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On the role of salt formation and structural similarity of co-formers in co-amorphous drug delivery systems

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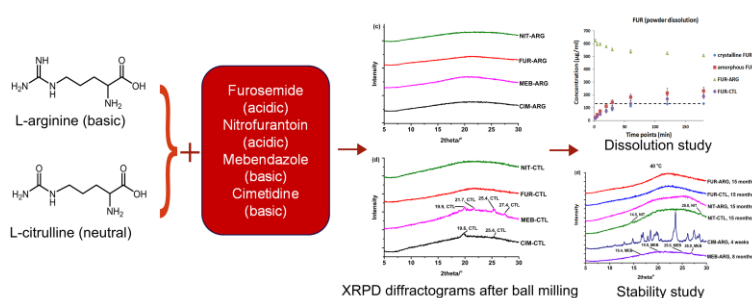
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Graphical abstract



Abstract

Co-amorphous drug delivery systems based on amino acids as co-formers have shown promising potential to improve the solubility and bioavailability of poorly water-soluble drugs. Potential salt formation is assumed to be a key molecular interaction responsible for amorphous stability and increased solubility. However, little is known about the importance of the overall structure of the co-former. In this study, the structurally related amino acids arginine (basic) and citrulline (neutral) were chosen together with four model drugs (acidic furosemide and nitrofurantoin; basic cimetidine and mebendazole) to investigate the importance of salt formation versus structural similarity of co-formers. Drug-amino acid mixtures were ball milled at a molar ratio of 1:1. Generally, arginine showed a higher tendency to successfully form co-amorphous systems with the model drugs compared with citrulline, irrespective of assumed salt formation. Salt forming mixtures showed

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