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Two Validated Spectrophotometric Methods for Quantitative Analysis of Amlodipine Besylate in Pharmaceutical Preparations by Redox Reaction

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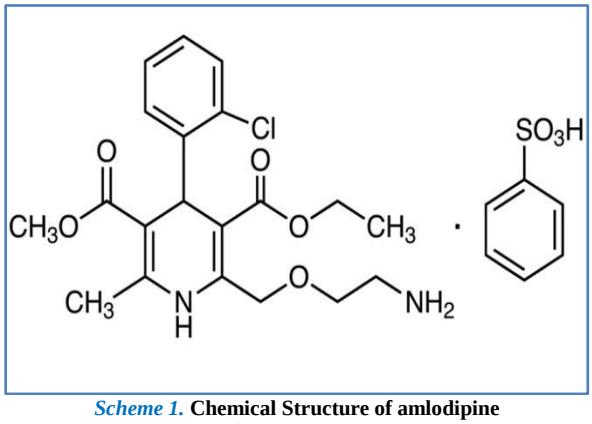
Abstract

This research aims to develop two spectrophotometric methods for the quantitative determination of amlodipine besylate (ADB) in its pure form and in pharmaceuticals. Both methods are characterized by simplicity, high accuracy, sensitivity, cost-effectiveness, and eco-friendliness. The underlying principle for both techniques is based on redox reactions. The first method (indirect) involves the reaction of ADB with a known excess of N-bromosuccinimide (NBS) in an acetic acid medium. The residual NBS is subsequently determined by its ability to bleaching the color of Orang G dye, with the remaining dye measured at λ max = 478 nm. The second method (direct) entails the reduction of potassium permanganate by ADB in an alkaline medium, resulting in the formation of a bluish- green manganate ion (MnO_4^{2-}) which exhibits maximum absorbance at λ max = 608 nm. Linearity for the two methods was observed in the ranges 1-35 and 1-70 µg. mL^{-1}, with determination coefficients (R^2) of 0.9989 for each method. The molar absorptivity values were 2.166 $\times 10^4$ and 0.98 $\times 10^4$ $L.mol^{-1}.cm^{-1}$, while Sandell's sensitivity index values were 0.0262 and 0.058 $\mu g.cm^{-2}$, respectively. The limit of detection (LOD) was found to be 0.196 and 0.567 $\mu g.mL^{-1,}$ while the limit of quantification (LOQ) was 0.653 and 1.89 $\mu g.mL^{-1}$, respectively. The proposed methods were effectively applied to evaluate ADB in pure forms and pharmaceutical preparations (tablets, capsules). The validity of these methods was confirmed through recovery studies using the standard addition method.

Keywords: Amlodipine besylate, Spectrophotometric determination, Orange G, Redox -Reaction.

Introduction

Amlodipine Besylate (ADB), with the IUBAC name 2-[(2-aminoethoxy), methyl]-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridin dicarboxylic acid 3-ethyl-5-methyl ester benzene sulfonate, is a white crystalline powder with a molar mass of 567.1 $g.mol^{-1}$. It is slightly soluble in water, freely soluble in methanol, and sparingly soluble in anhydrous ethanol. Scheme 1 illustrates the chemical structure of ADB [1,2].



Scheme 1. **Chemical Structure of amlodipine molecular formula: $C_{26}H_{31}ClN_2O_8S$**

ADB was first discovered in 1982 and approved by the FDA as a prescription drug in 1990 [3]. A long-acting, lipophilic, third-generation calcium channel blocker, it is mainly used for the treatment of hypertension, chronic stable angina, and vasospastic (prinzmetal's) angina [4]. It works by preventing the influx of calcium ions across cell membranes. Vascular smooth muscle cells and cardiac muscle cells work together to reduce peripheral vascular resistance and lower blood pressure [5].

It can also be used in the treatment of dilated myocardium and shows improvement in plasma and myocardial catecholamine levels, with a significant reduction in calcium deposition [6]. Amlodipine has anti-oxidant properties and an ability to enhance the production of nitric oxide (NO) [7]. Studies have shown that amlodipine inhibits calcium channels of the type Dihydropyridines can induce apoptosis, leading to cell cycle arrest and inhibition of cancer cell growth [8] underscoring its extensive clinical application. Amlodipine's pharmacokinetic profile is characterized by low renal clearance (7 mL/min/mg), extended half-life (35–50 h), and high bioavailability (60%–80%) [9]. The link between stroke and myocardial infarction (MI) has not been proven yet [10]. Side effects of amlodipine include edema, dizziness, facial flushing, palpitations, and even shock [11-12].

Due to the medical importance and therapeutic uses of ADB, various analytical methods were published in scientific literature for quantifying ADB in pharmaceutical preparations and biological fluids [13]. This includes gas chromatography [14], LC-MS/MS [15-18], high-performance liquid chromatography [19-26], thin-layer chromatography [27-28], electrochemical sensor [29], voltammetry [30], kinetic spectrophotometric [31-32], and spectrophotometric methods [33-47]. The present study aims to develop two oxidation reduction reaction based spectrophotometric methods that are simple, rapid, and highly cost- effective. Unlike previously reported methods, the suggested procedures eliminate the need for tedious extraction steps and avoid the use of expensive instrumentation. Moreover, the methods are environmentally friendly, as they do not involve toxic reagents or hazardous organic solvents, making them suitable for routine quality control in laboratories with limited resources. The two methods were successfully applied for the estimation of ADB in bulk form and in commercial dosage forms (tablets, capsules). The validity of the two methods was confirmed by a recovery study using standard addition methods.

Materials and Methods

Chemicals, Reagents and Materials

All chemicals and reagents used in this research characterized by a high degree of purity, Amlodipine besylate was obtained from the Samarra Drug Industry company, Iraq.

Instrumentation

Absorbance and absorption spectra were measured using a Shimadzu UV-Visible 1900i spectrophotometer (Japan) equipped with 1.0 cm quartz cells. A sensitive balance model Kern and Sohn analytical balance ABS 120-4N, Germany, was used to measure the weight.

Experimental

This section describes all reagents that are employed for the determination of amlodipine besylate.

Amlodipine besylate solution, 100 µg.mL^{-1}: Prepared by weighing 0.01 g of ADB and dissolved in distilled water to 100 mL in a volumetric flask, the solution was stable for one month.

Orang G dye solution, 500 µg.mL^{-1}: Prepared by dissolving 0.05 g of OG dye in distilled water (DW) and completed with DW to 100 mL in a volumetric flask.

N-Bromosuccinimide (NBS) solution, 400 µg.mL^{-1}: 0.04 g of NBS was weighed and dissolved in DW to 100 mL in a volumetric flask, the solution was prepared daily.

Hydrochloric acid, 0.1 M: Prepared by dilution of 0.83 mL of concentrated HCL (12.08 M) and diluting to 100 mL with DW.

Acetic acid 1 M: Prepared by dilution of 5.7 mL of acetic acid (17.4 M) and diluting to 100 mL with DW.

Stock solution of potassium permanganate, 0.02 N: 0.6321 g of pure $KMnO_4$ was weighed and dissolved in 75 mL of DW, heated for 5 min to complete the dissolution, then the solution was cooled, filtered through a sintered glass filter to remove manganese dioxide and diluted to 200 mL in a volumetric flask. The resulting solution is titrated with sodium oxalate, the solution was stable for one week.

Working solution $KMnO_4$, 1000 µg.mL^{-1}: 31.64 mL of $KMnO_4$ from stock solution was diluted to 100 mL with DW to the mark in a volumetric flask. The prepared solution was kept in an opaque vial and was stable for one week.

Sodium Hydroxide Solution, 2 M: One ampoule of NaOH was dissolved in DW and completed to 500 mL in a volumetric standard flask.

Pharmaceutical Solutions

Tablets Solution (2.5 mg and 10mg /tablet), 100 µg.mL^{-1}

Two tablet formulations of ADB (2.5 mg/ tablet from Hikma Pharmaceuticals, Jordan, and 10 mg/ tablet Ajanta, India were used. From each preparation, 10 tablets were accurately weighed, powdered, and well mixed. An amount of the tablet powder equivalent to 0.01 g of pure ADB was accurately weighed specifically, 0.3001 g was taken for the 2.5 mg tablets, and 0.179 g was taken for the 10 mg tablets. This portion was then dissolved in D.W, filtered, and quantitatively transferred into a 100 mL volumetric flask, and completed to the mark with D.W to obtain a 100 µg . mL^{-1} solution.

Capsule medicine solution, 100 µg. mL^{-1}

The contents of five capsules (5 mg/ capsule, from Hikma Pharmaceuticals, Jordan) were emptied and accurately weighed (0.5667 g). The powder was mixed well, and 0.2266 g of the powder, equivalent to 0.01 g of pure ADB, was dissolved in DW. The solution was then filtered and transferred to a 100 mL volumetric flask, and the volume was topped up with distilled water to the mark.

Indirect Method

Under optimal conditions, an increasing volumes of amlodipine besylate (100 µg.mL^{-1}) covering the concentration (0.1- 40 µg.mL^{-1}) are added to a series of 10 mL volumetric flasks. 0.5 mL of 0.1 M acetic acid and 0.7 mL of oxidizing agent NBS of 400 µg.mL^{-1} are added, then the solutions were left for 5 min at room temperature to complete the oxidation of ADB, then 1.0 mL of orange G dye (500 µg.mL^{-1}) was added and left for 5 min. After that the volume of each flask was adjusted up with DW, then the absorbance of residual dye measured versus the blank at a wavelength 478 nm.

Direct Method

Increasing amounts of the standard ADB solution (100 µg.mL^{-1}) covering the range of concentration (1.0-80 µg.mL^{-1}) were

transferred to a series of 10 mL volumetric flasks, 2.5 mL of $KMnO_4$ (100 µg.mL^{-1}) and 1.5 mL of NaOH (2 M) were added. After waiting 15 min to complete oxidation step of the ADB, the volume was adjusted with DW to the mark, the absorbance of each solution was measured at the wavelength 608 nm versus the reagent blank.

Calibration Curve

According to the optimal operation conditions, the linearity of the calibration curve was obtained over the concentration range of 1.0-35 and 1.0-70 µg.mL^{-1} of ADB with a molar absorption coefficient 2.166 × 10^4 L.mol^{-1}.cm^{-1} and 0.98 ×10^4 L.moL^{-1}.cm^{-1} for first and second methods, respectively. The values of Sandell's index were equal to 0.0262 and 0.058 µg.cm^{-2} for first and second methods, respectively. Fig.1 explains the calibration curves of both proposed methods (direct and indirect).

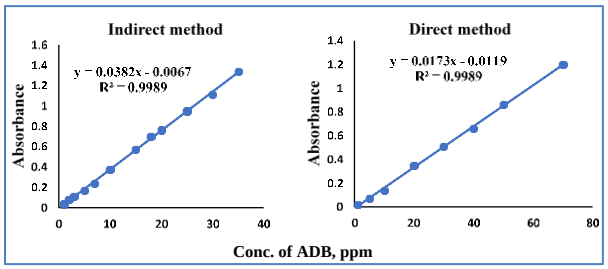


Figure 1. **Calibration curves of ADB determination for two methods**

Results and Discussion

Principle of the Two Methods

Indirect method: The determination of ADB includes the following steps:

The first step entails the oxidation of ADB using a known excess of NBS in an acidic medium:

ADB + NBS → Oxidized ADB + NBS
Excess Unreacted

The second step entails the reaction of unreacted NBS with OG dye and bleaching the reacted amount of orange G to a colorless compound in the same media. The orange color of the residual orange G dye is measured at 478 nm, which is proportional to the ADB concentration as shown in Fig. 2.

NBS + Orange G dye → Orang G dye oxidized + Orange Gdye
Residual *Colorless* *Reamining*

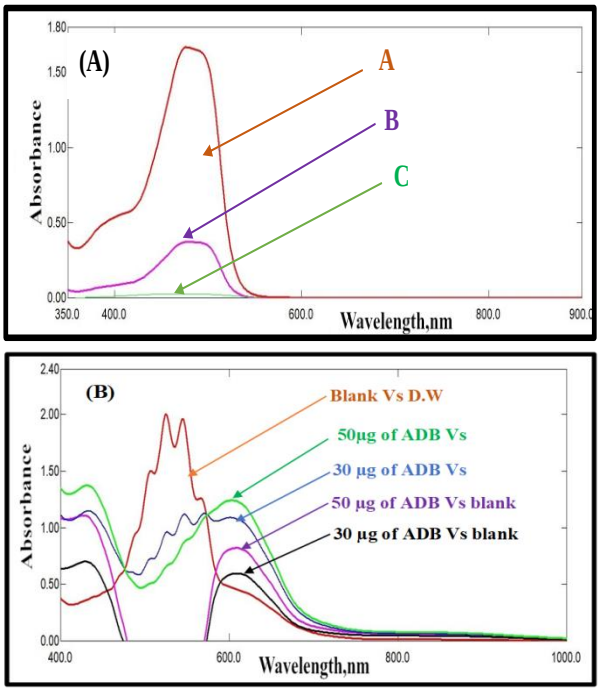


Figure 2. **(A) Absorption spectra of (A) OG. dye only vs. blank, (B) OG dye with 10 µg/mL ADB versus blank, (C) Blank versus DW. (B) Absorption spectra of two concentrations of ADB according to the proposed method**

Direct method: ADB is quantitatively oxidized by KMnO4 in the presence of a basic solution of sodium hydroxide to form a bluish – green color of the resulting manganate ion (MnO_4^{-2}), which exhibits maximum absorption at the wavelength 608 nm (Fig. 2).

Optimum Reaction Conditions of Indirect Method

All subsequent experiments were conducted using 1.0 mL of 100 µg/mL of ADB in 10 mL volumetric flasks, and the

absorbance of orange G dye was measured at 478 nm.

Study the Best Amount of OG Dye

To find the best quantity of OG dye that can be utilized in the determination of the ADB, that obey Beer-Lambert law, an increasing quantity of 500 µg.mL^{-1} OG dye solution was added to a number of 10 mL volumetric standard flasks containing 1.0 mL of 0.1 M HCl, after completing the volume with DW, the absorbance of the solutions was measured at 478 nm against their blank solution.

The results presented in Fig. 3 reveal that the calibration curve of Orange G (OG) dye exhibits excellent linearity over a concentration range of 20–90 ppm, strictly obeying Beer's law. The linear regression equation was found to be y = 0.0326x - 0.0294 with a high correlation coefficient (R^2 = 0.999), indicating the high sensitivity and reliability of the developed method for subsequent analytical applications.

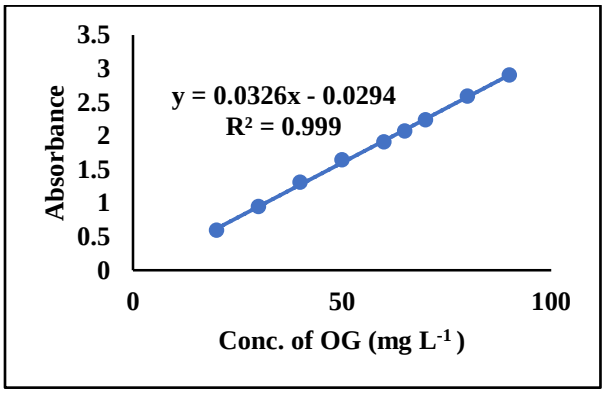


Figure 3. **Linear Regression graph of orange G dye**

Selection of the Best Oxidizing Agent

To choice the best oxidizing agent, several available oxidant agents (NCS, $K_2S_2O_8$, $KBrO_3$, Cu^{+2}, Ce^{+4}, KIO_4, NBS) were studied to determine the extent of their effect of bleaching the dye by using 1.0 mL of 400 µg/mL of each oxidizing agent separately in the presence of 1.0 mL of 0.1M HCl into 10 mL volumetric standard flask that contain 1.0 mL of OG dye (500 µg/mL), the absorbance was measured at 478 nm after competed the volume with DW. The results illustrate that NBS gives the best decolorization, so it was selected for subsequent steps.

Effect of Amount of NBS

The effect of the amount of NBS on the bleaching of OG dye color was studied by adding different volumes of it, while keeping other variables constant, to a set of 10 mL volumetric standard flasks. It was observed that 0.7 mL of 400 µg/mL NBS was sufficient to completely bleach the dye color. Therefore, this amount was relied upon in subsequent experiments.

Effect of the Acid Type and its Amount

Different types of acids were investigated to determine their effects on the oxidation of ADB and the decolorization of the orange G dye. The results explained that acetic acid was most effective. Furthermore, the effect of varying amounts of acetic acid were investigated. Table 1 indicates that the optimal final concentration of acetic acid was was 0.005 M, therefore it was adopted for subsequent procedures.

Table1. **Optimization of acetic acid concentration for the spectrophotometric determination of ADB.**

Con. CH_3COOH in M	Absorbance /µg of ADB mL^{-1}				R^2
	5	10	15	20	
0.003	0.193	0.351	0.601	0.7	0.9762
0.005	0.177	0.379	0.591	0.826	0.9988
0.010	0.195	0.371	0.556	0.786	0.9959
0.013	0.197	0.366	0.616	0.810	0.995
0.015	0.196	0.390	0.507	0.763	0.9805

Influence of Oxidation Time on Stability

The study aimed to optimize the time required for the complete oxidation of 10 µg/mL of ADB via waiting for different times after the addition of the NBS and before the addition of orange G dye, as well as waiting for different periods after adding orange G dye and then diluting with DW to the mark. The results illustrated that the time required for the oxidation of amlodipine was 5 min, and the suitable time for the oxidation of the dye to decolorize it was also 5 min.

Temperature Influence on Stability

The stability of absorbance value at different temperatures (5, 25, and 40 °C) was studied, the results show that the absorbance was stable for one hour at room temperature (25 ± 2 °C).

Influence of Adding Different Surfactant

The effect of adding different surfactants (negative, positive, neutral) on the absorption of the dye using various volumes of these substances to the components of the reaction was studied. The outcomes indicated that the addition of surfactants led to a decrease in the absorption of the dye, so their addition was excluded.

Optimum Reaction Conditions of Direct Method

All subsequent experiments were conducted using 0.3 mL of 1000 µg/mL of ADB in 10 mL volumetric flasks and measuring the absorption at 608 nm.

Effect of the Amount of $KMnO_4$

The effect of different concentrations (6.3×10^{-4} – 1.90×10^{-4}) of potassium permanganate on the absorbance of solutions containing increasing amounts of ADB (10-70 µg/mL) in the presence of 1.0 mL of 2 M sodium hydroxide solution was investigated. The results in Table 2 show that 1.58×10^{-4} of $KMnO_4$ was the optimal amount for the oxidation of ADB with a good correlation coefficient ($R^2 = 0.9987$).

Table 2. **Effect of potassium permanganate.**

Concentration of $KMnO_4$ (M)	Absorbance/ µg of ADB mL				R^2
	10	30	50	70	
6.3×10^{-4}	0.175	0.270	0.367	0.425	0.9797
9.5×10^{-4}	0.180	0.515	0.670	0.892	0.9764
1.26×10^{-4}	0.201	0.498	0.658	0.926	0.9754
1.58×10^{-4}	0.226	0.542	0.817	1.09	0.9987
1.90×10^{-4}	0.221	0.506	0.769	0.934	0.9867

Effect of Type and Amount of Base

The influence of various type (NaOH, KOH, Na_2CO_3, $NaHCO_3$) and their concentrations on the reaction absorbance was systematically investigated. The experimental outcomes revealed that a final concentration of 0.3 M sodium hydroxide provided the highest color intensity and stability. Consequently, this optimal alkaline condition was maintained for all subsequent analytical investigations

Effect of Oxidation Time

The required time to oxidize 30 µg of ADB was tested by waiting for different times after the addition of the base, and before completing with DW, to complete the oxidation process. The obtained results reveal that the time required to oxidize the ADB was 15 min., and the required time to complete the reaction in basic medium was 5 min.

Influence of Adding Different Surfactants

The effect of adding 1.0 mL of different types of surfactants, including SDS, CPC, CTAB (1×10^{-3} M), and Triton X-100 (1.0 %), on the absorbance values of the

colored product was studied. The results obtained showed that the addition of surfactants did not improve the absorbance value; So, their use was excluded from subsequent experiments.

The Nature of the Reaction

The mole ratio method [48] was used to determine the ratio between ADB and $KMnO_4$. The Fig. 4 showed that the ratio is 1:2 of (ADB: $KMnO_4$).

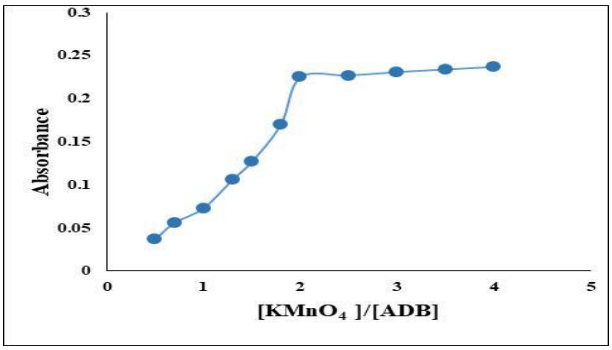
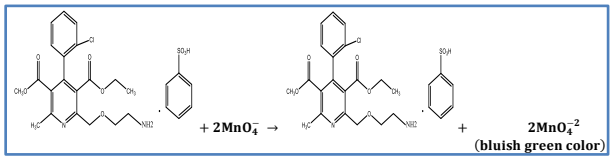


Figure 4. **Mole ratio between ADB and $KMnO_4$**

According to the obtained ratio, which was 1:2, the chemical reaction equation of ADB with $KMnO_4$ in basic medium can be written as:



Accuracy and Precision

To evaluate the accuracy and precision for two suggested methods (indirect and direct), two different concentrations (10, 15 µg.mL^{-1} and 3, 5 µg.mL^{-1}) of ADB, and five samples of each concentration were examined. Then, calculated the recovery ratio and relative standard deviation values, which ranged between (97.65-102.1% and 98.925-98.871%) and (0.53-0.58% and 1.625-1.03%), for the first and second methods, respectively. The results indicate that the developed method showed good accuracy and compatibility.

Pharmaceutical Applications

The proposed methods, indirect and direct, were carried out for the estimation of ADB in pharmaceuticals to test the efficiency and success using two different concentrations (15, 20 µg.mL^{-1} and 10, 20 µg.mL^{-1}, respectively) for different pharmaceutical preparations (tablets and capsules). The results shown in Table 3 demonstrated the successful application with high accuracy and good precision.

Table 3. **(A) Application of the indirect method (B) direct method.**

(A) Pharmaceutical preparations of ADB	Indirect method				t-test
	Amount of ADB taken (µg/mL)	Amount of ADB found (µg/mL)	Rec., %*	R.E%* RSD*	
Amlodipine besylate Tablets 2.5mg Jordan	15	15.30	102.00	2.00 1.275	2.20
	20	20.34	101.70	1.70 0.880	1.93
Amlodipine besylate Tablets 10 mg India	15	14.92	99.47	-0.53 0.860	2.03
	20	20.03	100.15	0.15 0.790	1.14
Amlodipine besylate Capsules 5 mg Jordan	15	14.86	99.06	-0.94 0.540	1.88
	20	20.26	101.30	1.30 0.885	0.80

*Average for five determinations

(B) Pharmaceutical preparations of ADB	Direct method				t-test
	Amount of ADB taken (µg/mL)	Amount of ADB found (µg/mL)	Rec., %*	R.E.%* RSD*	
Amlodipine besylate Tablets 2.5mg Jordan	10	10.02	100.20	0.20 1.625	1.68
	20	20.25	101.25	1.25 1.030	2.14
Amlodipine besylate Tablets 10 mg India	10	9.93	99.30	-0.70 1.870	1.38
	20	20.02	100.10	0.10 0.958	0.59
Amlodipine besylate Capsules 5 mg Jordan	10	10.03	100.30	0.30 1.390	0.84
	20	20.21	101.05	1.05 1.680	2.09

*Average for five determinations

Evaluation of the Two Methods

The selectivity and validity of the suggested methods for estimation of ADB in its pharmaceuticals, the standard method was applied [49]. Fig. 5 and Table 4 confirmed that the results are acceptable with the suggested methods.

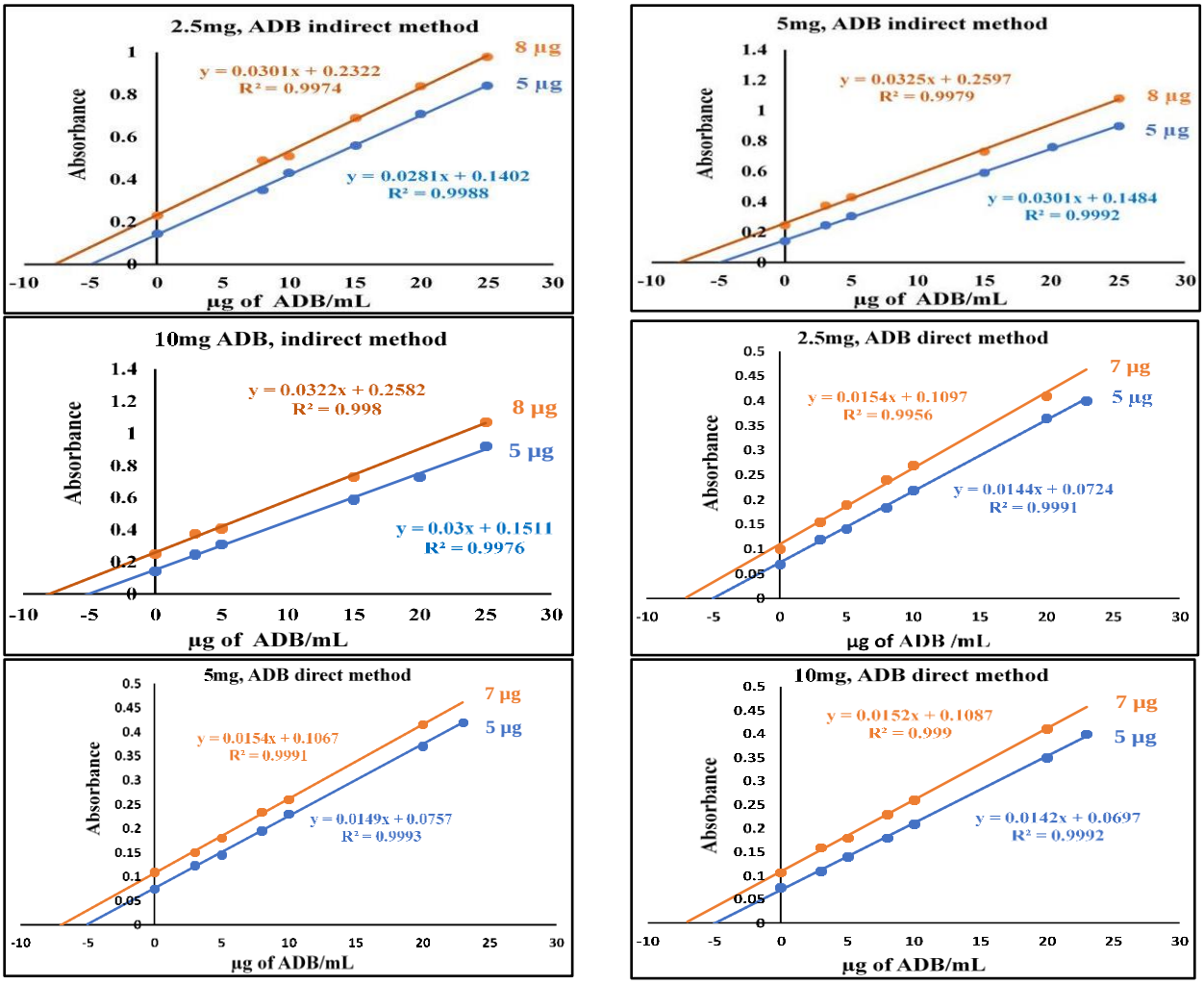


Figure 5. **Standard addition curves for estimation of AMD preparations**

Table 4. **Results of the standard addition method for the suggested methods.**

Pharmaceutical preparation	Indirect method			Direct method		
	Amlodipine besylate taken (µg/mL)	Amlodipine besylate found (µg/mL)	Recovery %*	Amlodipine besylate taken (µg/mL)	Amlodipine besylate found (µg/mL)	Recovery %*
Amlodipine besylate Tablet 2.5 mg Jordan	5	4.989	99.78	5	5.028	100.56
	8	7.714	96.42	7	7.123	101.76
Amlodipine besylate Tablets 10 mg India	5	4.930	98.60	5	5.080	101.60
	8	7.991	99.89	7	6.928	98.97
Amlodipine besylate Capsule 5 mg	5	5.037	100.74	5	4.908	98.16
	8	8.019	100.24	7	7.151	102.16

*Average for five determinations

Table 5. **Comparison of the developed methods with other spectroscopic methods.**

Methods	Type of reaction	λ max	Linearity range µg. mL^{-1}	Ɛ L.mol^{-1}.cm^{-1}	Reference
Suggested methods	Oxidation-reduction	478	1-35	2.166×10^4	Current work
	Bleaching color	608	1-70	0.98×10^4	Current work
	Derivatization with 2-Hydroxynaphthaldehyde	416	4-20	1.05×10^4	[43]
	Hydrotropic solubilization	243	5-25	2.0333×10^4	[44]
Spectrophotometric methods	condensation of ADB with sodium 1,2-naphthoquinone-4-sulphonate in an alkaline medium	459	10-20	2.24×10^4	[42]
	Condensation	592	1.0-56	1.92×10^4	[41]
	Ion pair Bleaching color	592	5-92.5	0.213×10^4	[47]
	Azotization and coupling reaction	368	10-200	0.342×10^4	
	Diazotization and coupling with sulfanilic acid	490	1-10	6.97×10^4	[45]
	UV Spectrophotometric	239	4-20	-	[46]

Comparison of Suggested Methods

As presented in Table 5, a comprehensive comparison was conducted between the two newly developed spectrophotometric methods and several previously reported analytical techniques for the determination of amlodipine besylate (ADB). The results demonstrate that the suggested methods exhibit exceptional sensitivity, as evidenced by their high molar absorptivity (Ɛ) values 2.166×10^4 L.mol^{-1}.cm^{-1} for the indirect method and wide linearity ranges 1 – 35 µg. mL^{-1} and 1-70 µg. mL^{-1}, which are superior to or highly competitive with many existing methods like the UV spectrophotometric and diazotization approaches. Furthermore, the indirect method operates at a remarkably convenient λ max 478 nm and the direct method at 608 nm, effectively minimizing potential spectral interferences from common pharmaceutical excipients. Crucially, unlike several published methods that rely on toxic organic solvents or complex derivatization steps (such as condensation with 1,2-naphthoquinone-4-sulphonate), the proposed methods are simple, cost-effective, eco-friendly, and utilize safe aqueous media, making them highly suitable for routine quality control analysis of ADB in pharmaceutical formulations

Conclusion

Two indirect and direct spectrophotometric methods were developed for the determination of ADB in pharmaceutical formulations (tablets and capsules), each method characterized by its fast, simplicity, inexpensive, eco-friendly, and sensitivity. The indirect method depends on the oxidation of ADB using excess NBS in an acidic medium. The unreacted NBS was then estimated using a fixed amount of OG dye, and the remaining dye's absorbance was measured at 478 nm. Indirect method, ADB reacts with $KMnO_4$ in a basic medium to form a bluish – green color of the resulting manganate ion, which exhibits maximum

absorption at 608 nm. Both methods proved to be effective and easy.

Acknowledgment

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Conflict of Interest

The researchers confirm that this work is free of any conflict of interest.

References

1. D. Alnohy, S. Morshedy, G. Omran, M.Mabrouk and W. Talaat, *Inter. J. Adv. Multidiscip. Res. Stud.*, 3 (2023) 249. https://www.multiresearchjournal.com/admin/uploads/archives/archive-1689236277.
2. British Pharmacopoeia, Her Majesty's Stationery Office, London, Vol. I, (2022) 159. https://doi.org/10.1111/j.2042-7174.1993.tb00725.x.
3. M.M. Heravi and V. Zadsirjan, *RSC Adv.*, 10 (2020) 44247. https://doi.org/10.1039/D0RA09193J.
4. A. Elsonbaty and K.H. Attala. *Erurj*, 2 (2023) 237. doi:10.21608/ERURJ.2023.202523.101
5. M.Y. Khan, S. Shetty, A. Oomman, P. Jain and K. Gaurav. *J. Cardiol. Cardiovasc. Sci.*, 5 (2021) 1. https://www.cardiologyresearchjournal.com/articles/amlodipine-and-landmark-trials-a-review.
6. M. Ozturk and Y. Kadioglu, *Int. J. Pharm.*, 1 (2021) 1. https://dergipark.org.tr/en/download/article-file/2897858.
7. S. K. Birajdar and M. S. Kalshetti, *Int. J. Sci. Res. Sci. Technol.*, 11 (2024) 456. https://doi.org/10.32628/IJSRST24113119
7. M.A.Y. Alqudah, R. Al-Samman, M. Azaizeh, K.H. Alzoubi, *Biomed. Reports*, 16 (2022) 1. doi:10.3892/br.2022.1533.
8. J.G. Wang, B.F. Palmer, A.K. Vogel and P. Sever, *J. Clin. Hypertens*., 25 (2023) 801. https://doi.org/10.1111/jch.14709.
9. S.S. Iyengar, J.C. Mohan, S. Ray, M.S. Rao, M.Y. Khan, U.R.H. Patted and K. Gaurav, *Cardiol. Ther*., 10 (2021) 429. https://doi.org/10.1007/s40119-021-00231-1.
10. M. Zhang, H. Li, L. Huang, Y. Liu, X.F. Jiao and L. Zeng, *Eur. J. Pediatr.*, 182 (2023) 4655. https://doi.org/10.1007/s00431-023-05146-2.
11. C. Wang, Q. Zhu, D. Tan, J. Walline and Y. Wang, *Cardiovasc. Toxicol.*, 24 (2024) 513. https://doi.org/10.1007/s12012-024-09849-2
12. J. E. F. Reynolds (Ed), Martindale: The Extra Pharmacopoeia, 31st Ed., Royal Pharmaceutical Society, London (1996) 404. https://doi.org/10.1177/106002809603001124.
13. S.C. Monkman, J.S. Ellis, S. Cholerton, J. M. Thomason, R. A. Seymour and J.R. Idle. *J. Chromatogr. B: Biomed. Appl.*, 678 (1996) 360. doi: 10.1016/0378-4347(95)00526-9.
14. P. Pongnarin, W. Thanakosai, P. Kingkhangphloo, W. Chandrani-papongse, S. Kongpatanakul and S. Chatsiricharoenkul. *Pharm. Sci. Asia*, 44 (2017) 217. doi: 10.29090/psa.2017.04.217.

15. L. Logoyda, S. I. Kovalenko, M. Gaafar, A. A. Ali, and F. A. Elbarbry. *Microchem. J.*, 155 (2020) 104700. https://doi.org/10.1016/j.microc.2020.104700.
16. A. Sirikatitham, K. Panrat, and N. Tanmanee. *Songklanakarin J. Sci. Technol.*, 30 (2008) 455. https://www.thaiscience.info/journals/Article/SONG/10617598.
17. N.U.H. Khan, S. Awais, N. Suleman, M.D. Qamar, M. Afridi, Mehwish, M.A. Zahid, and A. Munir. *Hist. Med.*, 10 (2024) 1331. https://doi.org/10.17720/3kx2b348/.
18. D. Dalawai, C. Aware, J. P. Jadhav and H. N. Murthy, *Nat. Prod. Res*., 35 (2021) 2239. https://doi.org/10.1080/14786419.2019.1662004
19. S. Jeelani and N. Kouznetsova, *Heliyon*, 9 (2023) 1. https://doi.org/10.1016/j.heliyon.2023.e19993.
20. R. A. Jiménez-Nava, L. G. Zepeda-Vallejo, F. Santoyo-Tepole, G. M. Chávez-Camarillo and E. Cristiani-Urbina, *Biomolecules*, 13 (2023) 1423. https://doi.org/10.3390/biom13091423
21. K. Verma, S. Rastogi, M. Dahiya, G.P. Singh, J. Chauhan, P. Tomar and S. Kumar, *Res. J. Pharm. Technol*., 17 (2024) 523. https://doi.org/10.52711/0974-360X.2024.00082.
22. F.O. Qasim, N.M.S. Mohammed, N.I. Yousi and M.H. Fattah, *Cihan Univ.-Erbil Sci. J.*, 8 (2024) 120. doi:10.24086/cuesj.v8n2y2024.pp120-127.
23. B. D. Patel, T. A. Nayak and S. Hussain, *Chin. J. Appl. Physiol.*, 40 (2024) e20240007. https://doi.org/10.62958/j.cjap.2024.007
24. F. Demir, S. Toker and S. Ünlü, *Istanbul J. Pharm*., 55 (2025) 274. https://doi.org/10.26650/IstanbulJPharm.2025.1465651
25. S. I. BeemaJainab, D. A. Prajapati, K. K. Sharma, S. K. Sharma, R. Priyadarshini, G. Durgadevi, A. Gautam and B. Sharma, *J. Pharm. Negat. Results*, 11 (2025) 3871. https://doi.org/10.64252/v5z60q27
26. S. Patel, H. Rohit, L. Patel, N. Raval, H. Kachhiya and J. Tandel. *J. Planar Chromatog.- Mod. TLC*, 38 (2025) 37. doi: 10.1007/s00764-025-00350-2.
27. N.W. Ali, N.S. Abdelwahab, M.M. Zaki, M. Abdelkawy. *J. Chromatogr. Sep. Tech.*, 3 (2012) 1. 1000134 doi: 10.4172/2157-7064. 1000134.
28. E. Arkan, Z. Karimi, M. Shamsipur and R. Saberd. *J. Rep. Pharm. Sci.*, 3 (2014) 99. doi:10.4103/2322-1232.222553.
29. R.N. Goyal, S. Bishnoi, *Bioelectrochem.*, 79 (2010) 234. doi:10.1016/j.bioelechem.2010.06.004.
30. B. Hemmateenejad, R. Miri and R.A. Kamali, *J. Iran. Chem. Soc.*, 6 (2009) 113. https://doi.org/10.1007/BF03246509.
32. A.M. Mahmoud, H.M. Abdel-Wadood, N.A. Mohamed. *J. Pharm. Anal.*, 2 (2012) 334. https://doi.org/10.1016/j.jpha.2012.03.002.
33. Z.A. Khdadad, A.I. Khaleel and Q.N. Rashid, *Int. J. Health Sci.*, 6 (2022) 7726. https://doi.org/10.53730/ijhs.v6nS1.6673
34. M.Y. Mohammad, M.S. Abdullah and S.S. Sabir, *Polytechnic J.*, 9 (2019) 25. https://doi.org/10.25156/ptj.v9n2y2019.pp25-29.
35. N. Rahman and M. N. Hoda, *J. Pharm Biomed. Anal*., 31(2003) 381. doi:10.1016/s0731-7085(02)00610-6.
36. D. Gupta, S. Bhardwaj, S. Sethi, S. Pramanik, D.K Kumar Das, R. Kumar, P. Pratap Singh and V.K. Kumar

Vashistha. *Spectrochim. Acta A: Mol. Biomol. Spectrosc*., 270 (2022) 120819. doi:10.1016/j.saa.2021.120819.

37. R. Alkhalil, A. Attal and A.A. Sakur, *Res. J. Pharm. Tech.*, 12 (2019) 3389. doi: 10.5958/0974-360X.2019.00572.9.
38. N. Alizadeh and Hemati F.(2014). *Bull. Faculty Pharm. Cairo Univ.*, 52 (2014) 109. https://doi.org/10.1016/j.bfopcu 2014.01.003 .
39. B. Gidwani, L. Patel, A. Gupta and C.D. Kaur, *J. Anal. Pharm. Res.*, 4 (2017) 187. doi: 10.15406/japlr.2017.04.00125.
40. N. Rahmanand S.N.H. Azmi, *Japan Soc. Anal. Chem.*, 16 (2000) 1353. https://doi.org/10.2116/analsci. 16.1353.
41. R. Alkhalil, A. Attaland A.A. Sakur. *Res. J. Pharm. Tech*., 12 (2019) 3389. doi:10.5958/0974-360X.2019.00572.9.
42. M. Sulyma, S. Vasyuk, Y. Zhuk, D. Kaminskyy, O. Chupashko and V. Ogurtsov, *Chem. Chem. Technol*., 12 (2018) 429. https://doi.org/10.23939/chcht12.04.429.
43. F. Almani, F.M.A. Rind, A.H. Memon, U.R. Mughal, M.G.H. Laghari, N. Memon, M.L. Maheshwari and M.Y. Khuhawar, *Asian J. Chem*., 22 (2010) 1205. https://doi.org/10.14233/ajchem.2010.AJC-7972
44. S. Bernard, M. Mathew and K. L. Senthilkumar, *J. Appl. Pharm. Sci*., 01 (2011) 177. https://www.japsonline.com/admin/php/uploads/248_pdf.pdf
45. S.A.B. Abdullah, R.M. Jihad and K.F. Alsamarrai, *Samarra J. Pure Appl. Sci*., 6 (2024) 98. https://doi.org/10.54153/sjpas.2024.v6i3(2).901
46. S. K. Birajdar, M. S. Kalshetti, *Int. J. Sci. Res. Sci. Technol*., 11 (2024) 456. https://doi.org/10.32628/IJSRST24113119
47. Z.A. Al-Mohsen Khdadad, A.I. Khaleel and Q.N. Rashid, *Int. J. Health Sci*., 6 (2022), 7726. https://doi.org/10.53730/ijhs.v6nS1.6673
48. H.H. Ahmed and S. A.Mohammed, *J. Turk. Chem. Soc. Section A: Chem.*, 10 (2023) 677. https://doi.org/10.18596/jotcsa.1260666.
49. D. C. Harris, Quantitative Chemical Analysis, 9th Ed., W. H. Freeman and Company, New York (2016) 106. https://nhathuocngocanh.com/wp-content/uploads/2023/09/Harris-Quantitative-Chemical-Analysis-8th-edition- nhathuocngocanh.pdf