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[Save Article to My Profile](#) [Download Citation](#)[< Previous Abstract](#) | [Next Abstract >](#)[Abstract](#) | [References](#) | Full Text: [HTML](#) | [Related Articles](#) | [Citation Tracking](#)**Research Article****High concentrations of cannabinoids activate apoptosis in human U373MG glioma cells**M. Widmer <sup>1 a</sup>, O. Hanemann <sup>2</sup>, J. Zajicek <sup>1 \*</sup><sup>1</sup>Clinical Neurology, Institute of Biomedical and Clinical Science, Peninsula Medical School, University of Plymouth, Plymouth, United Kingdom<sup>2</sup>Clinical Neurobiology, Institute of Biomedical and Clinical Science, Peninsula Medical School, University of Plymouth, Plymouth, United Kingdomemail: J. Zajicek ([john.zajicek@phnt.swest.nhs.uk](mailto:john.zajicek@phnt.swest.nhs.uk))<sup>\*</sup>Correspondence to J. Zajicek, Chair of Clinical Neurology, Peninsula Medical School, Tamar Science Park, Plymouth PL6 8BU, Devon, United Kingdom<sup>a</sup>Current address: Merck Chemicals Ltd., Boulevard Industrial Park, Padge Road, Beeston, Nottingham NG9 2JR, UK**KEYWORDS**

glioma • U373MG • cannabinoid receptors • CB1

**ABSTRACT**

Cannabinoids bind to two G-protein-coupled receptors, CB1 and CB2, expressed by neurons and cells of the immune system, respectively. Glioma cells (astrocyte-derived brain tumor cells) express cannabinoid receptors, and numerous in vitro and in vivo studies performed in rodents have concluded that apoptosis could be induced by cannabinoids in these cells. Whether this also applies to human cells is controversial; we, therefore, assessed the effect of cannabinoids on human glioma cell viability with the human astrocytoma cell line U373MG. We report here that U373MG human glioma cells are sensitive only to high concentrations of cannabinoids (>5  $\mu$ g/ml for  $\Delta^9$ -THC). Similar concentrations of the compounds promoted a rapid activation of extracellular-regulated kinase and c-Jun NH2-terminal kinase, suggesting that cannabinoid receptors are functional in U373MG cells. Nevertheless, these kinases are not involved in cannabinoid-induced cell death in U373MG cells, insofar as blocking their activation with specific inhibitors does not reduce cell death. CB1 is expressed in U373MG cells and is involved in cannabinoid-induced cell death, in that blocking its activation with a specific antagonist (AM251) almost totally prevented cell death following incubation of the cells with  $\Delta^9$ -THC. In addition, as already reported, some cannabinoids may have modest proliferative properties in U373MG cells. Human U373MG glioma cells are sensitive only to very high, pharmacologically irrelevant concentrations of cannabinoids, so it seems unlikely that cannabinoids would constitute promising molecules for treating malignant astrocytoma; they do not induce glioma cell death at doses that could be applied safely to humans. © 2008 Wiley-Liss, Inc.

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