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## Simultaneous Determination of Terbutaline Sulphate, Bromhexine Hydrochloride and Guaiphenesin in Three-component Tablet formulation by UV Spectrophotometry

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Derivative spectrophotometric and multiwavelength spectrophotometric methods have been developed for simultaneous determination of terbutaline sulphate, bromhexine hydrochloride and guaiphenesin in three-component tablet dosage forms. Methanolic hydrochloric acid (0.1 N) was used as the solvent. Terbutaline sulphate shows absorbance maximum at 279 nm, bromhexine hydrochloride shows two absorbance maxima, one at 318 nm and the other at 248 nm and guaiphenesin shows absorbance maximum at 274 nm. All the three drugs obey Beer's law in the concentration ranges employed for the methods. The methods have been validated statistically and by recovery studies.

Terbutaline sulphate (TBS) is a synthetic sympathomimetic agent and is used in bronchitis, asthma and other bronchospastic diseases<sup>1</sup>. Bromhexine hydrochloride (BH) is a mucolytic agent used in symptomatic treatment of respiratory disorders associated with viscid mucus<sup>2</sup>, whereas guaiphenesin (GP) is used as an expectorant<sup>3</sup>. The IP<sup>4</sup> and USP<sup>5</sup> describe spectrophotometric methods for the analysis of TBS in formulations, whereas USP<sup>6</sup> describes a HPLC method for the estimation of GP in formulations. For formulations containing BH, the IP<sup>7</sup> describes a spectrophotometric method. A number of methods<sup>8-13</sup> have been reported for the analysis of the bulk drugs as well as dosage forms of BH and GP. Various methods have also been reported<sup>14,15</sup> for quantitation of TBS in single as well as combined dosage forms. However, no analytical method is available for simultaneous estimation of these three drugs in a combination.

Shimadzu (Model: UV 160 A) UV/Visible recording spectrophotometer was used with instrumental parameters such as, spectral bandwidth:2 nm, scan speed 480 nm/min, wavelength sampling interval:0.1 nm (derivative spectroscopy) and 0.2 nm (multiwavelength spectroscopy). Terbutaline sulphate (IP), bromhexine hydrochloride (IP), guaiphenesin (USP), methanol (Qualigens, Spectroscopic grade) and hydrochloric acid (Ranbaxy, AR grade) were used for the present work.

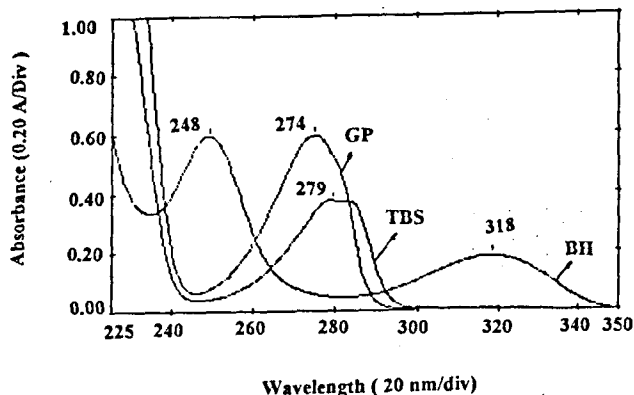
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From the overlay spectrum (Fig. 1) of TBS (50 µg/ml), BH (20 µg/ml) and GP (50 µg/ml), the wavelength selected for estimation of BH was 318 nm where TBS and GP showed zero absorbances. Standard calibration curve of BH was prepared in the concentration range of 4-40 µg/ml.

Estimation of GP was performed at 284.8 nm from the third order derivative spectrum ( $\Delta\lambda=6.3$  nm), where TBS and BH showed a common zero crossing point (Fig. 2). Standard calibration curve for GP was prepared using mixed standard solutions containing TBS:BH:GP in the concentration ratio of 2.5:4:25, 2.5:4:50, 2.5:4:75, 2.5:4:100 and 2.5:4:125 (mcg/ml). As BH and GP show zero absorbances at 284.2 nm in fourth order derivative spectrum ( $\Delta\lambda=5.4$  nm), this wavelength was used for determination of TBS (Fig.3). Standard calibration curve for TBS was prepared using mixed standard solutions containing TBS:BH:GP in the concentration ratio of 20:4:100, 25:4:100, 30:4:100, 35:4:100 and 40:4:100 (mcg/ml). These concentration ratios were chosen keeping in view the amount of three drugs in marketed formulation.

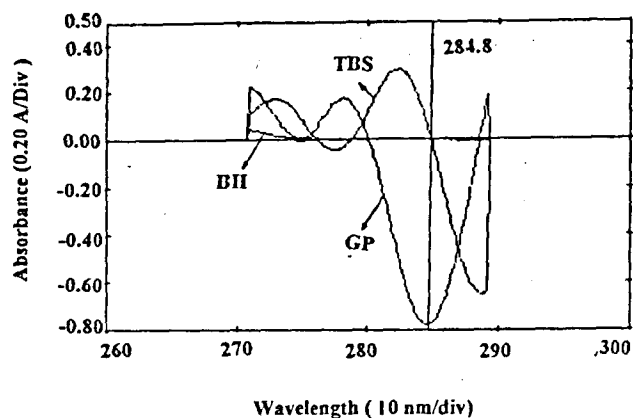
An accurately weighed quantity of the powdered tablets, equivalent to 100 mg of GP (4 mg of BH and 2.5 mg of TBS), was used for analysis. Tablet sample solutions were prepared using 0.1 N methanolic hydrochloric acid, by dissolution, filtration through Whatman filter paper



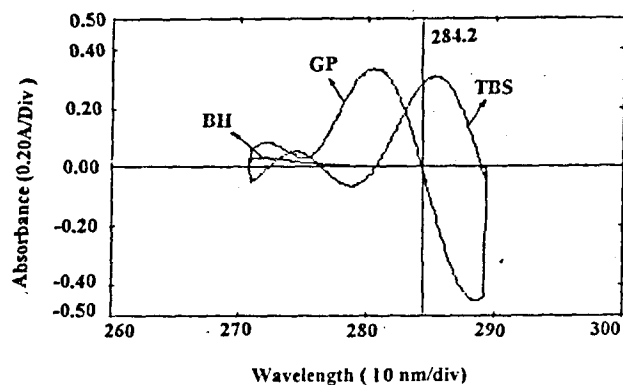
**Fig. 1 : Overlay Spectrum of Terbutaline Sulphate (TBS), Brohexine Hydrochloride (BH) and Guaiphenesin (GP)**

no. 41 and dilution to 100 ml (stock solution). Stock solution (5 ml) was diluted to 10 ml and absorbance of the resulting solution was measured at 318 nm and estimation of BH was carried out. For estimation of GP, 1 ml of the stock solution was diluted to 10 ml and absorbance of the resulting solution was measured from the third derivative spectrum at 284.8 nm. For estimation of TBS, 1 ml of the stock solution was taken, 1 ml of standard TBS (200 cg/ml) was added to it and absorbance of the resulting solution after diluting it to 10 ml was measured from the fourth order derivative spectrum at 284.2 nm. The results of analysis, obtained by repeating the method five time each with two different batches of the formulations, and results of recovery studies are given in Table 1.

For multiwavelength spectroscopy, nine mixed standards and four sampling wavelengths as 318, 279, 265 and 248 nm were selected for experimentation. The nine mixed standard solutions containing TBS, BH and GP in the concentration ratio of 50:0:0, 0:20:0, 0:0:50, 20:4:20, 30:8:40, 40:12:60, 50:16:80, 25:20:100 and 20:4:100 ( $\mu\text{g/ml}$ ) were prepared. All the mixed standard solutions were scanned over the range of 350 nm to 225 nm in the multicomponent mode using the four sampling wavelengths as mentioned. The spectral data obtained from the scan of nine mixed standards were used to determine the concentrations of all the drugs in the tablet sample solution, prepared as described under earlier method. Stock solution (1 ml) was taken, 1 ml of standard TBS (200 mcg/ml) was added to it and volume was made upto 10 ml. Spectrophotometric analysis of the resulting solution was carried out using the multicomponent mode of the instrument. The results of analysis and recovery were satisfactory and are shown in Table I.



**Fig. 2 : Third Order Derivative Spectrum of Terbutaline Sulphate (TBS), Brohexine Hydrochloride (BH) and Guaiphenesin (GP)**



**Fig. 3 : Fourth Order Derivative Spectrum of Terbutaline Sulphate (TBS), Brohexine Hydrochloride (BH) and Guaiphenesin (GP)**

Both the proposed methods were found to be simple and rapid for routine analysis of all three drugs in combined dosage forms. Derivative spectroscopy method utilises the Zero Crossing Point technique of measurement for estimation of TBS and GP. Rate of change of absorbance with respect to wavelength was nearly constant for BH over the wavelength region used for analysis and hence the particular wavelength range was selected for analysis. The standard deviation values and recovery studies were satisfactory keeping in view amount of drugs in the formulation.

In multiwavelength spectroscopy, the instrument collects and compiles the spectral data from the scan of nine mixed standards and produces the results by matrix calculations. Nine mixed standards and four

Table I - Analysis of Commercial Formulations

Method	BH			GP			TBS		
	Mean(%)* estimated	S.D.	R.S.	Mean(%)* estimated	S.D.	R.S.	Mean(%)* estimated	S.D.	R.S.
D.S.	99.34	0.97	98.9-100.8%	99.41	1.09	99.1-100.6%	98.96	2.14	98.8-102.1%
M.S.	99.47	0.86	99.4-101.1%	99.16	0.97	98.9-101.3%	99.09	1.81	100.1-101.7%

\* Average of five determinations each on two different batches of tablets containing BH, GP and TBS. D.S.=Derivative Spectroscopy, M.S.= Multiwavelength Spectroscopy, R.S.= Recovery Studies and S.D.= Standard Deviation.

sampling wavelengths were selected through experimentation keeping in view, the amount of drugs in the formulation and molar absorptivity coefficients of all the three drugs. The method requires no manual calculations.

In both the methods, additional but a known amount of TBS was added to the sample being analysed to increase its absorbance contribution which improve the accuracy of estimation.

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