

Cannabis (drug)

Cannabis, also known as **marijuana** among other names,^[n 1] is a psychoactive drug from the *Cannabis* plant intended for medical or recreational use.^{[17][18][19]}

The main psychoactive part of cannabis is tetrahydrocannabinol (THC), one of 483 known compounds in the plant,^[20] including at least 65 other cannabinoids.^[21] Cannabis can be used by smoking, vaporizing, within food, or as an extract.^[22]

Cannabis is often used for its mental and physical effects, such as a "high" or "stoned" feeling, a general change in perception, heightened mood, and an increase in appetite.^{[22][23]} Onset of effects is within minutes when smoked, and about 30 to 60 minutes when cooked and eaten.^{[22][24]} They last for between two and six hours.^[24] Short-term side effects may include a decrease in short-term memory, dry mouth, impaired motor skills, red eyes, and feelings of paranoia or anxiety.^{[22][25][26]} Long-term side effects may include addiction, decreased mental ability in those who started as teenagers, and behavioral problems in children whose mothers used cannabis during pregnancy^[22] Studies have found a strong relation between cannabis use and the risk of psychosis,^[27] though the cause-and-effect relationship is debatel.^[28]

Cannabis is mostly used recreationally or as a medicinal drug, although it may also be used for spiritual purposes. In 2013, between 128 and 232 million people used cannabis (2.7% to 4.9% of the global population between the ages of 15 and 65).^[29] In 2015, 43% of Americans had ever used cannabis, which increased to 51% in 2016.^[30] About 12% have used it in the past year, and 7.3% have used it in the past month.^[31] This makes it the most commonly used illegal drug both in the world and the United States.^{[22][29]}

The earliest recorded uses date from the 3rd millennium BC.^[32] Since the early 20th century, cannabis has been subject to legal restrictions. The possession, use, and sale of cannabis is illegal in most countries of the world.^{[33][34]} Medical cannabis refers to the physician-recommended use of cannabis, which takes place in Canada, Belgium, Australia, the Netherlands, Germany, Spain, and 31 U.S. states.^[35] Cannabis use started to become popular in the U.S. in the 1970s.^[36] Support for legalization has increased in the United States and several U.S. states have legalized recreational or medical use.^[37]

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Cannabis



A flowering cannabis plant

Product name	Cannabis
Pronunciation	Cannabis /ˈkænəbɪs/ Marijuana /ˌmærɪˈhwɑːnə/
Source plant(s)	<i>Cannabis sativa</i> , <i>Cannabis sativa</i> forma <i>indica</i> , <i>Cannabis ruderalis</i>
Part(s) of plant	Flower
Geographic origin	Central and South Asia ^[1]
Active ingredients	Tetrahydrocannabinol, cannabidiol, cannabinol, tetrahydrocannabivarin
Main producers	Afghanistan, ^[2] Canada, ^[3] China, Colombia, ^[4] India, ^[2] Jamaica, ^[2] Lebanon, ^[5] Mexico, ^[6] Morocco, ^[2] Netherlands, Pakistan, Paraguay, ^[6] Spain, ^[2]

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	Thailand, Turkey, United States ^[2]
Legal status	<u>AU</u> : S9 (Prohibited) <u>CA</u> : Schedule II (legal for medical use) will legalize recreational use on October 17, 2018 ^[7] <u>DE</u> : Medical cannabis from state-controlled production: Anlage III, other cannabis: I <u>UK</u> : Class B <u>US</u> : Schedule I (legal in 9 states for recreational use) <u>UN</u> : Narcotic Schedule I

Uses

Medical

Medical cannabis, or medical marijuana, can refer to the use of cannabis and its cannabinoids to treat disease or improve symptoms; however, there is no single agreed-upon definition.^{[38][39]} The rigorous scientific study of cannabis as a medicine has been hampered by production restrictions and other federal regulations.^[40] There is limited evidence suggesting cannabis can be used to reduce nausea and vomiting during chemotherapy, to improve appetite in people with HIV/AIDS, and to treat chronic pain and muscle spasms.^{[41][42][43]} Its use for other medical applications is insufficient for conclusions about safety or efficacy.

Short-term use increases the risk of both minor and major adverse effects.^[42] Common side effects include dizziness, feeling tired and vomiting.^[42] Long-term effects of cannabis are not clear.^[42] Concerns include memory and cognition problems, risk of addiction, schizophrenia in young people, and the risk of children taking it by accident.^[41]

Recreational

Cannabis has psychoactive and physiological effects when consumed.^[44] The immediate desired effects from consuming cannabis include relaxation and euphoria (the "high" or "stoned" feeling), a general alteration of conscious perception, increased awareness of sensation, increased libido^[45] and distortions in the perception of time and space. At higher doses, effects can include altered body

image, auditory and/or visual illusions, pseudohallucinations and ataxia from selective impairment of polysynaptic reflexes. In some cases, cannabis can lead to dissociative states such as depersonalization^{[46][47]} and derealization.^[48]

Some immediate undesired side effects include a decrease in short-term memory, dry mouth, impaired motor skills and reddening of the eyes.^[49] Aside from a subjective change in perception and mood, the most common short-term physical and neurological effects include increased heart rate, increased appetite and consumption of food, lowered blood pressure, impairment of short-term and working memory,^{[50][51]} psychomotor coordination, and concentration. Some users may experience an episode of acute psychosis, which usually abates after six hours, but in rare instances, heavy users may find the symptoms continuing for many days.^[52] A reduced quality of life is associated with heavy cannabis use, although the relationship is inconsistent and weaker than for tobacco and other substances.^[53] It is unclear, however, if the relationship is cause and effect.^[53]

Spiritual

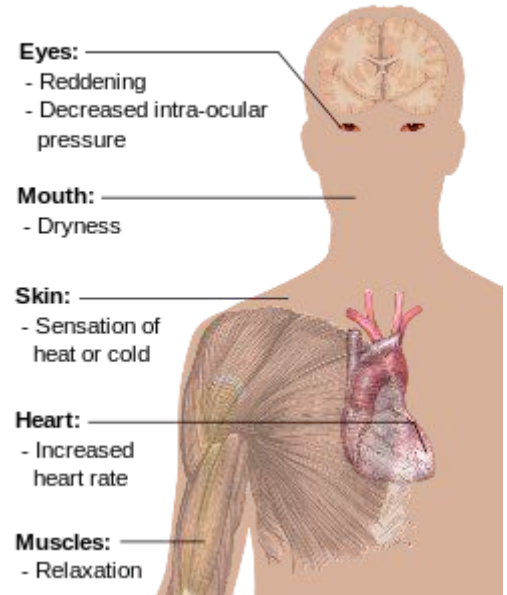
Cannabis has held sacred status in several religions. It has been used in an entheogenic context – a chemical substance used in a religious, shamanic, or spiritual context^[55] - in India and Nepal since the Vedic period dating back to approximately 1500 BCE, but perhaps as far back as 2000 BCE. There are several references in Greek mythology to a powerful drug that eliminated anguish and sorrow. Herodotus wrote about early ceremonial practices by the Scythians, thought to have occurred from the 5th to 2nd century BCE. In modern culture the spiritual use of cannabis has been spread by the disciples of the Rastafari movement who use cannabis as a sacrament and as an aid to meditation. The earliest known reports regarding the sacred status of cannabis in India and Nepal come from the Atharva Veda estimated to have been written sometime around 2000–1400 BCE.^[56]

Available forms

Cannabis is consumed in many different ways:^[57]

- smoking, which typically involves burning and inhaling vaporized cannabinoids ("smoke") from small pipes, bongs (portable versions of hookahs with a water chamber), paper-wrapped joints or tobacco-leaf-wrapped blunts, and other items.^[58]
- vaporizer, which heats any form of cannabis to 165–190 °C (329–374 °F),^[59] causing the active ingredients to evaporate into a vapor without burning the plant material (the boiling point of THC is 157 °C (315 °F) at 760 mmHg pressure).^[60]
- cannabis tea, which contains relatively small concentrations of THC because THC is an oil (lipophilic) and is only slightly water-soluble (with a solubility of 2.8 mg per liter).^[61] Cannabis tea is made by first adding a saturated fat to hot water (e.g. cream or any milk except skim) with a small amount of cannabis.^[62]
- edibles, where cannabis is added as an ingredient to one of a variety of foods, including butter and baked goods. In India it is commonly made into a beverage, bhang.

Bodily effects of Cannabis



Main short-term physical effects of cannabis



A woman smoking a marijuana "joint".



Process of making bhang in a Sikh village in Punjab, India. On the festival of colors called Holi, it is a customary addition to some intoxicating drinks.^[54]

Adverse effects

Short term

Acute effects may include anxiety and panic, impaired attention, and memory (while intoxicated), an increased risk of psychotic symptoms, and possibly an increased risk of accidents if a person drives a motor vehicle while intoxicated.^[64] Short-term cannabis intoxication can hinder the mental processes of organizing and collecting thoughts. This condition is known as temporal disintegration.^[65] Psychotic episodes are well-documented and typically resolve within minutes or hours. There have been few reports of symptoms lasting longer.^{[66][67]}

According to the United States Department of Health and Human Services, there were 455,000 emergency room visits associated with cannabis use in 2011. These statistics include visits in which the patient was treated for a condition induced by or related to recent cannabis use. The drug use must be "implicated" in the emergency department visit, but does not need to be the direct cause of the visit. Most of the illicit drug emergency room visits involved multiple drugs.^[68] In 129,000 cases, cannabis was the only implicated drug.^{[69][70]}

Marijuana is the most common illegal drug reported in motor vehicle accidents.^[71] A 2012 meta-analysis found that cannabis use was associated with an increased risk of being involved in a motor vehicle crash.^[72] A 2016 review also found a statistically significant increase in crash risk associated with marijuana use, but noted that this risk was "of low to medium magnitude."^[73] The increase in risk of motor vehicle crash for cannabis use is between 2 and 3 times relative to baseline, whereas that for comparable doses of alcohol is between 6 and 15 times.^[74]

Long term

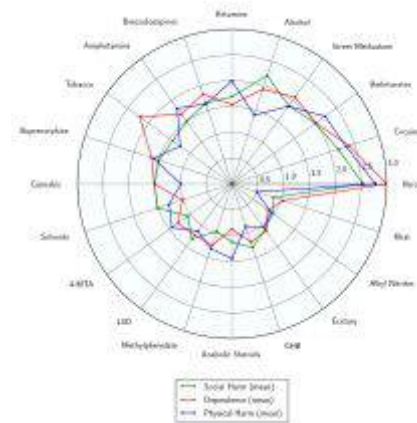
Heavy, long term exposure to marijuana may have biologically-based physical, mental, behavioral and social health consequences and may be "associated with diseases of the liver (particularly with co-existing hepatitis C), lungs, heart, and vasculature."^[75] It is recommended that cannabis use be stopped before and during pregnancy as it can result in negative outcomes for both the mother and baby.^{[76][77]} However, maternal use of marijuana during pregnancy does not appear to be associated with low birth weight or early delivery after controlling for tobacco use and other confounding factors.^[78] A 2014 review found that while cannabis use may be less harmful than alcohol use, the recommendation to substitute it for problematic drinking is premature without further study.^[79] Other side effects include cannabinoid hyperemesis syndrome.^[80]

A limited number of studies have examined the effects of cannabis smoking on the respiratory system.^[81] Chronic heavy marijuana smoking is associated with coughing, production of sputum, wheezing, and other symptoms of chronic bronchitis.^[64] The available evidence does not support a causal relationship between cannabis use and chronic obstructive pulmonary disease.^[82] Short-term use of cannabis is associated with bronchodilation.^[83]

Cannabis smoke contains thousands of organic and inorganic chemical compounds. This tar is chemically similar to that found in tobacco smoke,^[84] and over fifty known carcinogens have been identified in cannabis smoke,^[85] including; nitrosamines, reactive aldehydes, and polycyclic hydrocarbons, including benz[a]pyrene.^[86] Cannabis smoke is also inhaled more deeply than is tobacco smoke.^[87] As of 2015, there is no consensus regarding whether cannabis smoking is associated with an increased risk of cancer.^[88] Light and moderate use of cannabis is not believed to increase risk of lung or upper airway cancer. Evidence for causing these cancers is mixed concerning heavy, long-term use. In general there are far lower risks of pulmonary complications for regular cannabis



A joint prior to rolling, with a paper handmade filter on the left



Addiction experts in psychiatry, chemistry, pharmacology, forensic science, epidemiology and the police and legal services engaged in delphic analysis regarding 20 popular recreational drugs. Cannabis was ranked 11th in dependence, 17th in physical harm, and 10th in social harm.^[63]

smokers when compared with those of tobacco.^[89] A 2015 review found an association between cannabis use and the development of testicular germ cell tumors (TGCTs), particularly non-seminoma TGCTs.^[90] A 2015 analysis of six studies found little evidence that long-term or regular cannabis smoking was associated with lung cancer risk, though it could not rule out whether an association with heavy smoking exists.^[91] Another 2015 meta-analysis found no association between lifetime cannabis use and risk of head or neck cancer.^[92] Combustion products are not present when using a vaporizer, consuming THC in pill form, or consuming cannabis foods.^[93]

There is concern that cannabis may contribute to cardiovascular disease.^[94] As of 2018 evidence of an association is unclear.^[95]

Cannabis is believed to be an aggravating factor in rare cases of arteritis, a serious condition that in some cases leads to amputation. Because 97% of case-reports also smoked tobacco, a formal association with cannabis could not be made. If cannabis arteritis turns out to be a distinct clinical entity, it might be the consequence of vasoconstrictor activity observed from delta-8-THC and delta-9-THC.^[96] Other serious cardiovascular events including myocardial infarction, stroke,^[97] sudden cardiac death, and cardiomyopathy have been reported to be temporally associated with cannabis use. Research in these events is complicated because cannabis is often used in conjunction with tobacco, and drugs such as alcohol and cocaine.^[98] These putative effects can be taken in context of a wide range of cardiovascular phenomena regulated by the endocannabinoid system and an overall role of cannabis in causing decreased peripheral resistance and increased cardiac output, which potentially could pose a threat to those with cardiovascular disease.^[99] There is some evidence from case reports that cannabis use may provoke fatal cardiovascular events in young people who have not been diagnosed with cardiovascular disease.^[74] Smoking cannabis has also been shown to increase the risk of myocardial infarction by 4.8 times for the 60 minutes after consumption.^[100]

Neuroimaging

Although global abnormalities in white matter and grey matter are not associated with cannabis abuse, reduced hippocampal volume is consistently found. Amygdalar abnormalities are sometimes reported, although findings are inconsistent.^{[101][102][103]} Preliminary evidence suggests that this effect is largely mediated by THC, and that CBD may even have a protective effect.^[104]

Cannabis use is associated with increased recruitment of task related areas, such as the dorsolateral prefrontal cortex, which is thought to reflect compensatory activity due to reduced processing efficiency.^{[103][102][105]}

Cannabis use is associated with downregulation of CB₁ receptors. The magnitude of down regulation is associated with cumulative cannabis exposure, and is reversed after 1 month of abstinence.^{[106][107][108]}

There is limited evidence that chronic cannabis use can reduce levels of glutamate metabolites in the human brain.^[109]

Cognition

A 2015 meta analysis found that, although a longer period of abstinence was associated with smaller magnitudes of impairment, both retrospective and prospective memory were impaired in cannabis users. The authors concluded that some, but not all, of the deficits associated with cannabis use were reversible.^[110] A 2012 meta analyses found that deficits in most domains of cognition persisted beyond the acute period of intoxication, but was not evident in studies where subjects were abstinent for more than 25 days.^[111] Few high quality studies have been performed on the long-term effects of cannabis on cognition, and results were generally inconsistent.^[112] Furthermore, effect sizes of significant findings were generally small.^[111] One review concluded that, although most cognitive faculties were unimpaired by cannabis use, residual deficits occurred in executive functions.^[113] Impairments in executive functioning are most consistently found in older populations, which may reflect heavier cannabis exposure, or developmental effects associated with adolescent cannabis use.^[114] One review found three prospective cohort studies that examined the relationship between self reported cannabis use and intelligence quotient (IQ). The study following the largest number of heavy cannabis users reported that IQ declined between ages 7–13 and age 38. Poorer school performance and increased incidence of leaving school early were both associated with cannabis use, although a causal relationship was not established.^[106] Cannabis users demonstrated increased activity in task-related brain regions, consistent with reduced processing efficiency.^[115]

Psychiatric

At an epidemiological level, a dose response relationship exists between cannabis use and risk of psychosis.^{[116][117][118]} Although the epidemiological association is robust, evidence to suggest a causal relationship is lacking.^[119] Cannabis has also been associated with an earlier onset of psychosis.^[120]

It is not clear whether cannabis use affects the rate of suicide.^{[121][122]} Cannabis may also increase the risk of depression, but insufficient research has been performed to draw a conclusion.^{[123][117]} Cannabis use is associated with increased risk of anxiety disorders, although causality has not been established.^[124]

Reinforcement disorders

About 9% of those who experiment with marijuana eventually become dependent according to DSM-IV (1994) criteria.^[125] A 2013 review estimates daily use is associated with a 10-20% rate of dependence.^[41] The highest risk of cannabis dependence is found in those with a history of poor academic achievement, deviant behavior in childhood and adolescence, rebelliousness, poor parental relationships, or a parental history of drug and alcohol problems.^[126] Of daily users, about 50% experience withdrawal upon cessation of use (i.e. are dependent), characterized by sleep problems, irritability, dysphoria, and craving.^[106] Cannabis withdrawal is less severe than withdrawal from alcohol.^[127]

According to DSM-V criteria, 9% of those who are exposed to cannabis develop cannabis use disorder compared to 20% for cocaine, 23% for alcohol and 68% for nicotine. Cannabis abuse disorder in the DSM-V involves a combination of DSM-IV criteria for cannabis abuse and dependence, plus the addition of craving, minus the criterion related to legal troubles.^[106]

Overdose

THC, the principal psychoactive constituent of the cannabis plant, has low toxicity. The dose of THC needed to kill 50% of tested rodents is extremely high. Cannabis has not been reported to cause fatal overdose in humans.^[121]

Pharmacology

Mechanism of action

The high lipid-solubility of cannabinoids results in their persisting in the body for long periods of time.^[128] Even after a single administration of THC, detectable levels of THC can be found in the body for weeks or longer (depending on the amount administered and the sensitivity of the assessment method).^[128] A number of investigators have suggested that this is an important factor in marijuana's effects, perhaps because cannabinoids may accumulate in the body, particularly in the lipid membranes of neurons.^[129]

Not until the end of the 20th century was the specific mechanism of action of THC at the neuronal level studied. Researchers have subsequently confirmed that THC exerts its most prominent effects via its actions on two types of cannabinoid receptors, the CB₁ receptor and the CB₂ receptor, both of which are G protein-coupled receptors.^[130] The CB₁ receptor is found primarily in the brain as well as in some peripheral tissues, and the CB₂ receptor is found primarily in peripheral tissues, but is also expressed in neuroglial cells.^[131] THC appears to alter mood and cognition through its agonist actions on the CB₁ receptors, which inhibit a secondary messenger system (adenylate cyclase) in a dose-dependent manner. These actions can be blocked by the selective CB₁ receptor antagonist rimonabant (SR141716), which has been shown in clinical trials to be an effective treatment for smoking cessation, weight loss, and as a means of controlling or reducing metabolic syndrome risk factors.^[132] However, due to the dysphoric effect of CB₁ receptor antagonists, this drug is often discontinued due to these side effects.^[133]

Via CB₁ receptor activation, THC indirectly increases dopamine release and produces psychotropic effects.^[134] Cannabidiol (CBD) also acts as an allosteric modulator of the μ - and δ -opioid receptors.^[135] THC also potentiates the effects of the glycine receptors.^[136] It is unknown if or how these actions contribute to the effects of cannabis.

Chemistry

Detection in body fluids

THC and its major (inactive) metabolite, THC-COOH, can be measured in blood, urine, hair, oral fluid or sweat using chromatographic techniques as part of a drug use testing program or a forensic investigation of a traffic or other criminal offense.^[137] The concentrations obtained from such analyses can often be helpful in distinguishing active use from passive exposure, elapsed time since use, and extent or duration of use. These tests cannot, however, distinguish authorized cannabis smoking for medical purposes from unauthorized recreational smoking.^[138] Commercial cannabinoid immunoassays, often employed as the initial screening method when testing physiological specimens for marijuana presence, have different degrees of cross-reactivity with THC and its metabolites.^[139] Urine contains predominantly THC-COOH, while hair, oral fluid and sweat contain primarily THC.^[137] Blood may contain both substances, with the relative amounts dependent on the recency and extent of usage.^[137]

The Duquenois–Levine test is commonly used as a screening test in the field, but it cannot definitively confirm the presence of cannabis, as a large range of substances have been shown to give false positives. Despite this, it is common in the United States for prosecutors to seek plea bargains on the basis of positive D–L tests, claiming them to be conclusive, or even to seek conviction without the use of gas chromatography confirmation, which can only be done in the lab.^[140] In 2011, researchers at John Jay College of Criminal Justice reported that dietary zinc supplements can mask the presence of THC and other drugs in urine.^[141] However, a 2013 study conducted by researchers at the University of Utah School of Medicine refute the possibility of self-administered zinc producing false-negative urine drug tests.^[142]

Varieties and strains

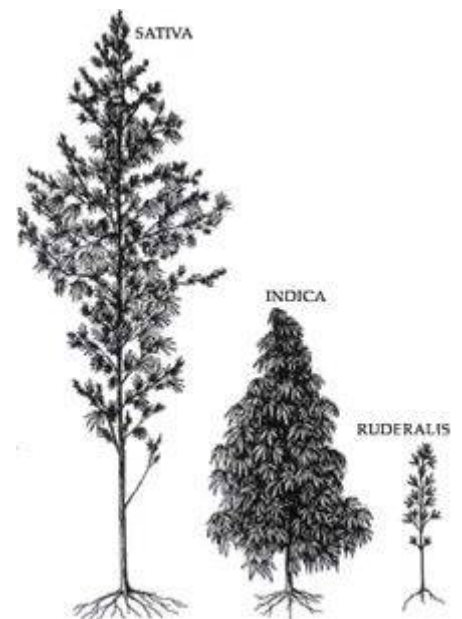
CBD is a 5-HT_{1A} receptor agonist, which may also contribute to an anxiolytic effect.^[143] This likely means the high concentrations of CBD found in *Cannabis indica* mitigate the anxiogenic effect of THC significantly.^[143] The cannabis industry claims that sativa strains provide a more stimulating psychoactive high while indica strains are more sedating with a body high.^[144] However this is disputed by researchers.^[145]

Psychoactive ingredients

According to the United Nations Office on Drugs and Crime (UNODC), "the amount of THC present in a cannabis sample is generally used as a measure of cannabis potency."^[146] The three main forms of cannabis products are the flower, resin (hashish), and oil (hash oil). The UNODC states that cannabis often contains 5% THC content, resin "can contain up to 20% THC content", and that "Cannabis oil may contain more than 60% THC content."^[146]

A 2012 review found that the THC content in marijuana had increased worldwide from 1970 to 2009.^[147] It is unclear, however, whether the increase in THC content has caused people to consume more THC or if users adjust based on the potency of the cannabis. It is likely that the higher THC content allows people to ingest less tar. At the same time, CBD levels in seized samples have lowered, in part because of the desire to produce higher THC levels and because more illegal growers cultivate indoors using artificial lights. This helps avoid detection but reduces the CBD production of the plant.^[148]

Australia's National Cannabis Prevention and Information Centre (NCPIC) states that the buds (flowers) of the female cannabis plant contain the highest concentration of THC, followed by the leaves. The stalks and seeds have "much lower THC levels".^[149] The UN states that leaves can contain ten times less THC than the buds, and the stalks one hundred times less THC.^[146]



Types of cannabis

After revisions to cannabis scheduling in the UK, the government moved cannabis back from a class C to a class B drug. A purported reason was the appearance of high potency cannabis. They believe skunk accounts for between 70 and 80% of samples seized by police^[150] (despite the fact that skunk can sometimes be incorrectly mistaken for all types of herbal cannabis).^{[151][152]} Extracts such as hashish and hash oil typically contain more THC than high potency cannabis flowers.^[153]

Preparations



Dried flower buds



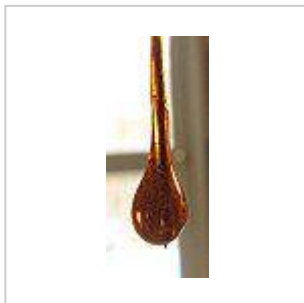
Kief



Hashish



Tincture



Hash oil



Infusion (dairy butter)



Pipe resin

Marijuana

Marijuana or marihuana (herbal cannabis),^[154] consists of the dried flowers and subtending leaves and stems of the female *Cannabis* plant.^{[155][156][157][158]} This is the most widely consumed form,^[158] containing 3% to 20% THC,^[159] with reports of up-to 33% THC.^[160] This is the stock material from which all other preparations are derived. Although herbal cannabis and industrial hemp derive from the same species and contain the psychoactive component (THC), they are distinct strains with unique biochemical compositions and uses. Hemp has lower concentrations of THC and higher concentrations of CBD, which decreases the psychoactive effects.^{[161][162]}

Kief

Kief is a powder, rich in trichomes,^[163] which can be sifted from the leaves and flowers of cannabis plants and either consumed in powder form or compressed to produce cakes of hashish.^[164] The word "kif" derives from colloquial Arabic كيف *kēf/kīf*, meaning pleasure.^[165]

Hashish

Hashish (also spelled hasheesh, hashisha, or simply hash) is a concentrated resin cake or ball produced from pressed kief, the detached trichomes and fine material that falls off cannabis flowers and leaves.^[166] or from scraping the resin from the surface of the plants and rolling it into balls. It varies in color from black to golden brown depending upon purity and variety of cultivar it was obtained from.^[167] It can be consumed orally or smoked, and is also vaporised, or 'vaped'.^[168] The term "rosin hash" refers to a high quality solventless product obtained through heat and pressure.^[169]

Tincture

Cannabinoids can be extracted from cannabis plant matter using high-proof spirits (often grain alcohol) to create a tincture, often referred to as "green dragon".^[170] Nabiximols is a branded product name from a tincture manufacturing pharmaceutical company.^[171]

Hash oil

Hash oil is a resinous matrix of cannabinoids obtained from the *Cannabis* plant by solvent extraction,^[172] formed into a hardened or viscous mass.^[173] Hash oil can be the most potent of the main cannabis products because of its high level of psychoactive compound per its volume, which can vary depending on the plant's mix of essential oils and psychoactive compounds.^[174] Butane and supercritical carbon dioxide hash oil have become popular in recent years.^[175]

Infusions

There are many varieties of cannabis infusions owing to the variety of non-volatile solvents used.^[176] The plant material is mixed with the solvent and then pressed and filtered to express the oils of the plant into the solvent. Examples of solvents used in this process are cocoa butter, dairy butter, cooking oil, glycerine, and skin moisturizers. Depending on the solvent, these may be used in cannabis foods or applied topically.^[177]

Medical use

Medical marijuana refers to the use of the *Cannabis* plant as a physician-recommended herbal therapy as well as synthetic^[178] THC and cannabinoids. So far, the medical use of cannabis is legal only in a limited number of territories, including Canada, Belgium, Australia, the Netherlands, Spain, and many U.S. states. This usage generally requires a prescription, and distribution is usually done within a framework defined by local laws. There is evidence supporting the use of cannabis or its derivatives in the treatment of chemotherapy-induced nausea and vomiting, neuropathic pain, and multiple sclerosis. Lower levels of evidence support its use for AIDS wasting syndrome, epilepsy, rheumatoid arthritis, and glaucoma.^[70]

History



Cannabis sativa from Vienna
Dioscurides, AD 512

Cannabis is indigenous to Central and South Asia,^[179] and its use for fabric and rope dates back to the Neolithic age in China and Japan.^{[180][181]} It is unclear when cannabis first became known for its psychoactive properties; some scholars suggest that the ancient Indian drug soma, mentioned in the Vedas, was cannabis, although this theory is disputed.^[182]

Cannabis was also known to the ancient Assyrians, who discovered its psychoactive properties through the Aryans.^[183] Using it in some religious ceremonies, they called it qunubu (meaning "way to produce smoke"), a probable origin of the modern word "cannabis".^[184] The Aryans also introduced cannabis to the Scythians, Thracians and Dacians, whose shamans (the kapnobatai—"those who walk on smoke/clouds") burned cannabis flowers to induce trance.^[185]

Cannabis has an ancient history of ritual use and is found in pharmacological cults around the world. Hemp seeds discovered by archaeologists at Pazyryk suggest early ceremonial practices like eating by the Scythians occurred during the 5th to 2nd century BC, confirming previous historical reports by Herodotus.^[186] It was used by Muslims in various Sufi orders as early as the Mamluk period, for example by the Qalandars.^[187] Smoking pipes uncovered in Ethiopia and carbon-dated to around c. AD 1320 were found to have traces of cannabis.^[188]

Following an 1836–1840 travel in North Africa and the Middle East, French physician Jacques-Joseph Moreau wrote on the psychological effects of cannabis use; Moreau was a member of Paris' Club des Hashischins (founded in 1844). In 1842, Irish physician William Brooke O'Shaughnessy who had studied the drug while working as a medical officer in Bengal with the East India company, brought a quantity of cannabis with him on his return to Britain, provoking renewed interest in the West.^[189] Examples of classic literature of the period featuring cannabis include *Les paradis artificiels* (1860) by Charles Baudelaire and *The Hasheesh Eater* (1857) by Fitz Hugh Ludlow.

Cannabis was criminalized in various countries beginning in the 19th century. The British colonies of Mauritius banned cannabis in 1840 over concerns on its effect on Indian indentured workers,^[190] the same occurred in British Singapore in 1870.^[191] In the United States, the first restrictions on sale of cannabis came in 1906 (in District of Columbia).^[192] It was outlawed in Jamaica (then a British colony) in 1913, in South Africa in 1922, and in the United Kingdom and New Zealand in the 1920s.^[193] Canada criminalized cannabis in *The Opium and Narcotic Drug Act, 1923*,^[194] before any reports of the use of the drug in Canada.



Cannabis propaganda sheet from 1935

In 1925 a compromise was made at an international conference in The Hague about the International Opium Convention that banned exportation of "Indian hemp" to countries that had prohibited its use, and requiring importing countries to issue certificates approving the importation and stating that the shipment was required "exclusively for medical or scientific purposes". It also required parties to "exercise an effective control of such a nature as to prevent the illicit international traffic in Indian hemp and especially in the resin".^{[195][196]} In the United

States in 1937, the Marihuana Tax Act was passed,^[197] and prohibited the production of hemp in addition to cannabis.

In 1972, the Dutch government divided drugs into more- and less-dangerous categories, with cannabis being in the lesser category. Accordingly, possession of 30 grams or less was made a misdemeanor.^[198] Cannabis has been available for recreational use in coffee shops since 1976.^[199] Cannabis products are only sold openly in certain local "coffeeshops" and possession of up to 5 grams for personal use is decriminalised, however: the police may still confiscate it, which often happens in car checks near the border. Other types of sales and transportation are not permitted, although the general approach toward cannabis was lenient even before official decriminalisation.^{[200][201][202]}

In Uruguay, President Jose Mujica signed legislation to legalize recreational cannabis in December 2013, making Uruguay the first country in the modern era to legalize cannabis. In August 2014, Uruguay legalized growing up to six plants at home, as well as the formation of growing clubs, and a state-controlled marijuana dispensary regime.

Following Canada's 2015 election of Justin Trudeau and formation of a Liberal government, in 2017 the House of Commons passed a bill to legalize cannabis on 1 July 2018.^[203] However, on 20 June 2018 it was announced that the legalization would be delayed until 17 October 2018 as provinces wanted more time to prepare.^[204]

The United Nations' World Drug Report stated that cannabis "was the world's most widely produced, trafficked, and consumed drug in the world in 2010", and estimated between 128 million and 238 million users globally in 2015.^{[205][206]}



Cannabis indica fluid extract, American Druggists Syndicate, pre-1937

Society and culture

Legal status

Since the beginning of the 20th century, most countries have enacted laws against the cultivation, possession or transfer of cannabis.^[207] These laws have impacted adversely on the cannabis plant's cultivation for non-recreational purposes, but there are many regions where, under certain circumstances, handling of cannabis is legal or licensed. Many jurisdictions have lessened the penalties for possession of small quantities of cannabis so that it is punished by confiscation and sometimes a fine, rather than imprisonment, focusing more on those who traffic the drug on the black market.

In some areas where cannabis use had been historically tolerated, new restrictions were instituted, such as the closing of cannabis coffee shops near the borders of the Netherlands,^[208]

and closing of coffee shops near secondary schools in the Netherlands.^[209] In Copenhagen, Denmark in 2014, mayor Frank Jensen discussed possibilities for the city to legalize cannabis production and commerce.^[210]

Some jurisdictions use free voluntary treatment programs and/or mandatory treatment programs for frequent known users. Simple possession can carry long prison terms in some countries, particularly in East Asia, where the sale of cannabis may lead to a sentence of life in prison or even execution. Political parties, non-profit organizations, and causes based on the legalization of medical cannabis and/or legalizing the plant entirely (with some restrictions) have emerged in such countries as China and Thailand.^{[211][212]}

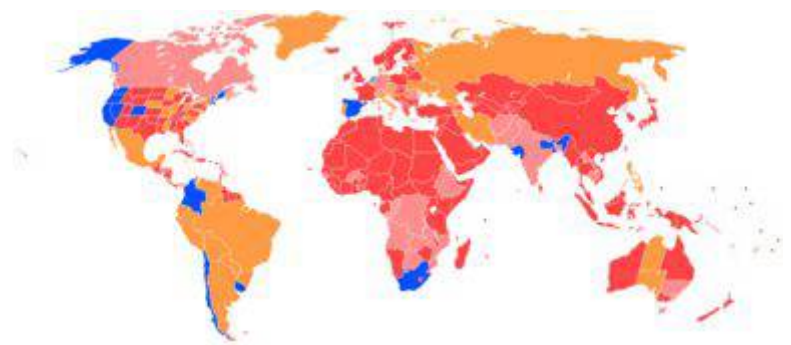
In December 2012, the U.S. state of Washington became the first state to officially legalize cannabis in a state law (Washington Initiative 502) (but still illegal by federal law),^[213] with the state of Colorado following close behind (Colorado Amendment 64).^[214] On January 1, 2013, the first marijuana "club" for private marijuana smoking (no buying or selling, however) was allowed for the first time in Colorado.^[215] The California Supreme Court decided in May 2013 that local governments can ban medical marijuana dispensaries despite a state law in California that permits the use of cannabis for medical purposes. At least 180 cities across California have enacted bans in recent years.^[216]

In December 2013, Uruguay became the first country to legalize growing, sale and use of cannabis.^[217] After a long delay in implementing the retail component of the law, in 2017 sixteen pharmacies were authorized to sell cannabis commercially.^[218] On June 19, 2018, the Canadian Senate passed a bill and the Prime Minister announce the effective legalization date as October 17, 2018.^[219] Canada is the second nation to legalise the drug.^[220]

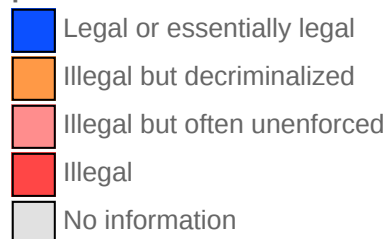
In November 2015, Uttarakhand became the first state of India to legalize the cultivation of hemp for industrial purposes.^[221]

On October 17, 2015, Australian health minister Sussan Ley presented a new law that will allow the cultivation of cannabis for scientific research and medical trials on patients.^[222] In December 2015, it was reported that the Canadian government had committed to legalizing cannabis, but at that time no timeline for the legalization was set out.^[223] On 20 June 2018, a legalization date was set for 17 October 2018, delayed from 1 July 2018.^[204]

As the drug has increasingly come to be seen as a health issue instead of criminal behavior, marijuana has also been legalized or decriminalized in: Czech Republic,^[224] Colombia,^{[225][226]} Ecuador,^{[227][228][229]} Mexico,^{[230][231]} Portugal,^[232] and Canada.^[233]



World laws on possession of small amounts of cannabis for personal use



Usage

In 2013, between 128 and 232 million people used cannabis (2.7% to 4.9% of the global population between the ages of 15 and 65).^[29] Cannabis is by far the most widely used illicit substance.^[235]

Global estimates of drug users in 2016 (in millions of users)^[234]

Substance	Best estimate	Low estimate	High estimate
<u>Amphetamine-type stimulants</u>	34.16	13.42	55.24
<u>Cannabis</u>	192.15	165.76	234.06
<u>Cocaine</u>	18.20	13.87	22.85
<u>Ecstasy</u>	20.57	8.99	32.34
<u>Opiates</u>	19.38	13.80	26.15
<u>Opioids</u>	34.26	27.01	44.54

United States

Between 1973 and 1978, eleven states decriminalized marijuana.^[236] In 2001 Nevada reduced marijuana possession to a misdemeanor and since 2012, several other states have decriminalized and even legalized marijuana.^[236]

In 2015, almost half of the people in the United States had tried marijuana, 12% had used it in the past year, and 7.3% had used it in the past month.^[31] In 2014, daily marijuana use amongst US college students had reached its highest level since records began in 1980, rising from 3.5% in 2007 to 5.9% in 2014 and had surpassed daily cigarette use.^[237]

In the US, men are over twice as likely to use marijuana as women and 18-29 year-olds are six times more likely to use as over 65-year-olds.^[36] In 2015, a record 44% of the US population has tried marijuana in their lifetime, an increase from 38% in 2013 and 33% in 1985.^[36]

Marijuana use in the United States is three times above the global average, but in line with other Western democracies. 44% of American 12th graders have tried the drug at least once, and the typical age of first-use is 16, similar to the typical age of first-use for alcohol but lower than the first-use age for other illicit drugs.^[235]

Economics

Production

It is often claimed by growers and breeders of herbal cannabis that advances in breeding and cultivation techniques have increased the potency of cannabis since the late 1960s and early '70s when THC was first discovered and understood. However, potent seedless cannabis such as "Thai sticks" were already available at that time. Sinsemilla (Spanish for "without seed") is the dried, seedless inflorescences of female cannabis plants. Because THC production drops off once pollination occurs, the male plants (which produce little THC themselves) are eliminated before they shed pollen to prevent pollination. Advanced cultivation techniques such as hydroponics, cloning, high-intensity artificial lighting, and the sea of green method are frequently employed as a response (in part) to prohibition enforcement efforts that make outdoor cultivation more risky. It is often cited that the average levels of THC in cannabis sold in the United States rose dramatically between the 1970s and 2000, but such statements are likely skewed because undue weight is given to much more expensive and potent, but less prevalent samples.^[238]



Woman selling cannabis and bhang in Guwahati, Assam, India

"Skunk" refers to several named strains of potent cannabis, grown through selective breeding and sometimes hydroponics. It is a cross-breed of *Cannabis sativa* and *C. indica* (although other strains of this mix exist in abundance). Skunk cannabis potency ranges usually from 6% to 15% and rarely as high as 20%. The average THC level in coffee shops in the Netherlands is about 18–19%.^[239]

Price

The price or street value of cannabis varies widely depending on geographic area and potency.^[240]

In the United States, cannabis is overall the number four value crop, and is number one or two in many states including California, New York and Florida, averaging \$3,000 per pound (\$6,600/kg).^{[241][242]} Some believe it generates an estimated \$36 billion market.^[243] Some have argued that this estimate is methodologically flawed, and makes unrealistic assumptions about the level of marijuana consumption. Other estimates claiming to correct for this flaw claim that the market is between \$2.1-\$4.3 billion.^[235] The United Nations Office on Drugs and Crime claims in its 2008 World Drug Report that typical U.S. retail prices are \$10–15 per gram (approximately \$280–420 per ounce). Street prices in North America are known to range from about \$40–\$400 per ounce (\$1.4–\$14/g), depending on quality.^[244]

The European Monitoring Centre for Drugs and Drug Addiction reports that typical retail prices in Europe for cannabis varies from €2 to €20 per gram, with a majority of European countries reporting prices in the range €4–16.^[245]

Gateway drug

The Gateway Hypothesis states that cannabis use increases the probability of trying "harder" drugs. The hypothesis has been hotly debated as it is regarded by some as the primary rationale for the United States prohibition on cannabis use.^{[246][247]} A Pew Research Center poll found that political opposition to marijuana use was significantly associated with concerns about health effects and whether legalization would increase marijuana use by children.^[248]

Some studies state that while there is no proof for the gateway hypothesis,^[249] young cannabis users should still be considered as a risk group for intervention programs.^[250] Other findings indicate that hard drug users are likely to be poly-drug users, and that interventions must address the use of multiple drugs instead of a single hard drug.^[251] Almost two-thirds of the poly drug users in the "2009/10 Scottish Crime and Justice Survey" used cannabis.^[252]

The gateway effect may appear due to social factors involved in using any illegal drug. Because of the illegal status of cannabis, its consumers are likely to find themselves in situations allowing them to acquaint with individuals using or selling other illegal drugs.^{[253][254]} Utilizing this argument some studies have shown that alcohol and tobacco may additionally be regarded as gateway drugs;^[255] however, a more parsimonious explanation could be that cannabis is simply more readily available (and at an earlier age) than illegal hard drugs. In turn alcohol and tobacco are easier to obtain at an earlier point than is cannabis (though the reverse may be true in some areas), thus leading to the "gateway sequence" in those individuals since they are most likely to experiment with any drug offered.^[246]

An alternative to the gateway hypothesis is the common liability to addiction (CLA) theory. It states that some individuals are, for various reasons, willing to try multiple recreational substances. The "gateway" drugs are merely those that are (usually) available at an earlier age than the harder drugs. Researchers have noted in an extensive review that it is dangerous to present the sequence of events described in gateway "theory" in causative terms as this hinders both research and intervention.^[256]

Research

Cannabis research is challenging since the plant is illegal in most countries.^{[257][258][259][260][261]} Research-grade samples of the drug are difficult to obtain for research purposes, unless granted under authority of national governments.

There are also other difficulties in researching the effects of cannabis. Many people who smoke cannabis also smoke tobacco.^[262] This causes confounding factors, where questions arise as to whether the tobacco, the cannabis, or both that have caused a cancer. Another difficulty researchers have is in recruiting people who smoke cannabis into studies. Because cannabis is an illegal drug in many countries, people may be reluctant to take part in research, and if they do agree to take part, they may not say how much cannabis they actually smoke.^[263]

A 2015 review found that the use of high CBD-to-THC strains of cannabis showed significantly fewer positive symptoms such as delusions and hallucinations, better cognitive function and both lower risk for developing psychosis, as well as a later age of onset of the illness, compared to cannabis with low CBD-to-THC ratios.^[264] A 2014 Cochrane review found that research was insufficient to determine the safety and efficacy to using cannabis to treat schizophrenia or psychosis.^[265]

See also

- [Occupational health concerns of cannabis use](#)
- [US National estimates of marijuana use](#)

Footnotes

1. Also referred to as "pot"^[8] "weed",^[9] "dope",^[10] and "ganja" /ɡɑːndʒə/,^[11] among many other nicknames^[12] ("grass",^[13] "herb",^[14] "skunk",^[15] "Mary Jane",^[16] etc.).

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