A Look at Cannabis Pharmacology, Medical Uses, and Adverse Effects

By

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Cannabis

Cannabis has been used for thousands of years for its medicinal and psychotropic qualities.[1] In the United States, cannabis was widely available in over-the-counter medicines during the 19th and early 20th centuries. Federal restriction of cannabis usage and sale first occurred in 1937, with the passage of the Marihuana (sic) Tax Act. Legal penalties for its use increased in the 1950's.[2] Many states have now legalized medical cannabis, and an increasing number of states have legalized recreational use as well.[1]

This article will discuss the pharmacology, medical uses, and adverse effects of cannabis. The term cannabis will be used preferentially unless the reference source specifically reported on marijuana usage.

Cannabis Pharmacology and Cannabinoid Receptors

Cannabis is a term for a genus of plants in the *Cannabaceae* family. Both marijuana and hemp are cannabis plants. The three strains of cannabis most frequently used are *Cannabis sativa*, *Cannabis indica*, and *Cannabis ruderalis.* *C*. *Sativa* contains a high amount of tetrahydrocannabinol (THC). *C*. *Indica* is a mixed THC-cannabidiol (CBD) plant, and *C*. *ruderalis* contains high amounts of CBD.[1] Hemp refers to cannabis that contains minimal THC levels with similar CBD levels to *C*. *ruderalis*. To qualify as hemp in the U.S. cannabis needs to contain less than 0.3% THC.[3]

Cannabinoid Receptors

The endocannabinoid system is thought to regulate body homeostasis.[1] There are two cannabinoid receptors present in humans, CB_1 and CB_2 which act by inhibiting adenyl cyclase. CB_1 receptors are located primarily in the central nervous system in brain and spinal cord presynaptic neurons, as well as within the peripheral nervous system.[1,4] CB_1 receptors are also found in the gastrointestinal system, spleen, heart, liver, uterus, bladder, and vas deferens.[1,4]

CB_1 receptors mediate many of the psychoactive effects of cannabinoids.[5] CB_1 receptor activation in the hypothalamus and pituitary gland results in modulation of the hypothalamic-pituitary system. Receptor activation leads to inhibitory effects on the release of growth hormone, thyroid hormone, prolactin, and luteinizing hormone.[4,6]

Activation of CB_1 receptors can result in decreased gastric acid secretion, lower esophageal sphincter relaxation, altered intestinal motility, visceral pain, and inflammation.[4]

CB_2 receptors are concentrated mainly in immune cells and tissues. CB_2 receptors appear to inhibit inflammation, visceral pain, and intestinal motility.[4] There is some suggestive early research that activation of CB_2 receptors might be useful in treating some inflammatory conditions.[7]

Cannabinoids

There are a number of cannabinoids in cannabis with delta 9-tetrahydrocannabinol (THC) being principally active.[4] THCa found in cannabis plants is the inactive precursor compound of delta 9-THC. It requires heat to convert THCa to the psychoactive delta 9-THC. The required heating can occur when smoking cannabis or heating it for edibles, such as baking cannabis brownies.[8] Delta-8 THC, a relative of delta-9 THC, has a similar molecular structure and is also sold in cannabis stores. Delta-8 THC has less psychoactive effect than delta 9-THC, and is found in lower quantities in cannabis plants than THCa.[9] THC acts as an agonist at both CB_1 and CB_2 receptors.[10]

Delta 9-Tetrahydrocannabivarin (THCV) is a naturally occurring analogue of THC and has an opposite effect to THC. It is an inverse agonist/selective antagonist of the CB_1 receptor. (It not only blocks the receptor from other agonists, it actually reverses the effects of receptor stimulation.) It lacks psychoactive effects, and in animal studies THCV decreased appetite, increased energy metabolism, and had positive effects on reducing glucose levels, and increasing insulin sensitivity. It is being investigated for use in the management of obesity and treatment of type 2 diabetes.[11,12]

Cannabidiol (CBD) and cannabigerol (CBG) are two additional cannabinoids found in cannabis. CBD is not psychotropic and has many opposite effects on the body to THC, acting to reduce the effects of THC on the CB_1 receptor,[10] as well as having anti-inflammatory properties. In low doses CBD has an anti-emetic effect, but higher doses may cause vomiting. It is also an agonist of other receptors in the body including the 5-HT_{1A} receptor. 5-HT_{1A} is a serotonin receptor that is one of the targets of antianxiety, antidepressant and antipsychotic medications.[13] CBG is a non-psychotropic cannabinoid with anti-inflammatory properties, but it acts as an antagonist at the CB_1 and 5-HT_{1A} receptors, and can reverse the anti-emetic actions of low-dose CBD at the 5-HT_{1A} receptor.[4,14,15]

Nearly 100 metabolites of THC have been identified, many of which also have pharmacologic actions. Some are psychotropic, others have anti-emetic, anti-inflammatory, ocular pressure lowering, or analgesic effects.[4]

There are a number of endogenous cannabinoids produced in the body that bind to cannabinoid receptors, the most well-known being anandamide and 2-arachidonylglycerol (2-AG). These are released by neurons and thought to be neurotransmitters or neuromodulators.[4]

THC is stored in body fat which becomes a long-term storage site, and contributes to the long length of time THC is able to be detected on urine drug screens, and may contribute to symptoms in the cannabis hyperemesis syndrome.[4,16]

Effects of Cannabinoids

Many people experience a pleasant euphoria and sense of relaxation with cannabis use. Other common effects, which may vary dramatically among users, include heightened sensory perception such as colors being brighter, laughing fits, altered perception of time, and increased appetite.[17]

Cannabis may also cause blurred vision, altered judgment, dysphoria, anxiety, paranoia, impaired motor coordination, or with use of higher doses, psychosis.[17] These negative effects are seen more often when a person uses too much, the cannabis has an unexpectedly high potency, or the user is inexperienced.[17] Because of the increased systemic absorption and longer time of onset of edible cannabis compared

with smoked cannabis, edible cannabis is more likely to result in adverse psychiatric and cardiovascular effects needing medical attention.[1] The effects of smoked cannabis typically lasts from one to three hours, and those of edible cannabis, such as ingesting cannabis brownies or gummies, may last much longer.[17]

THC stimulates the sympathetic nervous system while inhibiting the parasympathetic nervous system which causes an increase in heart rate, myocardial oxygen demand, supine blood pressure, and platelet activation. It has also been associated with endothelial dysfunction and oxidative stress. CBD has many opposite effects to THC and may cause a reduction in heart rate and blood pressure. CBD also has an anti-inflammatory effect. CBD has been shown to cause an improvement in vasodilation in models of endothelial dysfunction, and has been shown to reduce inflammation and vascular hyperpermeability in diabetic animal models.[1] The cannabinoid system also helps regulate the endocrine system.[18]

Note on Cannabis Literature

Interpretation of the current scientific data on both positive and adverse effects of cannabis is difficult, as much of it is observational or retrospective with a lack of blinded, randomized, prospective studies.[1]

Positive Effects of Cannabis[1]

Medical Indications for Use

Improvements in neuropathic and fibromyalgic pain

- There are a number of studies that demonstrate a reduction in symptoms in neuropathic pain with cannabis use.[19,21]
- A retrospective case series of 38 patients with fibromyalgia found a significant improvement in pain, severity, and disability symptoms with medical cannabis. However, almost half of the patients stopped therapy due to nonserious adverse side effects of the medication.[22]

Appetite stimulation and anti-emetic after chemotherapy

- THC increases appetite by stimulating CB_1 feeding centers in the hypothalamus.[18]
- Dronabinol (synthetic THC) and nabilone (a CB_1 receptor agonist) are two commercially available cannabinoids for the treatment of chemotherapy-induced nausea and vomiting.[4,19,21]

Decreased pain, decreased bladder dysfunction, and decreased spasticity in multiple sclerosis (MS)[21]

- Although the results were mixed, a metanalysis found limited efficacy of cannabinoids for the treatment of spasticity, pain, and bladder dysfunction in patients with MS.[23]
- There is limited evidence that dronabinol (synthetic THC), and other studied THC/CBD medications decrease pain, bladder dysfunction, and spasticity in multiple sclerosis.[21]
- Nabiximols, an oromucosal spray absorbed by the buccal mucosa, which contains equal parts CBD and THC, has been approved as a treatment for MS patients with moderate to severe spasticity in a number of countries, but is not currently available in the U.S.[24]

Reduction of attacks of drug-resistant epilepsy in both adults and children

- The CB_1 receptor provides protection against epilepsy by inhibition of both glutamate release as well as the harmful cascade of changes that can lead to seizures after an initial insult.[25]
- CBD appears to have anti-convulsant properties, whereas CB_1 agonists such as THC have been found to have either pro- or anti-epileptic properties.[21]
- Cannabidiol (oral CBD) has been found to be an effective treatment of childhood drug-resistant seizures in Dravet syndrome* and Lennox-Gastaut syndrome**, and has FDA approval for those indications.[21]
  [*Severe Myoclonic Epilepsy of Infancy]
  [**A childhood onset seizure disorder that induces several different types of seizures in those that suffer from it.]
- Observational studies have suggested CBD may cause a possible reduction in seizure frequency and an improved quality of life in adolescents with drug-resistant epilepsy.[21]

Possible Medical Uses, with Limited or Inconclusive Evidence

THC May help alleviate opioid withdrawal effects

- Pre-clinical studies suggest THC may alleviate some opioid withdrawal symptoms.
- Observational studies suggest that cannabis use could help alleviate opioid withdrawal symptoms, but as of yet the evidence is insufficient to draw firm conclusions.[21]

Improvement of dystonia

- Preclinical studies suggest cannabinoids may help with dystonia symptoms. Dystonia is a movement disorder that includes involuntary body movement or involuntary muscle contraction or spasm.
- There are mixed results from case studies and small trials with respect to use of cannabinoids for dystonia symptoms. One small trial found CBD had some efficacy.[21,26]

THC reduces intraocular pressure (IOP), but CBD raises it.

- One small study of six patients found a sublingual dose of THC reduced the IOP temporarily, and was well tolerated. Sublingual low doses of CBD did not reduce IOP, whereas higher doses produced a transient increase IOP rise.[27]
- THC is currently not an FDA recommended therapy for glaucoma. Issues with the use of THC for glaucoma treatment include the short length of time it works if the cannabis is smoked, development of tolerance, and unwanted side effects. Scientists are looking to try to create a long-acting THC eyedrop.[28,29]

Treatment of Alzheimer's disease and Parkinson's disease

- Pre-clinical studies suggest that THC and CBD may protect against oxidative stress and inflammation in animal models of Alzheimer's disease.[21]
- Limited case and observational studies suggest that oral THC and nabilone are associated with improvement in a number of symptoms associated with Alzheimer's disease, such as nocturnal motor activity, disturbed behavior, sleep, agitation, and resistiveness.[21]
- The evidence from a limited number of studies of the use of cannabinoids for symptoms of Parkinson's disease is mixed.[21]

Treatment of anxiety disorders[21]

- Evidence from pre-clinical and clinical studies suggests that THC exhibits biphasic effects on mood, with low doses of THC reducing anxiety and having mood-elevating effects, but high doses of THC potentially increasing anxiety and having mood-lowering effects.
- Limited evidence from a small number of clinical studies indicate that THC may improve symptoms of anxiety and depression in patients suffering from some chronic diseases such as HIV/AIDS, MS, and chronic neuropathic pain.

- Limited evidence from some observational studies suggests that medical cannabis with equal proportions of CBD and THC may cause less anxiety and depression than cannabis that is mostly THC.

Improvement of symptoms of inflammatory bowel disease

- According to a Cochrane database review, the effects of cannabis on Crohn's disease and ulcerative colitis is uncertain.[30]

Improved glycemic control in diabetics

- Observational studies suggest chronic cannabis use may lead to an improved metabolic profile. There is limited clinical evidence suggesting a potential beneficial effect of THCV on glycemic control in patients with type II diabetes.[21]

Treatment of sleep disorders

- Low doses of cannabis may improve sleep disorders, while high doses may worsen sleep patterns.[21,31]

Reducing the incidence of death in heart failure

- There is some limited observational, retrospective data showing decreased mortality in cannabis users versus non-users in patients with congestive heart failure.[1]

Protection against ischemia/reperfusion injury after ischemia

- Preclinical studies suggest that CBD and very low doses of THC may have some protective effects against ischemia/reperfusion injury due to CB_2 receptor anti-inflammatory properties.[1]

Topical CBD

- Although topical CBD is widely available, there is currently a dearth of scientific research on its effectiveness. The most common study cited as a positive result is one where topical CBD gel was found to reduce swelling, pain and synovial thickening in rats with induced osteoarthritis.[32]

Adverse Effects of Cannabis[1]

It is thought that most of the adverse effects of cannabis use arise from the THC component rather than CBD. However, CBD may cause diarrhea, decreased appetite, drowsiness, or mood irritability. CBD in very high doses has been found to cause hepatotoxicity in mice, although paradoxically it has also been found to improve symptoms of hepatic encephalopathy in mice.[33,34] CBD has also been found to cause reproductive system toxicity in animal studies including impairment of sexual behavior, reduced testosterone levels, testicular cell degeneration, and decreased fertilization rates.[35] Whether these animal studies of hepatic injury and sexual function are reflective of possible human toxicity is not known.

Cardiac Adverse Effects

Cannabinoid receptors are present in myocytes and platelets.[36] Cannabis use has been linked by case reports and observational studies to negative cardiovascular effects such as tachycardia, premature ventricular contractions, atrial fibrillation, and ventricular arrhythmias.[1]

- In states where cannabis has been legalized, there has been an observed increase in hospitalizations and emergency department visits for acute myocardial infarction (AMI).[1,37]
- Marijuana use in one study was associated with 3-fold higher mortality rate after AMI, and mortality was higher in subjects that used marijuana more frequently.[38] In the same study, the risk of triggering an AMI was elevated almost 5-fold within one hour after smoking marijuana.[39]
- Recent data suggest that marijuana use is present in 6% of patients ≤50 years of age who presented with their first AMI and is associated with worse all-cause and cardiovascular mortality. Marijuana use in that study was associated with a two times higher death rate among these patients, even after adjusting for tobacco use.[40]
- A small study of ten patients with coronary artery disease found that exercise time until angina onset was reduced after smoking one marijuana cigarette, as compared with a placebo.[41]
- A systematic analysis found an increased risk of both acute coronary syndrome and chronic cardiovascular disease associated with cannabis use.[42] The possible reasons smoking cannabis may increase cardiac risk include increased blood pressure, heart rate, myocardial oxygen demand, and carboxyhemoglobin levels.[40,41]
- Case reports have suggested associations of cannabis with stress cardiomyopathy[43] and myocarditis[44].

Arteritis

Delta-9 THC and delta-8 THC can induce peripheral vasoconstriction.[45-48] Cannabis arteritis resembling thromboangiitis obliterans (Buerger's disease) has been reported in male patients who developed distal ischemia leading to necrosis of fingers or toes.[45-48] While cigarette smoking is a confounding factor in many of these reported cases, it appears cannabis may be an aggravating factor in the development of arteritis.[48] It has also been found that rats exposed to secondhand marijuana smoke for one minute developed impaired femoral artery flow-mediated dilatation for at least 90 minutes, which was longer than the impairment by secondhand tobacco smoke. Femoral artery flow-mediated dilatation is a measure of vascular endothelial dysfunction.[49]

Stroke

A population survey found that weekly marijuana smokers experienced a 3.3 times higher rate of stroke or transient ischemic attacks than both non-users and infrequent users.[50]. In a case series of 17 patients who presented with ischemic stroke after or during cannabis use, three patients had stroke symptoms within 30 minutes after using cannabis, and five out of 14 had a recurrent stroke upon reuse of cannabis[51]. In contrast, a retrospective review and a systematic review found no correlation between marijuana smoking and stroke, but both of these reviews cited issues with the quality of the data.[52,53]

Pulmonary Effects

Chronic cannabis smoking can produce symptoms similar to those of tobacco smoking such as cough, sputum production, shortness of breath, and wheezing. The association between long-term cannabis smoking (without tobacco) and chronic obstructive pulmonary disease is unclear, but chronic bronchitis has been reported.[21,54] Cannabis smoking has been shown to worsen symptoms of chronic bronchitis, but if stopped does not increase the risk of later developing chronic bronchitis. Chronic marijuana smokers may develop an increase in FVC (forced vital capacity) as opposed to the decrease in FEV1 (forced expiratory volume in 1 second) seen in cigarette smokers.[55] Acutely, marijuana smoking causes a 5-fold increase in the blood carboxyhemoglobin level compared with tobacco, which may play a part in cannabis' negative cardiac effects.[53,54,56] There is no evidence for a link between cannabis smoking and lung cancer.[21]

Pregnancy

While there is a lack of definitive evidence on the adverse effects of cannabis on pregnancy, the American College of Obstetricians and Gynecologists recommends that women who are pregnant or contemplating pregnancy should discontinue marijuana

use. THC crosses the placenta and has been found in breast milk up to six days after cannabis use. Cannabis may potentially affect the newborn's brain development resulting in hyperactivity, poor cognitive function, or other possible long-term consequences.[1,54,57] A recent study found that maternal cannabis use during pregnancy was associated with greater anxiety, aggression, and hyperactivity in children three to six years old. They also found dampened activity in genes that make key immune-related proteins in the placentas of mothers using cannabis.[58,59]

Cannabis Hyperemesis Syndrome [4]

Cannabis hyperemesis syndrome (CHS) was first described in 2004, and is characterized by chronic cannabis use, cyclic episodes of nausea and vomiting, and use of hot showers to relieve symptomatology. The typical patient is a young adult with a history of daily cannabis use for a number of years. After cannabis was legalized in Colorado, there was a 29% increase in vomiting-related emergency department visits suggesting a possible connection.[60]

CHS is typically a recurrent problem, with initial symptoms of early morning nausea and abdominal discomfort. In the active phase there is persistent nausea and vomiting, leading to dehydration. Patients frequently learn that hot showers relieve some of their symptoms and may shower many times a day.[61] After an acute episode, the patient may go back to normal for days to months until the next episode occurs. The hyperemetic phase of CHS typically lasts for one to two days, and relapse is possible if the patient restarts cannabis use.

Treatment is supportive with intravenous rehydration if needed. Antiemetics may be tried, but are frequently unsuccessful in controlling the vomiting. As a number of these patients develop gastritis and esophagitis, a proton pump inhibitor is recommended.

Hot showers may improve symptoms of nausea and vomiting, abdominal pain, and decreased appetite during the acute phase. Topical capsaicin cream applied to the abdomen also seems to relieve symptoms. The precise mechanism by which they reduce the symptoms of CHS is unknown.

Transient receptor potential vanilloid subtype 1 (TRPV1) receptor is centrally involved in control of gastric motility and is activated by cannabinoids, high temperatures, and capsaicin. Chronic exposure to cannabinoids may downregulate or desensitize TRPV1 signaling, explaining how prolonged exposure to cannabinoids might lead to decreased TRPV1 signaling, altered gastric motility, and emesis.[62] This theory may explain why both hot showers and capsaicin work to relieve symptoms. Another theory to try to explain the efficacy of hot bathing suggests that heat may act to partially correct cannabis-induced thermoregulatory and digestive system disequilibrium in the hypothalamus.[4,61]

Cannabis and Psychiatric Disorders

There have been some studies that linked cannabis use to increased risk for psychiatric disorders, including psychosis, depression, anxiety, and substance use disorders.[63] To what extent cannabis actually precipitates these conditions is not always able to be determined, as people with psychiatric disorders may also use cannabis to self-medicate.[64]

Psychotic Disorders

Although there are variations depending on the study, the baseline median lifetime risk of a psychotic disorder in the general public is thought to be about 0.72%[65]

- In one study, daily users of low potency cannabis (< 10% THC) had 2.2 times the risk of psychosis over non-users. Daily users of high potency cannabis (>10% THC) were found to have 4.8 times the risk of psychotic disorder over non-users. The increased risk of psychosis varied across the three European cities in the study with the highest number of subjects using high-potency cannabis daily; there was a four times greater risk of psychosis in Paris, five times greater risk in London, and more than nine times greater risk in Amsterdam over non-users.[66]
- A 10-year longitudinal study of subjects 14 to 24 years old at baseline found cannabis use was a risk factor for the development of psychotic symptoms.[67]
- One study found that daily cannabis users carrying a variant of the *AKT1* gene, (which codes for an enzyme that affects dopamine signaling in the corpus striatum), had a seven times increased risk of psychosis over daily cannabis users without the genetic variant.[66,68]
- There is also increased risk of psychosis in people who use cannabis and carry a variant of the gene for *catechol-O-methyltransferase* which is responsible for degrading neurotransmitters such as dopamine and norepinephrine.[66]

Anxiety Disorders

The National Epidemiological Survey on Alcohol and Related Conditions found no increase in mood and anxiety disorders with cannabis use, but there was a correlation to other substance use disorders.[66,69] However, another meta-analysis of 112,000 people found a positive correlation between cannabis use and an anxiety disorder.[70]

Suicidality

There is some suggestive evidence from epidemiologic studies that there is a relationship between the heavy use of cannabis and suicidality, especially in men.[21,71] In addition, rimonabant, a synthetic CB_1 receptor antagonist was found to increase the risk of suicidality and was taken off the market.[21,72]

Cannabis Use Disorder and Cannabis Withdrawal Symptoms

It is estimated that about 10% of cannabis users will develop cannabis use disorder. The percentage is even higher in users that start before age 18, up to 16%.[73]

Cannabis use disorder is defined as a problematic pattern of cannabis use leading to clinically significant psychological impairment or distress, that has negative effects on the person's ability to function at work, school, home, and/or causes social or interpersonal problems.[74]

Cannabis withdrawal may be a part of cannabis use disorder. Symptoms may begin within a day after cessation, peak by the third day, and can last up to two weeks. It is most commonly seen after heavy, prolonged cannabis usage. Withdrawal symptoms occur only in some individuals on stopping cannabis, and may consist of irritability, anger, nervousness, anxiety, insomnia, nightmares, decreased appetite, weight loss, depressed mood, and possibly abdominal pain, shakiness/tremors, sweating, fever, chills, or headache.

Cannabis Overdose

Acute overdoses of cannabis almost all have a good prognosis. In a review of 985 pediatric accidental ingestions, the most common symptoms were drowsiness or lethargy, ataxia, agitation, and nausea or vomiting. There were a few patients that had respiratory depression, bradycardia, or hypotension, but there were no deaths.[75] There is one atypical case report in the literature of an 11-month-old child thought to have an acute cannabis ingestion, who developed lethargy, had a seizure and died from non-infectious myocarditis, There was no history of an ingestion, but screening tests for THC were positive.[76]

Other Adverse Effects

During cannabis intoxication, the user may for a short time experience impaired short-term memory, attention, judgment, and other cognitive functions as well as anxiety, paranoia, and, uncommonly, psychosis.

Persistent longer lasting, but not permanent symptoms include impaired learning, impaired coordination, and sleep disturbances.

Long-term cumulative effects of repeated use may include impairments in learning and memory with a potential small loss of IQ in heavy adolescent users,[77,78] increased risk of other drug and alcohol use disorders, and increased risk of psychosis in people with genetic vulnerability, or daily use of high potency cannabis.[66]

Driving Performance While Under the Influence of Cannabis

A study of subjects given vaporized THC, THC/CBD or CBD compared to placebo measured the standard deviation of lateral position(SDLP), which is a measure of lane

weaving, swerving, and overcorrecting. It was found that there was no difference between the performance of the CBD group versus the placebo at 100 minutes after taking the medication. There was some worsening of SDLP performance of the THC and THC/CBD groups at 40 to 100 minutes after cannabis use, which returned to normal by four to five hours. The impairment with cannabis in the THC group was modest and comparable to a blood alcohol level of 0.05%.[79]

A number of studies have looked at the rate of motor vehicle deaths after cannabis legalization versus pre-legalization, or compared to other states. While the issue is not resolved, there is no evidence of widespread motor vehicular fatalities after cannabis legalization. Some studies found no significant difference and some others minimal increases in motor vehicle fatalities, such as one study which reported an increase of 2.1 fatalities per billion miles driven in states where cannabis was legalized.[80-83]

Medical Cannabis Prescription Formulations[84]

Rimonabant was approved for use in Europe in 2006 for the treatment of anorectic obesity. It is a synthetic inverse agonist/selective antagonist of the CB_1 receptor. It was withdrawn from the market due to the high incidence of serious psychiatric side effects.

The FDA has approved **epidiolex (cannabidiol)** for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older.

Marinol and **syndros** are two synthetic cannabinoids containing **dronabinol**, a synthetic THC, that are FDA approved for the treatment of nausea associated with cancer chemotherapy, and for the treatment of anorexia and weight loss in AIDS patients.

Cesamet (nabilone), a synthetic cannabinoid similar to THC, is FDA approved for treatment of the nausea associated with cancer chemotherapy.

Sativex (nabixmols) is a 1:1 mixture of 9-delta-tetrahydocannabinol (THC) and cannabidiol (CBD) in a spray absorbed by the buccal mucosa, which is available in many countries, but not the U.S. It is approved as a treatment for multiple sclerosis patients with moderate to severe spasticity who do not adequately respond to first-line antispasticity therapy.[24]

Cannabis Drug Interactions

Cannabinoids can interfere with the action of multiple classes of cardiovascular medications by inhibiting cytochrome P450. This can lead to increased blood levels of some medications including calcium channel blockers, statins, warfarin, NSAIDS,

beta-blockers, and anti-arrhythmics such as flecainide, mexiletine, propafenone, amiodarone, quinidine, and lidocaine.[1]

A recent study found that both THC and CBD in vitro inhibited some UDP-glucuronosyltransferase (UGT) enzymes. UGT enzymes are found in both the liver and the kidney and have an important role in the metabolism and detoxification of a wide range of substances including acetaminophen, furosemide, carbamazepine, codeine, gemfibrozil, morphine, and NSAIDS. The concern is that by inhibiting the metabolization of these medications, especially in individuals with decreased hepatic or renal function, cannabis may possibly increase the chance of an adverse reaction, but further clinical study is needed.[85]

Conclusion

Cannabis has some proven medical benefit for conditions such as refractory epilepsy, nausea in cancer patients, and attenuating neuropathic pain. It is used by many people for anxiety reduction, although the evidence for that effect is far from conclusive. Most people can use cannabis without a problem, however a small percentage of people, especially frequent users of high potency cannabis, may experience adverse effects such as hyperemesis, psychosis, or negative cardiovascular effects. There is also the possibility of some adverse drug interactions. It appears THC is responsible for the majority of the negative effects due to its stimulatory properties, while CBD has fewer negative issues with its use. Knowledge of the full extent of both positive and negative effects of cannabis smoking or ingestion has been limited by a lack of well controlled scientific studies. As an estimated 48 million people in the U.S used cannabis in 2019,[86] clinicians should be aware of both the diseases that can be treated by cannabis, and the clinical problems it may cause.

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