Research Article

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DEVELOPMENT OF NEW VISIBLE SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF CINITAPRIDE IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT
Three simple and sensitive Spectrophotometric methods have been developed for the determination of Cinitapride (CNP) in pure and pharmaceutical dosage forms. Method A is based on the formation of charge transfer complex of the drug with chloranilic acid (λ_{max} : 550 nm). Method B is based on oxidative coupling of the drug with 3-methyl-2-benzothiazolinone hydrazone (λ_{max} : 420 nm). Method C is based on oxidation followed by complex formation with 1, 10-Phenanthroline (PTL) in the presence of ferric chloride to form a colored chromogen (λ_{max} : 510 nm). These methods have been statistically evaluated and found to be precise and accurate.
KEY WORDS: Cinitapride, Spectrophotometry, Chloranilic acid, MBTH, 1, 10-Phenanthroline and Validation

INTRODUCTION
Cinitapride (CNP)[1,2] is chemically 4-amino-N-[1-(3-cyclohexen-1-ylmethyl)- 4 – piperidinyl]-2-ethoxy-5-nitrobenzamide, with selective clinical activity against gastrointestinal disorders. A number of methods such as HPLC[3], LCMS[4-6] and polarographic methods have been reported for the determination of the active metabolite of CNP in human plasma and other biological fluids[7]. Literature survey reveals that few visible Spectrophotometric methods[8] have been reported for its quantitative determination in its pure form and pharmaceutical formulations. In the present investigation, three simple and sensitive Spectrophotometric methods have been developed for the determination of CNP. Method A is based on the formation of charge transfer complex of the drug with chloranilic acid. Method B is based on oxidative coupling of the drug with 3-methyl-2-benzothiazolinone hydrazone (MBTH). Method C is based on oxidation followed by complex formation with 1, 10-Phenanthroline[9-10] (PTL) in the presence of ferric chloride to form a colored chromogen. Beer's law is obeyed and results of analysis for the three methods have been validated statistically and by recovery studies.

MATERIALS AND METHODS
Instrument
A Systronics Model 2201 UV-VIS spectrophotometer was used for the measurements.
Reagents
All the chemicals used were of analytical grade. MBTH (0.2%w/v), Chloranilic acid (0.1%w/v), 1, 10-Phenanthroline (0.198%w/v), and Ferric Chloride (0.162%w/v) were prepared.
Standard drug solution
The stock solution (1 mg/ ml) of Cinitapride was prepared by dissolving 100 mg of the drug in 100ml of water and sonicated for about 10 minutes. This stock solution was further diluted to get 1000 µg/ml (for methods A and B) and 100 µg/ml of working standard solution (for method C).
Sample solution
Twenty tablets of CNP were weighed and powdered. A quantity of powder equivalent to 100mg was dissolved in 100 ml of distilled water. The solution was sonicated for 15min, filtered and made up to the mark with water. This stock solution was further diluted with sufficient volume of water to get 1000 µg/ml (for methods A and B) and 100 µg/ml of working standard solution (for method C).

ASSAY PROCEDURES
Method A
Aliquots of standard CNP solution ranging from 0.8-4 ml (1000µg/ml) were taken into a series of 10 ml volumetric flasks. To this added 1 ml of 0.1 % w/v chloranilic acid solution and allowed to stand at room temperature for 5 min. The final volume was made upto the mark with chloroform. The absorbance of the resulting solution was measured at 550 nm against the reagent blank. The amount of CNP was computed from its calibration graph.
Method B
Aliquots of standard drug solutions of CNP ranging from 0.2-0.6 ml (1000µg/ml) were taken into a series of 10 ml volumetric flasks. To each flask added 1.0 ml of ferric chloride (0.162% w/v) and 1 ml of MBTH, mixed well and the solution was allowed to react in the room temperature for about 15 min. And then the solution was made up to the mark with distilled water and the absorbance of the bluish-green colored chromogen thus formed was measured at 420 nm against reagent blank. The amount of CNP was computed from the Beer-Lambert's plot.
Method C
Aliquots of working standard solution (100 µg/ml) of CNP ranging from 0.5-2.5 ml were transferred into a series of 10 ml volumetric flasks. To these, 1.5 ml of ferric chloride and then 2ml of 1, 10-Phenanthroline was added. The volume was equalized with water and kept for boiling for 15 min. The flasks were cooled to room temperature and 2ml of O-phosphoric acid was added to each flask, finally the volume was brought to 10 ml with distilled water. The absorbance was measured at 510nm against reagent blank. The amount of CNP present in the sample solution was computed from its calibration curve.

RESULTS AND DISCUSSION
The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation and percent range of error (0.05 and 0.01 confidence limits) were calculated for all the three methods. The results are summarized in Table 1.The precision and accuracy were performed by analyzing six replicate samples containing known amount of drug and the results were summarized in Table1. The values obtained for the determination of CNP in pharmaceutical formulations (tablets) by the proposed methods are presented in Table 2. Studies reveal that the common excipients and other additives usually present in the tablets did not interfere in the proposed methods.

CONCLUSION

The proposed methods are applicable for the assay of CNP and have an advantage of wider range under Beer's law limits. The proposed methods are simple, selective and reproducible and can be used in the routine determination of CNP in pure form and formulations with reasonable precision and accuracy.

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Table 1: Optical characteristics, Precision and Accuracy of the proposed methods

Parameter	Method A	Method B	Method C
λ_{max} (nm)	550	420	510
Beer's law limit(μg/mL)	80-400	15-75	5-25
Sandell's sensitivity (μg/cm^2/0.001 abs. unit)	0.0354	0.04621	0.0362
Molar absorptivity (litre.mole^{-1}.cm^{-1})	0.897×10^4	8.259×10^5	2.63×10^4
Regression equation (Y*)			
Slope(b)	0.0023	0.0083	0.0313
Intercept(a)	0.0025	-0.0054	-0.0059
Correlation coefficient(r)	0.9993	0.9994	0.9996
%Relative standard deviation**	0.991	0.3996	0.8492
%Range of error			
0.05 significance level	0.827	0.4194	0.8913
0.01 significance level	1.224	0.6577	1.3978

*Y=a+bX, where Y is the Absorbance and X is the Concentration, ** For Six Replicates

Table 2: Estimation of Cinitapride in Pharmaceutical dosage Forms

Formulation	Labeled Amount (mg/tablet)	Amount found* by proposed methods (mg)			% recovery** by proposed methods		
		Method A	Method B	Method C	Method A	Method B	Method C
Tablet 1	5	4.98	4.96	4.94	99.94	99.82	100.53
Tablet 2	10	9.95	9.27	9.93	99.89	100.74	99.85

* Average of six determinations
**Recovery of amount added to the pharmaceutical formulation (Average of three determinations)

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