Poster

Supramolecular synthesis, crystallization, and co-crystallization of combination drugs for the inhibition of mycobacteria species

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In the quest to overcome the resistance of mycobacterium (MMTB) species against isoniazid (INH), a combination of INH and INH-derivatives with different moieties have been explored and are of continuous investigation [1]. Isoniazid is a drug that has long been used in the treatment of pulmonary and extra-pulmonary TB infections caused specifically by *M. tuberculosis*, *M. bovis* and *M. kansasii* and forms the backbone of TB treatment regimen [2]. However, most MTB strains have developed resistant mechanisms against isoniazid. It is for those aforementioned reasons that isoniazid was selected as the active pharmaceutical ingredients of interest and was to undergo covalent and supramolecular modification for the production of derivatives effective against clinically infectious MTB [3]. For modification and co-crystallization to be attained, a general one-pot synthesis method [1] and the mechanochemical synthesis process [4] of modified isoniazid crystals and co-crystals was adopted. Some novel derivatives were produced with others found to present with noteworthy inhibitory concentrations varying between 0.25 μg/mL and 11.36 μg/mL as single compounds, and 0.09 μg/mL and 0.59 μg/mL as combination drug treatment. These compounds were analysed using the single crystal x-ray diffractometer and investigated for their chemical relationship which plays a fundamental role in the observed synergistic activity that is highly depended on a particular order and concentration to elicit significant inhibitory effects.

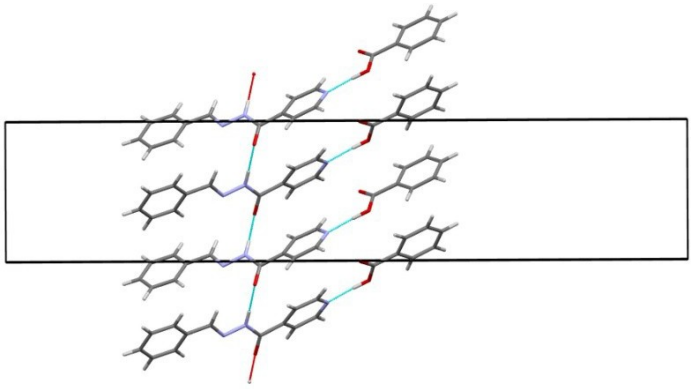

Figure 1. Isoniazid derivative co-crystal

[1] Smith, MG.; Forbes, RP.; Lemmerer, A.; *Cryst.Growth Des.* (2015), **15**, 3813 – 3821.

[2] Maitra, A., Bates, S., Kolvekar, T., Devarajan, P. v., Guzman, J.D. & Bhakta, S. (2015). Int. J. Infect. Dis., 32, 50–55.

[3] CDC. 2021. Infographic: Biosafety Lab Levels | CDC. https://www.cdc.gov/cpr/infographics/biosafety.htm

[4] Setshedi, I.B. & Smith, M.G. (2021). Z. für Kristallogr. – N. Cryst. Struct. **236**:1093–1095.