COLLAGEN-SILICA SCAFFOLDS AS POTENTIAL SYSTEMS FOR DRUG DELIVERY AND REGENERATION OF BONE TISSUE

Osteomyelitis is defined as a bone or bone marrow inflammation frequently caused by *Staphylococcus aureus* infection. Treatment of *osteomyelitis* remains a clinical challenge in orthopedic surgery. Currently, the most efficient therapy is the surgical removal of necrotic area followed by oral or parenteral long-term (4-6 weeks) administration of antibiotics. Ineffective treatment of chronic *osteomyelitis* may lead to deterioration of patients quality of life, disability, and an increased risk of mortality. The success of antibiotic-based therapy depends on two main factors: the susceptibility of bacteria colonized bone tissue to the administered drug (i) and local concentration of antibiotic at the site of infection (ii). Due to the low penetration of applied drugs into the bone tissue and decreased blood supply to affected area, systemic routes require an administration of high doses of antibacterial agents to provide an effective concentration at the site of infection. This strategy leads to severe systemic toxicity which affects overall condition of the patients. **Hence, local administration of antibiotics has gained an increasing interest in the treatment of bone tissue infections as more effective and safer therapy.** The implantable drug delivery system should: release of antibacterial agent for a long time (1) and initiate the regeneration of damaged bone (2). To our knowledge, there is no implantable biomaterial or composites which fulfils both these functions.

Silica materials due to their unique properties are examined in bone tissue engineering as drug delivery systems or agents for regeneration of bone tissue. First type of silica, bioglasses, due to the release of calcium and phosphate ions (osteogenic ions), are able to form a layer of bone-like apatite. This ability, called as mineralisation potential, is the key element of regeneration of bone tissue. Unfortunately, low specific surface area of bioglasses and disordered porosity limit their potential application as antibiotic delivery system. Another type of silicas, ordered mesoporous silica materials (e.g. MCM-41), due to their high adsorption capacity have been used as drug carriers in bone tissue diseases. However, the research showed that the MCM-41 reveals mineralisation properties only after introduction of osteogenic ions into its structure. According to conducted study, the direct modification of mesoporous silica with calcium and phosphates results in disruption of ordered porous structure that reduce the repeatability and effectiveness of drug sorption.

Among organic compounds, composites based on collagen have been intensively examined for their application in bone tissue engineering. Collagen type I produced by osteoblasts is the main structural protein in bone matrix. Commercially available freeze-dried collagen scaffolds (applied as substitutes of small bone defects) are characterised by proved biocompatibility, biodegradability, plasticity, high surface area, and pore size excellent for osteoblasts penetration, adhesion, and proliferation. Currently used methods of drug loading into collagen matrix result in carriers characterised by unfavourable rapid release of total drug content.

The aim of this project is to obtain three-dimensional collagen scaffolds with bioglass and drug-loaded MCM-41. Mesoporous silica will serve as a carrier of antibiotic, bioglass and collagen type I will enhance regeneration of bone tissue. This interdisciplinary project involves: obtaining of antibiotic-loaded collagen-silica scaffolds (1); characterisation of collagen-silica scaffolds in terms of physicochemical properties (2); and *in vitro* evaluation of dual function of scaffolds i.e. efficient release of antibiotic and bone-regenerative potential (using human osteoblasts) (3).

We assume that the collagen-silica scaffolds will: - release the antibiotic for a prolonged time; - exhibit antimicrobial activity against pathogenic strains involved in *osteomyelitis*; - form the bone-like apatite layer onto the scaffolds surface; - stimulate adhesion, proliferation, and differentiation of human osteoblasts *in vitro*.

The presented novel project may lead to development of an effective therapy for postsurgical and chronic infections of bone tissue.