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UV Spectrophotometric Analysis Of Prochlorperazine Maleate And Pyridoxine Hydrochloride In Tablet Dosage Form By Simultaneous Equation Method

Gajanan B. Bhagwat[1,2]*

[1]Department of Pharmaceutical Chemistry, Sharad Pawar College of Pharmacy, Wanadongri, Hingna Road, Nagpur 441 110 (M.S.) India.

[2]Department of Pharmaceutical Chemistry, Kasturi Shikshan Sanstha's College of Pharmacy, Shikrapur, Tal.Shirur, Dist.Pune 412208 (M.S.) India.

***Corres.author: rajbhagwat07@gmail.com**
Mob. No- +919404694494

Abstract: Prochlorperazine maleate and pyridoxine hydrochloride in combination are available as tablet dosage forms in the ratio of 1:5. A simple, reproducible and efficient method for the simultaneous determination of prochlorperazine maleate and pyridoxine hydrochloride in tablet dosage form has been developed. The developed method is based on the simultaneous estimation by UV Spectroscopy, using Simultaneous Equation Method. In this method 0.3M HCl was used as solvent. Wavelengths selected for estimation of prochlorperazine maleate and pyridoxine hydrochloride in simultaneous equation method were 254.5 nm and 290.5 nm respectively. Both drugs obey Beer-Lambert's law in concentration range of 1-5 µg/ml (prochlorperazine maleate) and 5-25 µg/ml (pyridoxine hydrochloride). The results of analysis have been validated statistically and by recovery studies.

Keywords: Prochlorperazine Maleate, Pyridoxine Hydrochloride, Simultaneous equation method, Standard addition, Validation.

INTRODUCTION

Prochlorperazine maleate (PCM), 2-Chloro-10-[3-(4-methylpiperazin-1-yl)propyl] 10 H phenothiazine bis[hydrogen(Z)-butenedioate] (fig. 1), is antiemetic and antipsychotic drug[1] while pyridoxine hydrochloride (PDH), 5-Hydroxy-6-methyl-3,4-pyridine dimethanol hydrochloride (fig. 2), is a nutritional component[2]. Both the drugs are official in IP, BP and USP. Literature survey revealed that HPLC[3,4] methods have been reported for pyridoxine hydrochloride with other drugs. However, no method is reported for simultaneous estimation of these two drugs in combined dosage form. This prompted us to develop simple, rapid, accurate, economical and sensitive simultaneous equation method for their determination in combination.

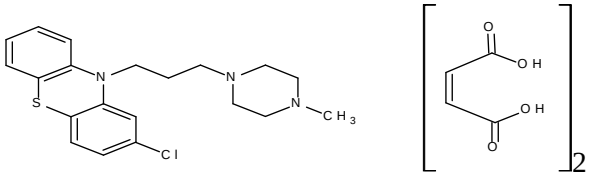
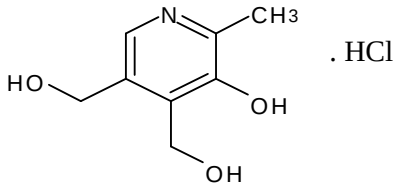


Figure 1: Structure of prochlorperazine maleate



. HCl

Figure 2: Structure of pyridoxine hydrochloride

EXPERIMENTAL METHODS

Shimadzu 1700 UV/Visible spectrophotometer with matched cuvettes was used for experimental work. The chemicals used were of analytical grade. Commercially available tablets of prochlorperazine maleate and pyridoxine hydrochloride in combination were procured from local market. Standard prochlorperazine maleate and pyridoxine hydrochloride were received as gift sample from FDA Mumbai.

Employing Simultaneous Equation Using Vierodt's method

Selection of Common Solvent:

A 0.3M HCl solution was selected as the suitable solvent for the estimation of prochlorperazine maleate and pyridoxine hydrochloride.

Preparation of standard stock solution:

Standard stock solutions of PCM and PDH were prepared separately by dissolving 25 mg each of standard PCM and PDH in 0.3 M HCl and making up the volume up to 100 ml (250 µg/ml).

Study of spectra, selection of scanning range and wavelength:

The aliquot portions of standard stock solutions of PCM and PDH were diluted individually with the solvent to obtain concentration 10µg/ml of each drug. The solutions were scanned in the range of 200nm–400nm in 1cm cell against blank. From the spectrum, wavelengths selected for the estimation of drugs were 254.5 nm as λ_{max} for PCM and 290.5 nm as λ_{max} for PDH. This is shown in fig. 3, 4 and 5.

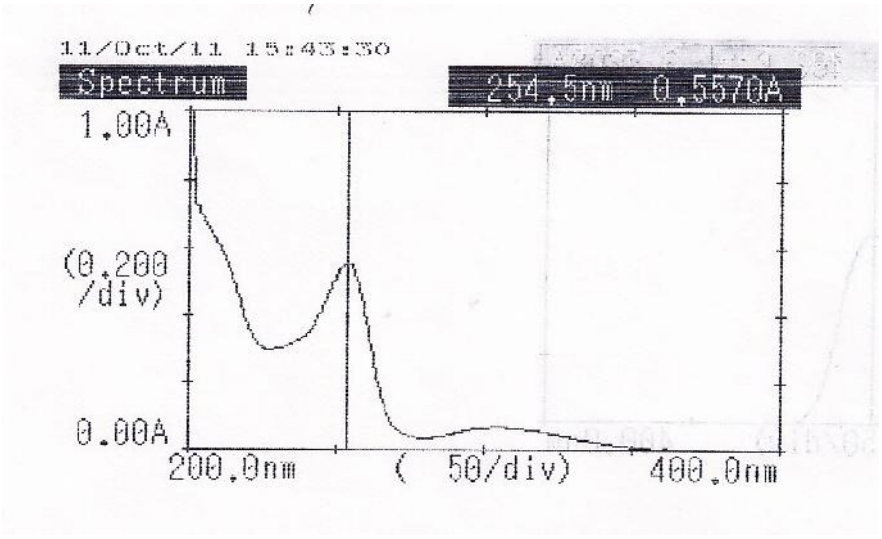


Figure 3: UV Spectrum of PCM

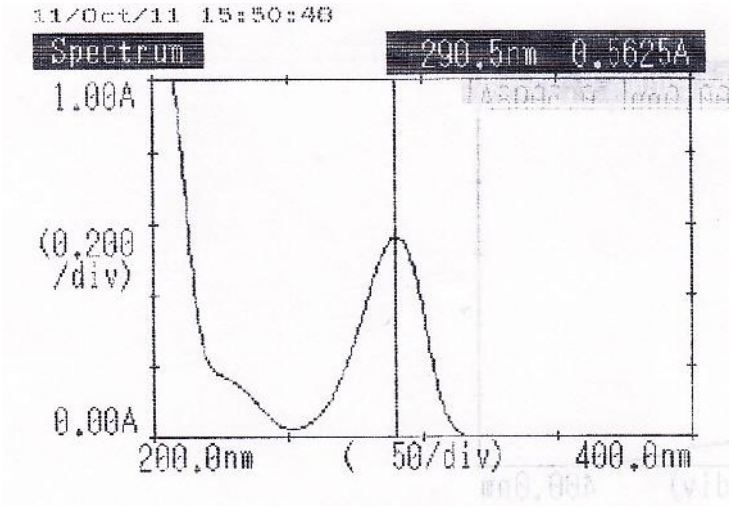


Figure 4: UV Spectrum of PDH

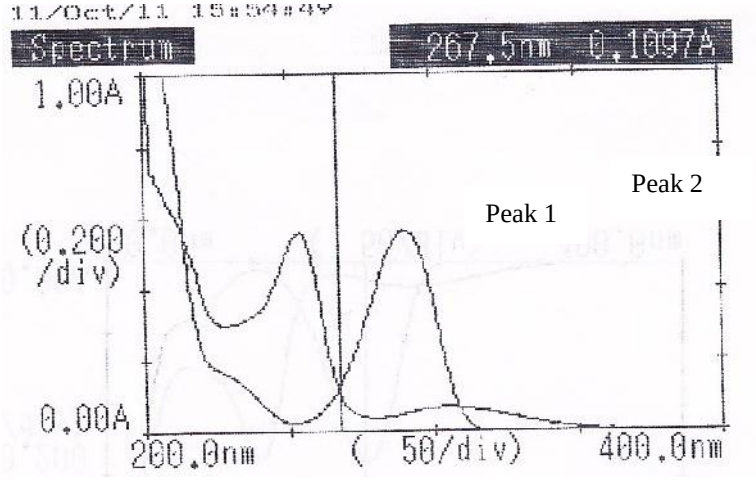


Figure 5: Overlain spectra of PCM and pyridoxine PDH in 0.3 M HCl.

Prochlorperazine maleate (PCM, Peak 1) at wavelength of 254.5nm, Pyridoxine hydrochloride (PDH, Peak 2) at wavelength of 290.5nm and 267.5nm is the isobestic point.

Study of Beer-Lambert's law:

The aliquot portions of standard stock solutions of PCM and PDH were diluted with the solvent to get a series of concentration between 1-5µg/ml and 5-25µg/ml respectively. The aliquot portions of above solutions of PCM and PDH were mixed (Std. Laboratory mixture) and diluted to get a series to maintain the ratio of 1:5 of PCM and PDH respectively. The absorbance of each solution was measured at 254.5 nm and 290.5 nm in 1 cm cell against solvent blank.

Study of Additivity of absorbance for PCM and PDH at selected wavelengths:

The data obtained in the study of Beer-Lambert's law was further used to study additivity of absorbance of PCM and PDH at 254.5 nm and 290.5 nm. Mixture of drugs shows additivity of absorbance at selected wavelengths.

Determination of Absorptivity (1%, 1cm) values of drugs at selected wavelengths:

Aliquot portions of PCM and PDH stock solutions were diluted with solvent i.e. 0.3 M HCl to obtain concentration of 10µg/ml of each drug. The absorbance of each solution was measured at 254.5 nm and 290.5

nm and absorptivity (1%, 1cm) for both drugs was found to be 664.4 and 62.6 for PCM, 46.1 and 679.5 for PDH at 254.5 nm and 290.5 nm respectively.

Analysis of Laboratory mixture by proposed method:

In order to see the feasibility of proposed method for simultaneous estimation of PCM and PDH in pharmaceutical formulations, the method was first tried for the estimation of drugs in standard laboratory mixture.

Accurately weighed quantities of PCM equivalent to 5 mg and PDH equivalent to 25 mg, were taken in 100 ml volumetric flask and dissolved in 0.3M HCl and the volume was made up to the mark with same solvent to get working solution of 5 and 25µg/ml of PCM and PDH respectively. The absorbance of resulting solutions was measured at 254.5 nm and 290.5 nm in 1 cm cell against blank.

Amount of each drug was determined by using formulae-

$$Cx = \frac{A2\ ay1 - A1\ ay2}{ax2\ ay1 - ax1\ ay2} \quad \text{---------- (1)}$$

$$Cy = \frac{A1\ ax2 - A2\ ax1}{ay\ ax2 - ay2\ ax1} \quad \text{---------- (2)}$$

$$\%\ Estimation = \frac{C \times d}{W} \quad \text{---------- (3)}$$

Where ,

Cx = Concentration of PCM in g/100 ml
C_y = Concentration of PDH in g/100 ml
A_1 = Absorbance of laboratory mixture at 254.5 nm
A_2 = Absorbance of laboratory mixture at 290.5 nm
a_{x1} = Absorptivity of PCM at 254.5 nm
a_{x2} = Absorptivity of PCM at 290.5 nm
a_{y1} = Absorptivity of PDH at 254.5 nm
a_{y2} = Absorptivity of PDH at 290.5 nm

$$\%\ Estimation = \frac{C \times d}{W} \quad \text{---------- (3)}$$

Where,

C = C_x or Cy = Concentration of PCM or PDH in g/100ml
d = Dilution factor
W = Weight of drug either PCM or PDH in laboratory mixture

Results of estimation of drugs in laboratory mixture are shown in Table-1.

Table 1: Results Of % Estimation Of Pcm And Pdh In Laboratory Mixture

Sr. no.	Wt. of pure drug (mg)	% Estimation*	SD	RSD	SE
1	PCM 5 mg	100.13	0.0258	0.0006	0.0005
2	PDH 25 mg	99.95	0.1963	0.0385	0.0385

*Results are mean of five replicates

Analysis of marketed formulation by proposed method:

Marketed tablets Emidoxyn Forte (Shreya Life Science Pvt Ltd., Mumbai) were used for the simultaneous estimation of PCM and PDH. Twenty tablets were accurately weighed. Average weight of tablet was calculated. A quantity of tablet powder equivalent to 5 mg of PCM and 25 mg of PDH was transferred to 100 ml volumetric flask and dissolved in 0.3M HCl and volume was made to 100 ml. The solution was filtered through Whatman filter paper no. 41. The aliquot portion of filtrate was further diluted with 0.03M HCl to get final concentration 5 µg and 25 µg of PCM and PDH respectively. The absorbance of resulting solutions was measured at 254.5 nm and 290.5 nm in 1 cm cell against blank. The content of PCM and PDH in tablet was calculated using the formula-

$$\%\ Label\ Claim = \frac{Cx\ or\ Cy \times W}{Wm \times L} \times 100 \quad \text{---------- (4)}$$

Where,

Cx or C_y = Concentration of PCM and PDH in g/100 ml
W = Average weight of tablet
Wm = Weight of sample
L = Label claim of sample taken

Results of % estimation of PCM and PDH in marketed formulation are shown in Table -2.

Table 2: Results Of Analysis Of Tablet Formulation And Statistical Data

Sr. no.	Label Claim mg/tablet	%Label Claim*	S.D	RSD	SE
1	PCM 5 mg	100.34	0.0207	0.0431	0.0344
2	PDH 25 mg	98.85	0.7696	0.5923	0.4738

*Results are mean of five replicates

Method Validation

The proposed method was validated on the basis of parameters namely accuracy, precision, specificity, ruggedness and linearity and range.

Accuracy:

Accuracy of an analytical method is the closeness of test results obtained by that method to the true value. It was ascertained on the basis of recovery studies performed by standard addition method. The preanalysed tablet powder equivalent to about 5 mg PCM was taken in 100 ml volumetric flask; to it standard solutions of PCM and PDH were added in the different proportions. The mixture was shaken for 15 minutes and volume was adjusted to the mark with 0.3M HCl and the solution was filtered through Whatman filter No.41. An aliquot portion of the resultant solution was appropriately diluted with 0.3M HCl to get final concentration within the range of mixed standard.

The % recovery was calculated by using the following formula

$$\%\text{Recovery} = \frac{A}{B + C} \times 100 \quad \text{----------(5)}$$

Where,

A= Total amount of drug estimated
B = Amount of drug found on preanalysed basis
C = Amount of pure drug added

Results of recovery studies are shown in Table-3.

Table 3: Results Of Recovery Study

Sr. no.	Wt. of tablet powder (g)	Amount of pure drug added (µg/ml)		% Recovery*	
		PCM	PDH	PCM	PDH
1	0.1384	1	05	100.2	100.0
2	0.1380	2	10	100.0	100.1
3	0.1388	3	15	100.1	100.1

*Results are mean of five replicates

Precision:

Precision of analytical method is the degree of agreement among individual results when the method is applied repeatedly to multiple readings of homogenous sample. It is expressed as the SD or RSD of series of measurements. It was ascertained by replicate estimation of the drugs by proposed method.

Specificity:

Accurately weighed quantities of tablet powder equivalent to 5 mg of PCM were taken in different 50.0 ml volumetric flasks and were stored for 24 hr under following conditions.

1. At room temperature (normal)
2. At 50^0C after addition of 1.0 ml of 0.1N NaOH (alkali)
3. At 50^0C after addition of 1.0 ml of 0.1N HCl (acid)
4. At 50^0C after addition of 1.0 ml of 3% H_2O_2(oxide)

The samples were diluted upto the mark with 0.3M HCl and filtered through grade-1 filter paper. Aliquot of the filtrate was diluted with 0.3M HCl to get 10 µg/ml concentration of PCM. The solution was analyzed as per the procedure described for analysis of laboratory mixture. The results of specificity studies are shown in Table-4.

Table 4: Results Of Specificity Study

Sr. No.	Sample	% Label claim*	
		PCM	PDH
1	Normal	100.11	100.20
2	Alkali	98.05	99.03
3	Acid	99.89	100.00
4	Oxide	101.01	101.21

*Results are mean of five replicates

Ruggedness:

Test for ruggedness was carried out by repeating the procedure under different conditions
A. Days (Intraday and Interday)
B. Different analysts
Results of ruggedness study are shown in Table -5.

Table 5: Results Of Ruggedness Study

Condition	% Label Claim*		S.D		RSD	
	PCM	PDH	PCM	PDH	PCM	PDH
Interday	100.27	99.99	0.03164	0.0223	0.10013	0.0004
Interday	100.08	99.18	0.1446	0.8176	0.02093	0.66823
Different analyst	100.01	99.20	0.1	0.6935	0.01	0.48103

*Results are mean of five replicates

Linearity and range

Accurately weighed quantities of tablet powder equivalent to 80, 90, 100, 110 and 120 % of label claim were taken and dilutions were done appropriately to obtain a concentration in the range of 80-120% of the test concentration and absorbance were recorded at 254.5 nm and 290.5 nm. PCM and PDH were found to be linear in 80-120% of the test concentration. The plot of linearity and range for PCM and PDH are shown in fig. 6.

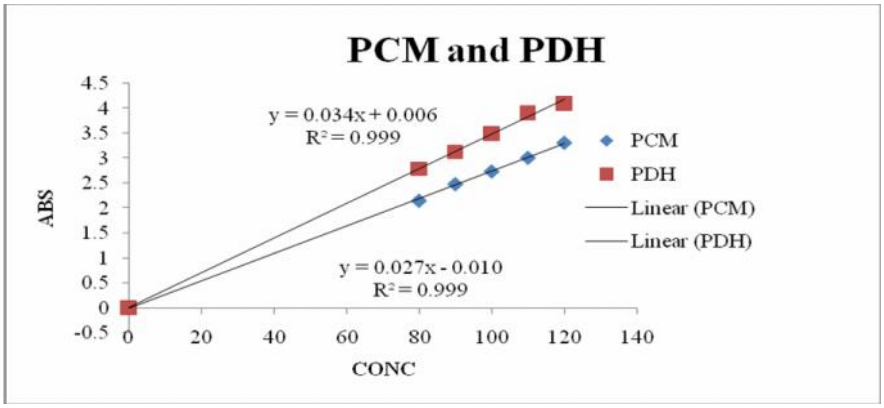


Figure 6: The plot of Linearity and range study for PCM and PDH.

Prochlorperazine maleate (PCM) its R^2 value is 0.999, Pyridoxine hydrochloride (PDH) its R^2 value is 0.999, ABS is absorbance, CONC is concentration of PCM and PDH respectively.

RESULTS AND DISCUSSION

An attempt has been made to develop a fast, sensitive, precise, reproducible and economical analytical method for simultaneous estimation of PCM and PDH in their combined dosage form. In this method drugs obey Beer's law in the concentration range 1-5 µg/ml for PCM and 5-25 µg/ml respectively. The absorption additivity study was carried out to see whether the drugs in mixture show additivity or not. It was observed that both drugs showed the additivity of absorbance at selected wavelength indicating that both drugs do not interact with each other in solvent system used. A (1%, 1cm) values were also calculated for both drugs. For PCM, A (1%, 1cm) was found to be 664.4 and 62.6, for PDH 46.1 and 679.5 for PDH at a wavelength of 254.5 nm and 290.5 nm, respectively.

The result of % estimation of drugs is shown in Table-2. The method was validated as per the ICH and USP guidelines[5,6,7] . The results of recovery study were found to be within the prescribed limit of 98-102%, proving the accuracy and showing that the method is free from interference from excipients. The results are shown in Table-3. For precision, replicate estimations of both PCM and PDH in the same batch of tablet were done by the proposed method, which yielded quite concurrent results, indicating reliability of the method. The values of SD or RSD are within the prescribed limit of 2%, showing high precision of method, as shown in Table-2.

In the specificity study, sample was exposed to different stress condition like acid, alkali, peroxide and heat. The results for specificity study are shown in Table-4. For ruggedness, proposed method was repeated under different conditions like at different time, on different days and by different analysts. The results shown in Table-5, prove that the method is reproducible. During the linearity study it was observed that absorbance values of PCM and PDH in marketed formulation were linear in the range of 80% to 120% of test concentration with R^2 close to 1 for this method of analysis. Plot of linearity and range is shown in fig. 6.

From the study of validation parameters namely accuracy, precision (SD and RSD), ruggedness (interday, intraday and different analyst), specificity, linearity and range, it was observed that the method is specific, accurate, precise, reproducible and rugged.

CONCLUSION

The proposed method for simultaneous estimation of PCM and PDH in their combined dosage form is quite accurate, precise, yield reproducible result and rugged. Moreover the method is economic, simple and rapid hence, the method can be employed for routine quantitative analysis of tablet dosage form containing PCM and PDH.

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