Dextromethorphan Hydrobromide and Bromhexine Hydrochloride : Simultaneous Estimation by Two-Wavelength and Derivative Spectroscopic Methods

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A simultaneous analysis of two component formulation containing dextromethorphan HBr and bromhexine HCl by two-wavelength and derivative spectroscopic methods has been achieved. Dextromethorphan HBr and bromhexine HCl show linearity in the range of 0-120 μg/ml and 0-40 μg/ml respectively. In the two wavelength method, wavelengths selected for dextromethorphan HBr were 278.2 nm and 333.4 nm and for bromhexine HCl were 245.0 nm and 294.6 nm. In derivative spectroscopy, estimation of dextromethorphan HBr and bromhexine HCl was carried out in the 4th order (N=9) at 259.0 nm and 255.4 nm respectively. The results of the analysis of both methods have been statistically validated and were found to be satisfactory. Both methods are simple, rapid and accurate.

DEXTROMETHORPHAN HBr (DXH) is a narcotic antitussive which acts centrally and reduces cough reflex. BP[1] specifies a non-aqueous titration method in powder form whereas, HPLC method is reported in IP[2] for its estimation in syrup form. Few spectrophotometric[3-5] and chromatographic[6-7] methods are reported for its estimation. Bromhexine HCl (BH) is a mucolytic drug, used for its expectorant action. IP[8] suggests alkalimetry titration method for estimation in powder form and BP[9] shows spectrophotometric estimation in tablet form for BH. The reported methods available for its analysis individually and in combination in formulations include spectrophotometric[10-11], chromatographic[12] and some other[13-14] methods. Commercially liquid oral formulation (syrup) of DXH (10 mg/10 ml) and BH (8 mg/10 ml) is available. But no method has yet reported for simultaneous estimation in combined dosage forms.

A Shimadzu UV/ VIS recording spectrophotometer (Model 160 A) was employed with spectral bandwidth of 3 nm, wavelength accuracy of 0.5 nm with automatic wavelength correction and a pair of 10 mm matched quartz cells. Dextromethorphan HBr (IP), bromhexine HCl (BP), hydrochloric acid (Ranbaxy, A. R. Grade), chloroform (Ranbaxy, A. R. Grade), sodium hydroxide (Qualigens, ExcelaR) and double distilled water were used in the present study.

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Stock solutions of DXH (600 μg/ml) and BH (200 μg/ml) were prepared separately in 0.1 N HCl. Standard solutions of DXH (120 μg/ml) and BH (40 μg/ml) were prepared by further dilution with 0.1 N HCl. DXH shows linearity in the range of 0-120 μg/ml and BH from 0-40 μg/ml. By least square method the slope, intercept and correlation coefficient for DXH were 145.6, 0.118 and 0.998 and for BH these were 38.0, 0.39 and 0.999 respectively.

From the overlain spectra (Fig-1) the wavelengths selected for estimation of DXH are 278.2 nm and 333.4 nm and for BH are 245.0 nm and 294.6 nm.

Fig. 1: Overlain spectra of Dextromethorphan hydrobromide (A) and bromhexine hydrochloride (B)

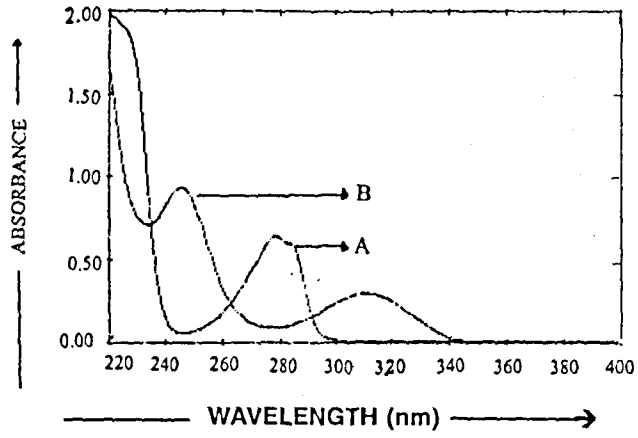


TABLE-1 : ANALYSIS BY THE PROPOSED METHODS

Method	Drug Conc.(μg/ml)		Estimated Conc. (μg/ml)		Percent Estimated	
	DXH	BH	DXH	BH	DXH	BH
	24	8	23.9	7.89	99.75	98.67
T.W.	60	20	60.7	20.20	101.2	101.25
	96	32	96.3	32.28	100.4	100.89
S.D.	0.731	0.810				
C.O.V.	0.727	0.808				
S.E.	0.422	0.467				
	24	8	23.7	7.78	98.87	97.25
D.S.	60	20	60.3	19.83	100.6	99.15
	96	32	93.6	32.07	97.50	100.24
S.D.	1.283	1.280				
C.O.V.	1.297	1.294				
S.E.	0.740	0.739				

TABLE - 2 : RESULTS OF ANALYSIS OF SYRUP FORMULATIONS

Method	Batch	Label Claim (mg/10 ml)		Found* (mg/10 ml)		Percent Found		S.D.		C.O.V.		S.E.	
		DX	BH	DX	BH	DXH	BH	DXH	BH	DXH	BH	DXH	BH
T.W.	B-I	10	8	9.91	8.06	99.17	100.7	1.001	0.90	1.01	0.96	0.451	0.43
	B-II	10	8	9.76	7.91	97.68	98.99	0.901	0.90	0.911	0.93	0.441	0.40
D.S.	B-I	10	8	9.75	8.08	97.52	101.0	1.201	1.10	1.221	1.02	0.540	0.49
	B-II	10	8	9.79	7.93	97.97	99.24	0.905	1.25	1.201	1.26	0.480	0.51

Six mixed standards having concentrations 0, 24, 48, 72, 96, 120 μg/ml of DXH and 40, 32, 24, 16, 8, 0 μg/ml of BH respectively were prepared by using the appropriate volume of standard solutions. Solutions were scanned at the selected wavelengths in the quantitative mode of the instrument and the absorbance difference were used to plot the calibration curves.

In order to assess the validity of the proposed method for assaying each drug in presence of other component, standard laboratory samples were prepared taking the concentration of each component as in the formulation under consideration as well as random samples and assayed. Results are recorded in Table -1 which are statistically validated.

TABLE - 3 : RECOVERY STUDIES BY PROPOSED METHODS

St. Parameters	T.W.				D.S.			
	B-I		B-II		B-I		B-II	
	DXH	BH	DXH	BH	DXH	BH	DXH	BH
Percent Mean**	99.72	98.87	99.87	100.7	99.76	100.7	99.55	100.9
S.D.	1.048	0.892	1.292	0.826	1.247	0.808	1.293	0.853
C.O.V.	1.059	0.902	1.293	0.820	1.250	0.802	1.238	0.845
S.E.	0.828	0.446	0.646	0.413	0.624	0.404	0.504	0.427

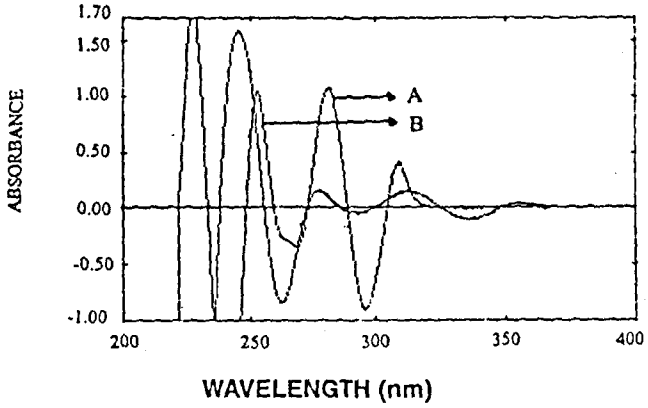
* Mean of Five Readings, ** Mean of Four Readings, T. W. = Two - Wavelength
D. S. = Derivative Spectroscoy, S. D. = Standard Deviation, S. E. = Standard Error
C. O. V. = Coefficient of Variance, DXH = Dextromethorphan HBr, BH = Bromhexine HCl

Ten ml of commercial syrup sample containing DXH and BH was taken and to it 14mg DXH was added (standard addition method). It was then made alkaline with 5 ml of IN NaOH. The resulting solution was extracted with successive amounts of chloroform (15 ml, 10 ml, 10 ml and 10 ml) and the extracts were collected. The solvent was driven off under vacuum. The residue was dissolved in 0.1 N HCl and the volume was made upto the 100 ml. This was treated as stock solution. The samples were scanned at selected wavelengths for DXH and BH from the absorbance difference values the concentration of each component was obtained from the calibration curves of the respective drugs. The results obtained by repeating the procedure with two different batches of syrup are recorded in Table-2 .Recovery study conducted by addition of different amounts of pure drugs to preanalysed syrup samples. The results are statistically validated and recorded in Table - 3.

The DXH and BH was estimated in fourth order (N=9) at 259.0 nm and 255.4 nm respectively. (fig.-2) Six mixed standards as mentioned under two-wavelength method were used to prepared the calibration curves. The absorbances of these mixed standards at 259.0 nm and 255.4 nm in the fourth order with sampling interval of 27 nm were used to plot the calibration curves for DXH and BH respectively.

Standard laboratory samples, similar to those in the above method, were prepared to validate the method. Results and their statistical validation are recorded in Table 1.

Fig. II: Fourth order (N=9) derivative spectra of dextromethorphan hydrobromide (A) and bromhexine hydrochloride (B)



Syrup samples were prepared as described under two wavelength method. Samples were derivatized in the fourth order (N=9) and absorbances were recorded at the specified wavelengths for DXH and BH. Concentration of each component in the sample solution was obtained from the calibration curves prepared. Results obtained by replicate analysis each time with two batches of syrups are statistically validated and are reported in Table 2. The recovery studies gave satisfactory recovery data which are tabulated in Table 3.

Both methods were found to be simple, rapid and accurate for routine simultaneous estimation of DXH and BH in syrup formulations. The values of standard deviation are low and recovery was close to 100 % indicating the

reproducibility and accuracy of the methods. The absorbance difference between two points on the mixture spectra is directly proportional to the concentration of the component of interest, independent of the interfering component is the basic principle underlying the two wavelength method of analysis.

In the second method employing derivative spectroscopy, first, second, third and fourth order derivative spectra of both the drugs were observed and fourth order spectra was selected keeping in view the resolution and sensitivity of the instrument used. Both the drugs did not interfere at the wavelengths used.

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Mucoadhesive Formulations of Theophylline

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Buccal mucoadhesive films and mucoadhesive gels of theophylline were prepared using Hydroxy Propyl Methyl Cellulose (HPMC), Ethyl cellulose (EC), and Carbopol. The drug release pattern and stability of these formulations were studied. The *in vitro* drug release and *in situ* intestinal drug absorption were higher with formulations containing Carbopol.

ONE of the significant approaches in the modern drug delivery systems is to target the drug to particular site of the body. In the living body, mucosal surfaces are available in the gastrointestinal tract, urogenital tract, air ways, nose, ear and eye. Nagai et al.[1] utilized the combination of HPMC and Carbopol 934 to prepare oral bioadhesive tablets for the administration of insulin. Studies using benzydamine and lidocaine employing carbopol have been reported[2]. Buccal mucoadhesive films of theophylline were prepared to avoid the gastrointestinal irritation commonly experienced on oral administration.

The films were prepared by a method employed by Roopa et al.[3] The composition of the films were as follows, Drug:Polymer-1:10, HPMC:EC-3:1, Carbopol -0.0%, 3.0% w/w. Drug was dissolved in ethanol. HPMC 15 cps, EC and Carbopol (940NE) were separately dissolved in ethanol. The two were mixed and the resulting mass was sonicated and poured on to specially designed rectangular glass mould (3X5 cm)lined with aluminum foils. It was

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