ANALYSIS OF THE POTENTIAL NEUROPROTECTIVE EFFECTS OF THE JM-20 MOLECULE AGAINST GLUTAMATERGIC NEUROTOXICITY IN *Caenorhabditis elegans.*

Arthur Belous[1]; Marcell Valandro Soares[1];Aline Franzen da Silva[1]; Adesina Babalola[1]; Sámili Silva[1]; Larissa Ilha[1]; Talita Chaves[1]; Amanda Campos[1]; Isabelle Peres[1]; Yanier Nuñez-Figueredo[2] ;Félix Alexandre Antunes Soares[1].

[1] Graduate Program in Biological Sciences: Toxicological Biochemistry, Centre of Natural and Exact Sciences, Federal University of Santa Maria, Santa Maria, RS, Brazil.

[2] Centro de Investigación y Desarrollo de Medicamentos, Ave 26, No. 1605 Boyeros y Puentes Grandes, CP, 10600 Habana, La Habana, Cuba.

INTRODUCTION: Glutamate-induced excitotoxicity has been associated with the development of neurodegenerative disorders such as Alzheimer's disease, epilepsy, and amyotrophic lateral sclerosis (ALS). The growing concern regarding these conditions has prompted the search for drugs and molecules with potential protective effects against glutamatergic excitotoxicity, including the compound JM-20 (3-ethoxycarbonyl-2-methyl-4-(2-nitrophenyl)-4,11-dihydro-1-pyrido[2,3-b][1,5]benzodiazepine), which is evaluated in the present study. Although JM-20 has shown promise, its mechanisms of action in the context of glutamate excitotoxicity remain unclear. In this scenario, the nematode Caenorhabditis elegans has emerged as a relevant experimental model in toxicology and pharmacology due to the conservation of glutamatergic pathways, making it a valuable tool for mechanistic studies of novel neuroactive compounds. **OBJECTIVE:** Assess the potential effects of JM-20 in response to quinolinic acid (QUIN) induced neurotoxicity in Caenorhabditis elegans. **MATERIALS AND METHODS:** Wild-type C. elegans (N2 strain) were chronically exposed to JM-20 (5 μM) from the L1 larval stage until adulthood. After this period, the animals were acutely exposed to QUIN (20 mM) for 1 hour. Behavioral assays were then performed, including responses to mechanical touch, 1-octanol avoidance (chemical latency), locomotion speed, and swimming movement pattern. Each experiment was independently replicated at least three times. **RESULTS:** Pre-treatment with JM-20 significantly preserved the touch response compared to animals exposed only to QUIN. However, no significant differences were observed in the 1-octanol latency test. Data on locomotion speed and movement patterns showed changes between the treated and untreated groups. **CONCLUSION:** JM-20 induced changes in some behavioral parameters in C. elegans exposed to QUIN, suggesting a possible role in modulating QUIN-induced toxicity. However, the underlying mechanism remains to be further investigated.

Keywords: Neuroprotection; Excitotoxicity; Neurodegeneration model.