

Design and characterization of multicomponent forms of miconazole: structural, biological, and solubility studies

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Fungal infections are among the most common diseases in humans, with immunocompromised individuals at increased risk [1]. Although typically superficial, these infections can progress into systemic forms [2]. *Candida* species and other opportunistic fungi pose a significant global health threat due to the severity of the diseases they cause [3]. Therefore, the development of effective antifungal drugs is essential. However, this remains challenging due to the poor water solubility of many active pharmaceutical ingredients, which is closely linked to limited bioavailability, reduced stability, and difficulties in the tableting process.

Multicomponent crystalline forms, including cocrystals, molecular salts, and their mixtures, offer a promising strategy to enhance the dissolution behaviour of poorly soluble drugs [4]. These modifications enable tuning of the physicochemical and pharmacokinetic properties without altering the molecular structure of the active substance, potentially even enhancing its therapeutic effect.

Miconazole, a well-known imidazole-class antifungal drug effective against various *Candida* species [5], but suffers from limited solubility. This project investigates new multicomponent forms of miconazole using cofomers such as benzoic and salicylic acids derivatives, along with selected heterocyclic carboxylic acids. These new forms have been characterized using single-crystal X-ray diffraction. The relationships between their biological activity and physicochemical properties, particularly solubility profiles, will be discussed. Additionally, pyridine-(2,*n*)-dicarboxylic acids (*n*=3,4,5,6) have been also employed as cofomers, as they are effective cocrystallizing agents that can improve the performance of pharmaceutical ingredients [6]. Notably, pyridinedicarboxylic acid molecules tend to form unique chain substructures, which are recognized as favourable motifs in the supramolecular architectures of miconazole-based multicomponent crystals [7].

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