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SPECTROPHOTOMETRIC DETERMINATION OF CISAPRIDE IN PHARMACEUTUCAL FORMULATIONS

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ABSTRACT

A simple and economical spectrophotometric method has been developed for the assay of cisaprode in pharmaceutical formulations. The method is based on the formation of a wine red coloured azo product by the diazotization of cisapride followed by a coupling reaction with p-hydroxy acetanilide. The absorbance of wine red coloured azo product is measured at 498 nm against reagent blank. Beer's law is obeyed in the concentration of 40-200 μg/mL of drug.

Key words : Cisapride, Spectrophotometric.

INTRODUCTION

Cisapride is chemically cis-4-amino-5-chloro-N-{1—3-(4-fluoro phenoxy)-propyl]-3-methoxy-4-piperidyl}-2-methoxy benzamide monohydrates. Cisapride stimulates gastro-intestinal motility and is used in the treatment of gastro-oesophagical reflux disease. Few colorimetric[1, 2] and HPLC[3, 4] methods have been reported in literature. However, only one spectrophotometric[5] method is reported for the estimation of cisapride in formulations.

In present method, cisapride is diazotized with sodium nitrite and hydrochloric acid at 0°C temperature. After diazotization, the diazonium salt is coupled with p-hydroxy acetanilide to produced wine red coloured chromogen. The wine red coloured chromogen is measured at 498 nm against reagent blank prepared in a similar manner without drug solution. An attempt has been made to develop simple, sensitive and economical method for determination of cisapride in bulk and pharmaceutical formulations.

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EXPERIMENTAL

Materials

Instrument : A Milton Roy 1001 plus spectrophotometer with 10 mm matched quartz cells was used for the spectral and absorbance measurements.

Reagent and solution : All the chemicals and reagents used were of AR grade. Double distilled water was used throughout the investigation. Hydrochloric acid (0.1N) was prepared and standardized with standard procedure. Sodium nitrite (0.1 N) was prepared by dissolving 0.69 g in 100 mL distilled water. Sodium carbonate (0.5 N) was prepared by dissolving 5.3 g in 100 mL distilled water. 4-Hydroxy acetanilide (1%) and urea (1%) solution were prepared.

Standard stock solution

About 50 mg of cisapride (pure) was accurately weighed and dissolved in 20 mL methanol in 50 mL volumetric flask and diluted upto the mark with methanol to obtain a stock solution of 1 mg/mL. The final concentration of cisapride was brought to 200 μg/mL with methanol.

Calibration curve procedure

Various aliquots of cisapride ranging from 0.2-1.0 mL were transferred into a series of 10 mL volumetric flask. To each flask, 1.0 mL of 0.1 N hydrochloric acid and 1.0 mL of 0.1 N sodium nitrite solutions were added. The resultant solution is mixed well and kept aside for 5 min. at 0-50^{o}C temperature for complete diazotization. Then 1.0 mL of 1% urea solution was added and shaken frequently to allow nitrogen gas to escape. After 2 min., 1.0 mL of 0.5 N sodium carbonate solution and 1.0 mL of 1% 4-hydroxy acetanilide solution were added. The volume in each flask was made up to the mark with methanol. After 10 min., the absorbance of wine red colored solution was measured at 498 nm against reagent blank prepared in a similar manner omitting drug solution. A calibration graph was constructed and the amount of cisapride was computed from calibration curve.

Estimation of cisapride in tablet dosage forms

The above proposed method in calibration curve was extended to cisapride in tablet forms. Twenty tablets of cisapride were weighed and powdered. The powdered equivalent to 50 mg of cisapride was transferred into 50 mL volumetric flask containing 20 mL methanol. The solution was shaken well and made up to the mark with methanol. Then the

solution was filtered through Whatman No. 1 filter paper. This solution contains 1.0 mg/mL of cisapride. The final concentration of cisapride was brought to 200 µg/mL with methanol. Further analysis was carried out as per the procedure described under calibration curve and the amount of cisapride present in sample was estimated from calibration graph. The results are tabulated in Table 1.

Table : Estimation of cisapride in tablets

Sample	Labelled amount (mg)	Amount found in mg		% Recovery*	*t_{cal}
		Proposed method ± S. D. *	Official method*		
Tablet 1	10	10.04 ± 0.20	10.0	99.90	0.4313
Tablet 2	10	9.90 ± 0.22	9.60	99.80	1.000
Tablet 3	10	9.82 ± 0.24	9.48	99.50	1.636
Tablet 4	10	9.96 ± 0.39	9.86	99.80	0.2387
Tablet 5	10	9.86 ± 0.15	9.90	99.60	2.067
Tablet 6	10	10.06 ± 0.24	10.02	100.0	0.5623

*Average of five determinations based on label claim.

RESULTS AND DISCUSSION

The experiment results were analyzed by using spectronic 1001 plus spectrophotometer. In this method, cisapride underwent diazotization when treated with sodium nitrite and hydrochloric acid. The excess nitrous acid during the diazotization could be removed by the addition of urea solution. The solution was shaken frequently to allow the nitrogen to escape. For this diazotization process, cisapride readily diazotized in acidic medium and that the diazonium cation would react with a coupling reagent, 4-hydroxy acetanilide by electrophilic substitution at the o-position of the coupling agent to produce a wine red azo product. This wine red colour shows maximum absorbance at 498 nm. The wine red azo product was stable for more than 24 hours. The results obtained from the proposed method are in good agreement with label claim and comparable with the results of the reported method. The percentage recovery was found in the range of 99.5-100%. The additives and excipients usually present in tablets do not interfere. The statistical analysis was carried out from the five replicate measurements of cisapride. The

standard deviation values are low, which indicates the reproducibility of the proposed method. The experimental 't' values are being less than the theoretical "t' values indicating that the proposed method does not differ significantly with the official method. The proposed method was found to be simple, precise, accurate and time saving, reproducible and can be conveniently adopted for routine analysis of estimation of cisapride in bulk drugs samples and pharmaceutical formulations.

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