Antiproliferative effect of cannabinoids and CBD-derived compounds in human cell lines

Margherita Gallicchio, Arianna Binello, Alessandro Barge, Valentina Boscaro.

Dipartimento di Scienza e Tecnologia del Farmaco, Università degli Studi di Torino, Torino

Background

Cannabis sativa possessed biological and therapeutic properties that are principally linked to cannabinoids, the main constituent of the plant. Its clinical use is limited by the psychoactive effects of delta-9-tetrahydorcannabinol (THC) contained in cannabis, also if the therapeutic potential of cannabinoids has become increasingly evident, particularly in neurodegenerative diseases [1]. Cannabinoids interact with CB1 and CB2, two G-protein coupled receptors, mainly expressed in the central nervous system and in the peripheral nervous system, respectively [2].

We studied the antiproliferative effect of cannabidiol (CBD), THC and some CBD-derived compounds synthetized in the laboratory of Organic Chemistry of Prof. Barge: monomethyil-CBD, dimetyl-CBD and bis(oxiranylmethyl)-CBD. We performed antiproliferative assay on four cell lines, SH-SY5Y, a neuroblastoma cell line, THP-1, a human monocyte cell line, HT-29 and HCT-116 two colorectal cancer cell lines. The firsts two cell lines were chosen since in literature the neuroprotective effects of cannabinoids have been correlated not only to neuronal activity, but also to effects on immune system; the other two as screening on tumoral cell lines. Moreover, we evaluated the ability of these substances to reduce the cytotoxicity induced by 6-hydroxydopamine (6-OHDA) in SH-SY5Y, a Parkinson model in vitro.

Methods

The phytocannabinoids and the compounds have been tested for times ranging from 48 to 72 hours and concentrations between 0,4 and 30 μM. The anti-proliferative effect was assessed using the Cell-Titer Glo (Promega) assay. In addition, the ability of CBD, THC and all the compounds to reduce the cytotoxicity induced by 6-hydroxydopamine (6-OHDA) in SH-SY5Y, a Parkinson model in vitro, was evaluated [3].

Results

CBD and THC showed no toxicity in all the cell lines tested after 48-72 hours of treatment. Among the compounds, only the monomethyil-CBD was able to inhibit cell viability in all cell lines, in a range of concentrations between 3,3-30 μM.

Conclusions

All the cell lines were insensitive to CBD, THC and other compounds. Only the monomethyil-CBD was able to reduce cell viability in all cell lines, in a concentration- but no time-dependent way. In the future, times of treatment will be modulated, and the compounds will be tested even in an in vitro Alzheimer model.

1. Campos AC, Fogaça MV, Sonego AB, Guimarães FS. Cannabidiol, neuroprotection and neuropsychiatric disorders. *Pharmacol Res*. **2016**;112:119–127.

2. Zou S, Kumar U. Cannabinoid Receptors and the Endocannabinoid System: Signaling and Function in the Central Nervous System. *Int J Mol Sci*. **2018**;19(3):833.

3. Lopes FM, Schröder R, da Frota ML Jr, et al. Comparison between proliferative and neuron-like SH-SY5Y cells as an in vitro model for Parkinson disease studies. *Brain Res*. **2010**;1337:85–94.