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Determination of rabeprazole in pharmaceutical formulations by kinetic spectrophotometric method

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ABSTRACT

An important and simple kinetic spectrophotometric method has been developed for the determination of rabeprazole in pharmaceutical formulations. Alkaline potassium permanganate is used in this method for oxidation of rabeprazole at room temperature. The increase in the absorbance at 610nm owing to the formation of MnO_4^{2-} was measured spectrophotometrically. Calibration curve procedure was adopted for the assay of the drug. The calibration curve was linear over the concentration ranges of 5-55µg ml^{-1}, with the corresponding calibration equations:

Rate = - 4×10^{-7} + 8.84×10^{-2}C

KEYWORDS

Rabeprazole;
Potassium permanganate;
Kinetic determination;
Spectrophotometry;
Pharmaceutical formulations.

INTRODUCTION

Rabeprazole, 2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]-methyl]sulfinyl]-1H-benzimidazole, is a newly developed benzimidazole proton-pump inhibitor, which suppress gastric acid secretion by specific inhibition of the H+/K+-ATPase enzyme system at the secretary surface of the gastric parietal cell[1]. Rabeprazole is used for the treatment of acid-peptic diseases, such as duodenal, gastric and oesophageal ulceration[2]. Literature survey reveals chromatographic methods for determination of RAB in tablet dosage forms[3,4] as well as spectrophotometric methods for rabeprazole determination in combination with other drugs[5,6]. Stability indicating[7] and bioanalytical chromatographic methods[8-11] for quantification of rabeprazole are also reported. Also high-performance liquid chromatography-ultra violet (HPLC–UV) method with column switching between sample pre-treatment column and analytical column was developed for the quantitation of rabeprazole in human plasma; on a Bio-Sample Analysis system has been reported[12]. The drug is effectively useful in the treatment of duodenal ulcer, gastric ulcer, reflux oesophagitis and helicobactor pylori infection. In addition to its efficacy in healing or maintenance treatment, it may provide amore effective system relief than other comparative agents. There is large number of branded products of rabeprazole available in the market. Owing to such an importance of the drug, a sensitive, simple and fast method for its determination is urgently needed.

Presently there is no kinetic spectrophotometric method available for the determination of the cited drug in the literature. The advantages in the application of a kinetic method are to be expected, such as selectivity due to the measurement of the evolution of the absorbance with the reaction time. In this paper, a kinetically based spectrophotometric method is proposed for the

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determination of rabeprazole in bulk and capsules by measuring the change in the absorbance at 610nm and 530nm, whereby the oxidation of the drug with alkaline $KMnO_4$ at 25±1°C is followed.

EXPERIMENTAL

Apparatus

A JASCO-505 UV/VIS. Spectrophotometer, Japan with matched quartz cells were used to measure the absorption spectra.

Reagents

All reagents used were of analytical grade from Loba Chemicals. The potassium permanganate solution, (6.0×10^{-3}M) should be freshly prepared and its apparent purity was assayed titrimetrically (Vogel 2002). Sodium hydroxide solution (1.0M) was prepared in distilled water.

Test solution

The rabeprazole solution (0.1% w/v) was prepared by dissolving 100mg of the reagent in 0.5ml of 0.10M NaOH and then diluting to 100ml with distilled water. The rabeprazole solution was freshly prepared and used within 5 hours.

Marketed products

The commercial pharmaceutical preparations of rabeprazole, i.e., RABEKIND (Mankind Ltd., New Delhi, India), ROLES (Ranbaxy Laboratories Ltd.Rexcel, India), RBZ(Glenmark Pharmaceuticals Ltd., Mumbai, India) and PRORAB(Wockhardt Ltd., Mumbai, India) were purchased from a local pharmacist.

Recommended procedure

0.1% rabeprazole solution was prepared and pipetted into a series of 10ml volumetric flaks to obtain find concentrations in the range 5-150μg ml^{-1}. Subsequently, 1.5ml of 1M NaOH was added followed by 2.0ml of 6.0×10^{-3}M potassium permanganate solution and then diluted to volume with distilled water. The contents of the flask were mixed well and immediately transferred to the spectrophotometric cell. The absorance at 605nm was recorded at 25±1°C as a function of time against prepared reagent blank. The initial rate of formation of MnO_4^{2-} at the different concentrations of rabeprazole was evaluated from the slope of the tangent to the absorbance-time curve. The calibration curve was constructed by plotting initial rate of reaction against the final concentration of rabeprazole in μg ml^{-1}. The amount of rabeprazole in unknown samples was calculated either from the calibration curve of the corresponding regression equation.

RESULTS AND DISCUSSION

The absorption spectrum of rabeprazole solution in distilledwater shows two absorption bands, peaking at 205 and 292nm (Figure 1 curve A) while that of potassium permanganate solution in alkaline medium exhibits and absorption band peaking at 535 nm (Figure 1 curve B). The course of the reaction commences on addition of aqueous alkaline potasium permanganate to the rabeprazole solution resulting in the formation of a new band peaking at 605nm (Figure 1 curve C). This band is attributed to the formation of manganate ions in the presence of the drug. Thus, the intensity of the green colored solution increased with time owing to the formation of MnO_4^{2}. MnO_4^{2-}. This fact was used to develop a kinetically based spectrophotometric method for the determination of rabeprazole. The optimum conditions affecting the formation of manganate ions were studied and maintained throughout the experiments.

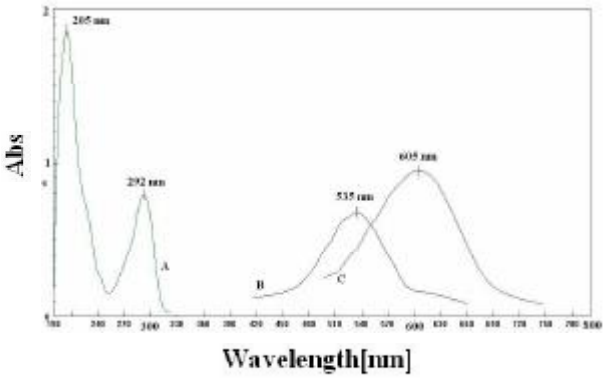

Figure 1: Absorption spectra of (A) 1.0ml of 2.707×10^{-4} M rabeprazole in distilled water (B) 1.0ml of 4.50×10^{-3} $MKMnO_4$+1.5ml of 1.0M NaOH solutions in distilled water and (C) 1.0 ml of 2.707×10^{-3}M rabeprazole + 2.0ml of 6.00×10^{-3} $MKMnO_4$ + 1.5ml of 1.0M NaOH solutions in distilled water. Each set was diluted with distilled water to 10 ml in a volumetric flask

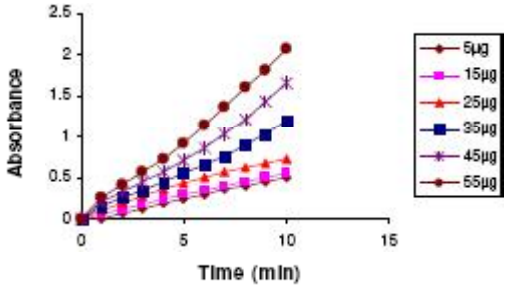

Figure 2: Absorbance of Rabeprazole at different concentrations in µg and time interval in minute at 605 nm

TABLE 1: Initial rate of reaction (formation of MnO_4^{2-}) at different concentrations of rabeprazole

Conc mol /lit.	Log conc mol / lit.	Initial rate in µg/ml/min	Initial rate in mol/l/s	log V
1.31E-05	-4.88244	0.0021	9.176E-05	-4.03735
3.93E-05	-4.40532	0.055	0.0024032	-2.6192
6.55E-05	-4.18347	0.1088	0.004754	-2.32294
9.18E-05	-4.03735	0.1611	0.0070393	-2.15247
0.000118	-3.9282	0.2141	0.0093551	-2.02895
0.000144	-3.84105	0.2671	0.011671	-1.93289

TABLE 2: Intra day and inter day assays: test of the precision of proposed method

Period of analysis	Amount in µg ml^{-1}		Recovery %	Standard error
	Amount taken	Estimated ± SD		
Intra day	20	19.99±0.03918	98.51	0.01752
analysis	50	50±0.05314	99.81	0.02377
Inter day	20	20.02±0.05224	101.2	0.02336
analysis	50	50 ± 0.02951	99.97	0.0132

TABLE 3: Results of analysis of commercial formulations

Drug	Label claim in mg/tablet	Estimated ± SD in mg/tablet	Recovery %
Rabekind	20	19.99± 0.04222	99.9
Prorab	20	20.01± 0.03701	100.1
Roles	20	20± 0.08178	100.03
RBZ	20	20± 0.07922	100.19

1.2×10^{-3}M $KMnO_4$ and 0.15 M NaOH in the final solution proved to be sufficient for the determinations. In this method, under the optimized experimental conditions, the determination of rabeprazole was carried out in an excess of potassium permanganate and sodium hydroxide with respect to the initial concentration of rabeprazole. As a result, pseudo zero order reaction conditions were obtained with respect to their concentrations.

Therefore, on the basis of the kinetic investigation, the kinetic equation for the oxidation of rabeprazole by KMnO4 in alkaline medium is written as:

$$\text{Rate} = k[C]^n[KMnO_4]^m[NaOH]^1 \quad (1)$$

For $[KMnO_4]\geq1.20\times10^{-3}$M and $[NaOH]\geq0.15$M equation (1) reduces to:

$$\text{Rate} = k\Psi[C]^n \quad (2)$$

where kψ is the pseudo-order rate constant, c is the concentration of rabeprazole and n is the order of the reaction with respect to rabeprazole of reaction. The logarithmic form of Equation (2) may be written as:

$$\text{Log (rate)} = \log k\Psi + n \log C \quad (3)$$

The initial rates of reaction were evaluated at different concentrations of rabeprazole by measuring the slopes of the initial tangent to the absorbance (at 610nm)- time curves during the first 10 min of the reaction (Figure 2). The values of the results are summarized in TABLE 1. The curve of log (rate) versus log c gave the following linear equation:

$$\text{Log (rate)} = 2.8451 + 1.2386 \log C \quad (4)$$

with a correlation coefficient (r) of 0.9998. The value of n in the equation confirmed that the reaction is first order with respect to rabeprazole with a constant of $700s^{-1}$.

The calibration curve was prepared by plotting the initial rate versus the concentration of rabeprazole and was found to be linear over the concentration range of 5-45µg ml^{-1}.The regression analysis of the calibration data yielded the following regression Equation:

$$\text{Rate} = -4\times10^{-7} + 8.84\times10^{-2}\ C$$

(N = 6, 95% confidence interval for difference: -0.009854 to -0.001846) with a coefficient of correlation, r = 0.9998. The variance was calculated[13] by statistical treatment of the calibration data at six concentration levels and found to be 9.688×10^{-6}µgml^{-1}. The low value of variance speaks for the negligible scattering of the experimental data points around the regression line.

The accuracy and precision of the proposed procedure was established by measuring the content of rabeprazole at two different concentration levels within one day and on five consecutive days shown in TABLE 2. The intra day and inter day assays were performed by performing five independent analyses at the 10.0 and 25.0 µg ml^{-1} concentration.

Results of analysis of commercial formulation are reported in TABLE 3. Low standard deviation values

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of determination indicate reproducibility of the method. Recovery studies were carried out by the addition of standard drug solution of equal quantity to preanalyzed and exhausted tablet sample solution at two different concentrations within the linearity of drug.

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