Abstract

Title of thesis: Miniaturized and fast method for solubility and level of supersaturation determinations of drug nanocrystals
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As a formulation strategy for improving the bioavailability of poorly water-soluble drugs, drug nanocrystals can be employed. Several studies have shown that drug nanocrystals exhibit higher dissolution rate compared to conventional drug formulations. However, when orally administered, various conditions in gastrointestinal tract, such as changes in pH may result in problematic absorption. In this work, the preparation of drug nanosuspension of itraconazole (ITZ), as model poorly water-soluble compound, was carried out. The nanosuspension was prepared by using wet milling method of preparation, with suitable stabilizers added (Poloxamer 407 and Hydroxypropyl methylcellulose). Hydrochloric acid buffer pH 1.2 was chosen to create an environment similar to gastric fluids. In order to investigate changes in solubility of ITZ nanosuspension, UV spectrophotometer was used. Measurement was performed at the wavelength 551 nm, where dissolved ITZ does not absorb light and no change in absorbance occurred. Subsequently, the conditions similar to those, when drug reaches the main site of absorption, i.e. small intestine, were simulated by raising the pH value to 7. Results showed rapid increase in absorbance caused by precipitation of ITZ in the analyzed sample. Thus, this simple method is a promising tool to determinate solubility and level of supersaturation of drug nanocrystals.

Key words: itraconazole, drug nanocrystals, supersaturated state, precipitation,