IV SIMPÓSIO INTERNACIONAL EM INVESTIGAÇÕES QUÍMICO-FARMACÊUTICAS

**Área: TOX**

# NEUROTOXICITY OF SULFENTRAZONE IN BV2 CELLS

Maria E. Vieira[1*], Carlos R. Vaz[1], Larissa Benvenutti[1], Fernanda C. Goldoni[1], Bruna de Araújo[1], Beatriz Z. Schlindwein[1], Andriéli R. Dutra[1], Ozana K. F. Fernandes[1], Marcelo Arbo[2], Nara L. M. Quintão[1], José R. Santin[1].

*[1]University of Vale do Itajaí, UNIVALI, Brazil. [2]Federal University of Rio Grande do Sul, UFRGS, Brazil.* *mvieira@edu.univali.br

## INTRODUCTION

Sulfentrazone is a widely used pesticide in the Southern Region to control invasive plants in crops such as soybeans and tobacco. There is a lack of studies evaluating the effects of this pesticide on the Central Nervous System (CNS). This study aims to assess its in vitro toxicity on the CNS using glial cells (BV2).

## MATERIALS AND METHODS

In silico toxicokinetic assessments were conducted using the online software SwissADME. For toxicological evaluations, the QSAR Toolbox computational software (version 4.7.1) was used. BV2 cells were cultured under appropriate growth conditions. To assess cell viability, two assays were performed: MTT and neutral red (NR). Cells were plated and treated with sulfentrazone at different concentrations [1 to 5,000 mg/L] for 24 hours. After the treatment period, optical densities (OD) were measured to determine the minimum inhibitory concentration (IC) values. Subsequently, a flow cytometry assay was conducted to evaluate the cell death profile using Annexin V and 7-AAD markers. Additionally, the supernatant from treated cells was used to quantify NO2- concentrations through the Griess reaction.

## RESULTS

Predictive in silico analyses indicate that sulfentrazone does not possess molecular characteristics that allow it to cross the blood-brain barrier (BBB). However, under conditions of high exposure, such as in agricultural workers, the BBB may become more permeable. Additionally, the high gastrointestinal absorption of sulfentrazone may lead to the formation of biotransformation products capable of crossing this barrier. Sulfentrazone also triggered an alert for the "hydrogen receptor pathway" in the in vivo mutagenicity test (micronucleus assay).

To evaluate cell viability, MTT and NR tests were performed after 24 hours of exposure to sulfentrazone at concentrations ranging from 1 to 5,000 mg/L. Based on the resulting curve, the inhibitory concentrations were determined: IC25 = 35 mg/L, IC50 = 110 mg/L, and IC75 = 340 mg/L. Flow cytometry indicated that sulfentrazone induced apoptosis, a programmed process that causes less damage to resident cells. Moreover, indirect quantification of nitric oxide (NO) in the supernatant of treated cells revealed a reduction in NO production at higher concentrations (IC50 and IC75). This effect may be related to cell death and the immunosuppressive properties of sulfentrazone.

## CONCLUSIONS

Exposure of microglial cells to the pesticide sulfentrazone induces apoptosis and compromises their immune function by reducing NO release. This effect suggests a potential immunotoxic property of the substance, impacting inflammatory responses and cellular defense.

## ACKNOWLEDGMENTS

CAPES, UNIVALI, UFRGS, FAPESC, CNPq, INCT-Inovamed.