

Cannabis and Cancer

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Outline

- **The recent studies of cannabis for cancer**
- **PubMed - Clinical Trial Medical cannabis for Cancer**
- **National Cancer Institute - Cannabis and Cannabinoids**
- **American Cancer Society - Marijuana and Cancer**
- **WebMD - Medical Marijuana and Cancer**

CANNABIS VS. CANCER

THERAPEUTIC RELIEF OR CANCER KILLER?



COPS - Cannabis and Cancer 23 Aug 2019 - Narisa Kamkaen

<https://myfloridagreen.com/blog/cannabis-vs-cancer-therapeutic-relief-or-miracle-cure-2>

The TRUTH About CANCER

educate • expose • eradicate

“One of the advantages of cannabinoid-based medicines would be that they target specifically tumor cells. They don’t have any toxic effect on normal non-tumoral cells. This is an advantage with respect to standard chemotherapy that targets basically everything.”

- Dr. Christine Sanchez
Microbiologist , Complutense University,
Madrid, Spain



The recent studies of cannabis for cancer

- “The combination of cannabidiol and Delta9-tetrahydrocannabinol enhances the anticancer effects of radiation in an orthotopic murine **glioma model**” (Molecular Cancer Therapeutics, 2014)
- “Cannabinoids inhibit the vascular endothelial growth factor pathway in **gliomas** (aka that halt their growth)” (The Journal of Cancer Research & American Journal of Cancer, 2004)
- “Cannabidiolic acid, a major cannabinoid in fibre-type cannabis, is an inhibitor of MDA-MB-231 **breast cancer** cell migration” (Toxicology Letters, 2012)
- “Cannabidiol inhibits **lung cancer** cell invasion and metastasis via intercellular adhesion molecule-1” (The FASEB Journal, 2012)

The recent studies of cannabis for cancer

- “Cannabinoids Induce Apoptosis of **Pancreatic Tumour** Cells via Endoplasmic Reticulum Stress–Related Genes” (Cancer Research, 2006)
- “Cannabis-based medicine reduces multiple pathological processes in **cancerous mice**” (Journal of Alzheimer’s Disease, 2015)
- “Inhibition of **skin tumour** growth and angiogenesis in vivo by action of cannabinoid receptors” (Journal of Clinical Investigation, 2003)

PubMed: clinical trial cannabis for cancer

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[Cannabis Use and Incidence of Testicular Cancer: A 42-Year Follow-up of Swedish Men between 1970 and 2011.](#)
Callaghan RC et al. **Cancer** Epidemiol Biomarkers Prev. (2017)

[A selective review of medical cannabis in cancer pain management.](#)
Blake A et al. Ann Palliat Med. (2017)

[Cannabis use among patients at a comprehensive cancer center in a state with legalized medicinal and recreational use.](#)
Pergam SA et al. **Cancer**. (2017)

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Complementary & Alternative Medicine (CAM)

CAM for Patients

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Cannabis and Cannabinoids (PDQ®)-Health Professional Version

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Cannabis Pharmacology

- When oral *Cannabis* is ingested, there is a low (6%–20%) and variable oral bioavailability.
- Peak plasma concentrations of delta-9-tetrahydrocannabinol (THC) occur after 1 to 6 hours and remain elevated with a terminal half-life of 20 to 30 hours.
- Taken by mouth, delta-9-THC is initially metabolized in the liver to 11-OH-THC, a potent psychoactive metabolite.
- Inhaled cannabinoids are rapidly absorbed into the bloodstream with a peak concentration in 2 to 10 minutes, declining rapidly for a period of 30 minutes and with less generation of the psychoactive 11-OH metabolite.

Cannabis Pharmacology

- Cannabinoids are known to interact with the hepatic cytochrome P450 enzyme system.
- In one study, 24 cancer patients were treated with intravenous irinotecan (600 mg, n = 12) or docetaxel (180 mg, n = 12), followed 3 weeks later by the same drugs concomitant with medicinal *Cannabis* taken in the form of an herbal tea for 15 consecutive days, starting 12 days before the second treatment.
- The administration of *Cannabis* did not significantly influence exposure to and clearance of irinotecan or docetaxel, although the herbal tea route of administration may not reproduce the effects of inhalation or oral ingestion of fat-soluble cannabinoids.

Cannabis Pharmacology

- **Highly concentrated THC or cannabidiol (CBD) oil extracts are being illegally promoted as potential cancer cures.**
- **These oils have not been evaluated in any clinical trials for anticancer activity or safety.**
- **Because CBD is a potential inhibitor of certain cytochrome p450 enzymes, highly concentrated CBD oils used concurrently with conventional therapies that are metabolized by these enzymes could potentially increase toxicity or decrease the effectiveness of these therapies.**

Patterns of *Cannabis* Use Among Cancer Patients

- A cross-sectional survey of cancer patients seen at the Seattle Cancer Care Alliance was conducted over a 6-week period between 2015 and 2016.
- In Washington State, *Cannabis* was legalized for medicinal use in 1998 and for recreational use in 2012. Of the 2,737 possible participants, 936 (34%) completed the anonymous questionnaire. Twenty-four percent of patients considered themselves active *Cannabis* users.
- Similar numbers of patients inhaled (70%) or used edibles (70%), with dual use (40%) being common. Non-mutually exclusive reasons for *Cannabis* use were physical symptoms (75%), neuropsychiatric symptoms (63%), recreational use/enjoyment (35%), and treatment of cancer (26%).

Patterns of *Cannabis* Use Among Cancer Patients

- The physical symptoms most commonly cited were pain, nausea, and loss of appetite.
- The majority of patients (74%) stated that they would prefer to obtain information about *Cannabis* from their cancer team, but less than 15% reported receiving information from their cancer physician or nurse.

Cancer Treatment

- No ongoing clinical trials of *Cannabis* as a treatment for cancer in humans were identified in a PubMed search.
- The only published trial of any cannabinoid in patients with cancer is a small pilot study of intratumoral injection of delta-9-THC in patients with recurrent glioblastoma multiforme, which demonstrated no significant clinical benefit.
- In a trial conducted in Israel, oral cannabidiol (CBD) was investigated as a single salvage agent for recurrent solid tumors.
- The study was projected to be completed in 2015; however, no results have been published.

Cancer Treatment

- A small exploratory phase II study was conducted in the United Kingdom that used nabiximols, a 1:1 ratio of THC:CBD in a *Cannabis*-based medicinal extract oromucosal spray, in conjunction with temozolomide in treating patients with recurrent glioblastoma multiforme.
- The study enrolled 21 patients. Final results have not been published.

Cancer Treatment

- Another Israeli group postulated that the anti-inflammatory and immunosuppressive effects of CBD might make it a valuable adjunct in the treatment of acute graft-versus-host disease (GVHD) in patients who have undergone allogeneic hematopoietic stem cell transplantation.
- The authors investigated CBD 300 mg/d in addition to standard GVHD prophylaxis in 48 adult patients who had undergone transplantation predominantly for acute leukemia or myelodysplastic syndrome.

Cancer Treatment

- The combination of CBD with standard GVHD prophylaxis was found to be safe.
- Compared with 101 historical controls treated with standard prophylaxis, patients who received CBD appeared to have a lower incidence of grade II to grade IV GVHD, suggesting that a randomized controlled trial (RCT) is warranted.

The Evidence for Cannabinoids

- **Several controlled clinical trials have been performed, and meta-analyses of these support a beneficial effect of cannabinoids (dronabinol and nabilone) on chemotherapy-induced nausea and vomiting (N/V) compared with placebo.**
- **Both dronabinol and nabilone are approved by the U.S. Food and Drug Administration for the prevention or treatment of chemotherapy-induced N/V in cancer patients but not for other symptom management.**

The Evidence for Cannabis

- There have been ten clinical trials on the use of inhaled *Cannabis* in cancer patients that can be divided into two groups.
- In one group, four small studies assessed antiemetic activity but each explored a different patient population and chemotherapy regimen.
- One study demonstrated no effect, the second study showed a positive effect versus placebo, the report of the third study did not provide enough information to characterize the overall outcome as positive or neutral.

The Evidence for Cannabis

- **Consequently, there are insufficient data to provide an overall level of evidence assessment for the use of *Cannabis* for chemotherapy-induced N/V.**
- **Apparently, there are no published controlled clinical trials on the use of inhaled *Cannabis* for other cancer-related or cancer treatment-related symptoms.**

The Evidence for Cannabis

- An increasing number of trials are evaluating the oromucosal administration of *Cannabis* plant extract with fixed concentrations of cannabinoid components, with national drug regulatory agencies in Canada and in some European countries that issue approval for cancer pain.
- At present, there is insufficient evidence to recommend inhaling *Cannabis* as a treatment for cancer-related symptoms or cancer treatment-related symptoms or cancer treatment-related side effects; however, additional research is needed.

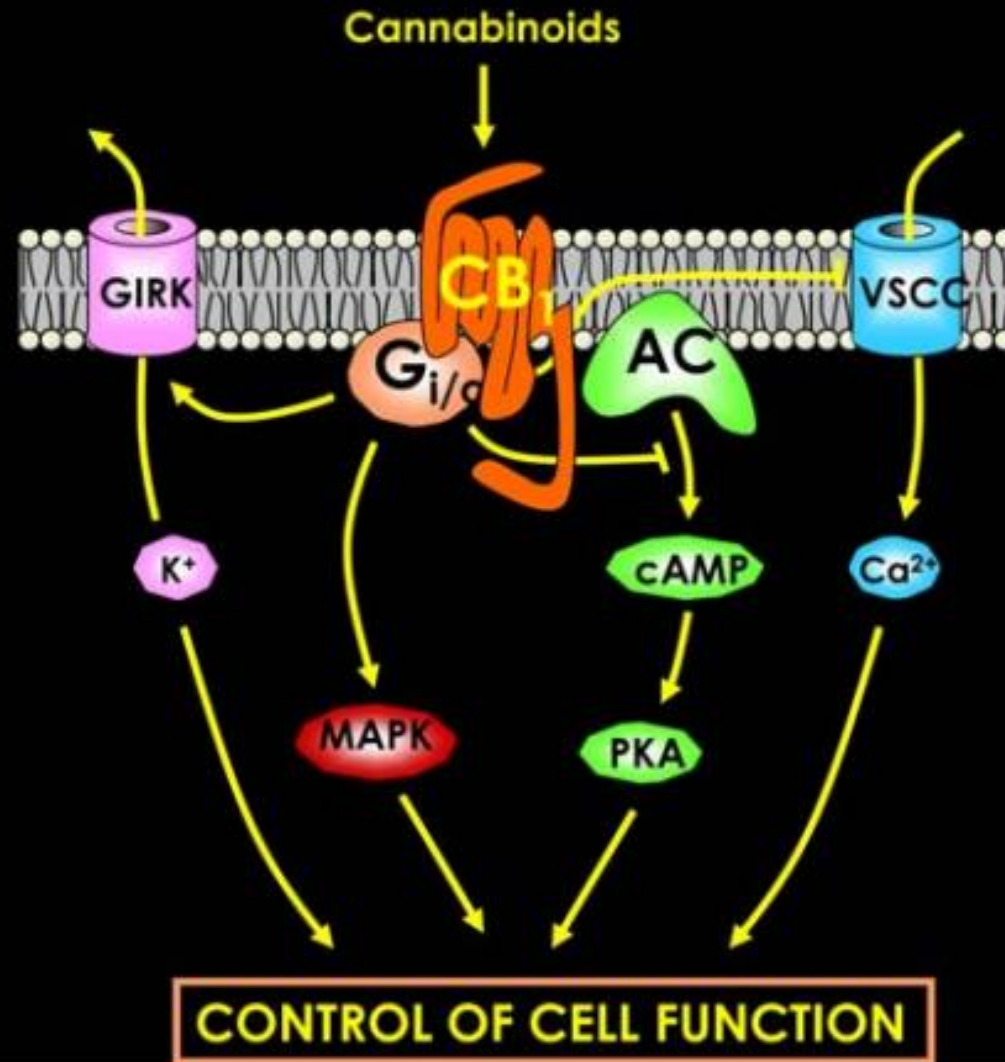
Cannabis in Cancer Care

- Cannabis has been used in medicine for thousands of years prior to achieving its current illicit substance status.
- Cannabinoids, the active components of Cannabis sativa, mimic the effects of the endogenous cannabinoids (endocannabinoids), activating specific cannabinoid receptors, particularly CB1 found predominantly in the central nervous system and CB2 found predominantly in cells involved with immune function.
- Delta-9-tetrahydrocannabinol, the main bioactive cannabinoid in the plant, has been available as a prescription medication approved for treatment of cancer chemotherapy-induced nausea and vomiting and anorexia associated with the AIDS wasting syndrome.

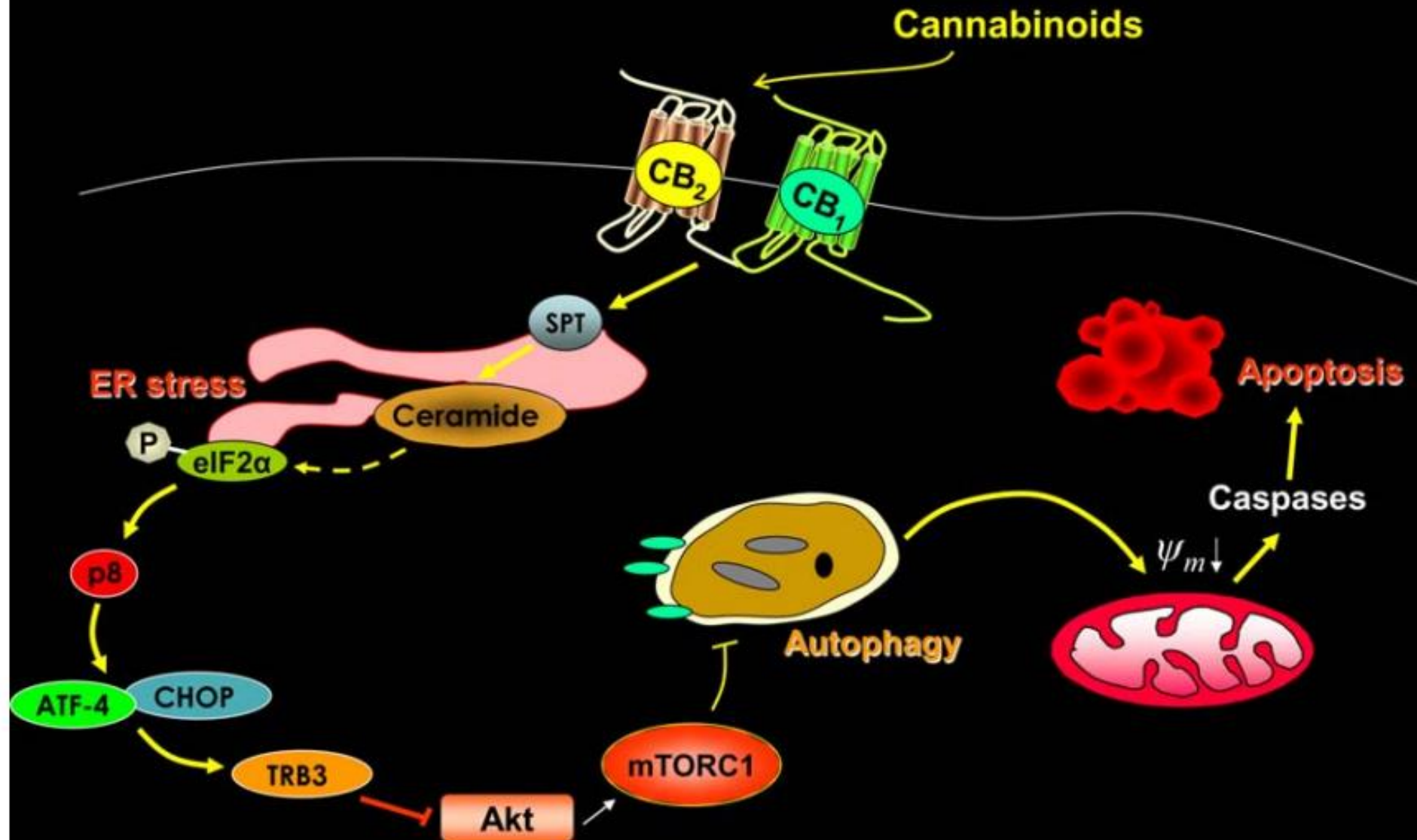
Cannabis in Cancer Care

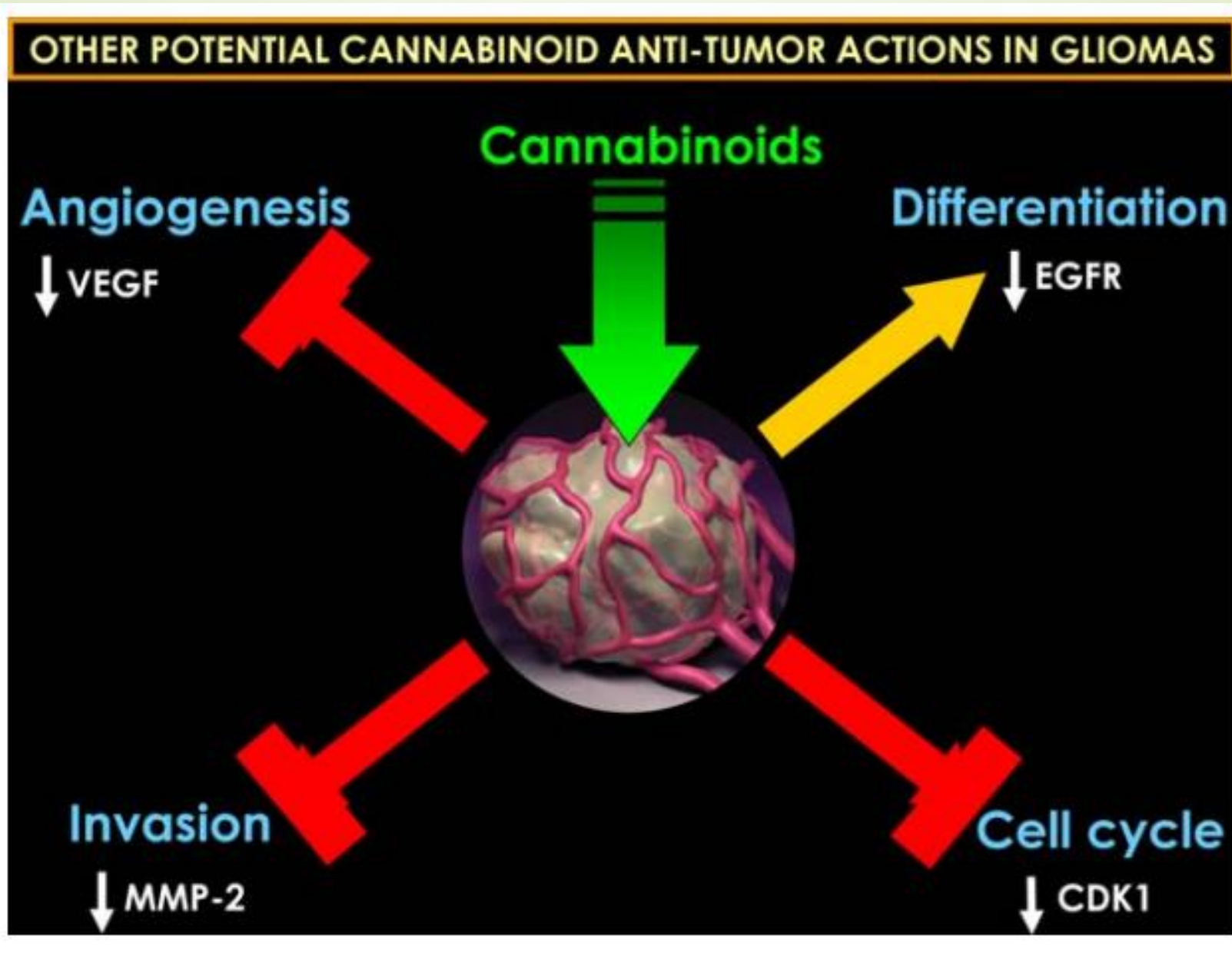
- Cannabinoids may be of benefit in the treatment of cancer-related pain, possibly synergistic with opioid analgesics.
- Cannabinoids have been shown to be of benefit in the treatment of HIV-related peripheral neuropathy, suggesting that they may be worthy of study in patients with other neuropathic symptoms.
- Cannabinoids have a favorable drug safety profile, but their medical use is predominantly limited by their psychoactive effects and their limited bioavailability.

CANNABINOID RECEPTORS: G-PROTEIN COUPLING



MECHANISM OF CANNABINOID-INDUCED CANCER CELL DEATH





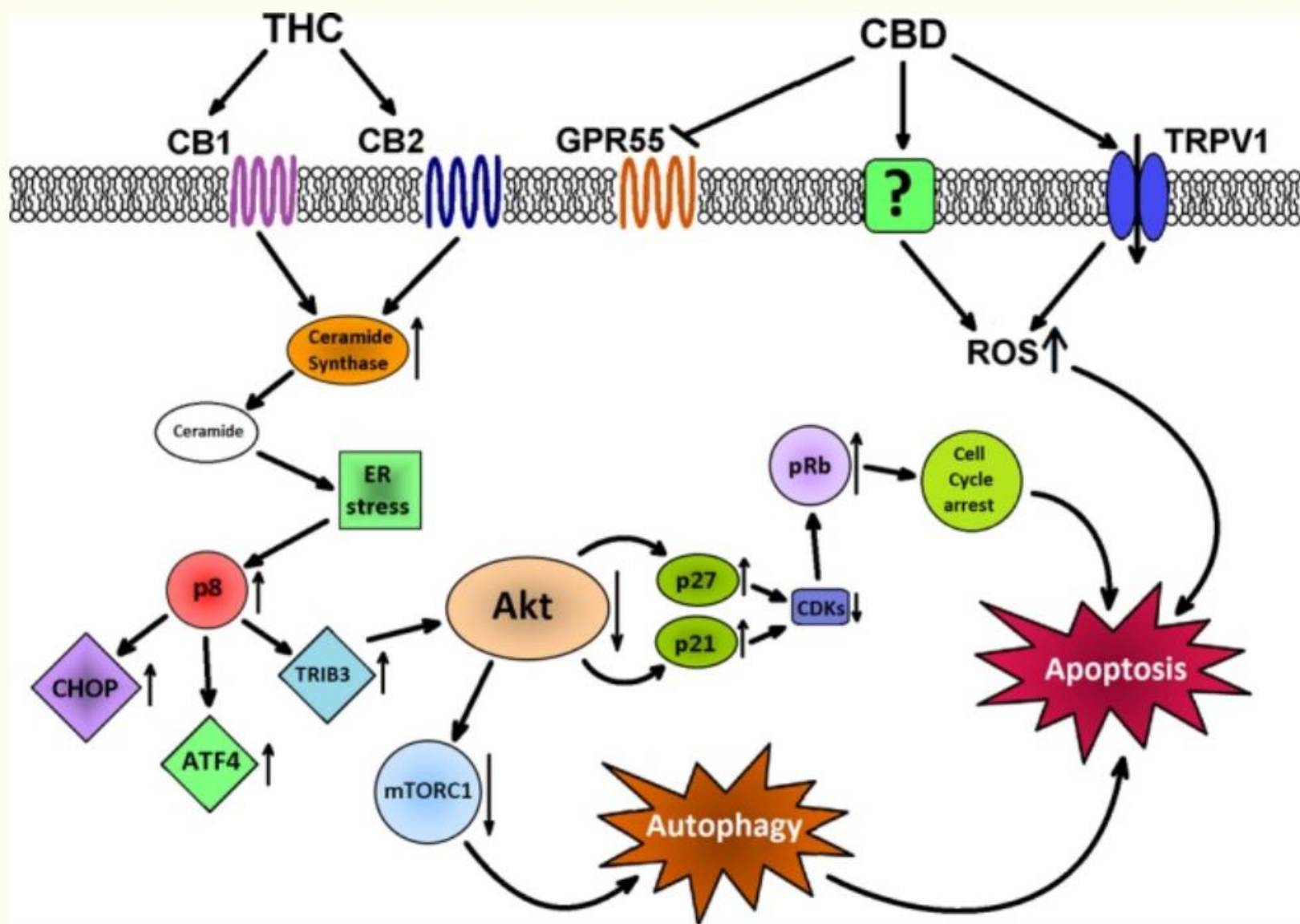


Table 1. Clinical Studies of *Cannabis*^a

Reference Citation	Type of Study	Condition Treated	No. of Patients: Enrolled; Treated; Control ^b	Strongest Benefit Reported ^c	Concurrent Therapy Used (Yes/No/ Unknown) ^d	Level of Evidence Score ^e
[38]	RCT	CINV	8; 8; None	None	Unknown	1iC
[39]	RCT	CINV	15; 15; None	Decreased N/V	Unknown	1iiC
[42]	Pilot RCT	CINV	16; 7; 9	Decreased/delayed N/V	5-HT3 receptor antagonists	1iC

CINV = chemotherapy-induced nausea and vomiting; RCT = randomized controlled trial; N/V = nausea and vomiting.

^aRefer to text and the NCI Dictionary of Cancer Terms for additional information and definition of terms.

^bNumber of patients treated plus number of patient controls may not equal number of patients enrolled; number of patients enrolled equals number of patients initially recruited/considered by the researchers who conducted a study; number of patients treated equals number of enrolled patients who were given the treatment being studied AND for whom results were reported.

^cStrongest evidence reported that the treatment under study has activity or otherwise improves the well-being of cancer patients.

^dConcurrent therapy for symptoms treated (not cancer).

Table 2. Clinical Studies of Cannabinoids^a

Reference Citation	Type of Study	Condition Treated	No. of Patients: Enrolled; Treated; Control ^b	Strongest Benefit Reported ^c	Concurrent Therapy Used (Yes/No/ Unknown) ^d	Level of Evidence Score ^e
[43]	RCT	Cancer-associated anorexia	469; dronabinol 152, megestrol acetate 159, or both 158; none	Megestrol acetate provided superior anorexia <u>palliation</u> among advanced cancer patients compared with dronabinol alone	Unknown	1iC
[44]	Pilot RCT	Appetite	21; 11; 10	THC, compared with placebo, improved and enhanced chemosensory perception	Unknown	1iC
[46]	RCT	Cancer-related anorexia-cachexia syndrome	243; <i>Cannabis</i> extract 95, THC 100; 48	No differences in patients' appetite or QoL were found	Unknown	1iC

[46]	RCT	Cancer-related anorexia-cachexia syndrome	243; <i>Cannabis</i> extract 95, THC 100; 48	No differences in patients' appetite or QoL were found	Unknown	1iC
[47]	RCT	Appetite	139; 72; 67	Increase in appetite	Unknown	1iC
[50]	Survey of RCTs	Pain		Decreased pain	Unknown	1iC
[54]	RCT	Pain	10; none; none	Pain relief	Unknown	1iC
[60]	Observational study	Pain	112; 47; 65	Decreased pain		

No. = number; QoL = quality of life; RCT = randomized controlled trial; THC = delta-9-tetrahydrocannabinol.

^aRefer to text and the NCI Dictionary of Cancer Terms for additional information and definition of terms.

^bNumber of patients treated plus number of patient controls may not equal number of patients enrolled; number of patients enrolled equals number of patients initially recruited/considered by the researchers who conducted a study; number of patients treated equals number of enrolled patients who were given the treatment being studied AND for whom results were reported.

^cStrongest evidence reported that the treatment under study has activity or otherwise improves the well-being of cancer patients.

^dConcurrent therapy for symptoms treated (not cancer).

^eFor information about levels of evidence analysis and an explanation of the level of evidence scores, refer to Levels of Evidence for Human Studies of Integrative, Alternative, and Complementary Therapies.

Marijuana and Cancer

Marijuana is the name given to the dried buds and leaves of varieties of the *Cannabis sativa* plant, which can grow wild in warm and tropical climates throughout the world and be cultivated commercially. It goes by many names, including pot, grass, cannabis, weed, hemp, hash, marihuana, ganja, and dozens of others.

Marijuana has been used in herbal remedies for centuries. Scientists have identified many biologically active components in marijuana. These are called *cannabinoids*. The two best studied components are the chemicals *delta-9-tetrahydrocannabinol* (often referred to as THC), and *cannabidiol* (CBD). Other cannabinoids are being studied.

At this time, the US Drug Enforcement Administration (DEA) lists marijuana and its cannabinoids as Schedule I controlled substances. This means that they cannot legally be prescribed, possessed, or sold under federal law. Whole or crude marijuana (including marijuana oil or hemp oil) is not approved by the US Food and Drug Administration (FDA) for any medical use. But the use of marijuana to treat some medical conditions is legal under



How can marijuana affect symptoms of cancer?

- A number of small studies of smoked marijuana found that it can be helpful in treating nausea and vomiting from cancer chemotherapy.
- A few studies have found that inhaled (smoked or vaporized) marijuana can be helpful treatment of neuropathic pain (pain caused by damaged nerves).
- Smoked marijuana has also helped improve food intake in HIV patients in studies.
- There are no studies in people of the effects of marijuana oil or hemp oil.
- Studies have long shown that people who took marijuana extracts in clinical trials tended to need less pain medicine.

How can marijuana affect symptoms of cancer?

- More recently, scientists reported that THC and other cannabinoids such as CBD slow growth and/or cause death in certain types of cancer cells growing in lab dishes. Some animal studies also suggest certain cannabinoids may slow growth and reduce spread of some forms of cancer.
- There have been some early clinical trials of cannabinoids in treating cancer in humans and more studies are planned. While the studies so far have shown that cannabinoids can be safe in treating cancer, they do not show that they help control or cure the disease.
- Relying on marijuana alone as treatment while avoiding or delaying conventional medical care for cancer may have serious health consequences.

Possible harms of marijuana

- Marijuana can also pose some harms to users. While the most common effect of marijuana is a feeling of euphoria ("high"), it also can lower the user's control over movement, cause disorientation, and sometimes cause unpleasant thoughts or feelings of anxiety and paranoia.
- Smoked marijuana delivers THC and other cannabinoids to the body, but it also delivers harmful substances to users and those close by, including many of the same substances found in tobacco smoke.
- Because marijuana plants come in different strains with different levels of active compounds, it can make each user's experience very hard to predict. The effects can also differ based on how deeply and for how long the user inhales. Likewise, the effects of ingesting marijuana orally can vary between people. Also, some chronic users can develop an unhealthy dependence on marijuana.

Cannabinoid drugs

- There are 2 chemically pure drugs based on marijuana compounds that have been approved in the US for medical use.
- Dronabinol (Marinol®) is a gelatin capsule containing delta-9-tetrahydrocannabinol (THC) that's approved by the US Food and Drug Administration (FDA) to treat nausea and vomiting caused by cancer chemotherapy as well as weight loss and poor appetite in patients with AIDS.
- Nabilone (Cesamet®) is a synthetic cannabinoid that acts much like THC. It can be taken by mouth to treat nausea and vomiting caused by cancer chemotherapy when other drugs have not worked.

Cannabinoid drugs

- **Nabiximols (Sativex®)** is a cannabinoid drug still under study in the US. It's a mouth spray made up of a whole-plant extract with THC and cannabidiol (CBD) in an almost one to one mix. It's available in Canada and parts of Europe to treat pain linked to cancer, as well as muscle spasms and pain from multiple sclerosis (MS). It's not approved in the US at this time, but it's being tested in clinical trials to see if it can help a number of conditions.

How can cannabinoid drugs affect symptoms of cancer?

- Based on a number of studies, dronabinol can be helpful for reducing nausea and vomiting linked to chemotherapy.
- Dronabinol has also been found to help improve food intake and prevent weight loss in patients with HIV. In studies of cancer patients, though, it wasn't better than placebo or another drug (megestrol acetate).
- Nabiximols has shown promise for helping people with cancer pain that's unrelieved by strong pain medicines, but it hasn't been found to be helpful in every study done. Research is still being done on this drug.

Side effects of cannabinoid drugs

- Like many other drugs, the prescription cannabinoids, dronabinol and nabilone, can cause side effects and complications.
- Some people have trouble with increased heart rate, decreased blood pressure (especially when standing up), dizziness or lightheadedness, and fainting.
- These drugs can cause drowsiness as well as mood changes or a feeling of being “high” that some people find uncomfortable.
- They can also worsen depression, mania, or other mental illness. Some patients taking nabilone in studies reported hallucinations.

Side effects of cannabinoid drugs

- The drugs may increase some effects of sedatives, sleeping pills, or alcohol, such as sleepiness and poor coordination.
- Patients have also reported problems with dry mouth and trouble with recent memory.

Side effects of cannabinoid drugs

- Older patients may have more problems with side effects and are usually started on lower doses.
- People who have had emotional illnesses, paranoia, or hallucinations may find their symptoms are worse when taking cannabinoid drugs.
- Talk to your doctor about what you should expect when taking one of these drugs.
- It's a good idea to have someone with you when you first start taking one of these drugs and after any dose changes.

False News of a Cannabis Cancer Cure

- **Background**
- **There is increasing concern among healthcare communities about the misinformation online about using cannabis to cure cancer. We have characterized this online interest in using cannabis as a cancer treatment and the propagation of this information on social media.**
- **Materials & methods**
- **We compared search activity over time for cannabis and cancer versus standard cancer therapies using Google Trends' relative search volume (RSV) tool and determined the impact of cannabis legalization. We classified news on social media about cannabis use in cancer as false, accurate, or irrelevant. We evaluated the cannabis-related social media activities of cancer organizations.**

False News of a Cannabis Cancer Cure

► Results

- The online search volume for cannabis and cancer increased at 10 times the rate of standard therapies (RSV 0.10/month versus 0.01/month, $p < 0.001$), more so in states where medical or recreational cannabis is legal. The use of cannabis as a cancer cure represented the largest category (23.5%) of social media content on alternative cancer treatments. The top false news story claiming cannabis as a cancer cure generated 4.26 million engagements on social media, while the top accurate news story debunking this false news generated 0.036 million engagements. Cancer organizations infrequently addressed cannabis (average 0.7 Tweets; 0.4 Facebook posts), with low influence compared to false news (average 5.6 versus 527 Twitter retweets; 98 versus 452,050 Facebook engagements, $p < 0.001$).

Cannabis for cancer - illusion or the tip of an iceberg

- **Article highlights**
- **Cannabis has historically been used as a healing herb and mild-altering plant and is currently approved in many countries for recreational and medicinal use.**
- **Favorable outcomes are shown in chemotherapy-induced nausea and vomiting and cancer pain, with evidence of advantageous neurological interactions.**
- **Cannabinoids have shown antineoplastic effects in preclinical studies in a wide range of cancer cells and some animal models, and distinct signaling pathways are implicated in these results.**

Cannabis for cancer - illusion or the tip of an iceberg

- **Article highlights**
- **Conflicting reports show that Cannabis contains immunosuppressive properties and oncogenic potential.**
- **Combining Cannabis with conventional cancer treatment modalities may cause enhancing or diminishing effects.**
- **Research is hampered by high variability and lack of standardization in trial construction and drug formulation and pharmacodynamics.**
- **Clinical trials and in-depth drug and patient analyses are needed to find the right constellation of drug composition, dose, and means of administration, to tailor specific Cannabis-based medicine per indication and per patient.**

Health Effects of Cannabis and Cannabinoids

*Current State of
Evidence and
Recommendations for
Research*

This report will be available to
download as a free pdf:
[Nationalacademies.org/CannabisHealthEffects](https://www.nationalacademies.org/CannabisHealthEffects)

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Experts weigh in on the health effects of marijuana

➤ Therapeutic Effects

- Patients with **chronic pain** who were treated with cannabis or cannabinoids were more likely to experience a significant reduction in pain symptoms.
- For adults with **multiple sclerosis-related muscle spasms**, there was substantial evidence that short-term use of certain oral cannabinoids improved their reported symptoms.
- In adults with **chemotherapy-induced nausea and vomiting**, there was conclusive evidence that certain oral cannabinoids were effective in preventing and treating those ailments.

Experts weigh in on the health effects of marijuana

- **Risks**
- Long-term cannabis smoking was associated with **worse respiratory symptoms** and **more chronic bronchitis episodes**.
- Cannabis use prior to driving increases the risk of being involved in a **motor vehicle accident**.
- Smoking cannabis during pregnancy was associated with **lower birth weight** in the child.

References

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