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7.1.15 Cytotoxicity and genotoxicity induced in human and murine cell assays by copper oxide nanoparticles

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Metal oxide nanoparticles (NPs) are already present in commercial products and their applications are expected to increase in the future. Among these, copper oxide (CuO) NPs are used as antimicrobial preparations, heat transfer fluids and semiconductors. Since CuO can induce toxic effects in several cell lines, we used CuO NPs from a commercial source to set up cytotoxicity and genotoxicity assays suitable for screening purposes of metal NP.

The induction of toxicity and genotoxicity following *in vitro* exposure to CuO NPs [mass concentration from 0.1 to 10^3 µg/ml] was assessed in three cell lines: the human A549 lung epithelial cells, the murine macrophage RAW 264.7 and the murine fibroblast Balb/3T3; to mimic possible interaction with blood cells, we also used peripheral blood monocytes (PBMC) from volunteers. Cytotoxicity was assessed by MTT and Colony Forming Efficiency (CFE) assays.

MTT assay revealed a significant dose-effect relationship between the testing concentrations and a decrease of cell viability in A549 and RAW 264.7 cells, both after 24h and 48h with. The CFE assay on A549 cells - that are able to form colonies - confirmed a dose-effect relationship at 24 h and 72 h in the same range of CuO NPs concentrations used for MTT, with an IC_{50} of about 4 µg/ml at 24h. The comet assay carried out on A549, RAW 264.7 cells and PBMC (2h and 24h treatment; dose range: 0.1 to 100 µg/ml) revealed that the primary DNA damage increased in a dose-dependent manner, with different sensitivity exhibited by the different cell type. The version of the Comet assay that allows to specifically detect the induction of oxidative damage to DNA was applied and both oxidised purines and pyrimidines showed significant increases in all the cell types studied. Moreover, the frequency of micronuclei in binucleated RAW 264.7 and A549 cells and PBMC increased in a dose-related manner (dose range: 0.1 to 100 µg/ml) with differences in sensitivity due to the specific cell type.

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