BOOK OF ABSTRACTS

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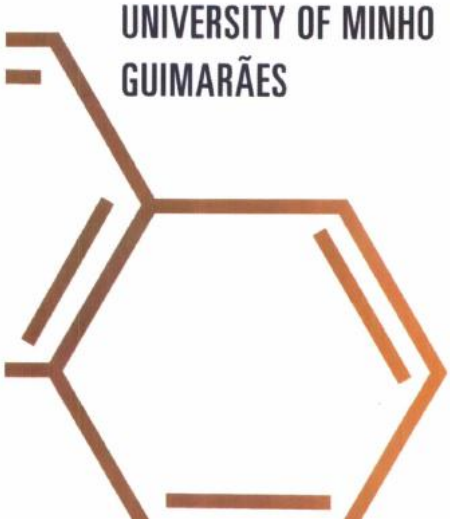

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SPB

The impact of phyto and synthetic cannabinoids in placental cytotrophoblast cells turnover [P8/07]

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Synthetic cannabinoids (SCs) were developed by the pharmaceutical industry to probe the endocannabinoid system or be used as potential therapeutics. Nevertheless, in recent years their use for recreational purposes, as psychoactive drugs in products such as "spice" is increasing and their impact in physiological processes is unknown. SCs have greater binding affinity to cannabinoid receptors (CBs) than Δ9-tetrahydrocannabinol (THC), the primary psychoactive compound of *Cannabis sativa*. A balanced proliferation, apoptosis and differentiation in cytrophoblast cells, the specialized placental epithelial cells, is crucial for placental development. Alterations in these processes are associated with gestational-related complications, such as preeclampsia, intrauterine growth restriction or miscarriages. In this study, we investigated the impact of the SCs WIN 55,212-2 and JWH-122 and of the phytocannabinoid THC on primary cultures of cytotrophoblasts and BeWo cell model. Cell viability was analysed by MTT assay and LDH release. Caspase -3/-7 and -9 activities were measured by luminescence whereas alterations in mitochondrial transmembrane potential (ΔΨm) and reactive oxygen species formation (ROS) were evaluated by fluorimetry. SCs are able to cause cytotrophoblast apoptosis. In primary cultures, WIN 55,212-2 induced caspase-3/7 and 9 activation, as well as loss in Δψm without ROS/RNS generation while in BeWo cells JWH-122 caspase activation and loss in Δψm were accompanied by ROS production. THC induced a decrease on cell viability in concentration-dependent manner though the underlying molecular mechanisms are under investigation. Being apoptosis essential for trophoblasts cell turnover our results highlight the impact of exogenous administration of cannabinoids either by recreational or medicinal use in placental development.

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