WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Determination of Naringenin Saturation Solubility in Diverse Dissolution Medium Using UV-Visible Spectrophotometric Analysis

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Doi : https://doi.org/10.55248/gengpi.5.0924.2703

A B S T R A C T

Naringenin is a flavanone from the flavonoid group of polyphenols, known for its decreased water solubility. Solubility parameters are essential in the formulation and development of drugs, with solubility being one of the most critical pre-formulation factors. The solubility of drug molecules significantly influences their bioavailability across various formulations. Consequently, permeability and solubility play vital roles in the bioavailability of parenteral and solid formulations, such as tablets and capsules.

This study uses a UV-visible spectrophotometer to investigate Naringenin's solubility across different pH media. The pH range studied spans from 1.2 to 7.4. Findings indicate that Naringenin exhibits the lowest solubility in distilled water, while it forms a clear solution when dissolved in phosphate buffer pH 7.4. This solubility behavior can be further utilized for analytical purposes, as there is a significant correlation between analyte concentration and absorbance.

Keywords: Saturated solubility, Naringenin, UV-Visible spectrophotometer

1. Introduction

Solubility is defined qualitatively as the spontaneous interaction of two or more substances to generate a uniform molecular dispersion. Quantitatively, it is defined as the concentration of solute in a saturated solution at a specific temperature. The solubility of drugs is outlined by the Indian Pharmacopoeia as the number of milliliters of solvent in which one gram of solute dissolves[1]. A solution is considered saturated when it contains the maximum amount of solute possible, such a solution will not dissolve if more solute is introduced. As a result, a solution that is in thermal equilibrium with the pure solute can be described as saturated. The concentration of the saturated solution, also known as the solubility of the substance, is a measurement of the drug's capacity to dissolve in the relevant solvent. In general, solubility is temperature-dependent[2].

The two key characteristics of the Biopharmaceutical Classification System (BCS) are permeability and solubility designed for actives, based on their aqueous solubility and in-vivo bioavailability. The scientific foundation for many regulatory decisions as well as the design of drug delivery devices is provided by the Biopharmaceutical Classification System (BCS). A drug taken orally initially dissolves in the gastrointestinal tract, then enters through the intestinal membrane and travels throughout the body. Based on available data, around 40% of therapeutic compounds do not meet this requirement due to sub-optimal biopharmaceutical qualities, such as aqueous solubility. Hence, Solubility determination is one of the first most important and extensively studies of preformulation which effects on the bioavailability of the drug[3,4].

One flavonoid, naringenin, also known by its IUPAC designation 5,7-dihydroxy-2-(4-hydroxyphenyl) chroman-4-one, is commonly present in grapefruit juice and found in tomatoes and tomato-based products at lower concentrations. There have been reports that this flavanone inhibits human cancer cells, and can show estrogenic, anticarcinogenic, and antioxidative properties. However, flavonoids are practically insoluble in water which affects the drug efficacy directly, as well as its future developments[5].

This experiment aims to determine the aqueous solubility of the drug in different dissolution mediums (such as distilled water, pH 1.2, pH 6.8, pH 7.4 buffers).

2. Experimental

2.1 Materials

Naringenin 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 prepared using a distillation unit in the research laboratory.

2.2 Determination of λmax of Naringenin in different dissolution medium

The wavelength at which maximum absorption of radiation takes place is called as λmax. The absorption maximum (λ-max) of Naringenin in different dissolution medium or solvents including distilled water, 0.2N HCl buffer of pH 1.2, phosphate buffer of pH 6.8, and pH 7.4 was ascertained by employing a UV-Visible spectrophotometer to scan the drug solution between 200 to 400 nm.

2.3 Standard calibration curve of Naringenin in different medium

The calibration curve of Naringenin was prepared in various dissolution mediums, including distilled water and buffer of pH 1.2, pH 6.8, pH 7.4. Accurately weighed 100 mg of naringenin was dissolved in methanol and taken in a clean 100 ml volumetric flask. The volume was made up to 100 ml with the dissolution medium mentioned above respectively, which gives a concentration of 1 mg/ml. From this standard solution, 10 ml was pipetted out in a 100 ml volumetric flask, and the volume was made up to 100 ml using dissolution mediums to obtain a concentration of 0.1 mg/ml. From the above stock solution, aliquots of 0.2, 0.4, 0.6, 0.8, and 1.0 ml each were transferred to a separate 10 ml volumetric flask, and the solution was made up to 10 ml to obtain a concentration of 2, 4, 6, 8, and, 10 µg/ml, respectively. The absorbance of each solution was measured at 290 nm. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve, and the r^2 value of this graph was calculated[6,7,8].

2.4 Saturated solubility study

- The saturated solubility of the drug Naringenin was determined in distilled water and various buffers from pH 1.2 to 7.4.
- In a 100 ml volumetric flask, 50 ml of distilled water and various buffers from pH 1.2 to 7.4 were taken.
- An excess amount of drug was added to each volumetric flask and closed with a stopper/ sealed with aluminum foil. These volumetric flasks were attached to an orbital-shaking water bath.
- The shaking was carried out for 48 hours with a speed of 50 rpm, and in the entire study, the temperature was maintained around 37 ± 0.5 °C.
- The resulting samples were filtered, and after suitable dilutions with the same solvent, the filtrates were collected and the absorbance of the drug was analysed with a UV visible spectrophotometer at the pre-scanned λmax in that particular solvent.
- The absorbance was converted into concentration using a standard curve of the drug in each concerned solvent[9,10,11].

3. Results and Discussion

3.1 Scanning of λmax of the drug in different dissolution medium

Scanning of λmax of the drug in different dissolution medium Table No. 1 displayed the drug's scanning wavelengths (λmax) in different dissolving mediums. The outcomes show that the drug's wavelengths were identical in each dissolving media, proving that the drug's wavelength is not influenced by the dissolution medium's pH.

3.2 Standard curve in different medium

The standard curves, which range from Figure No. 1 to Figure No. 4, are shown below for several kinds of dissolution media. The linear equation standard curves and coefficient correlation (r^2) values for a given medium are listed in Table No. 2. The results indicate that good correlation coefficients were achieved for each drug in the dissolving solution. The method can be utilized for analysis since there is a significant correlation between the analyte concentration and absorbance.

3.3 Saturated solubility study

The data for the saturated solubility analysis are shown in Figure No. 5. The solubility studies demonstrate that a drug's solubility is pH-dependent, increasing as the pH value increases. This drug's lowest solubility in distilled water may have something to do with the unionization of the compound. The results proved that the drug Naringenin can provide a clear solution when dissolved in Phosphate buffer, pH 7.4.

Table 1-The λmax of the drug in different dissolution medium

Sl. No.	Solvent used for study	Scanned drug λmax (nm)
1.	Distilled Water	290
2.	0.2N HCl Buffer (pH 1.2)	290

3.	Phosphate Buffer pH 6.8	290
4.	Phosphate Buffer pH 7.4	290

Table 2-Linear equation and correlation coefficient values in different medium

Sl. No.	Solvent used for study	Linear equation (y = mx + c)	Correlation Coefficient (r2)
1.	Distilled Water	0.0206x+0.0044	0.9937
2.	0.2N HCl Buffer pH 1.2	0.0238x+0.0074	0.9913
3.	Phosphate Buffer pH 6.8	0.0265x+0.0085	0.992
4.	Phosphate Buffer pH 7.4	0.0294x+0.0098	0.9964

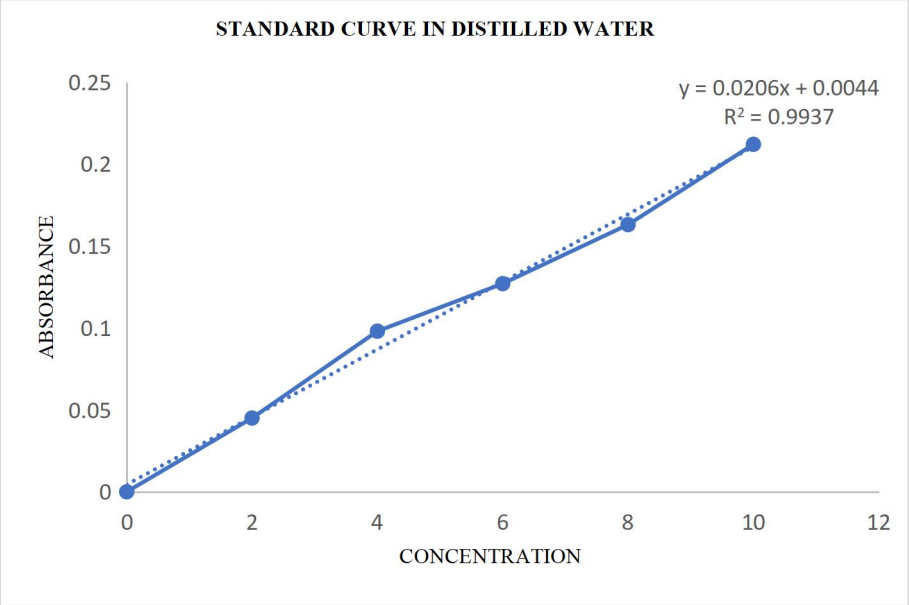

Figure 1- Standard curve in Distilled Water

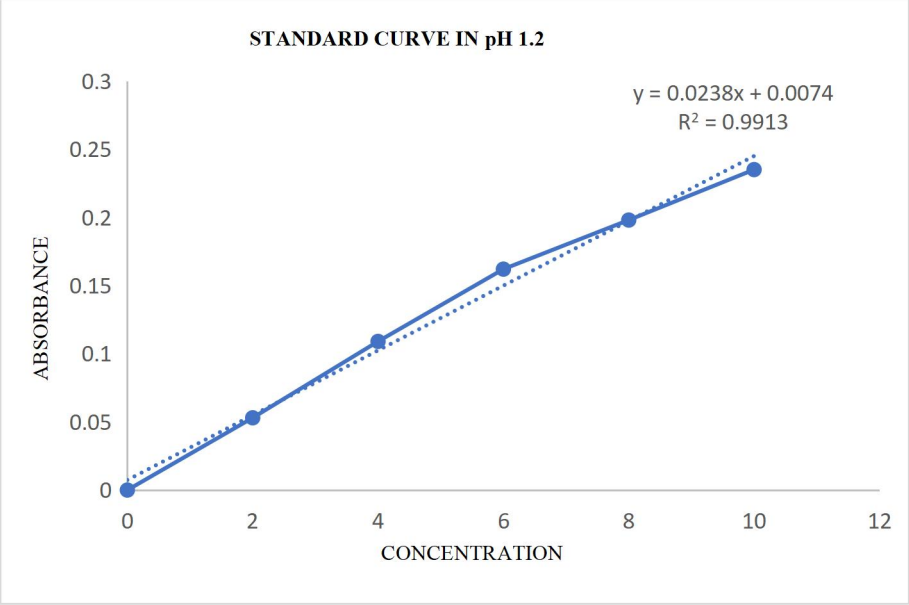

Figure 2- Standard curve in pH 1.2

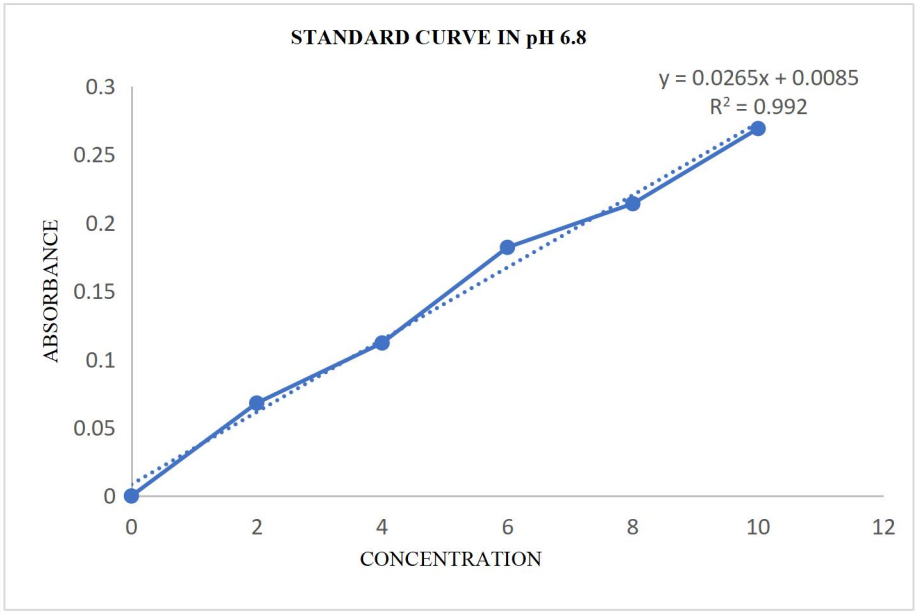

Figure 3- Standard curve in pH 6.8

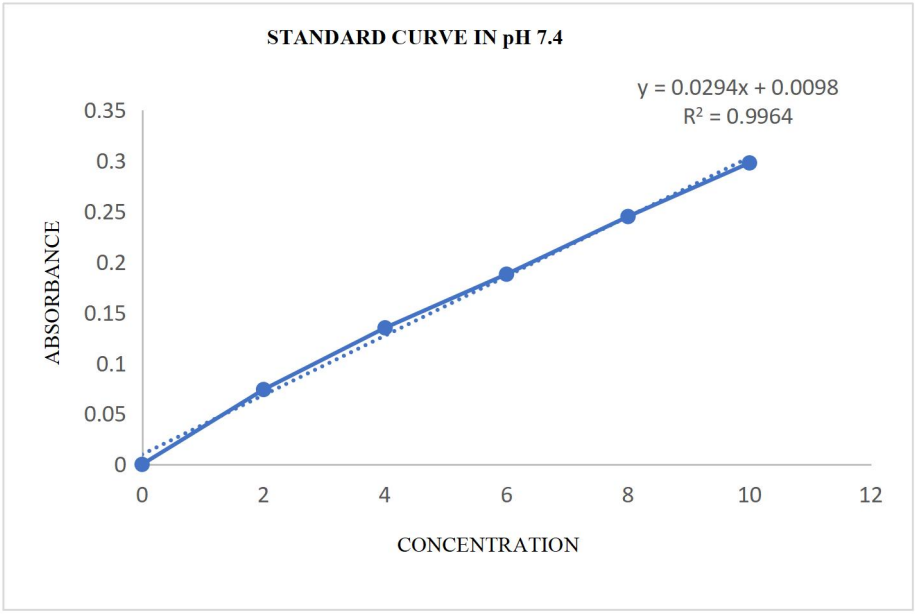

Figure 4- Standard curve in pH 7.4

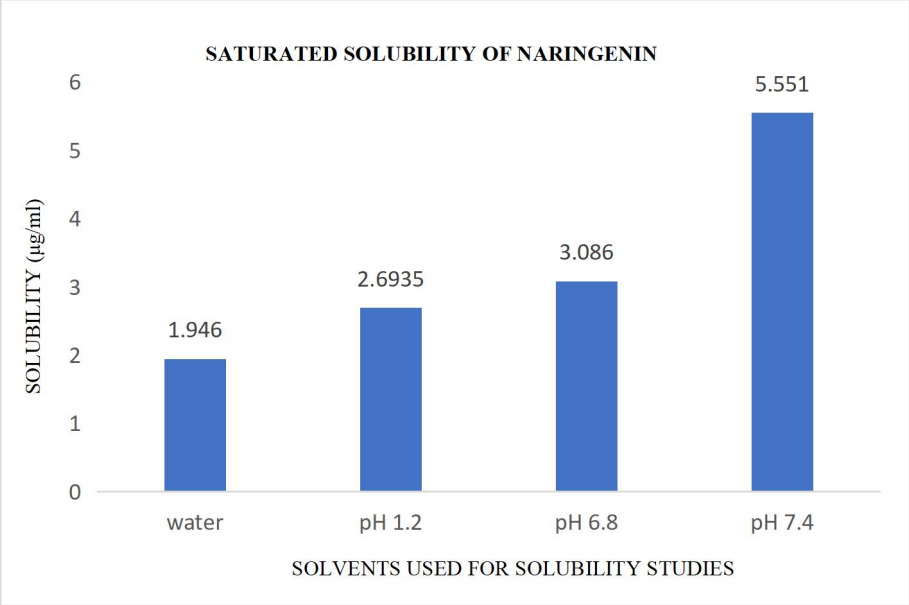

Figure 5- Saturated solubility of Naringenin

4. Conclusion

Drug development requires solubility determination in a range of pH media because it provides a comprehensive understanding of the drug's behaviour in a range of pH media. We can anticipate the drug absorption by using the solubility data. The current study finds that Naringenin has a pH-dependent solubility, indicating a limited bioavailability of the drug. According to saturated solubility research, the drug's low aqueous solubility is mostly to blame for its low bioavailability. Additionally, this investigation indicates that the drug's solubility in distilled water and an acidic media needs to be improved.

5. Acknowledgment

The authors wish to express their sincere gratitude to the Department of Pharmaceutics, T. John College of Pharmacy, Bangalore, India for providing the necessary facilities to carry out this research work.

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