Marijuana

Other common name(s): pot, grass, cannabis, weed, hemp, hash, marihuana, ganja, and dozens of others

Scientific/medical name(s): *Cannabis sativa*

Description

Cannabis sativa is an annual plant that grows wild in warm and tropical climates throughout the world and is cultivated commercially. The leaves and buds of the plant have been used in herbal remedies for centuries. Scientists have identified over 70 biologically active components, called *cannabinoids*, in marijuana. The best known component is the chemical *delta-9-tetrahydrocannabinol*, or THC, although cannabidiol (CBD) and some other active substances are now being studied.

Overview

The medical use of marijuana is limited because different strains of the plant contain different amounts of various compounds, which makes effects hard to predict. Medical researchers have isolated substances from the plant (cannabinoids) that can be used in precise doses alone and in combinations with other medicines to achieve more predictable effects. Certain cannabinoid drugs have been approved by the US Food and Drug Administration (FDA) to relieve nausea and vomiting and increase appetite in people with cancer and AIDS. Other marijuana extracts are still being tested.

How is it promoted for use?

THC and marijuana are promoted to relieve pain, control nausea and vomiting, and stimulate appetite in people with cancer and AIDS. Researchers also report that THC decreases pressure within the eyes, therefore reducing the severity of glaucoma.

Some supporters claim that marijuana has anti-bacterial properties, inhibits tumor growth, and enlarges the airways, which they believe can ease the severity of asthma attacks. Others claim that marijuana can be used to control seizures and muscle spasms in people who have epilepsy and spinal cord injuries.

> As of 2014, there are reports online suggesting that marijuana oil or “hemp” oil can cure cancer, as well as diabetes, ulcers, arthritis, migraines, insomnia, infections, and many other diseases. **These claims are largely unsupportable. Relying on marijuana alone as treatment while avoiding or delaying conventional medical care for cancer may have serious health consequences.**

What evidence, if any, supports these claims is discussed in the section “What is the evidence?”

What does it involve?

Marijuana leaves, stems, seeds, and flowers are typically shredded and dried before use. In this crude form, marijuana is most commonly smoked in pipes, homemade cigarettes, or hollowed out cigars. It also may be mixed with foods and eaten, or made into tea. It can be made into a more concentrated, resinous form called *hashish*, or a sticky black liquid, hash oil. This is similar to what is now being called marijuana oil or hemp oil, which is made by using solvents and heat to remove the oil from the plant. Possessing or selling crude or raw marijuana is illegal under federal law in the United States. Whole or crude marijuana (including marijuana oil or hemp oil) is not approved by the FDA for any medical use.

There are chemically pure drugs based on marijuana compounds that have been approved in the US for medical use. The cannabinoid THC has been available by prescription as dronabinol in pill form since 1985. This drug is approved to treat nausea and vomiting caused by cancer chemotherapy as well as weight loss and poor appetite in patients with AIDS. A second drug, nabilone, is a synthetic cannabinoid that acts much like THC. It is also a prescription drug, and is approved to treat nausea and vomiting caused by cancer chemotherapy when other drugs have not worked. More recently, a mouth spray containing a whole plant extract containing THC and cannabidiol (CBD) called nabiximols has become available in Canada and parts of Europe to treat pain linked to cancer as well as muscle spasms and pain from multiple sclerosis. It is not yet approved in the US as of 2014, but it is being tested in clinical trials to see if it will help a number of conditions.

What is the history behind it?

Marijuana plants were made into fiber for rope and textiles, oil was taken from its seeds, and some cultures used it in religious rituals. It was described in Indian and Chinese medical texts more than 3,000 years ago. It was used to treat conditions such as beriberi, constipation, gout, malaria, rheumatism, and absent-mindedness, as well as depression, insomnia, vomiting, tetanus, and coughs. In the middle ages, herbalists used it externally to help muscle and joint pain.

In the mid-1800s, the plant was mentioned as a treatment for gonorrhea and angina (chest pains related to heart disease). It was also used to treat intestinal pain, cholera, epilepsy, strychnine poisoning, bronchitis, whooping cough, and asthma. In the US and Europe, marijuana extracts were prepared and sold for medicinal use as sedatives and pain relievers, to help appetite and sexual problems. By the early 20th century, it was noted that the extracts varied in their effects. Their actions in the body varied based on where the marijuana came from, how it was prepared, and how old it was. Other medicines became available that were more predictable and easier to use.

Things were already changing in the US in 1937, when marijuana use (even by doctors) was taxed. Then Congress passed a law in 1951 that classified marijuana as a narcotic drug. In 1970, marijuana was defined in a new law, the Controlled Substances Act, as a Schedule 1 drug -- a drug with no accepted medical use and with the potential for abuse. While marijuana is legal in many parts of Asia and the Middle East, it remains illegal in most Western countries.

In recent decades, marijuana has been the subject of extensive medical research using more advanced methods of testing as specific active compounds have been isolated. But its status as an illegal substance, as well as concerns about potentially harmful side effects, have hampered the process of scientific inquiry in many countries, including the United States.

Despite this, researchers continue to study the compounds in marijuana for possible medical applications. As was discussed earlier, 2 prescription drugs based on marijuana compounds have been approved in the United States, and a third has been approved in Canada and Europe.

What is the evidence?

There are many challenges in marijuana research. The whole plant contains many compounds, which have different actions in the human body. For example, studies show that THC can raise anxiety and cause paranoia, while cannabidiol (CBD) may reduce them. Components of the whole plant can have nearly opposite effects in the human brain, so that one compound can change the effects of another.

Different cultivars (strains or types) and even different crops of marijuana plants can have varying amounts of these compounds. This means that studies that use the whole plant may find different effects based on the strain of marijuana used. At least one researcher has shown a wide range of ratios between THC and CBD in marijuana that was seized by law enforcement agents in California. Marijuana seized more recently had much more THC and much less CBD by comparison to past seizures.

Another issue is that effects vary depending on how marijuana compounds enter the body. When taken by mouth, the THC is processed by the liver, which produces another psychoactive compound (a substance that acts on the brain and changes mood or consciousness). When marijuana is smoked or vaporized (inhaled), cannabinoids enter the bloodstream quickly. The extra psychoactive compound is produced in smaller amounts than when marijuana is taken by mouth.

And finally, the studies discussed below may have been done on marijuana extracts (which would contain multiple

compounds in variable amounts) or on one or more purified components of marijuana such as THC or CBD.

A number of small studies of smoked marijuana found that it can be helpful in treating nausea and vomiting from cancer chemotherapy.

A few studies have found that inhaled (smoked or vaporized) marijuana can be helpful treatment of neuropathic pain (pain caused by damaged nerves).

Smoked marijuana has also helped improve food intake in HIV patients in studies.

Smoked marijuana did lower intraocular pressure in some studies from the 1970s and early 80's. However, this effect only lasted about 4 hours. One expert reasoned that patients would have to use marijuana around the clock in order to effectively treat glaucoma. Other medicines are generally more useful for people with glaucoma.

There are no studies in people of the effects of marijuana oil or hemp oil.

Studies have long shown that people who took marijuana extracts in clinical trials tended to need less pain medicine.

Oral cannabis extracts have been studied in multiple sclerosis. In 2014, the Guideline Development Subcommittee of the American Academy of Neurology examined the evidence and found that oral cannabis extract is effective in reducing spasticity (using patient-centered measures) and in treating central pain or painful spasms in patients with multiple sclerosis.

Nabimixols, which contains an equal mixture of CBD and THC, has also been studied in multiple sclerosis. In 2014, the Guideline Development Subcommittee of the American Academy of Neurology examined the evidence and found that nabiximols is "probably effective" in reducing spasticity (using patient-centered measures), central pain or painful spasms, and bladder dysfunction in patients with multiple sclerosis.

Nabiximols has shown promise for helping people with cancer pain that is unrelieved by strong pain medicines in some studies.

Based on a number of studies, dronabinol (THC taken by mouth) can be helpful for reducing nausea and vomiting associated with chemotherapy.

Dronabinol has also been found to help improve food intake and prevent weight loss in patients with HIV. In studies of cancer patients, though, it wasn't better than placebo or an alternative drug (megestrol acetate).

A small early study of CT-3, a substance related to delta-9-THC, looked at people with neuropathic pain (pain related to the nerves of the body). It tested CT-3 against a placebo, and found that patients reported lower pain levels 3 hours after receiving the CT-3 compared with placebo. Few other studies have been done on this compound, which is also called *ajulemic acid*.

An in-depth investigation into the medical use of marijuana was authorized by the US Government in 1997. The Office of National Drug Control Policy commissioned the Institute of Medicine (IOM) to assess the potential health benefits and risks of marijuana. The IOM is an independent research body affiliated with the National Academy of Sciences. The IOM issued its final report in 1999 and offered several conclusions regarding marijuana's usefulness.

First, it found that scientific data indicate that cannabinoids, particularly THC, have some potential to relieve pain, control nausea and vomiting, and stimulate appetite. Cannabinoids probably affect control of movement and memory, but their effects on the immune system are unclear. It found that some of the effects of cannabinoids, such as reduced anxiety, sedation, and euphoria, may be helpful for certain patients and situations and distressing for others. Based on the many studies reviewed, researchers also found that smoking marijuana delivers harmful substances and may be an important risk factor in the development of lung diseases and certain types of cancer. The IOM stated that because marijuana contains a number of active compounds, it cannot be expected to provide precise effects unless the individual components are isolated.

More recently, scientists reported that THC and other cannabinoids such as CBD slow growth and/or cause death in certain types of cancer cells growing in laboratory dishes. Some animal studies also suggest certain cannabinoids may slow growth and reduce spread of some forms of cancer. There have been some early clinical trials of cannabinoids in treating cancer in humans and more studies are planned. While the studies so far have shown that cannabinoids can be safe in treating cancer, they do not show that they help control or cure the disease.

Cannabinoid levels in marijuana are unpredictable and lower than doses used in most animal studies, so any benefit

from this compound would require use of a purified and concentrated form. This is also true of marijuana oil or hemp oil, since purified oils contain roughly the same ratios of compounds as the plants from which they are made. Even though some proponents of marijuana oil recommend using *Cannabis indica* (rather than *C. sativa*) for its higher cannabidiol levels and lower THC levels, the levels cannot be considered consistent or predictable.

Are there any possible problems or complications?

This substance may not have been thoroughly tested to find out how it interacts with medicines, foods, herbs, or supplements. Even though some reports of interactions and harmful effects may be published, full studies of interactions and effects are not often available. Because of these limitations, any information on ill effects and interactions below should be considered incomplete.

There is still concern that marijuana may cause toxic side effects in some people, and any benefits must be carefully weighed against its potential risks.

A number of reviewers have concluded that the scientific evidence does not support smoking marijuana as a medicine because of problems with dosing and the variable amounts of any one compound that might be delivered.

Inhaling or ingesting (eating or drinking) marijuana can cause a number of mental and emotional effects, including feelings of euphoria, short-term memory loss, difficulty in completing complex tasks, changes in the perception of time and space, sleepiness, anxiety, confusion, and inability to concentrate. Some people find the emotional and mental effects to be frightening, and a significant few have had problems like depression, paranoia, and hallucinations from marijuana or cannabinoid medicines. People who are prone to mental illness may have more serious mental and emotional effects from marijuana use.

Physical side effects include low blood pressure, fast heartbeat, dizziness, slow reaction time, and heart palpitations. Instances of serious heart problems are very rare.

Marijuana smoke contains many of the same carcinogens, or chemicals that can cause cancer, as tobacco smoke.

Studies have shown changes in the linings of the breathing passages in marijuana smokers.

Results of epidemiologic studies have not shown a clear link between marijuana and cancer risk. Many of these studies compared people with certain cancers that are linked to smoking and compared them to people without the cancer. Often, the people in these studies that smoked marijuana also smoked tobacco, which made it hard to see a separate effect of marijuana on cancer risk. Also, even heavy marijuana smokers don’t smoke as much or as often as most tobacco smokers. There is also concern that because marijuana has been largely illegal, people may not want to admit that they use the drug, making the studies less reliable. A few studies have linked testicular cancer to marijuana use in men, but the evidence isn’t conclusive.

Marijuana temporarily impairs driving skills, leading to an increased risk of motor vehicle accidents and injuries. These effects are worsened if the person uses alcohol or other drugs along with marijuana.

Heavy marijuana use over a long time can cause lung problems (chronic bronchitis), alter brain development, and worsen educational outcomes.

People who are susceptible to psychosis are more likely to use marijuana and there is concern that their illness may be accelerated or worsened by marijuana use.

One long term study suggests that chronic marijuana affects intelligence. Researchers tested brain function in over 1,000 13 year-olds and then followed up on them with interviews for 25 years, retesting them again at age 38. They found that those who used marijuana often had a decline in brain function, even after they controlled for education levels. People who started using marijuana as teens had the most notable effects, and those who used it chronically had greater declines in function. Stopping marijuana use did not fully restore brain function.

With chronic marijuana use, a few people develop a rare effect called Cannabinoid Hyperemesis Syndrome (CHS). This tends to happen after a few years or even decades of frequent use. CHS starts with morning nausea and mild belly pain, which can last for months before the vomiting phase starts. The person might use more marijuana at this point since it’s known to help relieve nausea, but in this case it doesn’t help. When vomiting starts, it happens frequently, up to 5 times an hour. People with CHS may get temporary relief from taking hot showers, but they might still need medical help staying hydrated. The nausea and vomiting finally stop but the same cycle can repeat later.

Contamination of marijuana plants with the *Aspergillus* fungus has caused serious lung infections in people with low immunity (such as those with cancer, HIV, or organ transplants). This fungus can grow on marijuana plants and be invisible to the naked eye. Other types of contamination can cause health issues too.

There is debate on whether marijuana is truly addictive, but evidence suggests that some people do develop unhealthy dependence on marijuana, meaning that they continue to use it even in the face of unwanted consequences in their lives. This happens more often in people who started as teens, and in those who use marijuana daily.

Frequent users may have withdrawal symptoms if they stop it suddenly. Restlessness, irritability, mild agitation, sleep disturbances, nausea and cramping have been observed. Withdrawal symptoms have also been demonstrated in animal studies.

Marijuana should not be used during pregnancy. Women who use marijuana in pregnancy are more likely to have a stillbirth. In addition, children born to women who used marijuana in pregnancy have an increase in problems with development.

THC crosses into breast milk, so women who are breastfeeding should not use marijuana.

Marijuana overdoses are not thought to directly cause death, but may cause mental impairment and distressing emotional states, such as paranoia, hallucinations, panic, and disconnection from reality. Rarely, people who have ingested too much marijuana have been reported to have caused harm to themselves or others, through such behaviors as jumping off buildings or attacking someone else while fearful or hallucinating. Overdose can also cause fast or disturbed heart rhythm, sleepiness, clumsiness, dry mouth, dizziness, and low blood pressure.

Although it is rare, European doctors have reported severe shutdown of blood circulation to the arms or legs in young people who smoked marijuana. In some cases, it was so severe that amputation was required. There is some debate as to whether this was truly from smoking marijuana or whether other factors, such as cigarette smoking, contaminates in the marijuana, or the use of other drugs, is really to blame.

Marijuana may also serve as a trigger for a heart attack on rare occasions, usually within an hour after smoking. Allergic reactions, some severe, have been reported.

Relying on marijuana alone as treatment while avoiding or delaying conventional medical care for cancer may have serious health consequences.

Accidental poisonings have become more of a problem since marijuana has become readily available in many states. Doctors report that more children have been finding and eating the candies, sweet drinks, and baked goods that it's often put into. Medical marijuana preparations are the biggest problem, since they are typically much more concentrated than non-medical preparations. It's easy for children who find medical marijuana-laced treats to take in far more than a typical adult dose. Children who overdose on marijuana can have hallucinations, trouble breathing, and other symptoms that require hospitalization.

The veterinary literature reports that pets are finding and eating marijuana more often as well. Dogs take longer to clear marijuana out of their systems, and there are reports of some deaths.

Drugs derived from marijuana also have side effects

Dronabinol and nabilone, prescription drug forms of THC, also can cause complications. Some people have trouble with increased heart rate, decreased blood pressure (especially when standing up), dizziness or lightheadedness, and fainting. These drugs can cause drowsiness as well as mood changes or a feeling of being "high" that some people find uncomfortable. They can also worsen depression, mania, or other mental illness. Some patients taking nabilone in studies reported hallucinations. The drugs may increase some effects of sedatives, sleeping pills, or alcohol, such as sleepiness and poor coordination. Sleepiness, dizziness, dry mouth, and trouble with recent memory are side effects even with controlled doses of THC and other purified components like it.

Driving, operating machinery, or hazardous activities that require clear thinking and good coordination are not recommended until the effects of THC-based drugs are known. People taking these drugs should be under the supervision of a responsible adult at all times when they start taking the medicine and after any dose changes.

Like marijuana, these drugs should not be used if a woman is breastfeeding because they can be concentrated in breast milk and passed to the baby. THC drugs are not recommended during pregnancy. People who have had

emotional illnesses, paranoia, or hallucinations may become worse when taking THC or marijuana-based drugs.

Older patients may have more problems with side effects and are usually started on lower doses.

What does the American Cancer Society say about the use of marijuana in cancer patients?

The American Cancer Society supports the need for more scientific research on cannabinoids for cancer patients, and on better and more effective therapies that can overcome the often debilitating side effects of cancer and its treatment. The Society also believes that the classification of marijuana as a Schedule I controlled substance by the U.S. Drug Enforcement Administration imposes numerous conditions on researchers and deters scientific study of cannabinoids. Federal officials should examine options consistent with federal law for enabling more scientific study on marijuana.

Ultimately, medical decisions about pain and symptom management should be made between the patient and his or her doctor, balancing evidence of benefit and harm to the patient, the patient's preferences and values, and applicable laws and regulations.

To learn more

More information from your American Cancer Society

The following information on complementary and alternative therapies may also be helpful to you. These materials may be found on our website (**www.cancer.org**) or ordered from our toll-free number (1-800-277-2345).

Complementary treatments and herbal medicines

Complementary and Alternative Methods and Cancer

Dietary Supplements: What Is Safe?

Placebo Effect

The ACS Operational Statement on Complementary and Alternative Methods of Cancer Management

Finding out about new ways to treat and prevent cancer

Learning About New Ways to Treat Cancer

Learning About New Ways to Prevent Cancer

References

Abrams DI, Jay CA, Shade SB, Vizoso H, Reda H, Press S, Kelly ME, Rowbotham MC, Petersen KL. Cannabis in painful HIV-associated sensory neuropathy: a randomized placebo-controlled trial. *Neurology*. 2007 Feb 13;68(7):515-21.

Ahmedzai S, Carlyle DL, Calder IT, Moran F. Anti-emetic efficacy and toxicity of nabilone, a synthetic cannabinoid, in lung cancer chemotherapy. *Br J Cancer*. 1983 Nov;48(5):657-63.

American College of Physicians. Supporting research into the therapeutic role of marijuana. (Position paper, 2008.) Accessed at http://www.acponline.org/advocacy/where_we_stand/other_issues/medmarijuana.pdf on January 13, 2012.

Bhattacharyya S, Crippa JA, Allen P, et al. Induction of psychosis by {delta}9-tetrahydrocannabinol reflects modulation of prefrontal and striatal function during attentional salience processing. *Arch Gen Psychiatry.* 2012 Jan;69(1):27-36.

Barsky SH, Roth MD, Kleerup EC, Simmons M, Tashkin DP. Histopathologic and molecular alterations in bronchial

epithelium in habitual smokers of marijuana, cocaine, and/or tobacco. *J Natl Cancer Inst*. 1998;90:1198-1205.

Beal JE, Olson R, Laubenstein L, Morales JO, Bellman P, Yangco B, Lefkowitz L, Plasse TF, Shepard KV. Dronabinol as a treatment for anorexia associated with weight loss in patients with AIDS. *J Pain Symptom Manage*. 1995 Feb;10(2):89-97.

Beal JE, Olson R, Lefkowitz L, Laubenstein L, Bellman P, Yangco B, Morales JO, Murphy R, Powderly W, Plasse TF, Mosdell KW, Shepard KV. Long-term efficacy and safety of dronabinol for acquired immunodeficiency syndrome-associated anorexia. *J Pain Symptom Manage*. 1997 Jul;14(1):7-14.

Bolla KI, Eldreth DA, Matochik JA, Cadet JL. Neural substrates of faulty decision-making in abstinent marijuana users. *Neuroimage*. 2005;26:480-492.

Burgdorf JR, Kilmer B, Pacula RL. Heterogeneity in the composition of marijuana seized in California. *Drug Alcohol Depend*. 2011 Aug 1;117(1):59-61.

Cannabis-In-Cachexia-Study-Group, Strasser F, Luftner D, Possinger K, et al. Comparison of orally administered cannabis extract and delta-9-tetrahydrocannabinol in treating patients with cancer-related anorexia-cachexia syndrome: a multicenter, phase III, randomized, double-blind, placebo-controlled clinical trial from the Cannabis-In-Cachexia-Study-Group. *J Clin Onc*. 2006;24:3394-3400.

Cottencin O, Karila L, Lambert M, et al. Cannabis arteritis: review of the literature. *J Addict Med.* 2010 Dec;4(4):191-196.

Disdier P, Granel B, Serratrice J, et al. Cannabis arteritis revisited--ten new case reports. *Angiology*. 2001;52:1-5.

DuPont RL. Examining the debate on the use of medical marijuana users. *Proc Assoc Am Physicians*. 1999;111:166-172.

Ellis RJ, Toperoff W, Vaida F, van den Brande G, Gonzales J, Gouaux B, Bentley H, Atkinson JH. Smoked medicinal cannabis for neuropathic pain in HIV: a randomized, crossover clinical trial. *Neuropsychopharmacology*. 2009 Feb;34(3):672-80. Epub 2008 Aug 6.

Flom MC, Adams AJ, Jones RT. Marijuana smoking and reduced pressure in human eyes: drug action or epiphenomenon? *Invest Ophthalmol*. 1975 Jan;14(1):52-5.

Fusar-Poli P, Crippa JA, Bhattacharyya S, et al. Distinct effects of {delta}9-tetrahydrocannabinol and cannabidiol on neural activation during emotional processing. *Arch Gen Psychiatry.* 2009 Jan;66(1):95-105.

Galli JA, Sawaya RA, Friedenberg FK. Cannabinoid hyperemesis syndrome. *Curr Drug Abuse Rev.* 2011 Dec;4(4):241-249.

Gates P, Jaffe A, Copeland J. Cannabis smoking and respiratory health: Consideration of the literature. *Respirology.* 2014 May 15. doi: 10.1111/resp.12298. [Epub ahead of print]

Gruenwald J. *PDR for Herbal Medicines*. 3rd ed. Montvale, NJ: Thomson PDR; 2004.

Guzmán M, Duarte MJ, Blázquez C, Ravina J, Rosa MC, Galve-Roperh I, Sánchez C, Velasco G, González-Feria L. A pilot clinical study of Delta9-tetrahydrocannabinol in patients with recurrent glioblastoma multiforme. *Br J Cancer*. 2006 Jul 17;95(2):197-203. Epub 2006 Jun 27.

Haney M, Rabkin J, Gunderson E, Foltin RW. Dronabinol and marijuana in HIV(+) marijuana smokers: acute effects on caloric intake and mood. *Psychopharmacology*. (Berl). 2005;181:170-178.

Haney M, Gunderson EW, Rabkin J, Hart CL, Vosburg SK, Comer SD, Foltin RW. Dronabinol and marijuana in HIV-positive marijuana smokers. Caloric intake, mood,and sleep. J Acquir Immune Defic Syndr. 2007 Aug 15;45(5):545-54.

Hashibe M, Morgenstern H, Cui Y, et al. Marijuana use and the risk of lung and upper aerodigestive tract cancers: results of a population-based case-control study. *Cancer Epidemiol Biomarkers Prev*. 2006;15:1829-1834

Hepler RS, Frank IR. Marihuana smoking and intraocular pressure. *JAMA*. 1971 Sep 6;217(10):1392.

Herman TS, Einhorn LH, Jones SE, Nagy C, Chester AB, Dean JC, Furnas B, Williams SD, Leigh SA, Dorr RT, Moon

TE. Superiority of nabilone over prochlorperazine as an antiemetic in patients receiving cancer chemotherapy. *N Engl J Med*. 1979 Jun 7;300(23):1295-7.

Jatoi A, Windschitl HE, Loprinzi CL, Sloan JA, Dakhil SR, Mailliard JA, Pundaleeka S, Kardinal CG, Fitch TR, Krook JE, Novotny PJ, Christensen B. Dronabinol versus megestrol acetate versus combination therapy for cancer-associated anorexia: a North Central Cancer Treatment Group study. *J Clin Oncol*. 2002 Jan 15;20(2):567-73.

Johnson JR, Burnell-Nugent M, Lossignol D, et al. Multicenter, double-blind, randomized, placebo-controlled, parallel-group study of the efficacy, safety, and tolerability of THC:CBD extract and THC extract in patients with intractable cancer-related pain. *J Pain Symptom Manage.* 2010 Feb;39(2):167-179.

Johnson JR, Lossignol D, Burnell-Nugent M, Fallon MT. An open-label extension study to investigate the long-term safety and tolerability of THC/CBD oromucosal spray and oromucosal THC spray in patients with terminal cancer-related pain refractory to strong opioid analgesics. *J Pain Symptom Manage*. 2013 Aug;46(2):207-18. Epub 2012 Nov 8.

Joy JE, Watson SJ Jr, Benson JA Jr. eds. *Marijuana and Medicine: Assessing the Science Base*. Washington, DC: Division of Neuroscience and Behavioral Health, Institute of Medicine, National Academy Press; 1999.

Kalb C. No green light yet: a long-awaited report supports medical marijuana. So now what? *Newsweek*. 1999;133:35.

Karschner EL, Darwin WD, Goodwin RS, et al. Plasma cannabinoid pharmacokinetics following controlled oral delta9-tetrahydrocannabinol and oromucosal cannabis extract administration. *Clin Chem.* 2011 Jan;57(1):66-75.

Karst M, Salim K, Burstein S, et al. Analgesic effect of the synthetic cannabinoid CT-3 on chronic neuropathic pain: a randomized controlled trial. *JAMA*. 2003;290:1757-1762.

Koppel BS, Brust JC, Fife T, Bronstein J, Youssof S, Gronseth G, Gloss D. Systematic review: efficacy and safety of medical marijuana in selected neurologic disorders: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2014 Apr 29;82(17):1556-63.

Lacson JC, Carroll JD, Tuazon E, et al. Population-based case-control study of recreational drug use and testis cancer risk confirms an association between marijuana use and nonseminoma risk. *Cancer*. 2012 Nov 1;118(21):5374-5383.

McAllister SD, Christian RT, Horowitz MP, Garcia A, Desprez PY. Cannabidiol as a novel inhibitor of Id-1 gene expression in aggressive breast cancer cells. *Mol Cancer Ther*. 2007;6:2921–2927.

Mehra R, Moore BA, Crothers K, Tetrault J, Fiellin DA. The association between marijuana smoking and lung cancer: a systematic review. *Arch Intern Med*. 2006;166:1359-1367.

Meier MH, Caspi A, Ambler A, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proc Natl Acad Sci U S A*. 2012 Oct 2;109(40):E2657-64. doi: 10.1073/pnas.1206820109. Epub 2012 Aug 27.

Meola SD, Tearney CC, Haas SA, et al. Evaluation of trends in marijuana toxicosis in dogs living in a state with legalized medical marijuana: 125 dogs (2005-2010). *J Vet Emerg Crit Care (San Antonio)*. 2012 Dec;22(6):690-696.

Meiri E, Jhangiani H, Vredenburgh JJ, Barbato LM, Carter FJ, Yang HM, Baranowski V. Efficacy of dronabinol alone and in combination with ondansetron versus ondansetron alone for delayed chemotherapy-induced nausea and vomiting. *Curr Med Res Opin.* 2007 Mar;23(3):533-43.

Merritt JC, Crawford WJ, Alexander PC, Anduze AL, Gelbart SS. Effect of marihuana on intraocular and blood pressure in glaucoma. *Ophthalmology*. 1980 Mar;87(3):222-8.

Mittleman MA, Lewis RA, Maclure M, Sherwood JB, Muller JE. Triggering myocardial infarction by marijuana. *Circulation*. 2001;103:2805-2809.

Musty RE, Rossi R. Effects of Smoked Cannabis and Oral Δ9-Tetrahydrocannabinol on Nausea and Emesis After Cancer Chemotherapy: A Review of State Clinical Trials. *Journal of Cannabis Therapeutics*. 2001; 1(1): 29-56.

Nahas G, Latour C. The human toxicity of marijuana. *Med J Aust*. 1992;156:495-497.

National Cancer Institute. Cannabis and cannabinoids (PDQ®) Health Professional Version, updated 12/14/11.

Accessed at www.cancer.gov/cancertopics/pdq/cam/cannabis/healthprofessional on May 27, 2014.

Nicolson SE, Denysenko L, Mulcare JL, Vito JP, Chabon B. Cannabinoid hyperemesis syndrome: a case series and review of previous reports. *Psychosomatics.* 2012 May-Jun;53(3):212-219.

Portenoy RK, Ganae-Motan ED, Allende S, Yanagihara R, Shaiova L, Weinstein S, McQuade R, Wright S, Fallon M . Nabiximols for opioid-treated cancer patients with poorly-controlled chronic pain: a randomized, placebo-controlled, graded-dose trial. *J Pain*. 2012 May;13(5):438-49. Epub 2012 Apr 5.

Power RA, Verweij KJ, Zuhair M, Montgomery GW, Henders AK, Heath AC, Madden PA, Medland SE, Wray NR, Martin NG. Genetic predisposition to schizophrenia associated with increased use of cannabis. *Mol Psychiatry*. 2014 Jun 24. [Epub ahead of print]

Radwan MM, Elsohly MA, Slade D, et al. Biologically active cannabinoids from high-potency Cannabis sativa. *J Nat Prod.* 2009 May 22;72(5):906-911.

Robson P. Therapeutic aspects of cannabis and cannabinoids. *Br J Psychiatry.* 2001 Feb;178:107-115.

Rog DJ, Nurmikko TJ, Young CA. Oromucosal delta9-tetrahydrocannabinol/cannabidiol for neuropathic pain associated with multiple sclerosis: an uncontrolled, open-label, 2-year extension trial. *Clin Ther.* 2007 Sep;29(9):2068-2079.

Ross SA, ElSohly MA, Sultana GN, et al. Flavonoid glycosides and cannabinoids from the pollen of Cannabis sativa L. *Phytochem Anal*. 2005 Jan-Feb;16(1):45-48.

Smigel K. Cancer problems lead list for potential marijuana research studies. *J Natl Cancer Inst*. 1997;89:1255.

Smith PF. New approaches in the management of spasticity in multiple sclerosis patients: role of cannabinoids. *Ther Clin Risk Manag*. 2010 Mar 3;6:59-63.

Tramér MR, Carroll D, Campbell FA, et al. Cannabinoids for control of chemotherapy induced nausea and vomiting: quantitative systematic review. *BMJ*. 2001;323:16-21.

Voelker R. NIH panel says more study is needed to assess marijuana's medicinal use. *JAMA*. 1997 Mar 19;277(11):867-8.

Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse Health Effects of Marijuana Use. *N Engl J Med.* 2014 Jun 5;370(23):2219-2227.

Voth EA, Schwartz RH. Medicinal applications of delta-9-tetrahydrocannabinol and marijuana. *Ann Intern Med*. 1997;126:791-798.

Wang GS, Roosevelt G, Heard K. Pediatric marijuana exposures in a medical marijuana state. *JAMA Pediatr.* 2013 Jul;167(7):630-633.

Ware MA, Wang T, Shapiro S, Robinson A, Ducruet T, Huynh T, Gamsa A, Bennett GJ, Collet JP. Smoked cannabis for chronic neuropathic pain: a randomized controlled trial. *CMAJ*. 2010 Oct 5;182(14):E694-701. Epub 2010 Aug 30.

Wilsey B, Marcotte T, Deutsch R, Gouaux B, Sakai S, Donaghe H. Low-dose vaporized cannabis significantly improves neuropathic pain. *J Pain*. 2013 Feb;14(2):136-48. Epub 2012 Dec 11.

Woolridge E, Barton S, Samuel J, et al. Cannabis use in HIV for pain and other medical symptoms. *J Pain Symptom Manage*. 2005;29:358-367.

Zuardi AW. History of cannabis as a medicine: a review. *Rev Bras Psiquiatr.* 2006 Jun;28(2):153-157. Available online at http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1516-44462006000200015&lng=en&nrm=iso&tlng=en. Accessed 1/12/12.

Note: This information may not cover all possible claims, uses, actions, precautions, side effects or interactions. It is not intended as medical advice, and should not be relied upon as a substitute for consultation with your doctor, who is familiar with your medical situation.

Last Medical Review: 08/26/2014
Last Revised: 08/26/2014