، والذي يتم دمجه بعد ذلك مع كواشف Naphthol (1-NPT) و 4-Naphthol-NPT و 1-Naphthol-2-NPT و (CFT-1-NPT) و (CFT-2-NPT) ، كانت حدود الكشف (545nm and 0.5466×104 L.mol1cm−1) على التوالي. تم اتباع قانون بير من حيث مدى التركيز على التوالي, وكانت الامتصاصية المولية (2.9.41×102 and 2.9.41×102 L.mol1cm−1) على التوالي, وكانت الامتصاصية المولية (0.5466×104 g.ml1) على التوالي. تم استخدام الأسلاوب المقترحتين لتحديد السيفتازيديم في المستحضرات الصيدلانية بنجاح حيث تميزت هذه الطريقة بالبساطة والسرعة والدقاقة والتكلفة المنخفضة.

الكلمات المفتاحية: صبغة الأزو, الدفعات سيتفتازيديم, الأزوتة, الحقن الجرياني. 1- النفوذ 2- نفوذ. الطيفية.