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Research Article

Validation of Spectrophotometric determination of Rabeprazole using Ferric Chloride ($FeCl_3$)

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ABSTRACT

Spectrophotometric determination of irreversible proton pump inhibitor Rabeprazole sodium has been developed, the procedure is based on the formation of 2:1 chelate of drug and metal in ethanol media to form an orange colour chelate having an absorption maximum at 455nm. The regression analysis of Beer's law showed a good correlation in the concentration range of 10 - 60µg/ml of pure Rabeprazole with Iron (Fe+3). The limit of detection was 1.98µg/ml and limit of quantification was 6.59µg/ml. The optimum assay conditions were investigated and the recovery of the drug from their dosage forms was found to be 99.8 – 100.3%. Good values of precision were obtained, intraday R.S.D was 0.1567 and interday R.S.D was 0.1792. .

Keywords: Rabeprazole sodium; Spectrophotometer; IronIII (Fe+3); metal chelate; validation

INTRODUCTION

H^+/K^+ Atpase inhibitor Rabeprazole sodium is effective in the treatment of gastric ulcers (British Pharmacopoeia 1993, Merck Index 1996). Rabeprazole is chemically 2-[{(4)3-methoxy-propoxy -3-methyl-2-pyridinyl} sulphinyl} 1-H benzimidazole sodium (Rosak et al., 2005, Strowing S.M et al., 2005, Wellington K 2005). The reported methods for the determination of Rabeprazole include HPLC, HPTLC, Polaography, electrophoresis and U.V Spectrophotometer concerning visible spectrophotometry very few methods (Moustae A.A.M et al., 1999, Patel P.M et al., 2007, Prasanna Reddy etal., Pattaturanayak P et al., 2007, Salama F et al., 2003) have been developed.

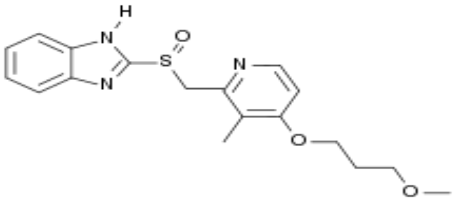

Figure 1: Structure of Rabeprazole

The purpose of this study was to develop stability indicating spectrophotometric procedure for the selective determination of Rabeprazole in presence of common excipients and to describe and validate the structural ability of the Rabeprazole to chelate certain metal ions which essentially present in biologically fluids. A prospective work will be a bioavailability study using the proposed chelation procedure.

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MATERIALS USED

Rabeprazole pure drug sample was kindly supplied by Rashmi Pharmaceuticals, Hyderabad. Rabo-10 and Rabo-20, Dr. Reddy's laboratory, Hyderabad was purchased from the market. U.V visible spectrophotometer (SCHIMADZU-160) was used to measure the absorbance. All reagents and chemicals used were of analytical grade. $FeCl_3$ $6H_2O$ (0.8%) and $1x10^{-3}$ M solution in ethanol standardized against standard $KMn0_4$ after reduction (Basset J et al., 1978). Rabeprazole 1mg/ml in ethanol, Rabeprazole $1x10^{-3}$ M solution in ethanol were used as standard solutions. Rabeprazole in ethanol was stable for 48hrs.

EXPERIMENTAL

Chelation of Rabeprazole sodium with Fe (III)

Accurately transfer volumes of standard drug solution in ethanol (1mg/ml) equivalent to 0.4-1mg Rabeprazole sodium into a series of 10ml volumetric flask add 0.5ml of 0.8% $FeCl_3$ and heated in a water bath at 60 ± 5^oC for 10 minutes, cool and complete volume with ethanol. Measure the absorbance of an orange chelate of Rabeprazole with Fe (III) at 455nm against reagent blank.

Application to Dosage form

20 tablets were weighed and made as fine powder. 25 mg of equivalent weight of Rabeprazole was taken into

a 25ml volumetric flask and dissolved in about 15ml of ethanol by shaking for 15minutes and the final volume was made with ethanol then filtered through Whatmann No. 41 filter paper. Analyze the clear alcoholic filtrate claimed to contain 1mg/ml Rabeprazole by chelation with Fe (III) as mentioned above.

Results and Discussions

The formation of metal complexes with organic compounds have been recognized, studying the structural formula of Rabeprazole showed that it is promising in forming metal chelate between the Imidazole -NH group, the oxygen of the sulfurdioxide chain and the N of the pyridine ring to form the chelate. Fig No. 2

Absorption spectra

The U.V spectra of Rabeprazole in methanol have a sharp peak at 284nm Fig No. 3. When reacting with Fe (III) in ethanol an orange coloured chelate was formed and have high absorption band at 455nm. Fig No. 4.

Optimization of reaction conditions

Ethanol was found to be the solvent of choice in which Rabeprazole and metal ion are stable and freely soluble. This ethanol solution was stable for 48hours.

Effect of time and temperature

At room temperature the chelation reactions were slow and it requires 2 hours to attain maximum absorbance at the relevant maxima. Thus different temperatures (50°C to 80°C) were tried using a thermostat water bath. Optimum heating time was found to be 10 min at 60°±5°C for chelation of Rabeprazole with Fe (III). The colour of the obtained chelate was stable for 60 min for Rabeprazole-Fe (III). Table 1

Table 1: Effect of temperature and time of heating on the absorbance intensity of chelate of Rabeprazole-Fe (III)

Time in min	absorbance of rabeprazole-Fe(III) Chelate at 455nm in different temperature			
	50°C	60°C	70°C	80°C
5	0.376	0.415	0.405	0.392
10	0.528	0.607	0.592	0.598
20	0.535	0.596	0.590	0.602
30	0.521	0.592	0.610	0.604
40	0.528	0.588	0.592	--
50	0.532	0.561	--	--
60	0.529	0.553	--	--

Effect of reagent concentration

Investigation of metal ion concentration revealed that 0.5-0.7ml o 1% $Fecl_3$ solution were optimum for maximum colour intensity of Rabeprazole using 50µg/ml concentration. Fig No. 5.

Interference study

To study the potential interference problem from the commonly used excipients and other additives, recovery studies were carried out under experimental conditions employed to a known amount of drug and excipients in different concentrations were added and analyzed. Results of recovery analysis were presented. Table 2.

Table 2: Determination of Rabeprazole sodium in presence of common excipients

Excipients	Recovery ± RSD%*
Lactose	99.8% ± 0.248
Talc	100.1% ± 0.215
Stearic acid	100.3% ± 0.1522
Microcrystalline cellulose	100.3% ± 0.2401

* average of five determinations

Table 3: Stability constants of Rabeprazole sodium – Fe(III) chelate in methanol by Job's method

Total molar concentration A/Aex	$1x10^{-4}$ M
A/Aex	0.960
β	$2.42x10^{8}$
Log β	8.38

Table 4: Results of assay validation of the proposed chelation procedure

Parameters	Rabeprazole-Fe(III)
Linearity range µg/ml	10-60
LOD µg/ml	1.98
LOQ µg/ml	6.59
Correlation coefficient	0.998
Accuracy%	100.3

*average of six determinations

Table 5: Results of determination of Rabeprazole sodium by proposed chelation procedure in their dosage form

Formulations	Recovery±RSD%*
Rabo-10	100.3±0.4132
Rabo-20	99.8±0.1409

*average of five determinations

Determination of chelate stability composition

The composition of the chelate of drug with metal ions using job's method, chelate of 2:1 ratio were obtained between drug and Fe (III). The stability constants were calculated (Inczedy J.et al., 1976) and the values of log B were around 8.38. Table No. 3.

Linearity range and quantification procedures

Beer's law was found to be obeyed in the ranges of 10-60µg/ml of pure Rabeprazole at 455nm upon chelation with Fe (III). The drug chelate absorbances were plot-

ted against the corresponding concentrations. Data were fitted to the equation Y= a+bx where Y is absorbance at the relevant maximum, x is the slope and "a" is the intercept of the calibration curve. The Regression parameters were shown in Table 4. The correlation coefficients "r" Was found to be 0.998. Commercial formulations of Rabeprazole were successfully analyzed by the proposed methods the values obtained were presented in Table 5.

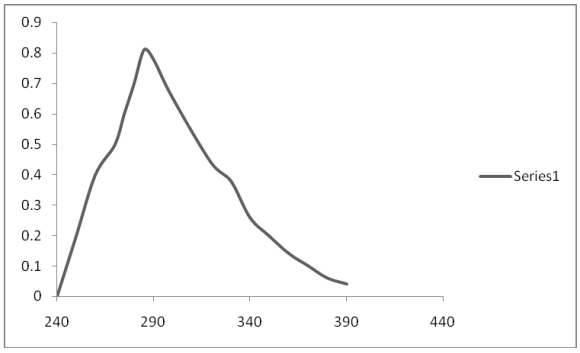

Figure 2: UV-VISIBLE Spectra of Rabeprazole in methanol

X-axis wavelength, Series1 Absorption spectra of Rabeprazole in methanol, Y-axis absorbance

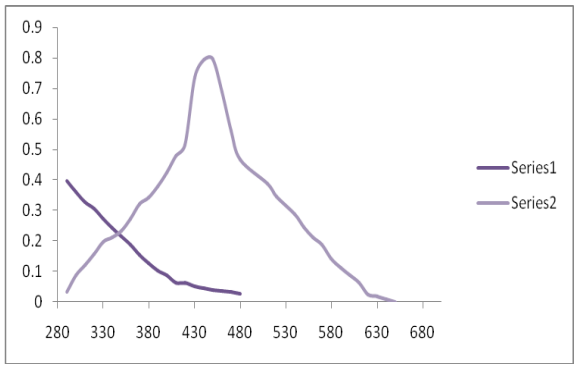

Figure 3: UV-VISIBLE Spectra of Rabeprazole (40µg/ml) –Fe(III) in ethanol

X-axis Wavelength in nm, Series1 reagent peak, Y-axis absorbance, Series2 Absorption band at 455nm

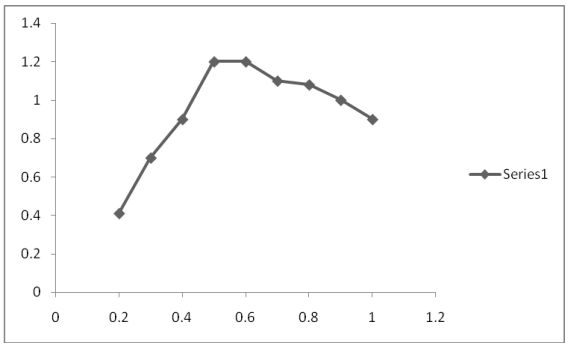

Figure 4: Effect of metal ion concentration on the absorbance of Rabeprazole-Fe (III) chelate using 0.8%Fecl3solution and 100µg/ml of Rabeprazole

X-axis volume of metal ion solution (0.8%), Y-axis absorbance

CONCLUSION

The drug obeys Beer's law in the concentration ranges employed for the method. The method is simple, rapid, accurate and can be adopted in routine analysis of drug formulation. The accuracy and reproducibility of the proposed method was statistically validated by recovery studies.

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