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Spectrophotometric determination of cefdinir in the pharmaceutical preparations

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***Abstract*---**Two simple, quick, and sensitive techniques for spectrophotometric determination of Cefdinir (Cef) in its pure form and pharmaceutical formulations have been devised. The proposed methods were: (I) synthesis of a Schiff's base between Cefdinir and 4-Chlorobanzaldehayde reagent in an alkaline medium to produce a yellow-colored product, (II) diazotization and coupling between (Cef) and Orthophenylenediamime in an alkaline medium to produce an intense yellow colored product. The highest absorptions were measured at 0.568 with the reagent 4-Chlorobanzaldehayde and 0.871 with the reagent Orthophenylenediamime. Beer's Law holds true for 4-Chlorobanzaldehayde and Orthophenylenediamime at concentrations of (10-200g/ml), (10-135g/ml), respectively, with molar absorptivity of 1.35×105 Lmol.cm and 1.66×105 Lmol.cm. The limits of detection (LOD) for 4-Chlorobanzaldehayde and Orthophenylenediamime were found to be 0.021g/ml and 0.022 g/ml, respectively. The proposed method proved successful in estimating "This medication" in both its pure form and in pharmaceutical formulations.

***Keywords*---**4-Chlorobanzaldehayde, Orthophenylenediamime, Cefdinir, Spectrophotometry.

1. Introduction

Cefdinir (Fig.1) is an antibacterial agent that can be taken orally [1], is an antibiotic of the third generation that is resistant to Gram-negative bacteria as well as some Gram-positive bacteria [2], it's used to treat urinary tract infections, acute hepatitis, rhinosinusitis, and pharyngitis (tonsillitis) [3] Several methods have been proposed for determination of this drug, such as HPLC [4,5], TLC [6],

HPTLC [7], UV-Voltammetry [8,9]. Spectrophotometry [10,11], UV-Vis. Spectrophotometry [12,13]. The research amis at finding a simple, fast, determining Cefidinir using reagent 4- Chlorobanzaldehayde in alkaline medium, and reagent Orthophenylenediamime in alkaline medium, as well as the success of the proposed methods for determining (Cef) in its pharmaceutical applications [14].

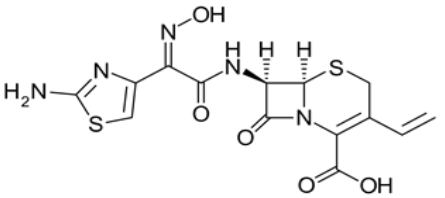


Figure (1): Chemical structure of Cefdinir

2. Experimental:

2.1. Chemicals used:

Cefidinir 99% from (SDI Samarra. Iraq), 99% 4- Chlorobanzaldehayde from (Marck), 97% Orthophenylenediamime from (Fluka), Sodium hydroxide 99% from (GCC), DMSO 99% from GCC,Ethanol 99% from (SDI Samarra. Iraq), Sodium Nitrate from (Marck), 25% Ammonium hydroxide from GCC, 99% Hydrochloric acid from GCC.

2.2. Devices used

UV- VIS Spectrophotometer. 2-T92+ UV Spectrophotometer ''PG INSTRUMMENTS with1cm PLastic cells. UV-VIS Spectrophotometer ''Single beam from Genesis UV10. -UV-VIS Spectrophotometer ''double beam from Shimadzu (model UV-1800 2- Balance Kern 770GS/GJ from Sartorius BL210S. Semi-Micro Analytical Balances. Oven from Memmert, Schutzart DIN 40050-IP20. Hot Plate.

2.3. Solutions

- Cefidinir stock solution (1000 µg\ml): an exactly (0.1000 gm) of (Cef) standard were dissolved in (100 ml) DMSO.
- Reagent solution (4-chlorobenzaldehyde) at a concentration of (0.08 M): It was prepared by dissolving 1.1244 g of it in 100 ml of ethanol and completing the volume with the same solvent to the mark.
- Sodium hydroxide solution (1M): A sodium hydroxide solution was prepared by dissolving 4 g of it in 100 ml of distilled water.
- Aammonium hydroxide solution (1M): The NH_4OH solution was prepared by taking 7.7 mL of concentrated base solution (6.49 M) and diluting the volume with distilled water to 50 mL.
- Preparation of $NaNO_2$ at a concentration of 0.001 molarity: The solution was prepared by taking a weight of 0.00344 g of it and dissolving it in 50 ml of distilled water.
- HCl acid solution with a concentration of 1 M.: The acid solution was prepared by diluting 8.6 ml of concentrated acid (11.68 M) to 100 ml of distilled water.

- Prepare a reagent Orthophenylenediamime solution at a concentration of 0.01 mol: The solution was prepared by dissolving 0.10814 g of it in 100 ml of ethanol.

2.4. Determination of (Cef) by 4-Chlorobanzaldehayde as reagent

The optimum conditions were reached after conducting an initial test as 1.5 ml of cefdinir solution at a concentration of 500 mcg/ml was added to a 10 ml volumetric vial, a and followed by 0.5 ml of NaOH at a concentration of 1 M. Volume was created with ethanol to the mark against its mock solution after adding 0.5 ml sodium hydroxide at a concentration of 1 ml 4-chlorobenzaldehyde reagent at a concentration of 0.08. the maximum absorption of the product is 0.568 at laboratory temperature at 460 nm versus its photo solution, while the photo solution did not give any absorption in this region [15-18].

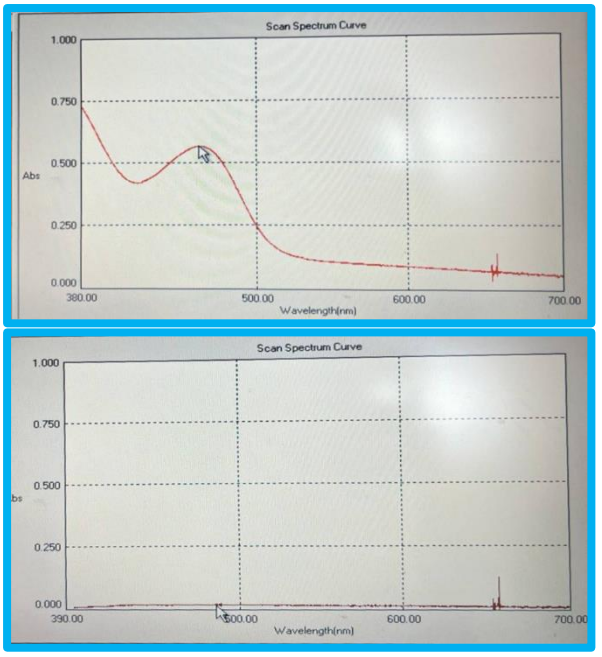


Figure (2): Absorption spectrum of (Cef) product against blank and Absorption spectrum of blank against

2.5. Application of proposed methods

The proposed method was used to estimate Cef in a pharmaceutical preparation in the form of tablets. The weight of ten tablets was 6.2030 g, and they were finely ground until they were converted into a fine powder. A weight of 0.1032 g of the preparation was taken, and it was dissolved in 100 ml of dimethyl sulfoxide, then the solution was filtered and three concentrations were taken from the filter to estimate Cef in a pharmaceutical preparation in the form of tablets, it was successful suggested methods of estimating (Cef) in various commercial tablets. [19-24]

3. Results and Discussion:

3.1. Optimal Conditions

3.1.1. Effect of (4-Chlorobanzaldehayde) reagent volume

When several volumes of the reagent with an initial concentration of 0.08M were added to the reaction of (4-Chlorobanzaldehayde), it was discovered that the best absorption was at a volume of 1ml, as indicated in the figure (3).

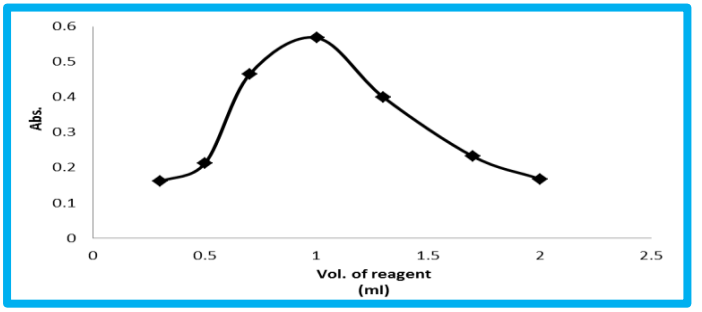


Figure (3): Effect the volum 4-Chlorobanzaldehayde of on product

3.1.2. Effect of base volume: To see how increasing volumes of sodium hydroxide solution with an initial concentration of 1M affect the resultant absorption values, the optimal added volumes were found to be 0.5 ml [25,26], as shown in figure (4).

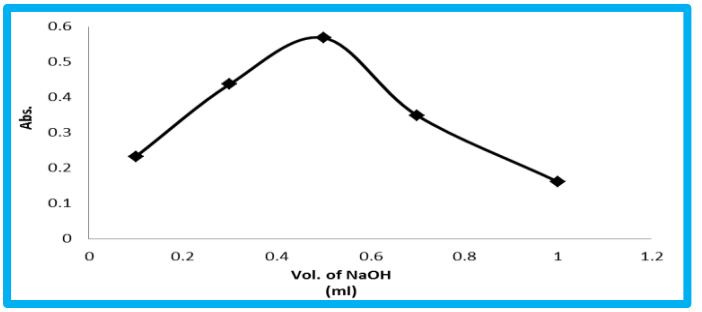


Figure (4): Effect the Volume of NaOH on the product

3.1.3. Effect of different bases: The best absorption was obtained when using NaOH, as shown in table (1), when using multiple base solutions (NaOH, KOH, NH_4OH) at a concentration of 1M and adding the same amount of 0.5 ml (1) [27-30].

Table (1): Effect of different bases on the product

Base	Absorbance
KOH	0.357
NH_4OH	0.029
NaOH	0.568

3.1.4. Effect of Time: The stability of the product formed by the interaction of the drug with the reagent is important in order to determine the length of time during which the formed product can remain constant, and the stability of the absorption values was observed at approximately 45 minutes in the experiments conducted, which is sufficient time to make the required measurements, as shown in the table (2).

Table (2): Effect of time on stability of product

Time(min)	5	10	15	20	25	30	35	40	45	50	55
Abs.	0.562	0.563	0.566	0.568	0.565	0.566	0.567	0.561	0.558	0.551	0.547

3.1.5. Effect of additives: The effect of additives on the composition of the product was studied, and not observed any effect, as shown in the table (3).

Table (3): Effect of interferences

RE%	Added con. g/ml	RE%	Added con. µg/ml	Interference
2.64	300	-1.14	150	Lactose monohydrate
3.36	300	2.89	150	Magnesium stearate
-2.11	300	0.53	150	Sodium lauryl sulfate
3.68	300	1.26	150	Cellulose

3.1.6. Calibration curve: As shown in figure (5), the calibration curve for (Cefdinir) using (4-Chlorobanzaldehayde) reagent showed linearity at concentrations ranging from (10-200) g/ml.

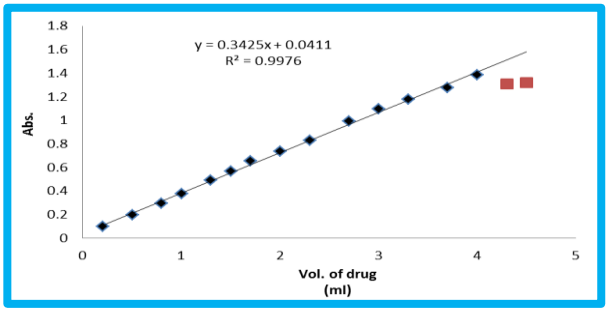


Fig. (5): Calibration curve of (Cef- 4-Chloroe) product

3.1.7. The stoichiometry of the product: The "equivalence of the product" was studied for the interaction of Cefdinir with the reagent under optimal conditions by the molar ratio method, as the initial concentration used was 5×10-3, as well as by the continuous change method at an initial concentration of 5×10-3, where the ratio of equivalence between the drug and the reagent was (1:1), (Figure 6).

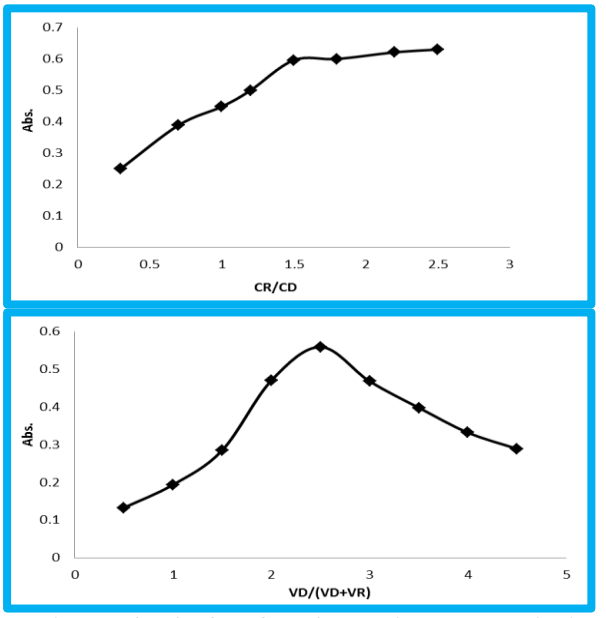
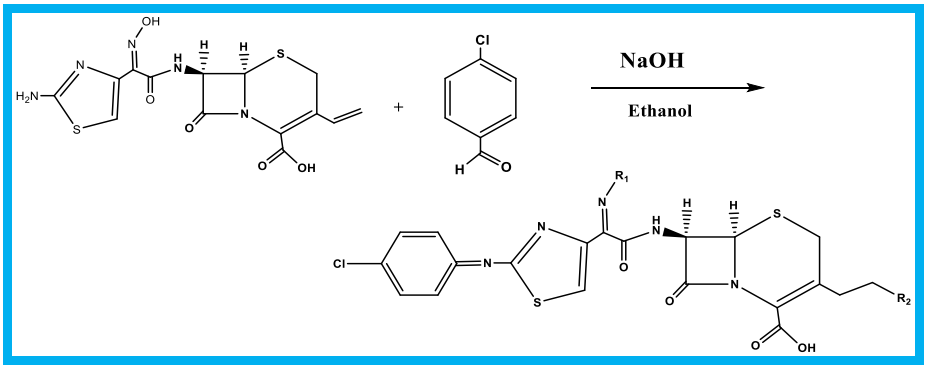


Figure (6): Mole-ratio method of Cef and Continuous variation method of Cef

3.1.8. Suggested interaction: The proposed reaction can be based on a condensation reaction between Cefdinir and 4-Chlorobanzaldehayde in a base medium to produce a dense, yellow colored product, (Schiff's base) [14]:



3.1.9. Application of the proposed method: the results of determination of (Cef) in the pharmaceutical preparations, as shown in table (4), (as tablets).

Table (4): Determination of Cef (as tablet)

Fharmaceuticai Preparation	Content (µg/ml) declared	Found(µg/ml) by proposed	Recovery%
Ceftinex	40	40.22	100.55
	85	84.98	99.98
	115	115.13	100.11

3.2. Determination of (Cef) by Orthophenylenediamime as reagent

The optimum conditions were reached after conducting preliminary experiments, as 3 ml of Ortho-vinylamine amine reagent at a concentration of 0.01 molar was added to a 10 ml glass vial, then 0.5 ml of the NaNO2 at a concentration of 0.001 was added, and 0.5 ml of HCl acid was added at a concentration 1.0 M, followed by the addition of 1.5 ml of cefdinir solution at a concentration of 500 mcg / ml, then 0.5 ml of a solution of NH4OH at a concentration of 2.0 M, and then the volume was supplemented with distilled water to the mark and after absorbing the product 0.871 at laboratory temperature at 413 nm against its mock solution While the mock solution did not give any absorption in this region.

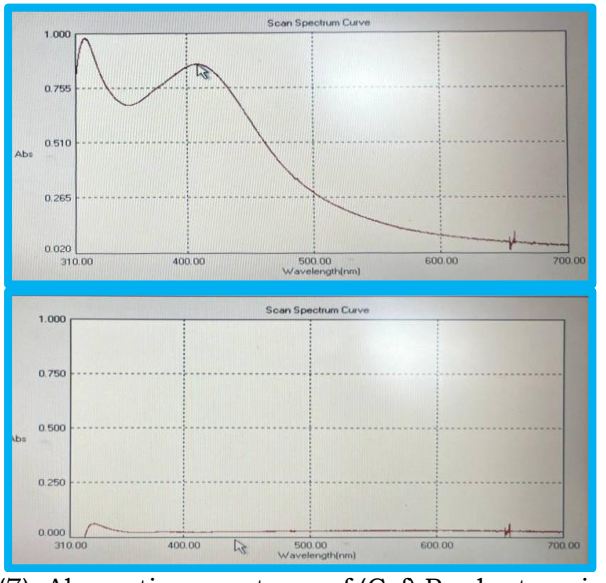


Figure (7): Absorption spectrum of (Cef) Product against blank

3.3. Optimal condition

3.3.1. Effect of acid volume: To determine the influence of the volume of the additional acid on the absorption value, increasing amounts of HCl were applied according to the stated data, the optimal volume for absorption is 0.5 ml, as indicated in figure (8).

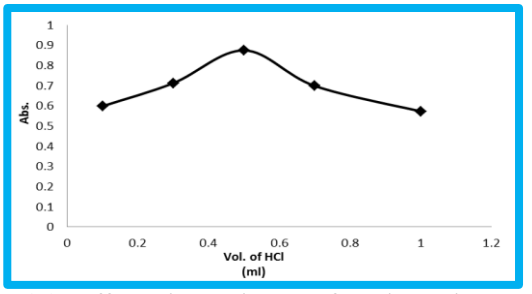


Figure (8): Effect the Volume of HCl on the product

3.3.2. Effect of the different acids: Used many acids, including the weak and strong ones (HCl, H_2SO_4, H1NO_3, CH_3COOH), and all of them have a

concentration of 1M, as well as the same added volume of 0.5 ml to find out which of the acids gives the best absorption of product formed, it has been shown that the best absorption is with HCl, as shown in table (5).

Table (5): Effect of different acids on the product

Acid	HCl	H_2SO_4	HNO_3	CH_3COOH
Abc.	0. 873	0.132	0.240	0.226

3.3.3. The effect of the volume of the nitrogenous agent: Volumes of NaNO2 were used with a concentration of 0.001M. The volume that gives the highest absorption was used, and the results are shown in fig. (9), it was found that the best volume of acid added is 0.5 ml.

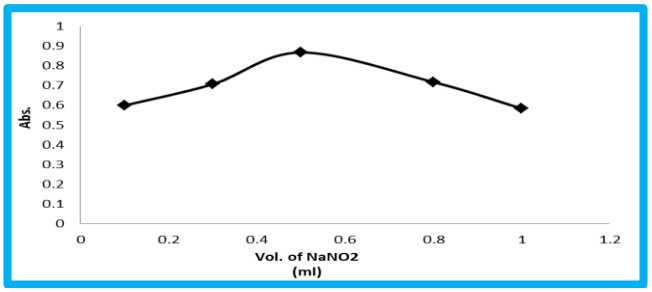


Figure (9): Effect the Volume of nitrogenous agent on the product

3.3.4. Effect of base volume NH_4OH: Increasing volumes of NH_4OH at a concentration of 2.0 molar were used to find out the volume that gives the highest absorption, and the results are shown in Figure (10), as it was found that the best volume added from the base is 0.5 ml.

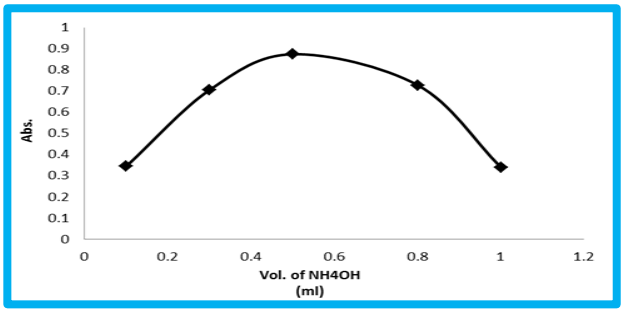


Figure (10): Effect of base Volume of (NH_4OH) on the product

3.3.5. Effect of Time: The stability of the formed product is important to know the time period during which the product remains constant, and Table (6) shows the results of following up the interaction with time under optimal conditions.

Table (6): Effect of Time on the product

Abs.	0.868	0.869	0.870	0.872	0.871	0.871	0.872	0.869	0.867	0.865	0.865	0.855	0.851	0.847
Time	0.00	10	20	30	40	50	60	70	80	90	100	120	130	140

From the table, the stability of the absorption values at a wavelength with time was observed, as the absorption value of the product was fixed for approximately (100) minutes, and this period is sufficient to make the required measurements.

3.3.6. Effect of reagent volume: Increasing volumes of ortho-vinyldiamine reagent were added with an initial concentration of 0.01 molar, to know the extent of their effect on the absorption of the product, as shown in figure (11), as it is noted that the best added volume of the reagent is 3 ml.

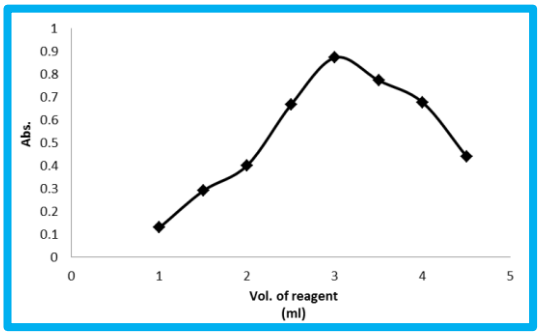


Figure (11): Effect the Volume of reagent volume

3.3.7. Effect of different bases: The bases NH_4OH, KOH, and NaOH were employed at 2.0 molar concentrations with the same supplied volume of 1.0 ml to determine which base produces the highest absorption when generating the product, with the best base being NH_4OH ammonium hydroxide, as shown in table (7).

Table (7): Effect of different bases

Bases	NH_4OH	NaOH	KOH
Abs.	0.869	0.233	0.342

3.3.8. Effect of additives: The effect of additives on the composition of the product was studied, and not observed any effect, as shown in the table (8).

RE%	Added con. µg/ml	RE%	Added con. µg/ml	Materials
1.77	300	1.56	150	Lactose monohydrate
1.49	300	2.83-	150	Magnesium stearate
1.65	300	0.98	150	Sodium lauryl sulfate
3.22	300	2.34	150	Cellulose

3.3.9. Calibration curve: The calibration curve for (Cef) pure form with (Orthophenylene diamime) showed the linearity at concentration rang of (10-135)µg/ml, as shown in figure 12.

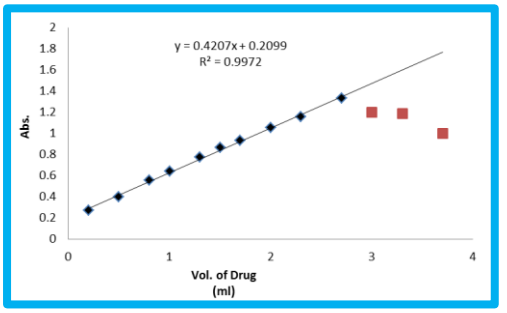


Figure (12): Calibration curve of (Cef- Orthophenylenediamime) product

3.3.10. The stoichiometry of the product: The equivalence of the product" was studied for the interaction of Cefdinir with the reagent under optimal conditions by the molar ratio method, as the initial concentration used was 8×10^{-4}, as well as by the continuous change method at an initial concentration of 8×10^{-4}, where the ratio of equivalence between the drug and the reagent was (1:1), (Figure 13).

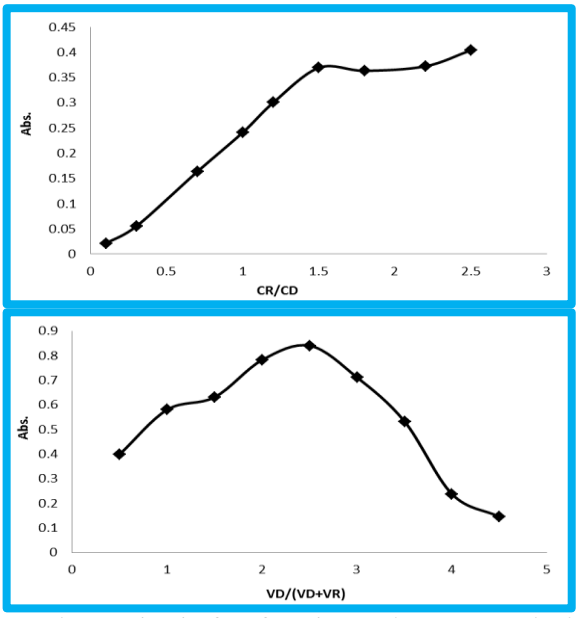
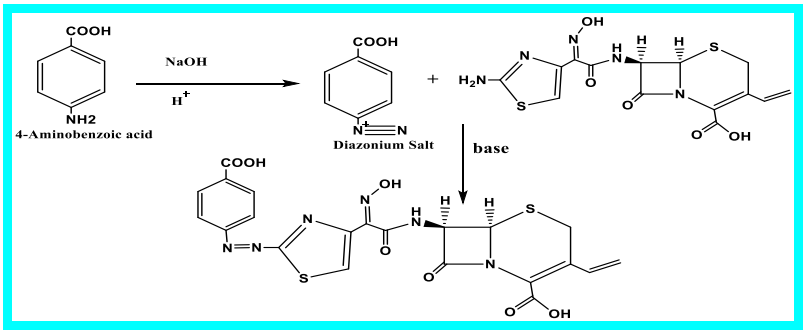


Figure (13): Mole-ratio method of Cef and Continuous variation method of Ce

3.3.11. Suggested interaction: The proposed reaction can be based on a condensation reaction between Cefdinir and Ortho-vinylamine in an acid medium to produce a dense, yellow colored product, [31-33]:



3.3.12. Application of the proposed method: The result of determination of (Cef) in the pharmaceutical preparations (as tablets).

Table (9): Determination of Cef (as tablet)

Fharmaceuticai Preparation	Content (µg/ml) declared	Found(µg/ml) by proposed	Recovery%
Ceftinex	25	24.99	99.96
	65	65.27	100.42
	85	85.53	100.62

4. Conclusion

These recommended techniques are straightforward and quick, and they do not necessitate difficult working circumstances,they were also faster than prior procedures since they provided color findings with low-cost chemicals,as a result these two methods can be combined to determine (Cef) in pharmaceutical formulations.

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