

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 and one pilot 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.[1] 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.[2] Researchers again confirmed cannabinoids' ability to inhibit tumor growth in animals in 2003.[3]

That same year, Italian investigators at the University of Milan, Department of Pharmacology, Chemotherapy and Toxicology, 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." [4]

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." [5]

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 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.[6] 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.[7]

Guzman and colleagues have also reported that THC administration decreases recurrent glioblastoma multiforme tumor growth in 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.[8] Several additional investigators have also recently called for further exploration of cannabis-based therapies for the treatment of glioma.[9-11] A separate 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.[12]

In addition to cannabinoids' ability to moderate glioma cells, separate studies demonstrate that cannabinoids and endocannabinoids can also inhibit the proliferation of other various cancer cell lines, including breast carcinoma,[13-17] prostate carcinoma,[18-22] colorectal carcinoma,[23-24] gastric adenocarcinoma,[25] skin carcinoma,[26] leukemia cells,[27-30] neuroblastoma,[31-32] lung carcinoma,[33-34] uterus carcinoma,[35] thyroid epithelioma,[36] pancreatic adenocarcinoma,[37-38] cervical carcinoma,[39] oral cancer,[40] biliary tract cancer (cholangiocarcinoma)[41] and lymphoma.[42-43]

Consequently, some experts now believe that cannabinoids "may represent a new class of anticancer drugs that retard cancer growth, inhibit angiogenesis and the metastatic spreading of cancer cells." [44-45] ... "[T]hese compounds are inexpensive to produce and making better use of their unique properties could result in much more cost effective anti-cancer drugs in future." [46] Israeli clinicians are presently recommending that cannabinoid treatment "be offered to ... patients in the earlier stages of cancer." [47]

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