BIFUNCTIONAL SILICA COMPOSITES FOR BONE TISSUE – THERAPEUTIC AND REGENERATIVE IMPLICATION

Currently, **the treatment of primary bone tumor** consists of both surgical removal of diseased bone tissue and long-term intravenous or intra-arterial chemotherapy. For most patients, such therapy is ineffective or a relapse is observed. The prognosis is worrying because it is estimated that in next 20 years, the malignant bone tumor incidence rate and mortality will be about 20 and 10 million, respectively.

After surgical removal of pathological bone tissue, substitute materials in a form of implants are used to replace the defects. Unfortunately, after implantation, **chronic bacterial infections of the tissue** might occur so additional antimicrobial therapy is required. This usually involves several weeks of antibiotic treatment, which often results in acquired antibiotic resistance. World Health Organization's forecasts suggest that in 2050, about 10 million people will die every year due to bone infections caused by antibiotic-resistant bacteria.

The treatment of bone tumors as well as bacterial bone infections is difficult due to the poor blood supply to the bone tissue and hence low bioavailability of the drug in affected area. Such treatment requires high drug doses in order to provide therapeutic effect. However, such high doses might be toxic to humans and cause side effects. **That is why increased attention is paid to targeted therapy involving local delivery of the drug directly to the diseased bone tissue using implantable drug carriers.** In such strategy, the implanted drug carrier would have two functions: (1) a carrier of anti-cancer drug or antibiotic with modified - prolonged drug release and (2) bone substitute material. The aim of targeted therapy is to maintain the concentration of the drug at the therapeutic level for a longer time period directly at the disease site without toxic effects on other tissues. Thus, the formulation and verification of an ideal local delivery system for the drug in the form of implant is the primary goal for many researchers and bone implants manufacturers.

Currently, mesoporous MCM-41 type silica biomaterials with ordered internal porous structure, due to confirmed non-toxicity and biocompatibility with the human body, are examined for the use as drugs carriers with modified drug release profiles. However, in the potential use of MCM-41 in targeted therapy to bone tissue, their mineralization potential is important, characterized as the ability to create on MCM-41's surface an apatite layer with a composition and structure similar to human bone apatite. The research so far indicated that **the MCM-41 material shows mineralization properties** only after introducing additional calcium and phosphate ions (so-called osteogenic ions) into its structure. However, the modification of MCM-41 with osteogenic ions has a major disadvantage where ordered porous structure becomes disorganized so the repeatable and effective drug loading is limited. In many cases the addition of osteogenic ions into the silica structure disqualifies such material as drug delivery system with controlled release. The solution to this problem may be the use of **bioglass** - a biomaterial which is commercially used in medicine to regenerate small bone defects. Bioglass shows higher mineralization properties compared to modified with osteogenic ions MCM-41. However, due to lack of ordered porous it cannot act as drug carrier.

Therefore, **the aim of our project is to design composite material in the form of spherical, porous granulates (pellets) and examine their physicochemical and biological properties** based on both MCM-41 with **adsorbed antibiotic (**which is commonly used in post-surgical, chronic bone infections) **or** with **adsorbed anticancer drug** (used in bone cancer chemotherapy) and based on bioglass - a biomaterial with well-known mineralization properties. In the future such pellets could be **the implants** which regenerate bone defects, prevent postsurgical bone tissue infections or support the treatment of primary bone tumors.