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DETERMINATION OF SATURATED SOLUBILITY OF EZETIMIBE 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, 6.8, 7.4 and acetate buffer pH4.5. This study concludes that the Ezetimibe has pH-dependent solubility.

INTRODUCTION

Low solubility drugs account for an estimated 40% of all new drugs developed and present a universal challenge for the drug development industry(1). Most of the new drug candidates are characterized by poor water solubility and consequently often by low bioavailability (2). Solubility is an essential parameter of preformulation 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 the permeation rate is also poor. Aqueous solubility affects the bioavailability of the drug. Orally administered drug initially get 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 Ezetimibe was received as a gift sample from Recipharmpharmaservicespvt ltd.,

karnataka, India. Potassium dihydrogen phosphate, sodium acetate, acetic acid, 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 4.5, pH 6.8, pH 7.4) was scanned using a UV Visible Spectrophotometer. In this study, the stock solution of Ezetimibe 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 methanol. Then the final volume was made up to the mark with a suitable solvent. Further, the λmax of Ezetimibe 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 Ezetimibe have been carried out in different dissolution mediums (or solvents) such as distilled water, pH 1.2, pH 4.5, 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 methanol. 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 decrease 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 solubility.

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)	230
3	Acetate Buffer pH 4.5	232
4	Phosphate Buffer pH 6.8	229
5	Phosphate Buffer pH 7.4	229

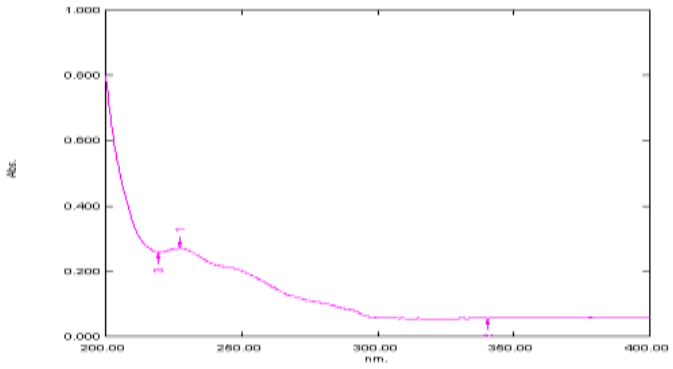

Fig.1. UV drug scanning in Distilled Water

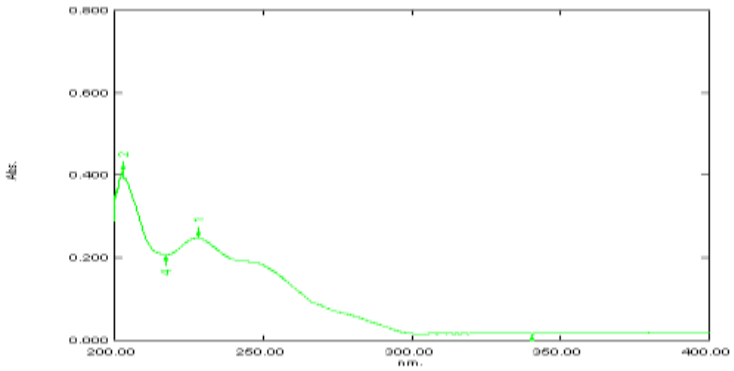

Fig.2. UV drug scanning in pH 1.2

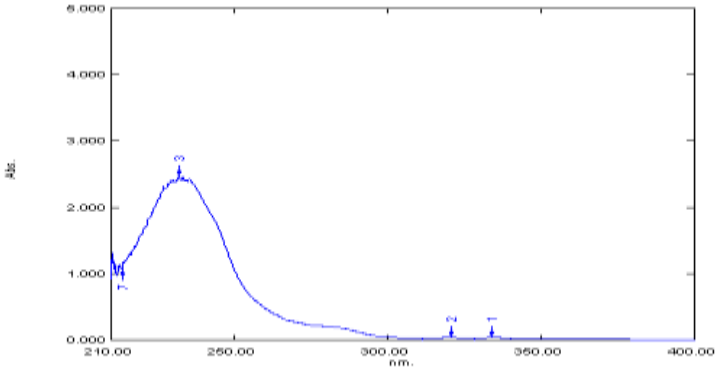

Fig.3. UV drug scanning in pH 4.5

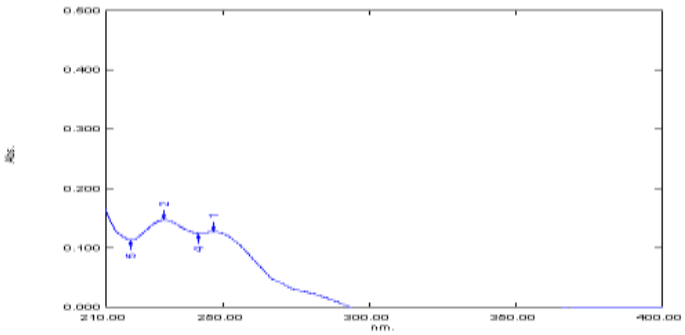

Fig.5. UV drug scanning in pH 7.4

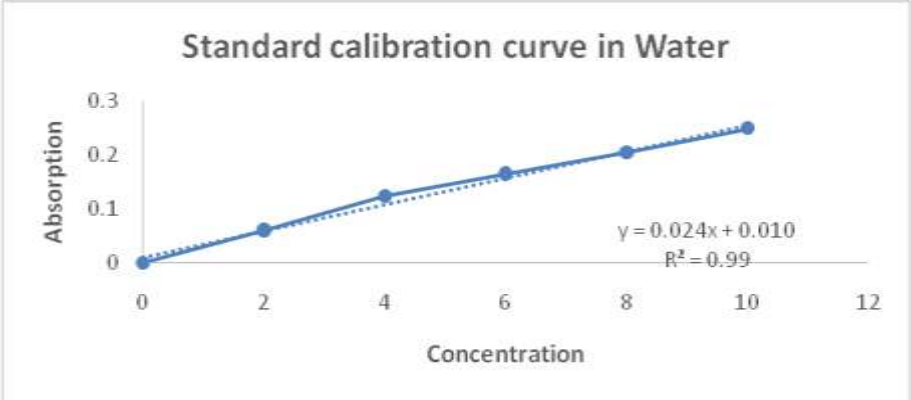

Fig.6. Standard Curve in Distilled Water

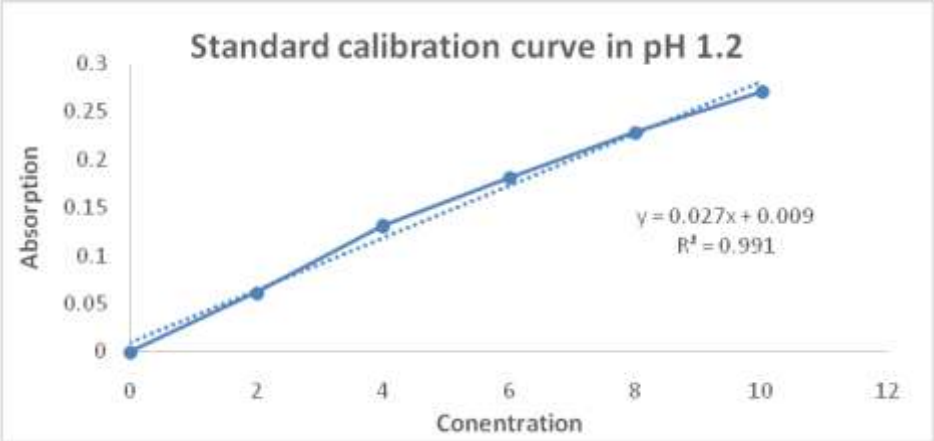

Fig.7. Standard Curve in pH 1.2

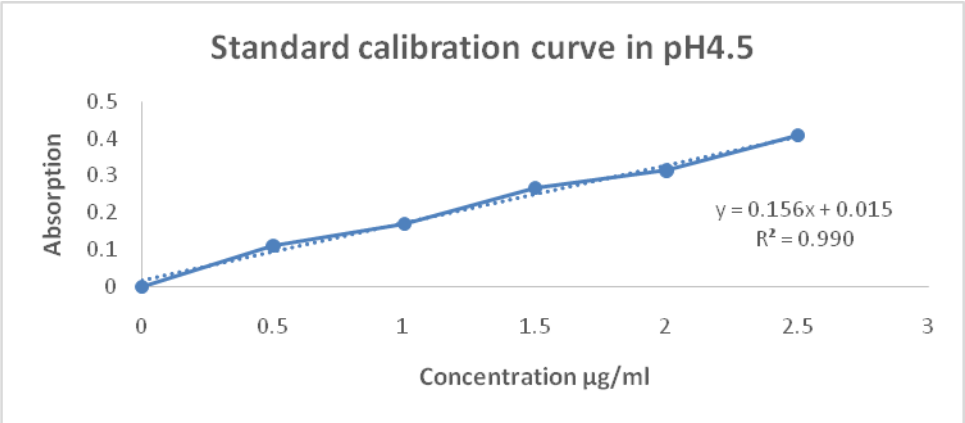

Fig.8. Standard Curve in pH 4.5

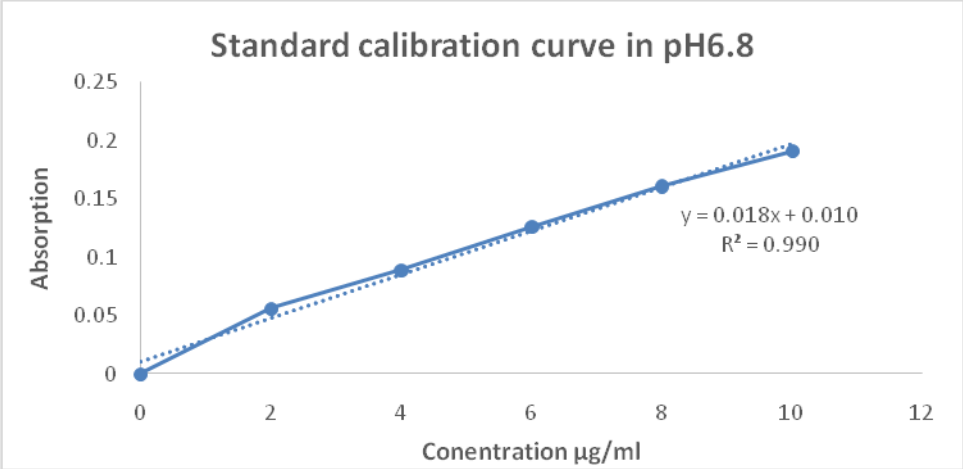

Fig.9. Standard Curve in pH 6.8

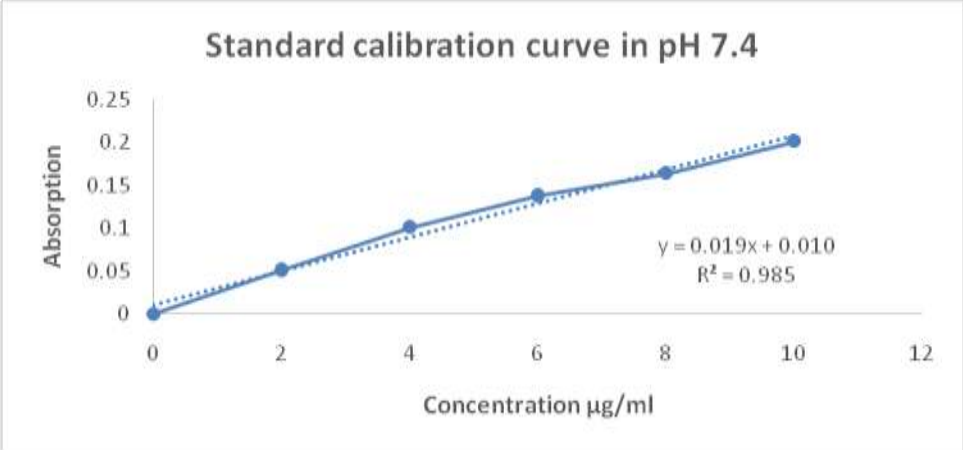

Fig.10. Standard Curve in pH 7.4

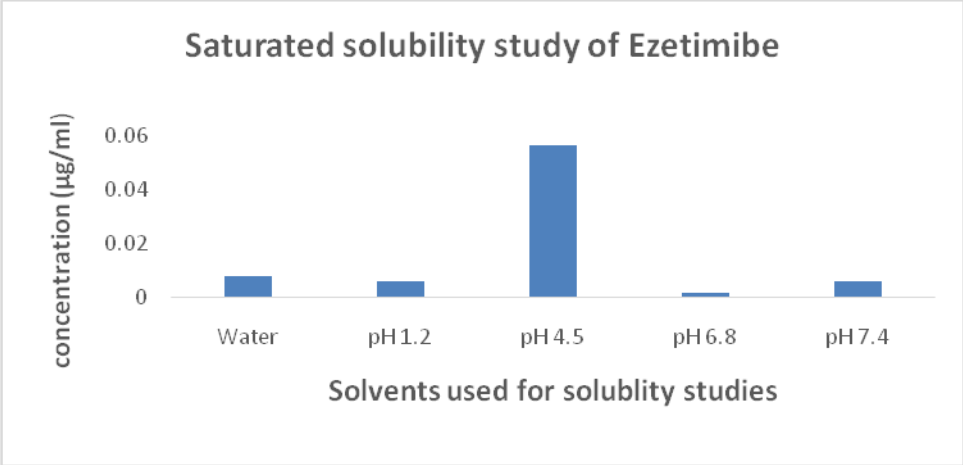

Fig.11. Saturated Solubility Studies of Ezetimibe

Table 2 Linear equation and correlation coefficient values in different medium

SI. No.	Solvent used for study	Linear equation (y = mx + c)	Correlation Coefficient (R^2)
1	Distilled Water	0.0245x + 0.0108	0.99
2	0.2 N HCl Buffer (pH 1.2)	0.0272x + 0.0094	0.9911
3	Acetate Buffer pH 4.5	0.1567x + 0.0152	0.9904
4	Phosphate Buffer pH 6.8	0.0187x + 0.0105	0.9901
5	Phosphate Buffer pH 7.4	0.0197x + 0.0105	0.9858

CONCLUSION

The present research study concludes that the Ezetimibe 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 alkaline medium and distilled water.

REFERENCES

1. Bohr A, Kristensen J, Stride E, Dyas M, Edirisinghe M. Preparation of microspheres containing low solubility drug compound by electrohydrodynamic spraying. International journal of pharmaceutics. 2011 Jun 30;412(1-2):59-67.
2. Colombo M, Staufenbiel S, Rühl E, Bodmeier R. In situ determination of the saturation solubility of nanocrystals of poorly soluble drugs for dermal application. International Journal of Pharmaceutics. 2017 Apr 15;521(1-2):156-66.
3. Larsson J. 2010. Methods for measurement of solubility and dissolution rate of sparingly soluble drugs. Examensarbetekemiteknik – Institutionen for Kemiteknik. Available from: http://www.chemeng.lth.se/exjobb/E272.pdf. Accessed on 05th June 2013.
4. Kumar L, Verma R. Determination of saturated solubility of propranololusing UV visible spectrophotometer. Der Pharmacia Lettre. 2016;8(17):196-201.
5. Kumar L, Suhas BS, Pai G, Verma R. Determination of saturated solubility of naproxen using UV visible spectrophotometer. Research Journal of Pharmacy and Technology. 2015 Jul 28;8(7):825-8.
6. Bala I, Bhardwaj V, Hariharan S, Kumar MR. Analytical methods for assay of ellagic acid and its solubility studies. Journal of pharmaceutical and biomedical analysis. 2006 Jan 23;40(1):206-10.
7. Wahbi AA, Abdel-Razak O, Gazy AA, Mahgoub H, Moneeb MS. Spectrophotometric determination of omeprazole, lansoprazole and pantoprazole in pharmaceutical formulations. Journal of Pharmaceutical and biomedical analysis. 2002 Nov 7;30(4):1133-42.
8. Kumar AA, Lavanya K, Suneetha P, Kumar AA. New simple UV spectrophotometric method for determination of rabeprazol sodium in bulk and pharmaceutical dosage forms. International Journal of Research in Pharmaceutical and Biomedical Sciences.3; 2012: 1070 – 1073. Available from: www.ijrpbsonline.com. Accessed on 05th Jan 2013.
9. Patel PM, Desai HJ, Patel RC, Patel NM. Spectrophotometric Method for Estimation of Rabeprazole. Indian Journal of Pharmaceutical Sciences. 2007 Mar 1;69(2).
10. Galande VR, Baheti KG, Indraksha S, Dehghan MH. Estimation of amlodipine besylate, valsartan and hydrochlorothiazide in bulk mixture and tablet by UV spectrophotometry. Indian journal of pharmaceutical sciences. 2012 Jan;74(1):18.