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RESEARCH ARTICLE

Drug–Drug Coamorphous Systems: Characterization and Physicochemical Properties of Coamorphous Atorvastatin with Carvedilol and Glibenclamide

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Abstract
Purpose In this study, coamorphous form of atorvastatin calcium (ATC) with two drugs, i.e., carvedilol (CVD) and glibenclamide (GLN) in 1:1 stoichiometry, were prepared from solvent evaporation method and they were characterized and their physicochemical properties determined.
Methods The coamorphous forms were characterized using differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FT-IR), and powder X-ray diffraction (PXRD). The kinetic solubility of coamorphous form of ATC with CVD (ATC–CVD) and GLN (ATC–GLN) were determined along with stability of supersaturated state of coamorphous forms using developed accurate and precise UV-net analyte signal standard addition method (chemometrics-based approach) and HPLC.
Results The results of DSC and analysis of glass transition temperatures (T_g), PXRD, and FT-IR indicated that the crystalline studied drugs were converted to coamorphous forms, with unique thermal behaviors, revealing a molecular interaction between two components. The kinetic solubility data revealed that coamorphous forms have better metastable solubility than those of crystalline state. In addition, these systems showed greater solution stability than those for amorphous form of single components reported in the literature.
Conclusion Coamorphous ATC–CVD and ATC–GLN were shown to have improved physicochemical and solution stability properties as compared to crystalline components.

Keywords Drug–drug coamorphous system · Supersaturation · Solubility · Atorvastatin–carvedilol · Atorvastatin–glibenclamide

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Introduction

Low solubility of marketed drugs (40 %) and drug candidates (75 %) is a challenge in different stages of drug discovery and development. The greatest concern of low solubility and dissolution rate of drugs is reduced and variable absorption after oral administration [1]. Biopharmaceutics Classification System (BCS) allows classification of drugs according to their solubility and permeability to four classes. Class II compounds have low solubility and high permeability and so they exhibit solubility-limited absorption [2]. Different methods were used for improving dissolution rate and solubility of drugs reviewed by Williams and coworkers [1]. One of the efficient methods is crystal engineering. Salt formation, polymorphs, solvate (or hydrate), amorphous forms and more recently, cocrystal and coamorphous systems are different crystal engineering strategies to improve the properties [3]. Cocrystal and coamorphous systems are single-phase materials composed of two or more different molecular and/or ionic compounds typically formed via strong hydrogen bonds in a stoichiometric ratio. They could be prepared in a metastable crystal form or an amorphous form [4, 5].

Despite of usefulness of amorphous forms, the main problem is their stability and crystallization under various conditions. Different compounds such as polymers can stabilize the amorphous systems and solid polymer dispersions are common methods to prepare stable amorphous