ABSTRACT

Bioapplication is an emerging field of metal-organic frameworks (MOF) utilization, but bio-compatible MOFs with permanent porosity are still a rarity in the field. In addition, biocompatibility of MOF constituents is often overlooked when designing bioMOF systems intended for drug delivery. In my research, I designed and synthesised a new bioMOF material which was characterized in detail, investigated the influence of various synthetic parameters on its properties, and demonstrated the suitability of the material for use as a delivery system for biologically active molecules.

Research I is focused on design and synthesis of a new bioMOF material with biocompatible constituents and no use of toxic solvents. After successful synthesis solving the crystal structure and a thorough characterization of its properties took place. I successfully synthesised and characterized a new bioMOF material, denoted bioNICS-1 (**N**ational **I**nstitute of **C**hemistry, **S**lovenia), since it is the first material of its kind developed at the Chemical Institute of Ljubljana. bioNICS-1 is a first MOF that utilizes ascorbic acid (Vitamin C) as an independent linker, while the »metal part« represents Zn^{2+} cations, which are located in three different coordinations and form a 3D unit with constant porosity - another novelty in the field.

In the second part of this research (Research II), the influence of compositional and process parameters, as well as activation conditions were studied in regards to the tunability of the material. By using simple monocarboxylic acids, size of the crystals could be controlled according to seesaw model, under different synthesis conditions. I also found that using propionic acid, either during or after synthesis (during the activation), can introduce point defects in the structure, which causes an overall increase in the amount of available acid metal sites – crucial feature for adsorption of therapeutic gas.

The final part – Research III was dedicated to demonstration of usability of the material. I have successfully encapsulated a molecular donor of nitrogen oxide - hydroxyurea and showed its release. Additionally, I have successfully incorporated 5,14 mmol/g of nitrogen oxide ($NO_{(g)}$) into the material, which is currently one of the highest reported values. Preliminary *in vitro* tests on human keratinocytes showed a concentration-dependent toxic effect, yet the material can still be classified as one of the safest bioMOFs based on Zn^{2+}. Results of NO loading and release kinetics, together with *in vitro* assay, demonstrate that toxicologically acceptable amounts of bioNICS-1 can be used to deliver a satisfactory amount of NO suitable for a therapeutic effect.

Keywords: metal-organic frameworks, tunability of structure, bioaplication, drug delivery, nitric oxide