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SIMULTANEOUS SPECTROPHOTOMETRIC ESTIMATION OF PHENYLPROPANOLAMINE HYDROCHLORIDE (PPM) AND CHLORPHENIRAMINE MALEATE (CPM) USING "SIMULTANEOUS EQUATION METHOD (VIERODT'S METHOD)"

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Abstract: With the help of UV Spectrophotometer a rapid and simple method for simultaneous determination of Chlorpheniramine Maleate (CPM) and Phenylpropanolamine Hydrochloride (PPM) by **"**Simultaneous Equation Method (Vierodt's Method)**"** has been developed in combined pharmaceutical dosage forms. The proposed method was successfully applied for the determination of drugs in physical mixture and commercial formulations. The earlier methods developed for simultaneous determination of Chlorpheniramine Maleate and Phenylpropanolamine Hydrochloride in combined pharmaceutical dosage forms were expensive and time consuming, so these studies may serve as a basis for simultaneous analysis of CPM and PPM in combined pharmaceutical dosage forms having results of good linearity, precision and reproducibility.

Key Words: Derivative, UV absorption, spectral overlap, principle maxima, wavelength range, analytical signal

INTRODUCTION

Combinations of two or more drugs in the pharmaceutical dosage forms are very much useful in multiple therapies. Market survey revealed that, day by day new drugs and their combination with another drugs are being introduced in market as they have more patient compliance than a single drug. The analytical chemistry hence has challenge in developing the methods for their analysis with the help of number of analytical techniques which are available for the estimation of the drugs and their combination. Analytical monitoring of pharmaceutical product or specific ingredients within the product is necessary to ensure its safety and efficacy throughout the shelf life, including storage, distribution and use.[1,2]

Chlorpheniramine maleate inhibits the effects of histamine on capillary permeability and bronchial smooth muscles. It is an anti-allergic drug, widely used in cough and cold preparations. Phenylpropanolamine (PPM) is indirectly acting sympathomimetic agent and is used in the symptomatic relief of nasal congestion. These drugs are either used alone or in combination. Besides the various official methods (IP & USP) the other analytical methods available in literature for determination of chlorpheniramine maleate, [3-11] phenylpropanolamine hydrochloride[12-19] and combination of chlorpheniramine maleate & phenylpropanolamine hydrochloride[20-22] have been mentioned. These methods are time consuming; therefore an alternative method Simultaneous Equation Method i.e. Vierodt's Method by UV spectrophotometry had been applied for estimation of combination of PPM and CPM in tablet formulation.

It obeys Beer's law at the working wavelengths and concentration of interest. The basic principle of this method is that "The absorbance at any point is sum of absorbance of both the component at that point".

MATERIAL AND METHODS

The simultaneous determination of CPM and PPM is not possible by direct UV absorption measurement method because of spectral overlap of their principal maxima. "The absorbance difference between two points on the mixture spectra is directly proportional to the concentration of the component of the interest independent of interfering components". The present work was undertaken to develop such method of analysis, which is a precise, accurate, simple, reliable and less time consuming method for estimation. Authentic samples of CPM and PPM were provides as a gift samples from M/S Plethico Pharmaceutical, Indore.

Precise Description of Solvent and Linearity Studies

The common solvent distilled water was used for the estimation of PPM and CPM using Simultaneous Equation Method.

Preparation of Stock Solutions

10mg. and 50mg. of CPM and PPM were weighed separately and transferred to 100 ml. volumetric flasks separately. 40ml. of distilled water was added in each volumetric flask for dissolving drugs and after dissolving the drugs volume was made upto the mark with distilled water. This gave stock solutions

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of CPM 100 mcg/ml and PPm 500 mcg/ml. From these stock solutions PPM 200 mcg/ml and CPM 32 mcg/ml were prepared.

Selection of "Wavelengths" and Determination of "Molar Absorptivity"

The stock solutions of CPM and PPM were scanned over the range 325- 200 nm. For PPM it showed λ_{max} at 257.0 nm and for CPM it showed λ_{max} at 262 nm. As we know at λ_{max} the drugs shows maximum sensitivity so these two λ_{max} were selected for estimation. The absorbance at 257 and 262 nm were denoted by A_1 and A_2 respectively. For estimation of PPM and CPM the simultaneous equations were calculated as follows.

$$A_1 = ax_1.b.cp + ay_1.b.cc \text{---------- (i)}$$

$$A_1 = ax_2.b.cp + ay_2.b.cc \text{---------- (ii)}$$

These above equations (i) and (ii) by rearrangement followed: -

$$Cp = \frac{A_2.ay_1 - A_1.ay_2}{ax_2.ay_1 - ax_1.ay_2} \quad \text{---------- (iii)}$$

$$Cp = \frac{A_1.ax_2 - A_2.ax_1}{ax_2.ay_1 - ax_1.ay_2} \quad \text{---------- (iv)}$$

Where,

A_1,A_2: Absorbances at 257.0 and 262.0 nm

ax_1, ax_2: molar absorptivity of PPM at 257 and 262 nm.

ay_1, ay_2: molar absorptivity of CPM at 257.0 and 262.0 nm.

Cp, cd: gm – mole / liter of PPM and CPM respectively.

b: path length (1 cm.).

After selection of two wavelength the standard solutions of both CPM (32 mcg/ml.) and PPM (400mcg/ml.) were scanned in the range of 325-200nm. Absorbance for both the drugs were noted separately at λ_{max} of both the drugs i.e. at 257.0 and 262.0nm and record in Table 1.

Table 1: Absorbance and Molar Absorptivity of PPM and CPM

Analytes/ Conc. mcg/ml.	Absorbance at 257 nm.	Molar absorptivity at 257 nm.	Absorption at 262 nm.	Molar absorptivity at 262 nm.
PPM 400	0.430	10.75	0.328	8.2
CPM 32	0.458	143.125	0.498	155.915

From the data as per Table 1, molar absorptivity was calculated at 257.0 and 262.0nm for both the drugs. With the knowledge of the values of A_1 and A_2 in samples (where both the drugs were present) the concentration of CPM and PPM were calculated as per formula devised below:

$$\text{Conc. of PPM} = \frac{A_2 \bullet 143.125 - A_1 \bullet 155.915}{8.2 \bullet 143.125 - 10.75 \bullet 155.915}$$

$$\text{Conc. of PPM} = \frac{A_1 \bullet 8.2 - A_2 \bullet 10.75}{8.2 \bullet 143.125 - 10.75 \bullet 155.915}$$

Validation of proposed Method using Laboratory Samples

Five mixed standard solutions were prepared having PPM 100, 125, 150, 200 and 250 mcg/ml and CPM 6, 7.5, 9, 12 and 15 mcg/ml respectively. Laboratory samples were scanned in the range of 325-200 nm and absorbance were noted at 257 and 262 nm for each sample. The values A1 and A2 Obtained at 257 and 262 nm respectively were used for the evaluation of concentration of PPM and CPM for each sample (by using equation (iii) and (iv)) in gm-mole/liter. The results of analysis are given in Table 2 and 3.

Table 2: Results of CPM and PPM by Analysis of Authentic Samples.

S.No.	Expected Conc. mcg/ml.		Found Conc. mcg/ml.		Percent Found	
	CPM	PPM	CPM	PPM	CPM	PPM
(i)	6	100	5.99	100.65	99.83	100.65
(ii)	7.5	125	7.57	124.26	100.93	99.41
(iii)	9	150	8.94	150.72	99.33	100.48
(iv)	12	200	12.20	198.46	101.66	99.23
(v)	15	250	14.77	254.48	98.46	101.79

Table 3: Statistical Estimation of results of CPM and PPM in Authentic, Commercial and Recovery Studies Samples.

Analysis	Mean	Standard Deviation	Standard error	Co-efficient of variation
Authentic sample				
PPM	100.312	0.9286	0.4153	0.9257
CPM	100.042	1.1368	0.5084	1.1363
Commercial samples				
PPM	100.18	0.7091	0.3171	0.7079
CPM	99.89	1.2256	0.5481	1.2269
Recovery studies				
PPM	100.53	1.3236	0.6618	1.3166
CPM	101.15	0.4506	0.2253	0.4455

Analysis of Commercial Formulation by Standard Addition Method

Twenty tablets were weighed and average weight was found (243.26 mg; labeled to claim 4 mg. of CPM and 25 mg. of PPM). The tablets were crushed to powder from and 243.26 mg. of table powder was weighed and transferred to 100 ml. volumetric flask. 50 mg. of PPM "standard drug" was weighed and transferred to same volumetric flask. 60 ml of distilled water was added and drug were dissolved by shaking vigorously for 10 minutes. The resultant mixture was filtered using Whatman filter paper, the volume was made up to mark with distilled water. The final solution labeled to claim 40 mcg/ml. of CPM and 750 mcg/ml. of PPM.

From this above stock solution different dilutions were prepared and used as unknown, and were analyzed by simultaneous equation method. These samples were scanned in the range of 325-200 nm at wave length 257 and 262 nm and the absorbance values A1 and A2 obtained were used for estimation of PPM and CPM in terms of gm-mole/liter. Results of analysis had been shown in Table 3 and 4.

Table 4: Results of CPM and PPM by Analysis of Commercial Formulation

S.No.	Expected Conc. mcg/ml.		Found Conc. mcg/ml.		Percent Found	
	CPM	PPM	CPM	PPM	CPM	PPM
(i)	4	75	4.059	75.260	101.47	100.34
(ii)	8	150	7.915	149.503	98.93	99.66
(iii)	12	225	11.77	223.745	98.09	99.44
(iv)	16	300	16.123	304.400	100.76	101.46
(v)	20	375	20.04	375.030	100.20	100.00

Table 5: Results of CPM and PPM by Analysis of Recovery Studies Samples

S.No.	Expected Conc. mcg/ml.		Found Conc. mcg/ml.		Percent Found	
	CPM	PPM	CPM	PPM	CPM	PPM
(i)	125	8	122.95	8.09	98.35	101.16
(ii)	150	10	152.46	10.07	101.64	100.68
(iii)	75	5.5	75.16	5.60	100.68	101.87
(iv)	175	12	178.36	12.11	101.92	100.88

Recovery Studies

The recovery study was carried out addition of pure drugs 125, 150, 75 and 175 mcg/ml of PPM and 8, 10, 5.5. and 12mcg/ml of CPM were added to pre analyzed 2 ml of stock solution of commercial tablet samples. These solution were scanned in the range of 325-200nm. Absorbance values A1 and A2 were noted at 257 and 262 nm and used for estimation of PPM and CPM respectively. The results and statistical data's are shown in Table 3 and 5.

RESULTS AND DISCUSSION

The basic principle utilized for developing proposed method is additive property of absorbance of two or more components. The λmax of both the drugs had been chosen for estimation. Because at λmax the method showed maximum sensitivity. The proposed method is economic, very simple and rapid because it does not require sample solution of derivative spectrophotometry. In this proposed method simply diluted sample solution of commercial tablets were scanned in the range of 325-200nm and the absorbance values obtained i.e. A1 and A2 at 257 and 262nm were used for the estimation of PPM and CPM in the simple solution by solving the equation (iii) and (iv). Various statistical calculations were performed for validation of proposed method and results obtained were found satisfactory.

CONCLUSION

Simultaneous analysis of CPM and PPM using simultaneous equation method gave satisfactory results which are better than other techniques. The method involves simple calculations using the molar absorptivity of CPM and PPM at 262 and 257nm. Where, 257 and 262 nm is absorption maxima for PPM and CPM respectively. The values of standard deviation for both CPM And PPM were found to be in-between 0.7 to 1.8 and recoveries of drug added were found to be between 97-103% which is quiet impressive.

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