Design and Synthesis of Pharmaceutical-based Biocompatible Metal Organic Frameworks as Efficient Multi-Drug Delivery Systems

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Metal-organic frameworks (MOFs) are a class of hybrid porous solid material formed through coordination between metal ions and organic ligands. MOFs exhibit desired features as drug carriers including high surface areas and large pore sizes that enable the encapsulation of large quantities of active pharmaceutical ingredients (APIs). Until recently the encapsulation of APIs into the MOF has been achieved through soaking the porous material in a saturated solution of the API. Through this method the release of the drug is achieved by desorption from the framework through an exchange with physiological media. An alternative approach consists of the direct coordination of the API to a metal ion to produce a MOF in which the bioactive molecule is the bridging ligand. APIs that exhibit a rigid molecular structure and multiple binding sites are the most suitable ligands for this approach. In this work, mast cell stabilizers, in particular, cromolyn sodium, nedocromil, lodoxamide and bufrolin, in combination with bioactive metal ions (Ca^{2+}, Mg^{2+}, Zn^{2+}, Fe^{3+}) are used to develop three-dimensional (3D) porous structures in which the API is directly incorporated into the framework. Mast cell stabilizers inhibit the activation of mast cells, preventing the release of histamine and other inflammatory substances in the body. The incorporation of these APIs as part of the framework could enhance the intestinal absorption of these drugs and possibly result in a multi-drug delivery system, if enough quantities of other APIs could be also encapsulated into the framework. Such multi-drug delivery approach could help to treat atherosclerosis, and other coronary artery diseases by increasing the systemic concentration of these drugs in the body.