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Gold nanoparticles uptake and cytotoxicity assessed on rat liver precision cut slices

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Nanotechnology research and development have been rapidly growing worldwide for the past decade. Although nanomaterials (NM)s provide great potential of commercial benefits, some of them have been claimed to be toxic in *in vivo* and *in vitro* tests and our knowledge on their toxicological properties is far from being comprehensive. With the current technological capabilities toxicological and environmental risk assessment of NPs struggles to keep up with all newly synthesized NMs. For this reason several authors have underlined the need to develop reliable in vitro models for studying their toxic effects. In order to set up a novel tool for the risk assessment of nanoparticles toxicity we evaluated cell uptake and toxicity of 5 nm gold nanoparticles (GNP)s coated with polyvynylpirrolidone (PVP) on an *in vitro* model system represented by rat liver "precision cut" slices. Rat liver precision cut slices were incubated individually at 37°C in RPMI 1640 medium for up to 24 h in the presence of GNPs at different concentrations. The presence of GNPs inside endocytotic vesicles of hepatocytes was appreciable already after 30 min incubation. From 2h onwards, GNPs cell uptake was substantiated by their presence inside endosome-like vesicles not only in hepatocytes, but also in endothelial and Kuppfer cells. After 6h GNPs could be spotted within lysosomes located close to the biliary pole of the hepatocytes. These results were confirmed in vivo with few experiments carried out upon i.p injection of GNPs. This did not translate into modification of both phase I and phase II of 7-ethoxycoumarin metabolism. Similarly, CYPs activities of slices microsomal preparations towards marker substrates resulted unaffected. Although GNPs were promptly taken up by slices, no signs of cytotoxicity were observed. In fact, LDH release, MTT reduction and GSH levels in GNPs-treated slices were not different from those of control slices. In conclusion, rat liver precision cut slices can be employed for assessing the consequences of the biological impact of nanoparticles

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