Advancing Tuberculosis Therapy with Co-crystals: A Comprehensive Review

Shagun Gogna[1,2,3], Jonathan J. Du[1], Paul W. Groundwater[1], Jan-Willem C. Alffenaar[1,2,3], David E. Hibbs[1,2*]

Affiliations

[1] Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, Camperdown, NSW, Australia

[2] Sydney Institute for Infectious Diseases, University of Sydney, Sydney, NSW, Australia

[3] Westmead Hospital, Sydney, NSW Australia

[*] Correspondence

David E. Hibbs, Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, Pharmacy and Bank Building (A15), Camperdown, NSW, 2006, Australia.
E-mail: david.hibbs@sydney.edu.au| Phone: +61 2 9351 6005| Fax: +61 2 9351 4391

Abstract

Co-crystallization has been a widely employed concept to enhance the bioavailability and physicochemical characteristics of drugs. As bioavailability of many anti-tuberculosis drugs is highly variable, co-crystals of these compounds are of interest. This review intends to give a comprehensive summary of studies conducted regarding co-crystals of medications used to treat tuberculosis, outlining the impact of different co-crystal structures on solubility and stability. Co-crystals of isoniazid, pyrazinamide, para-amino salicylic acid, fluoroquinolones, ethionamide and linezolid anti-tuberculosis drugs were reported and demonstrated to have increased solubility, increased stability, less side effects and synergistic effects with other anti-tuberculosis drugs. An important gap was identified as no co-crystals were found for bedaquiline, delamanid, pretomanid, ethambutol hydrochloride, cycloserine and rifapentine. As these drugs display variable bioavailability, co-crystals might increase absolute bioavailability while reducing variability. Another important gap identified is that co-crystals have not yet been used for any of the marketed generic products which justifies further investigation into hurdles of translation of findings. Designing co-crystals with improved characteristics that are clinically helpful in optimizing variability in the bioavailability, ensuring that patients consistently receive the intended dose and therapeutic effects will be the primary objective of future research.

Keywords: Anti-tuberculosis, Co-crystal, Drug-drug co-crystal, Stability, Solubility.