Review Article

Co-crystal: A pharmaceutical technique to improve physical characteristics of Active Pharmaceutical Ingredient

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Abstract

Co-crystal is defined as a material which contains two or more discrete molecular entities in the crystal structure. Co-crystals of many components are known for years in solid state chemistry. Pharmaceutical co-crystals are important because they can improve many properties of the parent API like solubility, dissolution rate, stability, crystallinity and many more. Biopharmaceutics Classification System (BCS) of drugs classifies drugs into four major categories based on their solubility and permeability behavior. BCS Class II and Class IV drugs suffer from poor aqueous solubility. Co-crystallization enhances solubility of BCS class II and class IV drug, in addition to BCS of drugs. The aim of this review is to present an extensive overview of the co-crystallization methods, focusing in the specificities of each technique, its advantages and disadvantages.

Keywords: Cocrystal, solubility enhancement, co-crystallization method

Introduction

Co-crystal is defined as a material which contains two or more discrete molecular entities in the crystal structure. Co-crystals of many components are known for years in solid state chemistry. However, it is only recently that pharmaceutical cocrystals have generated much commercial and academic interest. Pharmaceutical cocrystals are important because they can improve many properties of the parent API like solubility, dissolution rate, stability, crystallinity and many more (Almarsson and Zaworotko, 2004). Biopharmaceutics Classification System (BCS) of drugs classifies drugs into four major categories based on their solubility and permeability behavior. BCS Class II and Class IV drugs suffer from poor aqueous solubility. Poor aqueous solubility of hydrophobic drugs can result in poor absorption, low bioavailability and poses challenges for drug development process (Desimja, 2003a). Enhancing bioavailability of poorly water-soluble BCS class II and BCS class IV drugs therefore becomes necessary to improve drug's efficacy. Co-crystallization enhances solubility of BCS class II and class IV drug. In addition to BCS of drugs, Developability Classification System (DCS) of drugs also plays a significant role in determining the development of pharmaceutical formulations, especially the oral formulations based on its solubility in biorelevant media such as FaSSIF (Fast State Simulated Intestinal Fluid) and FeSSIF (Fed State Simulated Intestinal Fluid) rather than its solubility in buffers (Dunitz, 2003b; Jain and Patel, 2015, Vadher et al. 2019). Very few reports are available in the literature where researchers have determined the dissolution rate of cocrystals of poorly water-soluble drugs in biorelevant media. The studies illustrate that cocrystals exhibited enhanced dissolution rate in biorelevant media and buffer as well indicating that the DCS serves as a highly relevant tool in determining develop ability of cocrystals of poorly water-soluble APIs. Enhancing aqueous solubility of poorly water-soluble drugs without compromising on stability is one of the major challenges faced by the pharmaceutical industries during drug discovery and development processes (Sloed, 2013). Crystal Engineering is a tool which can be used to tailor the physicochemical properties of Active Pharmaceutical Ingredients (APIs) such as melting point, dissolution rate, aqueous solubility, refractive index, surface activity, hygroscopicity, density, electrostatic, mechanical and optical properties. Cocrystallization is one of

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Mozen JL, Townsend G. 2008. Method of Creating Crystalline Substances. U.S. Patent US20080280858 A1.

Malamatari M, Ross SA, Douroumis D, Velaga SP. 2017. Experimental cocrystal screening and solution based scale-up cocrystallization methods. Advanced Drug Delivery Reviews, 117:162–177.

Musumeci D., Hunter A.C., Prohens R., Scuderi S., McCabe F.J. 2011. Virtual cocrystal screening. Chem. Sci, 2:883–890.

Mathur V, Satrawal Y, Rajput MS. 2011. Bio-pharmaceutical performance and stability of co-crystal. International Journal of Pharmaceutical Frontier Research, 1(1):135-145.

Nair RH, Sarah JN, Adivaraha J, Swarbreek. 2007. Co-crystals: design, properties and formulation mechanism. Encyclopedia of Pharmaceutical Technology. 3rd ed. Vol. 1. New York: Informa Healthcare.

Ober CA, Gupta RB. 2012. Formation of Itraconazole–Succinic Acid Cocrystals by Gas Antisolvent Cocrystallization. AAPS PharmSciTech, 13:1396–1406.

Plata-Salamán CR, Videla CS, Tesson N, Trilla Castano M. 2012. Co-Crystals of Venlafaxine and Celecoxib. European Patent EP2515892.

Padrela L, Rodrigues AM, Velaga PS, Matos AH, de Azevedo EG. 2009. Formation of indomethacin–saccharin cocrystals using supercritical fluid technology. European Journal of Pharmaceutical Sciences, 38:9–17.

Pando C, Cabañas A, Cuadra IA. 2016. Preparation of pharmaceutical co-crystals through sustainable processes using supercritical carbon dioxide: A review. RSC Advances, 6:71134–71150.

Paradkar A, Pagire S. 2017. Effervescent Compositions Containing Co-Crystals of the Acid Part. U.S. Patent US20170128330 A1.

Rastogi RP, Bassi PS, Chadha SL. 1963. Mechanism of the reaction between hydrocarbons and picric acid in the solid state. Journal of Physical Chemistry A, 67:2569–2573.

Steed JW. 2013. The role of co-crystals in pharmaceutical design. Trends in Pharmacological Sciences, 34(3):185-93.

Shan N, Zaworotko MJ. 2008. The role of cocrystals in pharmaceutical science. Drug Discovery Today, 13:440–446.

Shan N, Toda F, Jones W. 2002. Mechanochemistry and co-crystal formation: Effect of solvent on reaction kinetics. Chemical Communications, 20:2372–2373.

Schultheiss NC, Bethune SJ. 2011. Pterostilbene Cocrystals. U.S. Patent US20110189275 A1.

Shekar HS, Rajamma AJ, Sateesha SB. 2017. Application of Ultrasound in Pharmaceutical Industry: An Overview. Journal of Pharmaceutics & Drug Delivery Research, 6.

Schultheiss N, Bethune S, Henck JO. 2010. Nutraceutical cocrystals: Utilizing pterostilbene as a cocrystal former. CrystEngComm, 12:2436–2442.

Trask AV, Motherwell WDS, Jones W. 2004. Solvent-drop grinding: Green polymorph control of cocrystallisation. Chemical Communications, 7:890–891.

Trask AV, Streek J, Motherwell WDS, Jones W. 2005. Achieving Polymorphic and Stoichiometric Diversity in Cocrystal Formation: Importance of Solid-State Grinding, Powder X-ray Structure Determination, and Seeding. Crystal Growth & Design, 5:2233–2241.

Takata N, Shiraki K, Takano R, Hayashi Y, Terada K. 2008. Cocrystal screening of stanolone and mestanolone using slurry crystallization. Crystal Growth & Design, 8:3032–3037.

Thipparaboina R, Kumar D, Chavan RB, Shastri NR. 2016. Multidrug co-crystals: Towards the development of effective therapeutic hybrids. Drug Discovery Today, 21:481–490.

U.S. Code Chapter 10 - Patentability of inventions. 100-105.

Vadher AH, Parikh JR, Parikh RH, Solanki AB. 2009. Preparation and characterization of co-grinded mixtures of aceclofenac and Neusilin US 2 for dissolution enhancement of aceclofenac. AAPS PharmSciTech, 10(2):606-14.

Weyna DR, Shattock T, Vishweshwar P, Zaworotko MJ. 2009. Synthesis and Structural Characterization of Cocrystals and Pharmaceutical Cocrystals: Mechanochemistry vs. Slow Evaporation from Solution. Crystal Growth & Design, 9:1106–1123.

Wang IC, Lee MJ, Sim SJ, Kim WS, Chun NH, Choi GJ. 2013. Anti-solvent crystallization of carbamazepine and saccharin. International Journal of Pharmaceutics, 450:311–322.

Yadav AV, Shete AS, Dabke AP, Kulkarni PV, Sakhare SS. 2009. Co-Crystals: A Novel Approach to Modify Physicochemical Properties of Active Pharmaceutical Ingredients. Indian Journal of Pharmaceutical Sciences, 71(4):359–370.

Yamashita H, Hirakura Y, Yuda M, Teramura T, Terada K. 2013. Detection of Cocrystal Formation Based on Binary Phase Diagrams Using Thermal Analysis. Pharmaceutical Research, 30:70–80.

Zaworotko M. 2005. Polymorphism in co-crystals and pharmaceutical co-crystals. Florence: XX Congress of the International Union of Crystallography.