

## **Effect of Methylphenidate and Nanoencapsulated Naringin on BV2 Microglial Cells in Culture**

Amanda Reis Cruz<sup>1</sup>; Daniela da Silva Araújo Martins<sup>2</sup>; Camila Medianeira da Silva D'Avila<sup>3</sup>; Bruno Silveira Levy<sup>2</sup>; Francine Carla Cadoná<sup>3</sup>; Carina Rodrigues Boeck<sup>2,3</sup>

<sup>1</sup>Biomedical Sciences, Universidade Franciscana-UFN, Santa Maria, RS, Brazil

<sup>2</sup>Graduate Program in Nanosciences, Universidade Franciscana-UFN, Santa Maria, RS, Brazil

<sup>3</sup>Master's Program in Health and Life Sciences, Universidade Franciscana-UFN, Santa Maria, RS, Brazil

### **Field: Nanotoxicology**

### **ABSTRACT**

**INTRODUCTION:** Methylphenidate (MPH), the primary drug used to treat ADHD (affecting ~3% of the global population), induces neural hyperactivity through dopamine and norepinephrine release and reuptake inhibition. Naringin, an antioxidant and anti-inflammatory flavonoid, modulates MPH's dopaminergic effects via redox homeostasis and mitochondrial function. Nanoencapsulation of naringin may enhance its action in the brain due to the increased bioavailability of natural compounds provided by nanomaterials. **OBJECTIVE:** Evaluate the effects of MPH on BV2 microglial cells and the association of free (F-NAR) or nanoencapsulated (NAR-NC) naringin on cell viability and proliferation. **METHODS:** BV2 cells were maintained in culture medium and incubated for 24 and 72 hours with F-NAR or NAR-NC (0.1; 1; 5; 10; or 50  $\mu$ g/mL), or with MPH (0.1; 0.5; 1; or 2 mM) to determine the concentration corresponding to toxicity (IC<sub>50</sub>). Cell viability and proliferation were assessed, along with nitric oxide and reactive oxygen species production. Statistical analysis was performed using one-way ANOVA followed by Tukey's post-hoc test ( $p < 0.05$ ). **RESULTS:** MPH exposure did not cause cell death at lower concentrations after 24 hours. However, after 72 hours, the IC<sub>50</sub> value decreased from 2 mM to 1 mM. F-NAR reduced cell viability at the highest concentration after 24 hours. NAR-NC induced a reduction in cell viability at 50  $\mu$ g/mL after 24 hours and decreased cell proliferation at all concentrations after 72 hours. **CONCLUSION:** The IC<sub>50</sub> for MPH was determined to be 2 mM. Naringin, in either free or nanoencapsulated form, did not demonstrate significant protective effects. The data suggest that redox status is not significantly altered in MPH-induced toxicity in BV2 cells and that

nanoencapsulated naringin may activate cell damage mechanisms in this cell type, which requires further confirmation.

**Keywords:** methylphenidate; BV2 cells; naringin; nanotechnology.