Nanotoxicity: gold nanoparticles under study

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The outstanding properties of nanoparticles along with their widespread use in consumer and industrial products have aroused global concern for the consequences of their interaction with biological systems in toxicological terms. In this regard, nanoparticles with applications in Biomedicine field, such as gold nanoparticles (AuNPs), require necessarily an exhaustive investigation on their possible adverse effects and how these can be alleviated.

Toxicity arising from nanoparticles is directly related to their ability for cellular internalization. Different mechanisms have been established to explain the cellular uptake of nanoparticles, most of which involve endocytic processes [1]. It should be noted that each type of nanoparticle exhibits a preferred internalization pathway which is mainly determined by its physicochemical properties including surface chemistry, size and shape. As far as surface chemistry is concerned, there are many examples in literature that associate the toxicity derived from AuNPs with the surfactant located on their surface and used for their synthesis and stabilization, in particular, CTAB [2]. On the other hand, positively charged AuNPs are likely to exhibit a greater cellular uptake as a consequence of their favored electrostatic interactions with negatively charged cell membrane [3]. Size-dependent toxicity of AuNPs has been also confirmed in several works where smaller AuNPs were more efficiently internalized than larger ones and therefore, caused a greater cytotoxicity [4]. As regards to nanoparticle shape, different cellular responses were reported for cells exposed to gold nanorods or gold nanospheres [5].

Once internalized and stored, AuNPs can induce harmful effects on cells principally due to their catalytic ability. It has described that AuNPs damage the DNA as a consequence of their strong affinity for DNA grooves, which have negative environment [6]. The endogenous production of reactive oxygen species (ROS) and the depletion of natural intracellular antioxidants represent other important mechanisms of toxicity induced by AuNPs, which may disturb the equilibrium between antioxidant and oxidant intracellular processes. ROS can be produced directly by the AuNPs themselves as a result of their surface reactivity, or degradation of their coating shell or inorganic core with the consequent leakage of free ions to the intracellular environment. Indirectly, AuNPs may also interact with intracellular organelles and biomolecules following the activation of oxidative stress response pathways. Moreover, protein and polyunsaturated fatty acid oxidation are other secondary effects derived from oxidative stress, and lead to mitochondrial alterations (e.g. increased membrane permeability) that ultimately prompt cell death. Lipid membrane thinning effects or alterations on protein conformation or activity are other potential toxicity mechanisms.

Methods for AuNP toxicity assessment include both in vitro and in vivo studies. However, the vast majority of the currently performed assays are in vitro and only allow examining the effects at cellular level. The scenario for evaluation of nanoparticle toxicity becomes even more complex when other additional influential factors come into play. In this respect, nanoparticles tend to aggregate in contact with cell media thus modifying their physicochemical properties and ultimately, their degree of interaction with cells. Different cell lines and culture media are other determinants that can modify the resulting toxicity even when the same nanoparticles are considered. In addition, interferences between AuNPs and some cytotoxicity assays have been also reported what definitely complicate the interpretation of the obtained results. Consequently, considerable efforts have to be made to overcome the limitations found in the currently available evaluation methods.

References

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