Gliomas/Cancer

Gliomas (tumors in the brain) are especially aggressive malignant forms of cancer, often resulting in the death of affected patients within one to two years following diagnosis. There is no cure for gliomas and most available treatments provide only minor symptomatic relief.

A review of the modern scientific literature reveals numerous preclinical studies, some case reports, and one controlled clinical study demonstrating cannabinoids' ability to act as antineoplastic agents, particularly on glioma cell lines.

Writing in the September 1998 issue of the journal *FEBS Letters*, investigators at Madrid's Complutense University, School of Biology, first reported that delta-9-THC induced apoptosis (programmed cell death) in glioma cells in culture. Investigators followed up their initial findings in 2000, reporting that the administration of both THC and the synthetic cannabinoid agonist WIN 55,212-2 "induced a considerable regression of malignant gliomas" in animals. Researchers again confirmed cannabinoids' ability to inhibit glioma tumor growth in animals in 2003.

Italian investigators that same year similarly reported that the non-psychoactive cannabinoid, cannabidiol (CBD), inhibited the growth of various human glioma cell lines *in vivo* and *in vitro* in a dose dependent manner. Writing in the November 2003 issue of the *Journal of Pharmacology and Experimental Therapeutics Fast Forward*, researchers concluded, "Non-psychoactive CBD ... produce[s] a significant anti-tumor activity both *in vitro* and *in vivo*, thus suggesting a possible application of CBD as an antineoplastic agent."

In 2004, Guzman and colleagues reported that cannabinoids inhibited glioma tumor growth in animals and in human glioblastoma multiforme (GBM) tumor samples by altering blood vessel morphology (e.g., VEGF pathways). Writing in the August 2004 issue of *Cancer Research*, investigators concluded, "The present laboratory and clinical findings provide a novel pharmacological target for cannabinoid-based therapies."

Investigators at the California Pacific Medical Center Research Institute reported that the administration of THC on human glioblastoma multiforme cell lines decreased the proliferation of malignant cells and induced cell death more rapidly than did the administration of the synthetic cannabinoid agonist WIN 55,212-2. Researchers also noted that THC selectively targeted malignant cells while ignoring healthy ones in a more profound manner than the synthetic alternative. A separate preclinical trial reported that the combined administration of THC and the pharmaceutical agent temozolomide (TMZ) "enhanced autophagy" (programmed cell death) in brain tumors resistant to conventional anti-cancer treatments.

Guzman and colleagues have also reported that THC administration decreases recurrent glioblastoma multiforme tumor growth in some patients diagnosed with recurrent GBM. In the first ever pilot clinical trial assessing the use of cannabinoids and GBM, investigators found that the intratumoral administration of THC was associated with reduced tumor cell proliferation in two of
nine subjects. "The fair safety profile of THC, together with its possible anti-proliferative action on tumor cells reported here and in other studies, may set the basis for future trials aimed at evaluating the potential antitumoral activity of cannabinoids," investigators concluded. Several additional investigators have also recently called for further exploration of cannabis-based therapies for the treatment of glioma. A case report, published in 2011 in the journal of the International Society for Pediatric Neurosurgery, also documents the spontaneous regression of residual brain tumors in two children coinciding with the subjects use of cannabis.

In addition to cannabinoids' ability to moderate glioma cells, separate preclinical studies demonstrate that cannabinoids and endocannabinoids can also inhibit the proliferation of other various cancer cell lines, including breast carcinoma, prostate carcinoma, colorectal carcinoma, gastric adenocarcinoma, skin carcinoma, leukemia cells, neuroblastoma, lung carcinoma, uterus carcinoma, thyroid epithelioma, pancreatic adenocarcinoma, cervical carcinoma, oral cancer, biliary tract cancer (cholangiocarcinoma), urological cancers, and lymphoma, among others. In some instances, improved anti-cancer activity has been reported when cannabinoids are administered in concert with one another, rather than in isolation. A 2013 case report published in the journal Case Reports in Oncology also reports successful treatment with cannabis extracts in a 14-year-old patient diagnosed with an aggressive form of acute lymphoblastic leukemia. Population studies also report an inverse relationship between cannabis use and the prevalence of various types of cancer, including lung cancer, head and neck cancer, and bladder cancer.

Experts acknowledge that there exists "solid scientific evidences supporting that cannabinoids exhibit a remarkable anticancer activity in preclinical models of cancer," and that cannabinoids may one day "represent a new class of anticancer drugs that retard cancer growth, inhibit angiogenesis and the metastatic spreading of cancer cells." Presently, medical cannabis use is prevalent among patients with various types of cancer, though many say that they "desire but are not receiving information about cannabis use during their treatment from oncology providers." Despite an absence of clinical trials, "abundant anecdotal reports describe patients having remarkable responses to cannabis as an anticancer agent, especially when taken as a high-potency orally ingested concentrate. … Human studies should be conducted to address critical questions related to the foregoing effects.

REFERENCES


The National Organization for the Reform of Marijuana Laws (norml.org)


27. Di Marzo et al. 2006. op. cit


The National Organization for the Reform of Marijuana Laws (norml.org)


50 Torres et al. 2011.op. cit.

51 Scott et al. 2013. op. cit.


The National Organization for the Reform of Marijuana Laws (norml.org)

Thomas et al. 2015. Association between cannabis use and the risk of bladder cancer: Results from the California Men's Health Study. *Urology* 85: 388-393.


Pergam et al. 2017. Cannabis use among patients at a comprehensive cancer center in a state with legalized medicinal and recreational use. *Cancer* [online ahead of print].