The Toxicity of Native and Oxovanadium (IV/V) Gatactomannan Complex on HepG2 Cells is Related to impairment of Mitochondrial Functions

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INTRODUCTION: Native and chemically modified polysaccharides have been extensively studied aiming different applications, such as antitumor agents.The biological effects attributed to them are related with their chemical structures. Then, chemical modifications as fragmentation of these polymers or their complexation with metals are frequently used. **OBJECTIVES:** The aim of this study was to evaluate the cytotoxic effects of the uncomplexed and complexed galactomannan with oxovanadium on cultured human hepatocarcinoma (HepG2) cells. **MATERIAL AND METHODS:** Native galactomannan (SAGM) from *Schizolobium amazonicum* was obtained by boiled in water extraction and fragmented by acidic hydrolysis (SAGMD). Both SAGM and SAGMD were complexed with oxovanadium resulting at SAMG:VO and SAGMD:VO, respectively. The complexation was confirmed by ^{51}V-NMR spectroscopy. Viability and cell proliferation were evaluated by MTT and violet crystal assays, respectively. The states of respiration: basal (absence of inhibitors or uncouplers, leak (presence of oligomycin) and uncoupled (presence of FCCP) were analyzed in intact cells by high-resolution respirometry (Oxygraph-2k, Oroboros®). The levels of Reactive oxygen species (ROS) and mitochondrial membrane potential ($\Delta\Psi m$) were measured using DCFH-DA and JC-1 probes, respectively. **RESULTS AND DISCUSSION**: The ^{51}V-NMR analysis showed different species of the complexes in the preparations. SAGM and SAGMD:VO (250 μg/mL) decreased the cell viability at ~50% after 72 h of treatment. At the same conditions, SAGMD:VO was more effective than the other polymers for inhibiting the cells proliferation. SAGM and SAGMD:VO (250 μg/mL) significantly inhibited all the states of respiration after 72 h of treatment . ROS levels were increased after the treatment with SAGMD:VO (250 μg/mL) by 72 of treatment while $\Delta\Psi m$ was decreased. **CONCLUSION:** SAGM and SAGMD:VO (250 μg/mL) after 72 h of treatment are toxic for HepG2 cells and this effect is related with the impairment of the mitochondrial functions linked to energy provision.

Key words: galactomannans, oxovanadium, HepG2 cells, mitochondrial functions
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