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Mini Review

Metal Organic Frameworks in Medicine

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Abstract

Metal–organic frameworks (MOFs) are porous coordination compounds exhibiting unique characteristics, such as high surface area, high porosity, and tunability. Recent years have seen an increasing number of studies focusing on MOFs. The application of these porous materials in several fields, including storage and separation of gases, sensors, catalysis, drug delivery and functional materials, has been widely investigated. In this editorial, we provide a brief discussion on the application of MOFs in drug delivery.

Keywords: Frameworks; MOFs; Materials

Introduction

After administration, curative drugs should reach the optimal concentration at which the highest efficacy is experienced without side effects. For this purpose, several drug delivery systems (DDS) have been formulated and investigated [1,2]. In the pharmaceutical field, looking for appropriate non-toxic carriers which are efficient for drug delivery to the body is a crucial challenge. Until now, a lot of different carriers, including organic polymers and inorganic porous materials, have been studied. However, their applications are limited either by low drug-loading capacity or by uncontrolled release. Among them, MOFs have recently emerged as innovative and promising DDS. MOFs are a new group of porous crystalline materials made of organic spacers connecting metal ions [3]. Thanks to their special properties such as high surface area, tunable pore size, high structural flexibility and strength, easy synthesis and high stability, MOFs have attracted particular attention in various fields including catalyst, selective adsorption and separation of gases, gas storage and drug delivery[4-7].

Drug delivery

High porosity, tunable pore size, and appropriate chemical stability are some of the advantages that make MOFs more competitive as drug containers over other conventional porous materials. Moreover, the presence of metal ions and specific functional groups in the MOF structure promotes the formation of strong interactions with drug molecules, thus increasing drug encapsulation efficiency [8,9]. Grard Ferey and co-workers examined MIL-100 (Cr) and MIL-101 (Cr). Though both materials showed remarkable ibuprofen adsorption, significantly different performances were observed [10]. While MIL-100 (based on trimesic acid and Cr, with pore size of 25 Å and surface area of 3100 m^2/g) encapsulated 0.35 g of ibuprofen/g of MOF, MIL-101 (obtained from terephthalic acid and Cr, with pore size of 34 Å and surface area of 5900 m^2/g) was able to achieve an impressive loading capacity, up to 1.376 g of ibuprofen/g of MOF,. Such high encapsulation performance is probably owing to its higher surface area and larger cage size. Figure 1 shows the release profile of ibuprofen from the loaded MOFs in simulated body fluid (SBF) at 37°C. The initial release from MIL-100, within the first 2 h, concerns weakly bound drug molecules, whereas the entire amount of ibuprofen was released in the later 3 days. In the case of MIL-101 the weakly adsorbed drug molecules were released in the first 8 h and complete release was achieved after 6 days. However, their use in the biomedical field is limited due to chromium toxicity. Sohrab Rohani and co-workers tested MIL-101 and MIL-53(Fe) as matrices for the adsorption and *in vitro* drug delivery of acetaminophen, progesterone, and stavudine [11]. MIL-53 exhibits reversible pore opening properties. Its pore width changes upon hydration, leading to a significant variation of surface area. When the pores are closed, the surface area of MIL-53 is only 15 m^2/g. In the presence of guest molecules the pores open, thus allowing drug encapsulation. Thanks to this property, MIL-53 was able to achieve

a loading capacity of 20 wt%, close to the performance of MIL-101, whose surface area is 2212 m^2/g. Nevertheless, the smaller pore size of MIL-53 (micropores), if compared to MIL-101 (mesopores), does not allow the encapsulation of the total amount of drug. As a result, a fraction of drug remains on the external surface of MIL-53 in the form of crystalline aggregates, as revealed by DSC analysis.

Figure 2 displays the cumulative release of acetaminophen, progesterone, and stavudine from loaded MIL-53 and MIL-101. Due to the larger pore diameter and host-guest interactions, the MIL-101 release kinetics were partly faster. However, both MOFs released the drugs with slow kinetics over a period of several days. Prolonging the release of drugs using MOFs may reduce many of the problems currently associated with traditional treatments [11].

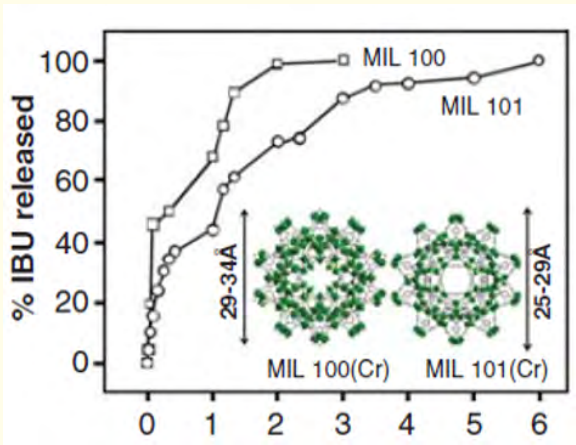

Figure 1: Ibuprofen release kinetics from MIL-100 (Cr) and MIL-101(Cr), in SBF at 37^{0}C [10].

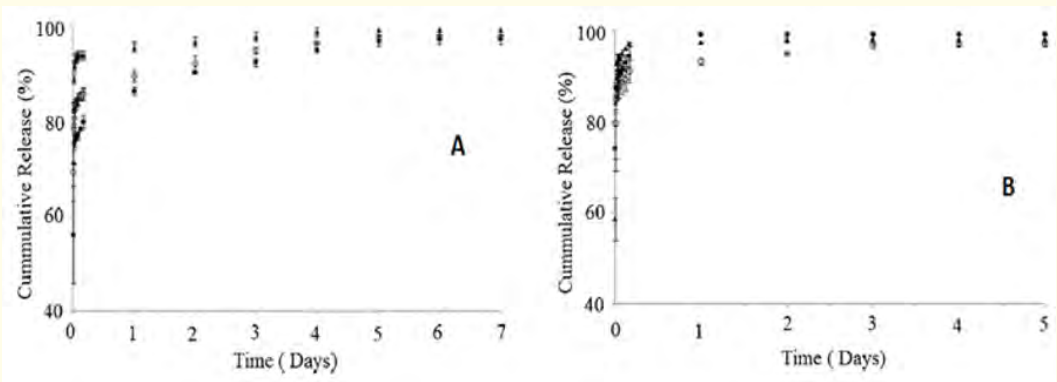

Figure 2: (A) Release profile of acetaminophen (■), progesterone (▲), and stavudine (○) from loaded MIL-53(Fe) in PBS at 37°C. (B) Release profile of acetaminophen (■), progesterone (▲), and stavudine (○) from loaded MIL-101 in PBS at 37°C [11].

Conclusions

MOFs, also called porous coordination polymers, are a unique family of hybrid porous solids. Compared to other traditional porous materials such as organic polymers or inorganic porous solids (zeolites or mesoporous silica), they exhibit many ideal features for drug delivery applications. Pore size, pore volume and chemical properties of MOFs can be easily tuned by changing the metal and/or the organic linker. In general, the higher the surface area of MOFs the higher the drug loading capacity. Furthermore, tunable pore size allows the encapsulation of a wide range of pharmaceuticals. However, to accomplish effective application of MOFs in biomedicine, several requirements need to be addressed and a lot of work still needs to be done, starting from pharmacokinetics and *in vivo* toxicity studies.

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