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Simultaneous Estimation of Phenylephrine Hydrochloride and Benzyl Alcohol by First Derivative Spectrophotometric Method

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ABSTRACT

A simple, precise and economical procedure for the simultaneous estimation of Phenylephrine Hydrochloride (PHE) and Benzyl Alcohol (BEN) in formulation has been developed. PHE is a Vasocostracting agentandBEN is a Local anaesthetic agent. The absorbance values 229.6 nm and 274.2 nm of first derivative spectrum was used for the estimation of PHE and BEN, respectively without mutual interference. This method obeyed beer's law in the concentration range of 25-250 µg/ml and 0.125-1.5 mg/ml forPHE and BEN respectively, in Methanol: Water (1:1) ratio.The slope and intercept for PHE were -0.001 and -0.008 and for BENwere -0.028 and -0.001 respectively as determined by the method of least squares. The results were found satisfactory and reproducible. The method was applied successfully for the estimation of PHE and BEN simultaneously in dosage form without the interference of common excipients.

Keywords: Benzyl Alcohol, Phenylephrine Hydrochloride, Derivative spectrophotometry, Simultaneous Estimation..

1. INTRODUCTION

Benzyl alcohol has been used as a local anesthetic for brief superficial skin procedures. Benzyl alcohol is an opium alkaloid used as a popular antiseptic in hundreds of products for its bacteriostatic properties[1]. It is commonly added to physiologic saline solution (0.9% benzyl alcohol– bacteriostatic saline solution) and ubiquitously available. The anesthetic effect of benzyl alcohol was first described in 1918, and its safety has been clearly demonstrated[2-3]. Benzyl alcohol has been used as a local anesthetic for brief superficial skin procedures; however, its efficacy for long-term dermal anesthesia has not been established[4-5] Benzyl alcohol is quantitatively determined by gas chromatography. Phenylephrine is a selective α1-adrenergic receptor agonist used primarily as a decongestant, as an agent to dilate the pupil, and to increase blood pressure.Derivative spectrophotometry is a very useful analytical technique for determining binary and multicomponent mixtures of drugs with overlapped spectra. Even though various analytical methods were reported for the estimation of BEN and PHE in their individual dosage forms as well as in combination with other drugs, none of the methods reported for simultaneous estimation of both compounds in the mixture by the present developed methods. Several analytical methods that have been reported for the estimation of benzyl alcohol formulations include derivative spectrophotometric method with other drugs[6]. Various methods have been reported in the literature for the analysis of phenylephrine hydrochloride including spectrophotometry[7-10], spectrophotometry with chromogenic reagent[11], High-performance liquid chromatography[12-15], and chromatography[16]. Micellar liquid chromatography[17], micellarelectrokinetic chromatography[18], capillary zone electrophoresis[19-20], spectro-fluorimetric and derivative spectrophotometric methods[21], have also been reported for the determination of phenylephrine hydrochloride.

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2. MATERIALS AND METHODS

Phenylephrine hydrochloride was obtained as a gift sample from Unichem Laboratories Ltd., Pithampur, and Benzyl alcohol was purchased from Sigma Aldrich.The water used in this work was doubly distilled and all other chemicals and reagents used were of analytical grade and were purchased from Sigma Aldrich.

2.1 Instrumentation

Derivative spectrophotometric method has been developed for the simultaneous estimation of BEN and PHE by using zero crossing first derivative spectroscopic method. The derivative UV spectra of standard and test solutions were recorded in 1 cm quartz cells using a Shimadzu UV/Vis-1601 double beam UV/Vis spectrophotometer (Japan) with a fixed slit width of 2 nm. The zero order and first derivative absorption spectra were recorded over the wavelength range 200-400 nm against the solvent blank.

2.2 Experimental

2.2.1 Study of Spectra and Selection of Wavelengths

The aliquot portions of standard stock solutions of PHE and BEN were diluted appropriately, with methanol: water (1:1) to obtain a concentration 20µg/ml of PHE and 20µg/ml of BEN respectively. The solutions were scanned in the range of 400-200nm in 1.0 cm cell against reagent blank. The overlain zero order spectra of PHE and BEN shows that the absorption maxima of BEN was overlapping with the absorption maxima of PHE, rendering the zero order determinations inaccurate. So a first order spectrum of both drugs in combination was developed. A 1st order overlain spectrum of PHE shows zero crossing points at 241.6nm, and 274.2 nm. 274.2nm was selected for the estimation of BEN because at this wavelength, BEN shows zero absorbance. A 1st order overlain spectrum of BEN shows zero crossing points at 229.6nm and 257.8nm. 229.6nm was selected for the estimation of PHE because at this wavelength, PHE shows zero absorbance figure 1.

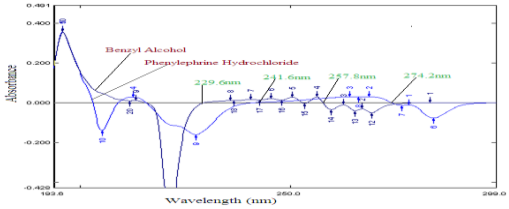

Figure 1: Overlain first order derivative spectra of Benzyl Alcohol and Phenylephrine Hydrochloride.

2.2.2 Standard Working Solutions

An accurately weighed quantity of PHE (100mg) and BEN (100mg) was dissolved in solvent (Methanol: water) in 100 ml volumetric flask and volume was made up to mark with solvent (1000µg/ml). Eight serial dilutions of PHE and BEN were prepared in mixed, from the stock solutions in the conc. range of 25–200µg/ ml and 0.125mg–1mg/ml respectively. The curves of the solutions were scanned in the range of 200nm – 400nm against methanol: water as the blank. This technique involves the differentiation of the normal spectrum with respect to the wavelength. The first derivative spectra of the PHE spectrum shows a zero crossing point at 274.2nm, BEN is measured at this wavelength.The first derivative spectra of the BEN spectrum shows a zero crossing point at 229.6 nm, BEN is measured at this wavelength in figure 2

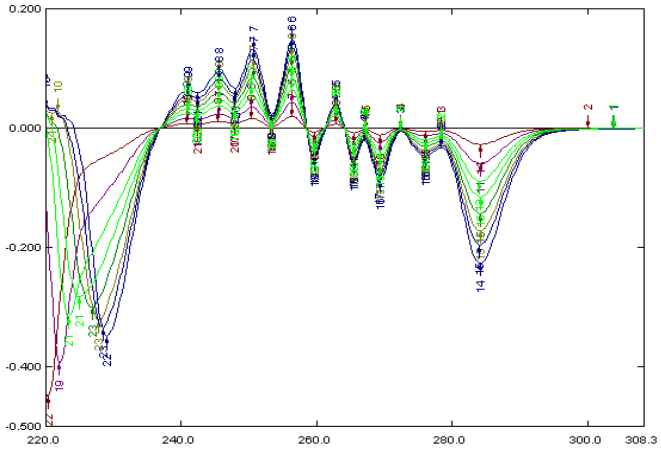

Figure 2: Overlain first order derivative spectra of Benzyl Alcohol and Phenylephrine Hydrochloride in combination.

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2.2.3 Calibration Curve of Phenylephrine Hydrochloride and Benzyl Alcohol by 1st Derivative Method

The stock solution of Phenylephrine Hydrochloride and Benzyl Alcohol was prepared in mixed, to obtain final strength of 1 mg/ml and 5mg/ml respectively.Standard solutions were prepared in the concentration range of 25-200µg/ml and 0.125-1.0 mg/ml by suitable dilutions of the stock solution in methanol: water and absorbance were taken at 229.6nm and 274.2nm for PHE and BEN respectively by UV Spectroscopy (as shown in figure 3 and Table 1).

2.2.4 Sample Analysis

The drug content of formulations was determined by 1st derivative spectroscopy. Briefly, 1ml formulation equivalent to

1mg of phenylephrine hydrochloride and 5 mg of benzyl alcohol was diluted with 50 ml methanol: water (1:1) and agitated for 30 minutes. The solution was filtered through whattman filter paper. After appropriate dilutions, the absorbances were measured and the concentration of phenylephrine hydrochloride and benzyl alcohol was determined by measuring the absorbance at 229.6nm and 274.2nm respectively, using spectrophotometer (Shimatzu 1601, Japan) after converting it in to 1st derivative graph, data given in table 2. The concentration of each analyte was determined with the equations generated from calibration curve of respective drugs.

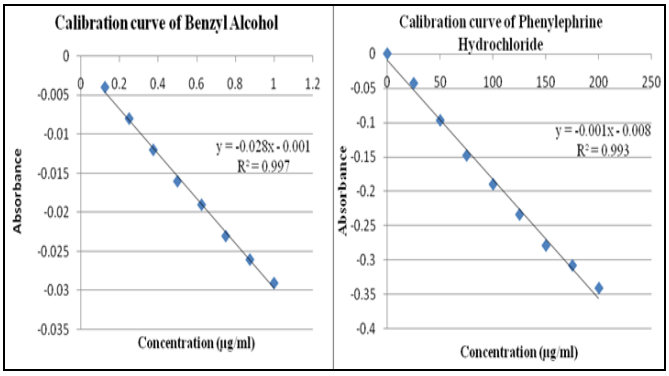

Figure 3: Calibration curve of Benzyl Alcohol and Phenylephrine Hydrochloride.

Table No.1 Calibration data of PHE and BEN

Compound	Conc. (µg/ml)	Absorbance	Correlation coeff.	Regression Equation
Phenylephrine Hydrochloride At 229.6nm	25	-0.043	**0.993**	**Y= -0.001x-0.008**
	50	-0.097		
	75	-0.148		
	100	-0.190		
	125	-0.234		
	150	-0.279		
	175	-0.308		
	200	-0.341		
Benzyl Alcohol at 274.2nm	0.125	-0.004	**0.997**	**Y= -0.028x-0.001**
	0.250	-0.008		
	0.375	-0.012		
	0.500	-0.016		
	0.625	-0.019		
	0.750	-0.023		
	0.875	-0.026		
	1.000	-0.029		

3. RESULTS AND DISCUSSION

The zero-order spectra of pure drugs were found to be overlapping making their simultaneous determination difficult. The first derivative spectrophotometric method was considered to be ideal to facilitate their quantitative determination. It was observed during initial study that first derivative spectra have ideal zero-crossing points for the estimation of BEN and PHE in their combined dosage form. The method utilizes eight mixed standard solutions which were scanned in a wavelength range of 200-400 nm against methanol: water (1:1) as blank. There was no interference of BEN at 229.6nm a signal of first derivative spectrum of PHE, thus this wavelength was selected for quantification of PHE, while there was no interference of PHE at 274.2nm a signal of first derivative spectrum of BEN, thus this wavelength was selected for quantification of BEN. For both the drugs eight point calibration curves were generated. Result of analysis of formulation showed % relative standard deviation value 0.8862 for BEN and 0.8538 for PHE, which indicates repeatability of the method.

Table No.2 Analysis of Formulation of Benzyl Alcohol and Phenylephrine Hydrochloride.

Sample No.	Conc.of BEN (mg)		%	Conc. of PHE (mg)		%
	Th.	Exp.		Th.	Exp.	
1.	5	5.05	101.1	1	0.99	99.0
2.	10	9.96	99.6	2	1.99	99.5
3.	15	14.92	99.53	3	3.02	100.66
Mean			100.07			99.72
SD			0.8869			0.8515
%RSD			0.8862			0.8538

4. CONCLUSION

A quick and accurate method for determining benzyl alcohol and phenylephrine hydrochloride was developed by using first derivative spectrophotometry. The advantage of this method is that both constituents can be determined directly in a single sample without the need to be separated. It was also found that auxiliary drug components had no effect on the results of determination obtained under established conditions.The derivative spectrophotometric method is relatively easy, fast and cheap for the determination of the benzyl alcohol and phenylephrine hydrochloride, because it does not require expensive solvents and reagents.

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