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Research Article

Development and Validation of UV Spectroscopic Method for Simultaneous Estimation of Pantoprazole and Cinitapride in Bulk and in Capsule Dosage Form

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ABSTRACT

A new, rapid, precise, selective and sensitive Vierodt's/simultaneous equation method is developed for the simultaneous estimation of pantoprazole (PNT) and cinitapride (CNT) in combined dosage form. In the developed method, absorbance was measured at 289 nm (λ max of Pantoprazole) and 267.2 nm (λ max of Cinitapride). The drugs obeyed the Beer's law in the concentration range of 13-65µg/ml and 1-5 µg/ml respectively for pantoprazole and cinitapride. Accuracy of the method was determined by recovery studies and was found to be 101.32 % and 98.9 % for Pantoprazole and Cinitapride respectively. The developed method is simple, precise, rapid and selective. It can be used for routine analysis of both drugs in bulk as well as in pharmaceutical formulations.

Keywords: Simultaneous Equation Method, Cinitapride, Pantoprazole.

INTRODUCTION

Pantoprazole sodium sesquihydrate is official in IP, BP, USP, EP. Pantoprazole sodium sesquihydrate is widely used as antiulcer drugs (proton pump inhibitors) through inhibition of hydrogen-potassium adenosine triphosphatase (H^+/ K^+-ATPase) in gastric parietal cells. Pantoprazole (PNT) reduces the gastric acid secretion regardless of the nature of stimulation.

Chemically PNT is Sodium5-(difluoromethoxy)-2-[(RS)-[3,4,-dimethoxypyridine-2-yl) methyl]sulphinyl] benzimidazole-ide- sesquihydrate. Cinitapride (CNT) is a substituted benzamide gastroenteric prokinetic agent acting via complex, but synergistic effects on serotonergic 5-HT2 (inhibition) and 5-HT4 (stimulation) receptor and dopaminergic D2 (inhibition) receptors in the neuronal synapses of the myenteric plexi.

Chemically CNT is 4-Amino-N-[1-(3-cyclohexen-1-ylmethyl)-4-piperidinyl]-2-ethoxy~5~nitrobenzamide. Potentiometric titration is the only available official method for the estimation of Pantoprazole in single dosage forms. CNT and PNT combination is not official in any pharmacopoeia, hence no official method is available for the estimation of these two drugs in combined dosage forms[1,2].

A literature survey regarding quantitative analysis of these drugs revealed that there were several analytical methods for PNT using extractive spectrophotometry[6], H PLC[7,8] and H PTLC[9]. Extractive spectrophotometry[10], RP-HPLC[11], HPTLC[12] methods have been reported for estimation of CNT. There is only first order derivative spectroscopic method[13] is reported for the estimation of these two drugs in combined dosage forms. So in present study simple, sensitive, specific, accurate and precise spectroscopic method is described for the estimation of these two drugs in combined dosage forms.

MATERIALS AND METHOD

Apparatus

Instrument used was an UV-Visible double beam spectrophotometer, SHIMADZU (model UV-1800) with a pair of 1 cm matched quartz cells.

Reagents and chemicals

Pantoprazole (PNT) was kindly supplied as a gift sample from Intas Biopharmaceutical Ltd. Ahmedabad, Gujarat (India). Cinitapride (CNT) was kindly supplied as a gift samples from Cadila healthcare pvt. Ltd, Ahmedabad, Gujarat (India).

Marketed formulation

The pharmaceutical formulation containing 40 mg of PNT and 3mg of CNT was procured from the local pharmacy.

Preparation of standard solution

The standard stock solution of CNT and PNT was prepared by dissolving 10 mg of each API in 10 ml of different volumetric flask with distilled water to produce 1 mg/mL of each solution.1mL of aliquot was taken in 10mL volumetric flask and diluted with

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distilled water to prepare standard stock solution of 100 µg/ml of each.

Selection of analytical wavelength

Standard solutions of CNT (10 µg/ml) and PNT (10 µg/ml) were scanned in the range of 200 to 400 nm for the determination of wavelength having maximum absorbance. Pantoprazole shows 289 nm Cinitapride shows 267.2 nm and as the wavelength

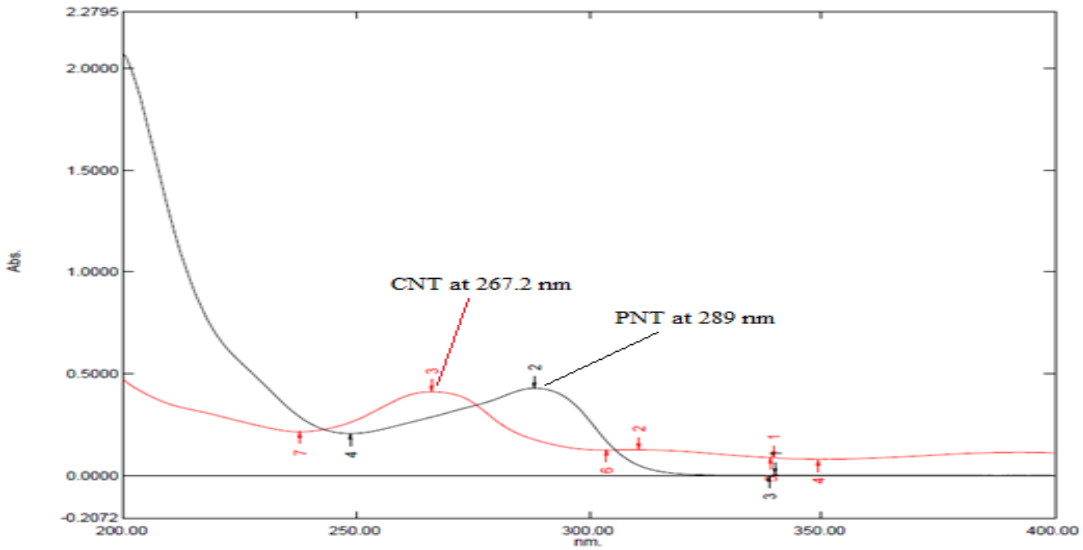

Figure 1: Overlain Spectra of pantoprazole (10µg/ml) and cinitapride (10µg/ml).

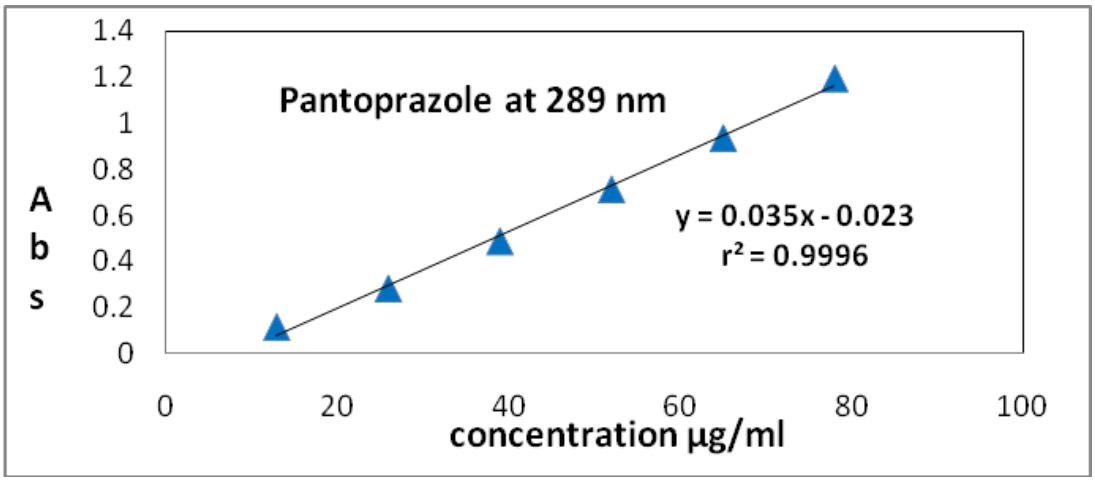

Figure 2: Calibration curve of standard PNT at 289 nm.

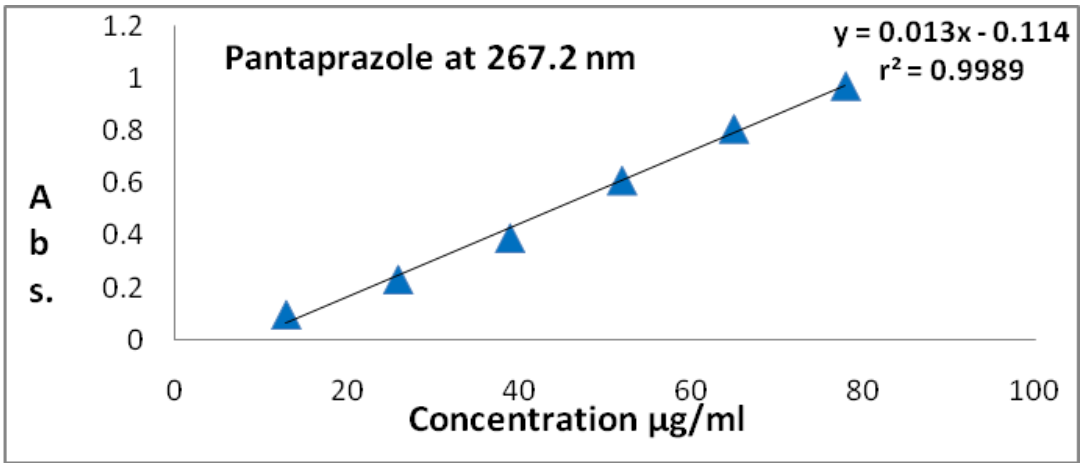

Figure 3: Calibration curve of standard PNT at 267.2 nm.

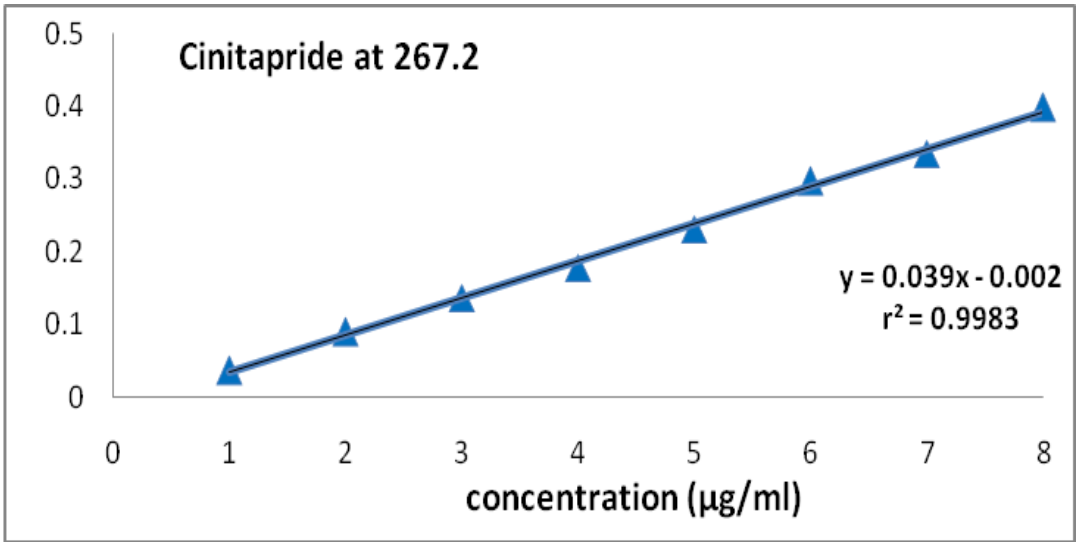

Figure 4: Calibration curve of standard CNT at 267.2 nm.

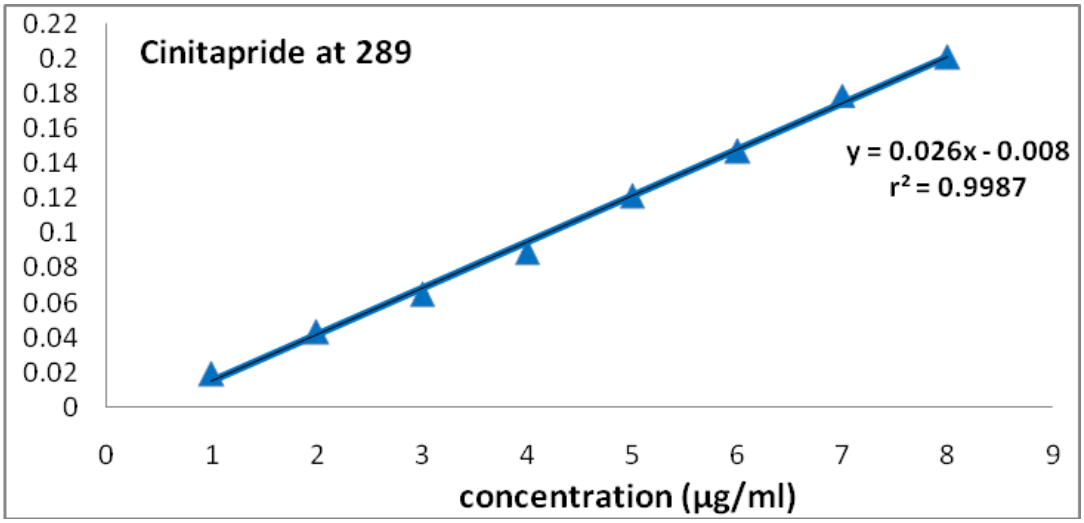

Figure 5: Calibration curve of standard CNT at 289 nm.

having maximum absorbance. From the overlain spectra, For the simultaneous equation method, 289 nm and 267.2 nm were selected as analytical wavelengths.

Vierodt's / Simultaneous Equation Method[3,4]

From overlain spectra (Fig 1.) 289 nm and 267.2 nm λmax for PNT were selected for formation of Absorbance ratio equation of two drugs. The absorbance at 289 nm and 267.2 nm for PNT and CNT were measured. The absorptivity values of each drug at both wavelengths were determined. The absorbance and absorptivity at this wavelength were substituted in following equations to obtain the concentration of both drugs.

Estimation of Pantoprazole and Cinitapride in synthetic mixture

Two simultaneous equations were formed using the above obtained absorptivity coefficient values 12.46 and 22.97 are absorptivities at 289 nm for Pantoprazole and Cinitapride respectively, while 10.28 and 45.62 are absorptivities at 267.2 nm for Pantoprazole and Cinitapride respectively.

$A_1 = 12.46\ C_x + 22.97\ C_y$ ..... (1)

$A_2 = 10.28\ C_x + 45.62\ C_y$ ..... (2)

Where, C_x and C_y are concentration of Pantoprazole and Cinitapride respectively in gm/liter in the sample solution. A_1 and A_2 are the absorbances of the mixture at 289 nm and 267.2 nm respectively in equation (1) and (2). The final concentration for synthetic mixture of Pantoprazole and Cinitapride was found to be in ratio of 13:1.

Validation of the proposed method[5]

Linearity (Calibration curve)

The calibration curves were plotted over a concentration range of and 13-65 µg/ml PNT 1-5 µg/ml for CNT. Accurately measured standard stock solutions of PNT (1.3, 2.6, 3.9, 5.2,6.5) and CNT (0.1, 0.2, 0.3, 0.4 and 0.5 ml) were transferred to a series of 10 ml volumetric flask separately and diluted up to the mark with methanol. The absorbance of solution was measured at 279 nm and 289.6 nm. The calibration curves were constructed by plotting absorbance versus concentration.

Method precision (repeatability)

The precision of the instrument was checked by repeated scanning and measurement of the absorbance of solutions (n = 7) of CNT (3 µg/ml) and PNT (39 µg/ml) without

Table 1: Recovery studies.

Mixture	Wavelength (nm)	Mean Recovery ± SD	% RSD
PNT:CNT	289 nm	Pantoprazole	Pantoprazole
		100.153 % ± 0.713	0.9575
	267.2 nm	Cinitapride	Cinitapride
		99.25 ± 0.602	0.3042

Table 2: Results of simultaneous estimation of CNT and PNT in marketed formulation.

Brand name	Label claim (mg)	Conc. Mean ± SD	Mean % ± SD	% RSD
CINTODEC	40 mg PNT+3 mg CNT	PNT 39.8625 ± 0.1537	PNT 99.66 ± 0.304	0.3053
		CNT 2.8815 ± 0.2098	CNT 98.76 ± 0.4197	0.4249

Table 3: Validation parameters.

Validation parameters		PNT	CNT
Specificity		% interference <0.5 %	
Range (µg/ml)	Working range	0.247-65	0.331-5
	Linear range	13-65	1-5
	Target range	31.2, 39, 46.80	2.4, 3, 3.6
	Target concentration	39	3
Accuracy (% Recovery)		100.153	99.25
Repeatability (% RSD)		1.417	1.003
Intraday analysis (% RSD)		0.360	0.243
Interday analysis (% RSD)		0.305	0.300
LOD		0.0820	0.1092
LOQ		0.247	0.331

changing the parameters of the proposed method.

Intermediate precision (reproducibility)

The intraday and interday precisions of the proposed method was determined by estimating the corresponding responses 3 times on the same day and on 3 different days over a period of one week for 3 different concentrations of standard solutions of PNT (31.2, 39 and 46.80 µg/ml) and CNT (2, 3 and 4 µg/ml). The results were reported in terms of relative standard deviation (% CV).

Accuracy (recovery study)

The accuracy of the method was determined by calculating the recoveries of PNT and CNT by the standard addition method. Known amount of standard solutions of PNT and CNT were added to prequantified sample solutions of CNT PNT (39 µg/ml) and (3 µg/ml) and. The amounts of PNT and CNT were obtained by applying regression line equations.

Limit of detection and Limit of quantification

The limit of detection (LOD) and the limit of quantification (LOQ) of the drug were derived by calculating the signal-to noise ratio (S/N, i.e., 3.3 for LOD and 10 for LOQ) using the following equations designated by International Conference on harmonization (ICH) guidelines.

LOD=3.3×S.D/S;

LOQ=10×S.D./S

Where, SD= the standard deviation of Y-intercept of 6 calibration curves and

S = the mean slope of the 6 calibration curves.

Assay of Capsule formulation

Twenty capsules were weighed and powdered. The quantity of the powder equivalent to 40 mg of PNT and 3 mg of CNT was transferred to a 100 ml volumetric flask. Add 60mL distilled water and sonicate it for 10min. The working solution was filtered through whatman filter paper (No. 41) and the volume was made up to the mark with the same solvent. The aliquot portions of above solutions were further diluted with solvent to get final concentration of about3 µg/ml CNT and 40 µg/ml of PNT and absorbance were measured at 289 nm and 267.2 nm against blank. The concentrations of two drugs in sample were determined by using equations 1 and 2. The results are reported in the table 2.

RESULT AND DISSCUSSION

The proposed method was validated as per ICH guideline. Method discussed in the present work provides a convenient and accurate way for simultaneous analysis of PNT and CNT. In Vierodt's / Simultaneous Equation method, wavelengths selected were 289 nm and 267.2 nm (λ_{max} of PNT). The plot of absorbance versus respective concentrations of PNT and CNT were found to be linear in the concentration range of 13-65 µg/ml for PNT and 1-5 µg/ml for CNT with correlation coefficient 0.9996 at 267.2 nm and 0.9989 at 289 nm as shown in table 3 and figures 2-4. Precision was calculated in terms of repeatability, intraday and interday variations and % CV (coefficient of variance) was found to be in acceptance range (table 3). The accuracy of method was determined by standard addition method. The % recovery ranges from 100-153 for PNT and 99.25 for CNT (table 1).

CONCLUSION

The low value of relative standard deviation for repeated measurement indicates that the method is precise. The value of % recovery is approximately 100%, which indicates that the method can be used for estimation of these two drugs in combined dosage forms without any interference due to the other components present in the formulations. Hence this study presents simple, accurate, precise and rapid spectroscopic analytical method for the simultaneous estimation of these two drugs in combined dosage form.

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