Role of copper oxide nanoparticles as antigenotoxic agents. Studies in *Drosophila*

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The biological reactivity of metallic nanomaterials is attributed to their redox characteristics, which would explain their pro- or anti-cancer properties depending on exposure circumstances. In this sense, CuO nanoparticles (CuONP) have been proposed as a potential antitumoral agent.

The aim of this study is to assess if CuONP can exert antigenotoxic effects using *Drosophila melanogaster* as an *in vivo* model. Genotoxicity was induced by two well-known genotoxic compounds, potassium dichromate (PD) and ethyl methanesulfonate (EMS). The wing-spot assay and the comet assay were used as biomarkers of genotoxic effects. In addition, changes in the expression of *Ogg1* and *SOD* genes were determined. The effects of CuONP cotreatment were compared with those induced by copper sulphate (CS), an agent releasing copper ions.

A slight but significant toxic effect was observed, according to the size of the emerging adults, CS being more toxic than CuONP. Neither CuONP nor CS were genotoxic in the wing-spot assay. Although CuONP was not able to reduce the genotoxic effects of EMS exposure, it had the ability to decrease the effects induced by PD. This effect was associated to a significant reduction in the frequency of mutant twin spots resulting from mitotic recombination. Similar results were obtained with CS. In addition, CuONP were able to reduce the primary DNA damage induced by PD, as measured by using the comet assay.

Since PD effects are associated with the induction of oxidative stress, changes in the expression of *Cu,ZnSOD* and *Ogg1* genes were determined after cotreatment conditions to explain the interferences observed in the cotreatment experiments. According to the results obtained, the antigenotoxic effects of environmental relevant and non-toxic doses of CuONP can be explained by its ability to restore the expression levels of the repair gene *Ogg1* and the antioxidant gene Cu,ZnSOD, inhibited by PD treatment.