

Marijuana: A Primer

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What is Marijuana/Cannabis?

The term 'marijuana' (sometimes spelled 'marihuana') is Mexican in origin and typically refers to any part of -- or any one of -- the three distinctive subspecies of the cannabis plant: *cannabis sativa* (which tends to grow tall and stalky), *cannabis indica* (which tends to grow smaller and bushier), or *cannabis ruderalis* (found primarily in Russia and Eastern Europe.) Grown outdoors, the cannabis plant typically achieves maturity within three to five months. Cultivated indoors under optimum heat and lighting, the plant may reach maturity within as few as 60 days.

Humans have cultivated and consumed the flowering tops of the female cannabis plant since virtually the beginning of recorded history. Cannabis-based textiles dating to 7,000 B.C. have been recovered in northern China, and the plant's use as a medicinal and euphoric agent date back nearly as far. In 2008, archeologists in Central Asia discovered over two pounds of cannabis in the 2,700-year-old grave of an ancient mummified shaman. After scientists conducted extensive testing on the material's potency, they affirmed, "[T]he most probable conclusion ... is that [ancient] culture[s] cultivated cannabis for pharmaceutical, psychoactive, and divinatory purposes."¹

Modern cultures continue to utilize cannabis for these same purposes, despite a present-day, nearly worldwide ban on the plant's cultivation and consumption imposed by various governments. In the United States, Congress initially imposed federal prohibitions outlawing cannabis' recreational, industrial, and therapeutic use by the passage of the Marihuana Tax Act of 1937. This federal prohibition was later reaffirmed by Congress' decision to classify marijuana - as well as all of the plant's active compounds, known as cannabinoids - as Schedule I substances under the Controlled Substances Act of 1970. This classification, which asserts by statute that cannabis is equally as dangerous to the public as heroin and is more dangerous than cocaine, defines cannabis and its dozens of distinct cannabinoids as possessing "a high potential for abuse ... no currently accepted medical use, ... [and] a lack of accepted safety for the use of the drug ... under medical supervision." By contrast, cocaine and methamphetamine - which remain illicit for recreational use but are allowed as prescription drug agents - are classified as Schedule II drugs. Examples of Schedule III and IV substances include anabolic steroids and Valium, respectively, while the law defines codeine-containing cough suppressants as Schedule V drugs, the federal government's most lenient classification.

Despite the U.S. government's nearly century-long prohibition of the plant, scientists in American and around the world have continued to closely study the plant and its effects on living organisms, including in clinical trials. In recent years, scientists' interest in the plant and its active constituents,

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known as cannabinoids, has increased exponentially. Scientific study of the cannabis plant has now identified over 60 unique, biologically active cannabinoids² - such as THC, THCV, CBD, THCA, CBC, and CBG, among others - many of which possess documented therapeutic properties. A recent meta-analysis of these compounds identifies well over a dozen therapeutic properties attributable to cannabinoids, including neuroprotective, anti-cancer, anti-bacterial, and anti-diabetic properties.³ To date, there are over 22,000 published studies or reviews in the scientific literature pertaining to the cannabis plant and its cannabinoids. Nearly one-half of these were published within the last five years. This total includes over 2,700 separate papers published in 2009, 1,950 papers published in 2010, another 2,450 published in 2011, and over 2,900 papers published in 2012, according to a key word search on PubMed, the U.S. government repository for peer-reviewed scientific research. A review of several hundred papers assessing cannabis' therapeutic properties is available here: <http://norml.org/library/recent-research-on-medical-marijuana>.

What Are Some Of The Uses Of Cannabis?

Historically, humans have used various parts of the cannabis plant for a multitude of purposes. Most people today are readily aware that cannabis is consumed socially as a mood-enhancer. By contrast, certain varieties of cannabis - as well as most parts of the plant, including the seeds and the stalk - contain virtually no psychoactive properties but may be utilized in other ways. For example, ground seeds from the cannabis plant contain high and balanced levels of essential amino acids and essential fatty acids and may be baked into a variety of nutritional food-stuffs, such as bread, butter, and salad dressing. Oil can also be processed from cannabis seeds and used for sautéing or consumed as a nutritional supplement.⁴ Since the seeds contain negligible amounts of the plant's primary psychoactive agent, the importation and domestic sale of certain cannabis-based foods, oils, and sterilized seeds is permitted in the United States under federal law.

The stalk of the marijuana plant, primarily of the cannabis *sativa* variety - which can grow as high as 20 feet in height - can also be harvested for bast fiber content. This renewable resource is a common source of paper, rope, and clothing. Most industrialized nations, including Canada, Japan, Australia, and the European Union, regulate the commercial production of low THC varieties of cannabis for industrial purposes.⁵ During World War II the U.S. government commissioned tens of thousands of domestic farmers to grow cannabis to assist with America's wartime needs. Following the War's conclusion, however, the United State's government imposed a complete ban on the domestic production of the plant, including the cultivation of non-psychoactive cannabis *sativa* varieties. That ban continues today.

The plant's cannabinoids are largely responsible for cannabis' physiological, mood-altering, and therapeutic effects. THC, the most studied of all the plant's cannabinoids, is psychoactive and is primarily responsible for the plant's influence on mood and behavior. It also possesses various therapeutic effects. Most acknowledged among these are pain relief, appetite stimulation, nausea

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and vomiting mitigation, anti-spasticity and anti-spasmodic effects, and intraocular pressure reduction in patients with glaucoma. An isolated stereoisomer of THC is presently available as an FDA-approved product Dronabinol, which is classified under federal law as a Schedule III substance. It is FDA-approved as an appetite stimulant and as an anti-emetic in patients with HIV/AIDS or undergoing chemotherapy treatment. A number of additional, non-psychotropic cannabinoids such as CBD also possess numerous therapeutic properties. A summary of many of these cannabinoids and their potential therapeutic applications may be found here: <http://www.alternet.org/drugs/5-marijuana-compounds-could-help-combat-cancer-alzheimers-parkinsons-if-only-they-were-legal>.

How Do Cannabinoids Interact With The Body?

Scientists have only recently begun to discover the answer to this question as researchers today are just beginning to understand the many complex ways that cannabinoids interact with the human body.

Subjects experience psychological and physiological effects after ingesting cannabis because cannabinoids, THC in particular, interact with a complex and dense receptor system within the body.⁶ The CB1 receptors, first identified in the late 1980s, reside predominantly in the nervous system and their stimulation is responsible for the plant's psychoactive and behavioral effects, among other functions. The CB2 receptors, identified in the early 1990s, reside primarily in the immune system and are involved in the moderation of a number of biological functions, including inflammation and pain response. Naturally occurring chemicals in human body (so-called endocannabinoids), which possess a similar molecular structure to herbal cannabinoids, act as neuromodulators and cytokine modulators within this receptor system to regulate many of the body's essential physiological functions -- including appetite, blood pressure, reproduction, bone growth, tumor modulation, immunity, inflammation, pain sensation, memory, and muscle tone, among others. It is theorized that a properly functioning endogenous cannabinoid receptor system is necessary for good health⁷ and that certain disease types may be the result of deficiencies within this system.⁸ According to a National Institutes of Health review, "[M]odulating the activity of the endocannabinoid system ... hold[s] therapeutic promise in a wide range of disparate diseases and pathological conditions, ranging from mood and anxiety disorders, movement disorders such as Parkinson's and Huntington's disease, neuropathic pain, multiple sclerosis and spinal cord injury, to cancer, atherosclerosis, myocardial infarction, stroke, hyper-tension, glaucoma, obesity/metabolic syndrome, and osteoporosis, to name just a few."⁹ A summary of this receptor system, its regulatory functions, and implications for the use of cannabinoids in therapeutic treatment is available here: <http://norml.org/library/item/introduction-to-the-endocannabinoid-system>.

What are some of the specific psychological and physical effects subjects will experience after consuming cannabis? The answer to this question often varies from subject to subject. Many of the plant's effects are dependent on percentage of THC and other cannabinoids present in the cannabis

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consumed. (The cannabinoid CBD, for instance, counteracts some of the psychoactivity of THC.) Moreover, cannabis naive users tend to experience different effects compared to more experienced users who have become tolerant to some of the cannabinoids' mood-altering and physiological qualities. If a less experienced user consumes too much cannabis at one time, he or she may experience a mix of unpleasant physical and psychological feelings, such as a tachycardia (rapid heart beat), dry mouth, and a growing sense of paranoia. (These adverse effects are commonly referred to as a 'panic attack.')

These feelings, while mildly unpleasant, are only temporary and pose little-to-no actual long-term risk to the user's health.

As cannabis consumers become more experienced with cannabis, they become more tolerant to some of the drug's physical effects. More experienced consumers also learn to better self-regulate (or 'titrate') their dosage to better avoid potentially dysphoric symptoms such as anxiety or paranoia.

What Is The Safety Profile of Cannabis?

Cannabinoids have a relatively unique safety record, particularly when compared to other therapeutically active substances. Most significantly, the consumption of cannabinoids -- regardless of quantity or potency -- cannot induce a fatal overdose because, unlike alcohol or opiates, they do not act as central nervous system depressants. According to a 1995 review prepared for the World Health Organization, "There are no recorded cases of overdose fatalities attributed to cannabis, and the estimated lethal dose for humans extrapolated from animal studies is so high that it cannot be achieved by ... users."¹⁰

Cannabinoids also appear to be largely non-toxic to healthy cells and organs. Writes Dr. Mitch Earleywine in the 2002 Oxford University Press publication, *Understanding Marijuana: A New Look at the Scientific Evidence*, "[C]annabis is essentially non-toxic."¹¹ A systematic review of clinical trials over a 40-year period, published in the *Canadian Medical Association Journal*, found no higher incidence of serious adverse effects from cannabis-consuming subjects compared to controls, and cited 'dizziness' as the primary reported non-serious adverse event reported.

¹² Additionally, in some initial trials, cannabinoids have demonstrated neuroprotective properties against toxic agents¹³ and have shown profound anti-cancer properties.¹⁴ Stated the National Academy of Sciences, Institute of Medicine in their 1999 review, *Marijuana and Medicine: Assessing the Science Base*, "Except for the harms associated with smoking, the adverse effects of marijuana use are within the range of effects tolerated for other medications."¹⁵ A more recent meta-analysis assessing the effects of long-term exposure to cannabis concludes, "Overall, by comparison with other drugs used mainly for 'recreational' purposes, cannabis could be rated to be a relatively safe drug."¹⁶

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Nonetheless, cannabis should not necessarily be viewed as a 'harmless' substance. Consuming cannabis will alter mood, influence emotions, and temporarily alter perception, so consumers are best advised to pay particular attention to their set (emotional state) and setting (environment) prior to using it. It should not be consumed immediately prior to driving or prior to engaging in tasks that require certain learning skills, such as the retention of new information. Further, there may be some populations that are susceptible to increased risks from the use of cannabis, such as adolescents, pregnant or nursing mothers, and patients with or who have a family history of mental illness. Patients with hepatitis C, decreased lung function (such as chronic obstructive pulmonary disease), or who have a history of heart disease or stroke may also be at a greater risk of experiencing certain adverse side effects from cannabis. As with any therapy, patients concerned about such risks should consult thoroughly with their physician before deciding whether the medical use of cannabis is safe and appropriate for them.

Does It Make Difference How One Consumes Cannabis?

Cannabis is most often inhaled - either through a cigarette (joint), pipe, water-pipe (also known colloquially as a 'bong'), or vaporizer. Consumers tend to prefer inhalation as a route of administration because they begin to experience cannabis' effects almost immediately after inhalation. This outcome allows them to moderate their dose as needed or in accordance with their particular preference, as well as to achieve immediate relief from pain, nausea, and other symptoms.

Regardless of whether a person is inhaling cannabis via a joint, pipe, or water-pipe, they are still subjecting their lungs to potentially noxious smoke. However, studies have, to date, failed to link cannabis inhalation - even over the long-term - to the sort of adverse pulmonary effects associated with tobacco smoking. According to a 2012 study published in the *Journal of the American Medical Association* (JAMA), lifetime, moderate cannabis smoking (defined as at least one joint per day for seven years or one joint per week for 49 years) was not associated with adverse affects on pulmonary function.¹⁷ Cannabis inhalation is also not associated with increased prevalence of certain types of cancers, such as melanoma, prostate cancer, or breast cancer.¹⁸ Nor has its use been associated with higher prevalence of tobacco-related cancers such as lung cancer.¹⁹ In 2006, the results of the largest case-controlled study ever to investigate the respiratory effects of marijuana smoking reported that cannabis use was not associated with lung-related cancers, even among subjects who reported smoking more than 22,000 joints over their lifetime. "We hypothesized that there would be a positive association between marijuana use and lung cancer, and that the association would be more positive with heavier use," one of the study's primary researchers, Dr. Donald Tashkin of the University of California at Los Angeles stated. "What we found instead was no association at all, and even a suggestion of some protective effect."²⁰

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The use of a water-pipe filtration system primarily cools cannabis smoke. However, this technology is not particularly efficient at eliminating the toxic byproducts of combustion. As a result, some cannabis consumers utilize vaporizers, which heat marijuana to a point where cannabinoid vapors form, but below the point of combustion. This technology allows consumers to experience the rapid onset of the plant's effects while avoiding many of the associated respiratory hazards associated with smoking -- such as coughing, wheezing, or chronic bronchitis. In several clinical trials, investigators have concluded that vaporization is a "safe and effective"²¹ cannabinoid delivery mode that "does not result in exposure to combustion gases."²² Researchers also report that vaporization results in higher plasma concentrations of THC compared to smoked cannabis.²³

Consuming moderate to high quantities of marijuana orally, such as in food or in a tincture (a liquid-based solution), will yield a different and sometimes more intense outcome. Consumers will typically not begin to feel any psychoactive or physiological effects of the plant for at least 45 minutes to 90 minutes after ingestion. This delayed onset makes it more difficult for subjects to regulate their dosage. Orally consumed cannabinoids tends to be stronger acting and last far longer (upwards of four to six hours is typical) than the effects of inhaled cannabis. This result is largely because of the way bodies metabolize THC. When cannabis is inhaled, THC passes rapidly from the lungs to the blood stream and to the brain. By contrast, when cannabis is consumed orally, a significant portion of THC is converted into the metabolite 11-hydroxy-THC before reaching the brain. (Inhaling cannabis produces only trace levels of this chemical.) Since this metabolite is believed to be slightly more potent than THC and possesses a greater blood-brain penetrability, the physical and psychoactive effects of substance may be magnified in some consumers.

Some users prefer these longer-lasting effects, particularly those seeking to treat chronic conditions. Other consumers, such as those seeking occasional symptomatic relief or those less experienced to cannabis' effects prefer the milder, shorter-lived effects associated with inhalation. Additional information regarding inhaled cannabis versus orally ingested THC is available here: <http://norml.org/component/zoo/category/marinol-vs-natural-cannabis>.

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³ Izzo et al. 2009. Non-psychoactive plant cannabinoids: new therapeutic opportunities from an ancient herb. *Trends in Pharmacological Sciences* 30: 515-527.

⁴ Chen et al. 2010. Analytical characterization of Hempseed oil from eight regions in China. *Journal of Dietary Supplements* 2: 117-129.

⁵ U.S. Congressional Research Service. *Hemp as an Agricultural Commodity*. January 2005.

⁶ Mitch Earleywine. *Understanding Marijuana: A New Look at the Scientific Evidence*. Oxford University Press: 2002.

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- ¹⁰ Wayne Hall. A comparative appraisal of the health and psychological consequences of alcohol, cannabis, nicotine, and opiate use. National Drug and Alcohol Research Centre, University of New South Wales, 1995.
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- ²³ Ibid.