

Iron-Metal-Organic Frameworks: Potential Application as Theranostics for Inhalable Therapy of Tuberculosis

Authors : Gabriela Wyszogrodzka, Przemyslaw Dorozynski, Barbara Gil, Maciej Strzempek, Bartosz Marszalek, Piotr Kulinowski, Wladyslaw Piotr Weglarz, Elzbieta Menaszek

Abstract : MOFs (Metal-Organic Frameworks) belong to a new group of porous materials with a hybrid organic-inorganic construction. Their structure is a network consisting of metal cations or clusters (acting as metallic centers, nodes) and the organic linkers between nodes. The interest in MOFs is primarily associated with the use of their well-developed surface and large porous. Possibility to build MOFs of biocompatible components let to use them as potential drug carriers. Furthermore, forming MOFs structure from cations possessing paramagnetic properties (e.g. iron cations) allows to use them as MRI (Magnetic Resonance Imaging) contrast agents. The concept of formation of particles that combine the ability to transfer active substance with imaging properties has been called theranostic (from words combination therapy and diagnostics). By building MOF structure from iron cations it is possible to use them as theranostic agents and monitoring the distribution of the active substance after administration in real time. In the study iron-MOF: Fe-MIL-101-NH₂ was chosen, consisting of iron cluster in nodes of the structure and amino-terephthalic acid as a linker. The aim of the study was to investigate the possibility of applying Fe-MIL-101-NH₂ as inhalable theranostic particulate system for the first-line anti-tuberculosis antibiotic - isoniazid. The drug content incorporated into Fe-MIL-101-NH₂ was evaluated by dissolution study using spectrophotometric method. Results showed isoniazid encapsulation efficiency - ca. 12.5% wt. Possibility of Fe-MIL-101-NH₂ application as the MRI contrast agent was demonstrated by magnetic resonance tomography. FeMIL-101-NH₂ effectively shortening T₁ and T₂ relaxation times (increasing R₁ and R₂ relaxation rates) linearly with the concentrations of suspended material. Images obtained using multi-echo magnetic resonance imaging sequence revealed possibility to use FeMIL-101-NH₂ as positive and negative contrasts depending on applied repetition time. MOFs micronization via ultrasound was evaluated by XRD, nitrogen adsorption, FTIR, SEM imaging and did not influence their crystal shape and size. Ultrasonication let to break the aggregates and achieve very homogeneously looking SEM images. MOFs cytotoxicity was evaluated in in vitro test with a highly sensitive resazurin based reagent PrestoBlue™ on L929 fibroblast cell line. After 24h no inhibition of cell proliferation was observed. All results proved potential possibility of application of ironMOFs as an isoniazid carrier and as MRI contrast agent in inhalatory treatment of tuberculosis. Acknowledgments: Authors gratefully acknowledge the National Science Center Poland for providing financial support, grant no 2014/15/B/ST5/04498.

Keywords : imaging agents, metal-organic frameworks, theranostics, tuberculosis

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