

# PEER REVIEWED CANNABIS MEDICAL STUDIES





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CANCER TREATMENT Cannabis and Cannabinoids (PDQ®)-Health Professional Version

## "Cannabinoids may

cause antitumor effects by various mechanisms,

including induction of cell death, inhibition of cell growth, and inhibition of tumor angiogenesis invasion and metastasis.[9-12] Two reviews summarize the molecular mechanisms of action of cannabinoids as antitumor agents.[13,14] Cannabinoids appear to kill tumor cells but do not affect their nontransformed counterparts..."

#### **Antitumor Effects**

One study in mice and rats suggested that cannabinoids may have a protective effect against the development of certain types of tumors.[3] During this 2-year study, groups of mice and rats were given various doses of THC by gavage. A dose-related decrease in the incidence of hepatic adenoma tumors and hepatocellular carcinoma (HCC) was observed in the mice. Decreased incidences of benign tumors (polyps and adenomas) in other organs (mammary gland, uterus, pituitary, testis, and pancreas) were also noted in the rats. In another study, delta-9-THC, delta-8-THC, and cannabinol were found to inhibit the growth of Lewis lung adenocarcinoma cells *in vitro* and *in vivo*.[4] In addition, other tumors have been shown to be sensitive to cannabinoid-induced growth

inhibition.[5-8]

Cannabinoids may cause antitumor effects by various mechanisms, including induction of cell death, inhibition of cell growth, and inhibition of tumor angiogenesis invasion and metastasis.[9-12] Two reviews summarize the molecular mechanisms of action of cannabinoids as antitumor agents.[13,14] Cannabinoids appear to kill tumor cells but do not affect their nontransformed counterparts and may even protect them from cell death. For example, these compounds have been shown to induce apoptosis in glioma cells in culture and induce regression of glioma tumors in mice and rats, while they protect normal glial cells of astroglial and oligodendroglial lineages from apoptosis mediated by the CB1 receptor.[9]

The effects of delta-9-THC and a synthetic agonist of the CB2 receptor were investigated in HCC.[15] Both agents reduced the viability of HCC cells *in vitro* and demonstrated antitumor effects in HCC subcutaneous xenografts in nude mice. The investigations documented that the anti-HCC effects are mediated by way of the CB2 receptor. Similar to findings in glioma cells, the cannabinoids were shown to trigger cell death through stimulation of an endoplasmic reticulum stress pathway that activates autophagy and promotes apoptosis. Other investigations have confirmed that CB1 and CB2 receptors may be potential targets in non-small cell lung carcinoma [16] and breast cancer.[17]

An *in vitro* study of the effect of CBD on programmed cell death in breast cancer cell linesfound that CBD induced programmed cell death, independent of the CB1, CB2, or vanilloid receptors. CBD inhibited the survival of both estrogen receptor–positive and estrogen receptor–negative breast cancer cell lines, inducing apoptosis in a concentration-dependent manner while having little effect on nontumorigenic mammary cells.[18] Other studies have also shown the antitumor effect of cannabinoids (i.e., CBD and THC) in preclinical models of breast cancer.[19,20] CBD has also been demonstrated to exert a chemopreventive effect in a mouse model of colon cancer.[21] In

this experimental system, azoxymethane increased premalignant and malignant lesions in the mouse colon. Animals treated with azoxymethane and CBD concurrently were protected from developing premalignant and malignant lesions. In *in vitro* experiments involving colorectal cancer cell lines, the investigators found that CBD protected DNA from oxidative damage, increased endocannabinoid levels, and reduced cell proliferation. In a subsequent study, the investigators found that the antiproliferative effect of CBD was counteracted by selective CB1 but not CB2 receptor antagonists, suggesting an involvement of CB1 receptors.[22]



Algunos Usos Terapéuticos Documentados:

#### 1 - Lung Cancer

https://www.ncbi.nlm.nih.gov/pubmed/22198381?do pt=Abstract

<u>FASEB J.</u> 2012 Apr;26(4):1535-48. doi:
10.1096/fj.11-198184. Epub 2011 Dec 23. **Cannabidiol inhibits lung cancer cell invasion and metastasis via intercellular adhesion molecule-1.**<u>Ramer R1</u>, Bublitz K, Freimuth N, Merkord J, Rohde H, Haustein M, Borchert P, Schmuhl E, Linnebacher

#### <u>M, Hinz B</u>.

#### Author information

Institute of Toxicology and Pharmacology, Department of General Surgery, University of Rostock, Schillingallee 70, D-18057 Rostock, Germany.

#### Abstract

Cannabinoids inhibit cancer cell invasion via tissue inhibitor increasing of matrix metalloproteinases-1 (TIMP-1). This study investigates the role of intercellular adhesion molecule-1 (ICAM-1) within this action. In the lung cancer cell lines A549, H358, and H460, cannabidiol (CBD; 0.001-3 µM) elicited concentration-dependent ICAM-1 up-regulation compared to vehicle via cannabinoid receptors, transient receptor potential vanilloid 1, and p42/44 mitogen-activated protein kinase.

2 - Anti Tumor / Hepato Carcinoma (Liver Cancer)

https://www.ncbi.nlm.nih.gov/pubmed/21475304?do pt=Abstract

Cell Death Differ. 2011 Jul;18(7):1099-111. doi: 10.1038/cdd.2011.32. Epub 2011 Apr 8. Anti-tumoral action of cannabinoids on hepatocellular carcinoma: role of AMPKdependent activation of autophagy. <u>Vara D</u>1, <u>Salazar M</u>, <u>Olea-Herrero N</u>, <u>Guzmán M</u>, <u>Velasco G</u>, <u>Díaz-Laviada I</u>.

#### **Erratum in**

Cell Death Differ. 2011 Jul;18(7):1237.

#### Abstract

Hepatocellular carcinoma (HCC) is the third cause of cancer-related death worldwide. When these tumors are in advanced stages, few therapeutic options are available. Therefore, it is essential to search for new treatments to fight this disease. In this study, we investigated the effects of cannabinoids. We found that  $\Delta(9)$ -tetrahydrocannabinol ( $\Delta(9)$ -THC, the main active component of Cannabis sativa) reduced the viability of the human HCC cell lines HepG2 (human hepatocellular liver carcinoma cell line)

#### 3 - Breast Cancer

https://www.ncbi.nlm.nih.gov/pubmed/21566064?do pt=Abstract

<u>Mol Cancer Ther.</u> 2011 Jul;10(7):1161-72. doi: 10.1158/1535-7163.MCT-10-1100. Epub 2011 May 12.

Cannabidiol induces programmed cell death in breast cancer cells by coordinating the cross-talk

#### between apoptosis and autophagy.

Shrivastava A1, Kuzontkoski PM, Groopman JE, Prasad A.

### Author information

#### Abstract

Cannabidiol (CBD), a major nonpsychoactive constituent of cannabis, is considered an antineoplastic agent on the basis of its in vitro and in vivo activity against tumor cells. However, the exact molecular mechanism through which CBD mediates this activity is yet to be elucidated. Here, we have shown CBD-induced cell death of breast cancer cells,

4 - Epilepsy

http://edition.cnn.com/2017/05/24/health/cannabidiol -epilepsy-study/index.html https://www.ncbi.nlm.nih.gov/pubmed/26282273

"These studies suggest that CBD avoids the psychoactive effects of the endocannabinoid system to provide a well-tolerated, promising therapeutic for the treatment of seizures, while whole-plant cannabis can both contribute to and reduce seizures."

<u>Neurotherapeutics.</u> 2015 Oct;12(4):747-68. doi: 10.1007/s13311-015-0375-5.

### **Cannabinoids and Epilepsy.**

Rosenberg EC1, Tsien RW1, Whalley BJ2, Devinsky O3.

### Author information

#### Abstract

Cannabis has been used for centuries to treat seizures. Recent anecdotal reports, accumulating animal model data, and mechanistic insights have raised interest in cannabis-based antiepileptic therapies.

#### <u>5 - Autismo</u>

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5535 348/

J Clin Diagn Res. 2017 Jun; 11(6): CE01–CE03. Published online 2017 Jun 1. doi: 10.7860/JCDR/2017/23862.9969 PMCID: PMC5535348 Role of Endocannabinoids on Neuroinflammation in Autism Spectrum Disorder Prevention Syed Shahid Habib,∞1 Khalid Al-Regaiey,2 Shahid Bashir,3 and Muhammad Iqbal4 Author information ► Article notes ► Copyright and License information ►



Dr Tashkin UCLA:

"Taking a hit of marijuana has been known to stop a full blown asthma attack." (Personal communication with Dr. Donald Tashkin, December 12, 1989 and December 1, 1997.)

(Tashkin, Dr. Donald, UCLA Pulmonary Studies (for smoked marijuana),

1969-97; Ibid., asthma studies, 1969-76; Cohen, Sidney & Stillman, Therapeutic Potential of Marijuana, 1976; Life Insurance Actuarial rates; Life shortening effects of childhood asthma, 1983.)

#### 7 - GLAUCOMA

Fourteen percent of all blindness in America is from glaucoma, a progressive loss of vision. Cannabis smoking would benefit 90% of our 2.5 million glaucoma victims, and is two to three times as effective as any current medicines for reducing ocular pressure! Cannabis use has no toxic side effects to the liver and kidneys; nor is there any danger of the occasional sudden death syndromes associated with the legal pharmaceutical glaucoma drugs/drops. Many California eye doctors, through the 1970s, '80s, and '90s, discreetly advised their patients to use "street" marijuana in addition to (or to mitigate) their toxic legal glaucoma medicines. Since November 1996, California doctors can legally recommend, advise or tacitly approve cannabis use by their glaucoma patients who may then grow and smoke their own marijuana, or go to the few remaining Cannabis Buyers' Clubs to acquire medical marijuana. (Harvard; Hepler & Frank, 1971, UCLA; Medical College of Georgia; U. of North Carolina School of Medicine, 1975; Cohen & Stillman, Therapeutic Potential of Marijuana, UCLA, 1976; National Eye Institute; Records of Bob Randolph/Elvy Musika, 1975, 1998.)

#### <mark>8 - TUMORS</mark>

A tumor is a mass of swollen tissue. Researchers at the Medical College of Virginia discovered that cannabis is an incredibly successful herb for reducing many types of tumors, both benign and malignant (cancerous). The DEA and other federal agencies had ordered these tumor studies done after hearing erroneous reports of possible immunicological problems associated with cannabis smoke. But, in 1975, instead of health problems, an apparent medical breakthrough occurred and successful tumor reductions were recorded! Following this remarkably positive discovery by the Medical College of Virginia, orders were immediately handed down by the DE and the National Institute of Health to defund all furter cannabis/tumor research and reporting! Millions of Americans who might be alive today are dead because of these and other DEA orders regarding marijuana. Since 1996, the Medical College of Virginia has again applied to receive grants for cannabis research and has been turned down by the DEA.

### <mark>9 - NAUSEA RELIEF (e.g., AIDS, CANCER</mark> THERAPY, SEA SICKNESS)

Though it is known to be extremely damaging to the immune system,

chemotherapy is claimed by practitioners to benefit cancer and AIDS patients. But chemo has some other serious side effects too, including nausea. "Marijuana is the best agent for control of nausea in cancer chemotherapy," according to Dr. Thomas Ungerleider, who headed California's Marijuana for Cancer research program from 1979 to 1984.

This is also true in AIDS and even in the unsettled otion in sickness. stomach common m Pharmaceutical nausea control drugs come in pills that are often swallowed by the patient, only to be thrown back up. Because cannabis can be ingested as smoke, it stays in the system and keeps working even if vomiting continues. Throughout the state's 10-year Compassionate Marijuana Medical law, George Deukmejian, both as attorney general and as governor, with no regard for the suffering or dying cancer patients, made it virtually impossible for them to get cannabis. Californa Governor Pete Wilson was following the same course until the medical marijuana initiative passed in November 1996.

#### <u>10 - EPILEPSY, MULTIPLE SCLEROSIS,</u> BACK PAIN, MUSCLE SPASMS

Cannabis is beneficial for 60% of all epileptics. It is definitely the best treatment for many, but not all types of epilepsy, and for victims' post-seizure mental traumas. Cannabis extract is more effective than Dilantin (a commonly prescribed antiepileptic with severe side effects). Medical World News reported in 1971: "Marijuana . . . is probably the most potent anti-epileptic known to medicine today." (Mikuriya, Tod H., M.D., Marijuana Medical Papers, 1839-1972, page xxii.) Cannabis users' epileptic seizures are of less intensity than the more dangerous seizures experienced by users of pharmaceuticals. Similarly, smoking cannabis has proven to be a major source of relief for multiple sclerosis, which affects the nervous system and is characterized by muscular weakness, tremors, etc. Aside from addictive morphine, cannabis, whether smoked or applied as an herbal pack or poultice, is also the best muscle relaxant, back spasm medicine and general antispasmodic medication on our planet. In September 1993, in Santa Cruz County, California, Sheriffs rearrested eqileptic Valerie Corral and confiscated the five marijuana plants she was growing for medicine even though 77% of the citizens of Santa Cruz voted in November 1992 to instruct local law enforcement not to prosecute medical marijuana users. Charges against Corral had been dropped earlier in March 1993 because she was the first person in California to meet all six points of a medical necessity defense. In 1997, Valerie, who runs a compassionate use club, was named Citizen of the Year in Santa Cruz. (Cohen & Stillman,

Therapeutic Potential of Marijuana, 1976; Consult U.S. Pharmacopoeia prior to 1937; Mikuriya, Tod H., M.D., Marijuana Medical Papers, 1839-1972.)

#### **11- ANTIBIOTIC CBD DISINFECTANTS**

Young un-budded hemp plants provide extractions of CBDs (cannabidiolic acids). There are many antibiotic uses of the cannabidiols, including treatment for gonorrhea. A 1990 Florida study indicated its use in treating herpes. The acid side of tetrahydrocannabinol, cannabidiols occur inversely to the amount of the plant's THC and is therefore more acceptable to prohibitionists because "it won't get you high." For virtually any disease or infection that can be treated with terramycin, cannabis derivatives did better in Czechoslovakian studies, 1952-1955. The Czechs in 1997 still published farm crop reports on strategies to grow cannabidiol rich hemp. (Also see Cohen & Stillman, Therapeutic Potential of Marijuana; Mikuriya, Tod H., M.D., Marijuana Medical Papers; Roffman, Marijuana as Medicine, 1982; International Farm Crop abstracts.)

### 12 - ARTHRITIS, HERPES, CYSTIC FIBROSIS AND RHEUMATISM

Cannabis is a topical analgesic.2 Until 1937, virtually all corn plasters, mustard plasters, muscle ointments, and fibrosis poultices were made from or with cannabis extracts. Rheumatism was treated throughout South America until the 1960s with hemp leaves and/or flower tops heated in water or alcohol and placed on painful joints. In fact, this form of herbal medicine is still widely used in rural areas of Mexico, Central and South America, and by California Latinos for relief of rheumatism and arthritis pain. Direct contact with THC killed herpes virus in a University of South Florida (Tampa) 1990 research study by Dr. Gerald Lancz, who warns that "smoking marijuana will not cure herpes." However, anecdotal reports indicate a faster drying and healing of the outbreak after topical application of "strong bud," soaked in rubbing alcohol and crushed into a paste.

#### **13 - LUNG CLEANER AND EXPECTORANT**

Cannabis is the best natural expectorant to clear the human lungs of smog, dust and the phlegm associated with tobacco use. Marijuana smoke effectively dilates the airways of the lungs, the bronchi, opening them to allow more oxygen into the lungs. It is also the best natural dilator of the tiny airways of the lungs, the bronchial tubes making cannabis the best overall bronchial dilator for 80% of the population (the remaining 20% sometimes show minor negative reactions). (See section on asthma - a disease that closes these passages in spasms - UCLA Tashkin studies, 1969-97; U.S. Costa Rican, 1980-82; Jamaican studies 1969-74, 76.) Statistical evidence - showing up consistently as anomalies in matched populations indicates that people who

smoke tobacco cigarettes are usually better off and will live longer if they smoke cannabis moderately, too. (Jamaicna, Costa Rican studies.) Millions of Americans have given up or avoided smoking tobacco products in favor of cannabis, which is not good news to the powerful tobacco lobby - Senator Jesse Helms and his cohorts. A turn-of-the-century grandfather clause in U.S. tobacco law allows 400 to 6,000 additional chemicals to be added. Additions since then to the average tobacco cigarette are unknown, and the public in the U.S. has no right to know what they are. Many joggers and marathon runners feel cannabis use cleans their lungs, allowing better endurance. The evidence indicates that cannabis use will probably increase these outlaw American marijuana-users' lives by about one to two years - yet they may lose their rights, property, children, state licenses, etc., just for using that safest of substances: cannabis.

#### **14 - SLEEP AND RELAXATION**

Cannabis lowers blood pressure, dilates the arteries and reduces body temperature an average of onehalf degree, thereby relieving stress. Evening cannabis smokers in general report more restful sleep. Using cannabis allows most people a more complete rest with a higher amount of "alpha time" during sleep as compared with prescription or sleep-inducing patent sedatives. Prescription sleeping pills (the so called "legal, safe and effective" drugs) are often just synthesized analogs of truly dangerous plants like mandrake, henbane and belladonna. As late 1991, doctors, as pharmacists and drug companies were fighting off new legislation to restrict these often abused compounds. (L.A. Times, April 2, 1991). Unlike Valium, cannabis does not potentiate the effects of alcohol. It is estimated that cannabis could replace more than 50% of Valium, Librium, Thorazine, Stelazine, other "-zine" drugs and most sleeping pills. It is unconscionable that, over the past two decades, tens of thousands of parents have committed their own children, aged 11 to 17, to be treated by massive doses of so-called "-zine" drugs in order to get them off pot, at the urging of parent groups, the PDFA, the feds and administrators and doctors from federally approved, private and highprofit drug rehabilitation centers. Often, "-zine" drugs do work to stop these youths from using pot. They also stop a kid from loving his or her dog, too - and children stand a one-in-four chance of suffering from uncontrollable shaking for the rest of their lives.\* But at least they're not high. \* The U.S. Centers for Disease Control in Atlanta said that 20-40% of "-zine" drug users have or will develop permanent lifetime pasies (shakes), November 1983. These prescription neurotoxins are chemically related to the pesticide and warfare nerve gas Sarin. Hundreds of private drugrehabilitation centers and their leaders keep this policy alive and in front of the media, often quoting discredited reports from NIDA or DEA (see Chapter 16, debunking) - because

they earn fat profits selling their useless or destructive "marijuana treatment" for children. After all, a relapse just means using marijuana against after a number of bouts with an "authority." This is mind control and an attempt to destroy individual free will.

#### **15 THERAPEUTIC EMPHYSEMA POTENTIAL**

Medical research indicates that light cannabis smoking might be useful for a majority of mild emphysema victims. It would improve the quality of life for millions of sufferers and extend their life spans. The U.S. government and DEA (since 1976) saky the side effect of being "high" is not acceptable, no matter how many years or lives it saves; even though some 90 million Americans have tried marijuana and 25 to 30 million Americans have tried marijuana and 25 to 30 million Americans have tried marijuana and 25 to 30 million still smoke marijuana relaxationally, or use it responsibly as a form of daily selfmedication, without one single death from overdoes - ever! All research into the oxygen blood transfer effects cause by cannabis indicates that the chest (lung) pains, extremity pains,

shallowness of breath, and headaches we may experience on heavy smog days are usually alleviated by cannabis smoking throughout the day. Dr. Donald Tashkin, the U.S. government's leading scientist on marijuana pulmonary research, told us in December 1989\*, and again in December 1997, that you cannot get or potentiate emphysema with cannabis smoking. \* See Tashkin's Marijuana Pulmonary Research, UCLA, 1969-1997. Since 1981, this author has personally taken part in these studies and has continuously interviewed Tashkin on cannabis' medical indications; last personal interview was in December 1997.

#### <u> 16 - STRESS AND MIGRAINE HEADACHE</u> RELIEF

Most of all: it is best for the world's number one killer - stress. It can safely curtail or replace Valium, Librium, alcohol, or even Prozac, for millions of Americans. While cannabis intoxication varies with psychological set and social setting, "the most common response is a calm, mildly euphoric state in which time slows and a sensitivity to sights, sounds and touch his enhanced." In contrast to marijuana's safe. therapeutic action, benzodiazepine (Valium) abuse is the number one drug abuse problem in the country, and is responsible for more emergency room admissions in the United States than either cocaine- related problems or morphone and heroinrelated admissions combined.\* While tobacco constricts arteries, cannabis dilates (opens) them. Because migraine headaches are the result of artery spasms combined with over- relaxation of veins, the vascular changes cannabis causes in the covering of the brain (the meninges) usually make migraines disappear. Evidence of vascular change caused by cannabis can be seen in the user's red eyes, which are

extensions of the brain. However, unlike most other drugs, cannabis has no apparent effect on the vascular system in general, except for a slightly increased heart rate during the onset of the high.

#### **17- TO INCREASE APPETITE**

Users of marijuana often (but not always) experience "the munchies," a stimulated appetite for food, which, at this time, makes cannabis the very best medicine on the planet for anorexia. Hundreds of thousands of Americans in old age, convalescent wards or hospital situations have anorxia. Most could be helped by cannabis - yet these Americans are being denied a healthy life by governmental policy dictated by government police! This effect can also extend the lives of AIDS and pancreatic cancer (eat or die). However, the DEA and U.S. government prevented any research or use of cannabis in pancreatic cancer therapy since 1976. They have effectively allowed tens of thousands of people to die each year, denying them the right to live otherwise normal, healthy and productive lives.

IN ADDITION...

#### 18 - AIDS, DEPRESSION & HUNDREDS OF OTHER PRIMARY MEDICAL USES

One well known effect of THC is to life the spirit, or make you "high." Cannabis users in Jamaica praise ganja's benefits for meditation, concentration, consciousness-raising and promoting a state of well being and self assertiveness.5 This kind of attitude adjustment, along with a healthier appetite and better rest, often represents the difference between feeling like you are "dying of" AIDS or cancer and feeling like you are "living with" AIDS or cancer. Cannabis also eases small pains and some big ones and helps senior citizens live with aches and pains like arthritis, insomnia and debilitating infirmities, and enjoy life in greater dignity and comfort. Legend has it, and medical evidence indicates, that cannabis is the best overall treatment for dementia, senility, and maybe Alzheimer's disease, for longterm memory "gain" and hundreds of other benefits. U.S. statistics of the 1970s indicated

"gain" and hundreds of other benefits. U.S. statistics of the 1970s indicated that you will live eight to 24 years longer if you substitute daily cannabis use for daily tobacco and alcohol use. New research is outlawed, of course.

#### ACCEPTABLE RISKS

Every U.S. commission or federal judge who has studied the evidence has agreed that cannabis is one of the safest drugs known. With all its therapeutic uses, it has only one side effect that has been exaggerated as a concern: the "high." The DEA says this is not acceptable, so cannbis continues to be totally illegal in utter disregard for both doctor and patient. Every day we trust physicians determine whether to the risks associated with therapeutic, yet potentially dangerous drugs are acceptable for their patients. Yet, doctors are not allowed to prescribe the herb that Federal Judge Francis Young in 1988 called "one of the safest therapeutically active substances known to man." We don't put out doctors in charge of stopping violent crimes. The police, prosecutors and prison guards should not be in charge of which herbal therapies people may use to treat their personal health problems.

Footnotes:

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2. Cohen & Stillman, Therapeutic Potential of Marijuana, UCLA, 1976; Mikuriya, Tod H., M.D., Marijuana Medical Papers 1839-1972, Medi-Comp Press, Oakland, CA, 1973. 3. The Antibiotic Effect of Cannabis Indica, 1952- 53-55. The Antibacterial Effect of Cannabis Indica, 1955, from Marijuana Medical Papers; Cohen & Stillman, Therapeutic Potential of Marijuana, UCLA, 1976.

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