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RESEARCH ARTICLE

Development and Validation of UV Spectrophotometric Method of Cinitapride in Bulk and Tablet Formulations

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ABSTRACT

The present research works discuss the development of a UV estimation method for Cinitapride. Simple, fast, accurate and cost efficient and reproducible. Spectrophotometric method has been developed for the estimation of Cinitapride at in bulk and tablet formulations. The wave length (λ max) selected for the Cinitapride at was 263 nm. The linearity for this drug at the selected wavelength is lies between 0.2 to1µg/ml. Beer's law[3,7] obeyed in this concentration range with correlation coefficient of 0.9999. The proposed method was successfully applied to the determination of cinitapride in pharmaceutical formulations without any interference from common excipients.

KEYWORDS

Cinitapride, Absorbance, Validation, Detection Limit

INTRODUCTION

Cinitapride is chemically 4-amino-*N*-[3-(Cyclohexan-1-yl-methyl)-4-piperidinyl]-2-ethoxy-5-Nitro benzamide (Figure 1), it is a substituted benzamide gastroenteric prokinetic agent acting via complex, but synergistic effects on serotonergic 5-HT_2 (inhibition) and 5-HT_4 (stimulation)receptor and dopaminergic D2 (inhibition) receptors in the neuronal synapses of the myenteric plexi[5,8].

A survey of literature revealed a polarographic method and LC-MS/MS methods for its determination[2]. The aim of the study is to develop a simple, sensitive, accurate and precise method for determination of Cinitapride in pharmaceutical formulations and bulk drugs using UV spectrophotometer.

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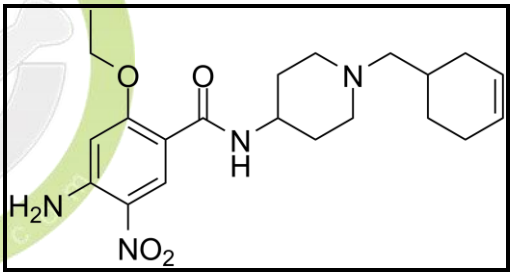


Figure 1: Structure of Cinitapride

EXPERIMENTAL

Instruments

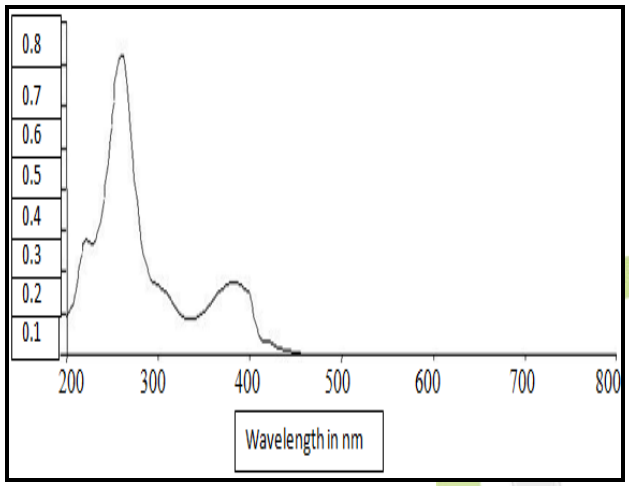
An analytical UV- Visible Spectrophotometer (UV-2080) with a matched pair of 10 mm quartz cells were used for experimental purpose.

Materials

Cinitapride was obtained as a gift sample from Cipla Pharma; Methanol AR was procured from MERCK Limited, Mumbai. The commercially available marketed tablet brand containing Cinitapride 1 mg in each tablet has been used for estimation.

Scanning and Determination of Maximum Wavelength (λmax)

In order to ascertain the wavelength of maximum absorption (λ max) of the drug, qualitative solution of the drug was prepared in methanol and scanned using UV spectrophotometer within the wavelength region of 200-400 nm against methanol as blank. The resulting spectra are shown below (Figure 2) and the absorption curve showed characteristic absorption maxima at 263 nm for Cinitapride.



Preparation of Standard Stock Solutions

Standard stock solution (primary) was prepared by dissolving 10 mg of cinitapride in 10 ml of methanol to get concentration of 1mg/ml (1000µg/ml). Secondary stock solution was prepared daily by diluting 1ml of the primary stock solution to final volume of 10 ml using methanol to get concentration of 0.1mg/ml (100µg/ml).

Preparation of Calibration Standard Solutions

The calibration standard solutions were prepared daily by diluting secondary stock solution with methanol to get calibration standard solutions of 0.2, 0.4, 0.6, 0.8 and 1 µg/ml of cinitapride to construct Beer's law plot for pure drug, the absorbance was measured at λmax 263 nm, against methanol as blank.

Procedure for Formulations

Twenty tablets of cinitapride were accurately weighed, finely powdered and mixed. A portion of the powder equivalent to 10mg of cinitapride was transferred into a 10 ml volumetric flask and 10ml of methanol was added. The content of the flask was sonicated for 15 min and diluted to volume with methanol. This solution was centrifuged for 15 min at 5000 rpm to separate out the insoluble excipients. Appropriate solutions were prepared by taking suitable aliquots of the clear supernatant and diluting them with methanol to give final concentration (10µg/ml). The absorbance of these solutions was measured at 263 nm. The amount of cinitapride per tablet was calculated using the calibration curve.

Validation

Validation is one of the most important steps in method development for analytical determinations[1]. The main validation parameters such as linearity and range, and precision, recovery and ruggedness were evaluated in developed method[4,6].

Linearity and Range

Under the experimental conditions, the calibration graphs of the absorbance versus concentration were found to be linear over the range of 0.2-1 µg/ ml for proposed method. The statistical analysis of data obtained for the estimation of cinitapride in pure solution indicated high level of accuracy for the proposed methods as evidenced by the low values of standard deviation and coefficient of variation (Table 1). The linear regression equation obtained was Y = 0.100X+0 where Y is the absorbance and X is the concentration (in µg/ml) of pure drug solution (Figure 3). Linearity of the regression equation and negligible scatter of points for the two drugs by the proposed methods were demonstrated from the highly significant ($p > 0.05$) correlation coefficient value. The reported slope values without intercept on the ordinate at 95% confidence limits, suggested that the calibration lines of cinitapride solutions in methanol did not deviate from the origin as the above-obtained values fall within the confidence limits. (Table 2).

Table 1: Linearity Table of Cinitapride

S.no	Concentration (µg/ml)	Absorbance
1	0.2	0.0207
2	0.4	0.0415
3	0.6	0.0621
4	0.8	0.0828
5	1.0	0.1035

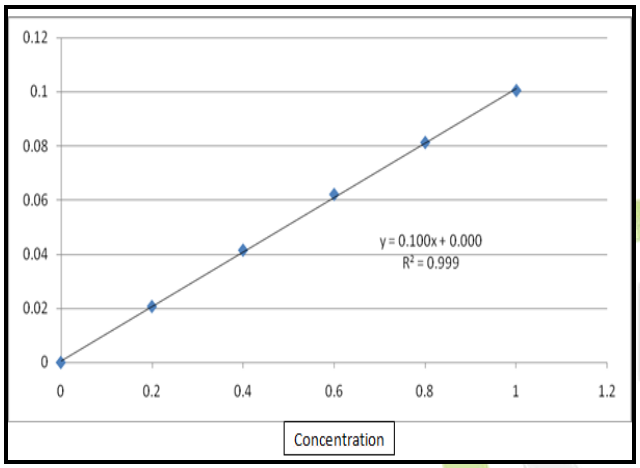


Figure 2: Linearity curve of cinitapride

Table 2: Regression Analysis of Data for the Estimation of Cinitapride from Standard Solution Statistical Parameters cinitapride

Precision

The precision of a method is defined as the closeness of agreement between independent test results obtained under optimum conditions. Three different concentrations of cinitapride in the linear range (0.3, 0.6 and 0.9 µg/ml) were analyzed in 5 independent series in the same day (intra-day precision) and 3 consecutive days (inter-day precision) The Results are shown in table 3.

Ruggedness

The ruggedness of the proposed method was evaluated by applying the developed procedures to assay of 10 µg/ml of cinitapride at using the same instrument by two different analysts under the same optimized conditions at different days. The obtained results were found to reproducible, since there was no significant difference between analysts. Thus, the proposed methods could be considered rugged. The results are shown in table 4.

Table 2: Intra Day & Inter Day Precision Readings

S.no	Conc (µg/ml)	Intraday	Inter day
1	0.3	0.0291	0.0310
2	0.6	0.0618	0.0612
3	0.9	0.0924	0.0983
4	Mean	0.0611	0.0635

Table 3: Ruggedness Data at 10 (µg/ml) by Two Analysts at Different Days

Test Conc (µg/ml)	Analyst-1	Analyst—2
10 µg/ml	0.9820	0.9846
10 µg/ml	0.9741	0.9813
10 µg/ml	0.9793	0.9902
10 µg/ml	0.9894	0.9857
10 µg/ml	0.9811	0.9814
Mean	0.9811	0.9846
S.D	0.0035	0.0026
%RSD	0.03567	0.2640

Table 4: % Recovery data of cinitapride

% label claim	Amount added	Amount found	%recovery
80	8	8.02	100.28
100	10	9.98	99.86
120	12	12.1	100.10

Table 5: Analysis of pharmaceutical formulation

Name of the formulation	Labeled amount in mg	Amount recovery in mg	% drug recovered	% SD
Cinitapride	1	1.005	100.48	0.286

Recovery

The absolute recovery of analytical method is measured as the response of a processed spiked matrix standard expressed as a percentage of the response of pure standard, which has not been subjected to sample pre-treatment and indicates whether the method provides a response for the entire amount of analyte that is present in the sample. It is best established by comparing the responses of extracted samples at low, medium and high concentrations in replicates of at least 6 with those non-extracted standards, which represent 100% recovery.

$$\text{Absolute recovery} = \frac{\text{Response of an analyte spike into matrix (processed)}}{\text{Response of analyte of pure standard (unprocessed)}} \times 100$$

If an internal standard is used, its recovery should be determined independently at the concentration levels used in the method. The Results are shown in table 5.

Analysis of Pharmaceutical Formulations

The optimized spectrophotometric method was applied to the direct determination of Cinitapride in tablet using calibration curve method. From the absorbance value, the drug content per tablet (on an average basis) was calculated. The results are shown in below table.

CONCLUSION

In this study a simple, fast and reliable UV spectrophotometric method was developed and validated for the determination of cinitapride in bulk drug and pharmaceutical formulations. This method was applied directly to the analysis of pharmaceutical dosage forms without the need of separation such as extraction steps prior to the drug analysis. From the results obtained, we concluded that the suggested method showed high sensitivity and precision. Moreover, this method is simple and in expensive and it can be employed for the routine quality control of cinitapride formulations.

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