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A New Validated Spectrophotometric Method for the Estimation of Rabeprazole Sodium in Tablet Dosage Forms

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ABSTRACT

The aim of this work is to develop and validate the derivative spectrophotometric method for determination of the proton pump inhibitor Rabeprazole sodium in pharmaceutical formulations. The technique was applied by using simple reagents 0.5% $KmnO_4$ and 2N NaOH solutions. The proposed method for the determination of Rabeprazole sodium showed molar absorptivity of 23.837x102. Linear regression of absorbance on concentration gave the equation y= 000087×-0.056with a correlation coefficient of 0.9991. The difference absorption spectrum of Rabeprazole sodium showed maximum absorbance at 695 nm and obeyed Beer's law in the concentration range of 20-100 g/ml. The proposed method is simple and rapid.

Keywords: Protonpumpinhibitor, molar absorptivity, linear regression, absorption spectrum, Beer's law.

INTRODUCTION

Pharmaceutical Analysis may be defined as "The science and art of determining the composition of materials in terms of the elements of compounds contained". More recently it also deals with biological samples in support of biopharmaceutical (1) and pharmacokinetic studies (2). Pharmaceutical analysis includes both qualitative and quantitative analysis.

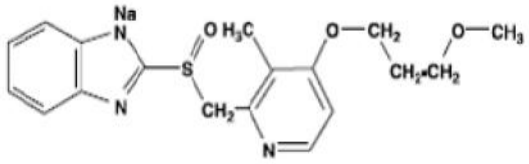
Qualitative analysis: Deals with identification of the substance.

Quantitative analysis: Deals with the determination of how much of the constituent is present. In pharmaceutical analysis it is of prime importance to gain information about the quantitative composition of substance and chemical species that is, to find out what a substance is composed of and exactly how much. Analytical method is a specific application of a technique to solve an analytical problem. The use of instrumentation is an exciting and fascinating part of chemical analysis that interacts with all areas of chemistry and with many other areas of pure and applied science. Analytical instrumentation plays an important role in the production and evaluation of new products. Instrument or physicochemical methods are based on the theory of relation between the content and the corresponding physicochemical and physical properties of the chemical system being analyzed. Changes in the system properties are either detected or recorded through the measurement of current, electrode potential, electrical conductivity, optical density, refractive index etc. with suitable and sensitive instruments. In instrument analysis physical property of a substance is measured to determine its chemical composition. Most important technique is into one of the three principal areas: spectroscopy, electrochemical and chromatography.

Introduction to Drug:

Rabeprazole sodium belongs to the class of anti-secretory compound, (substituted Benz imidazole proton-pump inhibitors) that do not exhibit anti cholinergic or histamine H2- receptor antagonist properties, but suppress gastric acid secretion by inhibiting the gastric H+, K+ATPase at the secretory surface of the gastric parietal cell. It is given orally as enteric coated Rabeprazole tablets and normally taken in the morning. In the treatment of severe ulcerative astrooesophogeal reflux disease, the usual dose is 20 mg once daily for 4 to 8 weeks; in the USA, a further 8-week course is permitted for healing of erosive oeophogistis (3). Chemically rabeprazole is 2-[{(4)3-methoxypropoxy-3-methyl-2-pyridinyl} sulphinyl} 1-H benzimidazole, its structure is shown in Fig.1. The aim of the present study was to develop a simple spectrophotometric method to determination of in Rabeprazole tablet dosage forms.

Fig1.1: structure of rabeprazole sodium



Method Development:

Materials and instruments: In this experiment the simple instruments are used. Double beam UV spectrophotometer Model spectro 2080 PLUS., Analytical technologies, Electronic digital balance JOE-ST-800G10 S.NO:#30E-169609, storm series and digital PH meter 152R are tabulated in table (2.1) reagents and chemicals are $KMnO_4$ procured from Universal laboratory pvt.ltd Mumbai batch No; E08185014, NaOH obtained from Merck specialties pvt.ltd batch no; ML8M583519 and distilled water used these are tabulated in table (2.2)

Tables.2.1: Instruments and materials used Instruments

S.NO	Name of instrument	Model
1	UV-Visible spectrophotometer	spectro2080PLUS,
2	Electronic digital balance	JOE-ST-800G10
3	Digital PH Meter	152R

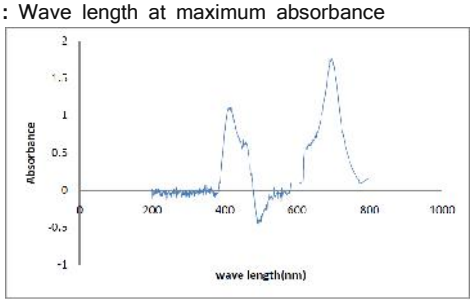
Tables.2.2: Reagents and chemicals

S.NO	Name of the reagent	Batch NO.	Manufactured by
1	$KMnO_4$	E08185014	Universal laboratorypvt.ltd
2	NaOH	ML8M583519	Mumbai Merck specialties
3	Distilled water		

Selection of solvent: The salt form of drug easily soluble in water hence we selected water as a solvent.

Determination of wave length (λmax): The chromophore was produced and scan in wave range of 400 to 800nm in a double beam UV visible spectrophotometer. the flat was constructed by taking wave length on X axis and absorbance's on Y axis, from the graph the maximum wave length of chromophore was optimized as 695nm .The spectrum was given in the fig (2.1).

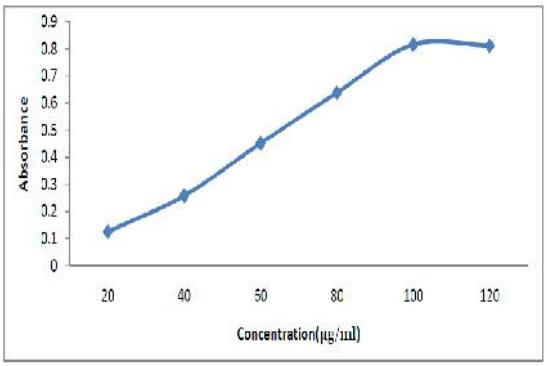
Fig2.1: Wave length at maximum absorbance



Preparation of stock solution: Accurately weighed quantity of 100mg Rabeprazole sodium was taken and transferred into 100ml volumetric flask which contains a small volume of water. After dissolving the drug the volume was made up to 100ml with to get the concentration about 1mg/ml.

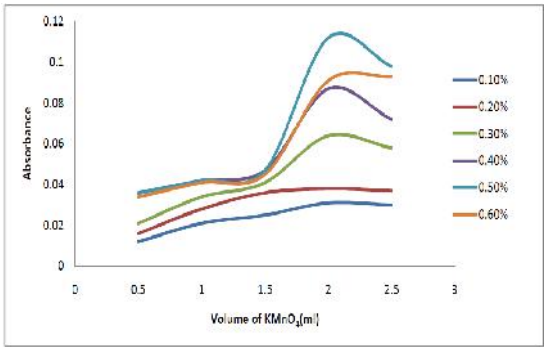
Beer's law optimization: From the stock solution different volumes of Rabeprazole sodium ranging from 0.2ml to1.2 ml were taken and transformed into a 6 different 10ml volumetric flasks. To this optimized volume of 0.5% of $KMnO_4$ and 2N NaOH was added. The solution was shaken for about 20 min to get dark blue Color chromophore. Then the solution diluted up to 10ml to get the concentration about 20,40,60,80,100 and 120µg/ml. The plot was constructed by taking concentration on X axis and absorbance was taken on Y axis. The result was tabulated (2.3) and graphically represented (2.2).

Fig2.2: Beer lamberts law optimization



Optimization of volume (ml) and concentration (µg/ml) of $KMnO_4$: Rabeprazole sodium gives the dark bluish to green Color in the presence of the alkaline condition. To the determination of the optimum concentration and optimum volume kept the drug concentration constant. Note the absorbance's at the obtained λ max 695nm from the obtained results were shown in table (2.4) and represented graphically (2.3).

Fig:2.3: Optimization of KMnO4 volume(ml) and concentration (%)

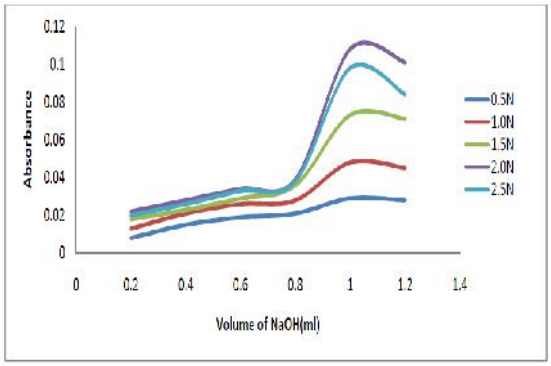


Tables.2.3: Beer lamberts law optimization

S.NO	Concentration (µg/ml)	Absorbance
1	20	0.125
2	40	0.258
3	60	0.451
4	80	0.638
5	100	0.816
6	120	0.812

Optimization of NaOH volume (ml) and concentration (%): Oxidation of weakly absorbing compounds produced a chromophpre that has much greater absorptivity than the parent component. Commonly used oxidizing reagents are alkaline $KMnO_4$, acidified $K_2Cr_2O_7$ and perchlorate solution in the present investigation the chromophore is produced in alkali conditions. The volume and strength of NaOH and remaining all conditions are kept constant. The absorbances were measured for different solutions containing varying concentration and volume .the result was shown in table (2.5) and in graph (2.4).

Fig2.4: Optimization of NaOH volume (ml) and concentration (N)



Tables.2.4: Optimization of KMno4 concentration and volume

S.NO	Volume of $KMnO_4$(ml)	Absorbance at different concentration (%)					
		0.1	0.2	0.3	0.4	0.5	0.6
1	0.5	0.012	0.016	0.021	0.036	0.036	0.034
2	1.0	0.021	0.028	0.034	0.042	0.042	0.041
3	1.5	0.025	0.036	0.041	0.047	0.047	0.045
4	2.0	0.031	0.038	0.064	0.087	0.112	0.091
5	2.5	0.030	0.037	0.058	0.072	0.098	0.093

Tables.2.5: Optimization of the NaOH concentration (N) and volume (ml)

S.NO	Volume of NaOH (ml)	Absorbance of NaOH (N) at different concentration				
		0.5	1.0	1.5	2.0	2.5
1	0.2	0.008	0.013	0.018	0.022	0.020
2	0.4	0.015	0.021	0.023	0.028	0.026
3	0.6	0.019	0.026	0.029	0.034	0.033
4	0.8	0.021	0.028	0.036	0.039	0.038
5	1.0	0.029	0.048	0.073	0.108	0.098
6	1.2	0.028	0.045	0.071	0.101	0.084

Order of addition: To find out whether the order of addition of reagents has any influence a set of solutions were prepared by mixing in different sequences without varying the amount of drug and reagents and the absorbance were measured .the best order of addition was $KMnO_4$, drug and reagent is given in the table (2.6).

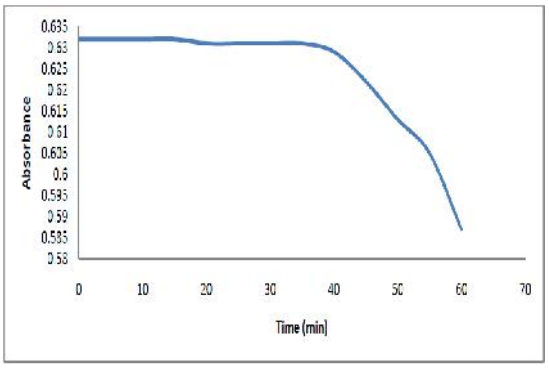
Tables.2.6 Optimization of order of addition

S.NO	Order of addition	Absorbance at 695nm
1	KMnO4+NaOH+DREG	No chromophore produced
2	KMnO4+DRUG+NaOH	Chromophore produced
3	NaOH+DRUG+ KMnO4	No chromophore produced

Effect of temperature: All experiments and absorbance measurements were carried out at laboratory temperature (28 ± 3^0C) at low temperature ($<20^0$C). The maximum Color development was delayed at the high temperature ($>30^0$C) the stability of the colored species was less. Hence the temperature was preferred in farther investigations.

Stability of the Color: The influence of the time for maximum Color development and stability of the colored species were studied and the results were given in the table (2.7) and graphically represented in fig (2.5).

Fig2.5: Color complex absorbance's at different time interval



Tables.2.7: Color complex absorbance's at different time interval

S.NO	Time(min)	Absorbance
1	0	0.6316
2	5	0.6316
3	10	0.6315
4	15	0.6316
5	20	0.6314
6	25	0.6314
7	30	0.6314
8	35	0.6312
9	40	0.6295
10	45	0.6223
11	50	0.6125
12	55	0.6052
13	60	0.5872

Preparation of solutions:

0.5% KMnO4 Solution: 0.5% of KMnO4 was prepared by dissolving the accurately weighed 0.5g of KMnO4 in 100ml of water.

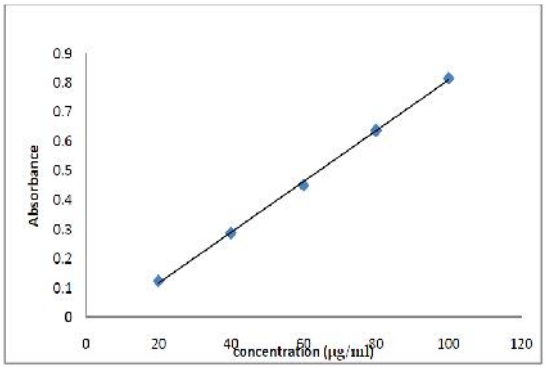
2N NaOH Solution: 2N NaOH was prepared by accurately weighed 8g of NaOH was taken in a 100ml volumetric flask and make up the volume up to 100ml.

Assay procedure: 10 tablets were taken and average weight of 10 tablets was determined. The tablets were triturated to get the powder. The powder which is equivalent to100mg of Rabeprazole sodium was calculated and weighed accurately. The powder was transferred into a 100ml volumetric flask dissolved and make up the volume with water. To get the concentration 1mg/1ml, from the stock solution 0.6 ml of solution was taken and transferred into the 10ml volumetric flask to this 2ml 0.5% KMnO4 and 1ml of 2N NaOH was added and shaken for 20min to get dark blue to green chromophore. The absorption of the resulting solution was measured and quantified by the standard plot (2.6). Y value and R_2 value are found from the standard plots are given below. The % purity of the different brands of the Rabeprazole sodium by using the standard plat and the % purity of the drugs was given in the table (2.8).

Regression equation: Y=0.0087×-0.056

Correlation coefficient: R2=0.9991

Fig2.6: standard plot of rabeprazole

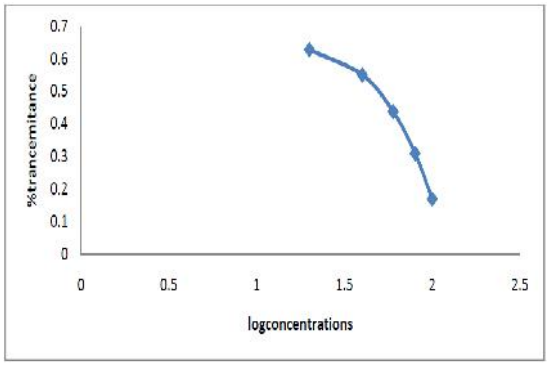


Tables.2.8: Assay for the Different formulations of the Rabeprazole:

S.NO	Brand name	Labeled claim(mg)	Estimated amount(mg)	% drug content
1	Rabeprazole sodium	20	21	105
2	Rabicip	20	19.7	98.5
3	Rabicer	20	20.2	101

Sandell's sensitivity: Number of micrograms of drug determined converted to the colored product, which in a column solution of cm2/cross-section, shows an absorbance of 0.001 or 0.005 (expressed as g of drug / cm2). These values are tabulate (2.9).

Fig2.7: Ringbom plot



Tables.2.9: Sandell's sensitivity and Molar extinction coefficient (Є) at different concentrations

S.NO	Concentration(µg/ml)	Molar extinction coefficient(Є)	Sandell's sensitivity
1	20	23.83767×10^{2}	15.99×10^{-2}
2	40	24.60×10^{2}	15.504×10^{-2}
3	60	28.668×10^{2}	13.304×10^{-2}
4	80	30.4171×10^{2}	12.538×10^{-2}
5	100	31.122×10^{2}	12.254×10^{-2}

Ringbom plots: Optimum photometric ranges are calculated from the linear portion of the Ringbom plot between present transmission V/s logarithms of the concentration of the drug (expressed as g/ml). Knowledge of the above - proposed method is necessary, for comparing the sensitivities of the proposed and reported methods to each drug. The values are tabulated in the table (2.10) and shown in the figure (2.7).

Tables.2.10: Ringbom plot table

S.NO	log Concentration	Absorbance	% Transmittance
1	1.3010	0.125	0.628
2	1.6020	0.258	0.550
3	1.7785	0.451	0.437
4	1.9030	0.638	0.308
5	2	0.816	0.168

Method of Validation;

A) Linearity

The solutions were prepared in concentrations ranging from 20-100µg/ml in water solvent the absorbance's of the solution was measured at the λ max 695nm and the result was shown in the table (2.11).

Tables.2.11: linearity table

S.NO	Concentration(µg/ml)	Absorbance
1	20	0.127
2	40	0.255
3	60	0.456
4	80	0.641
5	100	0.821

B) Accuracy of the method:

The accuracy of the method was determined by taking aliquots containing known quantity of Rabeprazole sodium (within beer's law limit) and analyzed by the proposed method and the results were compared with results of the reference method and tabulated in the table (2.12).

Tables.2.12: Accuracy or recovery of the method

	80%	100%	120%
Mean(n=3) %RSD	100.5	100.6	100.04
	99.99	100.1	99.54
	100.32	99.70	100.1
	100.27	100.13	99.99
	0.03835	0.08119	0.04342

C) Precision:

Precision is the measure of closeness of data values to each other for a number of measurements under similar analytical conditions. Precision may be considered at three levels according to ICH guidelines.

- Repeatability
- Intermediate Precision
- Reproducibility

- **Repeatability:** Expresses the precision under the same operating Conditions over a short interval of time. Repeatability is also termed Intra-assay precision.

- **Reproducibility:** Expresses the precision between laboratories.

- **Intermediate precision**: Expresses within laboratories variations: different days, different analysts, different equipment, etc. The inter day precision and intraday precision was found form the experimental values these are tabulated in table (2.13) and these values are given below.

  Intraday precision n = 6(100.243, 100.231, 100.323)
  Inter day precision + n=18(100.266)

Tables.2.13: Rabeprazole sodium inter day and intraday precision value

S.NO	Day1	Day2	Day3
1	100.3	100.1	99.99
2	100.5	100.9	100.4
3	100.7	99.96	100.6
4	100.89	100.2	99.95
5	100.1	99.93	100.6
6	99.97	100.3	100.4

RESULTS AND DISCUSSION

The absorption spectrum of Rabeprazole sodium was measured in the range of 800-400nm. The optical characteristics of Rabeprazole sodium is given in the table. 2.14. The standard solution show maximum absorbance at λ max 695nm as recorded from the optical characteristics of Rabeprazole sodium given in the table (2.14).

Tables.2.14: Optical characteristics of rabeprazole sodium

S.NO	Parameter	Optimized value
1	λ_{max}	695nm
2	Beer's law limits	20(µg/ml -100(µg/ml)
3	Strength of reagent($KMnO_4$)	0.5%
4	Volume of reagent added(kmno4)	2ml
5	Volume of 2n NaOH	1ml
6	Colour of chromophore	DARK BLUE COLOUR TO GREEN
7	Stability of colour	40min
8	Time taken for colour development	20min
9	PH of colour complex	13.2
10	Molar extinction coefficient	0.9991
11	Regression equation	0.0087x-0.056
12	Sandell's sensitivity(20µg/ml)	0.1599

The proposed method was validated by studying the following parameters as per ICH guidelines for the method validation. The proposed method for the determination of Rabeprazole sodium showed molar absorptivity of 23.837x102. Linear regression of absorbance on concentration gave the equation y= 000087×-0.056with a correlation coefficient of 0.9991. The difference absorption spectrum of Rabeprazole sodium showed maximum absorbance at 695nm and obeyed Beer's law in the concentration range obtained from the plat (2.2) the measured range is 20-100µg/ml. Accuracy data of the drug (Table.2.12) was shown good percentage recovery of the method was performed by recovery studies. The percentage recovery value indicates that there is no interference from the excipients present in the formulation. The specificity of the method was conducted to prove that they are free from determined interference of solvent and commonly used excipients. This is evidenced by the lack of absorbance at the specified λ max for the excipients in the blank solutions. The applicability of the proposed method for the assay of Rabeprazole sodium tablet formulation was examined by analyzing commercial formulations and the results were tabulated. The results obtained were in good agreement with the label Claims. The results of analysis of the commercial formulations and the recovery study of the drug suggested that there is no interference from any excipients.

CONCLUSION

The proposed method was found to simple rapid accurate and economic method for the determination of

Rabeprazole sodium in bulk and pharmaceutical dosage forms. The method was developed using simple reagents and chemicals which offers accurate estimation of Rabeprazole sodium without any errors. Hear by we concluded that the proposed method most suitable for rotten laboratory analysis of Rabeprazole sodium in bulk and pharmaceutical dosage forms. The proposed method is simple and rapid when compared to the other spectrophotometric methods reported in literature where as it is a new method not yet published.

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Conflict of interest: None Declared