RESEARCH PAPER

Accepted 26 July 1997
Received 27 June 1996
Indian J. Pharm Sci., 1997, 59(6) pp. 295-298

Simultaneous Determination of Salbutamol and Etofylline by Third Derivative Ultraviolet Spectroscopy

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Simultaneous determination of salbutamol and etofylline using third derivative ultraviolet spectroscopy with zero crossing technique is reported in this communication. Third derivative amplitudes at 233.8 and 303 nm were selected for the assay of salbutamol and etofylline in combination respectively. This method showed good linearity and precision. The proposed method is successfully applied to the combination of these drugs in laboratory mixture and in tablet dosage form.

SALBUTAMOL, chemically 2-t-butylamino-1-(4-hydroxy-3-methyl phenyl) ethanol causes bronchial smooth muscle relaxation and thus relieves bronchospasm[1]. Etofylline is hydroxyethyl theophylline, a xanthine derivative has bronchial smooth muscle relaxant action and also has stimulant effect on respiration. Salbutamol and etofylline in combination induce bronchodialation and have been used in bronchial asthma and other branchopastic diseases[1].

Salbutamol is official in I.P. and B.P. which describe non aqueous titrimetric assay procedure for bulk drug and column chromatography followed by spectrophotometry for tablets[2,3].

Other reported method for salbutamol as a bulk is colorimetry[4]. Salbutamol with terbutaline is assayed by derivative spectrometry[5,6] and with beclomethasone[7] by difference spectroscopy in tablet dosage form[8]. HPLC method was used in combination with theophylline[9], bamipine[10] and with combination of ipratropium bromide and terbutaline[11]. The reversed phase HPTLC was used with beclomethasone dipropionate[12]. Etofylline is official in I.P. and B.P. wherein non aqueous titrimetry[13,14] is reported. Other reported methods are spectrophotometry[15,16], colorimetry[17] and HPLC[18]. For combination of salbutamol and etofylline, only reversed phase HPLC has been reported[19].

EXPERIMENTAL

A Shimadzu (Model UV-160A) instrument was used for spectral measurement in 10 mm matched quartz cells. Instrumental parameters were ; spectral slit width-2 nm, scan speed-2400 nm/min., wavelength range-200 to 350 nm and absorbance scale setting an 0 to +2.5. Third derivative spectra was recorded using an inbuilt data processing facility.

Distilled water free from any particulate matter was used as a solvent. Salbutamol sulphate and etofylline were procured and used as such.

Different dilutions of salbutamol and etofylline ranging from 0 to 60 ug/ml were prepared. Each dilution was scanned in the uv range of 200 to 350 nm and converted to third derivative using key entry 7 ($\Delta\lambda$24.5 nm) selected through experimentation. Two working wavelengths, 233.8 and 303 nm were selected for salbutamol and etofylline, respectively. Amplitude of each dilution was measured at these selected wavelengths. A linear relationship was observed between 5 - 27.5 ug/ml and 5 - 31 µg/ml for salbutamol and etofylline, respectively.

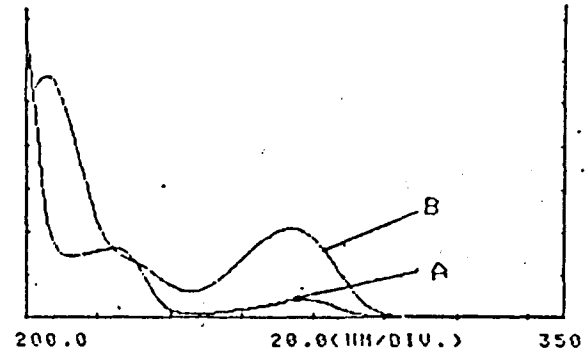

Fig. 1: Overlay Spectra of Salbutamol (A) and Etofylline (B)

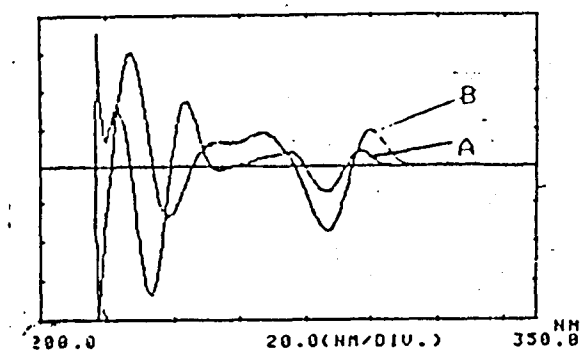

Fig. 2: Overlay Spectra of Salbutamol (A) and Etofylline (B) In Third Derivative Order at key entry 7(Δ λ 24.5 nm)

A mixed standard of salbutamol (11 mg) and etofylline (12.4 mg) was prepared in a 100 ml volumetric flask. Five different dilutions were prepared using 0.5, 1.0, 1.5, 2.0 and 2.5 ml of the mixed standard which were diluted to 10 ml with distilled water. Each solution was analysed on an uv spectrophotometer as described in the linearity study. Amplitude was measured and plotted against concentration to prepare a calibration graph (Analytical data shown in Table - 1).

Twenty tablets were powdered. An accurately weighed powdered sample equivalent to 2 mg of salbutamol and 124 mg of etofylline was transferred to a 100 ml volumetric flask, extracted with 10 ml of distilled water for 10 min and filtered. The filtrate

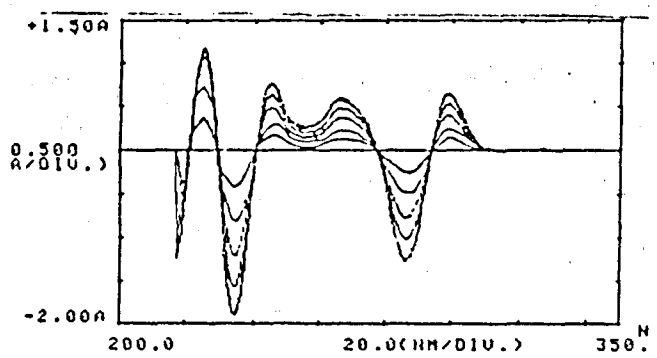

Fig. 3: Overlay Spectra of Salbutamol and Etofylline at different Concentrations In Third Derivative Order

was adjusted to 100 ml with distilled water. To 1 ml of filtrate, 10 ml of solution 'A' was added and final volume was adjusted to 100 ml with distilled water. The spectrophotometeric analysis of the resulting solution was carried out using distilled water as reference.

RESULTS AND DISCUSSION

The normal spectra of salbutamol and etofylline are shown in figure - 1. Etofylline showed peaks at 273 and 210 nm. However, salbutamol also absorbs over the same wavelength range with two peaks at 276 and 225 nm. Because of the extensive overlapping of the spectral bands of both these drugs, coventional uv spectroscopic method could not employed for the determination of two drugs in mixture. In the derivative mode of third order, spectra was resolved (Fig. - 2). Derivative spectrum was found suitable for the determination of both these drugs. The selection of wavelengths for the estimation of salbutamol and etofylline was on the basis of zero crossing method. Third derivative amplitude at 233.8 nm (zero crossing of etofylline) and 303 nm (zero crossing of salbutamol) was selected for the estimation of salbutamol and etofylline, respectively. Figure-3 shows third derivative spectra of salbutamol and etofylline at different concentration.

Linearity range of salbutamol was found between 5 and 27.5 ug/ml and for etofylline the range was

Table 1
Analytical Data for (A) Linearity (B) Calibration Graph for Salbutamol and Etofylline by Third Derivative UV Spectroscopy

S.No.	Drugs	Method	Linearity range (ug/ml)	Regression Slope	Parameter Intercept	Correlation coefficient
(A)						
1.	Salbutamol	$^3D_{233.8}$	5.0-27.5	0.0139677	0.008601	0.997325.
2.	Etofylline	$^3D_{303.0}$	5.0-31.0	0.0704724	-0.03215	0.999479.
(B)						
1.	Salbutamol	$^3D_{233.8}$	5.0-27.5	0.0653364	0.049550	0.999388.
2.	Etofylline	$^3D_{303.0}$	5.0-31.0	0.0152744	0.006400	0.999140.

Table 2
Results for the determination of Salbutamol and Etofylline in Standard Laboratory Mixture and Commercial Formulation by proposed Method and Recovery Results

	Salbutamol			Etofylline		
	Found (%)	SD	CV	Found (%)	SD	CV
Standard Laboratory Mixture	100.5	0.6545	0.5795	99.20	2.00	2.025
Tablet Formulation	99.63	1.4960	1.5030	100.91	1.715	1.700
Recovery Results (%)		97.215			99.440	

SD=Standard Deviation, CV= Coefficient of Variance.

5 to 31 ug/ml. Regression parameters and correlation coefficient for linearity and calibration curve is shown is Table-1. The parameters obtained were found satisfactory.

The validity of the proposed method was studied using a standard laboratory mixture and a marketed formulation. The composition of the standard mixture was kept similar to the marketed formulation (2 mg salbutamol and 124 mg etofylline). Results are shown in Table - 2.

Recovery results obtained for the two drugs, salbutamol and etofylline were 97.2 %, 99.4 % respectively, standard deviation ranges from 1.5 to 1.72 and coefficient of variance ranges from 1.5 to 1.7 for both the drugs in tablets formulation. The developed method is found to be accurate, precise, simple and rapid for the assay of a combination of salbutamol and etofylline in bulk powder as well as marketed formulations during routine analysis.

ACKNOWLEDGEMENTS

Authors are thankful to M/s Nicholas Piramal Ltd., Pithampur, Dist. Dhar (M.P.) for providing the gift samples of salbutamol and etofylline, the facilities provided by the Head, Department of Pharmacy,

S.G.S.I.T.S., Indore and the Director, S.G.S.I.T.S., Indore to carry out all the research work are thankfully acknowledged.

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