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NANOPARTICLES AS A POTENTIAL RISK FACTOR FOR HEALTH DAMAGE - PLATFORM FOR PHD PROGRAM

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Abstract

In addition to education – Faculty of Public Health of Slovak Medicine University in Bratislava - realizes also many research projects, which are focused on environmental health and cognition of causal links between environmental factors and human health. Many research projects of our faculty concern the exposure to adverse environment and occupational factors (for example: asbestos, industrial dust, radiation, polychlorinated biphenyls, nanoparticles, etc.) in relation to the impact on employees' health, child population and their subsequent preventive measures. Many of our projects are experimental – *in vivo or in vitro.*

We also teach students to apply for grants, enter and manage projects in these areas.
Many students – mainly internal PhD. students are directly involved in projects and they use results in writing PhD. theses.

Doctoral program - in our last 2 projects, solved in the laboratory of Respiratory toxicology - was part of projects: Centre of Excellence of „Environmental Health", ITMS No. 26240120033 - based on the support of operational research and development programme financed by the European Regional Development Fund and „NanoTest“ EU Project (7FP), No.19-40-10). The studies of our projects were focused on the effect of TiO_2 and magnetite - Fe_3O_4 nanoparticles (NPs) on the respiratory tract;

We examined many inflammatory and cytotoxic parameters of bronchoalveolar lavage after exposure to mentioned nanoparticles and monitored the time and dose dependence of NPs.

*Nanoparti*cles are particles smaller than 100 nm. Because they have nano dimensions, they probably can penetrate through various membranes and get from the bloodstream to other organs in the body. Massive expansion of nanotechnologies together with production of new nanoparticles - which had not been yet in contact with living organisms - may be potential problem for people health. For that it is necessary to investigate the impact of the NPs on the health after experimental and human exposure.

The ways of NP entry into the organism are: Lungs (work and environment); Skin (use of cosmetics, clothing); Gastrointestinal tract – (consumption contaminated foods, drugs that contain NPs). By inhalation NPs get into: Brain – and can contribute to diseases such as (Parkinson‘s, Alzheimer's diseases, autism etc.); Lungs (asthma, bronchitis, pulmonary emphysema, lung cancer); Circulatory system (arteriosclerosis, narrowing of blood vessels, thrombus, high blood pressure); Heart (arrhythmias and other heart diseases); Lymphatic system (Kaposi's sarcoma); Other organs (liver and kidney diseases of unknown origin).

Employees professionally exposed to NPs: workers involved in NP development, in NP research, in production of NPs and nanomaterials, workers in construction work, painters and pavers, welders, employees in nanotechnologies, professional drivers exposed to exhaust gas, in car maintenance and repair, employees exposed to raw nanomaterials and waste in the work processes, hairdressers, ealthcare workers, etc.
The aim of our study was:
a) to determine whether the NP investigated by us, do pass through the vascular system to the respiratory tract, and if so,
b) how they affect the selected inflammatory and cytotoxic parameters of bronchoalveolar lavage,
c) to compare the results (BAL parameters influenced by TiO_2 and Fe_3O_4) with a control group and with each other (Fe_3O_4 to TiO_2).
e) to find out dose and time dependence of mentioned nanoparticles.

Wistar rats were intravenously given (to a tail vein of an animal) a suspension of NPs TiO_2 and Fe_3O_4. 1) After time intervals 1, 7, 14 and 28 days, we sacrificed the animals under anesthesia, performed bronchoalveolar lavage (BAL) and isolated the cells. 2) Wistar rats were given 3 doses of suspension Fe_3O_4
- magnetite nanoparticles: 0,1% LD_{50} = 0.0364; 1,0% LD_{50} = 0,364 and 10,0% LD_{50} = 3,64 mg/kg body weight). Seven days later, we sacrificed the animals under anesthesia, performed BAL and isolated the cells from it.

We examined: a differential count of BAL cells (% of alveolar macrophages – AM, polymorphonuclear leukocytes – PMN, lymphocytes – Ly); viability and phagocytic activity of AM; the proportion of immature and polynuclear cells enzymes: cathepsin D – CAT D, lactate dehydrogenase – LDH and acid phosphatase – AcP).

Dose dependence – Magnetite nanoparticles (Fe_3O_4) *i.v.* injected into the tail vein pass into the respiratory tract and affect some BAL parameters. Of the 12 parameters examined by us, the highest dose of 10% LD/50 magnetite suspension affected 10 parameters, but statistically significant 7. Dose dependence we confirmed only partly. Questionable is, why are some of the BAL parameters in our study dose dependent, while others are not. Therefore, we assume the adverse effect of NPs probably does not correlate with the dose, but more with the size of the particles – with their surface area – as published by some authors. Smaller NPs have a bigger surface area and therefore may be more reactive.

Time dependence – The results shown, that TiO_2 and Fe_3O_4 nanoparticles used in our study were transferred from the bloodstream to the respiratory tract,

but in a 28-day phase after *i.v.* instil-lation have been eliminated by the defence mechanism from the respiratory tract. The results in our study are after a single, one-time exposure, but other could be situation after long-term, repeated exposure, for example in the work process.

Some NPs may represent new potential health risks. In fact, the normal human defence mechanisms may be unable to respond adequately to the newly created particles withunique features, because the human organism has not yet encountered them. Therefore, the impact of NPs on health has become a public health issue, resulting in an important need for further research.

Doctoral – PhD. programme within the mentioned EU projects in Faculty of Public Health (in Laboratory of respiratory toxicology) was highly effective. As part of the projects, several students completed their doctoral studies. PhD. programm brought valuable knowledge in the NP field. The results were published in domestic and foreign journals and presented at domestic and international forums. They guarantee the quality of PhD. theses, especially in terms of scientific approach.

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