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Estimation of Rabeprazole Sodium in tablet dosage form by rapid isocratic reversed phase high performance liquid chromatography using volatile buffer additives

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A simple, rapid and reproducible reverse phase high performance liquid chromatographic (RP-HPLC) assay method for determination of Rabeprazole Sodium (RS) in solid dosage form (20 mg) has been developed. Chromatographic separation was performed on YMC C_{18}, ODS-AM stainless steel column (250 mm x 4.6 mm ID; particle size 5µ). Mobile phase comprised of 50 m *M* ammonium acetate in water (pH 8) with ammonia and methanol. Detection was performed using PDA detector. Recovery of RS in tablets was 95.5-96.8%. Chromatographic response of the analyte (100-500 µg/ml) was linear with correlation coefficient more than 0.99. Runtime of the method is very short and mobile phase additives used are volatile that are also suitable for mass spectrometry analysis. Therefore, this method could be used for routine quality control analysis and in bio-analytical work.

Keywords: Rabeprazole Sodium, Reverse phase high performance liquid chromatographic (RP-HPLC) assay method, Volatile buffer additives
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Introduction

Rabeprazole Sodium (RS)[1], 2-[[[4-(3-methoxy-propoxy)-3-methyl-2-pyridinyl]-methyl] sulfinyl]-1H-benzimidazole sodium salt, is white to slightly yellowish-white solid, very soluble in water and methanol, freely soluble in ethanol, chloroform, ethyl acetate and insoluble in ether and n-hexane. RS is rapidly degraded in acid media and more stable under alkaline conditions. It is in a class of drugs called proton pump inhibitors (PPIs), which block acid production by the stomach. PPIs are used for treatment of ulcers and Zollinger-Ellison Syndrome caused by stomach acid. Few HPLC assay methods for quantitation of RS in pharmaceutical dosage form require borate buffers or dilute ammonium hydroxide solution as mobile phase additives, which are suitable for UV-VIS/PDA detector, however not for mass spectrometry analysis.

This study presents a simple and rapid isocratic HPLC assay method[2-5] for quantitation of RS in solid dosage form using the solvent and buffer compatible with mass spectrometry[6].

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Materials and Methods

RS (purity, 99.70%) was a gift sample from Wockhardt Pharmaceuticals Ltd., Aurangabad, India. Ammonium acetate and ammonia were of Analytical grade (Merck India Ltd.). Methanol and water were of HPLC grade (Qualigens). Commercially available tablets claimed to contain 20 mg of RS (Rabemac-20, Rabepro-20) were procured from local market.

Quantitative HPLC was performed on a high-pressure liquid chromatography (Shimadzu HPLC class 10AT) with four LC-10AT pumps, PDA detector (SPD-M10Avp), an SIL-10AD series auto sampler and C_{18} bonded stainless steel column (YMS ODS-AM, 250 mm x 4.6 mm ID, particle size 5µ). HPLC system was equipped with data acquisition and processing software "Class-LC-10 series" (Shimadzu).

Mobile phase comprised 50 m *M* ammonium acetate in water (pH 8) with ammonia and methanol (15:85 v/v). Diluent (pH 8) used was water and methanol (1:1 v/v) with ammonia. Mobile phase was filtered through a 0.45-µm membrane filter, degassed with a helium spurge for 20 min and pumped from the respective solvent reservoir to the column (flow rate, 1.0 ml/min), which yielded a column back pressure of 165-175 kgf. Run time was set at 5 min and column

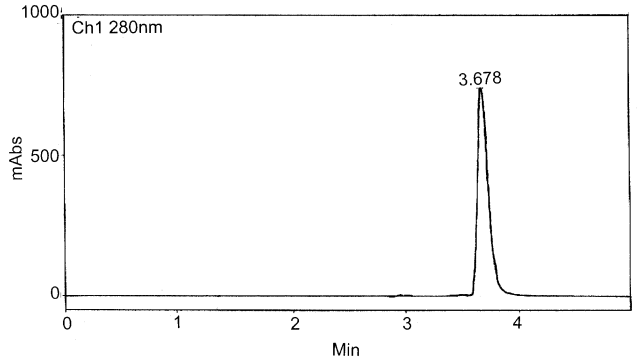

Fig.1— HPLC chromatogram of Rabeprazole Sodium

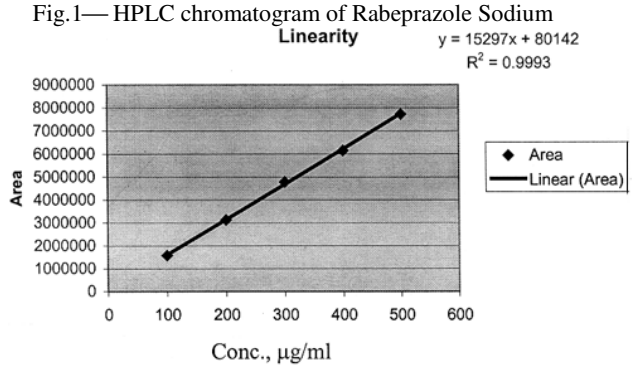

Fig. 2—Graph of peak area to drug concentration

Table 1— RSD and linearity

	Peak area	Conc. µg/ml	Area
	4797833	100	1572735
	4791915	200	3136073
	4801578	300	4775937
	4793389	400	6143583
	4788925	500	7717278
Average	4794728		
SD	4998.6		
RSD	0.104		

temperature was maintained at 30°C. Prior to the injection of drug solution, column was equilibrated for 60 min with mobile phase flowing through the system. Eluents were monitored at 280 nm and data were acquired, stored and analyzed with the software "Class-LC-10 series version 3.1" (Shimadzu).

A stock solution of drug was prepared by dissolving RS (100 mg) in a volumetric flask (100 ml) containing 25 ml of diluent, sonicated for 20 min and then made upto the volume with diluent. Working standard solution of RS (300 µg/ml) was prepared by suitable dilution of stock solution with diluent. Linearity solutions were prepared in diluent containing RS (100-500 µg/ml). Each of these drug solutions (10 µl) was injected into the column and the peak area and retention times were recorded.

Table 2— Recovery of Rabeprazole Sodium by new method

Drug	Label amount mg	Found amount mg	Recovery %
Rabemac-20	20.0	19.36	96.80%
Rabepro-20	20.0	19.11	95.55%

All results are mean of three observations

Tablets (10) were weighed to calculate the average tablet weight, then crushed and mixed well to prepare homogeneous mixture. A sample of the mixed material (50 mg of active ingredient) was taken in a volumetric flask (50 ml) containing 25 ml of diluent. This mixture was sonicated for 30 min to ensure the complete solubility of the drug and was then filtered through a 0.45 µm membrane filter, followed by addition of diluent to obtain a stock solution (1 mg/ml). An aliquot of this solution (15 ml) was transferred to a volumetric flask (50 ml) and volume was made upto the mark with the diluent to give the desired concentration (300 µg/ml). All the experiments were conducted in triplicate. The same procedure was repeated to estimate the concentration of drug in one or more commercial brand of Famotidine tablets.

Results and Discussion

Retention time for RS was found to be 3.67 min (Fig. 1). Relative standard deviation (RSD) for RS was 0.104 for peak area (Table 1). Graph of peak area to drug concentration (100-500 µg/ml) was linear (Fig. 2). Correlation coefficient (R^2) for RS was found to be 0.9993 (Table 1). Regression analysis of the calibration data was carried out to determine the relationship between the dependent variable (peak area) and the independent variable (drug concentration). Regression equation ($y = mx+c$) for RS was found to be

$$y = 15297x + 80142$$

RS recovery in the tablets by new method was 95.5-96.8% (Table 2). Low RSD value is indicative of accuracy and precision of method[7-8]. Correlation coefficient shows linear response.

Conclusions

Proposed method is accurate and precise for the analysis of Rabeprazole Sodium. No interference from excipients used in tablet formulation and hence the method is suitable for analysis of tablet formulation. The method is simple and has runtime of

5 min, which makes it especially suitable for the routine quality control analysis work.

Acknowledgements

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