RESEARCH PAPER

Simultaneous Estimation of Chlorzoxazone and Paracetamol from Solid dosage forms Employing Simultaneous Equations and Derivative Spectrophotometry

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Two accurate and economical procedures for simultaneous estimation of chlorzoxazone and paracetamol in two component tablet formulation have been developed. The methods employ first derivative ultraviolet spectrophotometry and simultaneous equations for the simultaneous estimation of the two drugs.
In 0.02 M sodium hydroxide, chlorzoxazone has two absorption maxima at 244 nm and 288 nm and paracetamol has an absorption maxima at 257 nm. Both the drugs obey Beer's law in the concentration ranges employed for these methods. The results of analysis have been validated statistically and by recovery studies.

THE U.S.P.[1] described a spectrophotometric method for the analysis of chlorzoxazone and its tablets. For the capsule formulation containing chlorzoxazone and paracetamol, the U.S.P.[1] describes a high performance liquid chromatographic (HPLC) method of analysis. The I.P.[2] and B.P.[3] suggest a spectrophotometric method for the analysis of paracetamol formulations whereas the U.S.P.[4] describes of HPLC method for the analysis of paracetamol formulations. Few HPLC methods for simultaneous analysis of chlorzoxazone and paracetamol[5] have been reported. A gas liquid chromatographic (GLC) method for simultaneous analysis of chlorzoxazone and paracetamol[6] has also been reported. This paper presents two simple, accurate, reproducible and economical methods for the simultaneous analysis of two components in tablet formulation.

EXPERIMENTAL

Shimadzu ultraviolet/visible recording spectrophotometer (Model : UV-160A) with a Spectral band width (Resolution) of 3 nm and Wavelength accuracy of ± 0.5 nm. (with automatic wavelength correction) was employed. Matched quartz cells corresponding to 10mm pathlength have been used.

Method-I : Employing Simultaneous Equations

The molar absorptivity coefficients of each of the two drugs were determined at 244 nm and 257 nm. A set of two simultaneous equations framed using these molar absorptivity coefficient values is given below.

$$A_1 = (9.837C_1 + 9.059C_2) \times 10^3 \quad \ldots \ldots \ldots \text{(I)}$$

$$A_2 = (3.329C_1 + 10.819C_2) \times 10^3 \quad \ldots \ldots \ldots \text{(II)}$$

where,

C_1 and C_2 are concentrations of chlorzoxazone and paracetamol respectively, in moles per litre in the sample solution. A_1 and A_2 are absorbances of the sample solution measured at 244 and 257 nm, respectively. 9.059×10^3 and 9.837×10^3 are the molar absorptivities at 244 nm of paracetamol and
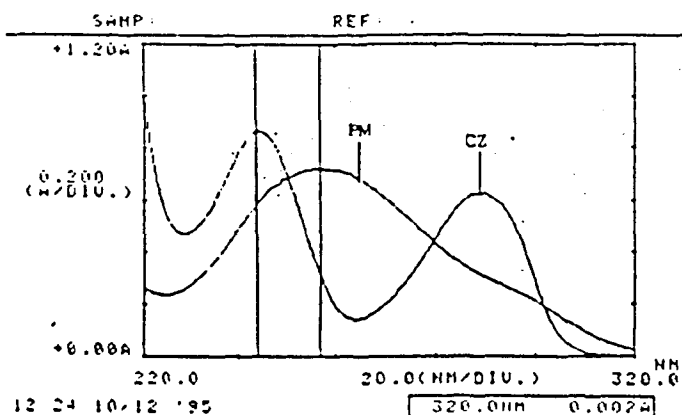
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Fig. 1 : Overlain Spectra of Paracetamol and Chlorzoxazone

Fig. 2 : Overlain First Derivative Spectra of Paracetamol and Chlorzoxazone

PM : Paracetamol
CZ : Chlorzoxazone

chlorzoxazone, respectively. 10.819×10^3 and 3.329×10^3 are the molar absorptivities at 257 nm of paracetamol and chlorzoxazone respectively. The molar absorptivities reported are a mean of five independent determinations.

By substituting value of C_1 from equation (I) into equation (II) the numerical value of C_2 can be obtained. Now substituting this value of C_2 in any of the above two equations the numerical value of C_1 can be obtained.

Preparation of Tablet Sample Solutions

Tablet samples from two different batches were separately used for analysis. Twenty tablets were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 50 mg of Paracetamol was transferred to a 100 ml volumetric flask. The powder was dissolved in about 75 ml of 0.02 M sodium hydroxide solution by intermittent shaking and the volume was made upto the mark. The solution was then filtered through Whatman Filter Paper No. 41 and the filtrate was diluted to get a final concentration of 10 mcg/ml each of paracetamol
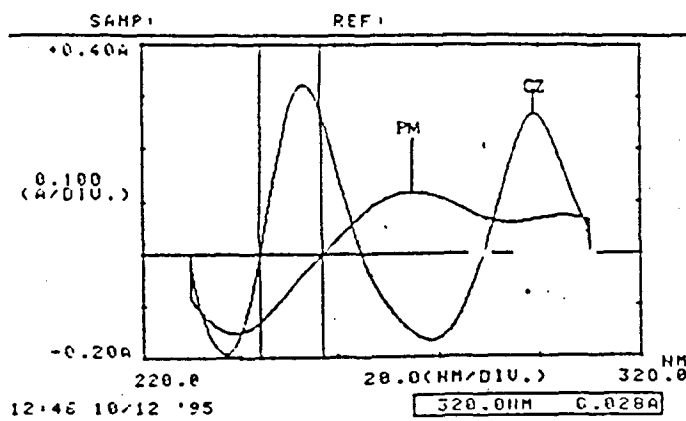
and chlorzoxazone. Absorbances, A_1 and A_2 of this sample solution were recorded at 244 and 257 nm, respectively, and the concentrations of the two drugs in the sample were determined using the above equations. The results of analysis of the tablet formulations are stated in Table - 1. Recovery studies carried out also gave satisfactory results which are stated in Table - 2. The overlain spectra of chlorzoxazone (17.5 mcg/ml) and paracetamol (10 mcg/ml) with markers at the wavelengths used for analysis is given as Figure - 1.

Method-II: Employing First Derivative Spectro-photometry

From the first derivative spectra of the two drugs (Figure-2) it was evident that chlorzoxazone and paracetamol showed zero absorbance at 244 and 257 nm respectively. As at the zero crossing point on the first derivative spectrum of one drug the other drug shows substantial absorbance, these two wavelengths can be employed for the estimation of paracetamol and chlorzoxazone, respectively, without any interference from the other drug in their combined formulation. Pure standard drug solutions

Table 1

Table 1

Results of Analysis of commercial tablets by proposed methods

Tablet	Label Claim mg./tab		% of Label Claim Estimated*					
			Method-I		Method-II		Reported method	
.	PM	CZ	PM	CZ	PM	CZ	PM	CZ
Batch-I	500	500	97.54	99.50	98.64	98.20	97.62	99.16
Batch-II	500	500	99.96	101.45	101.24	98.12	100.82	102.40

* Mean of five determinations.

Tablet	Standard Deviation					
	Method- I		Method- II		Reported method	
	PM	CZ	PM	CZ	PM	CZ
Batch-I	0.546	0.735	0.490	0.804	0.762	0.640
Batch-II	0.812	0.556	0.614	0.692	1.024	0.732

Table 2

Recovery Study Data

Sr. No.	Conc. of added amount of drug in the final dilution in mcg/ml.		% Recovery			
			Method-I		Method-II	
	PM	CZ	PM	CZ	PM	CZ
1.	2	2	99.80	101.44	100.50	98.64
2.	4	4	101.62	102.24	98.45	99.36
3.	6	6	98.28	98.56	102.05	99.48
4.	8	8	99.34	101.94	100.78	101.37
5.	10	10	100.80	99.38	99.18	98.06

PM : Paracetamol
CZ : Chlorzoxazone

in 0.02 M sodium hydroxide were used to plot calibration curves from the absorbances recorded from the derivative spectra. The curves show linearity in the concentration range of 0-25 mcg/ml for paracetamol and 0-35 mcg/ml for chlorzoxazone. Tablet sample solutions for both the batches of tablets were made as mentioned in the method-I.

Absorbances for the sample solutions were recorded at 244 and 257 nm from the first derivative spectra of the sample solution and the amount of drug present in the sample solution was obtained from the calibration curves plotted. The results of analysis using this method, along with the results of analysis of the same tablet samples by a reported method[7]

are also given in Table - 1. The results of recovery studies carried out are stated in Table - 2.

RESULTS AND DISCUSSION

The proposed methods were found to be accurate, simple and rapid for routine simultaneous estimation of the two drugs. The values of standard deviation were statisfactorily low and recovery was close to 100% indicating the reproducibility and accuracy of both the methods.

The first method, employing simultaneous equations, is a very simple method and can be employed for routine analysis of these two drugs in combined dosage forms using simple instrumentation. Once the molar absorbtivities are determined, very little time will be required for the routine analysis as it would only require determination of the absorbances of the sample solutions at the two selected wavelengths and few simple calculations.

The second method requires spectral data processing and hence can be applied only on recording spectrophotometers with such facilities like the instrument used for this work. The first derivative spectrophotometry was employed to totally eliminate the spectral interference from one of the two drugs while estimating the other drug. This was achieved by selecting the zero crossing point on the derivative spectra of each drug at the wavelength for estimation of the other drug. The method did not show any significant advantage over the first method except for eliminating the manual calculations required to solve the simultaneous equations.

The reported method[7] requires a sophisticated recording spectrophotometer with sufficient memory to store the spectral data obtained from a number of mixed standards of the two drugs. In addition, it requires an inbuilt programme for solving matrix equations. The first method presented in this paper is simpler as it does not require such a sophisticated spectrophotometer and yet is equally accurate and precise. The second method requires a spectrophotometer with spectral data processing facilities but does not require memory to store the spectral data and hence is better suited for routine analysis than the reported method. Both the methods presented in this paper are simpler than the reported method and also show slightly better reproducibility.

ACKNOWLEDGEMENTS

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