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Physico-chemical characterization, UV spectrophotometric analytical method development and validation studies of Rabeprazole Sodium

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ABSTRACT

*Rabeprazole sodium (RSM) is a proton pump inhibitor used against peptic ulcer disease to suppress excess acid secretion in the stomach. Physico chemical characterization studies showed that RSM has showed a melting point of 137^o C. The solubility of drug RSM followed the order distilled water > pH 9.0 > pH 8.0 > pH 7.5 > pH 2.5. The analytical method developed for the estimation of RSM in bulk fluids showed maximum absorbance λ_{max} of 272.2 nm in distilled water between 200 nm and 400 nm. Linearity studies indicated that estimation of RSM between 2.00 μ g /ml to 10.00 μ g /ml was found to be linear with regression equation of $y = 0.034 * X - 0.00267$; ($r^2 = 0.99961$). The accuracy, precision studies showed that the recovery of drug from bulk fluids and dosage form are highly accurate and precise with minimum error. The above analytical parameters indicated that the developed UV Spectrophotometric method for RSM was simple, accurate, precise and reproducible.*

Key words: Rabeprazole sodium (RSM), UV Spectrophotometric Method, Accuracy, Precision.

INTRODUCTION

Proton pump inhibitors (PPIs) are the most potent inhibitors of gastric acid secretion and are effective for treating all gastric acid-related disorders. Rabeprazole sodium, a substituted benzimidazole that inhibits gastric acid secretion. The stability of rabeprazole sodium is function of pH; it is rapidly degraded in acid media, and is more stable under alkaline condition.

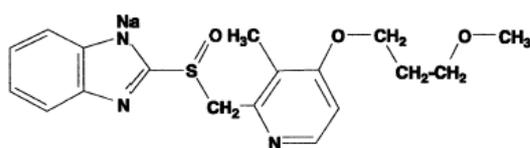
Rabeprazole sodium is chemically 2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]-methyl]sulfinyl]-1H-Benzimidazole sodium salt. Its molecular formula is $C_{18}H_{20}N_3NaO_3S$ with molecular weight of 381.43, half-life of 1-2 h and has a oral bioavailability of 52 % when administered orally [1]. Rabeprazole belong to a class of antisecretory compounds that do not exhibit anticholinergic or histamine H_2 –receptor antagonist properties, but suppress gastric acid secretion by inhibiting the gastric H^+ , K^+ ATPase at the secretory surface of the gastric parietal cell. Because this enzyme is regarded as the acid (proton) pump within parietal cell, rabeprazole has been characterized as a gastric proton –pump inhibitor. Rabeprazole blocks the final steps of gastric acid secretion [2]. It is used in the treatment of active duodenal ulcer and active benign gastric ulcer. It is also used in the treatment of gastro–oesophageal reflux disease (GORD). In combination with appropriate antibacterial therapeutic regimens it is being used for the eradication of *H. Pylori* in patients with peptic ulcer disease (PUD) [3].

Review of literature given in sight that very few spectrophotometric and high performance liquid chromatographic method for the analysis of Rabeprazole [4-6] Hence the present investigation was undertaken for drug candidate physico chemical characterization, to develop a simple and robust UV Spectrophotometric Method and validation for the quantitation of Rabeprazole sodium in bulk fluids and tablets.

EXPERIMENTAL SECTION

Theil's melting point apparatus was used for drug melting point determination. Dhona 200 D electronic balance (Mumbai) was used for weighing of all samples. Shimadzu UV 1700 double beam spectrophotometer (Japan) was used for all the spectrophotometric measurements. The absorption spectra of the reference and test solutions were carried out in a 1 cm quartz cells over the range of 200 - 400 nm. All laboratory glassware like volumetric flasks and pipettes were calibrated and used for experimentation.

Active pharmaceutical ingredient and Reagents:



RABEPRAZOLE SODIUM

Rabeprazole Sodium was kindly gifted by Danmed pharmaceuticals Pvt limited, Hyderabad, A.P, India) the drug was used without further purification. All the solvents and chemicals like n-octanol (INR Chemicals, Mumbai). Methanol (Pampasara distillaries). Potassium dihydrogen ortho phosphate and Sodium hydroxide pellets from S.d. Fine chemicals limited, Mumbai used in Spectrophotometric analysis were of LR grade.

Methods used for Physico-chemical characterization of the drug:

Melting point determination: Melting point of the drugs was determined by taking a small amount of drug in a capillary tube closed at one end and was placed in their melting point apparatus and the temperature at which the drug melts was noted. Average of triplicate readings was noted.

Solubility studies: The solubility of Rabeprazole Sodium was determined in distilled water, different buffers, viz., pH 2.5, pH 7.5, pH 8.0, pH 9.0 according to the method proposed by Diez et. al [7]. Triplicate readings were taken and average was calculated.

Partition coefficient [8]: The partition coefficient of the drug was determined by taking equal volumes of n-octanol and aqueous phases in a separating funnel. A drug solution was prepared and 1ml of the solution was added to octanol: water (50:50) was taken in a separating funnel and shaken for 10 minutes and allowed to stand for 1 h and is continued for 24 h. Then aqueous phase and octanol phase was separated, centrifuged for 10 min at 2000 rpm. The aqueous phase and octanol phase were assayed before and after partitioning using UV Spectrophotometer at their respective λ_{max} to get partition coefficient. Triplicate readings (n=3) were taken and average was calculated.

Analytical method developed for the estimation of rabeprazole Sodium drug either in bulk or in tablets:

Method used to estimate rabeprazole Sodium : The drug rabeprazole Sodium was dissolved in distilled water to get 10 $\mu\text{g/ml}$ solution. Further diluted with the same and scanned for maximum absorbance (λ_{max}) in a UV-VIS Spectrophotometer, (double beam) Shimadzu, Japan between a U.V range from 200 to 400 nm against distilled water as blank.

Calibration curve of rabeprazole: Stock solution of rabeprazole Sodium was prepared by dissolving 100 mg of accurately weighed amount of rabeprazole Sodium in 10 ml of distilled water and then the volume was adjusted to 100 ml with the same solution.

Procedure: The above stock solution of drug was subsequently diluted with distilled water to get 2 μg , 4 μg , 6 μg , 8 μg and 10 μg , of drug per ml. Then the absorbance of these dilute solutions was measured at a λ_{max} of 272.2 nm by using double beam U.V. spectrophotometer against a blank of distilled water. Average of triplicate readings was taken and tabulated. Regression equation was derived from the slope of the curve $y = 0.034 * X - 0.00267$; $r^2 = 0.99961$. The analytical method so developed was validated for precision, accuracy and linearity.

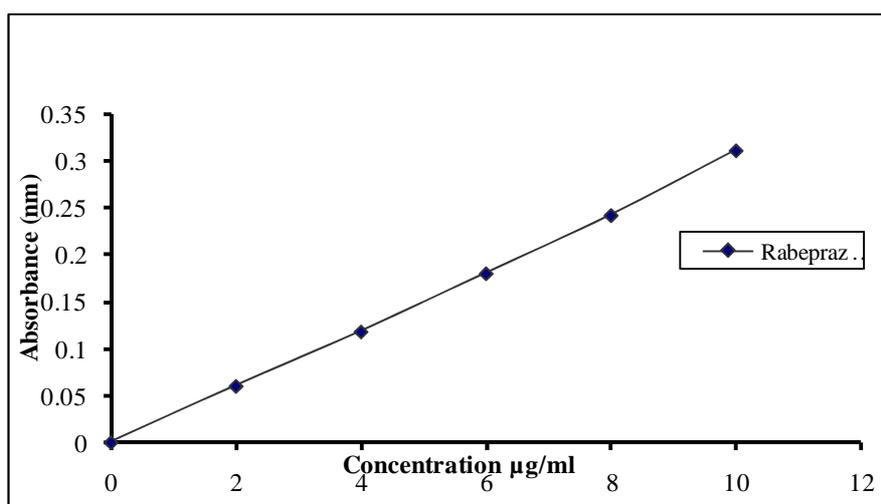
Table.1. Spectrophotometric data for the estimation of rabeprazole Sodium at 272.2 nm

Sl. No	Concentration ($\mu\text{g/ml}$)	Absorbance
1	0.00	0.00
2	2.00	0.06
3	4.00	0.118
4	6.00	0.180
5	8.00	0.242
6	10.00	0.311

Table 2. Linearity studies of Rabeprazole Sodium

Sl. No	Concentration ($\mu\text{g/ml}$)	Absorbance(nm)	Regression Data		
1	2	0.060	$m^* = 0.0314$	$c^* = -0.00267$	$r^* = 0.99961$
2	4	0.118			
3	6	0.180			
4	8	0.242			
5	10	0.311			

* m = slope; c = intercept; r = regression.



$$y = 0.034 * X - 0.00267; (r^2 = 0.99961)$$

Fig 1. Calibration curve of Rabeprazole Sodium at 272.2 nm

Validation of analytical method of Rabeprazole Sodium developed in the laboratory:

The analytical method so developed in the laboratory was validated for accuracy, precision and linearity.

Table 3. Accuracy and precision studies of Rabeprazole Sodium Tablets

Drug	Formulation	Amount of Drug added (mg/ml)	Amount recovered (mg/ml)	Accuracy	Precision
Rabeprazole Sodium	Cr -1	21.0	20.19	96.14%	0.11
	Cr -2	21.0	20.39	97.09%	0.26

Determination of Accuracy and precision studies of Rabeprazole Sodium enteric coated tablets with Acryl EZE:

Enteric coated tablet of rabeprazole Sodium was crushed into powder in a mortar and 100 mg of powder was taken in a volumetric flask containing pH 9.0 buffer and kept aside with constant shaking for 24 hours to extract the total drug present in the tablet. Then the absorbance of the solutions was measured after suitable dilution at 272.2 nm against drug devoid pH 9.0 buffers as

blank. Averages of triplicate readings were taken. The recovery content of the drug was calculated using the developed analytical method.

RESULTS AND DISCUSSION

The U.V. absorption maxima of rabeprazole sodium in distilled water were found to be 272.2nm which is nearly same as literature value 284 nm [9]. Melting point was found to be 137°C which corroborates with the literature value 140-141°C [10]. Results of studies on melting point and UV absorption maxima of drug suggested the values corroborating with previously reported literature values. The slope (m) of calibration curve of rabeprazole sodium was 0.0314. Linearity studies indicated that estimation of rabeprazole sodium between 2.00 µg / ml to 10.00 µg /ml was found to be linear with slope (m) 0.0314, intercept (c) is -0.00267 ($r^2 = 0.99961$). Later, solubility of rabeprazole in distilled water, acidic and alkaline pH buffers was studied. It was found to be 0.085 mg/ml in pH 2.5, 100.4 mg/ml in distilled water, 0.395 mg/mL in pH 7.5 and 0.567 mg/mL in pH 8.0, 0.878 mg/ml in pH 9.0 at 25°C. The log p value of rabeprazole was found to be 0.549 which corroborates to the reported literature value 0.60 [11]. The physico-chemical characterization studies showed that the bulk sample obtained was pure and analytical work for the estimation of rabeprazole sodium was found to obey Beer's limit in between 2.00 µg / ml to 10.00 µg /ml and the curve was found to be linear. Accuracy and precision studies of rabeprazole sodium tablets showed drug recovery rates of 96.14% and 97.09% in accuracy studies and 0.11 and 0.26 for precision studies of rabeprazole core 1 and core 2 tablets. Hence the developed analytical method for rabeprazole sodium by using UV spectrophotometer was found to be accurate and precise to analyze the drug sample in bulk and dosage forms. Using the proposed analytical technique, further quantitation work of prospective *in vitro* studies of RSM could be carried out.

CONCLUSION

The literature review encompasses the literature reports on various analytical methods of rabeprazole sodium estimation useful in the study. The corroborating experimental values suggest the bulk drug sample of rabeprazole sodium obtained was pure. The solubility studies of rabeprazole sodium suggests that It was also observed closely that, rabeprazole in the lower pH media (below pH 9) turns dark and degree of darkness is more in lower pH than higher pH and at pH 9 the drug did not dark and this may be due to the pH dependent stability of rabeprazole sodium. The analytical method developed using UV spectrophotometer is linear and accurate with minimum variation. Although there are reports and publications of either colorimetric and HPLC methods for rabeprazole estimation, but there is no report or publication corresponding to the intended investigation, development and validation of UV Spectrophotometric method of rabeprazole sodium. Therefore it could conclude that the proposed investigation is a novel work and the investigation would help in estimation of drug candidate spectrophotometrically in the bulk fluids and dosage forms.

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