Research Article

Validated First Order Derivative Spectroscopic Method for the Determination of Cinitapride and Omeprazole in Bulk and Pharmaceutical Dosage Form.

***Jagdish Jadav, Parul Parmar, Smita Talaviya, Sagar Solanki, Jignesh Patel, Mandev Patel.**

Department of Pharmaceutical Chemistry, K. B. Raval College of Pharmacy, Kasturinagar, Sertha, Gandhinagar – 382423, Gujarat, India.

ABSTRACT

A simple, accurate, precise and sensitive First order derivative spectrophotometric method was developed for the estimation of Cinitapride and Omeprazole in bulk and pharmaceutical dosage forms. The estimation of Cinitapride and Omeprazole were carried out at 254.6 nm (Zero Crossing Point of Omeprazole) and 236.0 nm (Zero Crossing Point of Cinitapride) respectively. The method was found to be linear and obeys Beer's law in the concentration range of 1.5-15 µg/ml (R^2=0.9998) and 10-50 µg/ml (R^2=0.9996) respectively. The developed method was validated according to ICH guidelines for linearity, accuracy, precision, LOD and LOQ. The LODs (Limit of detection) were found to be 0.3440 and 0.6029 for Cinitapride and omeprazole respectively and LOQs (Limit of quantification) were found to be 0.7515 and 1.4331 for Cinitapride and omeprazole respectively. The accuracy was found to be 99.61-101.35 and 101.01-101.66 for Cinitapride and omeprazole respectively. The % assay was found to be 98.5- 100.70 % for Cinitapride and 99.20-100.50 % for Omeprazole. Thus the proposed method can be successfully applied for the estimation of Cinitapride and Omeprazole in bulk and pharmaceutical dosage forms.

Keywords: Cinitapride, first order derivative spectroscopy, ICH guidelines, omeprazole, validation.

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***Address for correspondence:**
Jagdish Jadav
Department of Pharmaceutical Chemistry, K. B. Raval College of Pharmacy, Kasturinagar, Sertha, Gandhinagar – 382423, Gujarat, India.
E-mail: jagdishjadav26@gmail.com

INTRODUCTION[1-5]

Cinitapride (CNT) is, (RS)-4-amino-N-[1-(1-cyclohex-3-enylmethyl)-4-piperidyl]-2-ethoxy-5-nitro benzamide, a gastroprokinetic agent and antiulcer agent of the benzamide class. It acts as an agonist of the 5-HT1 and 5-HT4 receptors and as an antagonist of the 5-HT2 receptors. It is indicated for the treatment of gastrointestinal disorders associated with motility disturbances such as gastroesophageal reflux disease, non-ulcer dyspepsia and delayed gastric emptying.

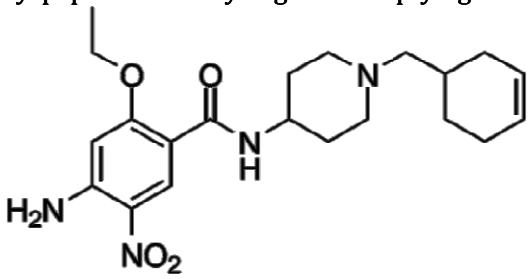

Figure I- Structure of Cinitapride (CNT)

Literature survey reports some of analytical method like, colorimetric method[6-7],UV spectroscopic method[8-9], RP-HPLC[10-11], polarography[12], LC-MS- plasma[13], UPLC[14] and HPTLC[15] methods, alone CNT and with other drugs.

Omeprazole (OME) is, 6-methoxy-2-((4-methoxy-3,5-dimethylpyridin-2-yl) methyl-sulfinyl)-1*H*-benzo[*d*]imidazole, a proton pump inhibitor used in the treatment of dyspepsia, peptic ulcer disease (PUD), gastroesophageal reflux disease (GORD/GERD), laryngopharyngeal reflux (LPR) and Zollinger–Ellison syndrome.

Literature survey reports some of analytical method like colorimetric method[16-17], UV spectroscopic method[18-19], LC-MS/MS[20], RP-HPLC[21-25], HPTLC[26], SFC[27] methods alone OME and with other drugs.

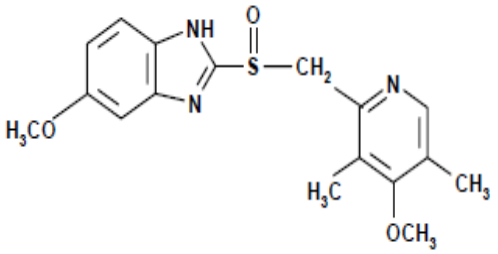

Figure II- Structure of Omeprazole (OME)

Only single spectroscopic method[28] is reported on combination of Cinitapride and Omeprazole so its worth will to do derivative method to get more accurate results.

This paper presents simple, rapid, reproducible and economical method for the simultaneous estimation of both the drugs by 1st Derivative UV Spectroscopic method.

MATERIALS AND METHODS

A Shimadzu UV-VIS Spectrophotometer 1800 with 1.0 cm matched quartz cells was used.

Standard gift samples of Cinitapride and Omeprazole were procured from Reschem Pharma Pvt. Ltd., Ahmedabad and Cadila Pharma Pvt. Ltd., Dholka, Ahmedabad, respectively**.** Combined dosage formulation containing Cinitapride and Omeprazole were purchased from local market (BURPEX, Zydus Cadila).

Preparation of standard stock solution (100 µg/ml).

The stock solution (100 µg/ml) of CNT and OME were prepared separately by dissolving accurately about 10 mg of drug in Methanol and the volume was made up to 100 ml with Methanol to prepare standard stock solution (100 µg/ml).

Determination of zero crossing point

The standard stock solution (100 µg/ml) of CNT and OME were further diluted to obtain the final concentration 1.5, 3, 6, 9, 12, 15 µg/ml and 10, 20, 30, 40, 50 µg/ml respectively. Both the solutions were scanned in the spectrum mode from 200.0 nm to 400.0 nm. The zero order spectrum thus obtained was processed to 1st derivative spectrum using Delta lambda 8.00 and Scalling factor 1.0. It appear that Cinitapride showed zero crossing point at 334.3 nm and 236.0 nm and omeprazole showed zero crossing point at 302 nm, 280.0 nm, 276.0 nm and 254.6 nm.

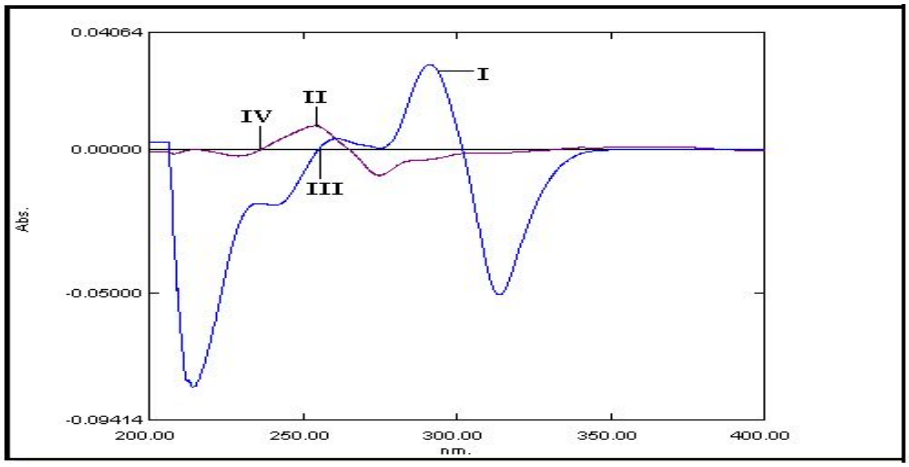

Figure: III. Overlay 1st derivative absorption spectra of Cinitapride and Omeprazole in methanol {I- Omeprazole, II- Cinitapride, III- Zero crossing point of Omeprazole (254.6 nm), IV- Zero crossing point of Cinitapride (236.0 nm)}.

Validation[29] The method was validated according to ICH guidelines to study linearity, accuracy, precision, LOD and LOQ.

Linearity

The measurement of linearity was evaluated by analyzing different concentrations of the standard solution of CNT and OME. For both the methods, the Beer law was obeyed in the concentration range 1.5-15 µg/ml and 10-50 µg/ml for CNT **(Figure II)** and OME **(Figure III)** respectively. The absorbance was plotted against the corresponding concentrations to obtain the calibration graphs.

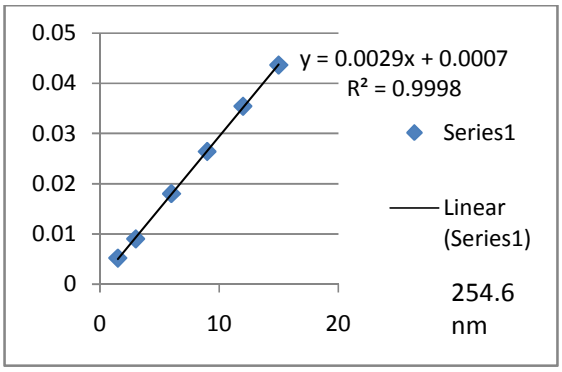

Figure: IV Calibration curve of Cinitapride at 254.6 nm

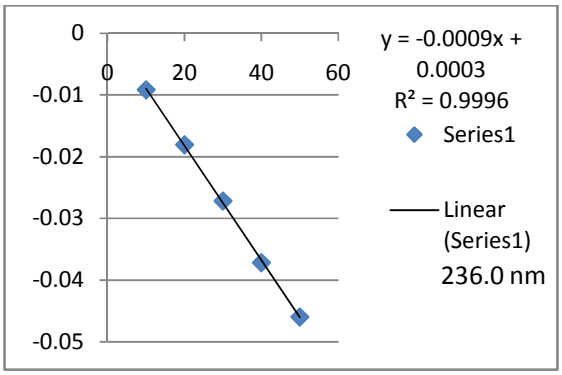

Figure: V Calibration curve of Omeprazole at 236.0 nm

Precision

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

Limit of Detection and Limit of Quantitation

The LOD and LOQ were separately determined based on calibration curve. The residual standard deviation of a regression line or the standard deviation of y- intercepts of regression lines were used to calculate the LOD and LOQ. The detection limit (LOD) may be expressed as: LOD = 3.3 σ/S and the quantitation limit (LOQ) may be expressed as: LOQ =10 σ/S Where, σ = the standard deviation of the response S = the slope of the calibration curve.

Accuracy (% Recovery studies)

To ascertain the accuracy of proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%). Percent recovery was calculated for CNT and OME, by this method **(Table 1)**. Here three times repetition done with proposed procedure.

Table 1: Result of Accuracy

Drug	Level of Recovery	Amt. of drug taken µg/ml	Amt of std. drug added (spiked amt) µg/ml	% of drug estimated(n=3)
CNT	0%	3	0	101.14
	80%	3	2.4	99.61
	100%	3	3	100.00
	120%	3	3.6	101.35
OME	0%	20	0	101.11
	80%	20	16	101.23
	100%	20	20	101.66
	120%	20	24	101.01

Table 2: Regression analysis and Validation Parameter

Parameters	Cinitapride	Omeprazole
Linearity Range	1.5-15 µg/ml	10-50 µg/ml
Correlation Coefficient	0.9998	0.9996
Precision (% RSD)	0.75-1.71	0.57-1.89
Intraday(n=3)	0.80-1.69	0.57-1.29
Interday (n=3)	0.75-1.71	0.98-1.89
LOD (µg/ml)	0.3440	0.6029
LOQ (µg/ml)	0.7515	1.4331
Accuracy(% Recovery)	99.61-101.35	101.01-101.66

RESULTS AND DISCUSSION

The present work provides an accurate, reproducible, sensitive method for the simultaneous analysis of CNT & OME in bulk and capsule formulation. Linear relationships between drug concentrations were obtained over the range of at 1.5-15 µg/ml & 10-50 µg/ml for CNT and OME respectively. Under experimental conditions described assay of capsule, linearity, accuracy studies and precision, LOD and LOQ were estimated. Correlation coefficient was found to be > 0.995. The results of commercial capsule formulation are presented in **(Table 1)**. The % assay was found to be 98.5- 100.70 % for CNT and 99.20-100.50 % for OME, and S.D. and R.S.D. for six determinations of capsule sample, by this method, was found to be less than 2.0 indicating the precision of this method. No interference was observed from the pharmaceutical excipients.

CONCLUSION

The UV spectrophotometric method was developed and validated as per ICH guidelines. The standard deviation and % RSD calculated for the proposed method are within limits, indicating high degree of precision of the method. The results of the recovery studies performed indicate the method to be accurate. Hence, it can be concluded that the developed spectrophotometric method is accurate, precise and can be employed successfully for the estimation of CNT and OME in bulk and formulation.

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