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Research Article

DEVELOPMENT OF NEW METHODS AND ITS VALIDATION FOR THE DETERMINATION OF RABEPRAZOLE IN BULK AND MARKETED FORMULATIONS

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ABSTRACT

Simple, sensitive, specific, and validated colorimetric methods have been developed for the quantitative estimation of Rabeprazole in bulk and pharmaceutical dosage form. Method A consists of redox reaction of Rabeprazole in presence of acidic medium reacts with excess amount of Cerric ammonium sulphate. The dye Safranin gave λmax of Rabeprazole at 516nm. Method B consist of redox reaction of Rabeprazole with ferric nitrate and the reduced ferrous ion than reacts with 1,10 Phenanthroline giving maximum absorbance at 511nm. The methods were validated as per ICH guidelines.

Keywords: Rabeprazole sodium, colorimetry, λmax, validation.

INTRODUCTION

Rabeprazole is an antiulcer drug in the class of proton pump inhibitors. Rabeprazole has anti Helicobacter pylori activity (MIC 4-16 mg/ml) and shows synergistic activity with some antibiotics. Rabeprazole has been demonstrated to be effective in patients with pathological hyper-secretory activity.[1,2]It is chemically known as 2-((4-(3-methoxypropoxy)-3-methylpyridin-2-yl)methylsulfinyl)-1H-benzo[d]imidazole. The molecular formula of Rabeprazole is $C_{18}H_{21}N_3O_3S$ and the Molecular mass is 381.4 Structure of Rabeprazole is given in Figure no. 1.

Several methods have been reported for determination of Rabeprazole in pharmaceutical formulation as well as in bulk form including UV-visible spectroscopy [3-7], derivative spectrophotometry[8], RP-HPLC[9-11], RP-UPLC[12], HPLC[13], Chemometry[14]. The proposed methods are simpler and cheaper.

MATERIALS AND METHODS

Instruments

JASCO V-630 series UV spectrophotometer and SHIMADZU-1700 with 1 cm path length.

Materials

1. Rabeprazole (YARROW CHEM PRODUCTS)
2. Commercial formulations.
3. Ceric ammonium sulphate 0.15%w/v. (HIMEDIA, Mumbai)
4. 2N Sulphuric acid. (HIMEDIA, Mumbai)
5. Safranin 0.03%w/v. (LOBA CHEMIE)
6. Ferric nitrate 1.50% w/v. (HIMEDIA, Mumbai)
7. 1,10 Phenanthroline 1.75% w/v. (HIMEDIA, Mumbai)

Preparation of standard stock solution for method A and B

100mg of Rabeprazole was taken in 100ml volumetric flask and dissolved in distilled water to get a concentration of 1000µg/ml. From this suitable dilutions were made to get concentration of 100µg/ml.

Method A

Seven 10 ml volumetric flask were taken and pipetted out into them 0.2ml, 0.4ml, 0.6ml, 0.8ml, 1.0ml, 1.2ml, and 1.4 ml of working stock solution

of Rabeprazole. To that 0.5ml of 0.15% w/v of Cerric ammonium sulphate was added followed by 1ml of 2N H_2SO_4. The flasks were set aside for 5 minutes for completion of reaction. Then 1ml of 0.03% w/v of Safranin was added. The contents were shaken well and diluted up to the mark with distilled water. The absorbance was recorded against reagent blank at 516nm. Results are given in Table no.1, Figure no. 2.

Method B

To the drug solution in the range of 5 -30 µg/ ml, 0.5ml of 1.50% w/v Ferric nitrate was added. To this 3ml of 1.75% w/v 1,10 Phenanthroline was added. Volume was made up to the mark with distilled water. A reddish yellow colour was obtained. Absorbance was recorded against reagent blank at 511nm. The results are given in Table no. 2 and Figure no. 3.

Results of assays of formulations are given in Table no.3 and 4. Studies of linearity were performed and results reported in Table no. 5 & 6 and figure no.6 & 7. Similarly results for accuracy, LOD and LOQ were reported in Table no. 7 and 8 respectively for both the methods.

RESULTS AND DISCUSSION

Method A

This method is based on oxidation-reduction reactions. In acidic condition Rabeprazole reacts with excess of Cerric ammonium sulphate, which is followed by reaction of unreacted oxidant with the dye Safranin. The colour developed is due to the excess of Safranin present, this is correlated with the concentration of the drug. The solution was analysed at λmax 516 nm. The reactions are given in Figure no. 4.

Method B

The proposed method for the estimation of RABEPRAZOLE was based on the reaction of alcoholic solution of 1, 10 phenanthroline with Ferric nitrate.The orange-red coloured complex was formed with ferric nitrate and 1,10 phenanthrolin. Ferric nitrate oxidises RABEPRAZOLE and itself gets reduced. The ferrous ion reacts with 1, 10 phenanthroline to form the complex, which showed λmax at 511nm. The reactions are given in Figure no. 5.

Table 1: Standard graph for Rabeprazole by method A

Sr.no.	Volume of working standard of drug in ml	Concentration of drug (µg/ml)	Absorbance at 516nm
1	0.2	2	0.149
2	0.4	4	0.253
3	0.6	6	0.365
4	0.8	8	0.461
5	1.0	10	0.570
6	1.2	12	0.679
7	1.4	14	0.753

Table 2: Standard graph for Rabeprazole by method B

Sr.no.	Volume of working standard of drug in ml	Concentration of drug (µg/ml)	Absorbance at 511nm
1	0.5	5	0.1466
2	1	10	0.2455
3	1.5	15	0.3538
4	2	20	0.4728
5	2.5	25	0.6131
6	3	30	0.7684

Table 3: Assay results of formulation by method A

Formulation	Actual concentration of Rabeprazole(µg/ml)	Amount obtained of Rabeprazole (µg/ml)	% Rabeprazole
CYRA tablets	5 µg/ml	4.937 µg/ml	98.74%

Table 4: Assay results of formulation by method B

Formulation	Actual concentration of Rabeprazole(µg/ml)	Amount obtained of Rabeprazole (µg/ml)	% Rabeprazole
ACIPHEX tablets	10 µg/ml	9.76µg/ml	97.6%

Table 5: linearity for Rabeprazole for method A

S. no.	Concentration in µg/ml	Absorbance at 516nm Mean ± S.D. (n=6)
1	2	0.1488±0.0011
2	4	0.2533±0.0012
3	6	0.3655±0.0010
4	8	0.4616±0.0015
5	10	0.5713±0.0012
6	12	0.6776±0.0012
7	14	0.7526±0.0010

Table 6: linearity for Rabeprazole for method B

S. no.	Concentration in µg/ml	Absorbance at 511nm Mean ± S.D. (n=6)
1	5	0.145667±0.001033
2	10	0.2445±0.001033
3	15	0.353333±0.001049
4	20	0.471333±0.001033
5	25	0.613±0.000816
6	30	0.767±0.000632

Table 7: Accuracy study of Rabeprazole by Method A and B

Method	Amount of sample Rabeprazole µg/ml	Amount of Pure drug Rabeprazole %	Amount of Pure drug Rabeprazole µg/ml	Amount of drug recovered Rabeprazole µg/ml	Mean % Recovery ± SD
A	6	80%	4.8	4.745	99.32±0.390
	6	100%	6	5.997	99.95±0.9558
	6	120%	7.2	7.195	99.94±0.6543
B	10	80%	8	7.95	99.44±0.3406
	10	100%	10	9.89	98.90±0.400
	10	120%	12	11.99	99.96±0.340

Table 8: statistical data of Rabeprazole by method A and B

Parameter	Method A	Method B
Linear Range (µg/ml)	2-14	5-30µg/ml
Sandell's Constant	6.691×10^{-3}µg/cm^2	1.6133×10^{-2}µg/cm^2
Regression Equation* y=bx+a	0.0534x+0.0304	0.0247-0.0003
Slope (b)	0.053367	0.0247
Intercept (a)	0.030417	0.0003
Correlation coefficien(R^2)	0.9957	0.9953
Standard Deviation of Slope	0.000103	0.0001169
Standard Deviation of Intercept	0.000778	0.000454
Limit of Detection (µg/ml)	0.006391	0.01563
Limit of Quantition(µg/ml)	0.0193	0.04736
Molar Absorptivity (L/mol.cm)	5.7×10^4	2.346×10^4
Repeatability Data(%RSD)	0.137-0.785	0.0823-0.712
Reproducibility:- Instrument 1 (%RSD) Instrument 2 (%RSD)	0.5703 0.2833	0.7124 0.9684

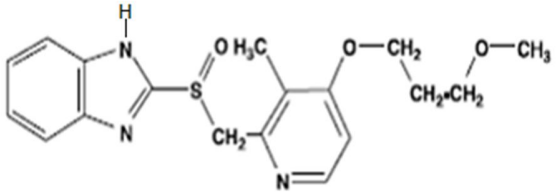


Fig. 1: Structure of Rabeprazole

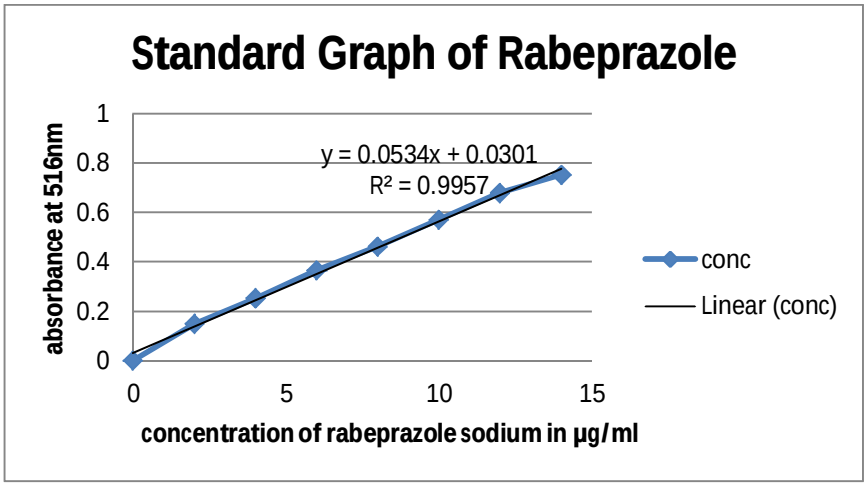


Fig. 2: Standard graph of Rabeprazole for method A

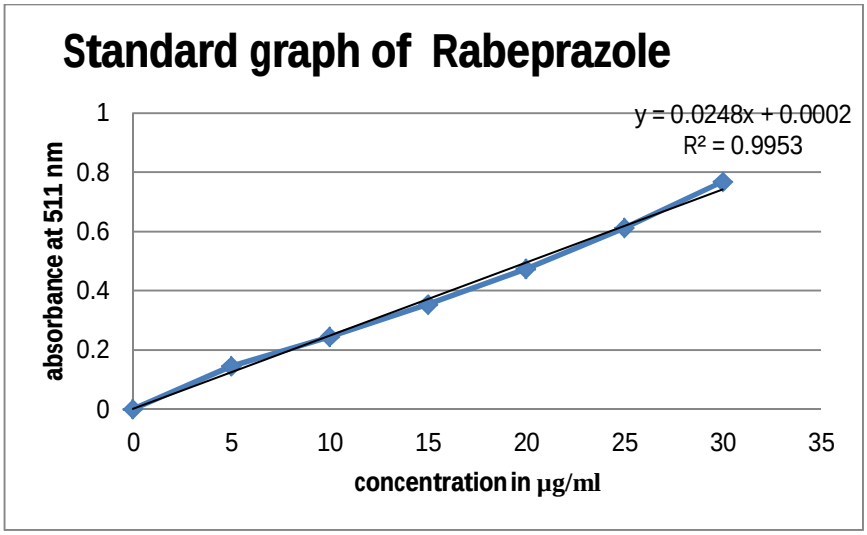
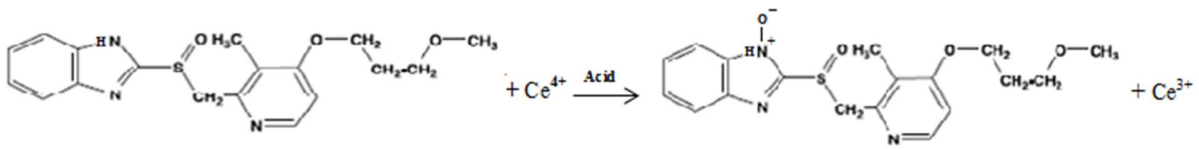
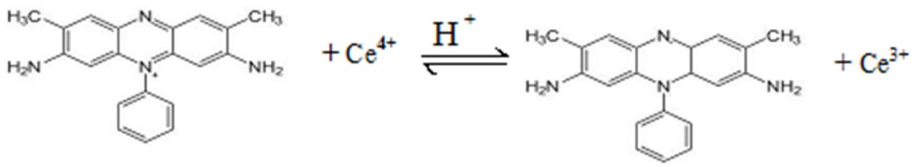


Fig.3: Standard graph of Rabeprazole for method B

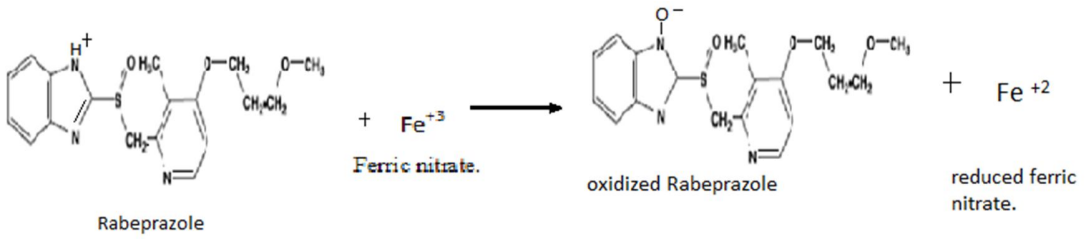


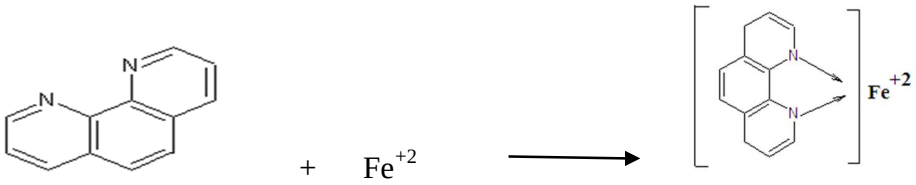
Rabeprazole **CAS** **Oxidized Rabeprazole** **Reduced CAS**



Safranin **unreacted CAS** **Safranin** **reduced Cerrous**

Fig. 4: Reactions for Method A





1,10 Phenanthroline **Reduced ferric nitrate (Ferrous ion)** **Orange red colour complex.**

Fig. 5: Reactions for Method B

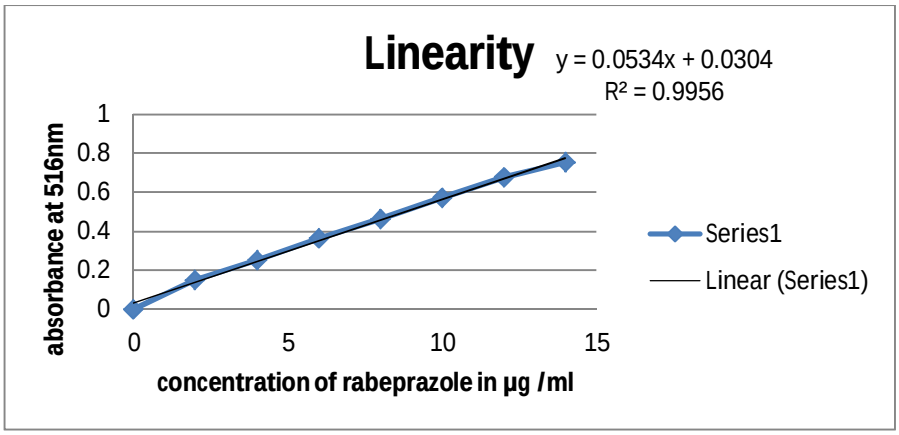


Fig. 6: linearity of Rabeprazole for method A

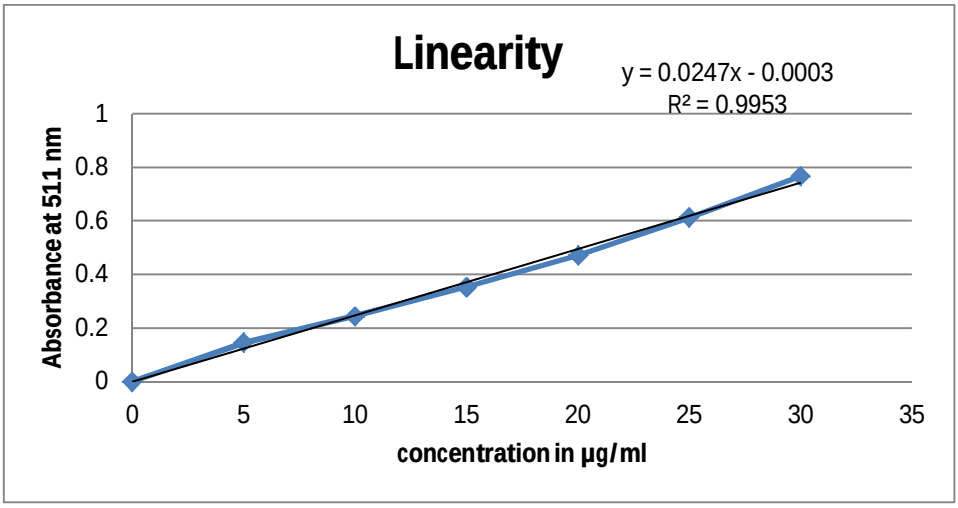


Fig. 7: linearity of Rabeprazole for method B

CONCLUSION

Simple and rapid colorimetric methods for the determination of Rabeprazole have been developed. The methods are easy to perform and do not contain any stringent experimental variables which effect the reliability of the results. There is no interference from the common additives and excipient. The methods thus can be used in the determination of Rabeprazole in pure and dosage forms.

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