Current Drug Delivery, 2021, *18*, 44-53

RESEARCH ARTICLE

Assessment of Effects of Solvents on Cocrystallization by Computational Simulation Approach

Manami Dhibar[1,*], Santanu Chakraborty[1] and Souvik Basak[1]

[1]*Dr. B.C. Roy College of Pharmacy & AHS., Formulation Development Research Unit, Pharmaceutics, Durgapur-06, West Bengal, India*

Abstract: ***Purpose*:** The sole purpose of this study is to improve the solubility and dissolution of telmisartan by cocrystallization technique and apply a computational simulation approach to assess the nature of chemical interactions between telmisartan and coformer as well as the solvent contribution to the molecules for furnishing cocrystallization.

Methods: The effects of various concentrations of coformer *i.e.* oxalic acid on physicochemical parameters and drug release were investigated.

***Results*:** Solubility studies suggested that cocrystallization technique with oxalic acid helps to increase the solubility of pure telmisartan of about 7 folds and drug release study revealed that telmisartan-oxalic acid cocrystals showed greater dissolution as compared to pure telmisartan. SEM study suggested that prepared telmisartan cocrystals showed rhomboid-shaped crystals with sharp edges and smooth surface. FTIR study revealed that shifting in the vibrational frequencies of C=O group of telmisartan in telmisartan-oxalic acid cocrystal indicates the formation of supra molecular hetero synthon of the cocrystal. DSC and XRD studies confirmed the formation of telmisartan-oxalic acid cocrystals. Computational simulation approach revealed that telmisartan and oxalic acid can interact with each other in the presence of methanol and water where oxalic acid can form interactions principally with the others. The interactions, thereof, may form several associations or bondings in between the drug and carrier modifying the planarity, bond energy, bond angles of both which subsequently lead to cocrystallization.

***Conclusion*:** So, the present research concluded that prepared telmisartan-oxalic acid cocrystal is a successful application of crystal engineering approach to improve the physicochemical properties as well as to enhance the solubility and dissolution of telmisartan.

ARTICLE HISTORY

Received: March 16, 2020
Revised: June 22, 2020
Accepted: July 13, 2020

DOI:
10.2174/1567201817666200804110837

Keywords: Computational simulation approach, cocrystals, telmisartan, solubility enhancement, interaction studies, bonding.

1. INTRODUCTION

Solubility and permeability are the two major challenges with respect to the oral bioavailability of an active pharmaceutical ingredient [1]. Among the newly developed drugs, around 70% APIs (active pharmaceutical ingredients) are poorly water soluble which leads to ineffective absorption, improper bioavailability and therapeutic failure [2]. Most of the pharmaceutical industries are facing a major challenge to improve the solubility as well as the dissolution of BCS class II drugs. Solubility is very much important for a drug because to permeate through the gastrointestinal barrier, the drug should dissolve in gastrointestinal fluid. Poorly soluble APIs when delivered through the oral route may lead to slow dissolution in biological fluids, insufficient and erratic systemic exposure and sub-optimal efficacy in patients [3]. Solubilization of poorly water-soluble APIs is one of the major challenges for screening studies of new chemical entities as well as in the fabrication of dosage form [4]. Several formulation strategies have been proposed to improve the solubility and dissolution of poorly water-soluble drugs such as pH adjustment, amorphization, solid dispersion, self-emulsifying drug delivery systems, supercritical fluid processing, particle size reduction, complexation, cocrystals, *etc*. [5].

Among these various approaches, cocrystallization technique has emerged as a particularly effective approach. Cocrystallization is a simple technique that helps to improve various physicochemical properties *i.e.* solubility, dissolution, stability, *etc*. of the API [6]. This technique is widely used in pharmaceutical research to alter the features of existing pharmaceutical solids and to fabricate a new entity (*i.e.* cocrystal) with desired physico-chemical properties without affecting its pharmacological activity [7]. In this cocrystallization method, poorly soluble API and coformer with a defined stoichiometric ratio are intermolecularly inter-

*Address correspondence to this author at the Dr. B. C. Roy College of Pharmacy & AHS., Formulation Development Research Unit, Pharmaceutics, Durgapur-06, West Bengal, India; Tel: +91-8942004362;
E-mail: manamidhibar@gmail.com

1875-5704/21 $65.00+.00