Co-crystals for Tuberculosis

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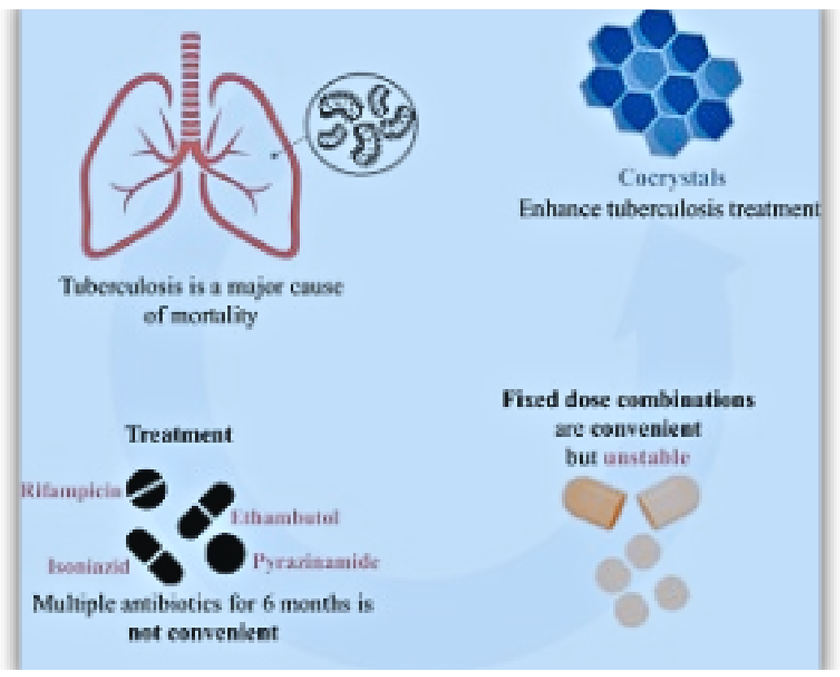
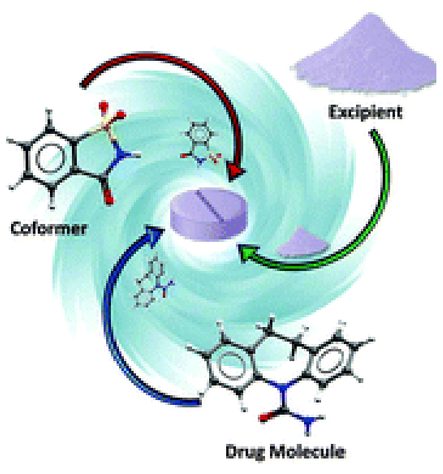
Background

Co-crystallization is a well-established pharmaceutical technique used to enhance the properties of active pharmaceutical ingredients (APIs). It involves binding the API and a coformer in crystal structures, with the coformer typically being an inactive substance chosen to improve aspects like dissolution, chemical stability, and antibacterial activity. In some cases, the API itself can serve as a coformer, reducing the need for multiple pills.

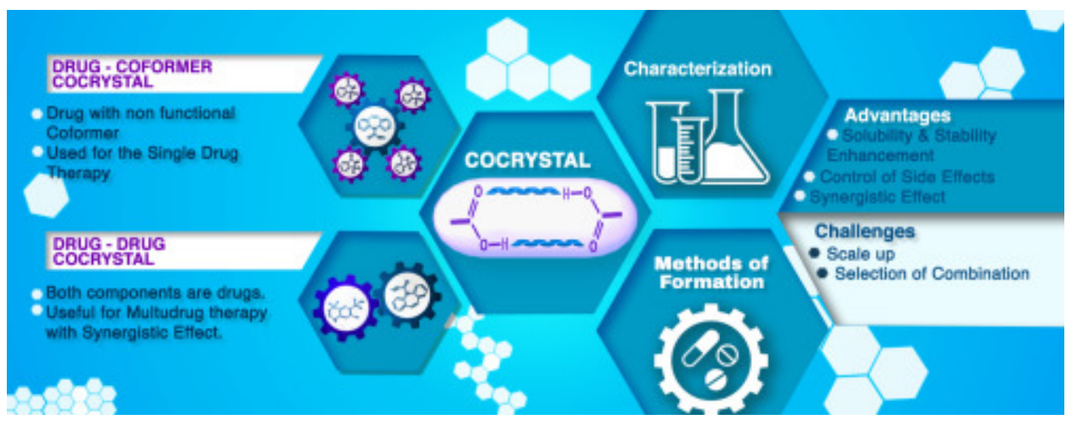
Tuberculosis (TB) remains a major global health concern, with 10.6 million cases and 1.6 million deaths in 2021. TB treatment involves drug combinations, but variable drug bioavailability poses challenges. Co-crystallization is explored as a solution to enhance TB drug effectiveness, especially for multidrug-resistant TB.





Method

To compile this review, 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.



Results

Co-crystallization has extensively explored various anti-tuberculosis drugs, yielding positive outcomes. It enhances drug solubility, notably in isoniazid, pyrazinamide, and para-amino salicylic acid, potentially improving drug absorption. Co-crystallization also stabilizes drugs like isoniazid and pyrazinamide, extending their shelf life.

Furthermore, co-crystals, often with hepatoprotective co-formers, improve dissolution and bioavailability in drugs like ethionamide, linezolid, and pyrazinamide, optimizing drug delivery. Certain co-crystals, especially those involving fluoroquinolones and other anti-TB drugs, exhibit synergistic effects in combination therapy, potentially enhancing overall treatment effectiveness. Importantly, co-crystallization may reduce side effects, potentially enhancing patient adherence and treatment compliance. These findings underscore the promise of co-crystals in improving anti-tuberculosis drug therapy.

Conclusion

In conclusion, co-crystals of anti-tuberculosis drugs show promise in improving the solubility, stability, and safety profiles of these medications. They also offer the potential for synergistic effects in tuberculosis treatment. However, there are notable gaps in the exploration of co-crystals for certain anti-TB drugs, such as Bedaquiline, Delamanid, Pretomanid, and Rifapentine, which exhibit variable bioavailability. Future research should focus on identifying clinically valuable co-crystals to enhance the treatment of tuberculosis and multidrug-resistant tuberculosis. The primary objective of this future research will be to design co-crystals with improved characteristics that are clinically beneficial, ultimately leading to more effective and accessible TB treatments. Public-private partnerships and grants will likely play a crucial role in supporting this research and development effort.