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Toxicokinetics of Insoluble Nanoparticles in Rodents after Different Routes of Administration

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Nanoparticles (NP) are increasingly used in a wide range of applications in science, technology and medicine. Since they are produced for specific purposes which cannot be met by larger particles and bulk material they are likely to be highly reactive, in particular, with biological systems. Direct routes of intake into the organism are (1) inhalation and deposition of NP in the respiratory tract and (2) oral intake of NP and ingestion. Recently there is evidence that nanoparticles can cross body membranes – such as the air-blood-barrier in lungs and the intestinal epithelium – reaching blood circulation and accumulating in secondary target organs. Therefore, direct intravenous administration of NP into circulation provides a powerful tool to shed light on the various interactions of crossing body membranes.

To quantitatively determine accumulated NP fractions in such organs the ultimate aim is to balance the NP fractions in all interesting organs and tissues including the remaining body and total excretion. Since these gross determinations of NP contents in organs and tissues do not provide microscopic information on the anatomical and cellular location of nanoparticles such studies are to be complemented by electron microscopy analysis as demonstrated for inhaled titanium dioxide nanoparticles.

Based on quantitative biokinetics after all three routes of administration in a rat model (lungs, blood, gastro-intestinal tract) we found small NP fractions (iridium, carbon, titanium dioxide, gold,) in all secondary organs studied including brain, heart and even in foetuses. Fractions per secondary organ were usually below 0.1% of the administered dose but depended strongly on particle size, material and surface modifications as well as on the route of intake.

The current knowledge on systemic translocation of NP and their accumulation in secondary target organs and tissues of man and animal models does not suggest to cause acute effects of translocated NP but chronic exposure may lead to elevated NP accumulations resulting eventually in adverse health effects.

In fact, there is growing evidence that ambient ultrafine particles and some of the engineered NP can induce acute adverse health effects in humans and in animal models not only in the respiratory tract but also in the cardio-vascular-system. Since NP translocation is so low these effects are likely to be triggered by mediators released in the organ of intake.