Galactosamine and sialic acid glycosystems based on nanosized MOFs for therapeutic strategies

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Multivalent carbohydrate systems, involving synthetic constructs featuring multiple carbohydrate units attached to a central core/scaffold, have shown exceptional potential in inhibiting cell binding and infectivity, thus opening new possibilities for the treatment of infections and cancers. Among these glycosystems, those based on carbohydrates linked to metal-organic frameworks (GlyconanoMOFs) have emerged as ideal contenders for drug diagnostic and therapeutic (theranostic) strategies, albeit still relatively limited in their development [1,2]. Of special interest are glycosystems derived from biocompatible Zr-MOFs referred to as "PCNs" (porous coordination networks), such as PCN-222, PCN-224, and PCN-225, composed of Zr(IV) nodes interconnected by porphyrinic ligands, showing large surface areas and chemical stability [3]. This study reports the design, synthesis, characterization, and evaluation of water-dispersible PCNs, carefully tailored to possess well-defined morphology and size-controlled structures (<100 nm).

These PCNs were modified with specific directional sulphate-PEG ligands functionalized with N-acetyl galactosamine (GalNAc-PEG-SO_4) and sialic acid derivatives (SA-PEG-SO_4) through the coordination of the sulphate group with the Zr. The incorporation of GalNAc aimed at exploiting its specificity towards the asialoglycoprotein receptor (ASGPR), overexpressed on hepatic cancer cells [4]. Additionally, the incorporation of SA derivatives, including 9-O-acetylated-SA, was targeted at developing anti-viral strategies, such as combating SARS-CoV-2 infections [5].

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