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ANALYZING THE SATURATED SOLUBILITY OF RABEPRAZOLE SODIUM IN DIFFERENT DISSOLUTION MEDIA VIA UV/VISIBLE SPECTROPHOTOMETER

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ABSTRACT

Solubility is a fundamental pre-formulation factor that significantly influences the formulation and development of drugs. It plays a crucial role in determining the bioavailability of solid dosage forms, such as tablets and capsules. For these forms to be effective, it is essential that drug molecules are adequately solubilized. This solubilization becomes even more important in the context of innovative drug formulations that aim to enhance therapeutic efficacy. In this study, the focus was on assessing the solubility of Rabeprazole sodium at varying pH levels. To achieve this, a UV-visible spectrophotometer was utilized to measure the drug's solubility in both pure water and buffer solutions, which had pH values ranging from 1.2 to 7.4. This method allowed for a precise evaluation of how different pH environments would influence the solubility characteristics of Rabeprazole sodium. The results clearly indicated that the solubility of Rabeprazole sodium is pH-dependent, which means that changes in the pH of the dissolution medium can significantly affect the solubility of the drug. This finding is particularly relevant for formulators, as it highlights the need to consider pH when developing tablets and capsules. By optimizing the solubility conditions, formulators can improve the bioavailability and therapeutic effectiveness of Rabeprazole sodium, ultimately leading to more successful treatment outcomes. Understanding these solubility dynamics is essential in the quest for effective pharmaceutical formulations.

KEYWORDS: Bioavailability, Rabeprazole sodium, UV-visible spectrophotometer and pH values.

INTRODUCTION

Solubility is a fundamental element in pharmacology, as it directly impacts a drug's concentration in the bloodstream and its therapeutic effectiveness. One of the most pressing challenges in creating new pharmaceuticals and generics is low water solubility. Research indicates that over 40% of new chemical entities are significantly insoluble, which can hinder their efficacy and bioavailability.[1]

To tackle these issues, the Biopharmaceutical Classification System (BCS) provides a structured framework for categorizing pharmaceutical compounds based on their water solubility and intestinal permeability. This classification system plays a crucial role in informing research and development efforts, as it takes into consideration both a drug's permeability and it's *in vitro* dissolution properties.[2] For instance, when a compound falls under categories such as BCS 2, BCS 3, or BCS 4, it signals to the discovery teams that there is an urgent need to enhance either its solubility or permeability to improve its therapeutic outcome.

Moreover, a classification outside of BCS 1 serves as a warning to clinicians regarding potential variability in drug exposure, which can significantly affect treatment outcomes. This is particularly important in terms of food interactions that may alter a drug's effectiveness. Additionally, these classifications alert manufacturing teams to possible formulation challenges during the development process, helping to ensure safer and more effective drug delivery. In summary, understanding solubility through the BCS framework is essential for advancing drug development and optimizing patient care in pharmacotherapy.[3-4] The purpose of this study is to determine the solubility of the drug across different dissolution media.

EXPERIMENTAL

Materials

Hydrochloric acid, disodium hydrogen phosphate, sodium hydroxide and potassium dihydrogen phosphate were purchased from Qualigens Fine Chemicals., Mumbai, India. The distilled water was produced in our research laboratory with a distillation unit.

Determination of λ max of Rabeprazole sodium in different dissolution medium

A standard stock solution of Rabeprazole sodium was prepared by dissolving 0.01 g of the drug in methanol and then adjusting the total volume to 100 ml, resulting in a concentration of 100 µg/ml. Following this preparation, working standard solutions of 10 µg/ml were scanned across the UV range of 200-400 nm. This scanning process enabled the identification of the λ max, which was found to be 284 nm. To further investigate the solubility characteristics of Rabeprazole sodium, six additional working standard solutions with varying concentrations—specifically 2, 4, 6, 8 and 10 µg/ml—were derived from the initial stock solution. The absorbance of these different solutions was measured precisely at the identified λ max. The resulting data allowed for the construction of a calibration curve, which is essential for analyzing linearity. This calibration curve then provided the necessary regression equation, thereby enabling a comprehensive evaluation of Rabeprazole sodium's solubility under various experimental conditions.[5]

Standard calibration curve of Rabeprazole sodium in different medium

Various dissolution media, such as distilled water and buffer solutions at pH levels of 1.2, 6.8, and 7.4, were utilized to develop standard curves for Rabeprazole sodium. This process began with the careful weighing of 100 mg of Rabeprazole sodium, which was then dissolved in 10 ml of methanol. The solution was diluted to a final volume of 100 ml using each corresponding pH buffer solution, resulting in a concentration of 1 mg/ml. For further analysis, 10 ml of this initial solution was diluted again with methanol, increasing the volume to 100 ml with the same buffer solution, thus yielding a concentration of 0.1 mg/ml. To create a range of concentrations for subsequent analysis, aliquots were prepared to achieve final concentrations of 2, 4, 6, 8, and 10 µg/ml. These solutions were subjected to analysis using a UV spectrophotometer, which was specifically calibrated to the wavelength (λ max) of 284 nm, where Rabeprazole sodium exhibits maximum absorbance. An absorbance versus concentration graph was plotted based on the recorded absorbance values, and the corresponding r^2 value was calculated to evaluate the linearity of the data obtained. This systematic approach enabled a thorough assessment of Rabeprazole sodium's solubility across different pH environments, thereby enhancing the understanding of its pharmacokinetic properties and offering insight into its behavior in various physiological conditions, which is crucial for optimizing its therapeutic effectiveness.[6-7]

Saturated solubility study

To explore the saturation solubility of the drug, various buffers with pH values ranging from 1.2 to 7.4, alongside distilled water, were incorporated into the experimental design. Each 100 ml volumetric flask was filled with 50 ml of either distilled water or the chosen buffer solution. Subsequently, additional amounts of the drug were added to each flask, which were then sealed with aluminum foil to prevent contamination. This meticulous preparation was critical for achieving accurate and reliable results. To ensure thorough mixing and effective solubilization of the drug in the selected solvents, the volumetric flasks were placed in a shaking water bath. The temperature was carefully maintained at approximately 37 ± 0.5°C while the flasks were agitated at a constant speed of 50 rpm for a continuous duration of 48 hours, allowing ample time for the drug to attain saturation solubility in each solution. Upon completion of the dissolution phase, the samples were filtered through syringe filters with a pore size of 0.22 µm to remove any undissolved particles that could affect subsequent analyses. The filtered samples were then diluted with the same solvent to ensure accuracy in measurement. The absorbance of the drug in these diluted samples was analyzed using a UV-visible spectrophotometer (UV-1800, Shimadzu Corporation, Japan) at the specific λ max predetermined for each solvent. Using established standard curves for the drug in the respective solvents, the concentration of the drug in each sample was calculated from its absorbance. This thorough methodological approach provided essential insights into the drug's solubility characteristics across different pH environments, which is vital for understanding its pharmacological properties and potential therapeutic applications.[8-9]

RESULTS AND DISCUSSION

Scanning of λmax of drug in different dissolution medium

The wavelengths (λmax) of the drug, measured in various dissolution media, are displayed in Table No. 1. The findings reveal that the drug exhibited the same wavelengths across all the tested media, indicating that the pH of the dissolution medium does not influence the drug's wavelength.

Standard curve in different medium

The standard curves for various aqueous media are presented below, ranging from Figure No. 1 to Figure No. 4. Table No. 2 lists the linear equations and correlation coefficients (r^2 values) for the standard curves of each specific medium. The results indicate that strong correlation coefficients were obtained for the drug in all dissolution media. Given the significant correlation between analyte concentration and absorbance, this method is suitable for analysis.

Saturated solubility study

Figure No. 5 presents the results of the saturated solubility analysis. The findings indicate that the solubility of the drug is influenced by pH, showing an increase in solubility with rising pH values. Notably, the drug exhibited the lowest solubility at a pH of 1.2 (0.1N HCl).

Table No. 1: The λmax of the drug in different dissolution medium.

Sl. no	Solvent use for study	Scanned drug λ max (nm)
1.	Distilled water	284
2.	0.1N HCl pH (1.2)	284
3.	Phosphate buffer pH (6.8)	284
4.	Phosphate buffer pH (7.4)	284

Table No. 2: Linear equation and correlation coefficient values in different medium.

SL no.	Solvent used in the study	Linear equation (y = mx + c)	Correlation Coefficient (r^2)
1	Distilled water	0.0257x + 0.0175	0.9824
2	0.1N HCl pH (1.2)	0.0278x + 0.0136	0.9914
3	Phosphate buffer pH (6.8)	0.0285x + 0.0139	0.9920
4	Phosphate buffer pH (7.4)	0.0308x + 0.0125	0.9917

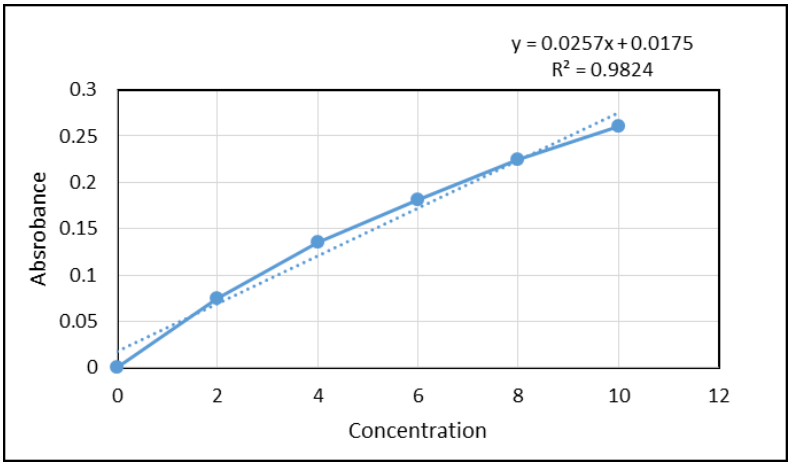

Figure No. 1: Standard curve in distilled water.

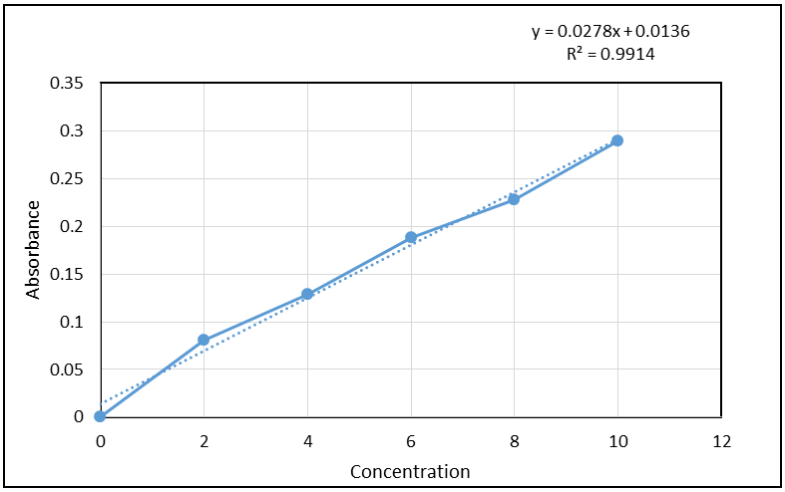

Figure No. 2: Standard curve in pH 1.2.

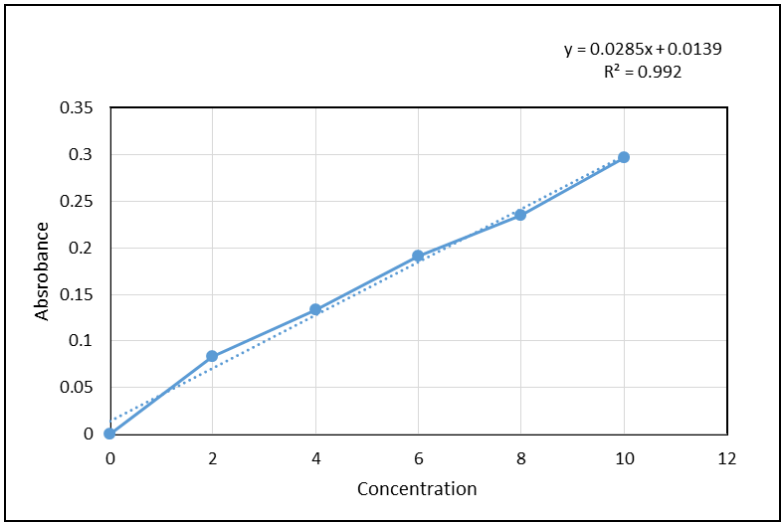

Figure No. 3: Standard curve in pH 6.8.

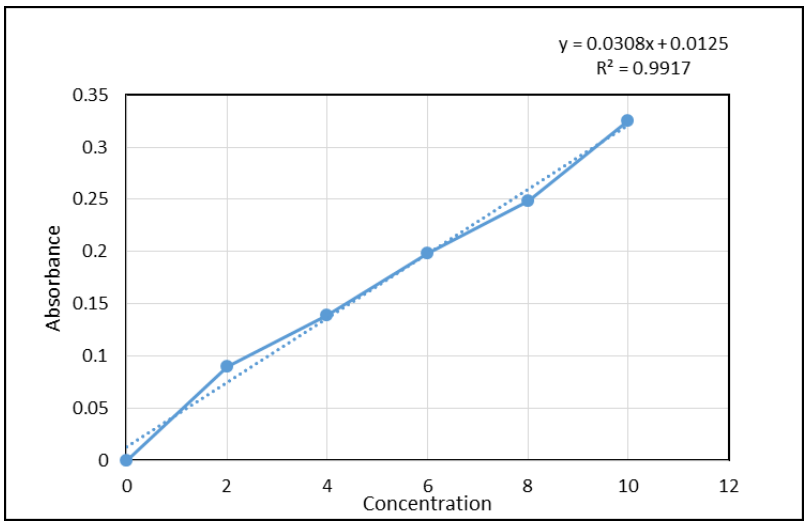

Figure No. 4: Standard curve in pH 7.4.

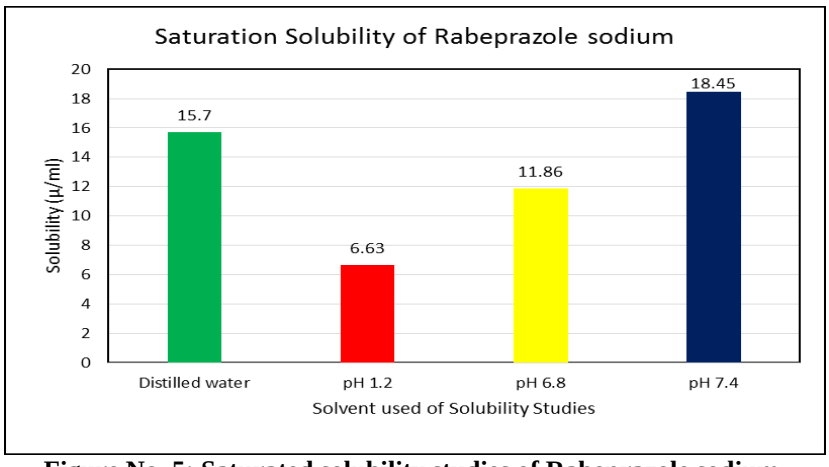

Figure No. 5: Saturated solubility studies of Rabeprazole sodium.

CONCLUSION

The current research indicates that Rabeprazole sodium exhibits pH-dependent solubility. The findings from the saturated solubility study reveal that the drug's low bioavailability is primarily attributed to its limited aqueous solubility. Additionally, the study highlights the necessity of enhancing the drug's solubility in acidic conditions.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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