Abstract

Introduction: Sulfasalazine is a sulfonamide used in the treatment of Crohn's disease, ulcerative colitis, and rheumatoid arthritis. This drug is a BSC class 4 compound and has poor solubility and permeability. Due to its limited solubility (0.6 μg/ml) and low bioavailability, high doses of the drug (1-3 g/day) are usually administered.To overcome these problems various solubility enhancement techniques are required. The objective of the present work is to employ the co-solvency method to improve the aqueous solubility of sulfasalazine. A various co-solvents including ethanol, methanol, acetone, 1,2-propanediol, glycerol, and PEG400 were utilized to study drug solubility in binary solvent mixtures. The effect of surfactant micellization is also investigated using cationic, anionic, and non-ionic surfactants. The effect of pH on drug solubility was studied in the range of 2-9. Moreover, the generated data from this study are correlated to some cosolvency model to represent the results as a mathematical model.

Methods: In this study, the shake-flask method is used, so that the surplus amount of drug has been added to different mass fractions of two-component solutions and reach saturation over a specified time (24 hours). The solutions were centrifuged and determined in the UV_VIS device at a wavelength of 365 nm. Also, 10 different concentrations of anionic (Sodium laurilsulfate), cationic (Benzalkonium chloride), and non-ionic (Tween20) surfactants at concentrations below and above CMC were used to study drug solubility. The effect of pH on drug solubility was studied in the range of 2-9. Finally, the experimental data prediction was evaluated with three models of Jouyban-Acree, CNIBS/R-K and the modified Wilson model.

Results: The solubility of sulfasalazine increased with increasing the composition of each solvents, so that the highest solubility was observed in pure PEG400. Also, the results of mycelialization with BAC and SLS indicated an increase in drug solubility, while Tween20 did not significantly increase the solubility. The correlation error of the predicted data was evaluated using three different models and the error percentage of each of them was obtained. Adding alkali to Sulfasalazine solution also increased its solubility. Mean relative deviation (MRD) of the three models was calculated.

Discussion and conclusion: The data show that PEG400, is a suitable solubilizing agent and BAC is a suitable surfactant to increase the solubility of sulfasalazine. In addition, error rate of correlated data with Joyban-Acree, Modifed Wilson and CNIBS/R-K is less than 20%, which indicates the strength of the Model is within an acceptable and reasonable range.

Key words: Sulfasalazine, solubility, co-solvency, micellization, Jouyban-Acree model, Modified Willson model, CNIBS/Redlich-Kister model, PH.