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BOOK OF ABSTRACTS

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Synthesis Monitoring of a Novel Isonicotinamide–Gemfibrozil Cocrystal via Raman Spectroscopy and Chemometrics, with Structural Elucidation by SCXRD

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Co-crystallization is a promising strategy in pharmaceutical development to improve the physicochemical properties of poorly soluble active pharmaceutical ingredients (APIs) without altering their chemical structure. Gemfibrozil, a lipid-lowering drug classified as BCS Class II, exhibits low aqueous solubility and variable oral bioavailability, limiting its therapeutic efficiency. In this study, a novel gemfibrozil–isonicotinamide co-crystal was successfully obtained via mechanochemical synthesis using an equimolar mixture and a catalytic amount of water. This solvent-free method enhances sustainability and scalability compared to conventional crystallization techniques.[1], [2]

A key innovation of the study was the use of in-situ Raman spectroscopy combined with Principal Component Analysis (PCA) to monitor the co-crystallization process in real time. The PCA revealed significant spectral changes that did not correspond to either of the pure components or their physical mixture, strongly suggesting the formation of a new solid phase. This new phase was subsequently confirmed through powder X-ray diffraction (PXRD) analysis, demonstrating the effectiveness of chemometrics in supporting process analytical technology (PAT) for solid-state transformations. [3], [4]

The novel co-crystal was characterized by X-ray diffraction (XRD) and thermal analysis. Single-crystal XRD confirmed a well-ordered crystalline lattice and revealed the specific intermolecular interactions responsible for the co-crystal's stability. Thermal analyses, including Differential Scanning Calorimetry (DSC) and Thermogravimetric Analysis (TG), demonstrated a significant enhancement in thermal stability compared to pure gemfibrozil. This improved thermal resistance is critical for pharmaceutical formulations, potentially increasing shelf-life and processing robustness.

Solubility studies revealed a clear advantage of the co-crystal over the free form of gemfibrozil, particularly in acidic media. These findings support the use of co-crystallization to enhance solubility and dissolution performance. Overall, this study highlights the potential of mechanochemistry and advanced analytical techniques in the discovery and development of innovative pharmaceutical co-crystals.

[1] D. J. Berry e J. W. Steed, (2017). Adv Drug Deliv Rev, 117,3–24.
[2] N. Schultheiss e A. Newman, (2009). Crystal Growth &Design, 9, 2950–2967.
[3] A. De Juan e R. Tauler, (2003). Analytica Chimica Acta, 195–210.
[4] L. X. Yu, R. A. Lionberger, A. S. Raw, R. D'Costa, H. Wu, e A. S. Hussain, (2004). Adv Drug Deliv Rev, 56, 349–369.

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