The aim of the project is to evaluate the mechanisms associated with iron deposition within tissues, the effect on the overall iron homeostasis of the body and possible toxic effects after oral administration of biodegradable ZnO nanoparticles doped with Fe (ZnO:Fe). Animal model for the experiment is an adult laboratory mouse of the Balb-c strain. The assumptions of the project are based on our promising, previously performed studies showing intestinal uptake of the biodegradable ZnO nanoparticles, their wide intra-organism distribution and gradual bio-degradation. Secondly, the pilot study with oral application of ZnO nanoparticles doped with iron was performed showing the accumulation of Fe within tissues important for iron metabolism.

The research hypothesis assumes, that oral administration of ZnO:Fe nanoparticles, will result in the effective absorption of iron in the nanoparticle form, followed by its distribution to tissues. As the mechanism of the nanoparticle uptake is independent from the standard paths of Fe absorption from the duodenum, this should led to a significant reduction of possible iron-related toxicity within cells as well as bypass of the iron-uptake bottleneck within the intestine, the divalent metal transporter channel, susceptible to interference with other 2+ metal ions (i.e. Cu, Zn, Mg, etc.). We assume, that administrated nanoparticles, following transfer to the tissues and organs involved with iron metabolism (predominantly liver), will undergo degradation with gradual release of iron ions from nanoparticle matrix preventing i. overoxidation of target tissue and ii. saturation of iron stores and activation of hepcidin, the control protein, preventing iron release to the blood.

The project assumes evaluation the effectiveness and safety of two forms of ZnO nanoparticles, doped either with Fe^{2+} or Fe^{3+}. Following initial experiment, the better form of Fe doping will be chosen for further examination of acute and sub-chronic exposure. Tissues collected from animals (spleen, kidneys, liver, bone, brain, adipose tissue and small intestine) and blood will be used to evaluate the bioavailability of iron, the level of proteins responsible for iron store and transport (ferritin), iron control (hepcidin), as well as iron accumulation within key tissues (in heme and non-heme form). Especially, changes in the liver mRNA content of hepcidin, the main protein controlling overall iron levels in the body, may depict the effect of ZnO:Fe NPs on the general iron homeostasis. Possible toxicity caused by ZnO:Fe nanoparticles will also be assessed.

The research subject has a major economic and social impact, due to the fact that in humans iron deficiency is the most frequent nutritional deficiency, the most commonly cause of anemia and affects up to 30% of the human population. It is also important issue for animal husbandry, specially pig farming, with iron deficiency in pig neonates. Here, our studies may give crucial information on the possible use of biodegradable nanoparticles as carriers of supplementary iron in the diet. Moreover, there is dynamically increasing popularity of studies on possible application Fe or Fe-doped nanoparticles for medical diagnostics or as drug carriers. There, the detailed investigation of the consequences of the use of Fe-containing nanoparticles on the iron metabolism is a key issue to evaluate the biosafety of proposed formulations.