

## ABSTRACT

Charles University  
Faculty of Pharmacy in Hradec Králové  
Department of Biochemical Sciences

Friedrich Schiller University Jena  
Faculty of Chemistry and Earth Sciences  
Institute for Organic and Macromolecular Chemistry

Candidate: Veronika Měrková

Supervisors: PharmDr. Hana Jansová, Ph.D., Prof. Dr. Felix H. Schacher

Title of diploma thesis:  $\text{Co}^{2+}$  loaded block copolymer micelles: Preparation and their uptake into macrophages

Since lots of patients suffer from post-operative infections resulting in sepsis, there were attempts to modulate immune system response in order to treat this pathological state. Cobalt is a biogenic trace element, however its direct administration may cause immunological reactions. The immune response can be inflammatory or anti-inflammatory mediated by macrophages ( $\text{M}\Phi$ ). Both are responsible for specific actions, regarding  $\text{M}\Phi$  activation and cytokine release. The aim of this study was to provoke such response in  $\text{M}\Phi$  and therefore to possibly control the inflammatory process. Nevertheless, free cobalt ions are toxic. In order to find a suitable and safe way of cobalt administration, the triblock terpolymer  $\text{PEO-}b\text{-PAGE}_{\text{COOH}}\text{-}b\text{-PtBGE}$  was synthesized and assembled into micelles in aqueous solution. Eventually the micelles were loaded with cobalt chloride to facilitate the detection in a biological *in vitro* test system of human monocyte-derived  $\text{M}\Phi$ . The micelles were characterized in their structure, size, shape, appearance and net charge. The amount of cobalt bound inside was determined as well. After the synthesis and chemical characterisation, the micelles were further characterized for their biological application suitability. Therefore, uptake into  $\text{M}\Phi$  and its impact on vitality and cytokine secretion was investigated. It was found out that the uptake was increased with increasing micelle concentration in the cell culture medium up to concentrations of 300  $\mu\text{g}/\text{ml}$  and that the process was not carried out by clathrin-mediated endocytosis. The vitality of the cells was not significantly affected by the micelles. The cytokine release measurement suggests that the  $\text{M}\Phi$  could have been activated into M2 anti-inflammatory state and that the micelles are potentially a suitable drug delivery system.