Bifunctional, pH-responsive zeolite-bisphosphonates complex as a base for the production of smart bone implant for osteoporotic fracture treatment

Bone is a dynamic tissue that undergoes remodeling in which damaged or old bone is removed by osteoclasts (bone-resorbing cells) and replaced with a new tissue by osteoblasts (bone-forming cells). Disturbance of balance between osteoclastic bone resorption and osteoblastic bone formation results in the development of osteoporosis. Therapies aiming to inhibit osteoclast formation and bone resorption are the foundation for osteoporosis treatment. The bisphosphonates are commonly used anti-bone resorption drugs. Their mechanism of action is related to inhibition of osteoclast recruitment and differentiation and induction of osteoclast apoptosis. In clinical use, bisphosphonates are mainly administrated orally. Nevertheless, long-term clinical use of bisphosphonates during pharmacological therapy is associated with serious complications including gastrointestinal reactions, hypocalcemia, and kidney failure. Furthermore, the charge of the bisphosphonates limits penetration of cell membranes causing a very low absorption in the gut (approx. 1-10%). Moreover, in the developing and aging population, there are still emerge thousands of cases of severe osteoporotic fractures requiring surgical intervention what increases burden to society.

The aim of this project is to develop pH-responsive zeolite-bisphosphonates complex that would be used as a base for the production of smart bone implant for osteoporotic fracture treatment applications. To enhance bone formation process, Ca^{2+} and Mg^{2+} ions will be introduced to the zeolites structure through ion-exchange process (Na^{+} ions will be exchanged to Ca^{2+} and Mg^{2+} ions). Mentioned ions are known to support osteoblast adhesion and their bone-forming activity. Moreover, bisphosphonates will be bonded to zeolites using pH-sensitive chitosan as a linker. Developed in this way pH-responsive zeolite-bisphosphonates complex-based bone implant will simultaneously support bone regeneration and decrease bone resorption by osteoclasts. After implantation, developed smart biomaterials will be exposed to an acidic pH (~ 4.0-4.5) which occurs during osteoclast-mediated bone resorption. In turn, acidic pH will initiate the release of bisphosphonates into the bone environment, inhibiting osteoclasts and accelerating regeneration of osteoporotic fractures.