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Research Article

SIMULTANEOUS DETERMINATION OF PANTOPRAZOLE SODIUM AND ITOPRIDE HYDROCHLORIDE IN PHARMACEUTICAL DOSAGE FORM BY FIRST ORDER DERIVATIVE UV SPECTROPHOTOMETRY

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ABSTRACT

Derivative spectrophotometry offers a useful approach for the analysis of drugs in multi-component formulation. In this study a first order derivative spectrophotometric method is applied for the simultaneous determination of Pantoprazole Sodium and Itopride Hydrochloride in capsule dosage form using the zero-crossing technique. The measurements were carried out at wavelengths of 238.5 and 288 nm for Pantoprazole Sodium and Itopride Hydrochloride, respectively. The method was found to be linear (r^2 - 0.9991) in the range of 3-15 µg/ml for Pantoprazole Sodium in the presence of 15 µg/ml of Itopride Hydrochloride at 238.5 nm. The linear correlation (r^2-0.9992) was obtained in the range of 5-40 µg/ml for Itopride hydrochloride in the presence of 4 µg/ml of Pantoprazole Sodium at 288 nm. The method was successfully used for simultaneous determination of Pantoprazole Sodium and Itopride Hydrochloride in capsule dosage form without any interference from excipients and prior separation.

Key words: Pantoprazole Sodium, Itopride Hydrochloride, Spectrophotometry, First order derivative method.

INTRODUCTION

Itopride Hydrochloride is chemically *N*-[4-[2-(dimethylamino) ethoxy]-benzyl]-3, 4-dimethoxybenzamide hydrochloride and it is a gastrokinetic agent and it increases the release of acetylcholine (Ach) through dopamine D2 receptor antagonistic action and inhibits decomposition of Ach through its acetylcholinesterase inhibitory action, resulting in enhancement of gastrointestinal motility[1]. Pantoprazole sodium is chemically 5-[difluoromethoxy]-2-{[(3, 4-dimethoxy-2-pyridinyl) methyl] sulfinyl}-1H-benzimidazole, is an irreversible proton pump inhibitor. The inhibition of the gastric proton pump or H^+/K^+ ATPase suppresses gastric acid secretion and hence hyperacidity can be controlled by pantoprazole[2].

Literature survey reveals spectrophotometric[3], HPLC[4, 5] and HPTLC[6] methods for the estimation of Itopride hydrochloride in bulk drugs, pharmaceutical formulation and biological samples whereas HPLC[7], RP-HPLC[8-10] methods for the estimation of Pantoprazole Sodium alone or in combination with other drugs in pharmaceutical formulation and biological samples.

Direct UV–visible spectrophotometric method is not suitable for simultaneous determination of Pantoprazole Sodium and Itopride Hydrochloride due to their spectral overlapping in the region of 200-400 nm. Application of derivative technique of spectrophotometry offers a powerful tool for quantitative analysis of multi-component mixtures[11-12]. When derivatised, the maxima and minima of the original function take zero values, and the inflections are converted into maxima or minima, respectively. The derivative curves are more structured than the original spectra, thus enabling very tiny differences between the original spectra to be identified. Derivative spectrophotometry provides selectivity and offers a solution in resolving the overlapping spectra in multi-component analysis without previous chemical separation[13]. In the last decades, this technique has rapidly gained application in the field of pharmaceutical analysis to overcome the problem of interference, due to substances other than analytes, commonly present in pharmaceutical formulations or for combination of two or more drug substances[14-15]. Lack of any published method for simultaneous spectrophotometric determination of Pantoprazole Sodium and Itopride Hydrochloride, therefore, provoked us to investigate the application of derivative spectrophotometry for simultaneous determination of these compounds in pharmaceutical dosage forms using zero-crossing method.

EXPERIMENTAL

Reagents and chemicals

Standard drugs of Pantoprazole Sodium and Itopride Hydrochloride were procured from Themis Laboratories Pvt. Ltd., Mumbai. The commercial formulation Pantocid-IT was purchased from the market.

Equipment

Absorption and derivative spectra were recorded in 1 cm quartz cell using a dual beam Jasco V-630 UV-visible spectrophotometer with a fixed bandwidth of 2 nm and data processing capacity. The zero-order absorption spectra were recorded over the wavelength range 200-400 nm against a solvent blank. The derivative spectra were obtained over the same range at different slit width (dλ). The ordinate, maximum and minimum, were adjusted to the magnitude of derivative values.

Procedure

Preparation of standard stock solution

Stock solution was prepared by diluting 10 mg of each drug in sufficient quantity of double distilled water in separate volumetric flask and volume was made up to 100 ml to get the concentrations of 100 µg/ml for each drug. Dilutions from stock solution were prepared in the range of 5-40 µg/ml for Itopride Hydrochloride and 3-15 µg/ml for Pantoprazole Sodium.

Spectrophotometric Measurements

Zero-order spectra of standard solutions of Pantoprazole Sodium (4µg/ml) and Itopride Hydrochloride (15 µg/ml) versus their solvent blank were recorded in the range of 200-400 nm (Figure 1). The first order derivative spectra of these solutions were obtained in the same range of wavelength against their blanks (Figure 2). The values of first derivative amplitudes for Pantoprazole Sodium in the presence of Itopride Hydrochloride and vice versa were measured at 238.5nm (zero-crossing of Itopride Hydrochloride) and 288 nm (zero-crossing of Pantoprazole Sodium), respectively. The calibration curves for derivative spectrophotometry were constructed by plotting the drug concentration versus the absorbance values of the first derivative spectrum, at 238.5nm for Pantoprazole Sodium and at 288 nm for Itopride Hydrochloride.

Linearity

Calibration curves were constructed using six replicates of Pantoprazole Sodium solutions between 3-15 µg/ml in the presence of 5-40 µg/ml of Itopride hydrochloride. The same procedure was used for solutions containing Itopride hydrochloride 5-40 µg/ml in the presence of 3-15 µg/ml of Pantoprazole Sodium. The calibration

curves were constructed (Figure 3 and Figure 4) and statistical analysis was performed.

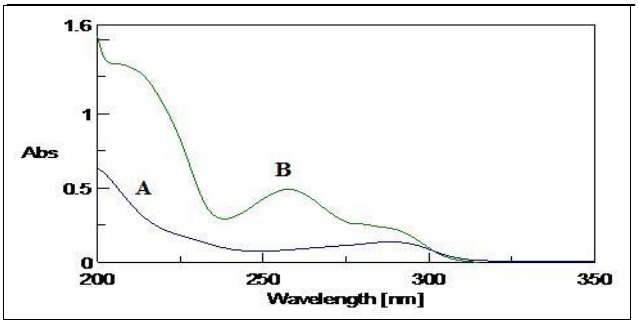

Figure 1: Zero order spectra (overlain) of Pantoprazole sodium (A) and Itopride hydrochloride (B)

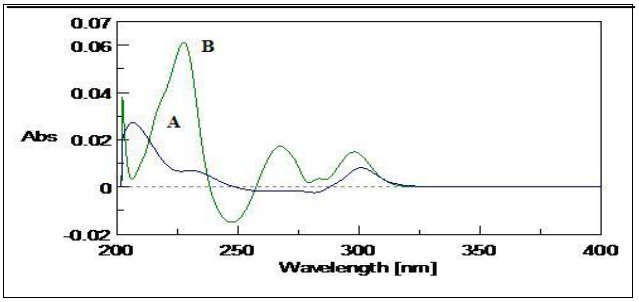

Figure 2: First order derivative spectra (overlain) of Pantoprazole sodium 4 µg/ml (A) and Itopride hydrochloride 15 µg/ml (B)

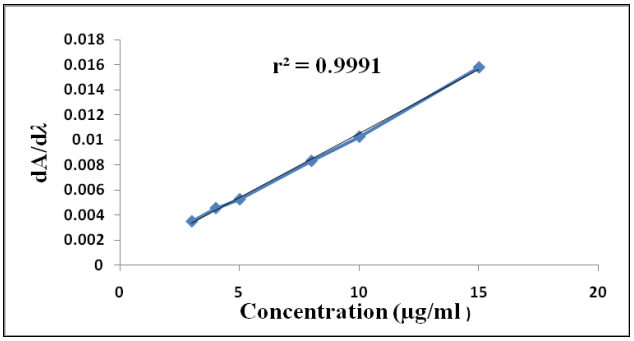

Figure 3: Calibration curve for Pantoprazole sodium at 238.5 nm

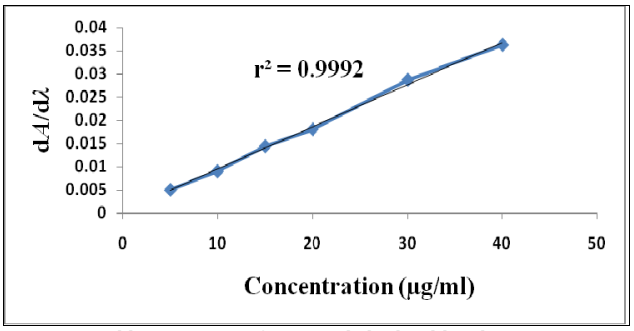

Figure 4: Calibration curve for Itopride hydrochloride at 288 nm

Precision

To establish the reliability of the proposed method, two series of solutions containing 3, 4, 5, 8 µg/ml of Pantoprazole Sodium with 15 µg/ml of Itopride Hydrochloride and 5, 10, 15, 20 µg/ml of Itopride Hydrochloride with 4 µg/ml Pantoprazole Sodium were prepared respectively and analyzed as discussed above. To evaluate the repeatability of this method six series of these mixtures were assessed in one day for intra-day precision using their corresponding calibration curves. Inter-day precision was performed by assessing six series of sample solution on different days.

Accuracy

For accuracy determination, the analysed samples were spiked with extra 80%, 100% and 120% of the standard solution of both drugs and the mixtures were reanalysed by the proposed method. The experiment was conducted in triplicate. This was done to check for the recovery of the drug at different levels in the commercial capsule formulations.

Analysis of commercial capsule formulation

Contents of 20 capsules were weighed and their average weight was determined and powdered. Accurately weighed powder equivalent to fill weight of one capsule was transferred to 100 ml calibrated flask containing 50 ml of double distilled water and sonicated for 30 minutes. The volume was then made up to the mark with double distilled water. The resulting solution was then filtered through whatmann filter paper (#41). From this solution, 10 ml was transferred to another 100 ml calibrated flask and diluted up to 100 ml. 1 ml of this solution was further diluted to 10 ml to get approximate concentration 4 µg/ml of Pantoprazole Sodium and 15 µg/ml of Itopride Hydrochloride.

RESULTS AND DISCUSSION

The overlain zero order absorption spectra of Pantoprazole Sodium and Itopride Hydrochloride is shown in Figure 1. The spectra shows considerable overlap and therefore simultaneous determination of these two drugs is not possible. The overlain of first order derivative spectra of both drugs is shown in Figure 2. Derivative spectrophotometry based on a mathematical transformation of the zero-order curve into the derivative spectra can overcome this problem. In derivative spectrometry the selection of the optimum wavelength for each component is based on the fact that the absolute value of the total derivative spectrum at these wavelengths has the best linear response to analyte concentration with an intercept very close to zero and least interference of other component. Therefore zero-crossing points of Pantoprazole Sodium (238.5 nm) and Itopride Hydrochloride (288 nm) were used for the analysis of the drugs from the pharmaceutical capsule dosage form.

Calibration curves and statistical analysis

Under the optimized conditions, the absorbance of the standard solutions of Pantoprazole Sodium and Itopride Hydrochloride were measured at the specified wavelengths. The calibration curves were constructed by plotting the first order values against Pantoprazole Sodium or Itopride Hydrochloride concentration over the range mentioned in Table 1. Separate determinations (six repetitions) at same concentration levels were performed. The linearity of the calibration curves and conformity of the proposed method are validated by the high values of correlation coefficients (r^2-0.999) of the regression equations and value of intercept on ordinate which is close to zero.

Accuracy and precision

The mean recoveries and %RSD are illustrated in Table 2. The data indicates that the proposed derivative spectrophotometric method is highly reproducible during one run and between different runs.

Stability

Stability of Pantoprazole Sodium and Itopride Hydrochloride in solutions during the analytical method showed that the analytes were stable for at least 24 h in solutions when protected from light.

CONCLUSION

From the results of this study it can be concluded that the proposed first order derivative spectrophotometric method can be used for simultaneous determination of Pantoprazole Sodium and Itopride Hydrochloride. This method is simple, rapid, practical, reliable and inexpensive and can be used for routine analysis of simultaneous determination of these compounds without any prior separation in quality control laboratories.

Table 1: Statistical data of calibration curve for pantoprazole sodium and itopride hydrochloride using first order derivative spectra

Parameters	Pantoprazole Sodium	Itopride Hydrochloride
Wavelength selected (nm)	238.5	288
Linearity range (µg/ml)	3-15	5-40
Regression equation	$y = 1.022 \times 10^{-3}x - 2.68 \times 10^{-4}$	$y = 9.13 \times 10^{-3}x - 2.97 \times 10^{-4}$
S.D of Slope	1.03×10^{-1}	2.7×10^{-2}
R.S.D. of Slope	0.89	0.96
Correlation coefficient	0.9991	0.9992

Table 2: Results of drug content and analytical recovery of pantoprazole sodium and itopride hydrochloride

Parameters	Pantoprazole sodium	% R.S.D	Itopride hydrochloride	% R.S.D
Labelled claim	40 mg	-	150 mg	-
% Drug content ± S.D	101.32 ± 0.3802	0.38	99.87 ± 0.5761	0.58
Analytical recovery at 80 % ± S.D	99.45 ± 0.1204	0.12	99.93 ± 0.1873	0.19
Analytical recovery at 100 % ± S.D	99.87 ± 0.1467	0.15	99.64 ± 0.1982	0.20
Analytical recovery at 120% ± S.D	99.95 ± 0.1751	0.18	99.78 ± 0.2118	0.21

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