

Coamorphous drug system to improve physicochemical properties of atorvastatin calcium

A. Shayanfar^{1,*}, A. Jouyban², H. Hamishehkar³,

¹Faculty of Pharmacy, Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

²Drug Applied Research Center and Faculty of Pharmacy, Tabriz University of Medical Sciences; Tabriz, Iran

³Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Background and Aims: Atorvastatin calcium (ATC) is classified as class II (low solubility and high permeability) drug according to the biopharmaceutical classification system (BCS) and its absolute bioavailability is ~12%. The amorphous form of ATC possesses higher solubility and dissolution rate than crystalline form. The amorphous form of ATC was prepared using different methods, such as antisolvent precipitation and spray drying process, melt quenching, supercritical antisolvent process. Coamorphous drug system is a method to prepare amorphous form of drugs. These systems are formed via strong hydrogen bond between drug and the coformer. In this study, coamorphous form of ATC and nicotinamide (NIC) was synthesized to improve intrinsic dissolution rate, kinetic and thermodynamic solubility values and of ATC.

Methods: Coamorphous ATC-NIC was prepared using solvent evaporation method. 0.1 mmol of ATC and 0.1 mmol of NIC were dissolved in 10 ml methanol and then the solvent was evaporated at 30 °C. The characteristics of the synthesized coamorphous were evaluated using DSC, FT-IR and XRD. The intrinsic dissolution rate, kinetic and thermodynamic solubility values of synthesized coamorphous were determined and compared with those of crystalline ATC.

Results: The results of FT-IR, DSC and XRD indicated that the crystalline form of ATC was converted to coamorphous form and the intrinsic dissolution, thermodynamic kinetic solubility of synthesized coamorphous is higher than crystalline form. The solution stability of the synthesized coamorphous is longer than the reported amorphous ATC in the literature.

Conclusions: The prepared coamorphous system improves the physicochemical properties of ATC i.e. intrinsic dissolution rate, thermodynamic, kinetic solubility and it has higher solution stability. In addition, this method is simple and rapid to convert ATC crystalline to coamorphous form.

Keywords: Coamorphous; Atorvastatin calcium (ATC); Nicotinamide; Solubility; Intrinsic dissolution rate