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DETERMINATION OF HYOSCINE BUTYLBROMIDE AND DIPYRONE IN PRESENCE OF EACH OTHER

Hesham S. Sharaf El-Din

Misr Pharmacy, Menia El-Kamh, Sharkia, Egypt

ABSTRACT

Determination of hyoscine butylbromide and dipyrone was performed in presence of each other using spectrodensitometry and derivative spectrophotometry.

INTRODUCTION

Spectrophotometric analysis of drugs in dosage forms and in biological fluid is often subjected to spectral interferences. This may lead to serious errors in the analytical growth curves of absorbances versus wavelength. Derivative spectrophotometry offers simple approach for resolving spectral overlap and for the quantitation of drugs in pharmaceutical and biological matrices[1].

Hyoscine butylbromide has a special site of at the parasympathetic ganglia in the walls of the viscera. Because of this, it exerts an anti-spasmodic action on the smooth muscle of the gastrointestinal, biliary and urinary tracts[2]. The most recent methods for the determination of hyoscine butylbromide include high pressure liquid chromatographic[3], volumetric[4-6] and spectrophotometric ones[7-9].

Dipyrone is a derivative of aminopyrone, it has a central analgesic antipyretic action as well as an anti-inflammatory effect[2]. Several methods have been recommended for dipyrone determination which include, titrimetric[10], polarographic[11], high pressure liquid chromatographic and spectrophotometric ones[13-15].

EXPERIMENTAL

Apparatus:

1- Shimadzu recording spectrophotometer, U.V. 260.

2- Shimadya CS-9000, dual wavelength flying-spot scanner.

3- Hamilton Microliter syringe, CH-7402 Bonad 42-Switzerland.

Materials:

Buscopan compositum tablets, labeled to contain 10 mg hyoscine butylbromide and 250 mg dipyrone per tablet Buscopan compositum suppositories for children labeled to contain 7.5 mg hyoscine butylbromide and 300 mg dipyrone per suppository (Chemical Industries Development Co., Egypt). HPTLC silica gel F-254, precated plates 20 x 20 cm (Merck, Germany) and methyl parahydroxy benzoic acid (Aldrich Co., USA).

Standard solutions:

Aqueous stock solutions of either hyoscine butylbromide or dipyrone (500 mg %) were prepared for derivative spectrophotometric technique.

Ethanolic stock solutions of hyoscine butylbromide, dipyrone or methyl parahydroxy benzoic acid (25 mg %) were prepared.

Procedures:

I- Derivative spectrophotometry:

Accurately measured equal aliquots of either dipyrone or hyoscine butylbromide aqueous stock solutions (0.2-8 ml) were pipetted into separate 50 ml volumetric flasks and completed to volume with distilled water. First and second derivative curves of dipyrone and hyoscine butylbromide were scanned against distilled water blank. Maxima were recorded at λ = 280 & 260.5 nm, respectively. Calibration curves were constructed.

Aliquots of dipyrone stock solution (0.2-8) accompanied by 0.2 ml aliquots of hyoscine butylbromide stock solution were pipetted into 50 ml volumetric flasks and completed to volume with distilled water. Absorbance was measured at λ = 280 nm against distilled water .

Aliquots of hyoscine butylbromide stock solution (0.2-8 ml) accompanied by 0.2 ml aliquots of dipyrone stock solution were pipetted into 50 ml volumetric flasks and completed to volume with distilled water. Absorbance was measured at λ = 260.5 nm against distilled water.

II- Spectrodensitometry:

Different aliquots from each stock solution of hyoscine butylbromide or dipyrone were transferred into 10 ml calibrated flask and 1 ml of methyl para hydroxy benzoic acid as an internal standard was added to each flask. The flasks were made up to volume with ethanol to form the desired solutions which contain 0.025 mg ml^{-1} of hyoscine butylbromide and dipyrone. Aliquot of each component (2 ul) was spotted by micropipette, on HPTLC-F254 plates scored into 1 cm lanes. The plates were developed with a suitable developing system (ethyl acetate, benzene, methanol in ratio 9:7:4, respectively) for about 6 cm from the base line. The spots were air dried and measured at the suitable wavelength. Calibration curve was made by plotting the area ratio versus concentration (ug per spot).

III- Application to pharmaceutical preparations:

1- For Buscopan compositum tablets:

The coat of twenty tablets was removed by cotton wool moisted with water. Tablets were dried for one hour until constant weights. An accurately weighed portion of the finely powdered tablets (equivalent to 10 mg hyoscine butylbromide and 250 mg dipyrone) was dissolved in 70 ml distilled water and complete to 100 ml with distilled water (for derivative spectrophotometric technique). For spectrodensitometric technique, other portion of the finely powdered tablets equal to the above weight was dissolved in 70 ml ethanol. The volume was completed to 100 ml with ethanol. The procedures were completed as mentioned under procedures I & II.

2- For Buscopan compositum suppositories for children:

Five suppositories were accurately weighed, cut into small pieces, transferred into a porcelain dish and melted on a boiling waterbath to complete homogenity. An amount of the resultant mass equivalent to 300 mg dipyrone and 7.5 mg hyoscine butylbromide was dissolved in 70 ml of boiling water or ethanol. The solutions were cooled and filtered into 100 ml volumetric flasks. The residues were washed with 10 ml portions of either boiling distilled water or ethanol. Filtrates and washings were completed to volume with distilled water (for derivative spectrophotometric technique) and with ethanol (for spectrodensitometric technique) after cooling. The procedures were completed as above.

RESULTS AND DISCUSSION

I- Derivative Spectrophotometry:

Fig. (1a) shows that hyoscine butylbromide having absorption maxima at λ = 252, 263 & 276 nm is overlaped

with dipyrone absorption spectrum. However, in the corresponding first derivative curves (Fig. 1b), dipryone maximum is located at zero crossing pointof coexisting compound (λ = 280 nm) while hyoscine butylbromide absorbance is nil. Moreover, the corresonding second derivative curves (Fig. 1c), hyoscine butylbromide maxima is located at zero crossing point of dipyrone (λ = 260.5 nm) while dipyrone shows nil interference.

Both components can be determined in presence of each other at the above mentioned wavelengths. The optimal parameters for the assay of these drugs are presented in Table 1. For comparison, the official methods[17] were applied. Statistical analysis of the results obtained for either authetic dipyrone of hyoscine butylbromide (Table 2) showed that, the suggested procedures are equally precise and accurate as the official ones.

In order to prove the validity and the applicability of the proposed methods, five dilutions of a laboratory prepared mixture as well as Buscopan compositum tablets and suppositories were analyzed for both dipyrone and hyoscine butylbromide applying the proposed methods. The results obtained compared with the modified Vierordt's methods[18] and showed high degree of accuracy and reproducibility for both dipyrone and hyoscine butylbromide in presence of each other.

II- Spectrodensitometry:

The quantitative thin layer chromatographic technique has been used for separating dipyrone from hyoscine butylbromide. It was found that various common excipients and coloring matter did not interfere in the separation process.

Methyl para hydroxy benzoic acid was chosen as an internal standard with suitable R_f value.

A calibration graph (peak area ratio versus concentration) for either dipyrone or hyoscine butylbromide was constructed. It was rectilinear at low concentration and curved at high concentration. It was valid from 0.05 to 0.25 ul^{-1} for each of them.

The regression equation for each component was listed as follows:

For dipyrone:

$$Y = 0.003 + 3.95\ x \qquad r = 0.988$$

For hyoscine butylbrxomide:

$$Y = 0.015 + 12.03\ x \qquad r = 0.995$$

Where : x is the concentration in micrograms

r is the correlation coefficient.

y is the peak area ratio

The suggested methods has been assessed by determination of authentic mixtures in ratios as those claimed in the pharmacentical preparations, then applied to the determination of Buscopan compositum tablets and suppositories, the results are shown in Tables 3 & 4.

Statistical analysis of the results shows that the proposed method is accurate as indicated from the relative error and percentage recovery. These methods are also precise as shown from the relative standard derivation (Tables 3 & 4).

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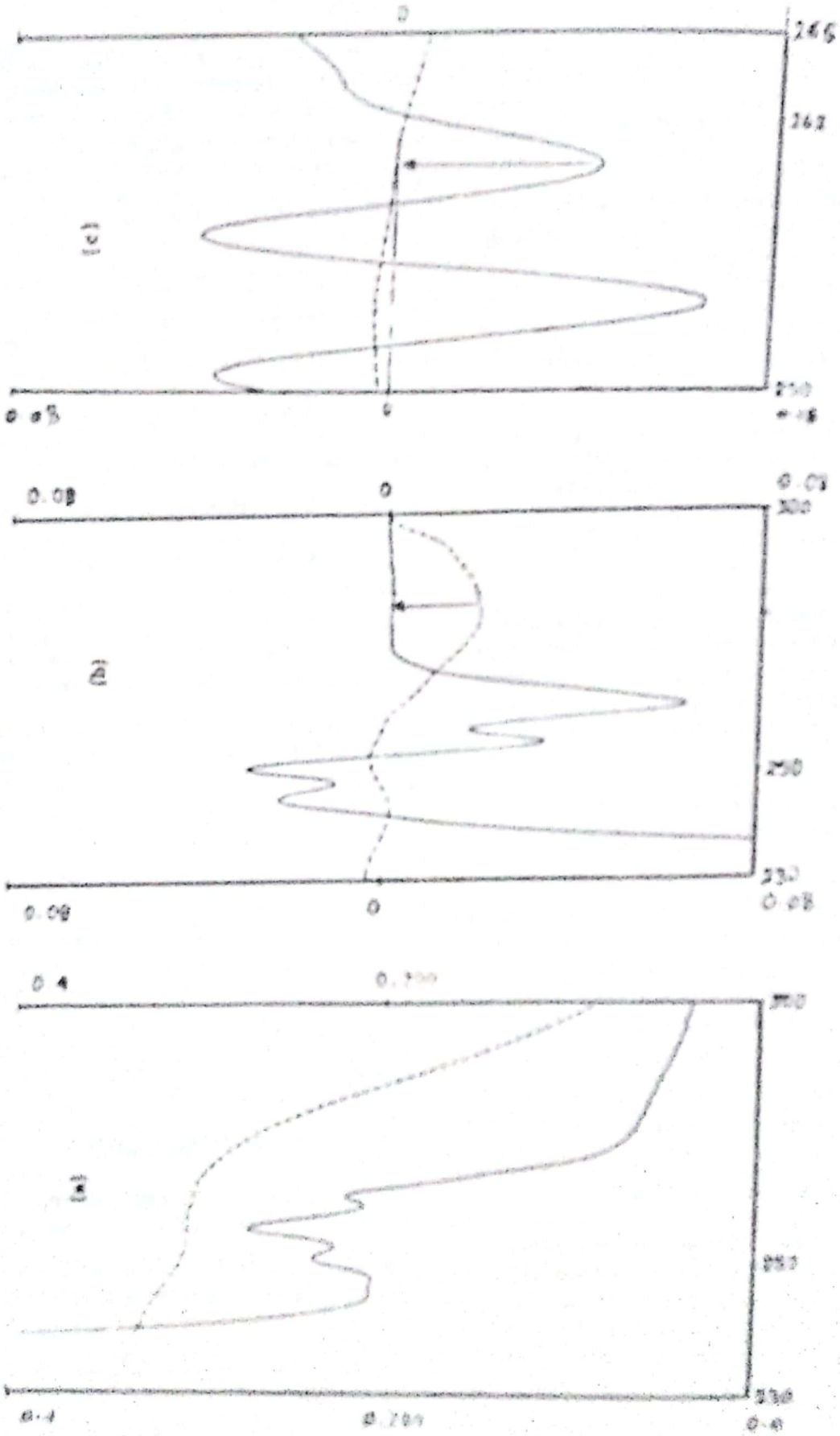

Fig 1 : U.V. absorption (a), ^1D (b) and ^2D (c) determination of dipyrone, 6 mg% (- - -) and hyoscine hydrobromide, 6 mg% (——)

Table (1): Optimum parameters for calibration curves construction.

Standard solution	Method	Concentration range mg%	λ nm	Regression analysis			C.V.%
				B	K	R	
Dipyrone (I)	^1D	2-10	280	-0.0159	16.7851	0.9998	0.9998
Hyoscine butylbromide (II)	^2D	2-10	260.5	0.0058	30.9814	0.9999	0.9999

C = B + KA.

Table (2): Results for the determination of the investigated drugs using the proposed and official methods.

Standard solution	Results, % mean ± S.D.		
	Official	Mod. Vierordt's method	Derivative spectrro.
Authentic dipyrone (I)	100.9 ± 0.78	-	100.7 ± 0.70 at (^1D) λ = 280 t = 0.22, F = 1.08
Authentic hyoscine butylbromide (II)	99.9 ± 0.51	-	100.2 ± 0.48 at (^2D) λ = 260.5 t = 0.95, F = 1.13
Lab. prep. mix. of I & II. for (I)	-	99.7 ± 0.38	99.9 ± 0.30 at (^1D) λ = 280 t = 0.18, F = 1.50
Lab. prep. mix. of I & II for (II)	-	99.8 ± 0.32	100.1 ± 0.32 at (^2D) λ = 260.5 t = 1.48, F = 1.00
Buscopan Comp. tab. for (I)	-	99.7 ± 0.38	99.8 ± 0.31 at (^1D) λ = 280 t = 0.67, F = 1.40
Buscopan Comp. tab. for (II)	-	99.8 ± 0.32	99.9 ± 0.31 at (^2D) λ = 260.5 t = 0.33, F = 1.00
Buscopan Comp. supp. for (I)	-	99.7 ± 0.38	99.6 ± 0.39 at (^1D) λ = 280 t = 0.19, F = 1.10
Buscopan Comp. supp. for (II)	-	99.8 ± 0.32	99.7 ± 0.28 at (^2D) λ = 260.5 t = 0.52, F = 1.25

* Means of five determinations. * P = 0.05. * t = (2.3), F = (5.05)

Table (3): Analysis of Buscopan compositum tablets using the proposed HPTLC method.

Dipyrone		Hyoscine butylbromide	
Conc. claimed. µg ul^{-1}	Recovery %	Conc. claimed ug µl-1	Recovery %
0.10	100.5	0.20	99.8
0.15	99.4	0.35	100.4
0.20	100.7	.50	99.7
0.25	99.8	0.65	99.5
0.30	100.3	0.80	99.9
Mean	100.1		99.8
SD	0.63		0.45
RSD	0.75		0.66
E rel.	0.50		0.40

Table (4): Analysis of Buscopan compositum suppositories using the proposed HPTLC method.

Dipyrone		Hyoscine butylbromide	
Conc. claimed. µg ul^{-1}	Recovery %	Conc. claimed ug µl-1	Recovery %
0.08	99.8	0.10	100.5
0.12	100.2	0.30	100.3
0.16	99.7	0.50	99.6
0.20	99.5	0.70	99.9
0.24	100.3	0.90	99.8
Mean	99.9		100.1
SD	1.10		0.7
RSD	9.80		0.5
E rel.	0.40		0.43

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تقدير الهيوسين بيوتيل بروميد والدايبيرون كل فى وجود الآخر

هشام سالم شرف الدين

صيدلية مصر - منيا القمح - الشرقية

فى هذا البحث تم فصل خليط من الهيوسين بيوتيل بروميد والدايبيرون بطريقة قياس الكثافة الضوئية على رقائق كروماتوجرافيا ذات التقنيه العالية لكل مكون دون تداخل من المواد الملونة أو أى مكونات أخرى الموجوده فى المستحضرات الصيدلية التى تحتوى على هذا المخلوط. كما تم تقدير كل منهما فى وجود الآخر بأستخدام طريقتى المشتقة التفاضلية الأولى والثانية لمنحنى الإمتصاص الطيفضوئى.

ولقد أوضحت النتائج المطبقة على مخاليط معملية وأقراص البوسكوبان كمبوزوتيم ولبوس البوسكوبان المركبة للأطفال أن الطرق المقترحة بسيطة وتماثل الطرق الدستورية المنشورة فى دقتها وتكرارها.