Enhancing Solubility and Dissolution of Celecoxib by Nanocrystal Formulation

Moloud Kazemi*, Majid Tabbakhian, Abolfazl Aslani

Abstract

Introduction: Celecoxib is a weakly acidic drug and has low aqueous solubility (3–7 µg/ml). Low solubility of drugs in water results in poor bioavailability because the solubility of a drug is an important factor in determining its absorption rate. According to the Noyes–Whitney equation, the saturation solubility and dissolution rate of poorly water soluble drugs can be enhanced by reducing the particle size, which increases the total surface area. Nanocrystals possess outstanding features enabling to overcome the solubility problems of poorly soluble drugs. The objective of this study was to investigate the dissolution behavior improving effects of differently sized nanocrystals of a poorly soluble model drug, Celecoxib.

Methods and Results: Nanocrystals were prepared by antisolvent precipitation followed by high pressure homogenization (HPH) technique in the presence of varying percentage of SLS as a stabilizer (0.2 or 0.4%) and rate of homogenization (26500 or 12500 rpm). The obtained nanoparticles were analyzed in terms of particle size distribution, polydispersity index, saturation solubility, thermal behavior (DSC) and dissolution behavior. The particle size of nanosuspensions was between 140 and 532 nm with poly dispersibility index less than 0.5. That minimum of particle size relate to formulation which contained 0.4% stabilizer with rate of 26500 rpm. This formulation also revealed the highest saturation solubility (18.1 µg/ml) and dissolution efficiency compared to pure Celecoxib. The DSC results indicated the absence of any interactions between drug and stabilizer. These studies showed a decrease in crystalinity of Celecoxib.

Conclusions: All microcrystals significantly ($P<0.05$) increased Celecoxib aqueous solubility and dissolution rate compared to plain drug. This result seemed to be due the significant particle size reduction and decreased drug crystallinity. Significant influence of increasing in rate of homogenizer on size reduction was observed. As well as, high stabilizer concentration and rate of homogenizer had Significant influence on saturated solubility of Celecoxib compared to pure drug ($P<0.05$). DSC study showed that there is no change in the crystal structure of Celecoxib during the process and showed that nanocrystals exhibited decreased crystallinity.

Key words: Celecoxib, Nanocrystal, Dissolution, DSC and HPH

Authors' Affiliations:
Department of Pharmaceutics, Novel Drug Delivery Systems Research Center, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran.

Abstract Presenter:
Moloud Kazemi; PhD candidate; Department of Pharmaceutics; Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: mk.pharm68@gmail.com

****Correspondence**:*
Moloud Kazemi; PhD candidate; Department of Pharmaceutics; Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: mk.pharm68@gmail.com

Grants: The authors are grateful to Isfahan University of Medical Sciences for the financial support of this work.