Combined Experimental and Molecular Dynamics Insight into Assembly of Fmoc-Amino Acid Building Blocks

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Low molecular weight gelators based on Fmoc-amino acids are versatile building blocks for functional supramolecular materials due to their simplicity, tunability and biocompatibility [1]. In this work, we investigate the self-assembly of Fmoc-Histidine (Fmoc-His), Fmoc-Cysteine (Fmoc-Cys) and their co-assembled system (Fmoc-Cys:Fmoc-His, 1:1) by combining molecular dynamics (MD) simulations with experimental characterization. MD simulations reveal distinct self-assembly pathways, where Fmoc-His forms fibril-like assemblies, Fmoc-Cys forms compact aggregates, while the co-assembled system gives rise to branched fibrous structures. Intermolecular interaction analysis shows that Fmoc-His primarily governs the morphology, whereas Fmoc-Cys contributes to increased compactness and may enhance intermolecular order within the co-assembled system. Co-assembly stabilizes interactions between Fmoc-His and negatively charged C-termini, as evidenced by coordination number analysis, modulating the local environment of Fmoc-His and potentially influencing its catalytic activity. Experimentally, scanning electron microscopy (SEM) also reveals distinct morphologies: Fmoc-His forms crystalline structures, Fmoc-Cys forms fibrous network and the co-assembled system develops fiber-bundle-like morphology and forms a hydrogel. These structural differences are accompanied by differences in catalytic activity, measured using p-nitrophenyl acetate (pNPA) hydrolysis, with the highest activity observed for Fmoc-His, followed by the co-assembled system and Fmoc-Cys. Overall, this study demonstrates that small changes in molecular building blocks strongly influence self-assembly pathways, resulting in distinct morphologies and functions. Co-assembly of Fmoc-Cys and Fmoc-His provides a simple strategy to obtain hydrogel and tune functional behaviour in minimalistic amino acid-based systems, while MD simulations offer molecular-level insight into the governing interactions.

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References:

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