

Review of Human Studies on Medical Use of Marijuana

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Summary: Human Studies on Medical Uses of Marijuana

There have been hundreds of studies on the medical uses of cannabis since its introduction to western medicine in the early nineteenth century. A review of the literature reveals over 65 human studies, most of them in the 1970s and early '80s.

- The best established medical use of smoked marijuana is as an anti-nauseant for cancer chemotherapy. Marijuana's efficacy was demonstrated in studies by half a dozen states, involving hundreds of subjects. Most research has found smoked marijuana superior to oral THC (Marinol). Many oncologists are currently recommending marijuana to their patients.
- Marijuana is widely used to treat nausea and appetite loss associated with AIDS, but the government has blocked research in this area. Studies have shown that marijuana helps improve appetite, and Marinol has been FDA approved for treatment of AIDS wasting syndrome. Nearly 10,000 PWAs were reported to be using marijuana through the San Francisco Cannabis Buyers' Club. However, the government has blocked efforts by Dr. Donald Abrams of the University of California at San Francisco to proceed with an FDA-approved study of marijuana and AIDS wasting syndrome, by refusing to grant him access to research marijuana. Research is badly needed on the relative merits of smoked and oral marijuana versus Marinol.
- There is much evidence, largely anecdotal, that marijuana is useful as an anti-convulsant for spinal injuries, multiple sclerosis, epilepsy, and other diseases. Similar evidence suggests marijuana may be useful as an analgesic for chronic pain from cancer and migraine as well as for rheumatism and a variety of auto-immune diseases. There is a conspicuous lack of controlled studies in this area; further research is needed.
- Cannabidiol, a constituent of natural marijuana not found in Marinol, appears to have distinctive therapeutic value as an anti-convulsant and hypnotic, and to counteract acute anxiety reactions caused by THC.
- It has been established that marijuana reduces intra-ocular pressure, the primary object of glaucoma therapy. Due to its psychoactivity, however, marijuana has not gained widespread acceptance in this application.
- Many patients report using marijuana as a substitute for more addictive and harmful psychoactive drugs, including prescription painkillers, opiates, and alcohol. Marijuana and Marinol have also been found useful as a treatment for depression and mood disorders in Alzheimer's and other patients. More research is needed.

Overview of Medical Marijuana Research

In its position paper, "Use of Marijuana as a 'Medicine,'" the California Narcotics Officers Association refers to "10,000 studies... documenting the harmful physical and psychological effects of smoking marijuana." This myth has been effectively debunked in a letter to Dr. Lester Grinspoon from NIDA's marijuana research librarian at the University of Mississippi, Beverly Urbanek, who writes, "We are totally in the dark as to where the statement that there are 10,000 studies showing the negative impact of marijuana could have originated." She explains that while her library has some 12,000 citations on cannabis, they cover a broad spectrum of economic, legal, horticultural, enforcement, and other non-health issues, and are not categorized by negative or positive effects. Pursuing the issue further, it is possible to enumerate an impressive number of studies on marijuana's therapeutic uses. There is no space here to list or summarize all of them. The book, "Cannabinoids as Therapeutic Agents," edited by Dr. Raphael Mechoulam (CRC, 1986), includes copious references to research articles on cannabis' pharmacological effects, as follows:

- Pharmacohistory of Cannabis Sativa - 90 references;
- Therapeutic Potential of Cannabinoids in Neurological Disorders -155 references
- Ocular Effects - 70 references
- Cannabinoids as Antiemetics in Cancer - 91 references
- Cannabinoids and Analgesia - 136 references
- Bronchodilator Action of Cannabinoids - 67 references

Of course, there are some duplicates, and by no means all of these 609 references actually detail medicinal benefits of marijuana, but it certainly seems reasonable to estimate that there have been 100s of studies on medical use of marijuana.

Human Studies

Following is a summary of the human clinical and epidemiological studies on marijuana's therapeutic applications. We have not attempted to detail the great bulk of research, which consists of animal and in vitro studies that are of more dubious relevance to human health. However, we have tried to include all human studies reported in the recent medical literature.

1. Anti-Nauseant for Cancer Chemotherapy

This is by far the best substantiated use of medical marijuana. There have been at least 31 human studies of marijuana and/or oral THC for cancer chemotherapy,¹ beginning with the pathbreaking work of Sallan and Zinberg, the first modern study of medical marijuana². This doesn't count the studies in which the sponsors of Marinol got it FDA approved as "safe and effective" for cancer chemotherapy. Smoked marijuana was shown to be an effective anti-nauseant in 6 different state-sponsored clinical studies: ³ New Mexico (250 patients),⁴ New York (199 patients),⁵ California (98),⁶ Tennessee (27),⁷ Georgia (119),⁸ and Michigan (165).⁹

Smoked marijuana was found to be superior to oral THC in the New Mexico and Tennessee studies, with efficacy rates of 90%. In New York and Tennessee, it was effective in patients who had not been helped by Marinol. In Michigan, patients found smoked marijuana preferable to a conventional prescription anti-nauseant (Torecan). Other researchers have also reported smoked marijuana to be superior to THC.¹⁰

The California study was the least satisfactory, being highly biased towards oral THC (2000 patients were given oral THC, versus only 98 for marijuana): still, it found that marijuana was effective in 59% of patients, versus 57% for oral THC; however, 30% rated oral THC "highly effective," versus only 17% for marijuana. This is the only state study showing smoked marijuana inferior to Marinol.¹¹

A survey of oncologists by Doblin and Kleiman reported that 44% of 1035 respondents had recommended marijuana to their patients (54% favored making it a prescription drug).¹²

2. Glaucoma

It is generally accepted - by the National Academy of Sciences and others -- that marijuana/THC reduces intraocular pressure (IOP), the basic aim of anti-glaucoma therapy.¹³ This was shown in a series of

experiments by Robert S. Hepler of UCLA, stemming from research aimed at finding out whether marijuana dilated pupils.¹⁴ Hepler found a "statistically significant" drop in IOP in 429 subjects treated with marijuana or THC; a subset of 29 patients showed continued benefits during 94 days of treatment with no signs of tolerance.¹⁵ The effects of THC/marijuana in reducing IOP were explored in a half-dozen other studies.¹⁶

Nonetheless, ophthalmologists have been reluctant to accept marijuana/THC because of its high psychoactivity. Efforts to develop topical cannabinoid eye drops as a non-psychoactive alternative have so far proven unfruitful.

The California Research Advisory Panel established a glaucoma research protocol under its cannabis research program of 1979-89, after finding interest in marijuana in its survey of ophthalmologists. The program flopped: only nine patients were treated; all chose to take Marinol instead of marijuana; and all eventually abandoned treatment.

3. AIDS & Appetite Stimulation

There have been no clinical studies on the use of marijuana for AIDS. Of course, one reason for this is that the government has blocked the study of Dr. Donald Abrams at the University of California at San Francisco by denying him access to research marijuana.

Nonetheless, Marinol has been FDA-approved as an appetite stimulant for treating AIDS wasting syndrome.¹⁷

There is also an extensive literature on smoked marijuana and appetite stimulation, including 4 clinical studies in which marijuana enhanced food intake and weight gain.¹⁸

Medical marijuana is widely used by AIDS patients. 80% of the SF Cannabis Buyers' Club's 11,000 customers are said to be PWAs.¹⁹ A recent survey of HIV-positive gays in Australia found that one-quarter were using marijuana therapeutically.²⁰

Many AIDS patients prefer smoked marijuana to oral THC, due to its quickness of action, ease of controlling the dose, and absence of side-effects. In addition to appetite stimulation, many AIDS patients use marijuana for pain associated with neuropathy, shingles, etc.

An important concern about smoked marijuana that critics emphasize is the danger of respiratory infection in AIDS patients due to smoking. In particular, critics have cited a worrisome study by Caiaffa et al.,²¹ showing a twofold increase in the rate of pneumocystis carinii pneumonia (PCP) among HIV positive injection drug users who smoke illegal drugs (88% marijuana, 26% cocaine, 9% crack). There are a few problems with the study, notably that almost all of the subjects also smoked cigarettes; therefore, it's difficult to say whether the PCP was really due to marijuana.

In any case, these problems can be avoided by ingesting marijuana orally, which many AIDS patients in fact do. It's not clear whether oral marijuana has any medical benefits over Marinol, though it could certainly be more economical.

Another problem that critics like to emphasize is the supposed threat to PWAs posed by the immunosuppressive properties of marijuana. Of course, these objections apply equally well to oral THC, which has been approved for treatment of AIDS. Studies of THC's effects on immunity have been contradictory, and do not lend themselves to easy interpretation.²² There are hints that THC might actually help stimulate the immune system in some ways.²³

Epidemiological studies have found no relation between marijuana use and development of AIDS.²⁴ One recent study of 354 HIV-positive males actually found marijuana to be associated with a decreased rate of progression to AIDS, though the difference was not significant when adjusted for parameters reflecting the initial health of the study subjects.²⁵

4. Muscle Spasticity, MS, Epilepsy & Spinal Injuries

The treatment of convulsions was the first major application of cannabis in Western medicine, attested by 19th-century authorities such as Dr. William O'Shaughnessy, the Ohio State Medical Committee, and

Dr. John Russell Reynolds (who prescribed it to Queen Victoria for menstrual cramps).²⁶ Although well authenticated in traditional practice, modern research into this usage has been scant, except for animal studies.

Altogether, there appear to be:

- 5 human case studies, involving a total of 8 patients, in which marijuana was reported to be useful for: epilepsy, multiple sclerosis, injury, and Tourette's syndrome;²⁷
- 1 study in which 5 out of 8 spinal cord injury patients reported benefits from marijuana;²⁸
- 3 more studies of THC for multiple sclerosis (total: 30 patients), in which benefits tended to be more subjective than objectively measurable;²⁹
- 1 case study of THC for spinal cord injury³⁰
- 2 clinical studies in which cannabidiol (CBD), a component of natural marijuana not found in Marinol, was found beneficial for grand mal epilepsy (15 subjects, double blind controls)³¹ and dystonia (5 patients, no controls).³²
- 1 study in which a THC-related cannabinoid benefitted 2 out of 5 severely epileptic children;³³
- 1 survey of 308 epileptic patients found that marijuana use appeared to delay the first onset of complex partial seizures.³⁴
- 1 survey of 43 spinal cord injury patients at VA hospitals found that 56% smoked marijuana, and 88% reported that it reduced their muscle spasms.³⁵

There have also been a couple of negative studies, finding no benefits of marijuana for Parkinsonism³⁶ or CBD for Huntington's corea.³⁷ Paradoxically, marijuana/THC has been reported to exacerbate spasticity or epilepsy on occasion, perhaps because of a rebound effect.

In a purported recent negative study on marijuana and multiple sclerosis, Dr. Harry Greenberg et al. at University of Michigan reported that marijuana impaired posture and balance in patients with spastic MS.³⁸ This should come as no surprise, since marijuana/THC also impairs balance in normal patients. In any event, MS patients don't use marijuana for posture/balance, but to reduce tremors and pain.

Cannabidiol:

There is considerable evidence from animal studies that CBD has distinctive anti-convulsant properties not found in THC.³⁹

In addition, there is evidence that CBD can reduce the risk of panic reactions associated with THC. A study by Zuardi found that CBD reduces the anxiety-stimulating effects of THC, a leading cause of adverse reactions to Marinol.⁴⁰ This may be a reason why many patients prefer natural cannabis.

A controlled study of 15 insomniacs found that CBD helped subjects sleep better.⁴¹

5. Analgesia & Pain

Many patients report using marijuana for some form of pain relief. Cannabis was used as an analgesic from ancient times through the nineteenth century. This usage declined with the introduction of more potent opiates such as injected morphine. Cannabis continued to be regarded as a drug of choice for migraine into the 20th century.

Modern research is scant. Animal studies have tended to show analgesic effects, while human studies have been more conflicting:

- In a preliminary study by R. J. Noyes, patients reported that marijuana relieved migraine, menstrual cramps, postsurgical pain.⁴²
- In a follow-up, Noyes found oral THC relieved chronic pain in 10 cancer patients.⁴³
- In a second follow-up with 36 cancer patients, THC was as effective as codeine, but had more side-effects.⁴⁴
- 2 other studies found marijuana and THC effective in reducing experimentally induced pain.⁴⁵
- 1 study reported that 3 patients began to experience migraines only after giving up marijuana.⁴⁶

Negative results have also been reported:

- 1 study failed to find THC beneficial for cancer pain, though it did help with depression and appetite.⁴⁷
- 1 study found THC useless for artificially induced pain.⁴⁸
- 1 study found marijuana increased sensitivity to electrically induced pain.⁴⁹
- 1 study found CBD useless for neuropathic pain (10 patients).⁵⁰

Inflammatory Diseases:

Marijuana is used by many patients for a wide variety of diseases characterized by inflammation. These include arthritis, rheumatism, lupus, multiple sclerosis, colitis, Crohn's disease, inflammatory gastritis, scleroderma, endometriosis, psoriasis, and pruritis. These diseases are thought to be auto-immune in nature. It is possible that the supposed immune suppressive properties of cannabis are beneficial for such conditions.

Unfortunately, there have been no clinical studies of this phenomenon. However, a variety of animal and laboratory studies have shown that cannabinoids have anti-inflammatory properties.⁵¹ One mouse study even suggested that a non-cannabinoid ingredient of marijuana may be involved.⁵²

Asthma:

Although this isn't (and shouldn't be) an indication of choice for medical marijuana, three human studies have shown that smoking marijuana produces bronchodilation, thereby relieving asthma attacks.⁵³ Two other studies confirmed the same effects with THC.⁵⁴ Efforts to develop a smokeless THC inhaler proved unsuccessful.

Depression & Mental Illness:

Opponents of medical marijuana such as the CNOA have charged that marijuana causes depression. In fact, marijuana is more often used to treat depression; hence its notorious reputation as a euphoriant. Human studies have been inconsistent. One study found that marijuana helped relieve depression in cancer patients;⁵⁵ another found no benefit for clinical depression.⁵⁶

A survey of 79 mental patients found that those who used marijuana reported relief from depression, anxiety, insomnia, and physical discomfort, as well as fewer hospitalizations;⁵⁷ a second survey also found fewer hospitalizations in schizophrenics who used marijuana.⁵⁸ Some psychiatrists are currently prescribing Marinol for depression.

A recent pilot study by the Unimed Corporation found that Marinol helped relieve mood disturbances and anorexia in 12 Alzheimer's patients.⁵⁹

Violence:

Many opponents absurdly charge that marijuana aggravates violence. To this, the best answer is that of the National Academy of Science in Marijuana and Health (1982, p. 128):

"Both retrospective and experimental studies in human beings have failed to yield evidence that marijuana use leads to increased aggression. Most of these studies suggest quite the contrary effect. Marijuana appears to have a sedative effect, and it may reduce somewhat the intensity of angry feelings and the probability of interpersonal aggressive behavior."

Alcoholism & Drug Dependence:

Cannabis is often used as a substitute for other, more dangerous drugs, including prescription narcotics, opiates and alcohol. Cannabis has been proposed as a treatment for alcoholism as well as opiate addiction.⁶⁰ However, a single controlled study of cannabis to treat alcoholics proved unsuccessful.⁶¹ There is some epidemiological evidence that substitution of marijuana for alcohol and other drugs tends to reduce drug abuse and accident costs.⁶² Many cannabis buyers club members say they use marijuana as a substitute for prescription narcotics.⁶³

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Footnotes

1 Includes (a) 25 studies of oral THC listed in M. Levitt, "Cannabinoids as Antiemetics in Cancer Chemotherapy," in *Mechoulam*, p. 73; (b) 6 state studies of marijuana listed below.

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3 For a summary, see Robert Randall, ed., *Marijuana, Medicine and the Law*, Vol. 2 (Galen Press, Wash. DC) 1989, pp. 36ff.

4 New Mexico: 250 patients; 90% relieved; only 3 adverse reactions (all w/THC): testimony of Daniel Dansak, MD in Robert Randall, ed., *Marijuana, Medicine and the Law*, Vol 1, pp. 125-33; Vol 2, pp. 36-8.

5 New York: 199 patients evaluated; all had failed previous anti-nauseants (some also failed THC); marijuana 89.7%-100% effective at 3 hospitals. ACT Official State Reports, Vol II, Exhibit 15, "Evaluation of the Antiemetic Properties of Inhalation Marijuana in Cancer Patients Receiving Chemotherapy Treatment," NY Dept of Health, Office of Public Health, Chapter 810, Laws of 1980 Article

33-A, Public Health Law, September 1981; ACT Exhibit 16-C, "Impressions from the National Conference on the Therapeutic Applications of Cannabinoids". Cited in Randall Vol 2, pp. 46-54.

6 California: 98 patients received marijuana; 59% found effective against strong emetics; 57% of 257 patients found THC-only effective; 17% rated marijuana "very effective" vs 30% for THC. "Cannabis Therapeutic Research Program," Report to the Cal. Legislature by California Research Advisory Panel, Jan. 1989. See also Randall, Vol 2, pp. 55-63.

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