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

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ABSTRACT

Solubility of the drug plays a crucial role in the formulation and development of the drug. Assessing the solubility of the drug is one of the most critical parameter in pre-formulation. Parenteral formulations require adequate solubility of the drug molecules. Correspondingly bioavailability from solid formulations such as tablets and capsules is also dependent on solubility and permeability. The objective of this study was to investigate the solubility of a drug in different pH mediums using a UV visible spectrophotometer. The drug solubility was studied in distilled water with a pH range of 1.2 to 7.4. This study concludes that the Bedaquiline has pH-dependent solubility.

INTRODUCTION

Most of the new drug candidates are characterized by poor water solubility and, consequently, low bioavailability [(1)]. Low solubility drugs account for an estimated 40% of all new drugs developed and present a universal challenge for the drug development industry[(2)]. Solubility is an essential parameter of pre-formulation studies. Solubility and permeability are the two essential properties of the Biopharmaceutical Classification System (BCS). The Biopharmaceutics Classification System given by U.S. Food and Drug Administration determines the absorption of the drug in the intestine. As per this, there are four classes of drugs; class I—drugs that are highly soluble and permeable, class II—drugs which have low solubility and high permeability, class III—It consists of less soluble and highly permeable drugs and class IV—Drugs which are significantly less soluble and permeation rate is also poor. Aqueous solubility affects the bioavailability of the drug. Orally administered drug initial gets dissolved in the gastrointestinal milieu. The dissolved drug then permeates through the intestinal membrane and reaches the systemic circulation. As per the literature, about 40% of the drug molecules fail to meet this process because of non-optimal biopharmaceutical properties like aqueous solubility [(3-5)]. The present study aims to determine the aqueous solubility of the drug in different dissolution mediums.

EXPERIMENTAL:

Materials

The Bedaquiline was received as a gift sample from Recipharm pharmaservices pvt ltd., Karnataka, India. Potassium dihydrogen phosphate, disodium hydrogen phosphate sodium hydroxide and hydrochloric acid were purchased from Thermo fisher scientific India Pvt. Ltd., Bangalore, India. The distilled water was produced in our research laboratory with a distillation unit

Scanning of λmax of drug in different dissolution medium

The λmax of the drug in various dissolution mediums (like distilled water, pH 1.2, pH 5.8, pH 6.8, pH 7.4) was scanned using a UV Visible Spectrophotometer. In this study, the stock solution of Bedaquiline was prepared in each medium. 100 mg of drug was taken in a 100 mL volumetric flask for a stock solution

and dissolved in 10 mL of 5% tween 80. Then the final volume was made up to the mark with a suitable solvent. Further, the λmax of Bedaquiline in all solutions was scanned under spectrum mode in the wavelength range from 200 – 400 nm, and the peak table in all solutions was recorded.

Standard curve in different medium

Standard curves of Bedaquiline have been carried out in different dissolution mediums (or solvents) such as distilled water, pH 1.2, pH 5.8, pH 6.8 and pH 7.4. In this study, the stock solution of the drug was prepared in each medium. For a stock solution, 100 mg of drug was taken in a volumetric flask and dissolved in 10 mL of 5% tween 80. Then the final volume was made up to the mark with a suitable solvent. Further, the dilutions were made using the same dissolution medium to make various concentration solutions for a standard curve. The λmax of the drug in each medium was scanned using UV Visible Spectrophotometer [6-7].

Saturated solubility study

The saturated solubility of the drug was determined in distilled water and various buffers from pH 1.2 to 7.4. The 50 mL distilled water or buffer of required pH were taken in a 100 mL volumetric flask. An excess amount of drug was added to each volumetric flask and closed with Aluminium foil. These volumetric flasks were attached in an orbital shaking water bath. The shaking was carried out for 48 hours with a speed of 50 rpm, and in the entire study, To maintained the temperature at around 37 ± 0.5 °C. Then the resulting samples were filtered using syringe filters with their pore size 0.22 µm. The filtrate was collected, and after suitable dilutions with the same solvent, the absorbance of the drug was analysed with UV Visible Spectrophotometer (UV– 1800, Shimadzu Corporation, Japan) at the pre-scanned λmax in a particular solvent. Then the absorbance was converted into concentration using the standard curve of a drug in each concern solvent [8-10].

RESULTS AND DISCUSSION:

Scanning of λmax of drug in different dissolution medium

The scanned wavelengths (λmax) of the drug in different dissolution mediums are given in Fig. 1 to Fig. 5 and Table 1. As shown in the results, the wavelengths of the drug in all dissolution mediums are the same, which shows the pH of the dissolution medium doesn't affect the wavelength of the drug.

Standard Curve in Different Medium

The standard curves in different aqueous mediums are given below from Fig.6 to 10. The linear equation and co-efficient correlation (r2) values of the standard curves in a different medium are given in Table 2. The results showed that excellent correlation coefficients were obtained for the drug in all dissolution mediums. This demonstrates a significant correlation between analyte concentration and absorbance, and hence the method is suitable for analysis.

Saturated solubility study

The data for the saturated solubility study is shown in Fig. 11. The solubility studies indicate that the drug solubility is dependent on pH, where an increase in pH value increases the solubility of the drug. Here the drug is found to be least soluble in distilled water which might be due to the unionization of the drug. The unionized form of the drug enables the permeability of the drug through the membrane but limits the drug.

Table 1. The scanned drug λmax values in different dissolution medium

SI No	Solvent used for study	Scanned drug λmax (nm)
1	Distilled Water	229
2	0.2N HCl Buffer (pH 1.2)	229
3	Phosphate Buffer pH 5.8	229
4	Phosphate Buffer pH 6.8	229
5	Phosphate Buffer pH 7.4	226

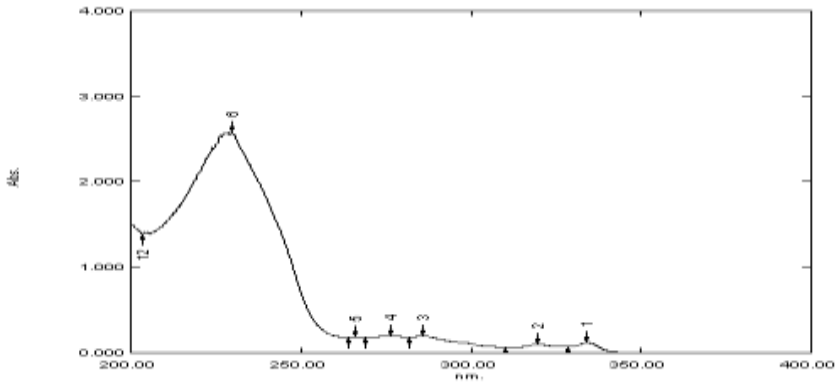

Fig.1. UV drug scanning in Distilled Water

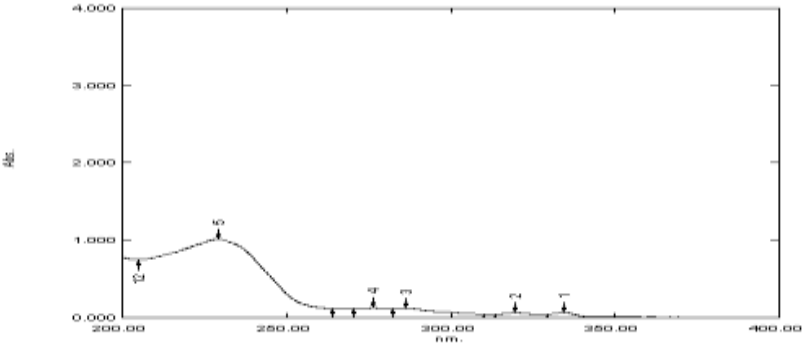

Fig.2. UV drug scanning in pH 1.2

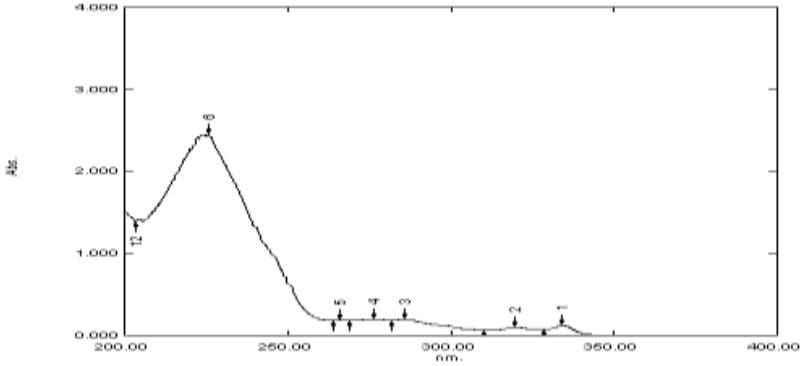

Fig.3. UV drug scanning in pH 5.8

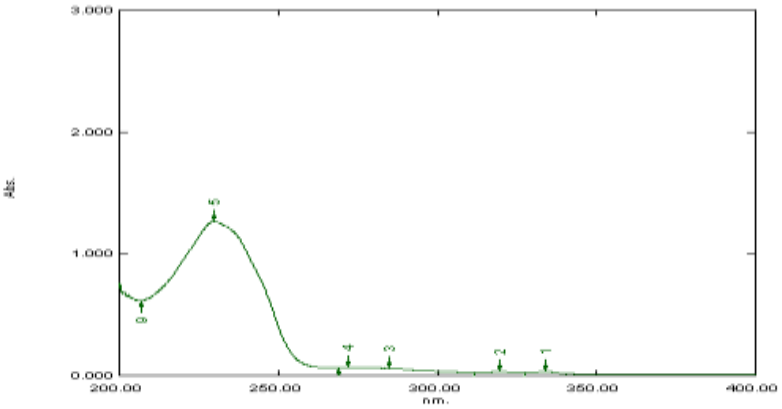

Fig.4. UV drug Scanning in pH 6.8

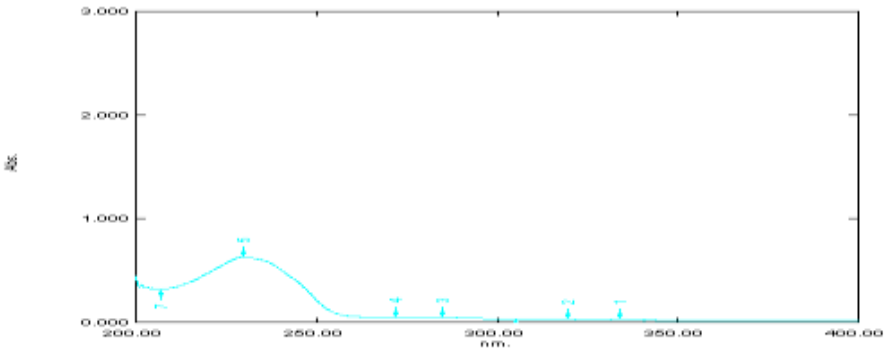

Fig.5. UV drug scanning in pH 7.4

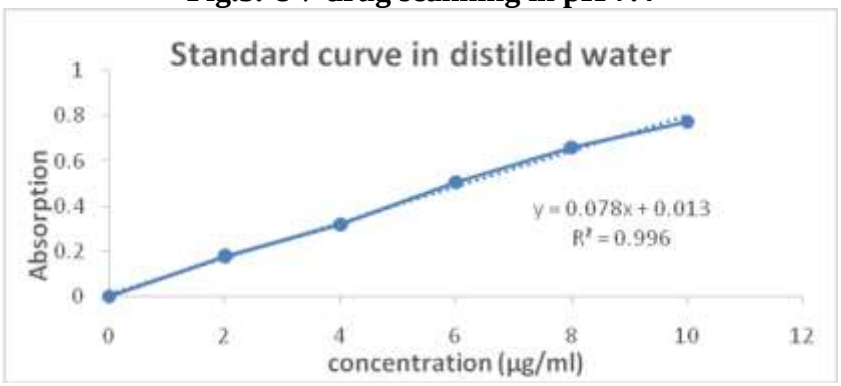

Fig.6. Standard Curve in Distilled Water

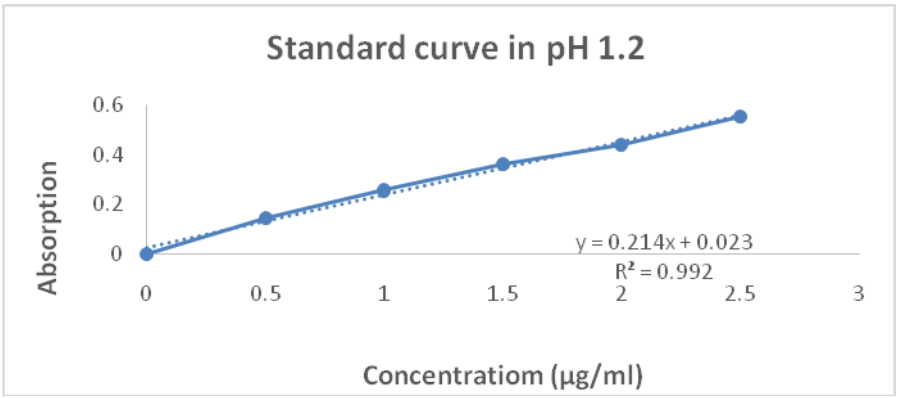

Fig.7. Standard Curve in pH1.2

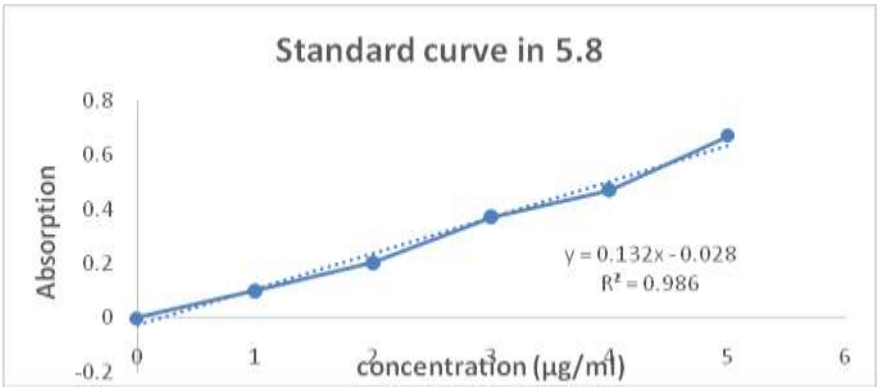

Fig.8. Standard Curve in pH 5.8

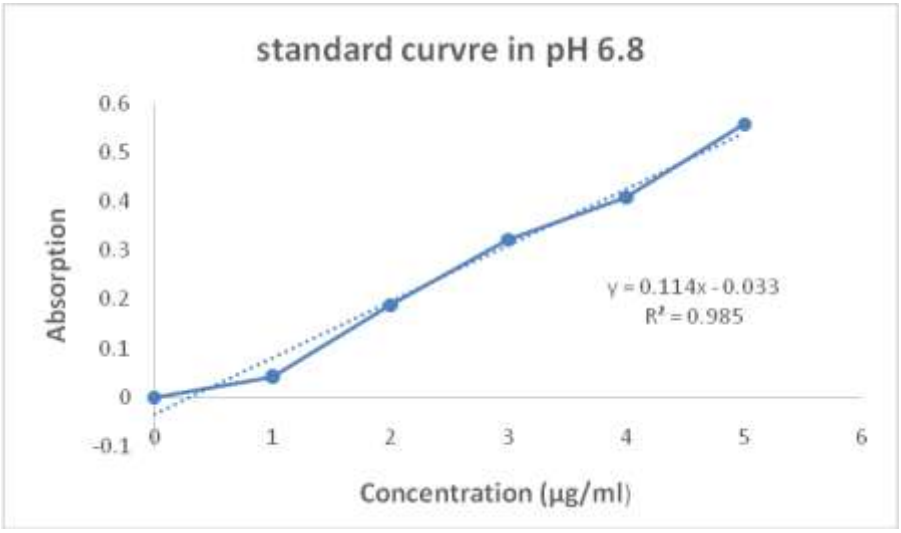

Fig.9. Standard Curve in pH 6.8

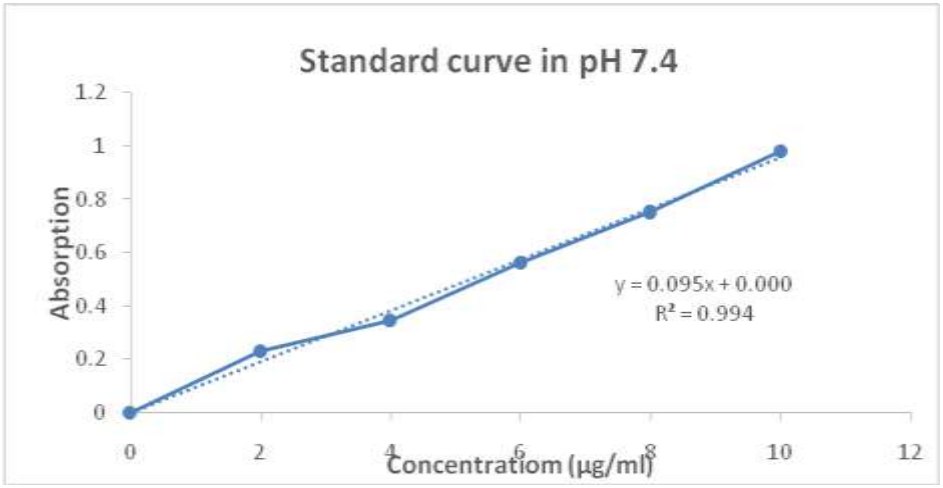

Fig.10. Standard Curve in pH 7.4

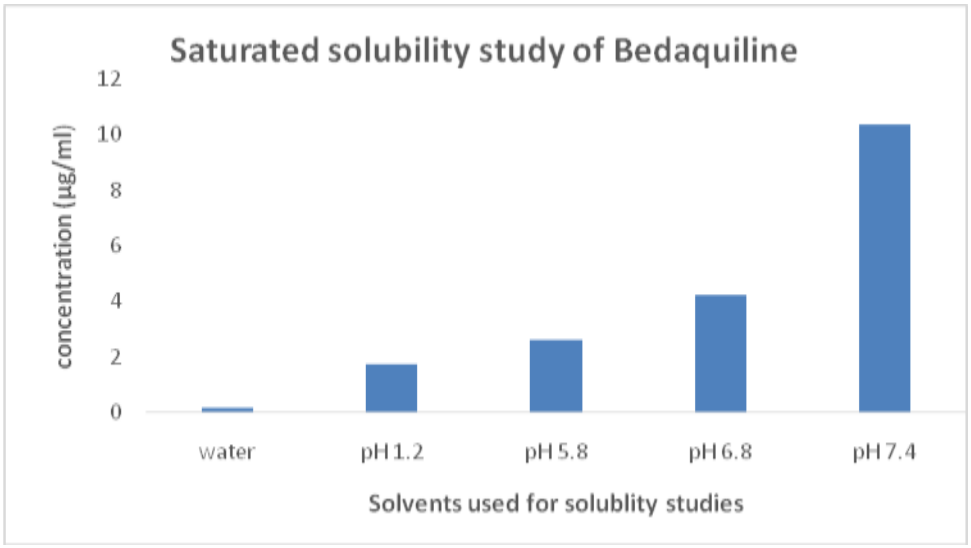

Fig.11. Saturated Solubility Studies of Bedaquiline

Table 2 Linear equation and correlation coefficient values in different medium

SI. No.	Solvent used for study	Linear equation (y = mx + c)	Correlation Coefficient (r2)
1	Distilled Water	0.0787x + 0.0134	0.996
2	0.2 N HCl Buffer (pH 1.2)	0.214x + 0.0237	0.9926
3	Phosphate Buffer pH 5.8	0.1323x + 0.0282	0.9865
4	Phosphate Buffer pH 6.8	0.1147x + 0.0338	0.9857
5	Phosphate Buffer pH 7.4	0.0957x +0.003	0.9943

CONCLUSION

The present research study concludes that the Bedaquiline has pH-dependent solubility, which means the drug has low 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 acidic medium and distilled water.

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