



Spectrophotometric determination of methyl dopa via diazotization- coupling and area under curve methods

Sahar Abdullah Fathi^{1*}, Nabeel Sabeeh Othman¹, Amer Thanoon AL-Tae¹

^{1,2,3} University of Mosul, College of Science, Chemistry Department, Mosul, Iraq.

*Corresponding author: nsn20002004@uomosul.edu.iq

Received: January 01, 2024

Accepted: February 02, 2024

Published: February 29, 2024

Cite this article as: Fathi., S. A., Othman., N. S., AL-Tae., A. T. (2024). Spectrophotometric Determination of Methyl dopa via Diazotization- Coupling and Area Under Curve Methods. Libyan Journal of Medical and Applied Sciences (LJMAS),2(1):19-27.

Abstract:

Two spectrophotometric methods have been proposed for measuring purified methyl dopa (MeD) in pharmaceutical preparations (tablets). The first procedure relies on the diazo - coupling of methyl dopa with diazotized p-Nitroaniline (D-PNA) in a basic medium in order to produce a stable and water-soluble azo dye with a colored pigment, measured at 610 nm. The calibration curve from 2 to 17 µg. mL⁻¹ and the molar absorptivity value is 0.7223 x10⁴ L.mol⁻¹. cm⁻¹. The LOD value was 0.0727 µg. mL⁻¹ and the LOQ value was 0.242 µg. mL⁻¹. The second method based on the area under the curve between 596 to 622 nm. The calibration curve from 1 to 20 µg. mL⁻¹ is more sensitive than first method and it has a molar absorptivity equal to 0.5470x10⁴ L.mol⁻¹. cm⁻¹. The two methods gave good recovery, accuracy and precision that applied in assay of MeD in it is dosages the tablets from two drug companies.

Keywords: Diazo-coupling reaction, area under curve, spectrophotometric determination of methyl dopa.

التقدير الطيفي للميثيل دوبا باستخدام طريقتي الاقتران الأزوي والمساحة تحت المنحني

سحر عبد الله فتحي^{1*}، نبيل صبيح عثمان¹، عامر ذنون الطائي¹
قسم الكيمياء، كلية العلوم، جامعة الموصل، الموصل، العراق.

الملخص:

تم اقتراح طريقتين طيفيتين لقياس الميثيل دوبا بشكله النقي (MeD) وفي مستحضره الصيدلاني (أقراص). تضمنت الطريقة الأولى على اقتران الميثيل دوبا مع بار-النايتروانيلين المؤزوت (D-PNA) في وسط قاعدي من أجل إنتاج صبغة الأزو الملونة مستقرة وقابلة للذوبان في الماء. وتم قياس الامتصاص عند الطول الموجي الأعلى 610 نانوميتر وكان المنحني القياسي لمدى التركيز من 2 إلى 17 مايكروغرام/مللتر ومعامل الامتصاص المولاري 0.7223x10⁴ لتر/مول.سم. كانت قيمتي حد الكشف والتقدير الكمي 0.0727 و 0.242 مايكروغرام/مللتر على التوالي. تعتمد الطريقة الثانية على المساحة تحت المنحني بين الطولين الموجيين 596 و 622 نانوميتر. وكان مدى الخطية 1 إلى 20 ميكروغرام/مللتر ومعامل امتصاص مولاري 0.5470 x10⁴ لتر/مول.سم. تم تطبيق الطريقتين في المستحضر الدوائي الأقراص من شركتين مختلفتين للأدوية. **الكلمات المفتاحية:** تفاعل الازوتة والاقتران، المساحة تحت المنحني، التقدير الطيفي للميثيل دوبا.

Introduction

Methyl dopa is an antihypertensive medication that acts centrally. It is decarboxylated to alpha-methyl noradrenaline in the central nervous system, which is used to decrease sympathetic tone and blood pressure. Methyl dopa is commonly used to treat hypertension during pregnancy. There is little evidence of adverse effects on fetal development [1]. Methyl dopa is a white or yellowish white crystalline powder or colorless or nearly colorless crystals that are slightly soluble in water, very slightly soluble in alcohol, and only partially soluble in ether. dissolves readily in diluted mineral acids. The structure of the MeD is depicted in Figure 1. [2].

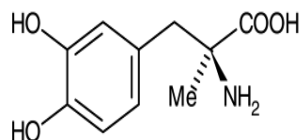


Figure 1. Chemical structure of methyl dopa.

For the estimation of the investigated compound (MeD), its dosage, and its presence in biological samples, a wide variety of analytical techniques were utilized. These procedures involve multiple categories of reactions with multiple types of reagents. Utilizing a variety of reagents, the oxidative coupling reaction has been used to quantify MeD in its purified form and in formulations. MDP was combined with Schiff's base new reagent in the presence of potassium periodate in an acidic medium [3]. Thiosemicarbazide in the presence of ferric nitrate [4]. The oxidation of 1, 5-diaminonaphthalene with ammonium Ceric (IV) nitrate [5]. Reagent 2,4-dinitrophenylhydrazine in the presence of potassium periodate [6]. p-Toluidine and sodium periodate Included in the determination of three pharmaceutical catechol amines were methyl dopa (I), dopamine (II), and adrenaline (III) [7]. Using cloud point extraction and flow injection spectrophotometric techniques, the methyl dopa and salbutamol concentrations were determined [4]. The oxidation of MeD with an excess of N-bromosuccinimide and residual N-bromosuccinimide contribute to the lightening of the color of Eriochrom black-T [8]. Also utilized is molybdate complexation [9]. Electrochemical methods using a modified glassy carbon electrode were used to determine methyl dopa [10]. Using modified pen-tip graphite electrodes with poly(p-aminobenzene sulfonic acid) and the Cyclic voltammetry (CV) technique, [11] investigated the effect of poly(p-aminobenzene sulfonic acid) on the conductivity of graphite. utilizing a nanocomposite graphene quantum dot (GQD) electrode for methyl dopa determination in biological samples [12]. For the determination of methyl dopa on the glassy carbon electrode (GCE) modified with poly P- aminobenzene sulfonic acid [13], differential pulse voltammetry was used. The concentration of MeD in human serum was determined by cleaning and separating the serum using mixed-mode liquid chromatography [14].

Experimental

Apparatus used

In spectral measurements, a UV-Visible spectrophotometer (Jasco modelV-630, Japan), an electronic balance (KERN & Sohn GmbH, Germany), and a professional Bench top pH meter (BP3001, Singapore) were utilized.

Chemicals and reagents used

All chemicals utilized were of analytical grade. Samara Drug Industry (SDI)-Iraq supplied the methyl dopa generously. It was prepared by dissolving 0.0100g of methyl dopa in warm distilled water to yield $100 \mu\text{g.mL}^{-1}$. The solution must be preserved in a tightly sealed, opaque bottle.

Sodium nitrite solution 9.144×10^{-3} M: This solution was made by dissolving 0.06313 g of sodium nitrite (supplied by BDH Company) in distilled water and bringing the volume to 100 mL in a volumetric flask with distilled water.

p-Nitroaniline solution 9.144×10^{-3} M: This solution was prepared by dissolving 0.12637 g of the reagent (supplied by Fluka Company) in 2 mL of 2 M hydrochloric acid, heating afterwards adding 10 mL of distilled water with heating and stirring then completing the volume to 100 mL in a volumetric flask with distilled water.

Pharmaceutical preparation

Tablet formulation of $100 \mu\text{g.mL}^{-1}$ (S.D.I.) Aldosam solution.

Five tablets containing 250 mg of MeD were weighed and then ground into a powder. Putting 0.0138 g of powder equivalent to 0.0100 g of purified MeD into a 100 mL beaker via weighing and transfer. The substance was dissolved in 100 mL of warmed distilled water using a calibrated flask to produce a $100 \mu\text{g MeD. mL}^{-1}$ solution, and then filled to the mark with distilled water.

Five tablets containing 250 mg of MeD were weighed and then ground into a powder. Putting 0.0143 g of powder equivalent to 0.0100 g of purified MeD into a 100 mL beaker via weighing and transfer. To produce $100 \mu\text{g.mL}^{-1}$ MeD, the powder was dissolved in warm distilled water, transferred to a 100mL calibrated flask, and then filled to the mark with distilled water.

Method

Recommended procedure and calibration curve

By adding a volume of 1 mL of p-Nitroaniline (9.144×10^{-3} M) to a series of volumetric flasks of 10 mL then adding 1 mL of sodium nitrite NaNO_2 (9.144×10^{-3} M) then adding 0.5 mL of nitric acid (1 M) and then adding increasing volumes of 0.2-1.7 mL of the methyldopa $100 \mu\text{g} \cdot \text{mL}^{-1}$ with shaking and then adding 1.5 mL of sodium hydroxide solution (1 M) for all solutions and completing the volumes to the mark with distilled water. At a wavelength of 610 nm, absorbance was measured against a blank solution after dilution. The standard straight curve that corresponds to Beer's law in the concentration range of 2 to $17 \mu\text{g} \cdot \text{mL}^{-1}$ is depicted in Figure 2, and it was determined that the molar absorptivity of the resulting azo dye is $0.7223 \times 10^4 \text{ L} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$ and Sandell's sensitivity index was $0.02 \mu\text{g} \cdot \text{cm}^{-2}$. The LOD was $0.0727 \text{ g} \cdot \text{mL}^{-1}$, and the LOQ was $0.242 \mu\text{g} \cdot \text{mL}^{-1}$.

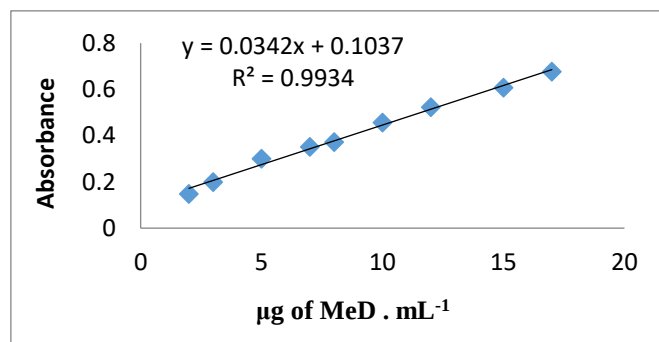


Figure 2. Calibration curve for the determination of Methyldopa according to the recommended procedure.

Results and discussion

Study of optimal conditions for the purpose of azo dye with high absorbance and suitable stability, the effect of various conditions on the absorbance of the resulting azo dye was studied.

The effect of the type of acid used

The acid used in the diazotization process of primary aromatic amines is one of the main reaction requirements as its presence is essential for the formation of the corresponding diazonium salt and to study its effect, 0.5 mL of various acids (1 M) was added and the absorbance of the azo dye formed was measured and the results are shown in Table (1).

Table 1. Selection of the type of acid

Acid used 1M	Abs	λ_{max} S(nm)	λ_{max} B(nm)	$\Delta \lambda$ *(nm)
HCl	0.2813	611	381	230
H ₂ SO ₄	0.0258	413	381	32
HNO ₃	0.2908	610	384	226
CH ₃ COOH	0.2602	615	382	233

$$*\Delta \lambda_{\text{max}} = \lambda_{\text{max}} \text{S} - \lambda_{\text{max}} \text{B}, \text{ When S=The azo dye, B=Blank}$$

It can be seen from Table 1 that nitric acid gave the highest absorbance of the azo dye formed and a good colour contrast so it was selected in subsequent experiments.

The effect of acid amount

The result of the effect of the amount of nitric acid on the absorbance of the azo dye formed was shown in Table 2, indicate that 0.5 mL of nitric acid (1 M) gave the highest absorbance of the azo dye formed so it was selected for the subsequent response.

Table 2. The effect of the amount of acid.

ml of HNO ₃	0.25	0.5	0.75	1.0	1.25
Absorbance	0.2679	0.2931	0.2426	0.1433	0.0074
pH	12.21	11.89	11.71	8.82	1.91

Effect of reagent amount

The effect of different volumes of p-nitroaniline reagent on azo dye absorbance was studied by preparing several volumetric flasks of 10 ml and each of them different volume of the reagent and equal volume of sodium nitrite to reagent were added in an acidic medium of nitric acid with different volumes as well as of the methyldopa and 1 mL of sodium hydroxide (1M) complete the volume with distilled water to the mark and the results are shown in the Table 3.

Table 3. Effect of reagent amount.

ml of reagent 9.144x10 ⁻³ M	Absorbance/ $\mu\text{g.ml}^{-1}$ of MeD						R2
	2	4	5	7	10	12	
0.2	0.0888	0.1664	0.1968	0.2337	0.3007	0.3206	0.9639
0.5	0.1081	0.1953	0.2488	0.3201	0.4559	0.4715	0.9787
0.7	0.0902	0.1592	0.2706	0.2949	0.3945	0.5456	0.9609
1.0	0.0967	0.1996	0.2940	0.3631	0.4665	0.5655	0.9817
1.2	0.1002	0.1975	0.2388	0.3483	0.4480	0.4857	0.9793

The results indicate that 1 mL of reagent is the best as it gave the highest absorbance and highest value of the determination coefficient, so it was adopted.

Effect of base type

The effect of various bases was studied to see the best of their effect on the absorbance of azo dye formed and the results are shown in Table 4.

Table 4. The effect of base type on absorbance and colour contrast.

Base used	Abs.	S λ_{max}	B λ_{max}	$\Delta\lambda$	pH
NaOH	0.2907	611	381	230	12.15
KOH	0.2450	611	387	224	12.07
Na ₂ CO ₃	0.1810	426	384	42	9.02
NaHCO ₃	Turbid				7.41

From the results in Table 4, we note that the formation of the azo dye needs a strong basic medium, so sodium hydroxide was chosen.

Effect of base amount.

After the optimal base type was achieved, the effect of the appropriate amount of sodium hydroxide 1M was studied, which achieves the highest absorbance and the results are shown in the Table 5.

Table 5. The effect of the NaOH amount.

NaOH added (ml, 1M)	Abs.	pH
0.25	0.0028	1.88
0.50	0.0093	2.37
0.75	0.2484	11.66
1.00	0.2907	12.13
1.25	0.2976	12.40
1.50	0.3019	12.51
1.75	0.2848	12.61

The volume of 1.5 mL of sodium hydroxide was chosen to give it the highest absorbance of the resulting azo dye, so it was adopted in subsequent experiments. The optimal conditions obtained from the above experiments are listed in Table 6.

Table 6. Optimal conditions for the proposed method

Parameters	Optimum conditions
$\lambda_{\max}$ (nm.)	610
Type and amount of acid, mL	HNO ₃ , 0.5
Type and amount of base, mL	NaOH, 1.5
Amount of reagent, mL	1
Amount of NaNO ₂ , mL	1
Temperature, °C	RT (23±2)
Solvent used in dilution	Distilled water

Final absorption spectra of the formed azo dye

Using the suggested procedure, the formed azo dye exhibits a final absorption spectrum with maximal absorbance at 610 nm relative to the blank, as depicted in Figure 3.

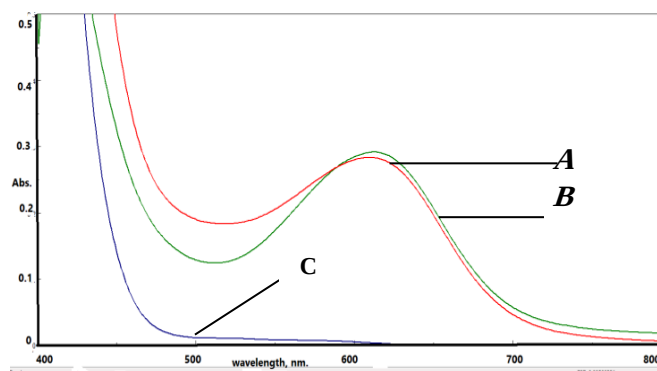


Figure 3. Absorption spectra 50 µg/10 ml methyl dopa measured according the suggested procedure (A) vs. the blank solution, (B) vs. distilled water (C) blank solution vs. distilled water

The wavelength 610 nm. Was fixed in all next experiments.

The stoichiometry of the chemical reaction

The mole ratio method was used to find the reaction ratio between the methyl dopa MeD and the diazotized reagent (D-PNA) under optimal experimental conditions, the absorbance of each sample was measured against its blank solution at wavelength of 610 nm. The reaction ratio was determined to be 1 MeD:1 D-PNA. Figure 4 demonstrates the results.

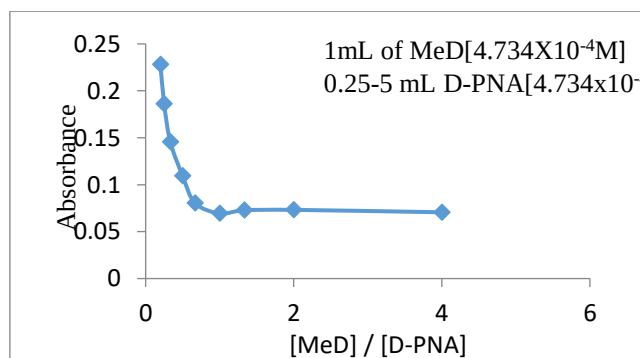
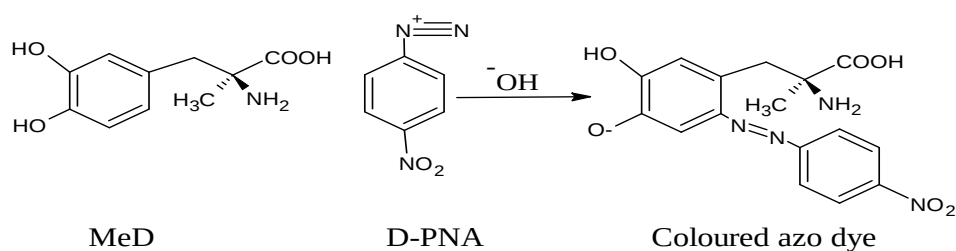


Figure 5. Curved molar ratios of azo dye resulting from the coupling D-PNA with methyl dopa.

Therefore, the proposed formulation of the formed azo dye is as follows [15].



Scheme 1. Proposed reaction equation

Accuracy and precision

The precision and accuracy of the proposed estimation method were evaluated. At a total of three different MeD concentrations of 5, 8, and 10 $\mu\text{g. mL}^{-1}$, four replicate measurements were conducted. According to Table 7, the relative standard deviation and relative error results demonstrated that the proposed method possesses outstanding accuracy and precision.

Table 7. Accuracy and precision of the proposed method

Amount of MeD taken, $\mu\text{g / mL}$	Recovery *%	Relative error, %	Relative standard deviation, %
5	98.20	-1.80	2.26
8	101.75	+1.75	0.43
10	100.50	+0.50	1.64

*Average of four determinations.

Application

The method was applied to the pharmaceutical preparation, tablets, and for three concentrations from different origins, and the results are shown in Table 11, by taking different concentrations (5, 10, and 12) $\mu\text{g/mL}$ of the prepared tablet solutions. Recovery percentage, relative standard deviation and drug content were calculated.

Table 8. Application of the method for the determination of MeD.

Drug	$\mu\text{g MeD present/mL}$	$\mu\text{g MeD measured/mL}$	Recovery*, %	Relative standard deviation, %	Drug content (mg)
Aldosam 250mg /Tablet S.D.I.,Iraq	5	4.96	99.20	0.25	248.00
	8	7.91	98.87	3.60	247.17
	12	12.11	100.91	1.92	252.27
Methyldopa 250mg/Tablet Accord, UK	5	4.88	97.60	2.36	244.00
	8	8.07	100.87	2.85	252.17
	12	11.75	97.91	1.66	244.77

*Average of four determinations

MeD estimation using the standard addition method

The outcomes of applying the standard addition method are depicted in Figures 7 and 8, as well as Table 9.

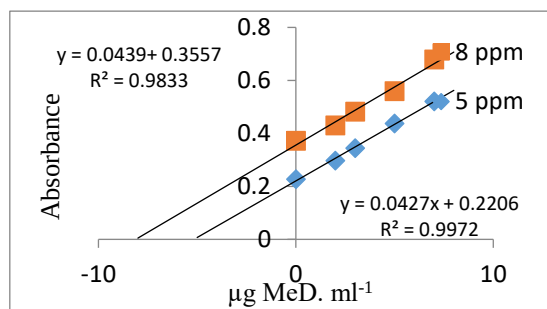


Figure 7. Standard addition method plot estimating of MeD in tablets SDI.

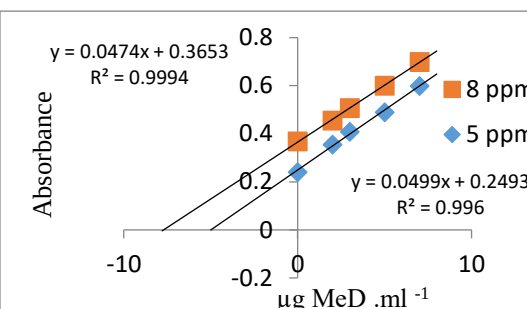


Figure 8. Standard addition method plot estimating of MeD in tablets Accord

Table 9. The results of assay MeD in tablets via standard addition method.

Drug content	MeD taken $\mu\text{g}/\text{ml}$	MeD found $\mu\text{g} \cdot \text{ml}^{-1}$	Recovery %	Drug content mg
Aldosam 250 mg / Tablet (S.D.I Iraq)	5	5.16	103.20	258.00
	8	8.10	101.25	253.12
Methyldopa 250 mg / Tablet (Accord, UK)	5	4.99	99.80	249.50
	8	7.70	96.25	240.62

We conclude that the proposed method of estimating the drug compound methyldopa in tablet dosage from two companies has successful and is free of interference for additives in manufacturing.

Area Under Curve (AUC)

The AUC (area under the curve) method was applicable when there was neither a sharp peak nor a broad spectrum. It entails calculating the integrated value of absorbance with respect to wavelength between the two wavelengths λ_1 and λ_2 . The area bounded by the curve and horizontal axis is computed by the area calculation processing item. By inputting the wavelength range over which the area must be calculated, the horizontal axis is determined [16]. The principle of the method is the same as mentioned in the first method. After the formation of the azo dye from methyldopa with the reagent D-PNA under the predetermined optimal conditions. The spectrum was taken for it and two wavelengths within the peak were identified and the area between them was recorded.

Absorption spectrum of the AUC

The absorption spectrum of methyldopa with a concentration of $8 \mu\text{g} \cdot \text{mL}^{-1}$ and the coefficient according to the method mentioned in the first method shows that the highest absorption peak was at the wavelength of 610 nm. The area under the curve of the peak between 596 to 622 nm. Was fixed in the next experiment. As shown in Figure 9.

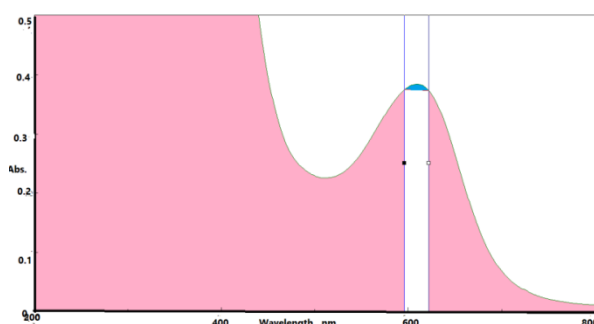


Figure 9. The area under the peak of $8 \mu\text{g} \cdot \text{ml}^{-1}$ of MeD

Recommended procedure and calibration curve

The standard curve of the method was prepared by adding 1 ml of 9.144×10^{-3} M of D-PNA to a series of volumetric flasks of 10 mL, then 1 mL of sodium nitrite NaNO_2 concentration of 9.144×10^{-3} M was added in an acidic medium by adding 0.5 mL of nitric acid then, increasing volumes of 0.1-2 mL of the methyl dopa $100 \mu\text{g} \cdot \text{mL}^{-1}$ were added with shaking, then 1.5 mL of a 1 M sodium hydroxide solution was added to each of the solutions. The volumes were adjusted with distilled water. The absorbance of the samples was then measured against a neutral solution after dilution, and two wavelengths between 596 and 622 nm were chosen. To compute the region under the peak, Figure 10 represents the standard straight curve to cover the concentration range of 1-20 $\mu\text{g} \cdot \text{mL}^{-1}$ and the molar absorptivity value was $0.5470 \times 10^4 \text{ L} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$ and Sandell's sensitivity index value was $0.0386 \mu\text{g} \cdot \text{cm}^{-2}$

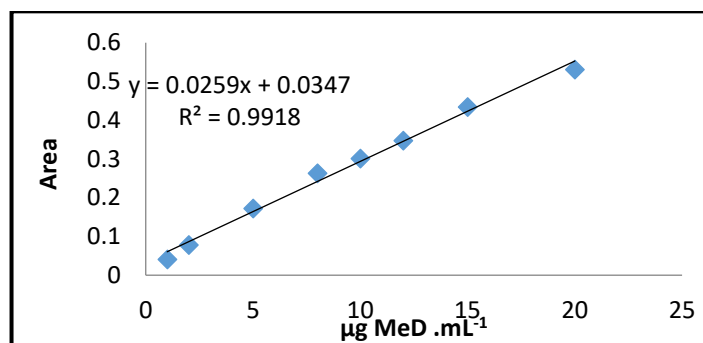


Figure 10. Standard curve for estimation of methyl dopa using area under curve

Accuracy and precision of the AUC method

By calculating the recovery and the relative standard deviation and applying the optimal conditions and choosing the two wavelengths 596-622 nm to estimate three different concentrations of the methyl dopa MeD, and the results in Table 10 indicate that the method has good accuracy and precision.

Table 10. Accuracy and precision of the proposed method

Amount of MeD $\mu\text{g}/\text{ml}$	Recovery *%	Relative error, %	RSD%
5	100.40	+0.40	1.57
10	97.70	-2.30	2.05
12	100.91	+0.91	1.62

*Average of three determinations.

Application

The method was applied to the pharmaceutical preparation, tablets, and for three concentrations from different origins, and the results are shown in Table 11, by taking different concentrations (5, 10, and 12) $\mu\text{g}/\text{mL}$ of the prepared tablet solutions. Recovery percentage, relative standard deviation and drug content were calculated.

Table 11. Application of the method for the determination of MeD

Drug	$\mu\text{g MeD}$ taken/mL	$\mu\text{g MeD}$ measured/mL	Recovery* %	Relative error, %	RSD%	Drug content (mg)
Aldosam 250mg /Tablet S.D.I., Iraq	5	5.09	101.80	+1.80	2.38	254.50
	10	9.91	99.10	-0.90	1.60	247.75
	12	11.57	96.42	-3.59	1.15	241.05
Methyl dopa 250mg/Tablet Accord, UK	5	4.85	97.00	-3.00	2.03	242.50
	10	9.80	98.00	-2.00	1.97	245.00
	12	11.55	96.25	-3.75	2.28	240.62

*Average of four determinations

The results indicated that the method successful in determination of MeD in tablet formulation.

Conclusion

Simple, fast and reliable Spectrophotometric Determination of Methyl dopa via diazo-coupling reaction with diazotized p-nitroaniline reagent and area under peak methods. for the routine analysis. No spectrophotometric methods for estimating the AUC of methyl dopa have been described. A different method of work was followed than what is commonly known, which is the preparation of the nitrous oxide agent In this method, sodium nitrite

was added in an amount equivalent to the concentration of the reagent p-nitroaniline, and there are no any excess of nitrous oxide and there is no any side reaction cooling use. The proposed spectrophotometric methods were characterized by accuracy and precision. The peak area method is more sensitive than diazo- coupling method and long range of linearity.

Disclaimer

The article has not been previously presented or published.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

References

1. Sweetman, SC . Martindale: The Complete Drug References. .35th ed. London, UK. Pharmaceutical press. [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3257481\(2007\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3257481(2007)).
2. British Pharmacopoeia on CD-ROM 3.0, a component ,BP(2007).
3. Shakkor, S. J. , Mohammed, N. ,Shakor, S. R Spectrophotometric method for determination of methyl dopa in pure and pharmaceutical formulation based on oxidative coupling reaction. Chemical Methodology ,2022; 6(11):851-860.
4. Abood, N.K.,Hassan, M. J. M , & AL-Damy, M. A. Spectrophotometric determination methyl dopa and salbutamol by oxidative coupling, cloud point and flow injection in pharmaceutical formulations, Inter. J. Drug Del.Tech.2019; 9(2): 182-192 .
5. Allah, N. M. G., Ahmed, A. M. K., & Tapabashi, N. OSpectrophotometric determination of methyl dopa in pure and pharmaceutical preparations by the oxidative coupling reaction with 1, 5-diaminonaphthalene in the presence of ammonium ceric (iv) nitrate. Kirkuk Univ. J. Sci. Stud. 2022;17(4):41-48..
6. AL-ghanam, D. N., & AL-Enizzi, M. S. Spectrophotometric determination of methyl dopa by oxidative coupling reactions using 2, 4-dinitrophenylhydrazine reagent. Tikrit J. Pure Sci.2022; 27(5): 16-22.
7. Abdulrahman, L. K., Al-Abachi, A. M., & Al-Qaissy, M. H. Flow injection-spectrophotometric determination of some catecholamine drugs in pharmaceutical preparations via oxidative coupling reaction with p-toluidine and sodium periodate. Analytica Chimica Acta.2005; 538(1-2):331-335 .
8. Dhamra, M.Y., & Al-Sabha, Th. NSpectrophotometric method for indirect determination of antihypertensive drugs in pharmaceuticals , Egypt. J. Chem.2020; 63(10): 3767 – 3777.
9. Gadkariem, E.A.,Ibrahim, K.E.E .,Kamil ,N.A.A., Haga, M.E.M., & El-Obeid, H.A. A new spectrophotometric method for the determination of methyl dopa, Saudi Pharma. J. 2009;17(4): 289– 293.
10. Antunes, R.S., Thomaz, D.V., Garcia, L. E., Gil, E.S., Somerset ,V. S., & Lopes, F. M. Determination of methyl dopa and paracetamol in pharmaceutical samples by a low cost genipa americana l. polyphenol oxidase based biosensor, Advanced Pharmaceutical Bulletin.2019; 9(3): 416-422.
11. Yanik, S., Kurt ,S. B., Ari ,B., Demirci, S. & Yilmaz, S. Development of electrochemical sensors for quantitative analysis of methyl dopa at modified-GCE and PGE electrodes by voltammetry , J.I Sci. Per. 2020;4(4): 223-236.
12. Sanati ,A. L. , &Faridbod, F. Electrochemical determination of methyl dopa by graphene quantum dot / 1-butyl-3-methylimidazolium hexafluoro phosphate nanocomposite electrode, Int. J. Electrochem. Sci.2017;12 , 7997 – 8005..
13. Erdodu, G. Yagci, S. Z., &Sava, E. K. Investigation of the voltammetric behavior of methyl dopa at a poly (p-aminobenzene sulfonic acid) modified sensor, Turk J Pharm. Sci.2019; 16(4): 450-6.
14. Zečević, M., Živanović, L. J., Agatonovic-Kustrin, S., & Minic, D. . The use of a response surface methodology on HPLC analysis of methyl dopa, amiloride and hydrochlorothiazide in tablets. J. Pharma. and Biomed. Anal.2001; 24(5-6), 1019-1025.
15. Saleem,M.;AL-Mtwaiti, S. M.; Al-Ramadhani, S. T.determination of salbutamol sulphate by coupling with diazotized 2,4- dinitroaniline. J. Edu. & Sci,2013;26 (2):55-64 .
16. Tagine, T. S. Estimation of valsartan in pharmaceutical formulation by area under curve spectrophotometric method. International Journal of Advances in Pharmaceutics. 2018; 7(1):1-4