Addressing the toxic potential of nanoparticles and potentially toxic elements mixtures: state-of-the-art and insight into project NanoLegaTox findings

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The industrialization and modernization processes, the development of new technologies and products, and the exploitation of natural resources results in a panoply of contaminants released into the environment. Consequently, humans are exposed to mixtures of substances and there is a pressing need to understand the potential adverse health effects resulting from the interactions between these substances. Existing data on mixtures' toxicity is rather limited, since the estimation of health risks from exposure to chemical mixtures is a complex issue, particularly if the chemicals have different modes of action.

One such example would be engineered nanoparticles (NPs) and potentially toxic elements (PTEs), such as metals and metalloids. Mixtures of these substances are of interest since:

I) Due to their growing production and application, NPs are increasingly discharged into the environment. The released NPs can potentially interact with pre-existing contaminants, leading to biological effects (bioaccumulation and/or toxicity) that are poorly understood. Indeed, the limited existing data suggests that NPs-metal(loid) interactions affect the behavior, uptake and toxicity of each individual contaminant (addition, antagonism, potentiation, and synergy, have all been reported).

II) PTEs, such as arsenic, cadmium, lead, and mercury, among others, have a particular affinity for NPs, namely significant accumulation of metal(loid) at NPs surfaces, and considering their persistent and toxic character it is imperative to assess the toxic profile resulting from these interactions.

Assessing the risk of NPs and PTEs mixtures is challenging and requires a dedicated approach. This presentation will: 1) summarize the current state-of-art and available data on toxicity resulting from NPs co-exposed with PTEs; 2) review *in vitro* and *in vivo* methods for investigating and evaluating joint effects of NPs and PTEs; 3) discuss knowledge gaps and future research directions to better understand the risk associated with NPs and PTEs co-exposure.

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