

Chapter 4: Common Medical Conditions Treated with Cannabis



Recent breakthroughs in cannabinoid analgesic research

In October 1997 Ian Meng presented research to the 27th annual meeting of the Society for Neuroscience in New Orleans. His team, working from the Department of Neurology at UCSF, presented breakthrough research that detailed the neurochemical effects of cannabinoids as they interfere with pain impulses in mammals. In order to understand the importance of this research it is necessary to understand the basic biochemical process of nerve impulse transmission.


Nerve-impulse transmission simplified

All nerve impulses, whether sensory (incoming) or motor (outgoing) are transmitted via either the peripheral or the central nervous system (PNS/CNS). The central nervous system is composed of bundles of nerve fibers that make up the spinal chord and part of the brain. Peripheral nerves are those outside of the brain and spinal chord, in the arms, legs and organs. Nerve impulses are chemically and electrically carried along nerve fibers to and from the brain and spinal chord. Individual nerve cells are called neurons. There is a space between each nerve cell, called a synapse. The synapse separates the end of one neuron from the beginning of the next. Nerve impulses move rapidly across the synapse in response to chemical neurotransmitters. Neurotransmitters are released by one neuron cell, move across the synapse and fit into specific sites—called receptor sites—on the next neuron. Receptor sites come in many different shapes, allowing many different chemical signals to activate the cell in different ways. Receptors will generally only accept a “chemical cousin” of similar shape. These pain receptors are activated by chemicals called agonists, which carry the same imprint.


How analgesics work

Most analgesics including morphine (an opiate), work by interfering with and modifying neuron receptor signals. They do this by chemically binding with the opiate receptors that are responsible for pain transmission. Morphine is also chemically similar to internally-produced, or endogenous, chemicals known as endorphins.¹


Morphine is considered the most potent analgesic in common use today and is often used for severe pain. Unfortunately it has significant “side effects” on specific vital areas in the central nervous system which




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are also receptor mediated. Morphine can slow or stop breathing, cause drowsiness or dizziness and effect many bodily functions that are regulated by the brain. In spite of morphine’s potentially lethal side-effects it is considered a mainstay in pain management because of its high therapeutic value. Morphine, placed in Schedule Two of the federal Controlled Substances Act, is available for controlled medical use.



Topical Cannabis preparation label, date unknown.

Image thanks to Farmacy

The cannabinoid receptor is “discovered”

In 1988, cannabinoid research took a quantum leap. That year, researchers first conclusively demonstrated the presence of human receptors to cannabinoids. (Many other receptor systems had been located, like opiate receptors.) The first cannabinoid receptor located was named “CB-1,” and was found only in the brain. CB-1 receptors were also found to be extremely abundant, indicating great importance. Brain areas of highest concentration include basal ganglia cells, cerebellum, hippocampus and cerebral cortex. These brain locations are also responsible for controlling body movement, coordination, learning and memory- all systems affected by Cannabis the drug.

In 1992 Doctor Raphael Mechoulam, working at Hebrew University in Israel, first described the presence in humans of an endogenous (internally-produced) cannabinoid. His research confirmed that humans possess a unique receptor-mediated system based upon chemicals similar to the cannabinoids found in Cannabis. He named the endogenous chemical *Anandamide* after the Sanskrit word “Ananda” which means bliss. It was found in the brain areas that control pain.

The discovery of the second cannabinoid receptor in humans, called “CB-2,” was announced in 1993. This remarkable discovery described an even more important biological role of the cannabinoid receptor system because, unlike centrally acting receptor systems located only in the brain, CB-2 receptors were found to be widespread in the immune system and throughout the body. This discovery opened up research possibilities aimed at describing the precise biochemical

details of the pain-soothing affects that are experienced and appreciated by many patients.

These discoveries led scientists to conclude that humans possess great numbers of cannabinoid receptors distributed throughout the body, which are activated by a chemical we produce ourselves, called anandamide. In other words, humans possess a unique cannabinoid-based analgesia system.

Before Doctor Meng's research, the specific process of nerve impulse transmission for this new cannabinoid receptor system was unknown. He elaborated upon the work of other teams in Europe and the U.S. by showing for the first time precisely *how* cannabinoids in marijuana bind to the CB-1 and CB-2 receptors and inhibit pain signals. He did this by administering a *synthetic cannabinoid* molecule known as WIN-55212 to laboratory rats and measuring the specific changes. (Synthetic cannabinoids are more effective for research purposes because of their standardized potency and purity).

After intravenous injection, Meng recorded the activity of specific *neurons* (nerve cells) in this cannabinoid receptor system and determined that cannabinoids reduce the pain signal transmission *from* the site of injury and up through the spinal chord. Cannabinoids do this by binding to pain receptors. He also determined that the *cannabinoid receptor system* works independently from *opioid receptor system*, by injecting *antagonists*² to both opioids and cannabinoids to see if the analgesic effect of one was diminished by the other.

In the experiments Nalaxone, the opioid antagonist, and SR-141716-A, the cannabinoid antagonist, were administered to rats previously treated with the respective agonist (morphine or WIN-55212). In all cases the opioid antagonist *failed* to counteract the effects of the cannabinoid, and the cannabinoid antagonist *failed* to counteract the effects of the opioid. The cannabinoid receptor "lock" would not accept the opioid "key". This demonstrated that the cannabinoid and opioid receptor systems are not the same. The researchers noted that this research not only proved that cannabinoids in marijuana have analgesic properties, but that cannabinoids could be the basis for an entirely new class of analgesic compounds.

Kenneth Hargreaves and his research team from the University of Minnesota took the same underlying cannabinoid research in a new direction. Their studies of cannabinoids showed that local (at the site of injury) administration of anandamide (the naturally occurring cannabinoid) produced pain relief without causing CNS effects. In other words, the cannabinoid worked locally-at the site of injury-and not in the brain as does morphine. In addition to relieving pain, anandamide decreased *hyperalgesia*, the increased sensitivity to pain occurring with tissue injury and inflammation. Other research teams confirmed these analgesic properties and presented their findings at the Society for Neuroscience conference.

The Society for Neuroscience presenters all described dramatic analgesic properties of cannabinoids. This research described, for the



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first time, the biochemical and neurological basis for the vast historical record of Cannabis use as an analgesic.



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Cannabis Indica, Squibb

Ground (30) for Pecolation tin, lb. \$2.50; 1/2 lb. \$1.29;
1/4 lb. 67c.

Cannabis Indica; Indian Cannabis or Indian Hemp. The dried flowering tops of female plant of *Cannabis sativa* (Fam. *Moraceae*), grown in the East Indies, gathered while the fruit is yet undeveloped and while it is carrying the whole of its natural resin. We use select tops only, no stems. This hemp produces galeonical preparations of a most satisfactory degree of activity. Narcotic, Sedative, Anodyne. Average Dose: 1 gr. (0.065 Gm.). (See also Extract; Fluidextract; Tincture.)

¶ The prices of Squibb Products are in all instances as low as quality and quantity of ingredients and expense of manufacture allow. They include containers, packing and boxing. When ordering or prescribing please specify SQUIBB'S.

Image thanks to Pharmacy

Advertisement for ground Indian Cannabis flowering tops, in pre-1938 Squibb catalog of pharmaceutical products.

Cannabis for cachexia/anorexia associated with AIDS wasting syndrome and cancer

Wasting syndrome is a debilitating or lethal complication, occurring in two-thirds of cancer patients and nearly 90% of AIDS patients. It is defined as greater than 10% loss of body weight. The debilitating disease processes of cancer and AIDS deplete the body's stores of protein by metabolizing muscle tissue to fuel critical functions. *Anorexia* and *cachexia* are the two complications that begin a downward nutritional spiral. Anorexia is the loss of appetite or desire to eat. Cachexia is a general term, which describes a wasting or malnourished process resulting from illness. Both anorexia and cachexia are probably caused by increased metabolism created by cancerous tumors or the AIDS virus combined with decreased absorption of nutrients. This depletion can quickly spiral out of control leading to nausea, vomiting, poor appetite, diarrhea and subsequent weakness which further blocks the body's ability to combat the disease. As patients are weakened, resistance to infection creates further stress. Opportunistic infections like *Pneumocystis carinii pneumonia*, *Giardia lamblia* and *cytomegalovirus* quickly develop. Patients suffering from these infections often die because they are too weak or sick to eat.

Anticancer treatments (like *chemotherapy*) involve repeated, large, powerful doses of drugs strong enough to interfere with and kill cellular processes of the tumor (hopefully without killing the patient). Protease inhibitor therapies are anti-viral drugs, which interfere with the Human Immunodeficiency virus replication (HIV). Unfortunately chemotherapy and protease inhibitor therapy is often non-specific, and normal healthy cells are affected as well, especially in the gastrointestinal tract. Nausea and vomiting are commonly associated with several common chemotherapeutic agents like Cisplatinum, Methotrexate, or 5-FU. Nausea and vomiting quickly sap energy and sometimes patients

terminate treatment rather than endure incapacitating side effects. Physicians, nurses and researchers continually search for remedies that will control nausea and vomiting.

Conventional medical management of anorexia/cachexia is aimed at restoring digestion and appetite, and increasing muscle mass. Treatments include *Total Parental Nutrition* (TPN), and medications. TPN is the direct intravenous infusion of solutions containing all necessary vitamins, minerals, carbohydrates, proteins and fats. Although it is often effective at reversing cachexia it has several drawbacks. These include diarrhea, expense (at least \$500 per day) and an intensive level of medical supervision. It also is administered via peripheral or central intravenous lines, which increase a patient's susceptibility to infections. Lastly, introducing and maintaining IV lines is painful and limits activity. TPN is usually considered as a short-term approach for use in critical situations.

Recent pharmacological advances have proven more effective than TPN. At this time two oral medications are approved by the FDA for use as appetite stimulants: *megestrol acetate* (Megace), and *dronabinol* (Marinol). Megace is supplied in 20 and 40 mg tablets and is commonly used as a treatment for breast or endometrial cancer. Its side effects include abnormal uterine bleeding, carpal tunnel syndrome, thrombophlebitis (blood clots) and alopecia (hair loss). Dronabinol is a synthetic tetra-hydro-cannabinol (THC) molecule in capsule form. It has been shown in clinical research to significantly increase appetite and body weight at a dosage level of 2.5-mg TID (three times per day), without euphoric effects associated with larger doses. Cannabis contains THC as its main pharmacological component, along with about 60 other lesser-known cannabinoids.

For short-term use during courses of cancer chemotherapy, inhaled Cannabis is a preferable treatment, partly because of its route. Using the lungs bypasses the gastrointestinal tract. Since the stomach and intestines are extremely sensitive from the chemotherapy, this is a huge advantage. Inhaled Cannabis is quickly absorbed in 1-10 minutes giving relief from either *anticipatory nausea* (before treatments) or actual nausea. Dronabinol is unsuited for severe nausea because of its slow onset and its oral route. The inhaled route is superior also because of ease of dosage titration (the ability to fine-tune the dose with experience) and rapid onset. Although the lungs are clearly harmed by inhaling any smoke, this situation still should be evaluated on a risk/benefit continuum. Also, vaporizers may offer an alternative to smoking.

The large amount of literature, both anecdotal and clinical, on the beneficial effects of Cannabis justifies its inclusion in the pharmacopoeia. Cachexia and wasting syndrome are severe, often fatal complications of disease process with few medical alternatives. Cannabis is a superior treatment for these conditions. Simply put, the minimal harm associated with short or medium-term use of Cannabis does not compare to the agonizing and rapid death brought on by cachexia or anorexia.



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Doctor Abrams described significant clinical improvement in health—measured weight gain—without increasing the viral load of the Human Immunodeficiency Virus (HIV) among participants who smoked Cannabis.



Increasing viral load is an indication that the virus that causes AIDS is replicating.



Protease inhibitors ... [interfere] with the reproduction of the HIV and keeps the level of the virus low enough to not allow opportunistic infections to develop.



The study evaluated the effect of Cannabis smoking, Marinol (dronabinol) and a placebo.

New research: Cannabis-smoking best treatment of all tried

In the first study to be approved by the labyrinthine U.S. Federal cannabinoid research bureaucracy in years, smoked Cannabis was found to be the most effective treatment of those treatments compared for HIV/AIDS, without causing negative drug-drug interactions.

Doctor Donald Abrams and his research team from the University of California at San Francisco compared the effects of Cannabis (smoked), Marinol (dronabinol) and a placebo on a population of HIV positive patients. He announced his preliminary results at the XIII International AIDS Conference in Durban, South Africa in July of 2000. There was little media coverage of this remarkable presentation. In his comments, Doctor Abrams described significant clinical improvement in health—measured weight gain—without increasing the viral load of the Human Immunodeficiency Virus (HIV) among participants who smoked Cannabis.

The “viral load”

One basic interpretation of HIV status is the measurement of a person’s “viral load”. The viral load is measured as a blood test that registers HIV RNA. ³

A result of fewer than 50 copies per milliliter (copies/ml.) of blood is considered “undetectable” or not significant enough to cause disease. Increasing viral load is an indication that the virus that causes AIDS is replicating.

Many HIV patients endure complicated and difficult regimes of drugs called *antiretrovirals*. *Protease inhibitors* are one type of antiretroviral drug. This class of drugs ideally interferes with the reproduction of the HIV and keeps the level of the virus low enough to not allow opportunistic infections to develop. Unfortunately, protease inhibitors have all kinds of serious side effects. Many patients report serious nausea, headache, anorexia, diarrhea and liver function abnormalities.

The UCSF research team used repeated measurement of viral load over the length of the study to determine the effect different cannabinoid-based therapies. The study evaluated the effect of Cannabis smoking, Marinol (dronabinol) and a placebo.

The study

The research protocol consisted of 67 initial subjects. (Sixty-two completed the study.) All the subjects were undergoing antiretroviral therapy with either of two common protease inhibitors, *indinivir* (30 subjects), or *nelfinavir* (37 subjects). Baseline measurements of viral load were taken twice on all subjects. At the beginning of the study over half the participants, thirty-seven, had viral loads less than 50 copies/ml. Ten persons had HIV RNA levels of 50-499 copies/ml., thirteen had levels of 500-9999 copies/ml., and seven persons had levels over 10,000 copies/ml.

All 67 participants were randomly divided into three groups. The first group consisting of 21 patients used smoked U.S. Government-grown Cannabis with a THC percentage of around 4%. (Four percent THC is considered medium quality). The second group of 25 patients was treated with Marinol (dronabinol). The third group of 21 received an oral placebo. ⁴

Blood measurements of viral load were taken eight times over the twenty-one day study. In the beginning weeks, viral load was measured every three to four days. Measurements were increased in frequency as the weeks progressed so that by the third week, viral load was measured every other day. The dosage of each drug was as follows: Cannabis smoking patients smoked one cigarette three times a day before meals. The dronabinol and placebo groups each received a 2.5-milligram capsule, or placebo, also three times per day before meals.

During the length of the study, five subjects left for various reasons. One subject left the smoked Cannabis section because of what were called “neuropsychiatric” symptoms. Two left the dronabinol section, one for “neuropsychiatric” effects and one for headache and nausea. Other minor side effects occurred including rapid heart rate.

The results

After the three-week study concluded, a statistical analysis was conducted comparing the baseline measurements of weight and HIV RNA, with those obtained at various intervals. This analysis showed that the 36 participants with undetectable viral loads (under 50 copies/ml) at the beginning of the study remained in the same category. This held true for the dronabinol, Cannabis and placebo users. The 26 participants who had measurable viral loads at the beginning of the study showed declines over time. The dronabinol/Cannabis groups showed greater declines in viral load than did the placebo group although this was statistically insignificant according to the researchers. What was of major importance was the conclusion that smoking Cannabis did not appear to interfere with the efficacy of protease inhibitor therapy or cause the HIV to increase. In other words, smoking Cannabis did not seem to lead to immunological compromise in this key indicator of HIV status. A more complex immunological analysis had not been done at the time of the Durban AIDS Conference. Future analysis may support or refute the conclusion that Cannabis does not interfere with more complicated immunological functions.

But there was another surprising and significant result of this study, something that HIV/AIDS patients have long since known: Cannabis stimulates appetite. This correlation was established because of the measurements of weight taken before and during the study that demonstrated significant weight gain among both the dronabinol and smoked Cannabis groups. Since Marinol is presently clinically indicated for appetite stimulation in HIV and cancer, this was not surprising. Of more importance was the comparison of weight gain between the Cannabis and Dronabinol groups. The Cannabis-smoking group



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Clearly, the Cannabis-smoking group demonstrated the greatest improvement in health as measured by weight gain.

gained an average of 3.5 kilograms (7.7 lbs.), more than any other group. The placebo group gained 1.3 kilograms (2.8 lbs.) and the dronabinol group gained 3.1 kilograms (6.8 lbs.). Clearly, the Cannabis-smoking group demonstrated the greatest improvement in health as measured by weight gain.

None of these results can conclusively establish that Cannabis is without serious adverse interactions in some people. Thus, the results will not settle this question and other researchers will look for more subtle interactions between Cannabis and HIV/AIDS. There could well be some other unknown factor that would make Cannabis use *not* desirable for people suffering from HIV. More extensive measurement of these results will shed some deeper understanding on how cannabinoids interact with protease inhibitors and immune function. But the study clearly demonstrated, in these circumstances at least, that smoked Cannabis was the most beneficial treatment of all studied- even using relatively poor quality government Cannabis. Whether these results, paid for by federal tax dollars, will lead to meaningful federal movement on the medical Cannabis issue is much more doubtful.



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| Tablets Zinc Phosphide, Cannabis and Nux, Squibb | | | |
|-------------------------------------------------------------|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| (Nerve Tonic No. 5) | | | |
| | Per 1000 | Per 500 | Per 100 |
| Chocolate-coated | \$1.80 | 95c. | 23c. |
| Zinc Phosphide | 1/8 gr. | } The action of these tablets is that of a Nerve Tonic and Stimulant. They are used mainly to control nervous irritability. Dose: 1 tablet with water after meals. | |
| Ext. Nux Vomica | 1/8 gr. | | |
| Ext. Cannabis Ind. | 1/8 gr. | | |
| Tablets Zinc Phosphide and Cannabis Compound, Squibb | | | |
| (Neuralgic, Dr. Kenyon) | | | |
| | Per 1000 | Per 500 | Per 100 |
| Plain | \$2.00 | \$1.05 | 25c. |
| Chocolate-coated | \$2.10 | \$1.10 | 26c. |
| Zinc Phosphide | 1/16 gr. | } These tablets are employed in pains caused by derangement of nerve functions. In neuralgias, sciatica, and spasmodic pains generally; they lessen nerve irritability and excitement, and, by improving the nutrition of the nerves, tend to prevent a recurrence of the neuralgic attacks. Dose: 1 tablet every two hours for three doses, then every three or four hours until relieved. | |
| Strychnine Sulph. | 1/60 gr. | | |
| Ext. Cannabis Indica | 1/8 gr. | | |
| Sodium Arsenite | 1/20 gr. | | |
| Aconitine | 1/400 gr. | | |

Image thanks to Pharmacy

Cannabis pharmaceutical tablets for neurological pain, pre-1938

Cannabis for spasticity and neurological disorders: Now we know “why”

One of the oldest and most dramatic indications for Cannabis is as a treatment to decrease spasticity associated with neurological disorders like *multiple sclerosis* (MS). Until recently, basic science had not

uncovered the precise biochemical mechanism underlying its efficacy. Thanks to research conducted in Britain, the scientific basis for Cannabis' use as an antispasmodic is now clear. Published in the March 2nd 2000 issue of the journal *Nature* is the article: "*Cannabinoids Control Spasticity and Tremor in Multiple Sclerosis Model.*" Scientific scrutiny is finally unlocking the secrets about *how* and *why* cannabinoids work.

Physiology of multiple sclerosis

Multiple sclerosis is a disease that progressively destroys the body's nervous system. It has several different clinical pictures that roughly translate into the speed and severity of the neurological collapse. Symptoms can intermittently wax and wane or quickly progress to severe incapacitation and death. The underlying cause of MS is not clear. Most medical researchers think that it is somehow caused as an immunological defect that may be brought on by a viral or bacterial illness. The viral illness triggers a process of deterioration in the protective coverings of the *Central Nervous System*. The CNS composes the brain and spinal chord. Simply put, it regulates the complex management of nerve impulses that control everything from thought processes to hormone release to bodily functions and reflexes. Multiple sclerosis is understood as a process of *demyelination* of the nerve coverings. The myelin sheath is a lipid (fat) covering that surrounds and protects the nerves in the spinal chord and brain. Nerve signals, or impulses, pass through the nerve cell at high speeds, carrying *sensory* or *motor* signals. These allow humans to feel pain (sensory) or physically act (motor). The myelin sheath probably enhances the signaling in somewhat the way that plastic coating protects electrical wires.

As MS progresses, the myelin sheath deteriorates in places over time. Plaques develop and alter nerve conduction pathways. This leads to abnormalities in many organ systems that depend upon nerve cells to signal environmental changes and carry chemical messages throughout the body. The *Autonomic Nervous System* (ANS) is severely affected by multiple sclerosis. The ANS controls many involuntary body functions like heart rate, sweating, and glands. ⁵ This is why MS can affect so many varied bodily systems.

Symptoms of MS are varied but include movement and coordination problems, visual or speech alterations, bladder and bowel control, emotional changes and spasms, cramps or tremors. These symptoms vary widely from patient to patient. They may be severe and incapacitating or mild and barely noticeable.

Common treatments for multiple sclerosis

The treatment for MS varies with the symptoms and severity of the disease. At this time there are no medical procedures to eliminate the disease. Mainly, treatment is supportive, relying on medications and physical therapy to help control the body functions. The pharmaceuticals in common use include dantrolene (Dantrum) and baclofen



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Physical therapy strengthens muscles, increases rang-of-motion, stimulates heart and lung function and decreases contractures and skin breakdown.



Several U.K. research teams...coordinated investigations into the anti-spasmodic properties of cannabinoids.

(Lioresal) to relax muscles, benzodiazapines like diazepam (Valium), sedatives and tranquilizers. Common side effects of these drugs range from minimal to incapacitating. Dantrolene can cause drooling, sweating, and pleural effusions, hepatitis and tachycardia. Xanax can cause nausea, constipation, drowsiness, benzodiazepine dependence headache and dry mouth. As with many pharmaceutical regimens, the dosage of the drug is increased as the severity of the disease increases. Thus, patients who suffer from the severest functional and sensory effects of MS also suffer from the worst effects of pharmaceuticals.

The other basic line of treatment for MS involves exercise and physical therapy. Lack of mobility increases many problems and can lead to skin breakdown, gastrointestinal problems, contractures and muscle wasting. Physical therapy strengthens muscles, increases rang-of-motion, stimulates heart and lung function and decreases contractures and skin breakdown. Exercise should be carefully monitored to not injure weak muscles. Some patients report that magnets also decrease spasticity, although this has not been scientifically established.

Herbal Cannabis decreases spasticity

Until recently, little or no research had evaluated the biochemical foundation for reports that Cannabis decreased spasticity. This is not surprising since research into medical uses of cannabinoids has been held hostage to United States governmental opposition. Research—undertaken mostly in the U.K.—has uncovered the physiological action of cannabinoids in controlling spasticity and, as the authors state: “...provides a rationale for patients’ indications of the therapeutic potential of Cannabis in the control of the symptoms of multiple sclerosis.”

Several U.K. research teams including The Multiple Sclerosis Society of Great Britain and Northern Ireland and the University College of London, coordinated investigations into the anti-spasmodic properties of cannabinoids. They used an “artificial” research model of MS called *chronic relapsing experimental allergic encephalomyelitis* or CREAE for short. Mice were given drugs to induce the CREAE, then used as research subjects to test the effectiveness of the different cannabinoid compounds. Researchers injected a total of four different cannabinoids (WIN 55212, Delta-9-THC, methanandamide, JWH-133) and measured the effect on the CREAE.

They pointed out that “cannabinoid (CB) receptor agonism using WIN 55212, Delta-9-THC, methanandamide, JWH-133 quantitatively ameliorated both tremor and spasticity in diseased mice.” Additionally, they injected cannabinoid *antagonists* (deactivators), into the mice and found that as the drugs bind with cannabinoid receptors, the spasms returned. Antagonists, by occupying receptor sites, make them unavailable for cannabinoid activators. This research demonstrated that mice, and by extension humans, possess an endogenous cannabinoid receptor system that helps regulate coordination, spasms and tremors.

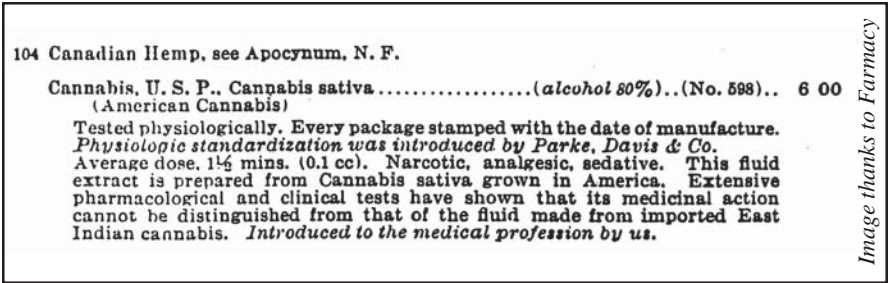


Image thanks to Farmacy

Cannabis pharmaceutical-grade elixer label, 1929-1930 catalog

Cannabis and glaucoma

Glaucoma is defined as an abnormal elevation in intraocular pressure (IOP) within the eye. It is caused by inadequate control of the fluid that lubricates and nourishes the eye—called *aqueous humor*. Aqueous humor is produced by an eye structure called the ciliary process. The aqueous humor passes through the eye and nourishes the tissues inside the eye. If there is a blockage of the valves that control the flow of aqueous humor out of the eye, pressure builds up. If there is excessive production of aqueous humor then pressure can also increase. Either condition causes degenerative changes including damage and destruction of the optic nerve. The eventual outcome is blindness for many patients. Normal IOP is 10-20 millimeters of Mercury (mm Hg.). IOP above 20 mm Hg. indicates glaucoma. Elevated IOP alone does not diagnose glaucoma. Damage to the optic nerve *caused* by the high pressure defines clinical glaucoma.

Glaucoma and diabetes are variously listed as the leading causes of blindness in the United States. At least 80,000 Americans are blind from glaucoma and three million Americans are afflicted with it. A higher percentage of African Americans suffer from glaucoma and blindness than do Caucasians.

The goal of medical management of glaucoma is to preserve the sight. Treatments for glaucoma include drugs and surgical intervention. Topical (applied directly to the eye) treatments include drugs containing beta-blockers like timolol maleate (Timoptic), miotic drugs which constrict the pupil to increase aqueous humor outflow like Pilocarpine, and carbonic anhydrase inhibitors like Diamox. Epinephrine may also be used. Side effects to these medications are varied in frequency and severity but include impaired night vision, blurred vision, fatigue, decreased appetite, weight loss, heart palpitations. As the degenerative process continues, topical agents are increased in dosage resulting in more significant side effects. Fifty percent of patients cannot tolerate the side effects of these medications, narrowing their available options. Surgical interventions carry significant risk of worsening the condition.

Cannabinoids have been shown in repeated research studies to reduce IOP to normal levels thereby slowing or arresting the disease. Pharmacological action on the formation and flow of aqueous humor is poorly understood. Tests using THC (tetra-hydrocannabinol) alone



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have not shown significant benefits. Several different cannabinoids within Cannabis seem to act in conjunction with one another.

Cannabis has some 60 different cannabinoid molecules. Many glaucoma sufferers report that inhaled Cannabis quickly reduces symptoms of elevated IOP. Some patients who use Cannabis report slowing or stopping of their loss of sight for long periods of time.

Cannabis therapy for glaucoma should be evaluated on the risk/benefit continuum. Research on long-term pulmonary effects of smoked Cannabis shows that cellular changes similar to tobacco occur with chronic use. The duration of action of Cannabis in lowering intraocular pressure is four to six hours. Thus, for long-term control of symptoms, patients need to dose four to six times per day. In general medical terms, this is not a desirable option. However, when compared to the incapacity of blindness or the increasingly dangerous medical options, Cannabis falls within an acceptable range. The patient and physician should be the ones to decide if the benefits outweigh the risks, by evaluating the patient's ability to maintain this therapy long-term.

In 1980, researchers in Jamaica formulated a topical eye drop made from *Cannabis sativa*. They named this compound *Canasol*. It has been used widely in Jamaica. Canasol is manufactured as a sterile solution and is dispensed in five milliliter (ml.) bottles for instillation into the eye. The IOP-lowering effects are similar to pilocarpine in degree. Canasol appears to work synergistically with pilocarpine, without the serious side effects. There have been no adverse effects noted as of 1998. There are no FDA clinical trials ongoing or planned to evaluate Canasol. As of 2001, this medicine is not available to patients in the United States.

Footnotes

¹ Endorphins are manufactured in the brain and are activated when a person is injured. As our natural pain-killing system, they are responsible when soldiers with grievous wounds feel no pain.

² Antagonists are chemical compounds that rapidly block and chemically counteract the effects of other substances by receptor-binding. People who overdose on heroin, (an opioid), are given Nalaxone, an antagonist, which quickly reverses the effects of heroin by competing for receptor sites occupied by the heroin.

³ Ribonucleic Acid (RNA) is a genetic structure that controls protein synthesis within all living cells. Since HIV is a virus, it contains RNA. Thus, measuring the RNA present in the AIDS virus gives a marker as to the extent of the virus.

⁴ A “placebo” is a “fake drug” that acts as a baseline control to evaluate the effect of no specific treatment. By using the placebo as a standard of comparison researchers are able to determine if the drug in question, in this case Cannabis, has any real effect. Patients and sometimes researchers do not know if the drug being evaluated is “real” or is a placebo. If neither the patient nor the researcher knows which it is then the test is called “double blind.” (There was no placebo Cannabis smoking group to establish a baseline for the Cannabis smokers in the study.)

⁵ The *Autonomic Nervous System* acts to slow or stimulate these systems in response to environmental situations in order to maintain *homeostasis* or physiologic equilibrium. In hot weather we perspire which releases heat from the body, reestablishing internal comfort.

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