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Determination of Saturated Solubility of Propranololusing UV Visible Spectrophotometer

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ABSTRACT

Solubility criteria plays a vital role in drug development and formulation. Many formulations require sufficient solubility of the drug molecules which affects their bioavailability. This study is based on the investigation of the solubility of drug in different pH medium using UV visible spectrophotometer. The pH range 1.2 to 7.4 was used to determine the solubility study. Thisstudy concludes that the Propranolol has pH dependent solubility.

Keywords: Saturated Solubility, UV Visible Spectrophotometer, Propranolol, pH range.

INTRODUCTION

Solubility is very important parameter of preformulation studies. Solubility and permeability are the two important properties of Biopharmaceutical Classification System (BCS).

The Biopharmaceutics Classification System (BCS) given by U.S. Food and Drug Administration determines the absorption of drug in intestine. Asper this there are four classes of drugs; class I— drugs which 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 very less soluble and permeation rae is also poor. Aqueous solubilityeffects on the bioavailability of the drug[1].

Solubility is important for a drug to achieve the desired concentration. Novel molecules with less solubility in water undergoes various problems while developing formulation as well as during generic drug development. Many drugs being weak acid or weak base are less soluble in water. The less solubility of drug results in poor absorption, variable bioavailability and is harmful to gastrointestinalmucosal tract. Dealing with drug dissolution problem is a big challenge for formulation scientist. Aim of thepresent study is to determine the aqueous solubility of drug in different dissolution medium [2].

MATERIALS AND METHODS

Materials

The Propranololwas received as a gift sample from Dr. Reddy's Laboratories Ltd., Hyderabad, India.Potassium dihydrogen phosphate, sodium hydroxide and hydrochloric acid were purchased from Spectrochem Pvt. Ltd., Bangalore, India.The distilledwater was produced in our research laboratory with distillation unit.

Scanning of λ_{max} of drug in different dissolution medium

The λ_{max} of drug in diverse dissolution medium (e.g.distilledwater, pH 1.2, pH 5.8, pH 6.8, pH 7.4) was scanned using a UV Visible Spectrophotometer. The stock solution of naproxen was prepared in each medium. For making stock solution, drug dissolution was done dissolving 100mg drug per ml methanol and making up the volume to 100ml in volumetric flask. Finally dilution was done till the mark using particular solvent. Further the λ_{max} of propranolol in all solutions was scanned under spectrum mode in the wavelength range from 200 – 400 nm record of peak table was taken [3].

Standard curve in different medium

Standard curves of Propranololwas carried out in different dissolution medium such as distilledwater, pH 1.2, pH 5.8, pH 6.8 and pH 7.4. The stock solution of drug was made in every medium. For making stock solution, 100 mg of drug was taken in a volumetric flask and dissolved in 1 mL of methanol. Finally dilution was done till the markusing particular solvent. Further the dilutions were made using the same dissolution medium to make different concentration solutions for standard curve. The λ_{max} of drug in each medium was scanned using UV Visible Spectrophotometer[4,5].

Saturated solubility study

For determining the saturated solubility of the drug in distilledwater and various buffers from pH 1.2 to 7.4, 3 mL medium of required pH were taken in 5 mL amber colored glass vials. After addingexcess amount of drug in each vial it was closed with stopper. Theseglass vials were attached in an orbital shaking water bath. The shaking was done for 48 hours at a speed of 50 rpm and the temperature mainteanance was done at around 37 ± 0.5 °C. Then resulting test samples were filtered using syringe filters with 0.22 µm pore size. The filtrate was collected and after suitable dilutions with the same solvent the absorbance of the drug was taken with UV Visible Spectrophotometer (UV – 1601PC, Shimadzu Corporation, Japan) at the pre-scanned λ_{max} in particular solvent. Then the absorbance was converted into concentration using standard curve of drug in each concerned solvent [6-9].

RESULTS AND DISCUSSION

λ_{max} of drug in diverse dissolution medium

Fig.1 to Fig.5 and Table 1 represents the scanned wavelengths (λ_{max}) of drug in diverse dissolution medium. Wavelengths of drug was found to be similar in all dissolution medium which shows that wavelength of drug is not affected by the pH of dissolution medium.

| Γable 1. The scanned drug $λ$ | _{nax} values in different | dissolution medium |
|--------------------------------------|------------------------------------|--------------------|
|--------------------------------------|------------------------------------|--------------------|

| S. No. | Solvent used for study | Scanned drug λ_{max} (nm) |
|--------|-------------------------|-----------------------------------|
| 1. | Distilled Water | 289 |
| 2. | 0.1N HCl (pH 1.2) | 289 |
| 4. | Phosphate Buffer pH 5.8 | 289 |
| 5. | Phosphate Buffer pH 6.8 | 289 |
| 6. | Phosphate Buffer pH 7.4 | 289 |



Fig.1. UV drug scanning in Distilled Water



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Standard Curve in various Medium

Fig.6 to 10 represents standard curve of drug in different aqueous medium. Table 2 shows the linear equation and co-efficient correlation (r^2) values of the standard curves in various medium. Results show excellent correlation coefficients for drug in various dissolution medium. A significant correlation between the analyte concentration and absorbance was found which proved the method to beappropriate for analysis.



Fig.6. Standard Curve in Distilled Water



Fig.7. Standard Curve in 0.1N HCl



Fig.8. Standard Curve in pH 5.8



Fig.9. Standard Curve in pH 6.8



Fig.10. Standard Curve in pH 7

Table 2 Linear equation and correlation coefficient values in different medium

| S. No. | Solvent used for study | Linear equation (y = mx + c) | Correlation Coefficient (r ²) |
|--------|-------------------------|---------------------------------|---|
| 1. | Distilled Water | y = 0.0181x + 0.0084 | 0.9865 |
| 2. | 0.1 N HCl (pH 1.2) | y = 0.021x + 0.0017 | 0.9933 |
| 4. | Phosphate Buffer pH 5.8 | y = 0.0191x + 0.0006 | 0.9908 |
| 5. | Phosphate Buffer pH 6.8 | y = 0.0224x + 0.0008 | 0.9966 |
| 6. | Phosphate Buffer pH 7.4 | y = 0.0173x - 0.0017 | 0.9971 |

Saturated solubility study

The data for the saturated solubility study is provided in Fig. 11. The solubility studies indicates that the drug solubility is dependent onpH where increase in pHvalue increases the solubility of the drug. Here drog is found to be least soluble in the distilled water which might be due to unionization of drug. Unionized form of the drug enables the permeability of drug through the membrane, but limits the drug solubility.



Fig.11. Saturated Solubility Studies of Propranolol

CONCLUSION

Present research study concludes that the Propranolol has pH dependent solubility which means the drug has low bioavailability in the stomach. Saturated solubility study concludes that the low bioavailability of drug is mainly due to low aqueous solubility. This study also suggests improvement of the drug solubility in acidic medium and distilled water.

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