Copper-Doped ZnO: Modulating Biocompatibility in Fruit Fly Models

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ABSTRACT

Zinc oxide (ZnO) nanocrystals (NCs) are extensively studied for their photocatalytic activity, bactericidal effects, and high chemical stability. However, concerns regarding their potential toxicity have prompted research into doping with transition metals, such as copper (Cu), as a strategy to enhance the physicochemical properties of these nanoparticles. This modification can influence the electronic and structural characteristics of ZnO, potentially increasing their biocompatibility. Nonetheless, the concentration of incorporated Cu can significantly impact biological interactions and requires careful evaluation. In this study, we synthesized, characterized, and assessed the biological properties of Cu-doped ZnO NCs. Characterization techniques, including optical absorption spectroscopy, X-ray diffraction, and chemical degradation analysis, confirmed the successful incorporation of Cu ions into the ZnO NCs. Notably, at concentrations exceeding 1.0 mg/mL, copper oxide formation was observed, leading to the creation of nanocomposites. The biological effects of Cu-doped ZnO NCs and the resulting Cu-doped ZnO/CuO nanocomposites were evaluated using first-instar larvae (L1) of *Drosophila melanogaster*, which were exposed to various concentrations (0.10, 0.25, 0.50, and 1.0 mg/mL) of these materials incorporated into standard Drosophila culture medium. A control group was maintained solely on standard medium. We conducted analyses of developmental outcomes and assessed locomotor function through negative geotaxis assays after a 24-hour exposure period. The results demonstrated that pure ZnO NCs exhibited significant toxicity, leading to reduced pupation and eclosion rates, as well as increased larval mortality, particularly at elevated concentrations. In contrast, Cu-doped ZnO NCs displayed enhanced biocompatibility, with pupation rates comparable to the control group and markedly reduced toxic effects. However, the ZnO/CuO nanocomposites revealed dose-dependent toxicity, as indicated by increased larval mortality and decreased eclosion rates at concentrations of 0.50 and 1.0 mg/mL. Importantly, the animals exposed to ZnO-Cu did not exhibit any negative effects in the negative geotaxis assays, suggesting preserved locomotor function. The antimicrobial activity assessment of ZnOXCu was performed using the broth microdilution method against the strains *Staphylococcus aureus* (ATCC 25923), *Staphylococcus epidermidis* (ATCC 31488), and *Enterococcus faecalis* (ATCC 10160). The minimum inhibitory concentration (MIC) of ZnO:0.4Cu was 125 µg/mL for S. aureus and *E. faecalis*, and 500 µg/mL for *S. epidermidis*. The performance of ZnO:4.0Cu was similar, with values of 125 µg/mL for S. aureus and *S. epidermidis*, and 250 µg/ml for *E. faecalis*. In conclusion, Cu doping significantly improves the biocompatibility of ZnO, especially at lower concentrations, while highlighting the necessity of optimizing Cu levels to mitigate toxicity and enhance the safety profile of ZnO nanomaterials for biological applications.