Asensitive colorimetric method for the determination of Methyldopa in pharmaceutical preparation via oxidative coupling organic reaction with Thiamine Hydrochloride in the presence of potassium periodate

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Abstract :

A simple, accurate and sensitive spectrophotometric method for the determination of Methyldopa in pure and pharmaceutical preparations has been developed .The proposed method uses Thiamine Hydrochloride as anew chromogenic reagent . The method is based on the oxidative coupling reaction of Methyldopa with Thiamine Hydrochloride with potassium periodate in neutral media to form orange water soluble dye product , that has a maximum absorption at λ_{max} 480 nm . Linear calibration graph was in the range of (1.00–25.00) $\mu g.ml^{-1}$ with molar absorptivity of (0.53×10^4 $L.mol^{-1}.cm^{-1}$) ,a sandall sensitivity of (4.49×10^{-5} $\mu g.cm^{-2}$) , correlation coefficient of (0.9997) , detection limit (0.38 $\mu g.ml^{-1}$) and the relative standard deviation of RSD% (0.97) . The method was applied successfully for the determination of Methyldopa in pharmaceutical preparations and the value of recovery % was better than (102%) .

طريقة لونية حساسة لتقدير عقار المثيل دوبا في المستحضرات الصيدلانية من خلال تفاعلات الأكسدة والازدواج العضوي مع ثيامين هيدروكلورايد بوجود بيرايودات البوتاسيوم

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مفتاح البحث : عقار المثيل دوبا ' التقدير الطيفي ، المستحضرات الصيدلانية

الخلاصة :

يتضمن البحث تطوير طريقة طيفية بسيطة ومضبوطة وحساسة لتقدير العقار مثيل دوبا في صيغته النقية وفي مستحضراته الصيدلانية . الطريقة المقترحة تعتمد على ازدواج مثيل دوبا مع الكاشف اللوني ثيامين هيدروكلورايد وبوجود بيرايودات البوتاسيوم في الوسط المتعادل حيث يتكون ناتج برتقالي يعطي امتصاص أعظم عند الطول الموجي (480) نانوميتر . أظهرت النتائج ان مدى الخطية بين (1.00 - 25.00) مكغم .مل$^{-1}$ وبمعامل امتصاص مولاري مقداره(0.53×10^4) لتر .مول $^{-1}$.سم$^{-1}$ ودلالة ساندل مقدارها (4.49×10^{-5}) مكغم .سم-2 وبمعامل ارتباط (0.9997) وحد كشف للطريقة (0.38) مكغم .مل$^{-1}$ وبمعدل انحراف قياسي نسبي (0.97%) .

طبقت الطريقة بنجاح لتقدير مثيل دوبا في مستحضراته الصيدلانية وكانت حدود الاسترداد المئوي أفضل من (102%) .

Introduction:

Methyldopa[3-(3,4-dihydroxypheny)2-methyl-L-alanine] is one of the catecholamine drugs that was discovered in 1960 and was used as hypotensive agents[1] in 1970. The pharmaceutical preparations containing this drug (Aldomate) is available for many years and several analytical procedures have been proposed for their control[2].Many methods have been developed to determine Methyl dopa in pharmaceutical preparations and other materials such as urine and blood. These include spectrophotometric[3,4] , chromatographic[5], potentiometric[6] and flow injection technique[7,8]. Oxidative coupling organic reactions seems to be one of the mostpopular spectrophotometric methods for the determination of several drugs such as sulphonamids[9] , paracetamol[10], phenylephrine HCL[11],methyl dopa[12] and folic acid[13].The proposed method is based on the reaction of the methyldopa drug with Thiamine Hydrochloride in the presence of potassium periodate in neutral medium to form an orange water soluble dye product which shows an absorption maximum at 480 nm .

Experimental parts

Apparatus:

All spectral and absorbance measurement were carried out in a Double beam UV-Vis spectrophotometer-1800 . Equipped with a 1 cm quarts cell .

- Water bath(Lab. Companion , BS - 11) .
- Electronic balance (Sartorius AG GÖTTINGEN B2 2105 Germany) .

Reagents:

All chemicals used were of analytical-reagent grade .

-Stock solutions from drug (100 $\mu g.ml^{-1}$) of Methyldopa(SDI - Iraq) were prepared by dissolving 0.01gm of Methyldopa in distilled water and diluting to the mark in 100 ml volumetric flask .Working solutions were prepared by diluting the solution in distilled water.

- Thiamine Hydrochloride (0.001M) stock solution was prepared by dissolving 0.0337gm of Thiamine Hydrochloride in distilled water and completed the volume to 100 ml in a volumetric flask with distilled water.
- potassium periodate(0.005M) stock solution was prepared by dissolving 0.115gm of KIO_4 in distilled water and diluting to the mark in 100 ml volumetric flask .

Recommended procedure :

In to a series of 25 ml volumetric flask , transfer increasing volume of Methyldopa solution(100.00$\mu g.ml^{-1}$)to cover the range of calibration curve (1.00– 25.00)$\mu g.ml^{-1}$,added (0.50) ml from (3.75×10^{-5}M) of Thiamine Hydrochloride and shake well . Added (2.50)ml from (5.00×10^{-3}M)of KIO_4 , dilute the solution to the mark with distilled water , and allow the reaction to stand for 10 min at room temperature (25 ^{o}c) . measure the absorption at λmax(480 nm) against a reagent blank prepared in the same way but containing no Methyldopa .

Procedure for pharmaceutical preparations :

Aldomate tablets, provided from (SDI) Samara-Iraq and from ASIA - Syria (10) tablets were grinded well and acertain portion of the final powder was accurately weighted to give an equivalent to about 10 mg of Methyldopa was dissolved in distilled water . The prepared solution transferred to 100 ml volumetric flask and made up to the mark with distilled water forming a solution of 100µg.ml^{-1} concentration . The solution was filtered by using a Whitman filter paper No. 42 to avoid any suspended particles .These solution were diluted quantitatively to produce a concentrations in the range of calibration curve .

Results and Discussion :

Absorption spectra :

It was found preliminary that the reaction of Methyldopa with Thiamine Hydrochloride and potassium periodate in neutral media forming an orange water soluble dye product , that has a maximum absorbance at λ_{max} (480 nm) Fig (1) . The above reaction can be utilized for the determination of Methyldopa using spectrophotometric method . Initial studies were directed toward optimization of the experimental conditions ,in order to establish the most favorable parameters for the determination of Methyldopa.

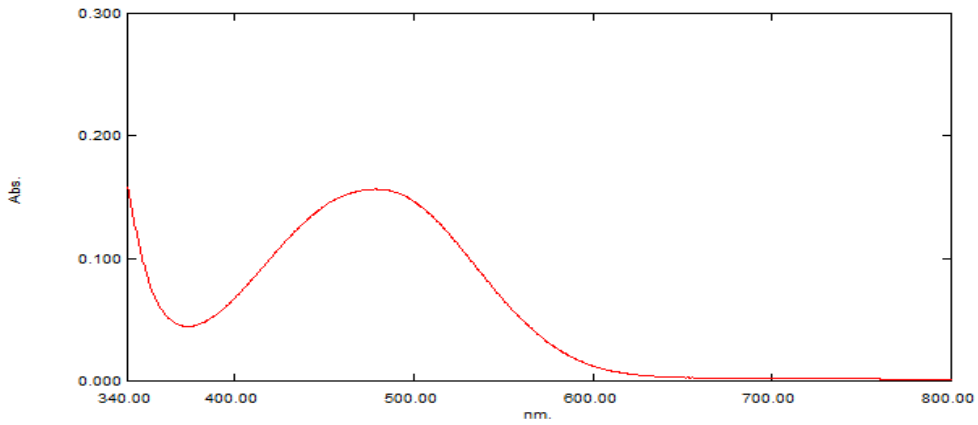


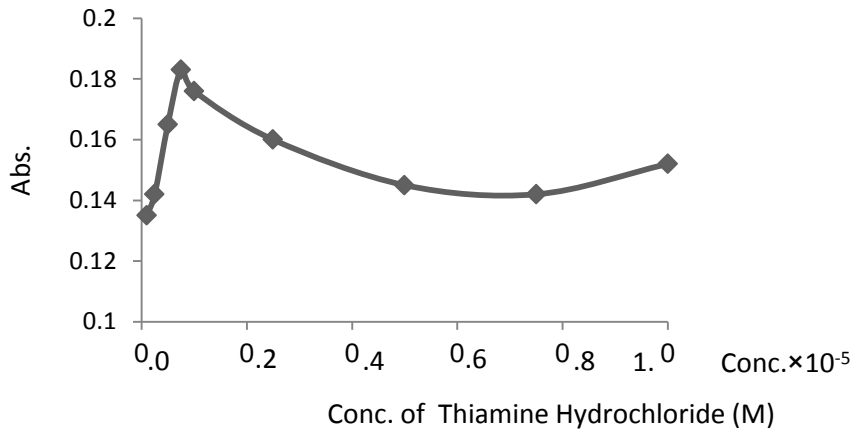
Fig (1) : Absorption spectra of (12.50 µg.ml^{-1}) of Methyldopa with Thiamine Hydrochloride(7.50 x 10^{-7})M , and KIO_4(5.00 x 10^{-4})M at room temperature and measured against blank solution.

Optimization of the Experimental Condition :

The influence of various reaction variables such as concentration of reactants , order of addition ,time and temperature were investigated .

Effect of Thiamine Hydrochloride Concentration :

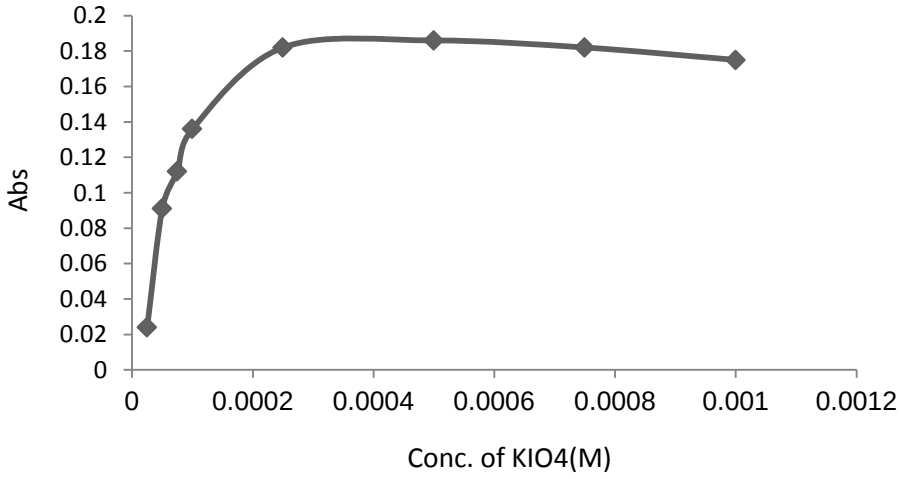
The effects of different concentration of Thiamine Hydrochloride in the range of (1.00 x 10^{-7} – 1.00 x 10^{-5})M were investigated .A Concentration of (7.50 x 10^{-7})M give the higher absorption intensity at λmax480nm for(15.00)µg.ml^{-1} of Methyl dopa and (1.00x10^{-4})M of KIO_4 Fig (2) and thus was chosen for further use .



Fig(2) :Effect of Thiamine Hydrochloride Concentration on Absorption spectra of (15.00 $\mu g.ml^{-1}$) of Methyldopa .

Effect of Potassium periodate KIO_4 Concentration :

The effect of KIO_4 Concentration in the range of (2.50×10^{-5} - 1.00×10^{-3})M was similarly studied . A Concentration of (5.00×10^{-4}) M of KIO_4give the higher absorption intensity at λ_{max} 480 nm for (15.00) $\mu g.ml^{-1}$ of Methyl dopa and (7.50×10^{-7}) M Thiamine Hydrochloride .Fig (3) and thus was chosen for further use .



Fig(3) :Effect of potassium periodate KIO_4 Concentration on Absorption spectra of (15.00 $\mu g.ml^{-1}$) of Methyl dopa .

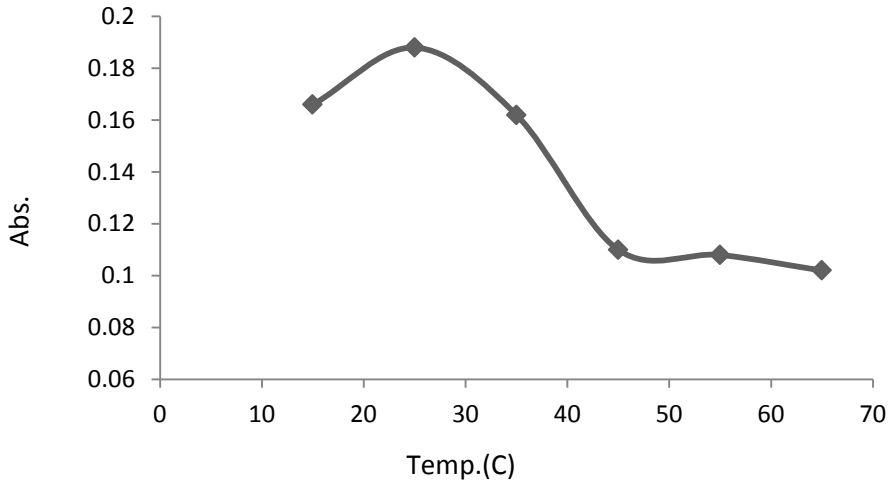
Order of addition :

The effect of order of addition on the absorption intensity of orange water soluble day was studied . Table (1) , shows the order of addition could be followed , Drug : Thiamine Hydrochloride : KIO4 . Due to give the higher absorption intensity .

Order of addition	Absorbance at λmax(480)nm
Drug :Thiamine Hydrochloride : KIO4	0.189
Drug: KIO4 : Thiamine Hydrochloride	0.119
KIO4 :Thiamine Hydrochloride : Drug	0.137
KIO4: Drug :Thiamine Hydrochloride	0.125
Thiamine Hydrochloride : Drug : KIO4	0.178
Thiamine Hydrochloride : KIO4 : Drug	0.141

Effect of Temperature :

The effect of Temperature on the color intensity of the product was studied in practice the highest absorption was obtained when the colored product was developed at room temperature (25ºc) . as shown in Fig (4)



Fig(4) :Effect of Temperature on Absorption spectra of (15.00 µg.ml^{-1}) of Methyldopa .

Effect of Time :

The color intensity reached a maximum absorption after Methyl dopa(15.00) µg.ml^{-1} has been reacted with Thiamine Hydrochloride and KIO_4 at 10 min . Therefore 10 min development time was chosen for further use . The results obtained are shown in Fig(5).

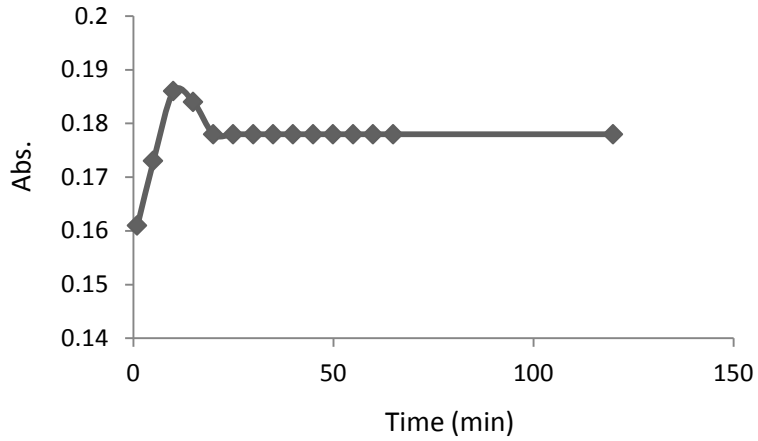


Fig (5) Effect of Time on Absorption spectra of (15.00 µg.ml^{-1}) of Methyl dopa .

Calibration Graph :

Under the optimum conditions , a linear calibration graph for the determination of Methyldopa was obtained over the concentration range of (1.00– 25.00)µg.ml^{-1}. The linear regression equation for the range of (1.00– 25.00)µg.ml^{-1} Methyldopa is Y=0.0118 X + 0.0116 and correlation coefficient of 0.9997 the linear calibration graph is shown in Fig (6) .

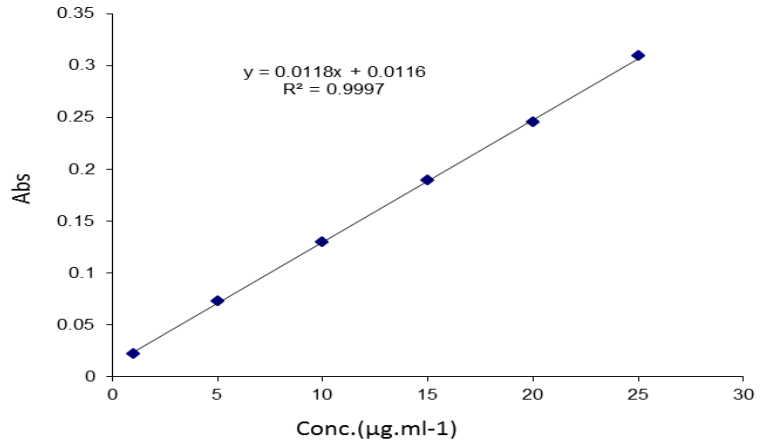
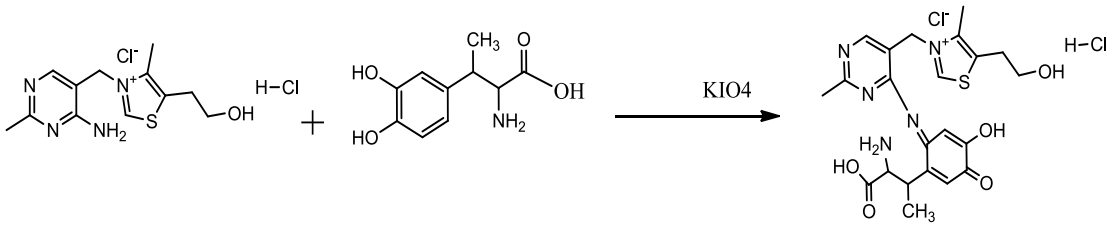


Fig (6) : Calibration graph for the determination of Methyldopa

Nature of the dye product :

The stoichiometry of the reaction between Methyldopa and Thiamine Hydrochloride was investigated using the mole ratio and Slope ratio method[14-17] under the optimized conditions . The results obtained Fig (7,8) , show a 1:1 drug to reagent product was formed .The formation of the dye may probably be occur as follows[18]:



Thiamine Hydrochloride Methyl dopa colored product

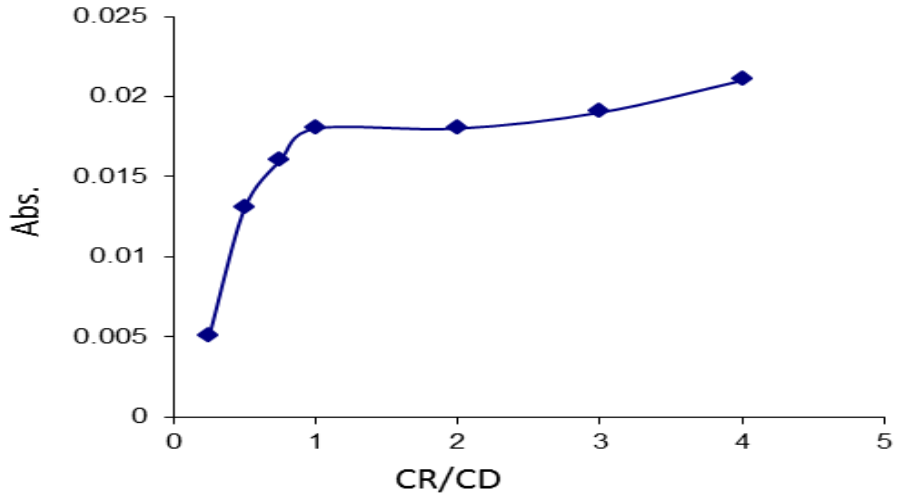


Fig (7) : Mole ratio of reagent to drug .

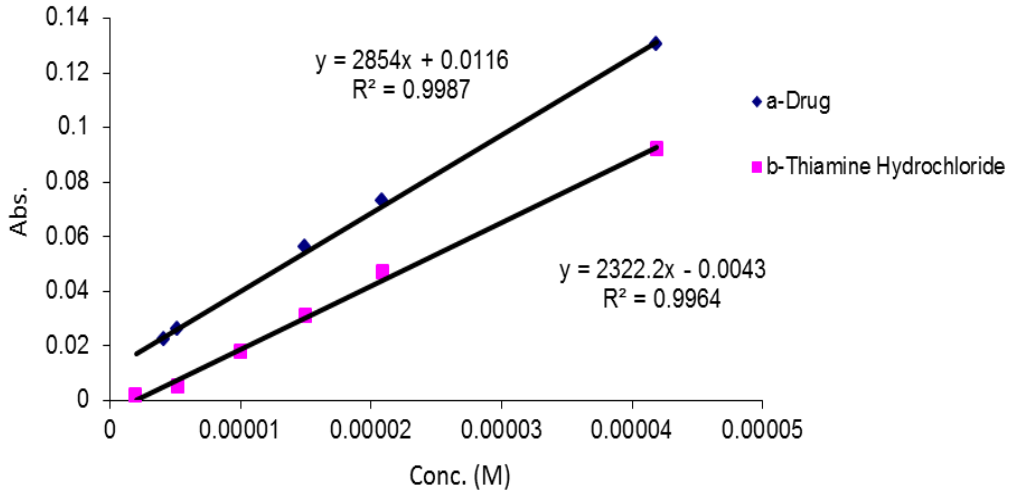


Fig (8) : Slope ratio method

(a) Absorbance vers concentration of drug at constant concentration of Thiamine Hydrochloride .
(b)Absorbance vers concentration of Thiamine Hydrochloride at constant concentration of drug .

Interferences :

Several pharmaceutical preparations are associated with flavoring agents, diluents and excipients. Table (2) shows the effect of interfering materials that may be present in pharmaceutical preparations, that indicate no influence effect on the proposed due to the value of recovery% change is less than (±5%) .

Table (2) : Influence of excipients and additives as interfering species in the determination of Methyldopa .

Foreign compound	Recovery (%) of 500µg Methyldopa per µg compound added				
	100	500	1000	2000	5000
Glucose	100.62	101.28	98.82	100.24	102.10
Lactose	100.48	101.63	100.73	102.21	102.43
Starch	102.12	101.95	100.17	100.41	99.61
Sucrose	98.89	101.15	102.21	101.26	99.72
Sodium chloride	101.55	101.87	102.18	98.72	102.68
EDTA	98.93	98.39	100.41	101.46	102.16
Citric acid	100.26	102.36	101.58	99.19	102.23
Magnesium setarate	102.41	101.31	98.73	99.12	102.38

Analytical Application :

The proposed method was applied for the determination of Methyl dopa drug in pharmaceutical preparations. Good accuracy and precision were obtained for the studied drugs . The results obtained were given in Table 1 which confirm Finally, the proposed method was compared successfully with the standard method Table(3).

Table (3) : Application of the proposed method for the determination of Methyldopa in pharmaceutical preparations .

Drug sample	Amount of Methyldopa(µg.ml^{-1})		Proposed Method			Standard Method
	Taken	Found	RSD %*	Error %*	Recovery %*	Recovery %[18]
Pure Methyldopa	5.00	4.92	0.88	-1.60	100.10	98.30
Aldomate(SDI)tablets	5.00	5.10	0.97	2.00	102.00	
	15.00	14.80	0.68	-1.33	98.67	
	20.00	19.89	0.53	-0.55	99.45	
Aldomate (ASIA) tablets	5.00	4.88	0.93	-2.4	100.12	
	15.00	15.25	0.71	1.66	99.75	
	20.00	20.15	0.48	0.75	99.85	

*Average of five determinations .

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