ABSTRACT

The aim of the present work was to prepare crystals of Mefenamic acid, Ketoprofen and piroxicam by different crystallization techniques (Spherical crystallization, crystallization by spray drying, crystallization by Freeze drying, super cooling crystallization and Recrystallization) using same solvent systems and study the influence of crystallization techniques on dissolution behavior of these poorly water soluble drugs.

All these drug candidates exhibited poor compression, tabletting properties and are highly adhesive in nature. Solvent composition for spherical crystallization was determined by constructing ternary diagrams. Solvent selection was based on the solubility of the drug substances. Water was used as poor solvent and isopropyl acetate was used as bridging liquid to cause the spherical crystallization and Tetrahydrofuran was the good solvent used for Mefenamic acid, while, for the Ketoprofen chloroform was used as bridging liquid to cause the spherical crystallization and Isopropyl alcohol (IPA) was the good solvent. Piroxicam, spherical crystallization was carried out using N, N-dimethylformamide (DMF) as the good solvent, water as poor solvent and chloroform as bridging liquid. Crystallization medium used for spherical crystals of Mefenamic acid were THF: Isopropyl acetate: water in the ratio of 20:70:10 respectively. For the spherical crystals of Ketoprofen the ratio was 25:60:15 of IPA: Chloroform: water. Piroxicam spherical crystallization was carried out using 25: 68: 7 of DMF: Chloroform: water respectively.

Operating conditions like stirring speed, mixing conditions of solvents and temperature difference between the drug solution and water were found to be the major determinants in obtaining spherical crystals. These variables influenced size, and yield of spherical crystals.
Using the same solvents system, crystals of mefenamic acid, ketoprofen and piroxicam were prepared by Spray drying, Freeze drying, super cooling and Recrystallization techniques and the important parameters were optimized.

All prepared crystals were evaluated for percentage yield, drug content, water content, solvent residuals and were characterized for their primary properties by differential scanning calorimetry, X-ray diffraction and FT-IR spectroscopy. Micromeritic and mechanical properties were evaluated. Dissolution studies for prepared crystals were carried out in pH 7.4 phosphate buffer. Tablets containing prepared crystals were prepared using directly compressible excipients.

Prepared crystals exhibited improved micromeritic and mechanical properties. Crystals exhibited smooth surfaces which were confirmed by SEM photographs.

Significant improvement in the dissolution was found with Mefenamic acid, Ketoprofen and Piroxicam crystals prepared by Spherical crystallization, crystallization by spray drying and crystallization by freeze drying. Mefenamic acid crystals prepared by super cooling crystallization, did not show improvement in the dissolution properties. The prepared crystals were stable for 6 month stability study. Tablets containing prepared crystals show almost same drug release profile that of marketed product except tablets containing Mefenamic acid prepared crystals. Hence Crystals prepared by Spherical crystallization, crystallization by spray drying, crystallization by freeze drying showed desirable tableting properties with improved dissolution characteristics and worthy for further investigation for scaling-up for direct tabletting.

**Key words:** Crystallization techniques; Spherical crystallization, freeze drying, spray drying, super cooling, Recrystallization techniques, Ternary diagram; Mefenamic acid, Ketoprofen, Piroxicam.