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Metal Organic Framework Nano Particles: Potential Contrast Agents for Magnetic Resonance Imaging

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Abstract

Metal-organic framework nano-particles are a type of novel organic-inorganic hybrid materials, which has been investigated as potential contrast agents in magnetic resonance imaging (MRI). This mini review focuses on recent research progress concerning the synthesis, stability and cytotoxicityof metalorganic framework nano-particles.

Keywords: Metal-organic framework nano-particles; Contrast agents; Magnetic resonance imaging

Introduction

Metal-organic frameworks (MOFs)assembled by metal ions (or metal clusters) and organic ligandsare under the pursuit of heavy research endeavor in the areas such as catalysis [1], gas separation [2], luminescence [3], drug delivery [4], and magnetic materials [5] in past decades. In contrast tozeolites, MOF smerit from relatively facile control of their composition and structural parameters (e.g., pore sizes and shapes) by a judicious choice of corresponding metal ions and organic ligands. In addition, good biocompatibility of MOFs obtained by using bioorganic linkers such as adenine [6] and nicotinic acid [7], make themselves favorable materials of candidate in biomedicine. In general, solvothermal MOFs synthesis promoted by microwave irradiation has been utilized to achieve high yields, and more importantly, to obtain size-control of nano-particle product [8], which further determines the chemical and physical properties of the particles. On the other hand, the delicacy of physiological systems requires the diagnostic process of diseases need to be precisely controlled in sizes. For example, parenteral treatments often choose stable a solution or suspension of nanoparticles with sizes smaller than 200nm in order to circulate freely through the smallest capillary vessels. In this regard, some functional metal-organic framework nano-particles have been investigated in the diagnostics for medical purposes.

This mini review will briefly discuss the current research using metal-organic framework nano-particles as potential contrast agents (CA) in magnetic resonance imaging (MRI). MRIis an important diagnostic medical technique owing to its nature of high spatial resolution and noninvasive measurement. In fact, the contrast in MR images is derived from a complex interplay between instrument parameters and intrinsic differences in the relaxation rates of tissue water protons [9]. CA such as a Gd^{III} chelateis generally used to increase the sensitivity of MRI by locally reducing the proton relaxation times. The magnitude of this effect on the longitudinal relaxation time T1 (or transverse relaxation time T2) is measured as the relaxivity R1 (or R2, respectively)and normalized to 1mM [CA] concentration at a given magnetic field strength. Maspoch reported the synthesis of a highly stable nanoscale Cu(II)/Gd (III) MOF system (CAMOF-1) and macro cyclic DOTP (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetramethylenephosphonic acid) [10], which has been investigated as a contrast agentof MRI. The nanoscale CAMOF-1 (The size of particles is less than 200 nm)demonstrates interesting relaxometric properties with 5 $mM^{-1}•s^{-1}$ of R1 at high field of 500 MHz and a maximum R1 = 15$mM^{-1}•s^{-1}$ at 40 MHz, three times higher than the corresponding relaxivity for [GdDOTP]5- at pH =7.4. Importantly, the reported CA property of nano-scale MOFs remains stable over a wide pH range and increases with temperature.

The leakage of free toxic Cu (II) and Gd (III) ions into physiological system can be prevented by strong chelation of DOTP towards these cations in solution, and the nano-scale CAMOF-1 does not show significant toxicity in the evaluated systems. In 2017, Chen's group reported the study of zwitter ionic manganese and gadolinium MOFs as efficient CA for in vivo MRI [11]. Two

water-stable Mn- andGd-based MOFs,{[Mn_2(Cmdcp)$_2$(H_2O)$_2$]•H_2O} n (1) and {[Gd(Cmdcp)-(H_2O)$_3$](NO_3)•3H_2O}n (2) (H_3CmdcpBr = N-(4-carboxybenzyl)-(3,5-dicarboxyl) pyridinium bromide), are hence prepared and the results of *in vitro* magnetic resonance imagingindicate that MOFs 1 and 2 possess relaxivity R1 values of17.50 and 13.46 $mM^{-1}•S^{-1}$, respectively, which are superior to that of Gd-DTPA (R1 = 4.87 $mM^{-1}•S^{-1}$, DTPA =di ethylene tri amine penta acetate) in the control experiments.In addition, the sizes of nano-particles can be controlled(less than 100nm). Encouragingly, smaller leakage rates and less cytotoxicity of these MOFs materials indicate that compounds 1 and 2 can be further exploited as contrast agents in MRI experiments.

Conclusion and Proposal for Further Research

This short review highlights the current studies of nano scale metal-organic frameworks materials with high stability and relativity in MRI. These MOFs systems merit from small leakage rates of metal ions and low cytotoxicity and therefore become quite promising in the application of MRI contrast agents. The effect of conglomeration of nano-particles in the flow of capillary vessels has to be modeled and evaluated in the settings of physiological environments on the next stage, because nano-particles tend to aggregate and may cause severe clot problems in tissues. More studies are still needed to clarify the MRI contrast agent path of nano-scale MOFs materials before any clinical trial.

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