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A COMPUTATIONAL STUDY OF METAL-ORGANIC FRAMEWORKS OXIDATIVE DEGRADATION FOR THE DESIGN OF TUNABLE SMART DRUG DELIVERY SYSTEMS

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Conventional strategies to discovery of new drug delivery platforms requires a tedious experimental screening procedures. Modern computational chemistry techniques can tremendously facilitate such a search by providing an insight into the structure-property relationships for selected classes of materials and guiding thus the experimental studies. In this work we employed such a computations-aided rational design strategy for the development of a novel drug delivery platform based on bio-compatible. Among different materials available, metal-organic frameworks (MOF). Here, the interactions of the bio-compatible Fe-MIL-101 material with a heparin blood thinning drug were investigated in detail [1]. The directed synthesis creates systems with sensitivity to the pathogenic cellular environment and allows you to encapsulate the required drug and to ensure its controlled release. These tasks are accomplished in this study by a parallel and complementary theoretical and experimental programs aimed at a systematic investigation of selected MOF materials for their interaction and response to model drugs and bio-mimicking environments.

Density functional theory (DFT) calculations were carried out to establish correlations between the structural properties of MOF, their interaction with the encapsulated drug and their stability towards the components of physiological environment. Calculations were carried out at the PBE0/6-31+G(d,p) level of theory with implicit polarized continuum solvation model to account for the bulk effects in the aqueous system. Computations were carried out on cluster models of the Fe-MIL-101 material as a nanocontainer for heparin blood thinning agent. Calculations targeted the identification of the optimal parameters for the controlled decomposition of the hybrid MOF nanocontainer in biological fluids. We found that specific interactions between the heparin drug with the structural Fe centers of the MOF are key to the prolonged drug release and its enhanced pharmaceutical activ¬ity as is also evidenced by the parallel experimental studies. When the interaction between heparin and MOF are limited to weak dispersion-type bonds, no activity enhancement and controlled drug-release effect was observed.

1. Bellido E. et al. *Adv Healthc Mater*, 2015, **4**: 1246 – 1257.