Academic Sciences Asian Journal of Pharmaceutical and Clinical Research
Vol 5, Suppl 4, 2012 ISSN - 0974-2441

Research Article

SPECTROPHOTOMETRIC SIMULTANEOUS ESTIMATION OF OMEPRAZOLE AND CINITAPRIDE IN BULK AND FORMULATION

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Received: 20 March 2012, Revised and Accepted: 18 May 2012

ABSTRACT

Two simple spectrophotometric methods have been developed for simultaneous estimation of Omeprazole (OMZ) and Cinitapride (CNT) in combined dosage forms has been developed. Method-I simultaneous equation method involves the measurement of absorbances at two wavelengths 267 nm (λmax of Cinitapride) and 302 nm (λ max of Omeprazole) in Methanol, Method-II involves, formation of Q-absorbance equation at 283 nm (isoabsorptive point) and 267nm (λmax of Cinitapride).The linearity lies between 3-18 µg/ml for both Omeprazole and Cinitapride for both methods. The accuracy and precision of the methods were determined and validated statically. Both methods showed good reproducibility and recovery with % RSD less than 2. Both method were found to be rapid, specific, precise and accurate and can be successfully applied for the routine analysis of Omeprazole and Cinitapride in combined dosage form.

Keywords: Cinitapride, Q-Absorbance ratio, Simultaneous equation.

INTRODUCTION

Cinitapride hydrogen tartarate (CNT) is chemically, 4-Amino-N-[1-(3-cyclohexen-1-ylmethyl)-4- piperidinyl]-2-ethoxy-5-nitrobenzamide hydrogen L-(+)-tartarate and a gastroprokinetic drug .[1]Cinitapride hydrogen tartarate is not official in any pharmacopeia. Literature survey reveals spectrophotometric[2-3] and HPLC[4] methods for determination of Cinitapride hydrogen tartarate in pharmaceutical dosage forms. Omeprazole (OMZ) is chemically, 5 methoxy-2 [[(4-methoxy-3, 5-dimetyl-2-pyridinyl) methyl] sulfinyl] 1H-benzimidazole and a proton pump inhibitor[5]. Omeprazole is official in Indian Pharmacopoeia (IP), British Pharmacopoeia (BP) and United State Pharmacopoeia (USP). The IP [6], BP [7] and USP [8] describe HPLC method for estimation of omeprazole. Literature survey reveals spectrophotometric [9], derivative UV spectroscopy [10], spectrofluorimetric [11], voltametric [12], LC-MS [13-14] and HPLC [15-17] methods for determination of omeprazole in pharmaceutical dosage forms as well as in biological fluids.

This combination is used in for the treatment of patient suffering from non-ulcer dyspepsia or gasteroesophageal reflux disease. The combination of these two drugs is not official in any pharmacopoeia; hence no official method is available for the simultaneous estimation of CNT and OMZ in their combined dosage forms. Literature survey reveals that there is no simple spectrophotometric method available for estimation of these drugs in combined dosage form. The present communication describes two simple, sensitive, accurate, precise, rapid and economical spectrophotometric methods for simultaneous estimation of CNT and OMZ in capsule dosage form.

MATERIALS AND METHODS:

Reagents and materials

Pure Cinitapride (CNT) & Omeprazole (OMZ) kindly gifted as a gift sample by Zydus Cadila Ankleshwar, Gujarat (India). BURPEX Capsule formulations Procured from market. All analytical grade chemicals and solvents were obtained from Merck (India), Qualigens and S D Fine chemicals Ltd. Methanol used as solvent in the study. Borosilicate Glassware was used in the study.

Instrumentation

A UV-visible spectrophotometer, model UV 1800 (Shimadzu) was used to measure absorbance of the resulting solutions. A Digital analytical balance and ultrasonic cleaner were used in the study.

Preparation of Standard Stock Solutions

The standard stock solution of CNT and OMZ were prepared by dissolving 100 mg of each drug in 100 ml volumetric flask separately using methanol. The standard stock solution having concentrations of CNT (1000 µg/ml) and OMZ (1000µg/ml).

PROCEDURE

Method I - Simultaneous equation method

3-18 µg/ml solution of OMZ was prepared in methanol and spectrum was recorded between 200-400 nm. Similarly 3-18 µg/ml solutions of CNT were prepared in Methanol and spectrum was recorded between 200-400 nm. OMZ showed λ_{max} at wavelength 302 nm and CNT showed λ_{max} at wavelength at 267 nm. The overlain spectrums of OMZ and CNT at different concentration were recorded. The Wavelength, for simultaneously detection of both drugs by Simultaneous Equation was 302 and 267 nm selected. The absorptivity coefficients of these two drugs were determined using calibration curve equation. In this method, the concentrations of both drugs are calculated by solving simultaneous equations.

Cx = (A1 aY2 - A2 Ay1) / (aX1 aY2 - aX2 aY1) ..... (1)

CY = (aX1 A2 - aX2 A1) / (aX1 aY2 - aX2 aY1) ..... (2)

Where Cx and Cy are concentration of CNT and OMZ respectively in gm/100 ml in the sample solution. A1 and A2 are the absorbances of the mixture at 267 nm and 302 nm respectively, aX1 is absorptivity of CNT at 267, aX2 is absorptivity of CNT at 302nm, aY1 is absorptivity of OMZ at 267 nm and aY2 =is absorptivity of OMZ at 302 nm.

Method II - Absorbance ratio method (Q-Analysis)

Absorbance ratio method uses the ratio of absorbances at two selected wavelengths, one which is an isoabsorptive point and other being the λ max of one of the two components. From the overlay spectra of two drugs, it is evident that CNT and OMZ show an isoabsorptive point at 283 nm. The second wavelength used is 267 nm, which is the λ max of CNT. Six working standard solutions having concentration 3, 6, 9, 12, 15 and 18 µg/ml for CNT and 3, 6, 9, 12, 15 and 18 µg/ml for OMZ were prepared in methanol, and the absorbances at 283 nm (isoabsorptive point) and 267 nm (λ max of CNT) were measured and absorptivity coefficients were calculated using calibration curve. The concentration of two drugs in the mixture can be calculated using equations

CX = [(QM – QY) / (QX -QY)] × A1/aX1 ..... (3)

CY = (A1/aX1) – CX ..... (4)

Where, A1 and A2 are absorbances of mixture at 283 nm and 267 nm, and aX1 and aY1 are Absorptivities of CNT and OMZ at 283 nm, aX2 and aY2 are absorptivities of CNT and OMZ respectively at 267 nm, and QM = A2 / A1, QX = aX2 / aX1 and QY = aY2 / aY1.

Analysis of CNT and OMZ in capsule dosage form

For determination of the content of CNT and OMZ in capsules, the powder from twenty capsules were collected and weighed. The powder equivalent to 3 mg of CNT or 20 mg of OME was transferred to 100 ml volumetric flask, dissolved in 50 ml of methanol and sonicated for 30 min, and volume was made up to mark with methanol. The solution was then filtered through Whatman filter paper no. 41. The solution was further diluted with methanol to get a final concentration of 3 µg/ml of CNT and 20 µg/ml of OMZ. For method I, the absorbances of the sample solution i.e. A1 and A2 were recorded at 267 nm and 302 nm respectively and concentration of two drugs in the sample were determined using above equation (1) and (2). For method II, the absorbances of the sample solution i.e. A1 and A2 were recorded at 283 nm (isoabsorptive point) and 267 nm (λmax of CNT) respectively, and ratios of absorbance were calculated, i.e. A2/A1. Relative concentration of two drugs in the sample was calculated using above equation (3) and (4). The analysis procedure was repeated six times with capsule formulation.

Validation

The method was validated according to ICH guidelines to study linearity, accuracy and precision.

Linearity

The linearity of measurement was evaluated by analyzing different concentrations of the standard solution of OMZ and CNT. For both the methods, the Beer law was obeyed in the concentration range 3-18 µg/ml for OMZ and CNT respectively. The correlation coefficient was found to be 0.999 at 267nm for Cinitapride and 0.997 at 302nm for Omeprazole.

Recovery studies (Accuracy)

To study the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels. A known amount of drug was added to pre analyzed capsule powder and percentage recoveries were calculated. The results of recovery studies were satisfactory and are presented in Table-2.

Precision

The reproducibility of the proposed methods was determined by performing Capsule assay at different time intervals on same day (Intra-day precision) and on three different days (Inter-day precision).

RESULTS AND DISCUSSION

For Both methods linearity was observed in the concentration range of 3-18 µg/ml for both Omeprazole and Cinitapride. Marketed brand of Capsule was analyzed and amount of drug determined by proposed methods ranges from 98.55 to 101.55 as shown in Table 1. The proposed methods were validated as per ICH guideline. The accuracy of method was determined by calculating mean percentage recovery. It was determined at 80,100 and 120 % level. The % recovery ranges from 99.25 to 102 for both methods and presented in Table 2. Precision was calculated as repeatability (% RSD is less than 2) and inter and intraday variations (%RSD is less than 2) for both drugs.

The proposed methods were found to be simple, accurate and rapid for the routine determination of Omeprazole and Cinitapride in formulation. To study the validity and reproducibility of proposed methods, recovery studies were carried out. The methods were validated in terms of linearity, accuracy, precision, specificity and reproducibility. Both methods can be successfully used for simultaneous estimation of Omeprazole and Cinitapride in combined dosage form.

CONCLUSION

The two spectrophotometric methods were developed and validated as per ICH guidelines. The standard deviation and % RSD calculated for the proposed methods are within limits, indicating high degree of precision of the methods. The results of the recovery studies performed indicate the methods to be accurate. Hence, it can be concluded that the developed spectrophotometric methods are accurate, precise and can be employed successfully form they estimation of Omeprazole and Cinitapride in bulk and formulation.

Table 1: Results of marketed formulation analysis

Method	Capsule content	Label claim(mg)	Label claim*(%)	±SD*	RSD (%)*
I	OMZ	20	99.83	0.0288	0.028
	CNT	3	101.55	0.5084	0.5
II	OMZ	20	101.51	0.5033	0.495
	CNT	3	98.55	0.6925	0.702

***Mean of six estimations. OMZ =Omeprazole, CNT = Cinitapride.**
Method I: Simultaneous equation
Method II: Q-Absorbance ratio

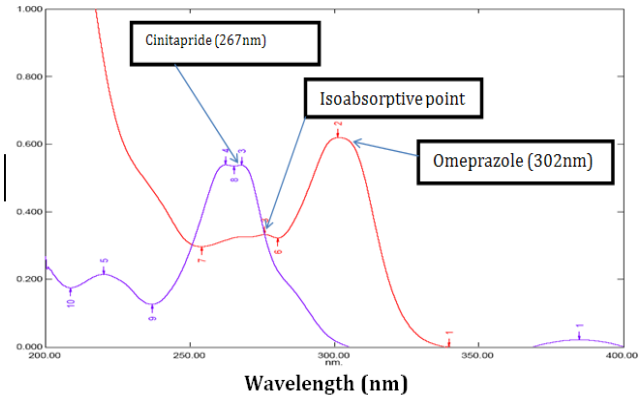

Figure 1: Overlay spectra of OMZ and CNT for both method

Table 2: Results of recovery studies

Level of recovery	Amt of drug Added µg/ml	Drug	Method I			Method II		
			Recovery (%)*	±SD*	%RSD	Recovery (%)*	±SD*	%RSD
80%	2.4	CNT	101.04	±0.213	0.21	99.253	±0.555	0.55
	36	OMZ	101.33	±0.627	0.61	102	±0.145	0.14
100%	3	CNT	101.55	±0.19	0.18	99.273	±0.417	0.42
	40	OMZ	100.7	±0.075	0.07	101.1	±0.16	0.15
120%	3.6	CNT	100.04	±1.009	1	101.06	±0.46	0.45
	44	OMZ	100.62	±0.319	0.31	100.35	±0.105	0.1

***Mean of six estimations. OMZ =Omeprazole, CNT = Cinitapride.**

Acknowledgements

The authors are very thankful to Dr. R.H PARIKH; Principal. We are thankful to Ramanbhai Patel College of Pharmacy and Charotar University of Science and Technology (CHARUSAT), Changa, for providing the research facilities. We are also thankful to Zydus Cadila Pharmaceuticals Ltd, Ankleshwar for providing the gift samples of CNT and OMZ for research work.

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