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Uio-68-Quercetin
As a drug delivery platform for Quercetin

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Abstract

The drug delivery application of Zeolites as a drug carrying platforms have been investigated due to their unique structures which can encapsulated different ions and molecules. In present study, UIO-68 was successfully prepared by applied for delivery of Quercetin. Using variety of analytical methods containing FTIR, FESEM, and EDS the synthesized nanostructure was characterized. Based on the in vitro cytotoxicity results, Uio-68-Quercetin was able to increase cytotoxicity compared to that of Quercetin on A549 cancerous cells indicating the remarkable role of this drug delivery system.

Keywords: Uio-68, drug delivery, Quercetin, Cytotoxicity, MOF

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1. Introduction

Heavy metal pollution is a global environmental problem, especially in the developing countries, which is caused by increasing industrial and agricultural activities as well as the improper release of metal ions from wastewater and domestic effluents (Boix et al., 2020, Li et al., 2018). These toxic metal ions including Cd (II), As (III and V), Cr (III and VI), Cu (II), Pb (II), and Hg (II) are bioaccumulated readily in humans and animals and believed to be serious threats to the ecological environment and human health (Ma et al., 2019, Zhao et al., 2019). For this purpose, it is much important to effectively remove these toxic pollutants from domestic or industrial wastewater. Many common techniques such as coagulation (Ma et al., 2008), chemical precipitation (Calo et al., 2013), solvent extraction (Cole and Brown, 1959), ion exchange (Crist et al., 1996, Khan et al., 2014), membrane filtration (Fang et al., 2017), electrochemical treatment (Lu et al., 2019) and flotation (Huang et al., 1995) have been used to treat the sewage, while most of them are costly along with having complex operation processes, and these approaches may cause secondary pollution, thus limiting their application (Cai et al., 2017, Ge and Li, 2018). In recent years, adsorption strategies provide a powerful method and have been widely used for the construction of simple and inexpensive platforms to realize high-efficiency removal of heavy metal ions from wastewaters (Sharma and Kumar, 2018, Zhang et al., 2020a, Zhang et al., 2020b, Zhao et al., 2019). In this interesting approach, depending on the strength of the interaction during the adsorption process, it allows an efficient transfer of analytes to the sorbent material. The sorbent is dispersed into the sample solution by magnetic stirring, eddy current or ultrasonic wave, thus increasing the contact area of analyte-sorbent. Therefore, it has become a trend to search for novel materials that can be used not only for adsorption but also for green analysis.

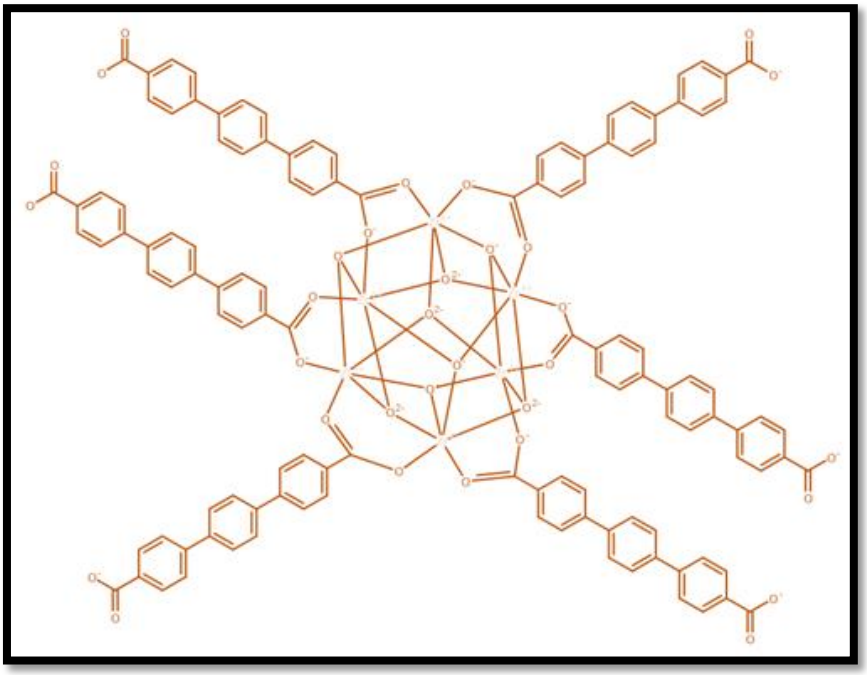

Fig1. UiO-68 Structure

In recent decades, metal-organic frameworks (MOFs) as novel organic-inorganic hybrid materials have been an increasing utilization in analytical chemistry. These novel substances are composed of metal ions (clusters or secondary building units (SBUs)) and organic ligands (linkers) through coordination bonds, have attracted wide attention because of their extraordinary properties (high ordered porosity, large surface area, uniform structural cavities, and thermal/chemical stability) (Kumar et al., 2017). Moreover, these properties have emerged in the research of ZIF, MOF, MIL, HKUST, PCN, and UiO, each of which fits the definition of prototype MOFs, implying that various metal and organic ligands can be combined satisfactorily (Winarta et al., 2020). Due to these fascinating properties, the adsorption of target molecules on the surface of MOFs can be effectively promoted. However, most MOFs have relatively lower hydrothermal and chemical stability, and their structures are easy to collapse under high temperatures, high pressure, or acid/alkaline environment. Besides, the structural stability of MOFs decreases as the length of the organic ligand increases, which inhibits the applications of MOFs. Fortunately, the three-dimensional porous nanocomposites constructed from Zr4+ and carboxylic acids of UiO-MOFs (featuring UiO-66, UiO-67, UiO-68, and UiO-69) have a relatively uniform, large pore size, specific surface area, strong stability as well as active Zr–O clusters, which has been widely studied and used in post-modification and application.

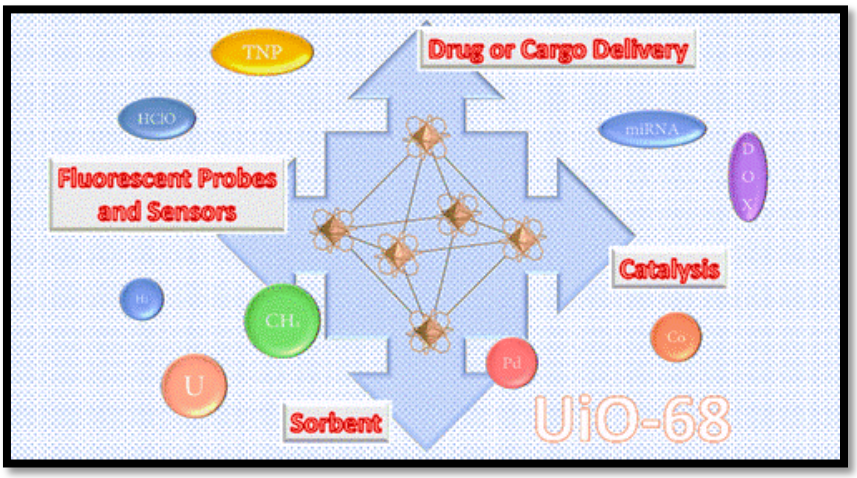

Fig2. UiO-68 and its applications

Furthermore, UiO-MOFs have many attractive active binding sites in the organic ligands compared with other MOFs. According to the hard-soft-acid-base (HSAB) theory, some metal ions can be preferred to specific functional ligands (amino, hydroxyl, sulfhydryl, phosphorous, etc.) by ion exchange, electrostatic interaction, or chelation. The specific functional ligands are Lewis bases and have a lone pair of electrons, which can be formed coordination bonds with heavy metal ions (Lewis acids). Therefore, the post-modification of UiO-MOF with specific functional groups to increase the active site for the adsorption of heavy metal ions is a hot topic as one of the promising adsorbents, which is considered as a reliable and advanced solid sorbent in the field of environment.

The purpose of this review was to focus on the potential of UiO series MOFs as the emerging MOFs material for the effective adsorption and separation of heavy metal ions from environmental samples. UiO-MOFs or functionalized UiO-MOFs composites have been widely applied as an efficient and selective adsorbent due to its structural diversity, excellent water stability, good biocompatibility, and other excellent properties (Mukhopadhyay et al., 2019, Yu et al., 2019, Zhao et al., 2019). Moreover, a comprehensive study about UiO-MOFs and their composites including the synthetic methods and the applications in the removal of heavy metal ions were presented in detail. Finally, the adsorption characteristics and mechanism of UiO-MOFs as solid sorbents for heavy metal ions were discussed, including adsorption isotherms equation, adsorption thermodynamics, and kinetics. Scheme 1 was a schematic illustration of the synthesis, characteristics, and application of UiO-MOFs in the environment.

Synthetic methods of UiO-MOFs

The premise for the synthesis of MOFs is experimental property research and practical application. UiO-MOFs are three-dimensional porous materials and constructed by Zr^{4+} and dicarboxylic acid ligands. Although the ligands of UiO-MOFs have different lengths, UiO-64, UiO-66, UiO-67, UiO-68, UiO-69, and various derivatives have the same reticular structure, the change of the ligand does not affect the thermal stability of UiO-MOFs. Zr(IV)-based MOFs is formed a similar cubic close-packed (CCP) structure with enlarged versions (Cavka et al., 2008, Nguyen et al., 2014), including ($Zr_6O_4(OH)_4(BDC)_6$ for UiO-66; $Zr_6O_4(OH)_4(BPDC)_6$ for UiO-67; $Zr_6O_4(OH)_4(TPDC)_6$ for UiO-68, and $Zr_6O_4(OH)_4$(2,6-NDC)$_6$ for UiO-69 (Xu et al., 2019, Kutzscher et al., 2016). As can be seen, $Zr_6O_4(OH)_4$ (as SBU) are coordinated with twelve bridge ligands separately to form a three-dimensional structure, which is consists of one octahedral center hole cage and eight tetrahedral corner cages. The theoretical values of pore volumes of UiO-MOFs (UiO-66, UiO-67, UiO-68) are 0.45, 1.05, and 1.82 cm^3g^{-1}, and the theoretical values of specific surface area are 1087, 3000, and 4170 m^2g^{-1} (Cavka et al., 2008), respectively. Therefore, due to the strong binding ability of Zr–O bond, the synthesis of UiO-MOFs is gradually concentrated on functionalization or changes in ligand length in order to control the physical/chemical properties, pore size, and morphology of UiO-MOFs. UiO-MOFs and functional UiO-MOFs composites are synthesized based on the node and connector approach and can maintain their topology structures and crystallinity when the organic ligands or the inorganic SBUs are enlarged, replaced, or functionalized. This may depend on the interaction forces such as coordination bond, hydrogen bond, π–π interaction, metal bond, and so on. The original pore characteristics of UiO-MOFs are determined by the properties of metal ions and linkers (Qiu and Zhu, 2009). The main structural characterizations can be influenced by the solvent, pH, reaction temperature, and so on. So far, some different synthesis strategies have been reported for UiO-MOFs such as solvent-thermal, microwave, volatilization, diffusion, template synthesis, ultrasonic, and mechanical stirring.

Quercetin

Quercetinis anticancer drugs which is able to induces cytotoxic and increase DNA damage[4]. Although, Quercetinfrequently applied, developed drug resistance and severe side effects affected its clinical application [5]. Encapsulate of Quercetinusing various DDS could be an effective idea[6]. In present work, the drug loading capacity of i for Quercetinas an anticancer drug was evaluated. Upon exposure by Uio-67-Quercetin the in vitro cytotoxicity against cancer cells were assessed.

Finally but contrary to the original goal of this project, which was to use a muff, because of the simpler and faster synthesis, we carried out this project with a MOF.

The purpose of this review was to focus on the potential of UiO series MOFs as the emerging MOFs material for the effective adsorption and separation of heavy metal ions from environmental samples. UiO-MOFs or functionalized UiO-MOFs composites have been widely applied as an efficient and selective adsorbent due to its structural diversity, excellent water stability, good biocompatibility, and other excellent properties (Mukhopadhyay et al., 2019, Yu et al., 2019, Zhao et al., 2019). Moreover, a comprehensive study about UiO-MOFs and their composites including the synthetic methods and the applications in the removal of heavy metal

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2. Results and discussion

Characterization

The chemical structure of the Uio-68 was characterized with different analytical methods such as XRD, SEM & TEM.

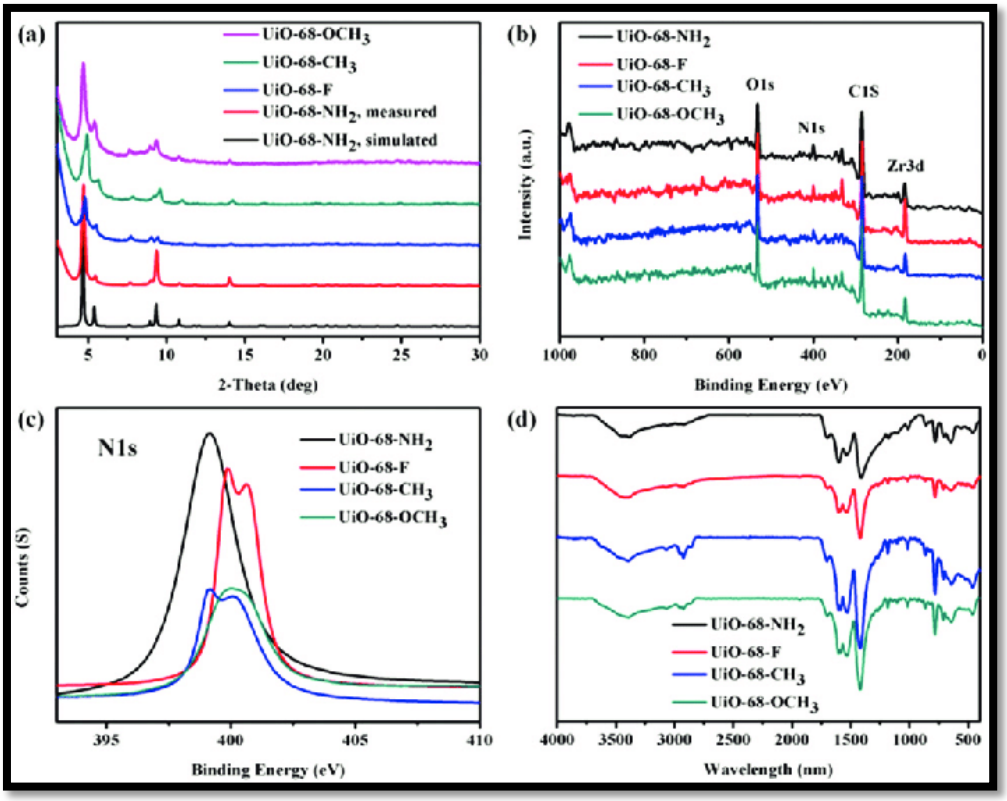

Fig4. (a) PXRD patterns of simulated and measured UiO-68-NH 2 , UiO-68-F, UiO-68-CH 3 and UiO-68-OCH 3 . (b) XPS, (c) XPS of N 1s and (d) IR spectra of UiO-68-NH 2 , UiO-68-F, UiO-68-CH 3 and UiO-68-OCH 3 [36]

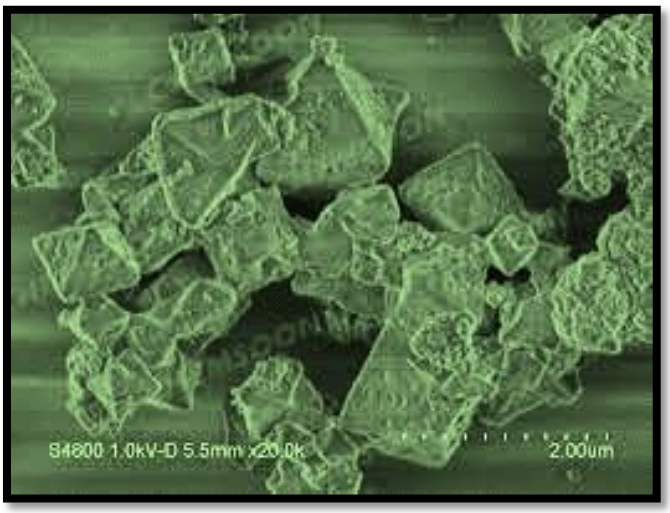

Fig5. TEM of UiO-68

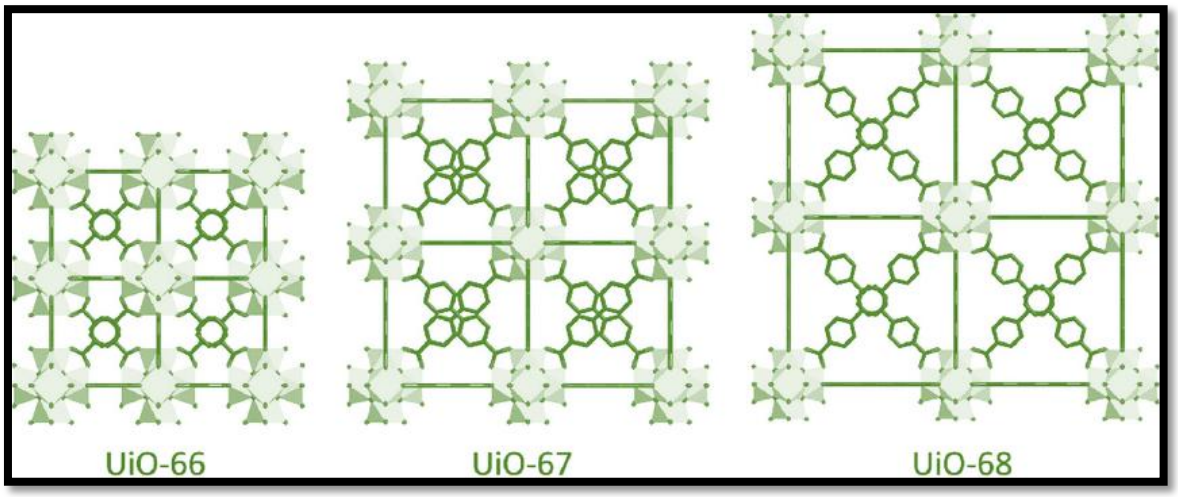

Fig6. Structures of UiO-66, 67, and 68[37]

Conclusions and perspective

In this study, Uio-68as a drug carrier was used for delivery of Quercetin. The obtained nanostructure poses spherical morphology with an average diameter of 20 nm. The high loading capacity (86%) and sustained drug release behavior was observed. Moreover, upon exposure by Uio-66-Quercetin, higher growth inhibition than those for Uio-68 and Quercetin drug against A549cells was determined. Collectively, Uio-68-Quercetin may could be a promising anticancer drug delivery system in the future.

Outlook for MOFs

The numerous advantages of MOFs, foremost their high surface area and modular composition, place them at a multidisciplinary crossroads. For good reason, MOFs are one of the most active research fields today, with aspects of their fundamental and applied properties permeating into disciplines as varied as electronics, chemical engineering, and optics. Whereas this Outlook does not attempt to delineate the developments and potential in all these areas, we have introduced some of the exciting prospects related to continued synthetic advances in the field. We further elaborated on three applied areas where MOFs are primed to excel: in challenging gas separations, as porous electrical conductors, and in heterogeneous catalysis. These examples are not exhaustive, but present subtleties that are applicable and relevant to many other applications of MOFs. The challenges and opportunities in these select applications, which span both the traditional and the modern aspects of the field, are illustrative of the continually expanding interest and bright future for MOF chemistry.

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