



AYAHUASCA MITIGATES OXIDATIVE STRESS AND SENESCENCE IN 6-OHDA-INDUCED SH-SY5Y CELLS

Wanderleya Toledo dos Santos^{1*}, Albert Katchborian Neto², Fernanda Brito Leite Dornellas¹, Dawidson Assis Gomes³, Fernanda Maria Pinto Vilela¹, Marisi Gomes Soares², Danielle Ferreira Dias², Paula Carolina Pires Bueno⁴, Daniela Aparecida Chagas de Paula², Ana Cláudia Chagas de Paula Ladvocat¹

wanderleyatoledos@gmail.com

1-Faculty of Pharmacy, Department of Pharmaceutical Sciences, Federal University of Juiz de Fora, Rua José Lourenço Kelmer, Juiz de Fora, Minas Gerais, 36036-900, Brazil. 2-Chemistry Institute, Federal University of Alfenas, Alfenas, Minas Gerais, 37130-001, Brazil. 3- Department of Biochemistry and Immunology, Federal University of Minas Gerais, Av. Antônio Carlos, 6627, Belo Horizonte, Minas Gerais, Brazil. 4- Leibniz Institute of Vegetable and Ornamental Crops, IGZ, Theodor-Echermeyer-Weg 1, 14979 Großbeeren, Germany.

Parkinson's disease (PD) is a neurodegenerative disorder, characterized by the progressive loss of dopaminergic neurons and symptoms such as resting tremor and muscle rigidity, as well as non-motor symptoms, including mood and gastrointestinal alterations. Current therapies are only symptomatic and often associated with significant adverse effects, highlighting the urgent need for new therapeutic approaches. In this context, natural products have emerged as promising sources of biologically active molecules. Ayahuasca (Aya), a traditional ritualistic beverage, mainly composed of *Banisteriopsis caapi* and *Psychotria viridis*, showed promising neuroprotective results. Thus, this study aimed to investigate the neuroprotective mechanisms of action of Aya in cellular PD model, using human neuroblastoma cells (SH-SY5Y) subjected to 6-hydroxydopamine (6-OHDA)-induced toxicity. Initially, the cytotoxicity of Aya and reference drug (L-DOPA), was evaluated by the MTT assay after 48 h of treatment. Subsequently, the neuroprotective mechanism of action was evaluated. The oxidative stress was measured using the MitoSOX Green probe. The cellular senescence was also evaluated. The results demonstrated that Aya exerted a neuroprotective effect, associated with reduced mitochondrial oxidative stress and decreased cellular senescence induced by 6-OHDA at the concentration of 1.25 µg/mL. These findings suggest the therapeutic potential of Ayahuasca for PD, although further studies are required to elucidate possible additional details regarding its mechanisms of action. Acknowledgments: CAPES, FAPEMIG RED-00213-23, APQ02882-24, APQ00443-18, CNPq 408115/2023-8, 304916/2025-0, FAPESP 24/04606-5.

Keywords: Parkinson's disease, neuroprotection, natural products, Ayahuasca.

