POSTER 159

Synthetic cannabinoids AMB-FUBINACA, ADB-FUBINACA, AB-CHMINACA and THJ-2201 impact on in vitro viability and proliferation of primary rat hippocampal neurons and SH-SY5Y cells

Rita Roque Bravo[1,2,*], Daniel Barbosa[3], Helena Carmo[1,2], João Pedro Silva[1,2], Félix Carvalho[1,2], Diana Dias da Silva[1,2,3]

[1]UCIBIO-REQUIMTE, Laboratory of Toxicology, Department of Biological Sciences, Faculty of Pharmacy, University of Porto, 4050-313 Porto, Portugal.

[2]Associated Laboratory i4HB – Institute for Health and Bioeconomy, Faculty of Pharmacy, University of Porto, 4050-313 Porto, Portugal.

[3]TOXRUN – Toxicology Research Unit, University Institute of Health Sciences, CESPU, CRL, 4585-116 Gandra, Portugal.

**✉rita.rdsb@gmail.com*

Doi: https://doi.org/10.51126/revsalus.v4iSup.426

Resumo

Introduction: Synthetic cannabinoids (SCs) are a subset of new psychoactive substances with pharmacological similarities to the main psychoactive principle of cannabis, Δ9-tetrahydrocannabinol (THC). However, unlike THC, which is a partial agonist of the cannabinoid receptors 1 and 2, SCs have proven to be more powerful agonists [1,2]. Recently, THC has been shown to promote senescence/aging [3,4]. As such, it is plausible that SCs are also capable to meddle with senescence processes and aggravate them, however this area is currently in need of research.**Objectives:** The present work aims to ascertain the effects of four SCs on cellular proliferation and viability, as a first approach to evaluate neuronal senescence. **Materials & Methods:** Two different in vitro models were employed, primary hippocampal neurons (PHN) isolated from Wistar rat embryos at E18-19 and the neuroblastoma cell line SH-SY5Y. Cells were exposed to AMB-FUBINACA, ADB-FUBINACA, AB-CHMINACA and THJ-2201, at the biologically-relevant concentrations 1pM, 1nM and 1μM. Cellular proliferation was evaluated in SH-SY5Y cells using the sulforhodamine B (SRB) assay, at 24h, 48h, 72, and 96h; cellular viability of PHN was assessed using the MTT reduction assay, after 24h exposure. Statistical treatment of data was done using a non-parametric analysis followed by the Kruskal-Wallis test for multiple comparisons. **Results:** The preliminary results obtained for viability assessment of PHN showed no significant differences between the solvent control (100±3.08%) and the tested SCs, with the highest concentration of AMB-FUBINACA and AB-CHMINACA showing 87.33±4.38 and 90.62±5.34% viability ($p<0.05$), respectively. In terms of the proliferation assessment, at 96h, SH-SY5Y cells exposed to AMB-FUBINACA and ADB-FUBINACA presented significant increases in proliferation rates at all concentrations (1μM, 1nM and 1pM, respectively: 1055%, 1152%, 1152% for AMB-FUBINACA; 977%, 1026%, 1067% for ADB-FUBINACA), compared to solvent control (821%) ($p<0.05$).

Conclusions: These results aid in enlightening SCs exposure effects over two distinct neuronal cells models (cell line vs. primary neurons) and how they affect natural neuronal senescence (since accelerated proliferation could precipitate senescence). Further studies using specific markers for senescence are the next step.

Keywords: synthetic cannabinoids; proliferation/senescence; neurons; new psychoactive substances

References:

[1] European Monitoring Centre for Drugs and Drug Addiction. Synthetic cannabinoids in Europe – a review, Publications Office of the European Union, Luxembourg, 2021

[2] Alves VL, Goncalves JL, Aguiar J, Teixeira HM, Camara JS. The synthetic cannabinoids phenomenon: from structure to toxicological properties. A review. Crit Rev Toxicol 50:359-82, 2020

[3] Battistella G, Fornari E, Annoni JM, Chtioui H, Dao K, Fabritius, M, Favrat, B, Mall, JF, Maeder, P, Giroud, C. Long-term effects of cannabis on brain structure. Neuropsychopharmacology 39:2041-8, 2014

[4] Vakonaki E, Tzatzarakis M, Tsiminikaki K, Nathena D, Fragkiadaki P, Kalliantasi, K, Kanaki, K, Vaki, G, Plaitis, S, Tsoukalas, D, Alegakis, A, Spandidos, DA, Tsatsakis, A. Effect of chronic and heavy drug abuse on biological aging. World Academy of Sciences Journal 1:67-73, 2019

Acknowledgements: This work was supported by FCT—Fundação para a Ciência e a Tecnologia (projects UIDP/04378/2021 and UIDB/04378/2021 of the Applied Molecular Biosciences—UCIBIO), the project LA/P/0140/2021 of the Associate Laboratory Institute for Health and Bioeconomy—i4HBM and the PhD grant 2020.04493.BD.