# NANOPARTICLES: TOXICITY AND PENETRATION ACROSS BIOLOGICAL BARRIERS

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Nanoparticles provide new opportunities for drug delivery and human therapy. To fulfill the therapeutical potential of nanoparticles two major aspects, toxicity and penetration across barriers of the body need to be studied. Different *ex vivo* and *in vitro* cell culture based models of the skin, nasal, lung, intestinal and blood-brain barriers have been established in our laboratory that can be used for both purposes. Three different types of nanoparticles were tested on the different models. Amorphous nanoparticles from the antiinflammatory drug meloxicam were obtained by by co-grinding with polyvinylpyrrolidone. Nanosized bilayered vesicles of non-ionic surfactants bearing glucose and amino acid ligands were prepared to specifically target solute carriers on the blood-brain barrier [1]. Poly(ferrocenyl silane) redox responsive polymer nanocarriers were also studied [2]. Several methods were applied parallelly to measure the toxicity of nanoparticles. In addition to colorimetric tests like MTT dye reduction assay, release of the cytoplasmic enzyme lactate dehydrogenase cellular events were also monitored in real time. By measuring impedance across microelectrodes covered with cells quantitative information on cell viability and intercellular adherence indicating paracellular permeability could be obtained. Co-culture models of the barriers prepared from primary cultures or human cell lines [3] served for permeability experiments to test the penetration of nanocarriers across cell layers. In the case of the blood-brain barrier a kinetic *in vivo* study in mice was also performed by near infrared fluorescence time-domain optical imaging. The results indicate that (i) toxicity measurements are very important to obtain the optimal dose of nanoparticles on living cells, (ii) nanonization of drugs can improve drug dissolution, absorption and pharmacokinetics, (iii) targeting of microvesicles increases their penetration across barriers.

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