IV Congresso Latino-Americano de Toxicologia Clínico-Laboratorial (ToxiLatin 2025)

DOSE-DEPENDENT EFFECT OF HEPARIN-FUNCTIONALIZED GRAPHENE OXIDE: IMPLICATIONS FOR ITS POTENTIAL ANTI-HERPETIC USE

Área: Nanotoxicologia

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INTRODUCTION: Graphene oxide (GO) is a promising nanomaterial in translational medicine, especially as a vehicle for controlled drug delivery. Its functionalization with heparin (GO@Heparin) has shown antiviral potential, particularly against herpesviruses, due to its structural similarity to heparan sulfate, a viral entry receptor. However, evaluating its safety and toxicity is essential for therapeutic use. OBJECTIVE: To assess the safety profile and biological effects of GO, GO@Heparin 5.0%, and heparin in VERO cells, focusing on cell viability and oxidative stress, after acute (24h) and chronic (72h) exposure. MATERIALS AND METHODS: This is an in vitro experimental study using VERO cells treated with different concentrations of GO, GO@Heparin 5.0%, and heparin. The following assays were performed: MTT (cell viability), PicoGreen (cell death via double-stranded DNA quantification), and nitrite determination (as a marker of oxidative stress). Statistical analysis was conducted using one-way ANOVA followed by Dunnett's post hoc test, with the aid of GraphPad Prism software. RESULTS: After 24 hours of exposure, GO and GO@Heparin stimulated cell proliferation at concentrations ranging from 3.9 to 125 µg/mL (GO) and up to 62.5 µg/mL (GO@Heparin), with a dose-dependent increase in nitrite levels ($p<0.0001$). Heparin significantly promoted cell proliferation at all tested concentrations without a notable increase in nitrite production, indicating a safe bio-stimulatory effect. After 72 hours, the dual nature of the nanomaterials became evident: GO and GO@Heparin maintained their proliferative effects at low concentrations but showed significant cytotoxicity at 250 µg/mL ($p<0.0001$), with increased cell death and reduced DNA detection. Heparin, on the other hand, continued to promote proliferation, with only a slight increase in oxidative stress at the lowest doses. CONCLUSION: GO and GO@Heparin demonstrated beneficial effects at low concentrations and toxicity at higher doses, especially after 72 hours. Functionalization with heparin did not completely eliminate toxicity at elevated concentrations but preserved part of the proliferative effect observed with free heparin, suggesting that the conjugation retains its bioactivity. This is particularly relevant in the antiviral context, given the potential of GO@Heparin as a nanocarrier with anti-herpetic activity provided that a safe therapeutic window is respected.

This study was supported by the Postdoctoral Fellowship Program (Auxílio Recém-Doutor) from FAPERGS – Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul.