April 2007 Volume 5 Issue 1-6

Trade Science Inc.

Analytical CHEMISTRY

An Indian Journal

Full Paper

ACAIJ, 5(1-6), 2007 [75-78]

Validated Simultaneous Estimation Of Rabeprazole Sodium And Itopride Hydrochloride In Pure And Pharmaceutical Capsule Formulation

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Received: 6th February, 2007
Accepted: 11th February, 2007

Web Publication Date : 15th April, 2007

ABSTRACT

A simple, rapid and precise RPHPLC method was developed for the simultaneous estimation of rabeprazole sodium and itopride hydrochloride in its pure and pharmaceutical capsule formulation. A gemini C_{18} column(4.6mm×25cm) in isocratic mode, with mobile phase potassium dihydrogen phosphate and acetonitrile(65:35) were used. The flow rate was 1ml/min and individual components were measured at 275nm. The retention time of rabeprazole sodium and itopride hydrochloride was found to be 9.6 and 6.4min respectively. Linearity for rabeprazole sodium and itopride hydrochloride were in the range of 0.012-0.02mg/ml and 0.09-0.21mg/ml. Amount found for rabeprazole sodium and itopride hydrochloride were found to be 19.83 and 146.22 mg/capsule respectively. Percentage recoveries for both the drugs were 100.08 and 99.82 for rabeprazole and itopride respectively. The proposed method is precise, selective and rapid for simultaneous estimation of rabeprazole sodium and itopride hydrochloride.

KEYWORDS

Rabeprazole sodium;
Itopride hydrochloride;
HPLC;
Capsule.

INTRODUCTION

Rabeprazole sodium[8] is chemically known as 2-{[4-(3-methoxy propoxy-3-methyl-2-pyridinyl]-methyl}sulfinyl)-1H benzimidazole sodium salt. Rabeprazole sodium is a proton pump inhibitor and itopride hydrochloride is a gastric prokinetic agent. Rabeprazole sodium suppresses gastric acid secretion by inhibiting the gastric H^+ K^+ ATPase at the secretary surface of the parietal cells. Very few analytical methods have been reported in the literature for the determination of this drug based on capillary electrophoresis, visible spectrophotometric methods[7], HPLC and HPTLC[9-14] methods. Itopride hy-

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drochloride is N-[4-(2-dimethyl amnio)ethoxy]-benzyl]-3,4-dimethoxy benzamide hydrochloride. Itopride hydrochloride increases the release of acetylcholine through dopamine D2 receptor antagonistic action and inhibits the decomposing of release acetylcholine through its acetylcholine esterase inhibitor action, resulting in enhancement of gastro intestinal motility. These combinations are mainly used in the treatment of gastro esophageal reflux disease. Fixed dose combination containing rabeprazole sodium and itopride hydrochloride is available only in capsule form in the market. This is the new combination dosage form recently introduced and no methods have been reported so far for simultaneous estimation of these drugs. The aim of this work was to develop a simple, rapid, precise, and accurate reverse phase HPLC method for the determination of rabeprazole sodium and itopride hydrochloride in pharmaceutical dosage form in capsule.

MATERIALS AND METHODS

Instrument

High performance liquid chromatograph, Shimadzu HPLC-LC 2010 CHT with class VP version 6.14 with auto injector with injection volume 20µl, UV-visible detector SPD-10 A vp. A gemini C_{18} column(4.6mm×25cm) forms stationary phase.

Chemicals and reagents

Capsule formulations containing 150mg of itopride hydrochloride and 20mg of rabeprazole sodium(rabium plus) were procured from the market. Acetonitrile HPLC grade, HPLC grade water, potassium dihydrogen orthophosphate and sodium hydroxide AR grade were used.

Mobile phase

Mixed acetonitrile and potassium dihydrogen ortho phosphate in the ratio of 35:65 and filtered through 0.45 micron filter. pH was adjusted to 3.5 sodium hydroxide.

Preparation of mobile phase

Weighed accurately 6.82gm of potassium dihydrogen ortho phosphate and 1.60g of sodium hydroxide in 1000ml volumetric flask dissolved and diluted to volume with water. The prepared mobile phase is then subjected to filtration and degassing.

Standard stock solution

Weighed accurately about 150mg of itopride and 20mg of rabeprazole sodium in 100ml volumetric flask dissolved and diluted to volume with mobile phase.

Working standard solution

From this 5ml of solution is pipetted into a 50ml volumetric flask and diluted to volume with mobile phase.

Sample preparation

The mixed contents of twenty capsules were weighed, a quantity of powder equivalent to one capsule were weighed and transferred to a 100ml volumetric flask. Dissolved and made up to volume with mobile phase. The above solution is filtered through syringe filter. Pipetted out 5ml of the filtrate in a 50ml volumetric flask and made up to volume with mobile phase.

Assay

20µl of mixed working standard and sample solutions(n=6) were injected in to an injector of liquid chromatograph and peaks were recorded. From the peak retention time(response factor) of rabeprazole sodium and itopride hydrochloride were recorded. And also, the amount of drug samples(n=6) were calculated. The values are given in the TABLE 1

TABLE 1: Assay of rabeprazole sodium and itopride hydrochloride

S.No	Sample	Label claim (mg)	Amount present (mg)	Percentage label claim
1	Rabeprazole sodium	20	19.83	99.15*
2	Itopride hydrochloride	150	146.22	97.48*

*Mean of six readings

Assay results

In replicate analysis(n=6) of two drugs by the proposed method showed, the content of rabeprazole sodium and itopride hydrochloride were found as 19.83mg/capsule and 146.22mg/capsule respectively.

Linearity and calibration

Linearity was assessed by performing measurement at several analyte concentration varying quantities of stock solution was diluted with the mobile phase to give a minimum of 5 concentration in the range of 0.09, 0.12, 0.15, 0.18, 0.21mg/ml of itopride and 0.012, 0.016, 0.02, 0.024, 0.028mg/ml of rabeprazole sodium respectively. Evaluation of two drugs were performed at 275nm. Peak area was recorded for all the peaks. The plot of a peak area verses the respective concentrations of rabeprazole sodium and itopride hydrochloride were found to be linear in range of 120-280µg/ml and 900-1900µg/ml respectively with coefficient of correlation (r=0.9965) and(r=0.9995) respectively.

Recovery study

To ensure the reliability and accuracy of the method recovery studies were carried out by mixing a known quantity of standard drug with preanalysed sample and content were reanalyzed by the proposed method. The values are shown in TABLE 2.

The lower the values of relative standard deviation(RSD) indicate the method is precise and accurate. The mean recoveries of rabeprazole sodium and itopride hydrochloride were 100.02 and 99.82 and show there is no positive or negative interference of excipients in capsule.

Method of validation

As per ICH guidelines[6] the method is validated and following parameters were evaluated. Accuracy of the method was checked by recovery studies. Precision of the method was studies by analysis of multiple samplings of homogenous sample and expressed as co-efficient of variance(CV). Specificity of the method was established by various parameters like resolution and plate count.

TABLE 2: Recovery studies of rabeprazole and itopride

S.No	Sample	Amount of drug added (mg)	Amount of drug recovered (mg)	Percentage recovery
1.	Rabeprazole (5%)	1	0.53	97.74
2.	Rabeprazole (10%)	2	2.5	102.42
3.	Itopride (5%)	7.5	5.72	98.95
4.	Itopride (10%)	15	15.8	100.7

System suitability test

As per USP-24, system suitability tests were carried out on freshly prepared standard stock solutions of rabeprazole sodium and itopride hydrochloride.

20µl of both drugs were injected into the chromatograph under the optimized chromatographic conditions and following parameters were studied to evaluate the suitability of the system.

1. Calibration range
2. Number of theoretical plates
3. Resolution
4. Retention time
5. Tailing factors
6. Limit of detection and Limit of quantification

The values of system suitability test were shown in TABLE 3

RESULTS

The TABLE 1 gives details of findings of assay, recovery studies and system suitability parameters.

DISCUSSION

The mobile phase composing phosphate buffer and acetonitrile in the volume ratio(65:35v/v) and pH adjusted with sodium hydroxide showed good resolution peaks with in a short run time. As per the current regulatory requirements resolution between the two component should be more than 3, tailing factor should be less than 2 and theoretical plates should be more than 2000. It is evident from TABLE 3 that method developed for these drugs in combination is

TABLE 3: System suitability parameters

S.No	Parameter	Rabeprazole sodium	Itopride hydrochloride
1	Resolution	9.935	
2	Tailing factor	1.25	1.38
3	Theoretical plate	11730.1	8340.1
4	Calibration range	0.09-0.19 mg/ml	0.012-0.02 mg/ml
5	Limit of detection	0.42	1.1
6	Limit of quantification	1.3	3.3

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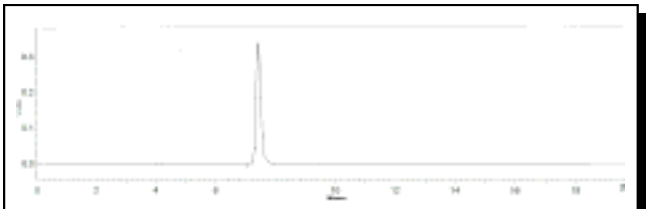
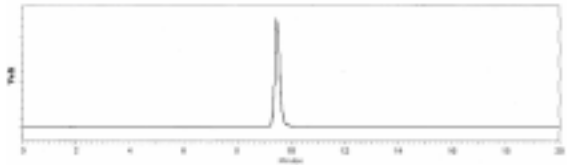
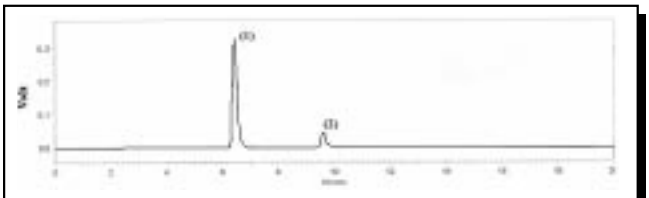


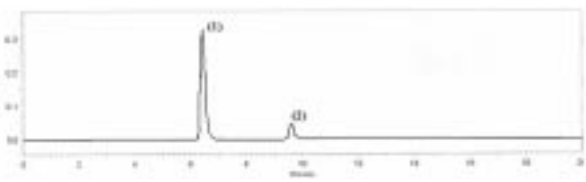
GRAPH 1: Identification chromatogram of itopride



GRAPH 2: Identification chromatogram of rabeprazole



GRAPH 3: Identification chromatogram for the assay of itopride (1) and rabeprazole (2)



GRAPH 4: Identification chromatogram for the recovery of itopride (1) and rabeprazole (2)

passing the standards of regulatory requirements. The method was found to be precise and accurate with low values of coefficient of variation. The TABLE 1 shows assay results which indicates that method is precise and accurate. The results of recovery study conform the accuracy of the method.

The proposed RP-HPLC method is accurate, simple, rapid and selective for the simultaneous estimation of rabeprazole sodium and itopride hydrochloride in capsule dosage form. Hence it is conveniently adopted for the routine analysis of the capsules.

ACKNOWLEDGMENTS

The authors are thankful to Themis Laboratories, Bombay for providing the gift samples of rabeprazole sodium and itopride hydrochloride.

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