

Determination of Amlodipine in Pharmaceutical Formulation by Charge Transfer Complex Method

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Keywords: Amlodipine, Schiff Base, Charge-Transfer Complex, Spectrophotometry, Pharmaceutical Formulation.

Abstract: Charge transfer complexes were attended by the interaction of Schiff base (amlodipine + Picolin aldehyde) with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to create a Compound that produced the maximum absorption at a wavelength of 436 nm by selecting the optimal conditions for the interaction between the two compounds which were adopted in subsequent experiments. The study covers the development of a straightforward and precise spectrophotometry for the measurement of amlodipine (AML) in pharmaceutical formulations and pure forms. The molar absorption rate was $1.4556 \times 10^4 \text{ l.mol}^{-1}.\text{cm}^{-1}$, the correlation coefficient was 0.9981, the sandal sensitivity was $0.0281 \mu\text{g}.\text{cm}^{-2}$, And the Beer's law limit was $5-40 \mu\text{g}.\text{ml}^{-1}$. When this technique was used to estimate the amount of AML in pharmaceuticals, the composition of the resultant compound revealed that the detection limit ($0.2596 \mu\text{g}.\text{ml}^{-1}$). The quantitative limit ($0.7865 \mu\text{g}.\text{ml}^{-1}$), and the Rec value (%103.1124-96.8260) were all within the range of 0.2257-0.6258. Additionally, AML measurement approach has proven effectively. Characterized complexes by U.V, FTIR and Spectrum of Mass.

1 INTRODUCTION

Spectrophotometric determination is a cornerstone technique in both quantitative analysis and quality assurance [1,2]. High blood pressure is a chronic illness that also increases the risk of cardiovascular disorders. Common all over the world. It is fairly significant to assess antihypertensive medications for medication safety because hypertension patients frequently need long-term medication to control their problems, such as amlodipine and other blood pressure-lowering medications [3]. Amlodipine (AML) is a dihydropyridine with special properties that set it apart from other medications in this family [4]. It belongs to the class of calcium channel blocking medicines[5,6]. It decreases the amount of calcium that enters cells by binding exclusively to voltage-gated L-type calcium. The coronary and peripheral blood arteries enlarge as a result of the relaxation of their smooth muscles. Its primary application is in the management of hypertension [7]. And angina [8]. Edema, palpitations, and redness are among the adverse effects of AML that are most frequently experienced at dosages more than 10 mg [4]. The chemical structure of AML is depicted

in Figure 1 [9]. AML pharmacological characteristics are displayed in Table 1 [10,11,12].

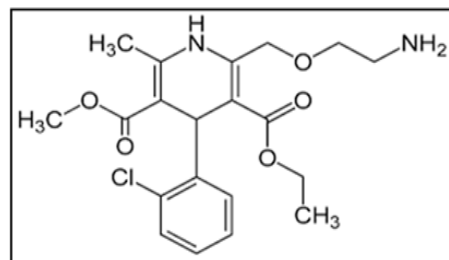


Figure 1: The chemical structure of AML.

Table 1: Some properties of AML.

Subject	Properties
Chemical Name (IUPAC)	3 - Ethyl - 5- methyl (±) - 2 - [(2-aminoethoxy) methyl] -4- (o-chlorophenyl) 1,4-dihydro-6 - methyl-3,5- pyridinedicarboxylate
Molecular Formula	$\text{C}_{20}\text{H}_{25}\text{ClN}_2\text{O}_5$
Molar mass	408.88 g / mol
Color	White

2 EXPERIMENTAL

Weights were determined using the four-ranked electrical scale, since the model is 220/C/1. Ultraviolet - visible spectroscopy technology was used in the Department of Chemistry, College of Education for Girls, Anbar University, Iraq model (Jasco V-650 double beam spectrophotometer) Japanese made with 1 cm plastic cells to measure the spectrum and absorbance.

The prepared samples were diagnosed at Samarra University, using an infrared technology model (Shimadzu FTIR-8400 S) Japanese-made, and mass spectrometry technology was also used model (Shimadzu - GCMS - QP 2010 Plus) Japanese-made.

2.1 Materials and Chemical Reagents Used

All of the synthetic materials utilized are of the best grade available.

2.2 Preparation of Schiff Base

Aldehyde condensation was used to create Schiff base (Picolin aldehyde). Reflux was used to dilute (0.2g, 0.002mol) of aldehyde with pure primary amine (AML) in ten milliliters of pure ethanol. After that, the resultant solution was put in a circular flask, and (0.8g, 0.002mol) AML, the main amine, was dissolved in 10 milliliters of 100% ethanol before being added.

Two to three Glacial acetic acid droplets were added as a stimulant to speed up the reaction. For three hours, the mixture was kept at 70⁰ C for the reaction escalation procedure.

After cooling the reaction mixture to room temperature, yellow crystals formed. For a full day, the stuff was kept in a baker's. Wash with cold distilled water to purify the precipitate and filter after the solvent has evaporated as much as possible. After that, the sediment was removed, dried, and stored [13].

2.3 Preparation of Solutions

2.3.1 Solution of Schiff Base (100 µg.ml-1)

A specific amount of Schiff Base (0.01 g) was dissolved in a predetermined volume of ethanol, and a volumetric flask containing ethanol was then filled with the solution until it reached 100 ml.

2.3.2 Solution of 8-Hydroxyquinoline (100 µg.ml-1)

After a specific amount of 8-Hydroxyquinoline (0.01 g) was dissolved in a predetermined volume of ethanol, the solution was made up to 100 ml in a volumetric flask.

2.3.3 Solution of 2,3-Dichloro-5,6-Dicyano-1,4-Benzoquinone (DDQ) (100 µg.ml-1)

In a 100 ml volumetric vial, 0.01 g of 2,3-dichloro-5,6 -dicyano- 1,4- benzoquinone was dissolved in ethanol to create the solution. The volume was then increased by the same solvent concentrically 100 µg / ml.

2.3.4 Solution of Chloranil (100 µg.ml-1)

In order that create the solution, 0.01 g of chloranil was dissolved in a 100 ml volumetric vial of ethanol. The same solvent was then used to fill the capacity to the brim, yielding a solution concentration of 100 µg/ml.

2.3.5 Solution of Hydrochloric Acid (0.5 M)

It was created by extracting 4.3 milliliters of HCl, a concentrated acid with an 11.64 M concentration. The acid was then progressively diluted by adding water, and the volume was adjusted using 100 ml of distilled water in a volumetric bottle.

2.3.6 Solution of Sodium Hydroxide (0.5 M)

In a 100 ml volumetric vial, 2 g of the pure material was dissolved in 100 ml of distilled water to create it.

2.4 Preparation of Pharmaceutical Preparation for Schiff Base

The preparation of the medication, among Indian made (Brand- Micro) comes in pill form. Five mg of AML are contained in each tablet, and the solutions were made as follows: Ten tablets were thoroughly pulverized after being weighed individually. One tablet has an average weight of 0.1906 g and contains 5 mg of AML. The active ingredient, as well as 0.2 g (0.002 mol) of less concentrated picoline aldehyde in ten ml of absolute ethanol, was then added to 0.8 g of pharmaceutical preparation and the powdered meal in 30 ml of absolute ethanol, and added to the solution.

Additionally, add to the reaction 2 to 3 drops of olive acid as a supporting element. After allowing the mixture to reflux for three hours at 70 degrees

Celsius, allow the interaction mix to cool to room temperature. After obtaining yellow crystals. The material was put in a Baker for a full day in order to evaporate the most solvent. The precipitate was then purified and the filter paper was named using cold distilled water. To remove things that have not disintegrated. After that, the precipitate was collected, dried, and preserved. 0.01 g of the precipitate and the least amount of ethanol were taken out, put in a 100 ml bottle, and the size was adjusted to the solvent's mark to reach a concentration of 100 µg/ml. as a practical remedy [13].

2.5 The Method of Work

This method depends on the formation of the ion-pair complex between the reagent and drug [14]. Using 1 ml of the drug's base lipids at a 100 µg/ml concentration and 1 ml of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone at a concentration of 100 µg/ml, the shipping transfer complex was created. Using distilled water and a wiping for wavelengths between 190 and 800 nm, add 0.5 ml of sodium hydroxide in a 10-milliliter container at a concentration of 0.5 M. The resultant complex is yellow and exhibits maximum absorption at 436 nm, which was utilized in subsequent experiments.

3 RESULTS AND DISCUSSION

3.1 The Choice of Type Reagent

To determine which of the following compounds would make the best reagent, a study was undertaken. 2,3 – dichloro - 5,6 – dicyano - 1,4 -benzoquinone, Chloanil and 8-Hydroxyquinoline and the reagent that provides the highest absorption value in comparison to other reagents was selected. Following the addition of 1 ml of the aforementioned reagents to a series of volumetric of 10 ml containing 1 ml of the sealing base at a 100 µg/ml concentration, followed by the addition of 0.5 ml of sodium hydroxide with a concentration of 0.5 M and finishing with distilled water, it was discovered that 2,3-dichloro-5,6-dicyano-1,4-benzoquinone with Schiff base provided the highest absorption in comparison to the other reagents that were examined. The results are displayed in Table 2.

Table 2: Effect of different reagents.

Reagent	max (nm) λ	Absorbance
2,3 - dichloro-5,6 – dicyano-1,4 - benzoquinone (DDQ)	436	0.467
8-Hydroxyquinoline	358	0.225
Chloranil	371	0.192

3.2 Effect of Reagent Volume

The increasing sizes have been added 0.5-4 ml of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone with a concentration of 100 µg/ml in a sequence of volumetric of 10 ml that contains a fixed size 1 ml of the base of the concentration of 100 µg/ml to determine the optimal size for the reagent 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, which gives the resulting complex the highest absorption. Next, 0.5 ml of sodium hydroxide solution with a concentration of 0.5 M is added, and finally, the size is completed using purified water to the point of the mark. Next, as indicated in Table 3, we noted the absorption values for the component that was generated in comparison to the Blanc solution.

Table 3: Effect of DDQ concentration.

V(ml) of 2,3_dichloro_5,6_dicyano-1,4-benzoquinone (DDQ) 100 µg/ml	Absorbance
0.5	0.387
1	0.467
1.5	0.526
2	0.558
2.5	0.577
3	0.589
3.5	0.563
4	0.549

According to the findings of the study to determine the ideal reagent size, which is displayed in the above table, the best reagent size from which the resultant complex is obtained is 3 ml of a solution containing 100 µg/ml of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. Because it had the highest absorption, it was chosen as the optimal reagent size.

3.3 Effect of Acid

A study of the effect of acid was conducted in which hydrochloric acid was used at a concentration of 0.5 molar. Different volumes of it, ranging from 0.5 - 1.5 ml, were added to the solution containing 1 ml of Schiff base with a concentration of 100 µg/ml and 3 ml of the reagent solution 2,3-dichloro-5,6-dicyano-1,4-benzoquinone with a concentration of 100. µg/ml and the absorbance values of the complex formed were recorded at each of these values as shown in the Table 4.

Table 4: Effect of acid volume on the complex.

V (ml) of 0.5 M hydrochloric acid	Absorbance
Without acid	0.589
0.5	0.577
1	0.525
1.5	0.442

Subsequent investigations avoided the use of acid since the findings of a study on its effect on the formation of a chelating complex for the medication AML indicated that adding acid decreased the absorption of the resultant complex.

3.4 Base Volume's Effect

A series of 10 ml volumetric bottles containing 1 ml of Schiff base for AML were filled with increasing volumes of sodium hydroxide at a particular concentration of 0.5 molar and in various volumes ranging from 0.5-2 ml with a concentration of 100 µg/ml, and 3 ml of the 2,3-dichloro-5,6-dicyano-1,4-benzoquinone reagent solution. The concentration was 100 µg/ml, and the Table 5 indicates that the absorption was measured at a wavelength of 436 nm.

Table 5: Effect of base volume on the complex.

V(ml) of Sodium Hydroxide 0.5 M	Absorbance
0.5	0.570
1	0.627
1.5	0.543
2	0.535

A study that looked at the effect of sodium hydroxide on the charge transfer complex formation reaction for the drug AML revealed that adding the basal medium in a volume of 1 ml gave the highest absorption value, which was utilized in subsequent studies.

3.5 Order of Additions

Several laboratory experiments were carried out using varying addition sequences to determine the best arrangement for the complex formed. Schiff base solution in one milliliter with 100 µg/ml and 3 ml of the 2,3-dichloro and 5,6-reagent solution were added. Table 6 displays the absorption values of dicyano-1,4-benzoquinone in different sequences, contingent on the optimal reaction conditions, and 100 µg/ml and 1 ml of NaOH solution at a concentration of 100 µg/ml 0.5 M.

Table 6: Impact of the addition sequence on the charge transfer complex's absorption.

Reaction component	Order number	Absorbance
D+R+B	I	0.627
D+B+R	II	0.615
B+R+D	III	0.597

Table 6 shows that the arrangement D+R+B, where (D) is the drug's Schiff base and (R) is 2,3-dichloro-5,6-dicyano-1,4-benzoquinone and (B) is base. has the best absorption of the final product. As a result, this arrangement was used in further studies.

3.6 Temperature's Effect

One of the crucial factors in the reactions that needs to be investigated is temperature. To determine which temperature is ideal for the resulting compound to exhibit the maximum absorption, 1 ml of Schiff base solution with a concentration of 100 µg/ml and 3 ml of the reagent solution 2,3-dichloro-5,6-dicyano-1,4-benzoquinone with a concentration of 100 µg/ml and 1 ml of NaOH solution with a concentration were added.

Table 7: Temperature's impact on the charge transfer system.

Temperature (C ⁰)	Absorbance
15	0.525
20	0.572
25	0.627
30	0.664
35	0.708
40	0.739
45	0.731
50	0.724

0.5 M solution was prepared, and distilled water was added to bring the volume to the desired level. Then, the absorbance measurement of the resultant

complex during the reaction was performed within a temperature range of 15–50 °C, as shown in Table 7.

The maximum absorption happens at 40° C. This temperature was therefore selected for use in subsequent experiments.

3.7 Time's Effect

A study was carried out to ascertain whether the compound created was stable between the Schiff base of the drug AML and the reagent 2,3-dichloro and 5,6-dicyano-1,4-benzoquinone by choosing the optimal time at which the complex formed gives the highest absorption.

A solution of sodium hydroxide with a concentration of 0.5 molar was added after 1 ml of the Schiff base with a concentration of 100 µg/ml was taken and 3 ml of the reagent solution with a concentration of 100 µg/ml was added with a volume

of 1 ml, and complete the volume up to the mark with distilled water and heating at a temperature of 40 C°.

Then the absorption of the complex was measured at different times, ranging from the beginning of the preparation of the complex to 20 minutes and Table 8 shows this.

Table 8: Time's impact on the charge transfer complex.

Time (min)	Absorbance
Moment of reaction	0.739
5	0.795
10	0.833
15	0.829
20	0.814

After 10 minutes, as shown in Table 8, the complex exhibits its maximum absorption, providing ample time for additional testing.

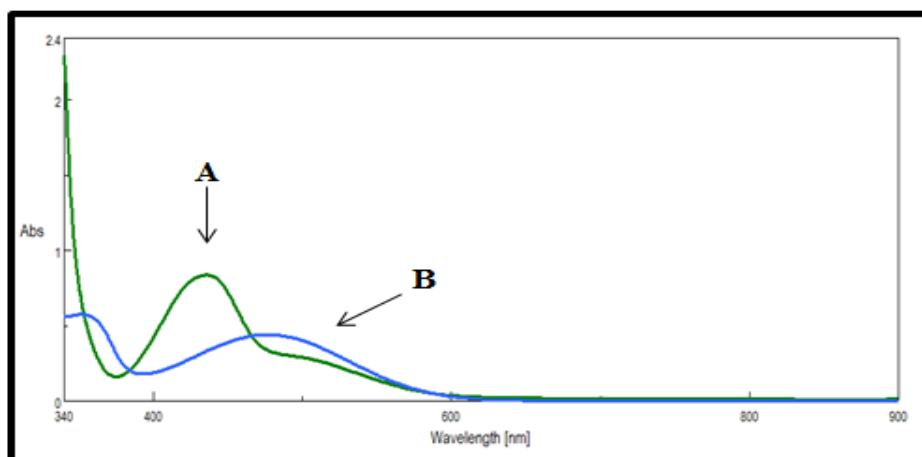


Figure 2: (A) Complex versus blank, (B) Reagent vs. ethanol.

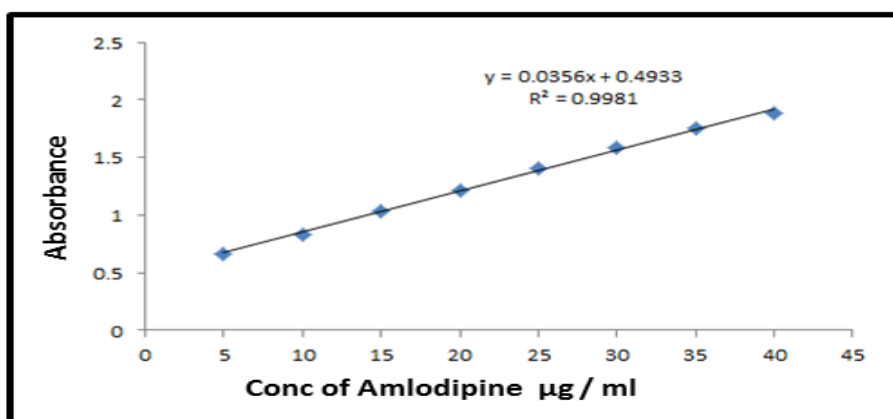


Figure 3: AML calibration curve of the proposed method.

3.8 Final Absorption Spectrum

One milliliter of Schiff base at a concentration of 100 $\mu\text{g/ml}$ was used to record the reaction's absorption spectra. and 3 ml of the reagent solution of 2,3-dichloro5,6-dicyano-1,4-benzoquinone with a concentration of 100 $\mu\text{g/ml}$, then adding 1 ml of sodium hydroxide solution with a concentration of 0.5 M, fixing the necessary temperature for the reaction at 40° C.

Then diluting with distilled water in a bottle. In a volumetric volume of 10 ml, the absorption spectra at wavelength 436 nm was recorded against the corresponding blank solution after the complex was allowed for 10 minutes to allow the reaction to finish, as shown in Figure 2.

3.9 Calibration Graph

A calibration curve, as shown in the figure, was created after the ideal conditions for the reaction were fixed. It demonstrates that the Beer-Lambert law was used to estimate AML for concentrations between 5 - 40 $\mu\text{g.mL}^{-1}$ with a final volume of 10 mL and a correlation coefficient ($r = 0.9981$). At higher concentrations, however, a deviation occurs. After calculation, the molar absorptivity came out to be $1.4556 \times 10^4 \text{ l.mol}^{-1}\text{cm}^{-1}$. Figure 3 shows that Sandal's index was 0.0281 $\mu\text{g.cm}^{-2}$.

3.10 Accuracy and Precision

For the calibration curve, three different concentration levels ranging from 10 to 40 $\mu\text{g.ml}^{-1}$ were chosen. To calculate the approach's precision (RSD%) and recovery (REC%), as shown in Table 9.

Table 9: The approach precision and accuracy in determining AML.

Conc. AML Taken $\mu\text{g/ml}$	Abs.*	Conc. AML found $\mu\text{g/ml}$	Rec%	RSD%
10	0.838	9.6826	96.8260	0.6258
25	1.411	25.7781	103.1124	0.2699
40	1.880	38.9523	97.3808	0.2257

3.11 Detection Limit and Quantitative Limit

The lowest analyte concentration in the test sample that can be consistently identified from zero is known

as the limit of detection (LOD). The boundary of The lowest concentration of a material that can be determined quantitatively is known as the limit of quantification (LOQ) [15].

Because the blank is colorless, as shown in Table 10, the detection limit and the quantitative limit have been established at the calibration curve's optimum misfortune (5 $\mu\text{g.ml}^{-1}$) [16].

Table 10: Quantitative Limit and Detection Limit.

Concentration $\mu\text{g/ml}$	Slope	s	LOD $\mu\text{g/ml}$	LOQ $\mu\text{g/ml}$
5	0.0356	0.0028	0.2596	0.7865

3.12 Application for Analysis

The suggested method for examining amlong 5 mg Indian made (Brand – Micro). A positive result was obtained after implementing the recommended strategy, as shown in Table 11.

Table 11: The analytical application, of the proposed approach.

Conc of AML $\mu\text{g/ml}$ pharmaceutical preparation	Abs.*	Conc. of AML found $\mu\text{g/ml}$	Rec%	RSD%
10	0.841	9.7669	97.6690	0.1880
25	1.409	25.7219	102.887	0.1587
40	1.889	38.2051	98.0128	0.1543

3.13 Characterization of Compound by IR and Mass

The infrared (IR) spectrum of the Schiff base is shown in Figure 5. This spectrum is compared with both the spectrum of the primary amine (AML) shown in Figure 4, In the infrared (IR) spectrum of the Schiff base, no absorption band appears at (3288) cm^{-1} , which belongs to the ν bond (NH_2), compared to the spectrum observed in the primary amine spectrum. The spectrum also does not show any absorption around the frequency (1713) cm^{-1} [17]. which is assigned to the bond $\nu(\text{C}=\text{O})$ of the aldehyde The spectrum of the Schiff compound also indicates the appearance of a new band at (1635) cm^{-1} belonging to $\text{C}=\text{N}$, which indicates the preparation of the new compound [18].The mass spectrum showed a peak at m/z 498, which represents the molecular weight of the Schiff base formed for AML, as show in Figure 6. Preparation of the Schiff base is shown in Figure 7.

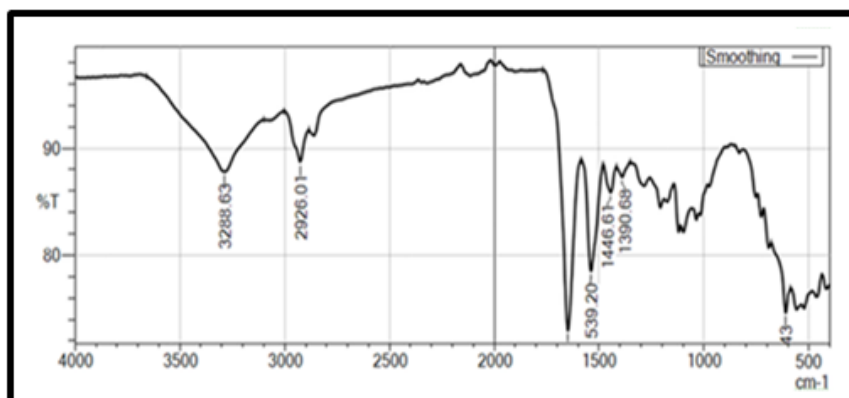


Figure 4: IR spectrum of AML.

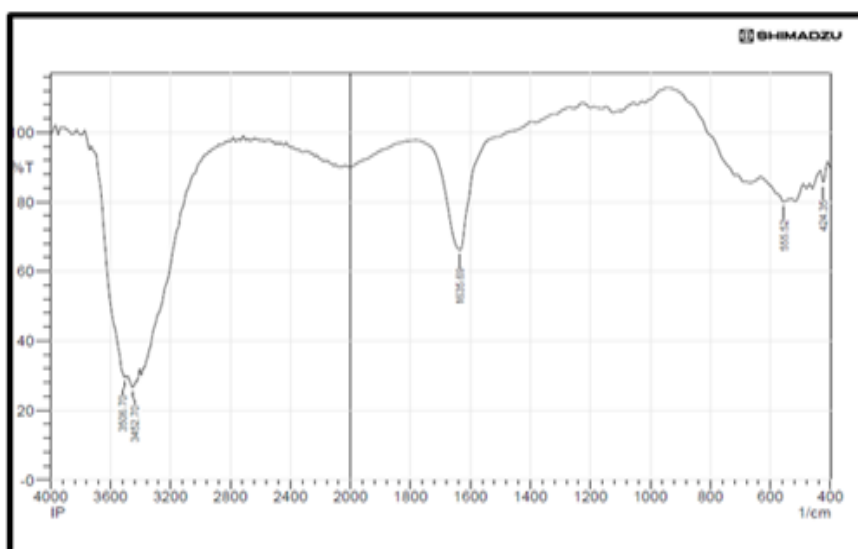


Figure 5: IR spectrum of Schiff base.

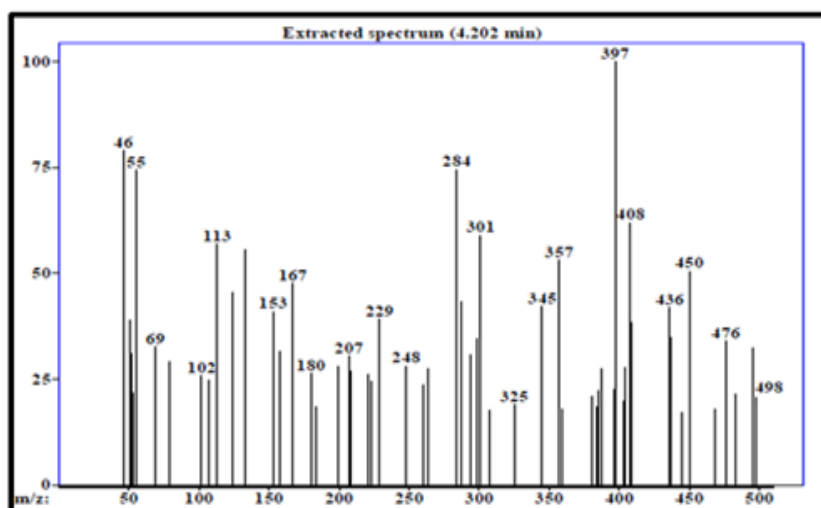


Figure 6: The mass spectrum of Schiff base.

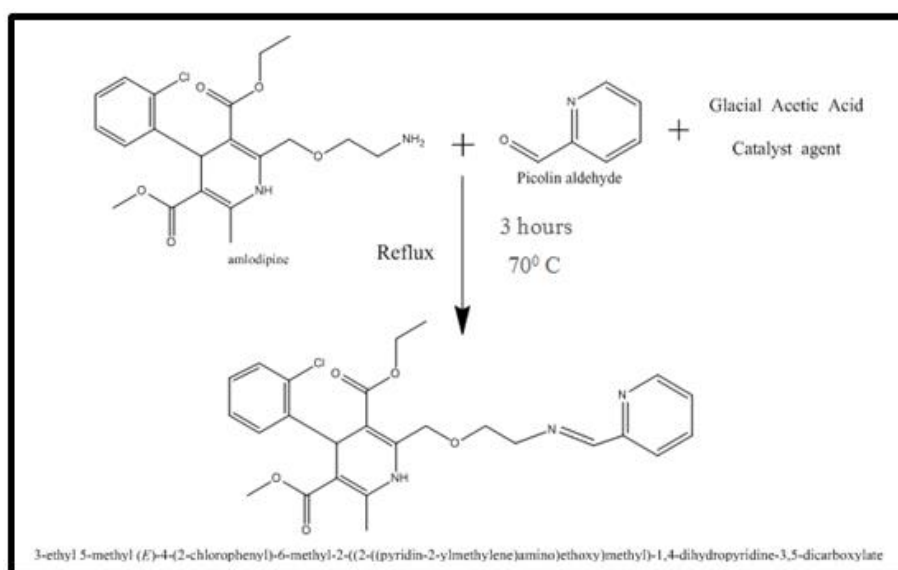


Figure 7: Schiff base preparation scheme.

4 CONCLUSIONS

In this study, a straightforward and reliable spectrophotometric method was successfully developed for the determination of Amlodipine (AML) in pharmaceutical formulations. The method is based on forming a yellow charge-transfer complex between a synthesized Schiff base of AML and DDQ reagent under basic conditions. A good and simple spectroscopic method has been developed to estimate AML through a complex charge transfer reaction with the reagent DDQ in the basic medium. The method is based on adding the reagent DDQ to a Schiff base and then adding sodium hydroxide and the temperature necessary to conduct the reaction 400 C, then the reaction's ultimate result, which is yellow in color, is created once the additions are finished, after which the absorption is measured at 436 nm. It follows Beer's law in the concentration range of 5-40 µg/ml. The method was successfully applied to AML in the pharmaceutical preparation Amlong 5 mg. The method demonstrated strong linearity across a concentration range of 5–40 µg/ml, with a high correlation coefficient ($R^2 = 0.9981$), excellent sensitivity, and low limits of detection ($LOD = 0.2596 \mu\text{g/ml}$) and quantification ($LOQ = 0.7865 \mu\text{g/ml}$). It also showed high precision and recovery rates, validating its accuracy for pharmaceutical analysis.

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