Medical marijuana


Cannabis is a plant with worldwide distribution, yielding fiber and food, as well as a psychoactive drug. The flowers have been used as a medicine for millennia. Investigation of its major chemical components has revealed their utility for the treatment of a wide variety of diseases. Delta-9-tetrahydrocannabinol is currently approved as an oral prescription drug for the treatment of the nausea and vomiting associated with cancer chemotherapy and for appetite stimulation in cases of the anorexia associated with AIDS. However, many patients find that smoking Cannabis offers a superior route of administration and therefore illicitly self-medicate.

Introduction

For those not familiar with marijuana and in need of it for medical purposes, the prospect of consuming an illicit drug may seem rather daunting. However, marijuana is used by 20-30 million people in the US and many times that number worldwide, under completely uncontrolled circumstances, with little apparent harm. It is the world's fourth most popular recreational drug behind caffeine, alcohol and nicotine. Unlike these latter drugs, Cannabis is not addictive and no one in the several thousand year history of its use is known to have died from its effects. The intent of this article is to provide the prospective medical user with an introduction to this drug as a possible therapeutic option. The basics of our subject start with the realization that this much-discussed drug, like many of the others we consume, is from a plant with an interesting natural history.

Cannabis, the plant

Cannabis is a dioecious annual producing approximately equal numbers of male and female plants. Marijuana comes from the flower-associated bracts of female Cannabis. The male plant is much less useful for this purpose. Almost all of the Cannabis found worldwide is classified as Cannabis sativa. Many taxonomists argue that Cannabis indica and Cannabis ruderalis are also valid species names (Emboden 1974, Schultes et al. 1974) although this remains controversial (Small and Cronquist 1976). However, even accounting for these additional species, 95% of the cultivated Cannabis in the world would still be classified as Cannabis sativa.

As it grows well at low temperatures, Cannabis is well adapted to temperate climates (Van der Werf 1994). Ancient northern Asian and European societies used Cannabis mostly for its fiber and seed. It is also an aggressive weed plant at higher latitudes worldwide. South Asian and African cultures used Cannabis mostly for its drug content, and the frost-free climates allowed more time for development of the psychoactive resin. Intense levels of ambient ultraviolet radiation and of insect predation in the tropics may also have contributed to a natural selection for these drug types (Pate 1983). In any case, Cannabis has evolved into two basic races. Plants grown for fiber and seed are universally called "hemp". Cannabis grown for its drug content is commonly called "marijuana" or "drug Cannabis". Its female flower bracts are covered with numerous small resin glands containing the pharmacologically active cannabinoids (Fig. 1) that are unique to this genus.

Figure 1. Some cannabinoids: a) THC, delta-9-tetrahydrocannabinol; b) CBC, cannabichromene; c) CBD, cannabidiol; d) CBG, cannabigerol.

Most of the psychoactive properties of marijuana can be attributed to its content of a cannabinoid (Fig. 1a) named delta-9-tetrahydrocannabinol (THC). In some literature, it is designated as delta-1-tetrahydrocannabinol due merely to a conflict between two methods of naming chemicals, but it is the very same molecule. Modern hemp varieties are nearly devoid of THC and, therefore, cannot be practically diverted into the drug trade. Hemp has been heavily selected for high fiber content, high stalk yield, high seed yield, and low (<0.3 %) inflorescence thc content (de meijer et al. 1992). Drug-type Cannabis varies widely in the content from approximately 1-2% in unselected strains to over 10% in the best modern varieties (Watson 1994). It is not feasible to "get high" on hemp, and most marijuana produces very little low-quality fiber. Hemp should never be confused with marijuana, as their roles cannot be reversed.

Cannabis, the medicine

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Cannabis has been recognized for centuries as a valuable therapeutic agent. Folk uses of Cannabis include treatment of insomnia, inflammation, various psychoses, digestive disorders, depression, rheumatism, migraine, neuralgia, fatigue, constipation, diarrhea, parasites, appetite disorders and it has also been employed by women to facilitate childbirth, stimulate lactation, and relieve menstrual cramping (Mechoulam 1986). These traditions continue in every region where Cannabis is available. Modern Western Cannabis users also frequently claim relief from many of these same medical complaints.

Cannabis or THC have been used experimentally to effectively lower the elevated intracranial pressure of glaucoma (Adler and Geller 1986) and have shown potential for the treatment of alcoholism (Rosenburg 1976) and drug dependence (Hine et al. 1975). THC has been used as a bronchodilator for the relief of asthma symptoms (Graham 1986) and may also be effectively used as an analgesic for pain relief (Segal 1986). It has even been shown to have antibacterial properties (Van Klingerenten and Ten Ham 1976).

The low toxicity of THC is best indicated by its widespread use with very few reports of anything even approaching an overdose. Occasionally, people may get too "high" for their psychic comfort, but their bodies continue to function fairly normally. The dosage necessary to kill half of the organisms tested (LD₅₀) for orally ingested THC is approximately 1 g/kg of body weight. Simply interpreted, this means an average sized human would have to consume 50-100 g of pure THC to reach the LD₅₀ level. Since high-potency Cannabis contains approximately 10% THC, a person would have to eat at least 500-1,000 g of this marijuana before having a 50% chance of death. A 1 g marijuana cigarette of 10% THC Cannabis contains 100 mg of THC and is usually shared among several smokers. Clinically effective oral doses for the relief of nausea start at 5-10 mg. This means that, even accounting for pyrotechnic decomposition and smoke loss, there is a several-thousandfold difference between an effective dose of THC and a potentially lethal one! For alcohol, this difference is only about twentyfold. Other common non-prescription drugs, such as aspirin, have similar relatively narrow margins of safe use. Research into the actions of the natural cannabinoids led to the creation of many artificial ones based on variations of their basic molecular structure. However, none of these artificial compounds are currently approved for medical use in the US. Nabilone proved to be toxic to laboratory test animals and in 1978, human tests were suspended, although it is available in Canada, Switzerland and the United Kingdom as Cesamet®. Levonathrodal, another synthetic cannabinoid analog, was not approved for use in the US, also following incidents of toxicity in test animals.

Other natural cannabinoids (Fig. 1b-d), such as cannabichromene (CBC), cannabidiol (CBD) and cannabigerol (CBG) have been shown to have potential therapeutic value, and can be isolated from both non-psychoactive as well as psychoactive Cannabis varieties. Epilepsy, multiple sclerosis, dystonias, and other neurological disorders have been experimentally treated with CBD (Consoe and Snider 1986). CBD has also been shown to relieve anxiety, especially the minor anxiety occasionally associated with the medical use of THC (Zuardi et al. 1982). CBC, CBD, and CBG and related analogs have been shown to have anti-microbial action (ElSohly et al. 1982, Van Klingerenten and Ten Ham, 1976). These non-psychoactive compounds are generally not restricted by international regulations prohibiting Cannabis and THC.

Various delivery systems for these cannabinoids, such as suppositories, time release encapsulation, eye drops, nasal sprays, aerosols, topical ointments, and transdermal patches will eventually become available. Several such cannabinoid delivery systems have already been patented (e.g., ElSohly 1990, Hussain 1984).

The only cannabinoid medicine currently available in the US is a synthetic THC encapsulated in sesame oil (generically known as "Dronabinol"). It is sold under the trade name Marinol® as a Schedule II controlled substance (allowing restricted prescription, similar to morphine and cocaine) and was afforded a narrow, specific legal exemption from the Schedule I status of other Cannabis products (forbidden from clinical use). It has been accepted and prescribed in the United States since 1985 as an anti-emetico toxic to the nerve association with cancer chemotherapy (Levitt 1986). Use as an appetite stimulant to correct the weight loss related to anorexia in AIDS patients was approved by the US Food and Drug Administration on December 22, 1992 (Anonymous 1992). THC is not a cure for cancer or AIDS, but helps to relieve suffering and improve quality of life, perhaps prolonging the lives of those afflicted. THC may also eventually win approval as a general appetite stimulant for anorexia nervosa and other appetite disorders.

Before other cannabinoids or Cannabis can become available to patients in the US, they must be similarly rescheduled. This also applies to the non-psychoactive compounds or even an otherwise identical, but plant-derived THC medicine! For alcohol, this difference is only about twentyfold. However, none of these artificial compounds are currently approved for medical use in the US. Marinol® ranges between $4.00 and $8.00 and the average patient cost ranges from $12.00 to $32.00 per day. Since Marinol® is expensive, narrowly prescribed and often less effective than crude Cannabis preparations, potent sinsemilla-type (seedless) marijuana remains the most viable form of Cannabis medicine, despite the fact that its illegality artificially inflates its cost. Physicians learned as much from their patients and began to publish guidebooks on the appropriate medical use of Cannabis (e.g., Roffman 1982), which is most often smoked or consumed in baked goods.

In some respects, it may be unfortunate that Cannabis has played such a prominent role in the American media's coverage of the counterculture movement since the 1960s. The popularization of Cannabis as the drug of choice increased its exposure to the general public, but government disinformation promoted the mainstream culture's confusion of it with hard drugs. It has been difficult for even the more knowledgeable patients and practitioners to view Cannabis as a genuine medicine rather than merely a recreational drug. Of course, many doctors are also reluctant to suggest Cannabis use because it is illegal. Marinol® is too expensive for many patients to afford and orally ingested anti-emetics are of questionable value because their application must be carefully timed to avoid vomiting the drugs. Many patients who both smoke Cannabis and swallow Marinol® report that THC absorbed through the lungs offers more immediate relief, better dose titration, fewer side-effects and shorter duration of action.

Conclusions

For millennia, Cannabis has been used as an effective medicine. Modern research has revealed the clear potential for this plant and...
its cannabinoid products to resume their place in the pharmacopoeia. Further work is urgently needed to determine how Cannabis can be best utilized as a clinical tool. Meanwhile, cancer and AIDS patients and members of the medical marijuana movement have taken responsibility for their own health and self-medicate without a doctor’s prescription.

References


Medical marijuana is a controversial topic. In the ceaseless battle of clashing opinions among journalists, police departments, attorneys, medical doctors, social activists, and legislators, itâ€™s all too easy to feel overwhelmed by media sensationalism and hyperbole. Unfortunately, this means the people who stand to benefit most from the use of medical marijuana â€“ individuals who suffer from serious health conditions â€“ are never given the chance to make informed decisions based on fact and evidence.