Co-crystals for Tuberculosis

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Abstract:

Co-crystallization has been a widely employed concept to enhance the bioavailability and physicochemical characteristics of drugs. As many anti-tuberculosis drugs suffer from variable bioavailability, co-crystals of these compounds are of interest. This review aims to summarize the research on antituberculosis drug co-crystals and presents the effect of various forms of co-crystals on solubility and stability. We conducted a comprehensive search of various databases, including Scopus, Embase, Medline (PubMed), Web of Science, and the Cambridge Structure Database (CSD). These databases were utilized to gather relevant information on anti-tuberculosis drug co-crystals. Co-crystals with appropriate characteristics can be made through co-former selection. 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 harmful side effects and synergistic effects with other anti-tuberculosis drugs. However, the potential impact of anti-tuberculosis drug crystals on of antimicrobial properties including synergy has not been fully explored. 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 bioavailability whilst reducing variability will be the primary objective of future research.

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