New cage-based imine and ester linked COF as a smart nanocarrier drug delivery system

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Covalent organic frameworks (COFs) are intrinsically designed to accommodate guest molecules in their tuneable, structurally regular pores, which are characterised by high surface areas and large pore volumes. The incorporation of active pharmaceutical ingredients (APIs) as guests, and the conjugation of stimuli-responsive molecules onto the surface, to create smart COF drug carriers, is a novel application of COFs to the field of therapeutics, which provides an alternative route to enhance the loading capacity of nanoparticle drug delivery systems, effectively increase drug solubility and protection from degradation in biological environments, and provide additional control on the distribution and release of the entrapped drug molecules. [1, 2]

Structure determination from laboratory PXRD data revealed the formation of a new cage-based COF. Modification of its unit cell parameters and atomic coordinates upon API loading and smart molecule conjugation, indicated the physical adsorption of the molecules into the pores and onto the surface of the framework, via strong intermolecular hydrogen bonds and π-π interactions. The new cage-based imine and ester linked COF was synthesised using liquid-assisted grinding (LAG) from a 4 + 2 + 9 condensation of the Ts linker 2-amino-2-(hydroxymethyl)propane-1,3-diol, with the widely-used C2 dialdehyde terephthalaldehyde, and the C2 linker pyridine-2,5-dicarboxylic acid, in the presence of a catalytic volume of 1:1 1,4-dioxane:1,3,5-trimethylbenzene as solvent. Conjugation of pH sensitive pyridine-2,6-dicarbaldehyde, electro sensitive 1,1’ferrocenedicarboxaldehyde, and UV sensitive 4-[4-aminophenyl]diazenyl]aniline followed the post-synthetic loading of 5fluoro-1H-pyrimidine-2,4-dione into the cages and onto the surface of this new extended network, to form the smart nanocarrier drug delivery system. Control on the release of the loaded API molecules was confirmed in vitro through improved stability at control conditions and a maximum of 42.2% enhanced release over the control, upon application of the target stimuli for 12 hours. [3] These complexes demonstrate the application of COFs as stimuli-responsive nanocarriers in drug delivery systems, going beyond the prevalent passive targeting nanocarrier applications.


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