MMP-019

New Jersey Department of Health
Medicinal Marijuana Program
PO 360
Trenton, NJ 08625-0360

MEDICINAL MARIJUANA PETITION
(N.J.A.C. 8:64-5.1 et seq.)

INSTRUCTIONS

This petition form is to be used only for requesting approval of an additional medical condition or treatment thereof as a "debilitating medical condition" pursuant to the New Jersey Compassionate Use Medical Marijuana Act, N.J.S.A. 24:6I-3. Only one condition or treatment may be identified per petition form. For additional conditions or treatments, a separate petition form must be submitted.

NOTE: This Petition form tracks the requirements of N.J.A.C. 8:64-5.3. Note that if a petition does not contain all information required by N.J.A.C. 8:64-5.3, the Department will deny the petition and return it to petitioner without further review. For that reason the Department strongly encourages use of the Petition form.

*This completed petition **must** be postmarked **August 1 through August 31, 2016** and sent by **certified mail** to:*

New Jersey Department of Health
Office of Commissioner - Medicinal Marijuana Program
Attention: Michele Stark
369 South Warren Street
Trenton, NJ 08608

Please complete each section of this petition. If there are any supportive documents attached to this petition, you should reference those documents in the text of the petition. If you need additional space for any item, please use a separate piece of paper, number the item accordingly, and attach it to the petition.

---

1. Petitioner Information

Name: [redacted]

Street Address: [redacted]

City, State, Zip Code: [redacted]

Telephone Number: [redacted]

Email Address: [redacted]

2. Identify the medical condition or treatment thereof proposed. Please be specific. Do not submit broad categories (such as "mental illness").

Rheumatoid Arthritis

3. Do you wish to address the Medical Marijuana Review Panel regarding your petition?

☐ Yes, in Person

☒ Yes, by Telephone

☐ No

4. Do you request that your personally identifiable information or health information remain confidential?

☒ Yes

☐ No

If you answer "Yes" to Question 4, your name, address, phone number, and email, as well as any medical or health information specific to you, will be redacted from the petition before forwarding to the panel for review.

RECEIVED
AUG 29 2016
OFFICE OF THE CHIEF OF STAFF

5. **Describe the extent to which the condition is generally accepted by the medical community and other experts as a valid, existing medical condition.**

   Rheumatoid arthritis (RA) is an auto immune disease recognized by the medical community. RA is a chronic inflammatory disease that primarily affects the joints. The disease may also affect other parts of the body including the skin, eyes, lungs, heart and blood vessels. It may also result in a low red blood cell count. Fever and low energy may also be present. Chronic and severe pain is present when the disease flairs.

6. **If one or more treatments of the condition, rather than the condition itself, are alleged to be the cause of the patient's suffering, describe the extent to which the treatments causing suffering are generally accepted by the medical community and other experts as valid treatments for the condition.**

   N/A

7. **Describe the extent to which the condition itself and/or the treatments thereof cause severe suffering, such as severe and/or chronic pain, severe nausea and/or vomiting or otherwise severely impair the patient's ability to carry on activities of daily living.**

   The condition causes chronic pain which at times can be severe and debilitating. When the joints are inflammed, loss/limit of function occurs which can impact several activities of daily living (ADLs) such as ambulation, dressing,and showering.Everyday normal tasks have to be thought through. For example, one has to think and plan ahead what needs to be brought up and down the stairs (laundry, shopping items) to reduce the number of trips,etc. Because of the pain, joint stiffness, and impaired sleep, the individual may experience loss of appetite and difficulty with concentration as well. Activities which were once enjoyable, such as a hand or foot massage while getting a manicure/pedicure are now no longer plesant. A person, even when their RA is controlled, experiences both good and bad days. During the bad days, rest seems the only option and then when the inflammation subsides, the person then spends the good day completing all their chores that piled up duirng the bad day. It becomes a cycle of balancing what needs to be done with what can actually be accomplished. Marijuana is a safe non addicting alternative to opioid pain management.

8. **Describe the availability of conventional medical therapies other than those that cause suffering to alleviate suffering caused by the condition and/or the treatment thereof.**

   Several forms of medication (pills, injections, infusions) are available but each of the medications have serious and extreme side effects including potential for infection and certain types of Lymphoma and other cancers particularly from those who use biologics. Even the chronic use of NSAIDs has potentially harmful cardiac, GI, and kidney side effects. These risks may be greater if they have comorbid heart disease or an increased risk for heart disease due to cigarette smoking, or family history. The gold standard treatment with Plaquenil can cause serious irreversible damage to the retina. For those who can not tolerate Plaquenil, then methotrexate is the next alternative. This medication also comes with serious side effects which include, birth defects, bone marrow suppression and stomach/intestinal disease (e.g. bleeding when used at the same time as NSAIDsa) lung disease and lung infections; which one is also susceptible to with RA. Folic acid must be taken daily to combat the side effects of Methotrexate. Prednisone is also routinely used to suppress inflammation. This drug also has a plethera of serious side effects which include metabolic, cardiac, endocrine, bone, immunologic, and psychiatric. This drug also increases the risk for infections so the option of taking an antiinflammatory medication, which also increases the risk for infections and bleeding, is compounded by the other standard medication treatments currently available for RA.

9. **Describe the extent to which evidence that is generally accepted among the medical community and other experts supports a finding that the use of marijuana alleviates suffering caused by the condition and/or the treatment thereof.** *[**Note:** You may attach articles published in peer-reviewed scientific journals reporting the results of research on the effects of marijuana on the medical condition or treatment of the condition and supporting why the medical condition should be added to the list of debilitating medical conditions.]*

   Due to the obstacles imposed by the Federal government since Marijuana is classified as a schedule 1 drug, research is limited. There is a disconnect between the Federal government and DEA regulations making obtaining consent for reaserch difficult and time consuming. For conditions such as epilepsy, cancer, AIDS, and MS; available research has shown, among other things, the use of medical marijuana to help alleviate pain, muscle spasm and increase appetite. All of which could be helpful for people who have RA. Those who are allowed to use medical marijuana ultimately may have a better quality of life and therefore have reflief from their pain, inflammation, and depression which they would otherwise have to contend with. Rather than being curative, medical marijuana's effiacy is one of symptom control.

10. **Attach letters of support from physicians or other licensed health care professionals knowledgeable about the condition. List below the number of letters attached and identify the authors.**

    There is not much medical research literature available concerning medical cannabis for RA. I've attached two articles. The first one is titled Arthritis & Medical Marijuana which appeared in the Americans for Safe Access booklet. Several physicians are mentioned in the article. They include Dr. Ethan Russo, Dr. Arnold Leff, and Dr. Harvey Rose. The second article titled Preliminary assessment of the efficacy, toleratility and safety of a cannabis-based medicine (Sativex) in the treatment of pain caused by rheumatoid arthritis. Dr. A.B. Hassell, Dr. D. Tull, Dr. M.J.B Duckworth, Dr. E. Montague and Dr. T.M. Johnosn provided collaboration.
    I would like to address the review panel, since I have been diagnosed with RA, but am extremely hesitant due to my profession [redacted] and my current place of employment. I am fearful of repercussion with my [redacted] license and loss of employment for taking a view of promoting a current schedule 1 drug for medical use.

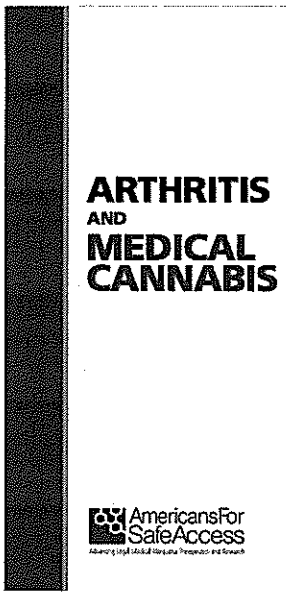
I certify, under penalty of perjury, that I am 18 years of age or older; that the information provided in this petition is true and accurate to the best of my knowledge; and that the attached documents are authentic.

Signature of Petitioner [redacted]	Date 8/7/16

Arthritis

Arthritis & Medical Marijuana

A Note from Americans for Safe Access



(http://www.amazon.com/Arthritis-and-Medical-Cannabis-ebook/dp/B00E5LYO66/ref=sr_1_15?s=digital-text&ie=UTF8&qid=1380152233&sr=1-15)We are committed to ensuring safe, legal availability of marijuana for medical uses. Today over one million Americans are legally using medical marijuana—or "cannabis," as it is more properly called—under the care of their medical professional, and nearly half the country lives in a state where this treatment is an option. This publication series is intended to help medical professionals, patients and policymakers better understand how cannabis may be used safely and effectively as a treatment for many medical conditions. You will find information on:

Why Cannabis is Legal to Recommend (http://www.safeaccessnow.org/arthritis_booklet#cannabis_legal)

Overview of the Scientific Research on Medical Cannabis (http://www.safeaccessnow.org/arthritis_booklet#science)

Cannabis and Arthritis (http://www.safeaccessnow.org/arthritis_booklet#arthritis)

Comparison of Medications: Efficacy and Side-Effects

While the federal prohibition of cannabis has limited modern clinical research and resulted in considerable misinformation, a scientific consensus on its therapeutic value has emerged, based on a growing body of successful clinical trials and preclinical research. The experience of patients, medical professionals and research has revealed that cannabis can safely treat a remarkably broad range of medical conditions, often more effectively than conventional pharmaceutical drugs. For some of the most difficult to treat conditions, such as multiple sclerosis and neuropathic pain, cannabis often works when nothing else does.

Many of its therapeutic uses are well known and documented, and medical researchers are learning more each day. Cannabis and its constituent components show potential to fight tumors, autoimmune disorders, and serious neurological conditions for which treatment options are limited. As of July 2014, 23 states and the District of Columbia have laws allowing its use under a doctor's supervision, and cannabis or a dose-controlled whole-plant extract of it is available by prescription in 11 countries and approved for 13 more.

This publication is only a starting point for the consideration of applying cannabis therapies to specific conditions; it is not intended to replace the training and expertise of medical professionals with regard to medicine, or attorneys with regard to the law. But as advocates for the hundreds of thousands of patients who have found relief with cannabis, we know there are millions more for whom it may be the best medicine.

Why Cannabis is Legal to Recommend

Medical professionals have a legal right to recommend cannabis as a treatment in any state, as protected by the First Amendment. That was established by a 2004 United States Supreme Court decision to uphold earlier federal court rulings that doctors and their patients have a fundamental Constitutional right to freely discuss treatment options. State rules for qualifying an individual patient for legal protections when using medical cannabis differ as to who may make the recommendation and for what conditions, as well as how that recommendation is communicated to the appropriate state authorities. Medical professionals and individual patients should familiarize themselves with the applicable laws and regulations in their state. ASA provides state-by-state resources to help at:
AmericansForSafeAccess.org/state_by_state_recommending_cannabis (http://www.safeaccessnow.org/state_by_state_recommending_cannabis)

Under federal law, cannabis may not be prescribed, but its therapeutic use can be recommended without any legal jeopardy. The court rulings that protect medical professionals stem from a lawsuit brought by a group of doctors and patients led by AIDS specialist Dr. Marcus Conant. The suit was filed in response to federal officials who, within weeks of California voters legalizing medical cannabis in 1996, had threatened to revoke the prescribing privileges of any physicians who recommended cannabis to their patients for medical use.[1] Dr. Conant contended that such a policy would violate the First Amendment, and the federal courts agreed.[2, 3]

What doctors may and may not do. In *Conant v. Walters*, the Ninth Circuit Court of Appeals held that the federal government could neither punish nor threaten a doctor merely for recommending the use of cannabis to a patient.[4, 5] But it remains illegal for a doctor to "aid and abet" a patient in obtaining cannabis.[6] This means physicians and other medical professionals may discuss the pros and cons of medical cannabis with any patient, and recommend its use whenever appropriate. They may put that in writing or otherwise participate in state medical cannabis programs without fear of legal reprisal.[7] This is true even when the recommending medical professional

knows the patient will use the recommendation to obtain cannabis through a state program.[8] What physicians may not do is provide cannabis directly to a patient[9] or tell patients how or where to obtain it.[10]

Patients protected under state law, not federal.

As of July 2015, 23 states and the District of Columbia provide legal protections for qualified individuals participating in their state medical cannabis program. However, all use of cannabis remains illegal under federal law, and in June 2005, the U.S. Supreme Court in *Gonzales v. Raich* ruled that state medical cannabis laws do not provide protections for patients and providers from federal prosecution.[11] Under the Obama Administration, the Department of Justice has issued three memos providing guidance to federal prosecutors, each indicating that individual patients and caregivers should not be federal enforcement priorities. The latest memo indicates enforcement should be left to states so long as they have effective regulations in place for use and distribution. An analysis by ASA of existing state laws and local regulations found that all reflect the same general enforcement priorities as the 2013 federal guidelines.[12]

For assistance with determining how best to write or obtain a legal recommendation for cannabis, please contact ASA at 1-888-929-4367.

Medical Professionals Say Cannabis is Medicine

Thousands of studies published in peer-reviewed journals indicate cannabis has medical value in treating patients with such serious conditions as AIDS, glaucoma, cancer, epilepsy, and chronic pain, as well as a variety of such neurological disorders as multiple sclerosis, Parkinsonism, and ALS.

A 2013 poll conducted by the New England Journal of Medicine found that three out of four clinicians would recommend the use of medical cannabis for a hypothetical cancer patient.13 The use of medical cannabis has been endorsed by numerous professional organizations, including the American Academy of Family Physicians, the American Public Health Association, and the American Nurses Association. Its use is supported by such leading medical publications as The New England Journal of Medicine and The Lancet. The International Cannabinoid Research Society was formally incorporated as a scientific

research organization in 1991 with 50 members; as of 2014, there are nearly 500 around the world. The International Association for Cannabinoid Medicines (IACM), founded in 2000, publishes a bi-weekly bulletin and holds international symposia to highlight emerging research in cannabis therapeutics.

The safety and efficacy of cannabis has been attested to by numerous government studies and reports issued over the past 70 years. These include the 1944 LaGuardia Report, the Schafer Commission Report in 1972, a review commissioned by the British House of Lords in 1997, the Institutes of Medicine report of 1999, research sponsored by Health Canada, and numerous studies conducted in the Netherlands, where cannabis has been quasi-legal since 1976 and is currently available from pharmacies by prescription.

Scientific Research Advances

While modern research has until recently been sharply limited by federal prohibition, the last few decades have seen rapid change. More than 15,000 modern peer-reviewed scientific articles on the chemistry and pharmacology of cannabis and cannabinoids have been published, as well as more than 2,000 articles on the body's natural cannabinoids and the receptors they attach to.[14] The discovery of the endocannabinoid system (ECS) opened a door to new understandings of how the body regulates internal systems and how the phytocannabinoids found in the cannabis plant interact with it. Endocannabinoids are crucial to bioregulation, and evidence suggests they play a role in inflammation, insulin sensitivity, and fat and energy metabolism, as well as chronic neurologic and immune conditions. The cannabinoid receptors CB1 and CB2 are identified targets for treating a remarkable variety of serious medical conditions.[15-18]

A 2009 review of controlled clinical studies with medical cannabis conducted over a 38-year period found that "nearly all of the 33 published controlled clinical trials conducted in the United States have shown significant and measurable benefits in subjects receiving the treatment."[19] The review's authors note that the more than 100 different cannabinoids in cannabis have the capacity for analgesia through neuromodulation in ascending and descending pain pathways, neuroprotection, and anti-inflammatory mechanisms. Research into the therapeutic potential of cannabis and

cannabinoids has expanded considerably in the past decade. As of May 2014, the Center for Medicinal Cannabis Research, a state-funded $8.7-million research effort at University of California campuses, had completed 13 approved studies. Of those, seven published double-blind, placebo-controlled studies examined pain relief, and each showed cannabis to be effective.[20]

No adverse health effects related to medical cannabis use have been reported, even among the most seriously ill and immune-compromised patients. Research on CD4 immunity in AIDS patients found no negative effects to the immune systems of patients undergoing cannabis therapy in clinical trials.[21] A complete health assessment in 2002 of four of the patients enrolled in the U.S. Investigational New Drug program who had used cannabis daily for between 11 and 27 years found cannabis to be clinically effective for each with no negative health consequences.[22]

In the United Kingdom, GW Pharmaceuticals has been conducting clinical trials for more than a decade with its cannabis medicine, Sativex® Oromucosal Spray, a controlled-dose whole-plant extract. GW's Phase II and Phase III trials show positive results for the relief of neurological pain related to: multiple sclerosis (MS), spinal cord injury, peripheral nerve injury (including peripheral neuropathy secondary to diabetes mellitus or AIDS), central nervous system damage, neuroinvasive cancer, dystonias, cerebral vascular accident, and spina bifida. They have also shown cannabinoids to be effective in clinical trials for the relief of pain and inflammation in rheumatoid arthritis and also pain relief in brachial plexus injury.[23-26]

Sativex® was approved in Canada for symptomatic relief of neuropathic pain in 2005, in 2007 for patients with advanced cancer whose pain is not fully alleviated by opiates, and in 2010 for spasticity related to multiple sclerosis. As of 2014, Sativex has been made available or approved for named patient prescription use in 24 countries, including the UK, Spain, Italy and Germany.

In the US, GW was granted an import license for Sativex® by the DEA following meetings in 2005 with the FDA, DEA, the Office for National Drug Control Policy, and the National Institute for Drug Abuse. Sativex® is currently an investigational drug in FDA-approved clinical trials as an adjunctive analgesic

treatment for patients with advanced cancer whose pain is not relieved by opioids. In 2013, GW Pharmaceuticals received FDA approval to test a highly purified cannabinoid extract (cannabidiol or CBD) named Epidiolex® on a limited number of US children with seizure disorders. As of January 2014, seven US pediatric epilepsy specialists have been approved to treat 125 children with Dravet syndrome, Lennox-Gastaut syndrome, and other pediatric epilepsy syndromes.

CANNABIS AND ARTHRITIS

More than 31 million Americans suffer from arthritis. There are two main types of arthritis: rheumatoid arthritis and osteoarthritis. Both affect the joints, causing pain and swelling, and limiting movement.

Rheumatoid arthritis (RA) is caused by a malfunction of the immune system. Instead of fighting off intruders such as bacteria or viruses, the body attacks the synovial membranes, which facilitate the movement of joints, eventually destroying cartilage and eroding bones. Rheumatoid arthritis is most common among the aged, whose immune systems are no longer as robust or efficient as they were when younger.

Osteoarthritis (OA), or arthritis of the bones, is also found primarily among the elderly, where cartilage has been worn away through many years of use. Arthritis may also manifest as chronic inflammation of the joints as the result of injuries. OA is the most common form of arthritis, affecting more than 10 million people worldwide. Currently, no drugs are available to treat or modify this disease, and treatment is primarily focused around the use of pain killers, which often have limited benefits and hazardous side effects.

An important aspect of arthritis pathology relates to maintaining healthy bone. As people age, bones undergo extensive remodeling, which can lead to destruction or functional degradation of synovial joints. Drugs which can not only modulate pain from arthritis but also protect bones are of great importance. Cannabis and cannabinoids represent a promising treatment which can reduce arthritic pain and inflammation and positively modulate bone growth and maintenance. It has already been demonstrated that cannabinoids

can effectively treat some types of arthritic pain, but recent evidence suggests that the cannabinoids are also important for bone growth and maintenance throughout life.[27-32]

The importance of cannabinoids in bone health has been established in transgenic mice that are missing either the CB1 or CB2 receptor. These mice develop osteoporosis much more quickly than normal or wild mice. Research has recently shown that mice missing both cannabinoid receptors have extremely weak bones, a condition that underlies osteoporosis and osteoarthritis pathology.[33-35]

Based on genetic screening techniques, a correlation between cannabinoids and bone is emerging in humans as well. Three studies in three distinct ethnic groups have demonstrated that mutations in the type 2 cannabinoid receptor correlate to bone diseases. One study even showed that hand bone strength weakness is very well correlated with dysfunctional/mutant CB2 receptors.

Arthritis of any type can be an extremely painful and debilitating condition that presents challenges for pain management. The use of cannabis as a treatment for musclo-skeletal pain in western medicine dates to the 1700s.[36,37] Evidence from recent research suggests that cannabis-based therapies are effective in the treatment of arthritis and the other rheumatic and degenerative hip, joint and connective tissue disorders. Since these are frequently extremely painful conditions, the well-documented analgesic properties of cannabis make it useful in treating the pain associated with arthritis, both on its own and as an adjunct therapy that substantially enhances the efficacy of opioid painkillers.

Cannabis has also been shown to have powerful immune-modulation and anti-inflammatory properties,[38-41] suggesting that it could play a role not just in symptom management but treatment of arthritis. In fact, one of the earliest records of medical use of cannabis, a Chinese text dating from ca. 2000 BC, notes that cannabis "undoes rheumatism," suggesting its anti-inflammatory and immune modulating effects were known even then.[42]

Modern research on cannabidiol (CBD), one of the non-psychoactive cannabinoid components of cannabis, has found that it suppresses the immune response in mice and rats that is responsible for a disease resembling arthritis, protecting them from severe damage to their joints and markedly improving their condition.[43,44]

Human studies have repeatedly shown cannabis to be an effective treatment for rheumatoid arthritis, and it is one of the enumerated conditions for which many states allow legal medical use. Cannabis has a demonstrated ability to improve mobility and reduce morning stiffness and inflammation. Research has also shown that patients are able to reduce their usage of potentially harmful Non-Steroidal Anti-Inflammatory drugs (NSAIDs) when using cannabis as an adjunct therapy.[45,46]

Medical researchers at Hebrew University in Jerusalem found that when cannabidiol is metabolized, one result is the creation of a compound with potent anti-inflammatory action comparable to the drug indomethacin, but without the considerable gastrointestinal side effects associated with that drug. [47]

In addition, when the body metabolizes tetrahydrocannabinol (THC), one of the primary cannabinoid components of cannabis, it produces a number of related chemicals. At least one of these metabolites has anti-inflammatory and pain-relieving effects. By modifying this metabolite, researchers have produced a synthetic carboxylic acid known as CT-3 (also called dimethylheptyl-THC-11 oic acid or DMH-11C), which is more powerful than the natural metabolite itself, and thus can be given in smaller doses. Animal tests found CT-3 effective against both chronic and acute inflammation, and it also prevented destruction of joint tissue from chronic inflammation.

The remarkable 5,000-year safety record of cannabis - there has never been a recorded death from an overdose - and the fact that a metabolite with the desired anti-inflammatory effect is produced in the body when cannabis is used, indicates that the development of targeted, safe, and effective anti-inflammatory drugs in this class are possible.[48] CT3 has also demonstrated

considerable analgesic effects in animals. In some cases, the dose-dependent effect of THC was equivalent to morphine, but with a much greater duration of action and far less toxicity.[49,50]

In contrast to the NSAIDs commonly prescribed arthritis sufferers, CT3 did not cause ulcers at therapeutically effective doses. Moreover, it does not depress respiration, produce dependence, induce body weight loss, or cause mutations, as many commonly prescribed drugs do. Studies on its mechanism of action are currently underway, with cytokine synthesis one of the pathways being studied.[51}

Cannabis may also help combat rheumatoid arthritis through its well-recognized immune-modulation properties.[52] Rheumatoid arthritis is characterized by ysregulation of the immune system in response to an initial infection or trauma. Over-activity of the immune system's B-cells causes antibodies to attack and destroy the synovial tissues located in the joint.

The immuno-modulatory properties of a group of fats found in cannabis, known as sterols and sterolins, have been used as natural alternatives to conventional rheumatoid arthritis treatments that employ highly toxic drugs to either suppress the entire immune response of the body or to palliate pain and the inflammatory process without correcting the underlying immune dysfunction.

Cytokines play a role in either fuelling or suppressing the inflammation that causes damage in rheumatoid arthritis and some other diseases. The release of selected cytokines is impaired by cannabis, but the findings differ by cell type, experimental conditions, and especially the concentration of the cannabinoids examined.[53-56] A sterol/sterolin combination has been experimentally demonstrated to reduce the secretion of the pro-inflammatory cytokines controlled by the TH2 helper cells and to increase the number of TH helper cells that regulate the secretion of antibodies from the B cells. This selective activation and inhibition of the immune system results is an effective control of the dysfunctional auto-immune response.

Similarly, ajulemic acid (another non-psychoactive cannabinoid) has been found to reduce joint tissue damage in rats with adjuvant arthritis.[57] Tests on human tissue done in vitro showed a 50% suppression of one of the body's chemicals (interleukin-1beta) central to the progression of inflammation and joint tissue injury in patients with rheumatoid arthritis.[58]

Conventional Arthritis Medications

Over 100 medications are listed by the Arthritis Foundation website for use with arthritis or other related conditions, such as fibromyalgia, psoriasis, osteoporosis and gout. These medicines include aspirin, ibuprofen and other oral and topical analgesics that dull pain. The most commonly used analgesic, acetaminophen (aspirin-free Anacin, Excedrin, Panadol, Tylenol) is usually not associated with side effects, though long-term use of acetaminophen is thought to be one of the common causes of end-stage renal disease.. To effectively control arthritis, aspirin must be taken in large, continuous doses (1000-5400 mg daily), which can cause stomach pain or damage; it is believed to cause more than 1,000 deaths annually in the United States. For that reason, some doctors prescribe one of several chemical variations referred to as nonacetylated salicylates, such as CMT, Tricosal, and Trilisate, which can cause deafness or ringing in the ears in large doses.

Much stronger analgesics are also prescribed for arthritis, sometimes along with acetaminophen. These are: **codeine** (Dolacet, Hydrocet, Lorcet, Lortab); **morphine** (Avinza, Oramorph); **oxycodone** (Vicodin, Oxycontin, Roxicodone); **propoxyphene** (Percocet, Darvon, Darvocet) and **tramadol** (Ultram, Ultracet). These medicines can cause psychological and physical dependence, as well as constipation, dizziness, lightheadedness, mood changes, nausea, sedation, shortness of breath and vomiting. Taking high doses or mixing with alcohol can slow down breathing, a potentially fatal condition.

Analgesics don't treat the inflammation that can cause severe arthritis pain. For inflammation, steroids, NSAIDs and newer COX-2 inhibitors are prescribed. **Corticosteroids** (Cortisone), **prednisone** and related medications can cause bruising, cataracts, elevated blood sugar, hypertension, increased appetite, indigestion, insomnia, mood swings, muscle weakness, nervousness or restlessness, osteoporosis, susceptibility to infection and thin skin.

Twenty NSAIDs are available with a doctor's prescription, with three of those also available over the counter. They are **diclofenac** (Arthrotec, Cataflam, Voltaren); **diflunisal** (Dolobid); **etodolac** (Lodine); **fenoprofen calcium** (Nalfon); **flurbiprofen** (Ansaid); **ibuprofen** (Advil, Motrin IB, Nuprin); **indomethacin** (Indocin); **ketoprofen** (Orudis); **meclofenamate sodium** (Meclomen); **mefenamic acid** (Ponstel); **meloxicam** (Mobic); **nabumetone** (Relafen); **naproxen** (Naprosyn, Naprelan); **naproxen sodium** (Anaprox, Aleve);**oxaprozin** (Daypro); **piroxicam** (Feldene); **sulindac** (Clinoril); and **olmetin sodium** (Tolectin).

Side effects of NSAIDs include abdominal or stomach cramps, edema (swelling of the feet), pain or discomfort, diarrhea, dizziness, drowsiness or lightheadedness, headache, heartburn or indigestion, nausea or vomiting, gastric ulcers, stomach irritation, bleeding, fluid retention, and decreased kidney function. This is because NSAIDs act on arthritis by inhibiting prostaglandins, which protect the stomach lining, promote clotting of the blood, regulate salt and fluid balance, and maintain blood flow to the kidneys. The gastrointestinal complications of NSAIDS are the most commonly reported serious adverse drug reaction, though NSAIDs are reported to cause more than 10,000 deaths and 100,000 hospitalizations annually.

The newer group of arthritis drugs is known as cyclo-oxygenase-2 inhibitors (COX-2), which include **Celebrex**, **Bextra** and **Vioxx**. These medications have the same side effects as NSAIDS, except they are less likely to cause bleeding stomach ulcers and increase susceptibility to bruising or bleeding.

Non-selective NSAIDS have been associated with an increased risk of congestive heart failure. Less is known or has been concluded about the cardiovascular effects f COX-2 inhibitors, though a retrospective analysis of the risk of hospital admission for heart failure done by the Institute for Clinical Evaluative Sciences in Toronto, Canada suggests some may have serious side effects. The study of 130,000 older patients found that those using **Vioxx** had an 80% increased risk of hospital admission for congestive heart failure. Those using non-selective NSAIDS had a 40% increased risk, and those using **Celebrex** had the same rate of heart failure as people who had never used NSAIDS.

Antipyretic and anti-inflammatory effects of NSAIDs can mask the signs and symptoms of infection. Their use can interfere with the pharmacologic control of hypertension and cardiac failure in patients who take beta-adrenergic antagonists, angiotensin-converting enzyme inhibitors, or diuretics. Long-term use may damage chondrocyte (cartilage) function.

About 60% of patients will respond to any single NSAID. Approximately 10% of rheumatoid arthritis patients will not respond to any NSAID. Biologic response modifiers such as **adalimumab** (Humira); **etanercept** (Enbrel); **infliximab** (Remicade), and **anakinra** (Kineret) are prescribed to either inhibit or the supplement the immune system components called cytokines. Rare reports of lupus (with such symptoms as rash, fever and pleurisy) have been linked to treatment with **adalimumab**, **etanercept** and **infliximab**. Lupus symptoms resolve when the medication is stopped. Multiple sclerosis has rarely developed in patients receiving biologic response modifiers. Seizures have been reported with **etanercept**.

Cannabis: By comparison, the side effects associated with cannabis are typically mild and are classified as "low risk." Euphoric mood changes are among the most frequent side effects. Cannabinoids can exacerbate schizophrenic psychosis in predisposed persons. Cannabinoids impede cognitive and psychomotor performance, resulting in temporary impairment. Chronic use can lead to the development of tolerance. Tachycardia and hypotension are frequently documented as adverse events in the cardiovascular system. A few cases of myocardial ischemia have been reported in young and previously healthy patients. Inhaling the smoke of cannabis cigarettes induces side effects on the respiratory system. Cannabinoids are contraindicated for patients with a history of cardiac ischemia. In summary, a low risk profile is evident from the literature available. Serious complications are very rare and are not usually reported during the use of cannabinoids for medical indications.

Is cannabis safe to recommend?

"The smoking of cannabis, even long term, is not harmful to health...." So began a 1995 editorial statement of Great Britain's leading medical journal, The Lancet. The long history of human use of cannabis also attests to its safety - nearly 5,000 years of documented use without a single death. In the same year as the Lancet editorial, Dr. Lester Grinspoon, a professor emeritus at Harvard Medical School who has published many influential books and articles on medical use of cannabis, had this to say in an article in the *Journal of the American Medical Association* (1995):

One of marihuana's greatest advantages as a medicine is its remarkable safety. It has little effect on major physiological functions. There is no known case of a lethal overdose; on the basis of animal models, the ratio of lethal to effective dose is estimated as 40,000 to 1. By comparison, the ratio is between 3 and 50 to 1 for secobarbital and between 4 and 10 to 1 for ethanol. Marihuana is also far less addictive and far less subject to abuse than many drugs now used as muscle relaxants, hypnotics, and analgesics. The chief legitimate concern is the effect of smoking on the lungs. Cannabis smoke carries even more tars and other particulate matter than tobacco smoke. But the amount smoked is much less, especially in medical use, and once marihuana is an openly recognized medicine, solutions may be found; ultimately a technology for the inhalation of cannabinoid vapors could be developed.

The technology Dr. Grinspoon imagined in 1995 now exists in the form of "vaporizers," (which are widely available through stores and by mail-order) and recent research attests to their efficacy and safety.[59] Additionally, pharmaceutical companies have developed sublingual sprays and tablet forms of the drug. Patients and doctors have found other ways to avoid the potential problems associated with smoking, though long-term studies of even the heaviest users in Jamaica, Turkey and the U.S. have not found increased incidence of lung disease or other respiratory problems. A decade-long study of 65,000 Kaiser-Permanente patients comparing cancer rates among non-smokers, tobacco smokers, and cannabis smokers found that those who used only cannabis had a slightly lower risk of lung and other cancers as compared to non-smokers.[45] Similarly, a study comparing 1,200 patients with lung, head

and neck cancers to a matched group with no cancer found that even those cannabis smokers who had consumed in excess of 20,000 joints had no increased risk of cancer.[60]

As Dr. Grinspoon notes, "the greatest danger in medical use of marihuana is its illegality, which imposes much anxiety and expense on suffering people, forces them to bargain with illicit drug dealers, and exposes them to the threat of criminal prosecution." This was the conclusion reached by the House of Lords, which recommended rescheduling and decriminalization.

Cannabis or Marinol?

Those committed to the prohibition on cannabis frequently cite Marinol, a Schedule III drug, as the legal means to obtain the benefits of cannabis. However, Marinol, which is a synthetic form of THC, does not deliver the same therapeutic benefits as the natural herb, which contains at least another 100 cannabinoids in addition to THC. Recent research conducted by GW Pharmaceuticals in Great Britain has shown that Marinol is simply not as effective for pain management as the whole plant; a balance of cannabinoids, specifically CBC and CBD with THC, is what helps patients most. In fact, Marinol is not labeled for pain, only appetite stimulation and nausea control. But studies have found that many severely nauseated patients experience difficulty in getting and keeping a pill down, a problem avoided by use of inhaled cannabis.

Clinical research on Marinol vs. cannabis has been limited by federal restrictions, but a review of state clinical trials conducted in the 70's and 80's published in 2001 reports that ". . . the data reviewed here suggested that the inhalation of THC appears to be more effective than the oral route... Patients who smoked marijuana experienced 70-100% relief from nausea and vomiting, while those who used THC capsules experienced 76-88% relief."[61] Additionally, patients frequently have difficulty getting the right dose with Marinol, while inhaled cannabis allows for easier titration and avoids the negative side effects many report with Marinol. As the U.K. House of Lords report states, "Some users of both find cannabis itself more effective."

THE EXPERIENCE OF PATIENTS

Dorothy Gibbs

In 1911, at the age of one, I contracted the polio virus. . . The early onset of polio caused permanent damage in my legs, spine, and back, resulting in significant weakness and atrophy in my legs. As a result, I have never been able to walk without the assistance of crutches and braces or a wheelchair. Approximately 30 years ago, my condition began to deteriorate. I began to suffer from increasing levels of pain and weakness in my legs and back as well as severe osteoarthritis in my hands, arms, and joints. Over time, my deteriorating medical condition has been exacerbated by my pain, leaving me increasingly immobilized. . .

By May, 1996, my physician [Dr. Arnold Leff, M.D.] had tried various prescription medications to relieve my pain, including: Tylenol #3, Ultram, Daypro, Tegretol, Soma, Valium, steroid injections into the trigger point, Dilantin, Duragesic, Zofran and Comapazine for the nausea caused by the opioid pain relievers, and Doloboid and Lodine a nonsteroids. Nothing seemed to work, and the pain persisted. I was growing increasingly depressed by the inability of anything to relieve my pain. . .

During this period it was clear to me, my caretaker and my physician that nothing was working to combat my pain. My caretaker, Pat, had heard of the success some people experience with the medicinal use of marijuana for pain management. Sometime during the end of 1997, she obtained a sample for me. Although I had never used marijuana in my previous eighty-seven years of life, I was willing to try anything that could alleviate even part of the pain.

The relief I experienced from medical marijuana was almost immediate. I was so pleased with the result that I wrote to Dr. Leff about my use of medical marijuana and we talked about the benefits of the medicine. Dr. Leff examined me and noted that medical marijuana helped me experience less chronic pain and nausea, leading him to recommended medical marijuana as part of my daily pain care regimen....

Ever since trying medical marijuana, my life has drastically improved. Although chronic pain, related to my post-polio syndrome will always be a part of my life, medical marijuana had helped me manage this pain by providing fast and

effective relief for my muscle spasms, acute pains, and arthritis. . . Since I began using medical marijuana, my pain is no longer persistent or debilitating. When I do suffer from pain, I am usually able to "get ahead of it" by using medical marijuana and make it manageable. . .

Margaret

I am a 45-year-old granny, and I smoke marijuana for medicinal reasons. I was 25 when I was diagnosed with rheumatoid arthritis. The doctor told me it was a painful, crippling disease and I would end up in a wheel chair. He gave me prescriptions for the arthritis and pain and sleeping pills.

Some of the pills had side effects and I would have to change to different ones. My arthritis was getting worse and I was depressed all the time. I started taking anti-depressants. For years I abused codeine, anti-depressants and sleeping pills. I don't smoke tobacco or drink alcohol. My friends smoked marijuana but it didn't interest me to try it.

I smoked my first joint when I was 30. One night I was in a lot of pain and feeling terribly uncomfortable. My friend Ed was with me and said he had heard marijuana helps relieve pain. I was willing to try anything and had a few tokes. After a few minutes I was relaxed and the pain seemed to have dulled. I was also more limber with my joints. I had a very restful sleep that night. I have been smoking marijuana every day since then. I have also been happier and no longer need anti-depressants. I now control my pain with marijuana.

Alfred

I'm a 23-year-old male currently employed as an accounting assistant. This fall I began work on my Master's Degree. I am inflicted with Gout, a hereditary form of arthritis, which I have had for 6 years. When an attack arises the pain is in the main joint of my left foot and on the side of my big toe. When these attacks happen it is virtually impossible for me to walk.

I take Vicodin for the pain. I'm also given steroid shots for the pain in the doctor's office. In addition, I take Allopurinol, this helps my body to get rid of the uric acid build up which leads to the pain of Gout. The reason that I have uric acid build up is because my kidneys do not function properly and rid my body of the uric acid.

The main side effects of Vicodin and Allopurinol are drowsiness, which are very bad if you are a full time college student and also employed. But, I have to have some kind of pain medicine to be able to walk, I have learned that marijuana helps a great deal with the pain, and I have found that I am able to walk and also function much better on marijuana than Vicodin. Allopurinol takes a terrible toll on my stomach. I would say 73% of the time I puke the medication up. I tried using marijuana in combination with the Allopurinol and I've found that this has helped drop the number of times that I throw the medication up. Now, I puke it up around 18% of the time, which is a big deal to me.

Matt Glandorf

I have arthritis in both hands and my chest, but here is the real kicker-- I am severely allergic to aspirin. I can't even take a Motrin without breaking out into a rash. I was born with a chest deformity called pectus excavatum (funnel chest and encaved chest are a couple other names for it.) I had corrective surgery in 1976 to try to make my rib cage bigger. In that surgery they break all the ribs and actually break the sternum in half, remove it, flip it over, and put it back together after removing most of the cartilage and muscle. Now I have arthritis along with lung problems and asthma. I usually spend two to three weeks a year in the hospital with lung infections and make numerous visits to the doctor for chest pain.

Needless to say, I have eaten a lot of pain killers and tried nerve blocks and so on. All have had little success and make me so stoned that I can't even drive a car. So I started using pot and went from four Vicodin a day to one, and with watching my activities and a healthy diet I can go with no doctor's meds for weeks on end.

Bob Burrill

I am a Canadian medical marijuana advocate. Osteoarthritis of the cervical spine is my problem. I have constant severe pain from many large bone spurs, compressed discs, and so on. Many narcotic and other types of pain reduction prescriptions have been tried with limited success. I have self-medicated with marihuana for the past 7 or 8 months, under my doctor's care, with great

success. My doctor and I have applied to the Canadian government to obtain a written ministerial exemption from prosecution so that I can cultivate and consume marijuana for a medical purpose.

Without medical marihuana, I have no life. I am restricted to bed or the couch and stuck inside the house. It's about time governments and the public alike awakened to the fact that this is not "Cheech and Chong medicine" but one of the safest and user-friendly herbs on the planet. I only wish I had tried it a lot sooner. I can't say enough about the merits and benefits of medical marijuana

The Experience of Doctors

Ethan Russo, M.D.

Patients have long told us that cannabis has been helpful to them in the treatment of their arthritic conditions. Science has now demonstrated that the THC component of cannabis is a very effective analgesic (pain killer), and that the CBD (cannabidiol) component has unique immunomodulatory benefits as an antagonist of tumor necrosis factor-alpha, supporting benefits in treatment of rheumatoid arthritis, as well as Crohn's disease and psoriasis. It appears that cannabis-based medicines will likely be an important component of arthritis treatment in the 21st century.

Ethan Russo, MD, is a board-certified child and adult neurologist in Missoula, MT, and researcher in migraine, ethnobotany, medicinal plants, cannabis and cannabinoids in pain management. Dr. Russo currently serves in a consultancy position as Senior Medical Advisor to the Cannabinoid Research Institute, the division of GW Pharmaceuticals established to promote exploratory research. He holds faculty positions as adjunct associate professor in the Department of Pharmaceutical Sciences of the University of Montana, and clinical associate professor in the Department of Medicine of the University of Washington. He has published numerous articles in scientific journals and is co-editor of Cannabis and Cannabinoids: Pharmacology, Toxicology and Therapeutic Potential. Dr. Russo is the founding editor of Journal of Cannabis Therapeutics.

Arnold S. Leff, M.D.

I currently treat at least 20 patients for whom I believe marijuana is medically appropriate in responding to treatment-induced nausea or for appetite stimulation. In my medical judgment, in some cases medical marijuana may be the only effective medicine.

Two of my patients, Hal Margolin and Dorothy Gibbs, have benefited tremendously from [medical cannabis]. Both suffer from chronic pain. Ms. Gibbs, who is 93 years old and who had not previously tried marijuana until joining WAMM, has found marijuana to be a highly effective analgesic for treating acute and chronic pain associated with post-polio syndrome and complications arising there from [including arthritis].

Ms. Gibbs turned to marijuana only after trying a wide range of conventional prescription pharmaceuticals and therapies prescribed by me, but to little or no avail. These treatments, including powerful and highly addictive opioid analgesics, either did not work, gradually lost their efficacy, or caused such debilitating side effects (particularly nausea and dizziness) that Ms. Gibbs found intolerable.

Ms. Gibbs is a good example of a patient who experiences episodic acute pain for which Marinol is too slow-acting and who, when stricken with acute pain, often requires the faster analgesic and antiemetic effects produced by smoked marijuana. I have been pleasantly surprised at the degree to which marijuana has afforded Ms. Gibbs relief from the agony that she suffered.

Dr. Leff has been an advisor on national drug control policy and public health to the administrations of Presidents Nixon, Ford and Carter. He has worked with the Department of Defense and State Department developing drug abuse programs in foreign countries and for U.S. military troops, and has consulted with local law enforcement officials on drug treatment. He served as Director of Health Services for Contra Costa County, California and has held teaching positions on the medical school faculties of the University of Cincinnati and the University of California.

Harvey L. Rose, M.D.

Both my research and my many years as a clinician have convinced me that marijuana can serve at least two important roles in safe and effective pain management. Ample anecdotal evidence and clinical observations, as well as significant research findings, strongly indicate that marijuana, for whatever reason, is often effective in relieving pain. This is true across a range of patient populations, including the elderly, the terminally ill seeking comfort in their final days, young adults stricken with life-threatening conditions, and cancer patients unable to tolerate the devastating effects of potentially life-saving therapies. Marijuana is also widely recognized as an antiemetic that reduces the nausea and vomiting often induced by powerful opioid analgesics prescribed for chronic, severe pain, as well as the nausea, vomiting and dizziness which often accompany severe and/or prolonged pain. I have had the benefit of consultations on this subject over many years with a range of treatment providers, including physicians, oncologists, pharmacologists, family practitioners, hospice workers, and pain specialists. . .

Specifically, I have found that cannabis can have an important opioid-sparing effect for pain patients. That is to say, that patients who are prescribed high doses of opioid analgesics can significantly reduce their reliance on these medications and improve their daily functioning by incorporating cannabis into their pain care regimen.

Marijuana not only has important analgesic properties but it also is an effective and important adjuvant therapy for patients suffering acute and/or chronic pain. No experienced and respected physician will deny that for such patients opioid therapy is central to palliative care. By the same token, the same experienced physicians will readily acknowledge that opioids often induce nausea and vomiting. For a number of pain patients, standard prescription antiemetics (e.g., Compazine, Zofran and Reglan) simply do not substantially reduce their nausea. For many, those medications are substantially less effective, or produce more debilitating side effects, than marijuana. . .

Quite simply, marijuana can serve much the same function for pain patients undergoing opiate therapy that it does for cancer patients undergoing chemotherapy: it suppresses the nausea and vomiting associated with

treatment, and reduces the pain associated with prolonged nausea and retching, thereby increasing the chances that the patient will remain compliant with the primary treatment. With both chemotherapy and long-term pain management, failure to obtain and continue proper palliative and adjutant care can have dire, even fatal, consequences. . .

Finally, it is important to note that in my clinical experience observing patients who ingest cannabis for relief from pain and nausea and/or to stimulate appetite, I have witnessed no adverse complications. By contrast, many of the first-line pharmaceuticals used to combat cancer, HIV/AIDS, and pain associated with these and other illnesses can induce a variety of iatrogenic effects, including, in some instances, death. While patients may face serious legal implications related to their use of medical marijuana, as a physician I have yet to encounter a medical downside to their cannabinoid therapy. . .

[A]gainst the backdrop of a growing body of scientific research, the reports of myriad pain patients, and the burgeoning clinical experience of physicians like myself, it is my considered opinion that cannabis can constitute an acceptable and sometimes necessary medicine to alleviate the immediate suffering of certain patients. Dr. Rose served as a medical officer in the Air Force before entering private practice. During his 40-year career, he has taught at UC Davis School of Medicine and consulted with state legislative bodies.

Dr. Rose served as a medical officer in the Air Force before entering private practice. During his 40-year career, he has taught at UC Davis School of Medicine and consulted with state legislative bodies.

THE HISTORY OF CANNABIS AS MEDICINE

While the federal government has resisted restoring cannabis to its place in the US Pharmacopeia, its own research studies acknowledge that the "use of cannabis for purposes of healing predates recorded history" and that it was included in "the 15th century BC Chinese Pharmacopeia, the Rh-Ya."[62] Ancient Egypt, India and Persia all made medical use of it more than 2,000 years ago. British herbalists in the 17th century noted its medicinal properties, but it did not become widely used in British medicine until the mid-nineteenth century. In

1890, Queen Victoria's personal physician, Sir Russell Reynolds, wrote in the first issue of The Lancet, "When pure and administered carefully, [it is] one of the most valuable medicines we possess."[63]

William O'Shaughnessy, a British East Indian Company surgeon who studied its use while posted in India, expanded western understanding of its range of applications and championed its use upon his return to Britain in 1841 and election to the Royal Society, the scientific advisory body to the British government. Between 1840 and 1900, European and American medical journals published more than 100 articles on the therapeutic applications of cannabis, known then as Cannabis Indica or Indian hemp. Common indications for its use in the nineteenth century included "muscle spasms, menstrual cramps, rheumatism, and the convulsions of tetanus, rabies and epilepsy; it was also used to promote uterine contractions in childbirth, and as a sedative to induce sleep."[64]

The American Medical Association in an article on the first federal law restricting legal access to cannabis noted that "No evidence has been produced to show the existence of addiction to cannabis arising out of the medicinal use of the drug."83 The AMA's lobbyist, Dr. William C. Woodward, testified to Congress that "The American Medical Association knows of no evidence that marihuana is a dangerous drug," and that any prohibition "loses sight of the fact that future investigation may show that there are substantial medical uses for Cannabis."

The first state medical cannabis law was passed in 1996 by California voter initiative. Since then, 23 states, the District of Columbia, and the US Territory of Guam have removed criminal penalties for their citizens who use cannabis on the advice of a physician and established legal means of obtaining it. Ten of those states plus the District of Columbia established their medical cannabis laws through voter ballot initiative, while the legislatures in 13 others have enacted similar bills. Limited bills that allow only the use of specific cannabis extracts for highly restricted conditions have been passed by the legislatures in 15 other states. Currently, nearly 50 percent of the U.S. population resides in a state with a medical cannabis program, and legislation is introduced in more states each year.

Federal Policy is Contradictory

Federal policy on medical cannabis is filled with contradictions. Cannabis was widely prescribed until the turn of the century, and an estimated one million Americans currently use it under medical supervision. Congress in 1970 classified cannabis is a Schedule I drug, defined as having no medicinal value and a high potential for abuse, yet its most psychoactive component, THC, is legally available as Marinol and is classified as Schedule III. The U.S. federal government also grows and provides free cannabis for a small number of patients today as part of an Investigational New Drug (IND) compassionate access research program created by court order in 1976. Though the program provided up to nine pounds of cannabis a year to these patients, and all reported being substantially helped by it, the application process was extremely complicated, and few physicians became involved. In the first twelve years, the government accepted only a handful of patients. But in 1989 the FDA was deluged with new applications from people living with AIDS, and 34 patients were approved within a year. In June 1991, the Public Health Service announced that the program would be suspended because it undercut the administration's opposition to the use of illegal drugs. The program was discontinued in March 1992 and the remaining patients had to sue the federal government on the basis of medical necessity to retain access to their medicine. Today, four surviving patients still receive medical cannabis from the federal government.

Despite this successful federal program, thousands of scientific articles, and dozens of successful clinical trials, as well as an unparalleled safety record, cannabis remains classified as a Schedule I substance. Healthcare advocates have tried to resolve this contradiction through legal and administrative channels. In 1972, a petition was submitted to reschedule cannabis in order to remove barriers to medical research and patient access. The DEA stalled hearings for 16 years, but after exhaustive hearings in 1988 their chief administrative law judge, Francis L. Young, ruled that "marijuana, in its natural form, is one of the safest therapeutically active substances known... It would be unreasonable, arbitrary and capricious for the DEA to continue to stand between those sufferers and the benefits of this substance." The DEA refused to implement this ruling based on a procedural technicality and continues to insist cannabis is a substance with no medical use. In 2009 the American Medical

Association, the nation's largest organization for physicians with a quarter million members, joined the chorus of professional medical groups calling on the federal government to reconsider the classification of cannabis and urging comprehensive clinical trials.

Widespread support, state laws passed, new policy issued

Public opinion is strongly in favor of ending the prohibition of medical cannabis and has been for some time, with every national poll conducted over the past two decades showing a substantial majority in support. A CBS News national poll in January 2014 found that 86 percent of Americans think doctors should be allowed to prescribe cannabis for patients suffering from serious illnesses. In 2004, the 35 million-member American Association of Retired Persons (AARP) released a national poll of older Americans showing 72 percent of seniors agreed that "adults should be allowed to legally use marijuana for medical purposes if a physician recommends it." Every national poll for more than a decade has found similar super-majorities of support.

The refusal of the federal government to act on this widespread public support has meant that advocates have had to turn to the states for action. Currently, laws that effectively remove state-level criminal penalties for growing and/or possessing medical cannabis are in place in: Alaska, Arizona, California, Colorado, Connecticut, Delaware, Hawaii, Illinois, Maine, Maryland, Massachusetts, Michigan, Minnesota, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, Oregon, Rhode Island, Vermont, Washington, the District of Columbia, and Guam. Another 15 states have established limited laws that allow the legal medical use of a cannabis plant extract. Thirty-six states have symbolic medical cannabis laws (laws that support access to medical cannabis but do not provide patients with legal protection under state law).

On August 29, 2013, the U.S. Department of Justice issued new guidance to federal prosecutors, telling them medical cannabis dispensaries should no longer automatically be considered targets for prosecution. The memo from Deputy Attorney General James M. Cole to all U.S. Attorneys reverses previous federal policy on prosecuting medical cannabis providers and businesses. The new guidance says state and local officials can avoid federal interference in

their medical cannabis programs if they "implement strong and effective regulatory and enforcement systems" that reflect eight federal enforcement priorities. The memo does not change federal law, nor does it preclude prosecution of any individual or business, as the U.S. Attorneys' offices are autonomous, and federal prosecutors make independent decisions about which cases to pursue.

REFERENCES

Legal Citations

1. See "The Administration's Response to the Passage of California Proposition 215 and Arizona Proposition 200" (Dec. 30, 1996). https://www.ncjrs.gov/txtfiles/215rel.txt
2. See Conant v. McCaffrey, 172 F.R.D. 681 (N.D. Cal. 1997).
3. See id.; Conant v. McCaffrey, 2000 WL 1281174 (N.D. Cal. 2000); Conant v. Walters, 309 F.3d 629 (9th Cir. 2002).
4. 309 F.3d 629 (9th Cir. 2002).
5. Id. at 634-36.
6. Criminal liability for aiding and abetting requires proof that the defendant "in some sort associate[d] himself with the venture, that he participate[d] in it as something that he wishe[d] to bring about, that he [sought] by his action to make it succeed."Conant v. McCaffrey, 172 F.R.D. 681, 700 (N.D. Cal. 1997) (quotation omitted). A conspiracy to obtain cannabis requires an agreement between two or more persons to do this, with both persons knowing this illegal objective and intending to help accomplish it. Id. at 700-01.
7. 309 F.3d at 634 & 636.
8. Conant v. McCaffrey, 2000 WL 1281174, at *16 (N.D. Cal. 2000).
9. 309 F.3d at 634.
10. See id.. at 635; Conant v. McCaffrey, 172 F.R.D. 681, 700-01 (N.D. Cal. 1997).
11. Gonzales v. Raich, 545 U.S. 1 (2005) 352 F.3d 1222.
12. Third Time the Charm? State Laws on Medical Cannabis Distribution and Department of Justice Guidance on Enforcement. Americans for Safe Access. November 25, 2013. http://americansforsafeacess.org/dojwhitepaper.

Research Citations

13. Adler JN, Colbert JA. Medicinal Use of Marijuana — Polling Results. N Engl J Med 2013; 368:e30. May 30, 2013. DOI: 10.1056/NEJMclde1305159
14. Hanus LO. Pharmacological and therapeutic secrets of plant and brain (endo)cannabinoids. Med Res Rev. 2009 Mar;29(2):213-71. doi: 10.1002/med.20135.
15. Grant I, Rael Cahn B. Cannabis and endocannabinoid modulators: Therapeutic promises and challenges, Clinical Neuroscience Research, Volume 5, Issues 2-4, November 2005, Pages 185-199.
16. Alexandros Makriyannis, Raphael Mechoulam and Daniele Piomelli, Therapeutic opportunities through modulation of the endocannabinoid system, Neuropharmacology, Volume 48, Issue 8, June 2005, Pages 1068-1071.
17. Cecilia J. Hillard and Abbas Jarrahian, Accumulation of anandamide: Evidence for cellular diversity, Neuropharmacology, Volume 48, Issue 8, June 2005, Pages 1072-1078.
18. Pacher, P., & Kunos, G. (2013). Modulating the endocannabinoid system in human health and disease–successes and failures. FEBS Journal.
19. Aggrawal S et al. 2009. Medicinal use of cannabis in the United States: historical perspectives, current trends, and future directions. J Opioid Manag. May-Jun;5(3):153-68.
20. Grant I, Atkinson JH, Gouaux B, Wilsey B. (2012). Medical Marijuana: Clearing Away the Smoke. The Open Neurology Journal. 2012 May 4, 6:18-25. DOI: 10.2174/1874205X01206010018.
21. Abrams DI et al (2003). Short-Term Effects of Cannabinoids in Patients with HIV-1 Infection: A Randomized, Placebo-Controlled Clinical Trial. Ann Intern Med. Aug 19;139(4):258-66.5.
22 Russo EB, Mathre ML, et al. (2002). Chronic Cannabis Use in the Compassionate Investigational New Drug Program: An Examination of Benefits and Adverse Effects of Legal Clinical Cannabis. Journal of Cannabis Therapeutics 2(1).
23. Russo EB. (2008) Cannabinoids in the management of difficult to treat pain. Therap and Clincial Risk Manag 4(1) 245-259.
24. Barnes MP (2006). Sativex: clinical efficacy and tolerability in the treatment of symptoms of multiple sclerosis and neuropathic pain. Expert Opin Pharmacother, 7:607-15.

25. Perez J (2006) Combined cannabinoid therapy via an oral mucosal spray. Drugs Today (Barc.), 42:495-501.
26. Selvarajah D et al (2010). Randomized placebo-controlled double-blind clinical trial of cannabis-based medicinal product (Sativex) in painful diabetic neuropathy. Diabetes Care. 33(1):128-30.
27. Bab I and Zimmer A (2008). Cannabinoid receptors and the regulation of bone mass. Br J Pharmacol 153(2):182-188.
28. Buckley NE, et al (2000) .Immunomodulation by cannabinoids is absent in mice deficient for the cannabinoid CB(2) receptor. Eur J Pharmacol 396(2-3):141-149.
29. Idris AI, et al (2009). Cannabinoid receptor type 1 protects against age-related osteoporosis by regulating osteoblast and adipocyte differentiation in marrow stromal cells. Cell Metab 10(2):139-147.
30. Ofek O, et al (2006). Peripheral cannabinoid receptor, CB2, regulates bone mass. Proc Natl Acad Sci U S A 103(3):696-701.
31. Tam J, et al (2006). Involvement of neuronal cannabinoid receptor CB1 in regulation of bone mass and bone remodeling. Mol Pharmacol 70(3):786-792.
32. Tam J, et al (2008). The cannabinoid CB1 receptor regulates bone formation by modulating adrenergic signaling. Faseb J 22(1):285-294.
33. Huang QY, et al (2009). Multiple osteoporosis susceptibility genes on chromosome 1p36 in Chinese. Bone 44(5):984-988.
34. Karsak M, et al (2005). Cannabinoid receptor type 2 gene is associated with human osteoporosis. Hum Mol Genet 14(22):3389-3396.
35. Karsak M, et al (2009). The cannabinoid receptor type 2 (CNR2) gene is associated with hand bone strength phenotypes in an ethnically homogeneous family sample. Hum Genet.
36. Russo EB (2002). Role of cannabis and cannabinoids in pain management. In: Weiner RS, editor. Pain management: A practical guide for clinicians. 6th ed. Boca Raton, FL: CRC Press. p. 357-375.
37. Marcandier M (1764). Treatise on hemp. London: T. Becket and P.A. de Hondt.
38. Formukong E et al (1988). Analgesic and Antiinflammatory Activity of Constituents of Cannabis Sativa L. Inflammation 12: 361.
39. Barret ML et al (1985). Isolation from Cannabis sativa L. of Cannflavon - a novel inhibitor of prostaglandin production. Biochem. Pharmacol. 34: 2019

40. Burstein SH et al (1989). Antagonism to the actions of platelet activating factor by a nonpsychoactive cannabinoid. J Pharmacol. Exp. Therap. 251: 531-5
41. Sofia RD (1989). Antiedemic and analgesic properties of delta-9-THC compared with three other drugs. Eur. J. Pharamacol. 41: 705-9
42. Zurier RB et al (1998). Dimethylheptyl-THC-11 Oic Acid: A Nonpsychoactive Antiinflammatory Agent with a Cannabinoid Template Structure. ARTHRITIS AND RHEUMATISM January; volume 41, number 1, pages 163-170.
43. Costa B et al (2004). Oral anti-inflammatory activity of cannabidiol, a non-psychoactive constituent of cannabis, in acute carrageenan-induced inflammation in the rat paw. Naunyn Schmiedebergs Arch Pharmacol. Mar;369 (3):294-9. Epub 2004 Feb 12.
44. Malfait AM et al (2000) .The nonpsychoactive cannabis constituent cannabidiol is an oral anti-arthritic therapeutic in murine collagen-induced arthritis. Proc Natl Acad Sci U S A. Aug 15 97(17):9561-6.
45. James JS (1998). Marijuana, inflammation, and CT-3 (DMH-11C): cannabis leads to new class of antiinflammatory drugs. AIDS Treat News. Jan 23;(No 287):1, 5.
46. Straus SE (2000). Immunoactive cannabinoids: Therapeutic prospects for marijuana constituents. Proc Natl Acad Sci U S A. Aug 15 97(17):9563.
47. Shohami E (2001). Nature. Oct 4;413(6855):527-31.
48. Burstein SH (2000). Ajulemic acid (CT3): a potent analog of the acid metabolites of THC. Curr Pharm Des. Sep 6(13):1339-45.
49. Burstein SH et al (2004). Ajulemic acid: A novel cannabinoid produces analgesia without a "high". Life Sci. Aug 6;75(12):1513-22.
50. Devane WAet al1(1992). Isolation and structure of a brain constituent that binds to the cannabinoid receptor. Science.258:1946-1949.
51. Barg J et al (1995). Cannabinomimetic behavioral effects of andadenylate cyclase inhibition by two new endogenous anandamides. Eur J Pharmacol.;287:145-152.
52. Klein TW et al (1998). Cannabinoid receptors and immunity. Immunol Today. 797:225-233.
53. Daaka Y et al (1996). Cannabinoid receptor proteins are increased in jurkat, human T-cell line after mitogen activation. J Pharmacol Exp Ther. 276:776-783.
54. Kaminski NE (1996); Immune regulation by cannabinoid compounds through the inhibition of the cyclic AMP signaling cascade and altered gene

expression. Biochem Pharmacol; 52(8):1133-40.
55. Di Marzo V (1998). 'Endocannabinoids' and other fatty acid derivatives with cannabimimetic properties: biochemistry and possible physiopathological relevance. Biochimica et Biophysica Acta.1392(2-3):153-75.
56. Smith PB et al (1994). The pharmacological activity of anandamide, a putative endogenous cannabinoid in mice. J Pharmacol Exp Ther. 270:219-227.
57. Burstein SH (2000). Ajulemic acid (CT3): a potent analog of the acid metabolites of THC. Curr Pharm Des. Sep;6(13):1339-45.
58. Zurier RB et al (2003). Suppression of human monocyte interleukin-1beta production by ajulemic acid, a nonpsychoactive cannabinoid. Biochem Pharmacol. Feb 15;65(4):649-55.
59. Hazekamp A et al (2006). Evaluation of a vaporizing device (Volcano(R)) for the pulmonary administration of tetrahydrocannabinol. J Pharm Sci 95 (6) Apr 24: 1308-1317.
60. Sidney S et al (1997). Marijuana Use and Cancer Incidence. Cancer Causes and Control; 8: 722-728.
61. Tashkin D (2006). Marijuana Use and Lung Cancer: Results of a Case-Control Study. American Thoracic Society International Conference. May 23, 2006.
62. Musty R, Rossi R (2001). Effects of smoked cannabis and oral delta-9-tetrahydrocannabinol on nausea and emesis after cancer chemotherapy: a review of state clinical trials. Journal of Cannabis Therapeutics. 1: 29-56.
63. Lancet 1; 1823.
64. United States Assumes Control of Cannabis. JAMA. 1937;109(13):31B-38B. doi:10.1001/jama.1937.02780390177058.

In This Section

Purchase Arthritis and Medical Cannabis On Kindle (/purchase_arthritis_and_medical_cannabis_on_kindle)

(/purchase_arthritis_and_medical_cannabis_on_kindle)

Oxford Journals Medicine & Health Rheumatology Volume 45, Issue 1 Pp. 50-52.

Rheumatology
rheumatology.oxfordjournals.org

Rheumatology (January 2006) 45 (1): 50-52. doi: 10.1093/rheumatology/kei183
First published online: November 9, 2005

Preliminary assessment of the efficacy, tolerability and safety of a cannabis-based medicine (Sativex) in the treatment of pain caused by rheumatoid arthritis

D. R. Blake, P. Robson [1], M. Ho [2], R. W. Jubb [3] and C. S. McCabe
+ Author Affiliations

Correspondence to: D. R. Blake, Royal National Hospital for Rheumatic Diseases, Upper Borough Walls, Bath BA1 1RL, UK. E-mail: David.Blake@rnhrd-tr.swest.nhs.uk

Received July 6, 2005.; Revision received October 5, 2005.

Abstract

Objectives. To assess the efficacy of a cannabis-based medicine (CBM) in the treatment of pain due to rheumatoid arthritis (RA).

Methods. We compared a CBM (Sativex) with placebo in a randomized, double-blind, parallel group study in 58 patients over 5 weeks of treatment. The CBM was administered by oromucosal spray in the evening and assessments were made the following morning. Efficacy outcomes assessed were pain on movement, pain at rest, morning stiffness and sleep quality measured by a numerical rating scale, the Short-Form McGill Pain Questionnaire (SF-MPQ) and the DAS28 measure of disease activity.

Results. Seventy-five patients were screened and 58 met the eligibility criteria. Thirty-one were randomized to the CBM and 27 to placebo. Mean (S.D.) daily dose achieved in the final treatment week was 5.4 (0.84) actuations for the CBM and 5.3 (1.18) for placebo. In comparison with placebo, the CBM produced statistically significant improvements in pain on movement, pain at rest, quality of sleep, DAS28 and the SF-MPQ pain at present component. There was no effect on morning stiffness but baseline scores were low. The large majority of adverse effects were mild or moderate, and there were no adverse effect-related withdrawals or serious adverse effects in the active treatment group.

Conclusions. In the first ever controlled trial of a CBM in RA, a significant analgesic effect was observed and disease activity was significantly suppressed following Sativex treatment. Whilst the differences are small and variable across the population, they represent benefits of clinical relevance and show the need for more detailed investigation in this indication.

Key words Cannabis-based medicine Sativex Pain Rheumatoid arthritis Disease activity

Evidence from basic science and human trials suggests that cannabis-based medicines (CBM) may have therapeutic potential in a range of medical conditions, particularly in the treatment of intractable pain [1, 2]. Cannabis has been used historically in the treatment of pain due to rheumatoid arthritis (RA), but this has never been formally evaluated in a clinical trial. Δ-9-Tetrahydrocannabinol (THC) and cannabidiol (CBD) are recognized as key therapeutic constituents that act synergistically together and with other plant constituents [3]. THC has analgesic activity in both nociceptive and neuropathic pain [1, 2]. Both THC and CBD have anti-

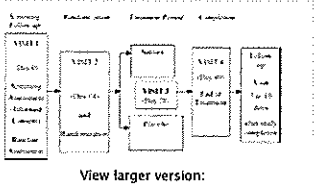
inflammatory effects [4], and CBD was found to block progression of disease and produce clinical improvement in a murine model of RA [5]. In a recent survey [6] of 2969 people who agreed to fill in a questionnaire about medicinal cannabis, 947 (32%) stated that they had obtained the drug from the black market for symptom relief. Of these, 155 (16%) gave symptom relief for arthritis (type not specified) as the reason for smoking cannabis. This was the fifth-commonest indication after multiple sclerosis, neuropathy, chronic pain and depression.

We present the results of the first controlled trial of a CBM in the symptomatic treatment of RA in humans.

Patients and methods

This was a preliminary multicentre, double-blind, randomized, parallel-group comparison of a CBM (Sativex) and placebo administered for 5 weeks in the treatment of pain caused by RA. Sativex consists of a blend of whole plant extracts which delivers approximately equal amounts of THC and CBD. This ratio was selected to reflect the proportions found in cannabis used historically for medicinal purposes, and to maximize the potential for synergism [7]. Minor cannabinoids, including cannabinol, cannabichromene and cannabigerol, are also present in trace quantities. All three of these have been found to have anti-inflammatory properties in laboratory studies, as have other plant components, such as terpenoids and flavonoids [3]. Sativex was administered by oromucosal spray, each activation delivering 2.7 mg THC and 2.5 mg CBD. Eligible patients had a diagnosis of RA meeting ACR criteria, with active arthritis not adequately controlled by standard medication. NSAID and prednisolone regimes had to have been stabilized for 1 month and DMARDs for 3 months prior to enrolment, and were maintained constant throughout the study. Exclusion criteria included a history of psychiatric disorders or substance misuse, severe cardiovascular, renal or hepatic disorder, or a history of epilepsy. Dosing was restricted to the evening to minimize possible intoxication-type reactions, with randomized treatment allocation using permuted blocks of four. Starting dose was one actuation within 0.5 h of retiring, and this was increased by one actuation every 2 days to a maximum of six actuations according to individual response. Stable dosing was then maintained for a further 3 weeks. Patients gave written informed consent to participate, and the study was approved by each local research ethics committee.

Primary efficacy variable was pain on movement measured by a 0–10 numerical rating scale (NRS) each morning. Baseline score (obtained as an average of the last 4 days of the 14-day baseline period) was compared with the average of the last 14 days of treatment. Secondary outcomes included NRS measures of pain at rest, sleep quality and morning stiffness, the Short-Form McGill Pain Questionnaire (SF-MPQ) and the 28-joint disease activity score (DAS28). The study plan is shown in Fig. 1. Based on previous results for pain on movement, it was calculated that 23 patients/group would be required to detect 2 units difference with 90% power. A minimum of 54 patients were to be recruited to allow for dropouts. Normally distributed data were to be analysed using one-way analysis of covariance. Change from baseline to endpoint was to be compared between the two treatment groups with the baseline score considered as a covariate. Non-parametric analysis was to be used if there was considerable departure from normality.



View larger version:

FIG. 1.
Plan of the study.

In this page In a new window
Download as PowerPoint Slide

Results

The protocol and all study documentation was approved by the Independent Research Ethics Committee representing each of the eight participating centres. Seventy-five patients were screened and 58 met the eligibility criteria. Written informed consent, as specified by the Declaration of Helsinki (2000), was obtained from all patients prior to screening. Thirty-one of the eligible patients were randomized to CBM and 27 to placebo. One patient withdrew from the active treatment group (unrelated surgery) and three from placebo (adverse events). There were no significant differences in demographics between groups (Table 1). Mean (S.D.) daily dose achieved in the final treatment week was 5.4 (0.84) actuations for CBM and 5.3 (1.18) for placebo.

View this table:
In this window In a new window

TABLE 1.
Summary of demography and patient baseline characteristics (intention-to-treat population)

Efficacy endpoints are shown in Table 2. Statistically significant improvements in pain on movement, pain at rest, quality of sleep, DAS28 and the SF-MPQ pain at present component were seen following CBM in comparison with placebo.

View this table:
In this window In a new window

TABLE 2.
Efficacy endpoints: difference between change from baseline between CBM and placebo after 5 weeks of treatment

Adverse effects (AE) occurring in two or more patients are shown in Table 3. AE in CBM group were all of mild or moderate intensity except for two (6%) rated severe (constipation; 'malaise') compared with six (22%) in the placebo group. Eight patients (26%) receiving CBM experienced transient dizziness at some point, though in all cases this was rated as mild. The exact timing of these episodes was recorded in six of these patients: four occurred during the initial 2-week titration period, the other two at 16 days. There were no withdrawals due to AE in the CBM group compared with three (11%) for placebo, and no serious AE following the active treatment compared with two (7%) in the placebo group.

View this table:
In this window In a new window

TABLE 3.
Adverse events recorded as 'possibly', 'probably' or 'definitely' related to study drug occurring in more than one patient

Discussion

Cannabis was first proposed as a useful analgesic for a spectrum of rheumatic diseases in 2800 BC. By 1997 the British Medical Association had concluded that herbal cannabis was unsuitable for medical use. Whilst there is extensive data—though often anecdotal—supporting an analgesic effect of cannabis, many trials have produced equivocal results. There are hundreds of different compounds in herbal cannabis, more than 60 of which are unique to the plant (cannabinoids), and many of these may interact, with additional synergistic or antagonistic effects [3]. There are at

least two and probably three cannabinoid receptors. These are found in high concentration in areas of nociceptive transmission within the CNS and on nociceptive peripheral nerves. CB1 receptors are potentially important targets for pharmacological modification. CB2 receptors are located primarily within the immune system.

We have assessed the analgesic and anti-inflammatory activity of a standardized whole-plant CBM with defined ratios and dosages of THC and CBD in a cohort of rheumatoid patients, with disease of extended duration and with poor analgesic control. A significant analgesic effect was observed and disease activity was significantly suppressed. Whilst the differences are small and variable across the population, they represent benefits of clinical relevance and indicate the need for more detailed study of dosage, formulation and ideal patient subgroup. The suppression of pain on movement, the primary endpoint, suggests a peripheral analgesic action. The suppression of pain at rest may suggest a more central effect. The modest suppression of the present gold standard inflammation activity measure, the DAS28, might indicate an influence on the immune effector system. This is consistent with the observation that cannabidiol suppressed a murine model of chronic arthritis, suppressing lymphocyte proliferation, the granulocytic cell reactive oxygen burst and lipopolysaccharide induced cytokine (TNF) production [5]. The improvement in sleep, a relevant clinical bonus, was probably due mainly to nocturnal symptom relief rather than a specific hypnotic effect since this was not observed in a sleep laboratory study of the compound at this dosage [8]. There was no effect on morning stiffness, but baseline scores were surprisingly low. The trial did not demonstrate significant toxicity and CBM was generally well tolerated.

We believe this to be the first controlled study of a CBM in rheumatoid arthritis, and the results are encouraging. The beneficial effects occurred in the context of a dosing regime restricted to evening dosing in order to minimize any possible intoxication-type reactions. However, 24-h dosing with this CBM (Sativex) using a self-titration regime in the context of multiple sclerosis resulted in only minimal intoxication scores [9]. Larger, more prolonged studies of CBM in rheumatoid arthritis are indicated.

Acknowledgments

The study was funded by GW Pharmaceuticals. We are grateful to Dr A. B. Hassell, Dr D. Tull, Dr M. J. B. Duckworth, Dr E. Montague and Dr T. M. Johnson for their collaboration in the study, to Mr Peter Clark for statistical advice and analysis, and to the clinical research team at the Cannabinoid Research Institute for their invaluable practical support.

The protocol was developed with a company that sent a donation to the Royal National Hospital for Rheumatic Diseases charity. P.J.R. is Medical Director of GW Pharmaceuticals. D.R.B. and C.S.M received honoraria from GW Pharmaceuticals for their work on the study design and protocol development.

References

1. Pertwee RG. Cannabinoid receptors and pain. Prog Neurobiol 2001;63:569-611. CrossRef Medline Web of Science

2. Robson P. Human studies of cannabinoids and medicinal cannabis. In: Pertwee RG, ed. Handbook of experimental pharmacology. Vol. 168. Cannabinoids. Berlin: Springer-Verlag, 2005:719-56.

3. McPartland J, Russo E. Cannabis and cannabis extracts: greater than the sum of their parts? J Cannabis Ther 2001;1:103–32.

4. Formukong EA, Evans AT, Evans FJ. Analgesic and anti-inflammatory activity of constituents of Cannabis sativa L. Inflammation 1998;12:361–71.

5. Malfait AM, Gallily R, Sumariwalla PF *et al.* The non-psychoactive cannabis-constituent cannabidiol is an oral anti-arthritic therapeutic in murine collagen-induced arthritis. Proc Natl Acad Sci USA 2000;97:9561–6.
Abstract/FREE Full Text

6. Ware MA, Adams H, Guy GW. The medicinal use of cannabis in the UK: results of a nationwide survey. Int J Clin Pract 2005;3:291–5.

7. Whittle BA, Guy GW. Development of cannabis-based medicines: risks, benefit and serendipity. In: Guy GW, Whittle BA, Robson PJ, eds. The medicinal uses of cannabis and cannabinoids. London: Pharmaceutica Press, 2004:427–66.

8. Nicholson AN, Turner C, Stone BM, Robson PJ. Effect of delta-9-THC and cannabidiol on nocturnal sleep and early morning behaviour in young adults. J Clin Psychopharmacol 2004;24:305–13.
CrossRef Medline

9. Wade DT, Makela P, Robson P, House H, Bateman C. Do cannabis-based medicinal extracts have general or specific effects on symptoms in multiple sclerosis? A double-blind, randomized, placebo-controlled study on 160 patients. Mult Scler 2004;10:434–41.
Abstract/FREE Full Text

10. Melzack R. The short-form McGill Pain Questionnaire. Pain 1987;30:191–7.
CrossRef Medline Web of Science

Articles citing this article

Expanding Medical Marijuana Access in Canada: Considerations for the Rheumatologist
The Journal of Rheumatology (2015) 42 (2): 143-145
Full Text (HTML) Full Text (PDF)

Efficacy and Safety of Neuromodulators in Inflammatory Arthritis: A Cochrane Systematic Review
The Journal of Rheumatology Supplement (2012) 90 (0): 28-33
Abstract Full Text (HTML) Full Text (PDF)

Evidence for the efficacy of complementary and alternative medicines in the management of rheumatoid arthritis: a systematic review
Rheumatology (Oxford) (2011) 50 (9): 1672-1683
Abstract Full Text (HTML) Full Text (PDF)

Identification of the Synthetic Cannabinoid R(+)WIN55,212-2 as a Novel Regulator of IFN Regulatory Factor 3 Activation and IFN-{beta} Expression: RELEVANCE TO THERAPEUTIC EFFECTS IN MODELS OF MULTIPLE SCLEROSIS
J Biol Chem (2011) 286 (12): 10316-10328
Abstract Full Text (HTML) Full Text (PDF)

Plasma Cannabinoid Pharmacokinetics following Controlled Oral {Delta}9-Tetrahydrocannabinol and Oromucosal Cannabis Extract Administration
Clin. Chem. (2011) 57 (1): 66-75
Abstract Full Text (HTML) Full Text (PDF)

Systematic Review and Meta-analysis of Cannabis Treatment for Chronic Pain
Pain Medicine (2009) 10 (8): 1353-1368
Abstract Full Text (HTML) Full Text (PDF)

Adverse effects of medical cannabinoids: a systematic review
CMAJ (2008) 178 (13): 1669-1678
Abstract Full Text (HTML) Full Text (PDF)

Inhibition of Human Neutrophil Chemotaxis by Endogenous Cannabinoids and Phytocannabinoids: Evidence for a Site Distinct from CB1 and CB2
Mol. Pharmacol. (2008) 73 (2): 441-450
Abstract Full Text (HTML) Full Text (PDF)

Cannabidiol, a nonpsychoactive Cannabis constituent, protects against myocardial ischemic reperfusion injury
Am. J. Physiol. Heart Circ. Physiol. (2007) 293 (6): H3602-H3607
Abstract Full Text (HTML) Full Text (PDF)