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**Research Article**

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# Study of pH - Dependent Drugs Solubility for BCS Class 2 and Class 4

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**Abstract** Drug solubility is considered as a fundamental property that has to be evaluated in the early stages of drug discovery. Various parameters will have an effect (polarity of drug and solvent, particle size), and they are in addition to the parameters associated with the solution process (temperature, agitation) [1]. This research deals with one of the most important problems of modern pharmacy and pharmacology, and that is the problem of degree of solubility of active pharmacological ingredients, which are being used for wide variety of human disorders and diseases, which, in terms of this particular academic work, has to do with naproxen sodium (Non-Steroidal Antiinflamatory drug –NSAID) and sulpiride (atypical antipsychotic drug). Solubility of medicaments active ingredients, whether it is under significant influence of physiological (features of body fluids) or pathological factors (pathological alterations of physiological factors, especially of pH value of body fluids, due to pathological changes in form of inflammation, tumors, etc.) is the most important factor that determins bioavailability of active pharmacological ingredients in human organism, which, in turn, determins their clinical and therapeutic efficiency [2, 3, 4]. BCS biopharmaceutical system gives specific categories of medicaments according to solubility (and subsequential bioavailability) of their active ingredients, and determins procedures of practical determination of this parameter, and practical measures for its improvemets as well. This research has come to conclusion that the solubility (and subsequent bioavailability and clinical efficency) of naproxen sodium and sulpiride can be significantly improved by means of pH alterations [5].

**Keywords** solubility; bioavailability; naproxen sodium; sulpiride

## Introduction

The Biopharmaceutics Classification System (BCS) is a scientific framework for classifying drug substances based on their aqueous solubility and intestinal permeability. When combined with the dissolution of the drug product, the BCS takes into account three major factors that govern the rate and extent of drug absorption from immediate release (IR) solid oral dosage forms: dissolution, solubility and intestinal permeability. According to the BCS, drug substances are classified as follows:

Class 1: High Solubility – High Permeability
Class 2: Low Solubility – High Permeability
Class 3: High Solubility – Low Permeability
Class 4: Low Solubility – Low Permeability [6].

The aim of this work is to demonstratedsolubility for two different drugs (one from BCS class 2, other form class 4) with an increase in pH.

## Materials and Methods

### Instruments

Instrumentation Spectrophotometer (Shimadzu) was employed for analysis. Spectrophotometric data was acquired using class VP software. pH meter was from Eutech and ultrasonic bath from Sonis.

### Reagents and Materials

Naproxen sodium and sulpiride were supplied by Sigma-Aldrich. Hydrochloric acid, sodium hydroxide, potassium chloride and potassium dihydrogen phosphate were from Semikem. Buffer solutions were prepared as is in USP described (pH 1.2; 4.5; 6.8 and 7.4) [7].

### Preparation of Naproxen Sodium Solutions

Standard solution: Prepared in concentration 50µg/ml in phosphate buffer pH 7.4. Sample solutions are prepared separated in buffer solutions pH 1.2; 4.5; 6.8; 7.4 and water to.

### Preparation of Sulpiride Solutions

Standard solution: Prepared in concentration 50µg/ml in hydrochloric buffer pH 1.2. Sample solutions are prepared separated in buffer solutions pH 1.2; 4.5; 6.8; 7.4 and water to.

### Procedure

Standard and sample solution for naproxen sodium are scanned at 332 nm using phosphate buffer pH 7.4 as blank.
Standard and sample solution for sulpiride are scanned at 291 nm using hydrochloric buffer pH 1.2 as blank.

## Results

Analysis of the solubility profile of naproxen sodium, as selected substance from BCS class 2, confirmed that the solubility substance increases with increasing pH. Based on our research, semiquantitative determination, naproxen sodium is soluble in water and pH 7.4, sparingly soluble in pH 6, 8 and pH 4.5, very sparingly soluble in pH 1.2 (Figure 1; Table 1).

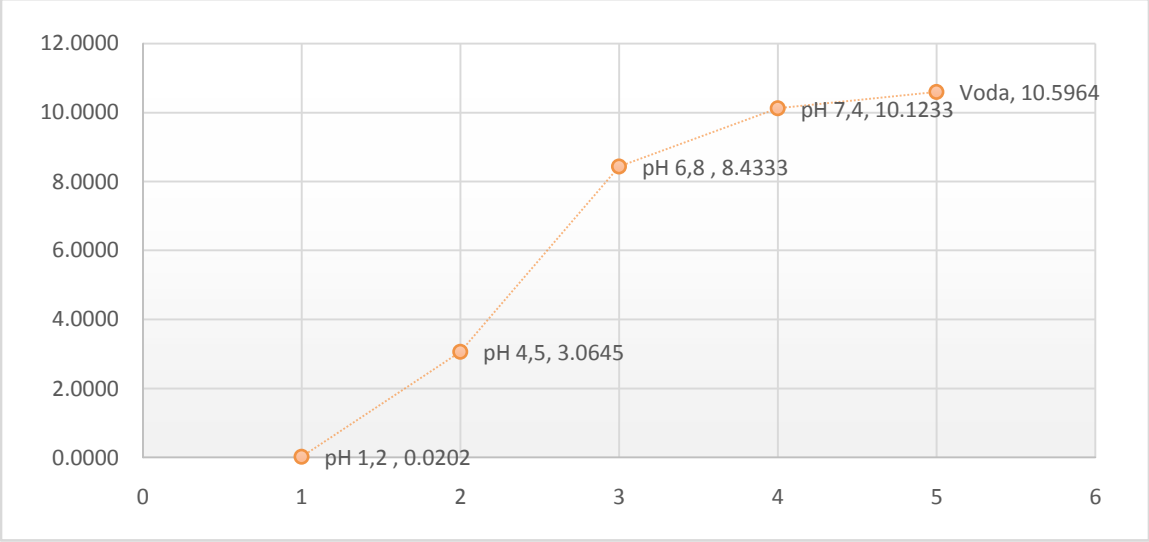


*Figure 1: Solubility profile for naproxen sodium*

**Table 1:** Solubility data for naproxen sodium

| pH | mg/ml |
|---|---|
| pH 1.2 | 0.0202 |
| pH 4.5 | 3.0645 |
| pH 6.8 | 8.4333 |
| pH 7.4 | 10.1233 |
| Water | 10.5964 |

Analysis of the solubility profile of sulpiride, as the selected substance from BCS class 4, confirmed that the solubility of the substance is lower at higher pH values, it increases at lower pH values. Based on our conducted research, semiquantitative determination, sulpiride is moderately soluble in pH 1.2, sparingly soluble in pH 4.5; 6, 8 and pH 7.4, and very sparingly soluble in water (Figure 2; Table 2).

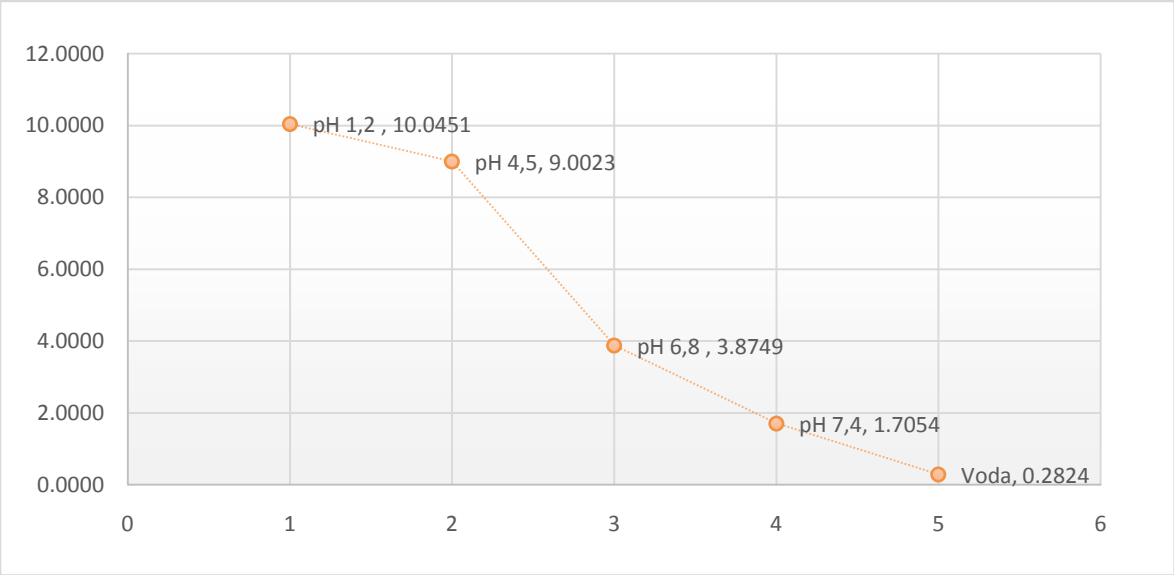


*Figure 2: Solubility profile for sulpiride*

**Table 2:** Solubility data for sulpiride

| pH | mg/ml |
|---|---|
| pH 1.2 | 10.0451 |
| pH 4.5 | 9.0023 |
| pH 6.8 | 3.8749 |
| pH 7.4 | 1.7054 |
| Water | 0.2824 |

**Conclusion**

This paper gives specific examples and descriptions of physicochemical properties of two substances from different biopharmaceutical classes (BCS), naproxen sodium, as a representative of BCS class 2 (with low solubility and high permeability) and sulpiride, as a representative BCS class 4 (low solubility and low permeability).

From the experimental part, naproxen sodium is very poorly soluble in acid media and it show highest solubility in basic (alkaline, high pH values) and neutral media (such as water).The systems that are developed for class 2 drugs are based on micronisation, lyophilization, addition of surfactants, formulation as emulsions and microemulsions system use of complexing agents like cyclodextrins.

In the case of sulpiride, the situation is diametrically reversed, dissolves very poorly in solutions with higher pH values, and well in solutions with lower pH values, as proved here for pH 1.2. The systems that are developed

for class 4 drugs present a major challenge for development of drug delivery system and the route of choice for administering such drugs is parenteral with the formulation containing solubility enhancers.

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