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DETERMINATION OF SATURATED SOLUBILITY OF RANOLAZINE ON DIFFERENT DISSOLUTION MEDIUM USING UV/VISIBLE SPECTROPHOTOMETER

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ABSTRACT

The solubility of the drug is essential for the formulation and development of the drug. One of the most important pre-formulation parameters is the solubility of drug. The drug molecules must be adequately solubilized for parenteral preparations. Solubility and permeability are also essential for the bioavailability of solid formulations like tablets and capsules. The aim of the study was to use a UV-visible spectrophotometer to examine the solubility of the drug in various pH environments. Buffers with a pH range of 1.2 to 7.4 and also distilled water were used for studying the solubility of drug. The results of this study confirmed that the solubility of Ranolazine is pH-dependent.

KEYWORDS

Saturated solubility, UV visible spectrophotometer, Ranolazine and pH range.

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INTRODUCTION

Poor water solubility and low bioavailability are common characteristics of novel drug candidates[1]. Drugs with low solubility make almost 40% of all newly created medications, which is a global concern for the pharmaceutical industry[2]. In pre-formulation investigations, solubility is considered as a crucial characteristic. The two crucial characteristics of the Biopharmaceutical Classification System (BCS) are solubility and permeability. The U.S. Food and Drug Administration's Biopharmaceutics Classification System is used to categorize pharmaceutical products. According to this, there are four different

classes of medications: Class I, which includes highly soluble and permeable medications, class II, which includes low-soluble and highly permeable medications, class III, which includes less soluble and highly permeable medications, and class IV, which includes medications that are significantly less soluble and have poor permeation rates. The bioavailability of the medicine is impacted by its aqueous solubility. Drugs taken orally dissolve at first in the gastrointestinal environment. The drug is dissolved, and after passing through the intestinal membrane, it enters the bloodstream. According to the literature, roughly 40% of drug molecules are unable to pass this process due to poor biopharmaceutical characteristics including water solubility[3-5]. The objective of this investigation is to ascertain the solubility of drug in various dissolution media.

EXPERIMENTAL

Materials

The Ranolazine was received as a gift sample. 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 λmax of Ranolazine in different dissolution medium

The UV Visible Spectrophotometer was used to scan the drug's maximum concentration in various dissolution mediums (such as distilled water, pH 1.2, pH 6.8, and pH 7.4 buffers). The stock solutions of ranolazine were made in each media for this study. Ranolazine 10µg/ml concentration were prepared in different pH buffers. The solutions were scanned from 200-400nm by UV spectrophotometer and a spectrum were observed for absorption maxima.

Standard calibration curve of Ranolazine in different medium

Various dissolution mediums (or solvents), including distilled water, pH 1.2, pH 6.8 and pH 7.4, had been used to conduct standard curves of Ranolazine.

100mg of accurately weighed Ranolazine was dissolved in 10ml of methanol and make up to 100ml with different pH buffer solution (1mg/ml).

10ml of the above solution was diluted with methanol and make up the volume upto 100ml with different pH buffer solution (0.1mg/ml).

From the above solution 2, 4, 6, 8 and 10µg/ml were prepared and analyzed by UV spectrophotometer at λmax 272 nm.

The graph of absorbance v/s concentration in µg/ml was plotted and r^2 value of this graph was calculated[6,7].

Saturated solubility study

Various buffers with pH ranges between 1.2 and 7.4 and distilled water were used to measure the drug's saturation solubility. In a 100mL volumetric flask, 50mL of distilled water or a buffer with the required pH was added. To each volumetric flask, additional drug was poured and sealed with aluminum foil. In a water bath that was orbitally shaking, these volumetric flasks were fastened together. Throughout the entire investigation, the temperature was kept at around 37± 0.5°C by applying 50rpm of shaking for the duration of 48 hours. Syringe filters with pore sizes of 0.22 m were then used to filter the final samples. After appropriate dilutions with the same solvent, the filtrates were collected, and the absorbance of the drug was examined using a UV-visible spectrophotometer (UV-1800, Shimadzu Corporation, Japan) at the pre-scanned λmax in that solvent. The concentration was then calculated from the absorbance using the drug's standard curve in each relevant solvent[8,9].

RESULTS AND DISCUSSION

Scanning of λmax of drug in different dissolution medium

The drug's scanned wavelengths (λmax) in various dissolving media were shown in Table No.1. The results demonstrate that the drug's wavelengths were identical in all dissolving mediums,

demonstrating that the pH of the dissolution medium has no impact on the drug's wavelength.

Standard curve in different medium

The standard curves for several aquatic media are provided below, ranging from Figure No.1 to Figure No.4. In Table No.2, the standard curves for a particular medium's linear equation and co-efficient correlation (r2) values are listed. The findings demonstrated that for the drug in each dissolving media, good correlation coefficients were obtained. Since the analyte concentration and absorbance show a significant correlation, the method can be used for analysis.

Saturated solubility study

Figure No.5 displays the data for the saturated solubility analysis. The solubility investigations show that the solubility of drug is pH-dependent, with a decrease in pH value the solubility increases. Here, the drug was shown to be least soluble in distilled water, which may be related to the substance's unionization. The drug's membrane permeability was enabled yet constrained by its unionized structure.

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

S.No	Solvent used for study	Scanned drug λmax (nm)
1	Distilled Water	272
2	0.2N HCl Buffer (pH 1.2)	272
3	Phosphate Buffer pH 6.8	272
4	Phosphate Buffer pH 7.4	272

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

S.No	Solvent used for study	Linear equation (y = mx + c)	Correlation Coefficient (r2)
1	Distilled Water	0.0118x + 0.0193	0.9971
2	0.2 N HCl Buffer (pH 1.2)	0.0677x + 0.0082	0.9978
3	Phosphate Buffer pH 6.8	0.0411x + 0.0278	0.9853
4	Phosphate Buffer pH 7.4	0.0271x + 0.0131	0.9898

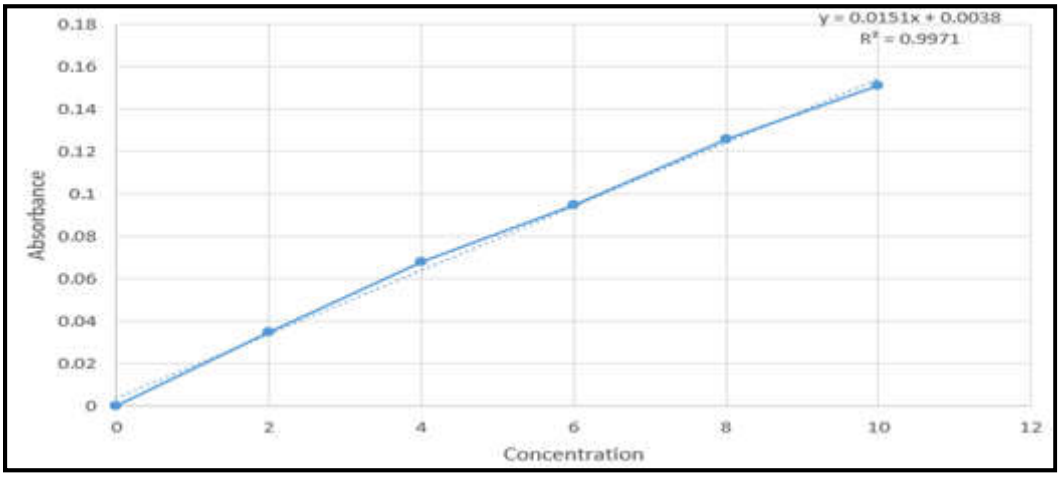

Figure No.1: Standard curve in distilled water

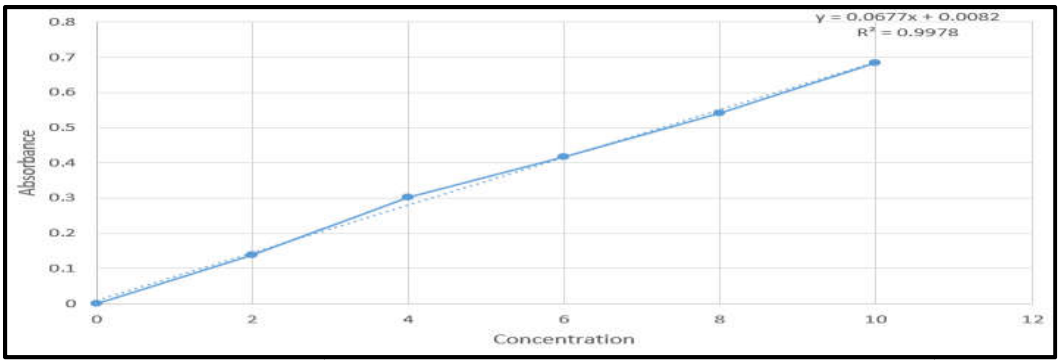

Figure No.2: Standard curve in pH 1.2

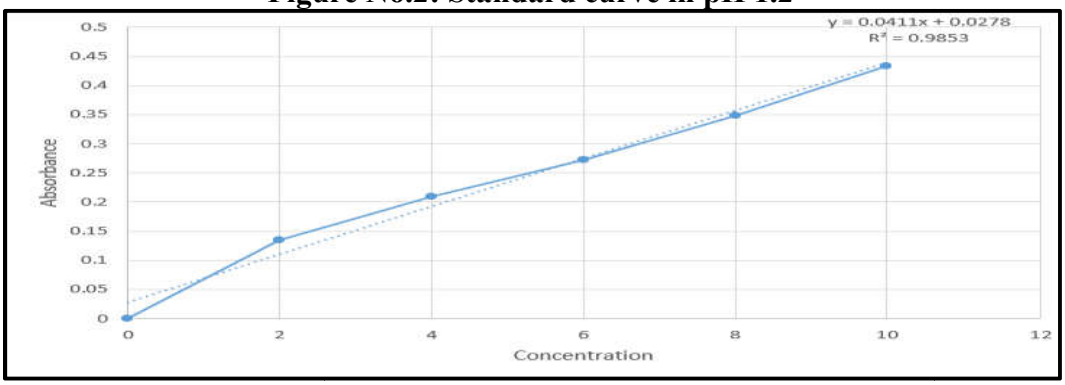

Figure No.3: Standard curve in pH 6.8

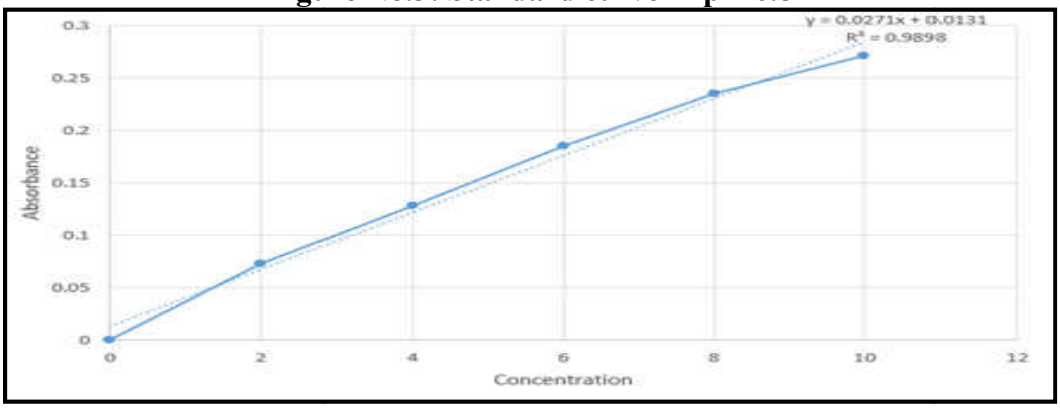

Figure No.4: Standard curve in pH 7.4

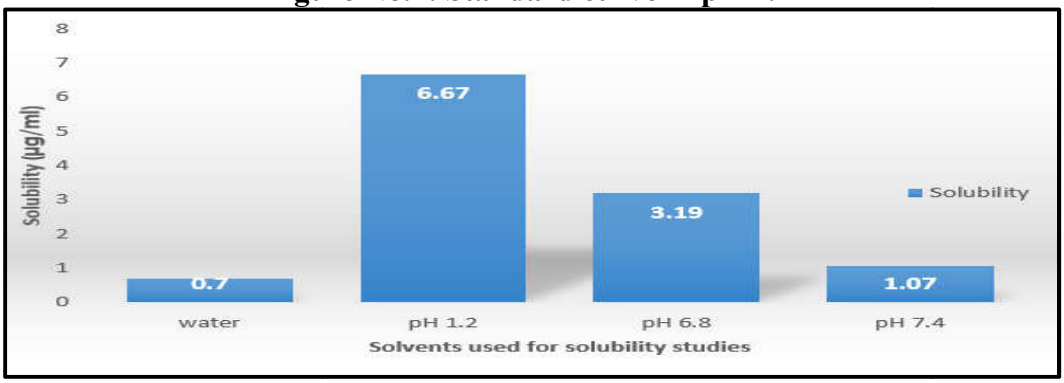

Figure No.5: Saturated solubility studies of ranolazine

CONCLUSION

The present research study concludes that the Ranolazine has pH-dependent solubility, which means the drug has high bioavailability in the stomach. The saturated solubility study concludes that the low bioavailability of the drug is mainly due to low aqueous solubility. This study also suggests a need to improve the solubility of the drug in the basic medium and distilled water.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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