

**1. Medical condition proposed:**

diabetes

**2. Provide justification for why this medical condition should be included as a qualifying debilitating medical condition for the use of medical marihuana. Be specific as to why medical marihuana should be used for this condition.**

367 medical marijuana patients in Arizona were surveyed.

26 patients reported using medical marijuana for treatment of Diabetes.

General relief from Diabetes symptoms was 38.4%.

Relief by medical marijuana compared to other medications was 37.5%

Less frequent use of other medications was 54.1%

<https://www.ncbi.nlm.nih.gov/pubmed/26317379>

Diabetes is one of the top 10 causes of death in the United States.

Number of deaths for leading causes of death:

Diabetes: 79,535

<https://www.cdc.gov/nchs/fastats/deaths.htm>

Anecdotal data has shown that medical marijuana helps treat symptoms of Diabetes and pre-diabetes.

<https://www.thediabetescouncil.com/diabetes-and-marijuana-a-possible-treatment/>

Clinical data has shown medical marijuana to regulate a person's metabolism and blood sugar levels into a more normal range via the endocannabinoid system.

<http://healthland.time.com/2013/05/21/marijuana-the-next-diabetes-drug/>

The US Department Of Health And Human Services has determined through thorough medical research and analysis that the cannabinoids including THC and CBD specifically from the marijuana plant can be used safely in treating diseases such as diabetes.

A method of treating diseases caused by oxidative stress, comprising administering a therapeutically effective amount of a cannabinoid that has substantially no binding to the NMDA receptor to a subject who has a disease caused by oxidative stress.

Oxidative associated diseases include, without limitation, free radical associated diseases, such as ischemia, ischemic reperfusion injury, inflammatory diseases, systemic lupus erythematosus, myocardial ischemia or infarction, cerebrovascular accidents (such as a thromboembolic or hemorrhagic stroke) that can lead to ischemia

or an infarct in the brain, operative ischemia, traumatic hemorrhage (for example a hypovolemic stroke that can lead to CNS hypoxia or anoxia), spinal cord trauma, Down's syndrome, Crohn's disease, autoimmune diseases (e.g. rheumatoid arthritis or diabetes), cataract formation, uveitis, emphysema, gastric ulcers, oxygen toxicity, neoplasia, undesired cellular apoptosis, radiation sickness, and others.

As used herein, a "cannabinoid" is a chemical compound (such as cannabinol, THC or cannabidiol) that is found in the plant species Cannabis sativa (marijuana)

<http://www.google.com/patents/US6630507>

The National Academy of Medicine (formerly the Institute of Medicine IOM) issued a comprehensive review of research on cannabinoids including THC and CBD from the Cannabis Sativa plant. Even though they were specifically looking for harms and risks of marijuana use, they were at a loss to explain why the majority of the research showed marijuana users had a lower BMI and obesity.

<https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state>

Counterintuitively, the majority of the reviewed studies showed that cannabis was associated with a lower BMI or a lower prevalence of obesity, or both (Hayatbakhsh et al., 2010; Le Strat and Le Foll, 2011; Smit and Crespo, 2001; Warren et al., 2005), or to have no association with BMI or obesity (Rodondi et al., 2006).

FDA approved prescription medications for diabetes and insulin related diseases can cause serious side effects or death.

<https://www.fda.gov/downloads/Drugs/DrugSafety/UCM204269.pdf>

Serious side effects can happen in people taking JANUVIA, including inflammation of the pancreas (pancreatitis) which may be severe and lead to death.

<https://www.drugs.com/januvia.html>

Januvia side effects

Get emergency medical help if you have signs of an allergic reaction to Januvia: hives; difficulty breathing; swelling of your face, lips, tongue, or throat.

Stop taking Januvia and call your doctor right away if you have symptoms of pancreatitis: severe pain in your upper stomach spreading to your back, nausea and vomiting, loss of appetite, or fast heartbeats.

Call your doctor at once if you have:

- severe autoimmune reaction - itching, blisters, breakdown of the outer layer of skin;
- little or no urinating;
- symptoms of heart failure - shortness of breath (even while lying down), swelling in your legs or feet, rapid weight gain; or
- severe skin reaction - fever, sore throat, swelling in your face or tongue, burning in your eyes, skin pain followed by a red or purple skin rash that spreads (especially in the face or upper body) and causes blistering and peeling.

Common Januvia side effects may include:

- runny or stuffy nose, sore throat;
- headache, back pain, joint or muscle pain; or
- nausea, stomach pain, diarrhea, constipation.

<https://www.fda.gov/Drugs/DrugSafety/ucm557507.htm>

FDA Drug Safety Communication: FDA confirms increased risk of leg and foot amputations with the diabetes medicine canagliflozin (Invokana, Invokamet, Invokamet XR)

The FDA continues to approve prescription drugs, with a lack of research on long term effects. The FDA refuses to approve of the safe and non-toxic and non-increased-risk-of-amputations marijuana as a drug.

A safety profile of Medical Marijuana can be found in the first year report of the Minnesota medical marijuana program. The Minnesota Department of Health surveyed 1500+ patients enrolled in the program.

Adverse Side Effects: At this point, the safety profile of the medical cannabis products available through the Minnesota program seems quite favorable. Approximately 20-25% of enrolled patients report negative physical or mental side effects of some kind, with the majority – around 60% - reporting only one and 90% reporting three or fewer. The vast majority of adverse side effects, around 90%, are mild to moderate in severity. An assessment of the 30 patients reporting severe side effects, meaning “interrupts usual daily activities,” found no apparent pattern of patient age, medical condition, or type of medical cannabis used. The most common adverse side effects are dry mouth, drowsiness, and fatigue. Fortunately, up to the present no serious adverse events (life threatening or requiring hospitalization) have been reported.

<http://www.health.state.mn.us/topics/cannabis/about/firstyearreport.html>

Medical Marijuana's mild to moderate side effects of dry mouth, drowsiness and fatigue are easily tolerated by the vast majority of patients.

The Mayo Clinic website has assembled dosage information on Medical Marijuana.

<http://www.mayoclinic.org/drugs-supplements/marijuana/dosing/hrb-20059701>

Drugs and Supplements  
Marijuana (Cannabis sativa)

Dosing

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.

Adults (18 years and older)

To treat amyotrophic lateral sclerosis (nerve cell disease), 10 milligrams of THC has been taken by mouth daily for two weeks.

To prevent nausea and vomiting caused by chemotherapy, five milligrams per meter squared of dronabinol (Marinol®) has been taken by mouth 1-3 hours before chemotherapy, then every 2-4 hours after chemotherapy, for a total of 4-6 doses daily. A dose of two milligrams of nabilone has been taken by mouth the night before chemotherapy, 1-3 hours before and after chemotherapy. A dose of 2-3 milligrams of nabilone has been taken by mouth 2-4 times daily. A dose of three milligrams of nabilone has been taken by mouth three times daily as a one-time dose, a four-day duration, and the duration of two cycles of chemotherapy. Cannabinoids have been taken by mouth over a 24-hour period as follows: 1-8 milligrams of nabilone daily as 1-4 milligrams daily, one milligram 3-5 times daily, or two milligrams 2-4 times daily or 24-50 milligrams per meter squared of dronabinol daily as 10 milligrams per meter squared 4-5 times daily, 12 milligrams per meter squared twice daily, or 15 milligrams twice daily. A dose of one milligram of nabilone has been taken by mouth 8-12 hours before chemotherapy, followed by 0.5-2 milligrams of nabilone 2-3 times daily after chemotherapy, depending on body weight. A dose of 10 milligrams per meter squared of THC has been taken by

mouth two hours before and four, eight, 16, and 24 hours after chemotherapy. Cannabinoids have been injected into the muscle over the course of 24 hours in the form of 0.5-1 milligrams of levonantradol three times daily.

To treat atopic dermatitis (itchy, scaly skin rashes), hemp seed oil has been taken by mouth for 20 weeks.

To increase appetite in people with cancer, 2.5 milligrams of THC has been taken by mouth with or without one milligram of CBD for six weeks.

To treat chronic pain, cannabinoids have been taken by mouth in the form of capsules or sprayed into the mouth as THC, benzopyranoperidine (BPP), cannabidiol (CBD), nabilone, dronabinol, or synthetic nitrogen THC analogs (NIB), with doses of 2.5-20 milligrams for an average of 25 days. Cannabis-based medicines have been used for 1-6 weeks. Ajulemic acid has been used for one week. Doses of nabilone of 0.25-2 milligrams have been used daily for 4-6 weeks. Doses of smoked cannabis of 1-9.4 percent have been used for six hours to 14 days. Cannabis has been smoked 3-4 times daily for five days. Doses of dronabinol of 10-20 milligrams have been used daily for six hours to six weeks. In people with cancer, 5-20 milligrams of delta-9-THC has been taken by mouth daily, as have the following doses: 2-8 milligrams of nabilone by mouth daily; 0.25-1 milligram of nabilone by mouth daily for four weeks; 1-2 milligrams of nabilone twice daily for a year; 1-2 milligrams of nabilone twice at an eight-hour interval; and 0.5 milligrams of nabilone twice daily for seven days, followed by two milligrams daily for three weeks. A dose of 0.5-1 milligrams of nabilone has been taken twice daily. A dose of 10 milligrams of THC has been taken by mouth, increasing to a maximum tolerated dose for six weeks. A mouth spray has been used in divided doses of 2.5-120 milligrams for two weeks. Doses of Sativex® have been sprayed into the mouth, up to 48 sprays daily, for 1-2 weeks, then 10-15 sprays daily, or 4-8 sprays, with eight being the maximum one-time dose or within a three-hour period.

To improve appetite in people with cystic fibrosis (mucus buildup in the organs), a dose of 2.5 milligrams of dronabinol has been taken by mouth, increasing to a maximum of 10 milligrams daily for 1-6 months.

To treat dementia, 2.5 milligrams of dronabinol has been taken by mouth twice daily for six weeks.

To treat eating disorders, 7.5-30 milligrams of THC has been taken by mouth daily for four weeks.

To treat epilepsy, 200-300 milligrams of CBD has been taken by mouth daily for up to 4.5 months.

To improve fatty acid status, hemp seed oil has been taken by mouth.

To treat movement problems caused by Huntington's disease, 1-2 milligrams of nabilone has been taken by mouth daily for five weeks. A dose of 10 milligrams per kilogram of CBD has been taken by mouth daily for six weeks.

To treat sleep disorders, 40-160 milligrams of CBD has been taken by mouth.

To treat multiple sclerosis symptoms, 2.5 milligrams of dronabinol (Marinol®) has been taken by mouth daily, increasing to a maximum of 10 milligrams daily for three weeks. A dose of 15-30 milligrams of cannabis extract capsules has been taken by mouth in five-milligram increments, based on tolerance, for 14 days. Cannabis extracts, including Cannador®, have been taken by mouth for 2-4 weeks. Cannabis plant extracts containing 2.5-120 milligrams of a THC-CBD combination have been taken by mouth daily for 2-15 weeks. A mouth spray (Sativex®, containing 2.7 milligrams of THC and 2.5 milligrams of CBD) has been used at a dose of 2.5-120 milligrams in divided doses for up to eight weeks. Eight sprays within any three hours, up to 48 sprays in a 24-hour period, have been used. Sativex® has been sprayed into the mouth for 6-14 weeks.

As a nutritional supplement, 15-30 milliliters of hemp oil has been taken by mouth daily.

To treat schizophrenia, 40-1,280 milligrams of CBD has been taken by mouth daily for up to four weeks.

To treat Tourette's syndrome, gelatin capsules containing 2.5-10 milligrams of THC have been taken by mouth as a single dose. A dose of 2.5 milligrams of THC has been taken by mouth daily, increasing to 10 milligrams daily in 2.5-milligram intervals over a four-day time period for six weeks.

To treat rheumatoid arthritis, up to six sprays of Sativex® have been used once daily 30 minutes before bed for five weeks.

As evidenced by the included medical marijuana patient surveys in other states and countries, adults are using medical marijuana to treat these diseases. Patients will continue to use medical marijuana to treat symptoms whether or not you approve these conditions. Approving these conditions to add them to the list of Qualifying Conditions in the MMMA has the only effect of protecting sick people from arrest or penalty, who are currently breaking the law by using a safe and non-toxic plant that they can grow themselves versus dangerous prescriptions that cost thousands of dollars per month.

LARA and the Medical Marihuana Review Panel are not the FDA.

LARA and the Medical Marihuana Review Panel are not tasked with "calling for more research".

LARA and the Medical Marihuana Review Panel are not deciding “if marihuana is a medicine”, the people of Michigan already decided and declared that in 2008.

The director of LARA, in previous denials of petitions, stated that there are a “lack of studies” on using medical marijuana with the conditions presented. A fact that is true. That is the whole point of medical marijuana laws. The people of 29 states and the District of Columbia know there is a lack of research on medical marijuana, but they created laws to protect patients who are using medical marijuana anyway. BECAUSE MEDICAL MARIJUANA WORKS. Research on medical marijuana has been stymied by the US federal government (DEA and FDA Denials on rescheduling marijuana for research purposes), blocked by NIDA and the NIH (requiring researchers to have extreme hoops to jump through, these hoops are not required to study any other drug).

Health professionals, Medical Marihuana Review Panel members and the Director of LARA have all called for more research. I fully agree more research is required and useful and beneficial for all. How long must sick patients wait for research? Must they wait for more research until they die?

All because the FDA wants a mono chemical therapy instead of a whole botanical plant medicine?

As an example for how long people have been waiting for “more research”, look at this study: “Chronic administration of cannabidiol to healthy volunteers and epileptic patients.” 1980.

<https://www.ncbi.nlm.nih.gov/pubmed/7413719>

Epileptics have been waiting 37 years for CBD research and medication. 37 YEARS of waiting for a safe non-toxic plant chemical that reduces or eliminates seizures. Do you have any idea how many intractable epileptic patients have died in those 37 years? THOUSANDS of epileptics whose diseases were uncontrolled by prescription medications have died in those 37 years. Or millions of patients in the 100 years since cannabis was banned federally and globally for racist reasons.

That is 37 years from that single study. Historically, medical marijuana has been used for seizures for over 5000 years. Because it works.

If you deny this petition for “lack of research”, please detail how many years patients should continue to wait. Please detail exactly how many people you are accepting to die waiting just because you think there is some risk of medical marijuana use that will manifest itself. Even though people have been using medical marijuana for 5000+ years. As well as 21 years since California started its medical marijuana law in 1996. Plus the US Federal Government IND program, started in 1978, which still currently sends 8 ounces of medical marijuana (300 cigarettes in a metal tin) to two people in the USA each month. That is 6+ pounds of medical marijuana each year for 35 years that Irv Rosenfeld has smoked, every day, to treat his bone tumor condition.

[https://en.wikipedia.org/wiki/Compassionate\\_Investigational\\_New\\_Drug\\_program](https://en.wikipedia.org/wiki/Compassionate_Investigational_New_Drug_program)

There is a study on the IND patients and medical marijuana safety here:

[http://www.cannabis-med.org/jcant/russo\\_chronic\\_use.pdf](http://www.cannabis-med.org/jcant/russo_chronic_use.pdf)

Further, if you deny this petition, please provide articles published in peer-reviewed scientific journals reporting the results of research on the effects of marihuana on the medical condition supporting why the condition should not be added to the list of debilitating medical conditions under the Michigan Medical Marihuana Act.

NIDA finds it difficult to put the words together, but finally admits there is no gateway theory of marijuana use.

These findings are consistent with the idea of marijuana as a "gateway drug." However, the majority of people who use marijuana do not go on to use other, "harder" substances.

<https://www.drugabuse.gov/publications/research-reports/marijuana/marijuana-gateway-drug>

NIDA also finds it very difficult to backtrack on the propaganda research they grant. When other researchers tried to duplicate the results of the first study on marijuana and IQ points, they were unable to find any IQ loss due to marijuana use. I hope that any knowledge you have on marijuana is up to date, and that you are paying attention when NIDA's biased research grants backfire on them, over and over again.

In a recent study sponsored by NIDA and the National Institute of Mental Health, teens who used marijuana lost IQ points relative to their non using peers. However, the drug appeared not to be the culprit. The new findings contribute to an ongoing scientific exploration of the drug's impact on users' cognition.

<https://www.drugabuse.gov/news-events/nida-notes/2016/08/study-questions-role-marijuana-in-teen-users-iq-decline>

**3. Provide a summary of the evidence that the use of medical marihuana will provide palliative or therapeutic benefit for this medical condition or is a treatment for this condition.**

1. [http://www.amjmed.com/article/S0002-9343\(13\)00200-3/fulltext](http://www.amjmed.com/article/S0002-9343(13)00200-3/fulltext)

In this large, cross-sectional study, we found that subjects who reported using marijuana in the past month had lower levels of fasting insulin and HOMA-IR, as well as smaller waist circumference and higher levels of HDL-C. These associations were attenuated among those who reported using marijuana at least once, but not in the past 30 days, suggesting that the impact of marijuana use on insulin and insulin resistance exists during periods of recent use.

In the present study, we demonstrate a significant association between current marijuana use and lower levels of fasting insulin and insulin resistance in multivariable adjusted analyses even after excluding participants with prevalent diabetes mellitus.

With the recent trends in legalization of marijuana in the United States, it is likely that physicians will increasingly encounter patients who use marijuana and should therefore be aware of the effects it can have on common disease processes, such as diabetes mellitus. We found that current marijuana use is associated with lower levels of fasting insulin, lower HOMA-IR, and smaller waist circumference.

2. <https://www.ncbi.nlm.nih.gov/pubmed/26317379>

367 medical marijuana patients in Arizona were surveyed.

26 patients reported using medical marijuana for treatment of Diabetes.

General relief from Diabetes symptoms was 38.4%.

Relief by medical marijuana compared to other medications was 37.5%

Less frequent use of other medications was 54.1%

3. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3349875/>

Natural cannabinoids, such as CBD and THCV, also have tremendous therapeutic potential. CBD is a potent antioxidant and anti-inflammatory agent that does not appear to exert its beneficial effects through conventional CB receptors and is already approved for human use. THCV and its derivatives, which may combine the beneficial effects of simultaneous CB1 inhibition and CB2 stimulation, are still under intense preclinical investigation. It will be interesting to see how newly developed, peripherally restricted CB1 receptor antagonists and/or CB2 receptor agonists and certain natural cannabinoids, such as CBD and THCV, will influence the clinical outcomes of diabetic patients. We hope that some of these new approaches will be useful in clinical practice in the near future to aid patients with diabetes.

4. <https://www.ncbi.nlm.nih.gov/pubmed/25978795>

Recently active cannabis smoking and diabetes mellitus are inversely associated.

5. <https://www.ncbi.nlm.nih.gov/pubmed/19441010>

These findings highlighted the beneficial effects of cannabis extract treatment in attenuating diabetic neuropathic pain, possibly through a strong antioxidant activity and a specific action upon nerve growth factor.

6. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4718895/>

Fourteen percent (13.8%) of current marijuana users and 17.5% of past marijuana users presented with metabolic syndrome compared to 19.5% of never users ( $p=0.0003$  and  $p=0.03$ , respectively). Current marijuana users had lower odds of presenting with metabolic syndrome than never users. Among emerging adults, current marijuana users were 54% less likely than

never users to present with metabolic syndrome. Current and past middle-aged adult marijuana users were less likely to have metabolic syndrome than never users.

7. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3289985/>

Marijuana use was independently associated with a lower prevalence of DM. Further studies are needed to show a direct effect of marijuana on DM.

8. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5152762/>

Our short-term, single session, crossover study in general found a dose dependent reduction in pain intensity in response to inhaled cannabis in patients with DPN. Overall, our finding of an analgesic effect of cannabis is consistent with other trials of cannabis in diverse neuropathic pain syndromes.

9. <https://www.ncbi.nlm.nih.gov/pubmed/21144973>

Collectively, these results coupled with the excellent safety and tolerability profile of CBD in humans, strongly suggest that it may have great therapeutic potential in the treatment of diabetic complications, and perhaps other cardiovascular disorders, by attenuating oxidative/nitrative stress, inflammation, cell death and fibrosis.

10. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2755639/>

Clinical studies largely affirm that neuropathic pain patients derive benefits from cannabinoid treatment.

11. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3579247/>

*In vivo*, CBD treatment does not appear to have any effect on resting blood pressure or heart rate, but does reduce the cardiovascular response to various types of stress. *In vivo, CBD treatment has a protective role in reducing the effects of cardiac ischaemia and reperfusion, or in reducing cardiac dysfunction associated with diabetes.* Similarly, CBD has a protective role in reducing the ischaemic damage in models of stroke, partly due to maintaining cerebral blood flow.

12. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5045244/>

Endocannabinoid regulation of  $\beta$ -cell functions: implications for glycaemic control and diabetes

13. <https://www.ncbi.nlm.nih.gov/pubmed/21484568>

On the other hand, evidence is emerging that some nonpsychotropic plant cannabinoids, such as cannabidiol, can be employed to retard  $\beta$ -cell damage in type 1 diabetes. These novel aspects of endocannabinoid research are reviewed in this chapter, with emphasis on the biological effects of plant cannabinoids and endocannabinoid receptor antagonists in diabetes.

14. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4818362/>

These findings highlight that THC treatment may attenuate slightly the oxidative stress in diabetic rats. The excretion rate of THC may vary in the type 2 diabetes mellitus status.

15. <https://www.ncbi.nlm.nih.gov/pubmed/21868374>

Additionally, after adjustment for sex and age, the use of cannabis was associated with body mass index differences in both samples. The authors conclude that the prevalence of obesity is lower in cannabis users than in nonusers.

16. <https://www.ncbi.nlm.nih.gov/pubmed/25557382>

Cannabis use was highly prevalent in the study population (57.4%) and was statistically associated with lower body mass index (BMI) ( $P < 0.001$ ), lower % fat mass ( $P < 0.001$ ), lower fasting insulin ( $P = 0.04$ ), and lower HOMA-IR ( $P = 0.01$ ), after adjusting for numerous confounding variables. Further adjustment for BMI rendered fasting insulin and HOMA-IR differences statistically nonsignificant between past-year cannabis users and nonusers.

Mediation analysis showed that the effect of cannabis use on insulin resistance was indirect, through BMI. In multivariate analysis, past-year cannabis use was associated with 0.56 lower likelihood of obesity (95% confidence interval 0.37-0.84).

17. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4669115/>

THC reduced weight gain, fat mass gain and energy intake in DIO but not lean mice. DIO-induced changes in select gut microbiota were prevented in mice chronically administered THC. THC had no effect on locomotor activity or whole gut transit in either lean or DIO mice.

Chronic THC treatment reduced energy intake and prevented high fat diet-induced increases in body weight and adiposity; effects that were unlikely to be a result of sedation or altered gastrointestinal transit. Changes in gut microbiota potentially contribute to chronic THC-induced actions on body weight in obesity.

18. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3714514/>

Chronic cannabis smoking was associated with visceral adiposity and adipose tissue insulin resistance but not with hepatic steatosis, insulin insensitivity, impaired pancreatic  $\beta$ -cell function, or glucose intolerance.

19. <https://www.ncbi.nlm.nih.gov/pubmed/20936991>

The existing data suggest lower prevalence of overweight and obesity among young adult cannabis users. Further research is needed to examine the mechanism of this association.

20. <https://www.ncbi.nlm.nih.gov/pubmed/16186086>

Linear regression revealed a negative correlation between BMI group and percent marijuana use ( $R^2 = 0.96$ ;  $P = 0.0173$ ).

21. <https://www.ncbi.nlm.nih.gov/pubmed/23410498>

Obesity is one of the highest preventable causes of morbidity and mortality in the developed world [1]. It has been well known for a long time that exposure to cannabis produces an increase of appetite (a phenomenon referred to as the 'munchies'). This phenomenon led to an

exploration of the role of the endocannabinoid system in the regulation of obesity and associated metabolic syndrome. This effort subsequently led to the development of a successful therapeutic approach for obesity that consisted of blocking the cannabinoid CB1 receptors using ligands such as Rimonabant in order to produce weight loss and improve metabolic profile [2]. Despite being efficacious, Rimonabant was associated with increased rates of depression and anxiety and therefore removed from the market. We recently discovered that the prevalence of obesity is paradoxically much lower in cannabis users as compared to non-users and that this difference is not accounted for by tobacco smoking status and is still present after adjusting for variables such as sex and age. Here, we propose that this effect is directly related to exposure to the ?(9)-tetrahydrocannabinol (THC) present in cannabis smoke. We therefore propose the seemingly paradoxical hypothesis that THC or a THC/cannabidiol combination drug may produce weight loss and may be a useful therapeutic for the treatment of obesity and its complications.

22. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4204468/>

Marijuana is a clinically controversial substance, but one potential medical benefit may be weight gain. According to available studies, appetite stimulation as well as weight gain may occur in patients with physical debilitation due to HIV/AIDS and/or cancer. However, while weight gain may occur, it is not greater than currently available agents for inducing weight gain (e.g. megestrol). As for the effects of marijuana on body weight in the general population, use appears to be associated with a lower body mass index. This observation may be partially explained by differences in short-term versus long-term use, comorbid polydrug use, and/or the intriguing theory that food and drugs may compete for the same reward sites in the brain. Alternatively, marijuana may genuinely be a regulatory compound, increasing weight in those with low weight, but not in those who are normal or overweight. Only additional research will unravel the answer to the seemingly multi-faceted weight effects of marijuana.

23. <https://www.ncbi.nlm.nih.gov/pubmed/16644197>

The study thus shows that Cannabis sativa and the cannabinoids, THC and CBN, display anticoagulant activity and may be useful in the treatment of diseases such as type 2 diabetes in which a hypercoagulable state exists.

24. <https://www.ncbi.nlm.nih.gov/pubmed/19011363>

This action is of therapeutic relevance: cannabinoid agonists are currently used to alleviate anorexia and nausea in AIDS patients, whereas the cannabinoid receptor CB1 antagonist rimonabant was recently found to be effective in the treatment of obesity.

25. <https://www.ncbi.nlm.nih.gov/pubmed/16148436>

Moreover, there is strong evidence of an endocannabinoid role in energy metabolism and fuel storage. Recent developments point to potential clinical benefits of cannabinoid receptor antagonists in the management of obesity, and of agonists in the treatment of other disorders of eating and body weight regulation.

26. <https://www.ncbi.nlm.nih.gov/pubmed/22133305>

These findings are consistent with modulation of appetite hormones mediated through endogenous cannabinoid receptors, independent of glucose metabolism.

27. <https://www.ncbi.nlm.nih.gov/pubmed/19367510>

The ability of Cannabis sativa to promote eating has been documented for many centuries, with the drug reported by its users to promote strong cravings for, and an intensification of the sensory and hedonic properties of food. These effects are now known to result from the actions of cannabinoid molecules at specific cannabinoid receptor sites within the brain, and to reflect the physiological role of their natural ligands, the endocannabinoids, in the control of appetite. Recent developments in the biochemistry and pharmacology of endocannabinoid systems have generated convincing evidence from animal models for a normal role of endocannabinoids in the control of eating motivation. The availability of specific cannabinoid receptor agonists and antagonists raises the possibility of improved therapies for disorders of eating and body weight: not only in the suppression of appetite to counter our susceptibility to the over-consumption of highly pleasurable and energy-dense foods; but also in the treatment of conditions that involve reduced appetite and weight loss.

28. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC166302/>

Nevertheless, as the smoke continues to clear, the cannabinoid system may prove to be an extremely promising target for the development of medications for obesity and cachexia (9).

29. <https://dmsjournal.biomedcentral.com/articles/10.1186/1758-5996-2-5>

Thus, endocannabinoid antagonists could be utilized for the treatment of the type of obesity associated with specific eating disorders such as 'sweet and snack-eating' and compulsive eating episodes.

30. The Health Effects of Cannabis and Cannabinoids:

<https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state>

31. Minnesota Medical Cannabis Program: Patient Experiences From the First Year

<http://www.health.state.mn.us/topics/cannabis/about/firstyearreport.html>

**4. Provide articles published in peer-reviewed scientific journals reporting the results of research on the effects of marihuana on the medical condition or treatment of the medical condition and supporting why the medical condition should be added to the list of debilitating medical conditions under the Medical Marihuana Act. Attach a copy of all articles that are discussed in this section. Please do not attach articles that are not discussed in this section.**

See enclosed.



