COULD CANNABINOIDS COMBAT NEUROINFLAMMATION? INSIGHTS FROM AN *IN VITRO* STUDY

Júlia Maiara dos Santos[1], Amanda Kolinski Machado[2], Elaine Aparecida Del Bel Belluz Guimarães[3], Alencar Kolinski Machado[2], Antonio Cardozo dos Santos[1]

[1]Neurotoxicity & Neuroprotection Research Laboratory, Department of Clinical Analyses, Toxicology and Food Sciences, School of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo, Ribeirão Preto, São Paulo, Brazil

[2]Cell Culture & Bioactive Effects Laboratory, Franciscan University, Santa Maria, Rio Grande do Sul, Brazil

[3]Department of Morphology, Physiology, and Basic Pathology, Ribeirao Preto Dentistry Faculty, University of São Paulo, Ribeirão Preto, Brazil

Institution where the work was carried out: Franciscan University, Santa Maria, Rio Grande do Sul, Brazil

INTRODUCTION: Inflammation serves as a protective mechanism under physiological conditions. However, when dysregulated, it triggers the excessive release of pro-inflammatory mediators, causing tissue damage and contributing to pathologies. The NLRP3 inflammasome, a key player in inflammation, has garnered significant scientific attention due to its central role in immune regulation. While essential for homeostasis, NLRP3 overactivation contributes to chronic neuroinflammation. Understanding the cellular mechanisms underlying these processes is crucial for developing novel anti-inflammatory therapies. One promising source of bioactive compounds is *Cannabis sativa*, which contains a variety of pharmacologically active molecules. Among these, cannabinoids stand out for their therapeutic potential. Cannabigerol (CBG), a lesser-known cannabinoid, has been proposed as a modulator of NLRP3 activity, with claims of anti-inflammatory properties. However, the safety profile of CBG and the mechanisms underlying its purported anti-inflammatory effects remain poorly understood. OBJECTIVE: To evaluate the safety profile and anti-inflammatory efficacy of CBG in an in vitro model of neuroinflammation using BV-2 microglial cells. MATERIALS AND METHODS: CBG was tested at concentrations ranging from 0.01 uM to 100 uM to assess its effects on DNA damage, cellular viability, nitric oxide (NO) production, and reactive oxygen species (ROS) levels. BV-2 cells were exposed to lipopolysaccharide (LPS) and Nigericin to induce NLRP3 inflammasome activation, followed by treatment with CBG. MCC950, a well-established NLRP3 inhibitor, served as a positive control, while dimethyl sulfoxide was used as the vehicle control. Key parameters were re-evaluated post-treatment to determine the effects of CBG. RESULTS AND CONCLUSION: At 100 uM, CBG significantly reduced cell viability (~80%) and increased NO (~400%), and ROS (~900%) levels compared to untreated controls, leading to its exclusion from further analysis. At lower concentrations, only 0.01

uM CBG demonstrated no genotoxic effects. While certain CBG concentrations partially mitigated LPS + Nigericin-induced reductions in cell viability and NO elevation, they unexpectedly increased ROS levels in the neuroinflammation model. These findings suggest that CBG exhibits a favorable safety profile at low doses but produces inconsistent anti-inflammatory effects. Further studies are necessary to fully elucidate the therapeutic potential of CBG and its mechanisms of action.

Keywords: Cannabigerol; Microglia; Inflammation; Oxidative stress; *in vitro* toxicology

Acknowledgments: CAPES