

GASTRO- INTESTINAL DISORDERS

AND

MEDICAL CANNABIS



AmericansFor
SafeAccess

Advancing Legal Medical Marijuana Therapeutics and Research

A Note from Americans for Safe Access

We are committed to ensuring safe, legal availability of marijuana for medical uses. This brochure is intended to help doctors, patients and policymakers better understand how marijuana—or "cannabis" as it is more properly called—may be used as a treatment for people with serious medical conditions. This booklet contains information about using cannabis as medicine. In it you'll find information on:

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We recognize that information about using cannabis as medicine has been difficult to obtain. The federal prohibition on cannabis has meant that modern clinical research has been limited, to the detriment of medical science and the wellness of patients. But the documented history of the safe, medical use of cannabis dates to 2700 B.C. Cannabis was part of the American pharmacopoeia until 1942 and is currently available by prescription in the Netherlands and Canada.

Testimonials from both doctors and patients reveal valuable information on the use of cannabis therapies, and supporting statements from professional health organizations and leading medical journals support its legitimacy as a medicine. In the last few years, clinical trials in Great Britain, Canada, Spain, Israel, and elsewhere have shown great promise for new medical applications.

This brochure is intended to be a starting point for the consideration of applying cannabis therapies to specific conditions; it is not intended to replace the training and expertise of physicians with regard to medicine, or attorneys with regard to the law. But as patients, doctors and advocates who have been working intimately with these issues for many years, Americans for Safe Access has seen firsthand how helpful cannabis can be for a wide variety of indications. We know doctors want the freedom to practice medicine and patients the freedom to make decisions about their healthcare.

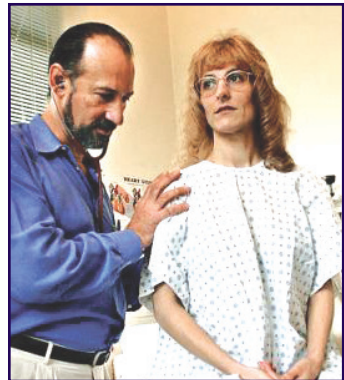
For more information about ASA and the work we do, please see our website at **AmericansForSafeAccess.org** or call **1-888-929-4367**.

Is Cannabis Legal to Recommend?

In 2004, the United States Supreme Court upheld earlier federal court decisions that doctors have a fundamental Constitutional right to recommend cannabis to their patients.

The history. Within weeks of California voters legalizing medical cannabis in 1996, federal officials had threatened to revoke the prescribing privileges of any physicians who recommended cannabis to their patients for medical use.¹ In response, a group of doctors and patients led by AIDS specialist Dr. Marcus Conant filed suit against the government, contending that such a policy violates the First Amendment.² The federal courts agreed at first the district level,³ then all the way through appeals to the Ninth Circuit and then the Supreme Court.

What doctors may and may not do. In *Conant v. Walters*,⁴ 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.⁵ But it remains illegal for a doctor to "aid and abet" a patient in obtaining cannabis.⁶ This means a physician may discuss the pros and cons of medical cannabis with any patient, and issue a written or oral recommendation to use cannabis without fear of legal reprisal.⁷ This is true regardless of whether the physician anticipates that the patient will, in turn, use this recommendation to obtain cannabis.⁸



Angel Raich & Dr. Frank Lucido

What physicians may not do is actually prescribe or dispense cannabis to a patient⁹ or tell patients how to use a written recommendation to procure it from a cannabis club or dispensary.¹⁰ Doctors can tell patients they may be helped by cannabis. They can put that in writing. They just can't help patients obtain the cannabis itself.

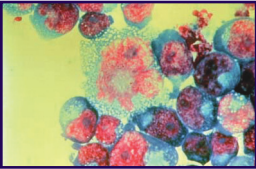
Patients protected under state, not federal, law. In June 2005, the U.S. Supreme Court overturned the *Raich v. Ashcroft* Ninth Circuit Court of Appeals decision. In reversing the lower court's ruling, *Gonzales v. Raich* established that it is legal under federal law to prosecute patients who possess, grow, or consume medical cannabis in medical cannabis states. However, this Supreme Court decision does not overturn or supersede the laws in states with medical cannabis programs.

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

Scientific Research Supports Medical Cannabis

Between 1840 and 1900, European and American medical journals published more than 100 articles on the therapeutic use of the drug known then as Cannabis Indica (or Indian hemp) and now simply as cannabis. Today, new studies are being published in peer-reviewed journals that demonstrate cannabis has medical value in treating patients with serious illnesses such as AIDS, glaucoma, cancer, multiple sclerosis, epilepsy, and chronic pain.

The safety of the drug has been attested to by numerous studies and reports, including the LaGuardia Report of 1944, the Schafer Commission Report of 1972, a 1997 study conducted by the British House of Lords, 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.



T4 Immune Cells

Recent published research on CD4 immunity in AIDS patients found no compromise to the immune systems of patients undergoing cannabis therapy in clinical trials.¹¹

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.

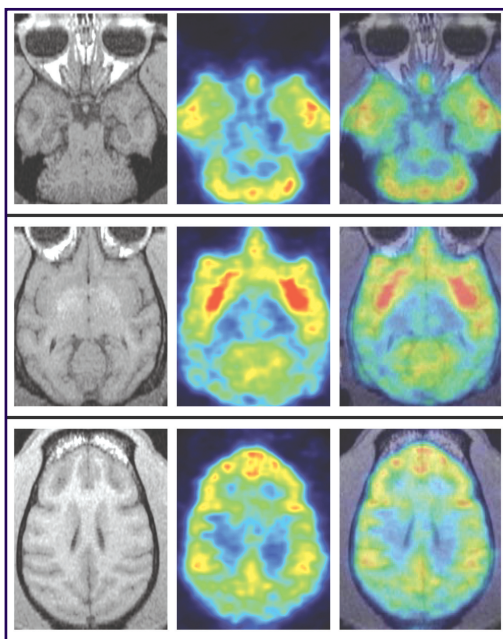
Recent Research Advances

While research has until recently been sharply limited by federal prohibition, the last few years have seen rapid change. The International Cannabinoid Research Society was formally incorporated as a scientific research organization in 1991 with 50 members; as of 2010, there are nearly 500 around the world. The International Association for Cannabis as Medicine (IACM), founded in March 2000, publishes a bi-weekly bulletin and holds international symposia to highlight emerging research in cannabis therapeutics. In 2001, the State of California established the Center for Medicinal Cannabis Research to coordinate an \$8.7-million research effort at University of California campuses. As of 2010, the CMCR had completed six of 14 approved studies. Of those, five published double-blind, placebo-controlled studies studied pain relief; each showed cannabis to be effective.

In the United Kingdom, GW Pharmaceuticals has been conducting clinical trials with its cannabis-based medicine for the past decade. GW's Phase II

and Phase III trials of cannabis-based medicine 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.

As of December 2010, the company has obtained regulatory approval in Spain, New Zealand, and the UK for Sativex® Oromucosal Spray, a controlled-dose whole-plant extract. 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 opioids, and in 2010 for spasticity related to multiple sclerosis. Sativex has been made available either for named patient prescription use or for clinical trials purposes in a total of 22 countries.



Cannabinoid receptors in the brain

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 strong opioids.

CANNABIS AND GI DISORDERS

The effectiveness of cannabis and its derivatives for treating gastrointestinal disorders has been known for centuries. Recently, its value as an anti-emetic and analgesic has been proven in numerous studies and has been acknowledged by several comprehensive, government-sponsored reviews, including those conducted by the Institute of Medicine (IOM), the U.K. House of Lords Science and Technology Committee, the Australian National Task Force on Cannabis, and others.



A doctor performing an endoscopy

The IOM concluded, "For patients . . . who suffer simultaneously from severe pain, nausea, and appetite loss, cannabinoid drugs might offer broad-spectrum relief not found in any other single medication."¹²

The most common gastrointestinal disorders—Irritable Bowel Syndrome and Inflammatory Bowel Disease—affect millions of people. The disorders are different, but they each cause a great deal of discomfort and distress and both can be disabling. Painful cramping, chronic diarrhea or constipation, nausea, and inflammation of the intestines are all symptoms of these GI disorders that can be alleviated by cannabis.

Irritable Bowel Syndrome (IBS) is a common disorder of the intestines that leads to stomach pain, gassiness, bloating, constipation, diarrhea

or both. Chronic, painful abdominal cramping is common. The cause of IBS is not known, and there is no cure. Researchers have found that the colon muscle of a person with IBS begins to spasm after only mild stimulation. IBS is at least partly a disorder affecting colon motility and sensation.

Inflammatory Bowel Disease (IBD) refers to both Ulcerative Colitis and Crohn's Disease. Ulcerative colitis causes inflammation of the lining of the large intestine, while Crohn's disease causes inflammation of the lining and wall of the large and/or small intestine. The causes of IBD are not known, but there are indications that the disease has a genetic component. The immune system changes that accompany IBD suggest that it may be an immune disorder.

The most common symptoms of Crohn's Disease are pain in the abdomen, diarrhea, and weight loss. There may also be rectal bleeding and fever. The most common complications of Crohn's Disease are blockage of the intestine and ulceration that breaks through into surrounding tissues. Surgery is sometimes required.

The symptoms of Ulcerative Colitis include diarrhea, abdominal cramps, and rectal bleeding. Some people may be very tired and have weight loss, loss of appetite, abdominal pain, and loss of body fluids and nutrients. Joint pain, liver problems, and redness and swelling of the eyes can also occur. Hospitalization and surgery are sometimes needed.

Research on cannabis and GI disorders

Research demonstrates that cannabis and cannabinoids are effective in treating the symptoms of these GI disorders in part because it interacts with

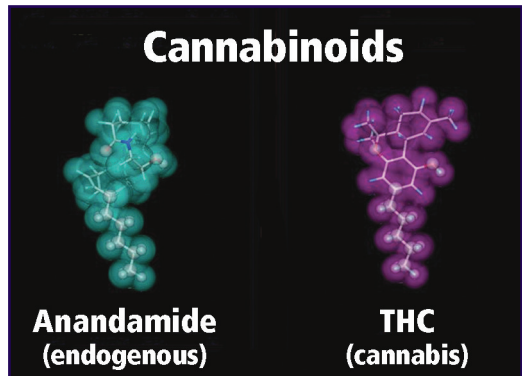
the endogenous cannabinoid receptors in the digestive tract, which can result in calming spasms, assuaging pain, and improving motility. Cannabis has also been shown to have anti-inflammatory properties¹³⁻¹⁵ and recent research has demonstrated that cannabinoids are immune system modulators, either enhancing or suppressing immune response.¹⁶⁻¹⁷

Cannabis has a long documented history of use in treating GI distress, going back more than a century in western medicine, and far longer in the east. While clinical studies on the use of cannabis for the treatment of gastrointestinal disorders have been largely limited to investigations on nausea suppression and appetite stimulation—two conditions for which cannabis has been consistently shown to be highly effective¹⁸⁻²⁹—the evidence in support of cannabis therapy for other gastrointestinal diseases and disorders is also strong. There is now extensive anecdotal evidence from patients with IBS, Crohn's disease and other painful GI disorders that cannabis eases cramping and helps modulate diarrhea, constipation and acid reflux. Recent laboratory research on the endogenous cannabinoid system in humans has identified that there are many cannabinoid receptors located in both the large and small intestine.³⁰⁻³⁵

Cannabis and new cannabinoid drugs are attractive for GI treatment because they can address a number of symptoms at once with minimal side-effects. Cannabinoids alter how the gut feels, affect the signals the brain sends back and forth to the gut, and modulate the actions of the GI tract itself.³⁶⁻³⁸ For instance, cannabidiol (CBD), the second most abundant cannabinoid on the plant, has been shown to reduce hypermotility, inflammation, and tissue damage in experimental models of GI diseases.³⁹⁻⁴⁰

Beginning in the 1970s, a series of human clinical trials established cannabis' ability to stimulate food intake and weight gain in healthy volunteers. In a randomized trial, THC significantly improved appetite and nausea in comparison with placebo. There were also trends towards improved mood and weight gain. Unwanted effects were generally mild or moderate in intensity.

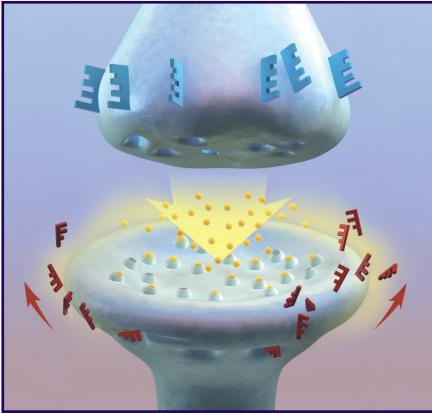
Cannabis helps combat the painful and often debilitating cramping that accompanies many GI disorders because cannabinoids relax contractions of the smooth muscle of the intestines. In fact, the smooth muscle-relaxant properties of cannabinoids are so well established that preparations of



Plant and endogenous cannabinoids are similar

guinea-pig intestine are routinely used as an in vitro screening tool to test the potency and function of synthetic cannabinoids.

Research on a variety of rodents has shown that endogenous cannabinoids play crucial neuromodulatory roles in controlling the operation of the gastrointestinal system, with synthetic and natural cannabinoids acting powerfully to control gastrointestinal motility and inflammation. Cannabinoid receptors comprise G-protein coupled receptors that are predominantly in enteric and central neurones (CB1R) and immune cells (CB2R). The digestive tract contains endogenous cannabinoids (anandamide and 2-arachidonylglycerol) and cannabinoid CB1 receptors can be found on myenteric and submucosal nerves. Activating cannabinoid receptors has been demonstrated to inhibit gastrointestinal fluid secretion and inflammation in animal models.⁴¹⁻⁵²



CB1 receptor

In the last decade, evidence obtained from the use of selective agonists and inverse agonists/antagonists indicates that manipulation of CB1R can have significant results.⁵³ Research has also shown that in the case of intestinal inflammation, the body will increase the number of cannabinoid receptors in the area in an attempt to regulate the inflammation by processing more cannabinoids.⁵⁴ The abundant cannabinoid receptors in the gut represent an excellent target to treat GI disorders, as the receptors are shown to be up-regulated in the intestinal tissue of patients suffering from IBD.⁵⁵ The activation of these hyper-expressed cannabinoid receptors can have protective and therapeutic effects against disorders of the GI tract.⁵⁶

Cannabinoids have a demonstrated ability to block spinal, peripheral and gastrointestinal mechanisms that promote pain in IBS and related disorders.⁵⁷ Animal research also indicates that cannabinoids work well in controlling gastroesophageal reflux disease, a condition in which gastric acids attack the esophagus and for which commonly prescribed medications, such as atropine, have serious, adverse side effects.⁵⁸⁻⁶⁰

From this evidence, many researchers have concluded that pharmacological modulation of the endogenous cannabinoid system provides new treatment options for a number of gastrointestinal diseases, including nausea and vomiting, gastric ulcers, irritable bowel syndrome, Crohn's disease, secretory diarrhea, paralytic ileus and gastroesophageal reflux disease.⁶¹⁻⁶⁴ The experience of patients with these GI disorders shows that for broad-spectrum relief, cannabis is highly effective and frequently helps when other treat-

ment options prove ineffective.⁶⁵

How Cannabis Compares to Other Treatments

The medications currently employed to fight chronic GI disorders include many that produce serious side effects. These side effects frequently threaten the health of the patient and require other medications to combat them. Drugs commonly prescribed to combat GI disorders include:

Megestrol acetate (Megace), an anticachectic. Serious side effects of this medicine include high blood pressure, diabetes, inflammation of the blood vessels, congestive heart failure, seizures, and pneumonia. Less serious side effects of this medicine include diarrhea, flatulence, nausea, vomiting, constipation, heartburn, dry mouth, increased salivation, and thrush; impotence, decreased libido, urinary frequency, urinary incontinence, urinary tract infection, vaginal bleeding and discharge; disease of the heart, palpitation, chest pain, chest pressure, and edema; pharyngitis, lung disorders, and rapid breathing; insomnia, headache, weakness, numbness, seizures, depression, and abnormal thinking.

Prednisone (Delatasone), like all steroids, can have serious adverse musculoskeletal, gastrointestinal, dermatologic, neurologic, endocrine, and ophthalmic side effects. These include: congestive heart failure in susceptible patients, potassium loss, hypokalemic alkalosis, sodium retention, and hypertension. Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, tendon rupture, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, and pathologic fracture of long bones. Peptic ulcer with possible perforation and hemorrhage; pancreatitis; abdominal distention; ulcerative esophagitis. Impaired wound healing, thin fragile skin, petechiae and ecchymoses, facial erythema. Increased intracranial pressure (pseudo-tumor cerebri) usually after treatment, convulsions, vertigo, and headache. Menstrual irregularities; development of Cushingoid state; secondary adrenocortical and pituitary unresponsiveness; decreased carbohydrate tolerance; manifestations of latent diabetes mellitus. Posterior subcapsular cataracts, increased intraocular pressure, glaucoma, and exophthalmos.

Metronidazole (Flagyl) has been shown to be carcinogenic in mice and rats. Two serious adverse reactions reported in patients treated with Metronidazole have been convulsive seizures and peripheral neuropathy,

INSTITUTE OF MEDICINE

"Nausea, appetite loss, pain and anxiety . . . all can be mitigated by marijuana.... For patients, such as those with AIDS or undergoing chemotherapy, who suffer simultaneously from severe pain, nausea, and appetite loss, cannabinoid drugs might offer broad spectrum relief not found in any other single medication."

**Marijuana and Medicine:
Assessing the Science Base, 1999**

the latter characterized mainly by numbness or paresthesia of an extremity. The most common adverse reactions reported have been referable to the gastrointestinal tract, particularly nausea reported by about 12% of patients, sometimes accompanied by headache, anorexia, and occasionally vomiting; diarrhea; epigastric distress, and abdominal cramping. Constipation has been reported.

Sulfasalazine (Azulfidine)—The most common adverse reactions associated with sulfasalazine are anorexia, headache, nausea, vomiting, gastric distress, and apparently reversible oligospermia. These occur in about one-third of the patients. Less frequent adverse reactions are pruritus, urticaria, fever, Heinz body anemia, hemolytic anemia and cyanosis, which may occur at a frequency of one in every thirty patients or less.

Chlordiazepoxide/Clidinium (Librax)—Drowsiness, ataxia and confusion have been reported in some patients, particularly the elderly and debilitated. Adverse effects reported with use of Librax are those typical of anticholinergic agents, i.e., dryness of the mouth, blurring of vision, urinary hesitancy and constipation. Withdrawal symptoms, similar in character to those noted with barbiturates and alcohol (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating), have occurred following abrupt discontinuance of chlordiazepoxide.

Hyoscyamine Sulfate (Levsin)—Adverse reactions may include dryness of the mouth; urinary hesitancy and retention; blurred vision; tachycardia; palpitations; mydriasis; cycloplegia; increased ocular tension; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; allergic reactions or drug idiosyncrasies; urticaria and other dermal manifestations; ataxia; speech disturbance; some degree of mental confusion and/or excitement (especially in elderly persons); and decreased sweating.

Mesalamine CR (Pentasa)—The most common side effects are diarrhea, headache, nausea, abdominal pain, dyspepsia, vomiting, and rash.

Phosphorated carbohydrate (Emetrol)—Side effects include: fainting; swelling of face, arms, and legs; unusual bleeding; vomiting; weight loss; yellow eyes or skin. Less common—more common with large doses: Diarrhea; stomach or abdominal pain.

Dicyclomine (Bentyl)—The most common side effects occurring with dicyclomine are due to its anticholinergic activity: dry mouth, blurred vision, confusion, agitation, increased heart rate, heart palpitations, constipation, difficulty urinating, and occasionally seizures can occur. Other potential side effects include changes in taste perception, difficulty swallowing, headache, nervousness, drowsiness, weakness, dizziness, impotence, flushing, difficulty falling asleep, nausea, vomiting, rash, and a bloated feeling.

Ciprofloxacin (Cipro)—The most frequent side effects include nausea, vomiting, diarrhea, abdominal pain, rash, headache, and restlessness. Rare allergic reactions have been described, such as hives and anaphylaxis.

Methotrexate (Rheumatrex, Trexall)—can cause severe toxicity when taken in high doses. The most frequent reactions include mouth sores, stomach upset, and low white blood counts. Methotrexate can cause severe toxicity of the liver and bone marrow, which require regular monitoring with blood testing. It can cause headache and drowsiness, which may resolve if the dose is lowered. Methotrexate can cause itching, skin rash, dizziness, and hair loss. A dry, non-productive cough can be a result of a rare lung toxicity.



Diphenoxylate and atropine (Lotomil)—The most common side effects include drowsiness, dizziness, and headache, nausea or vomiting, and dry mouth. Euphoria, depression, lethargy, restlessness, numbness of extremities, loss of appetite, and abdominal pain or discomfort have been reported less frequently. Although the dose of atropine in Lomotil is too low to cause side effects when taken in the recommended doses, side effects of atropine (including dryness of the skin and mucous membranes, increased heart rate, urinary retention, and increased body temperature) have been reported, particularly in children under two.

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 ischemias. 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.⁶⁶ Additionally, pharmaceutical companies have developed sublingual sprays and tablet forms of the drug. Patients and doctors



Angel Raich using a vaporizer in the hospital

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.⁶⁷ 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.⁶⁸

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 same 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 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 with inhaled cannabis.

Clinical research on Marinol vs. cannabis has been limited by federal restrictions, but a 2001 review of clinical trials conducted in the 70's and 80's reports that "...the inhalation of THC appears to be more effective than the oral route."⁶⁷ 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 House of Lords report states, "Some users of both find cannabis itself more effective."

THE EXPERIENCE OF PATIENTS

Bruce Buckner

My name is Bruce Buckner. I am a 48-year old computer pre-press technician and webmaster from Seattle, WA. I play music with a couple different bands for fun and profit as well.

I remember my first bouts of abdominal cramping and diarrhea around the age of nine or ten. I was told I was suffering from colitis, that it was just a "nervous stomach." It was always particularly bad on days I woke early to go somewhere, so the "nervous stomach" diagnosis kind of made sense. The cramping and frequent bowel movements continued. I was going to the bathroom a dozen times a day. I was always of slight build but by the age of twelve my weight had dropped off the "low normal" range of the height/weight charts. I became drastically underweight (I am a 48-year-old male who weighs 114 lbs.)

While attending the University of Oregon in Eugene, I was suffering from a particularly bad flare-up. I developed psoriasis, and started getting little red bumps on my lower legs, which I scratched into sores. I was very fortunate

that the young doctor I saw was very familiar with Crohn's (his wife had it). He was able to diagnose it right away, although he still made me undergo a colonoscopy the following week, which confirmed his diagnosis. He started me on sulfasalazine. This caused severe nausea and vomiting. The cure was much worse than the disease. The doctor gave me steroids (prednisone). This made me lay awake all night sweating. I was making all kinds of stupid mistakes—I backed my car into a light post, I lost my temper easily, I couldn't handle the sleep deprivation and stopped taking the steroids. In 1972 my doctor told me his wife found that smoking pot helped. Whenever I was cramping, I smoked a couple joints from that point on.

Through the seventies and eighties, I worked in the music business. My occupations allowed me to wake slowly, work late hours, and smoke lots of pot. Coincidentally, my Crohn's was in almost total remission. I still had occasional bouts of leg sores and cramping and diarrhea, but the cramping and bowel movements would subside after a couple hours and I would be OK the rest of the day. I was still underweight, but I could eat two or three times a day.

After changing jobs and suffering through several years of flare ups, I realized smoking a little pot helped lessen the cramping, increased my appetite and helped me feel a little better. But smoking a lot of pot (a big joint every hour and a half) would keep the disease in a state of almost total remission. I would have only one to three bowel movements in the morning, minimal morning cramping, I could eat any food I wanted; even my leg sores would go away.

I have several relatives with Crohn's Disease. Every one of them has had major surgery. Every one of them has had complications from the steroids and immune suppressors they have been prescribed. Most no longer have functioning excretory systems and are wearing pouches.

I went to a specialist who stated "Frankly, I can't believe you could have gone thirty years with Crohn's without major medical intervention, I have to question whether you really have Crohn's." He ordered an "enteroclysis" (a horrible procedure that I wouldn't wish on anyone) which showed definite scarring and narrowing in my terminal ileum. The doctor had to admit that I did have Crohn's and that I had kept the disease in control with marijuana.

I am firmly convinced that I would be in the same condition as my relatives with Crohn's, if I hadn't used pot. The medical use of marijuana has saved my colon and my quality of life.

Fernando Mosquera

I have personally been waging a lifelong battle with Crohn's disease, a battle in which medical marijuana has proven to be a great ally. Crohn's disease

causes inflammation affecting the entire gastrointestinal tract. During flare-ups, the symptoms can be paralyzing; over the past ten years my life has been brought to a stop by sharp, debilitating stomach pain, constant diarrhea (at its worst I spent entire days on the toilet screaming in pain), blood in the stool and severe weight loss. Medicine has made little progress in the search for a cure and doesn't even fully understand the cause of the illness. The most popular way to control Crohn's is with Prednisone, a multi-purpose steroid drug that can cause psychosis, stunted growth, high blood pressure, weak bones and glaucoma.

The manufacturer of Prednisone recommends it be used in short spurts to minimize side effects, but during my adolescence I was

kept on high doses of the drug for prolonged periods of time. Prednisone couldn't control my illness, and even worse it went to work on my body and mind, stunting my growth, causing mood shifts and water retention, and putting me at risk for osteoporosis. I tried all the treatments available, even attempting an "elemental diet:" breakfast, lunch and dinner served through a tube that ran up my nose and down to my stomach. This failed too, and I had to be home-schooled through high school, spending my days lying in bed clutching my stomach in agony, hoping the constant diarrhea would stop.

A writing career led me to California, where I discovered a medical marijuana regimen of smoking before and after meals made the symptoms of my Crohn's disease disappear. Under California's Proposition 215, I had the legal right to use a medicine that proved far more effective than anything my doctors had tried.

The alternative is Marinol, a legal prescription medicine that contains a synthetic version of tetrahydrocannabinol (THC), the main active ingredient in natural marijuana. Marinol has several disadvantages: 1) It takes much longer to work, especially after meals when I need relief the most; 2) It is difficult to have the right amount. I either end up being too stoned to function or not medicated enough; and 3) THC is not the only active compound in marijuana, and research shows the anti-inflammatory effect of marijuana is likely a result not of THC, but of cannabidiol, a separate chemical not contained in Marinol.

FEDERATION OF AMERICAN SCIENTISTS

"Based on much evidence, from patients and doctors alike, on the superior effectiveness and safety of whole cannabis compared to other medications,... the President should instruct the NIH and the FDA to make efforts to enroll seriously ill patients whose physicians believe that whole cannabis would be helpful to their conditions in clinical trials"

FAS Petition on Medical Marijuana, 1994

Rose Wheeler

I'm a 40-year-old wife and mother of two young boys who was diagnosed with Crohn's disease in September of 1993, while my husband was stationed in Austria. The best way I could describe my symptoms was that food was POISON to me. When I ate or drank ANYTHING, within 5 minutes I was on the toilet bent over in severe pain and experiencing hot flashes. I spent more time in the bathroom than any other place in my home. I was very weak, nauseated. With every bowel movement there was much blood and mucus, and I became seriously depressed. It was very difficult for me to care for my children.

At this time, not knowing what was wrong with me, I could only think that I was actually going to die. My abdomen felt bruised all the time, and the

last thing I wanted to do was eat. I then began what seemed a roller coaster ride of seeing different doctors and having different tests done, which to say the least made me in more pain than ever. The doctors told me the small bowel series revealed findings consistent with Crohn's disease. I was still not prescribed any meds for my symptoms. The doctors felt it was better to give me a consult to see a doctor for further

testing, and to begin my treatment after our return to the States.

I then was introduced to marijuana before leaving Austria, and within 1 hour I could not believe that the pain, bowel movements and ALL my other symptoms were relieved. Now my major concern was the illegality of marijuana, and putting my husband at risk in his military career. I had serious thoughts of getting busted and my children being taken from me. I quit the marijuana after a week of smoking it, only to have all those terrible symptoms return.

Once we returned to the states I began taking 750mg of flagyl, 1500mg of azulfidine, and 1mg of folic acid per day. My life started to turn for the better. But after two years, I began experiencing migraines and feeling as though I was going to pass out at times. I then chose to try smoking marijuana. I felt no one could know I was smoking, not even my husband. I wanted to so badly tell my doctor how much smoking marijuana had relieved my symptoms, but knew I couldn't. I will never forget my last visit to my doctor, telling him that my symptoms were gone and I wanted to quit the meds. He agreed with me that the migraines and dizzy spells were a side effect of the meds. I have not taken any prescription meds for my

AMERICAN NURSES ASSOCIATION

In 2003 the American Nurses Association passed a resolution that supports those health care providers who recommend medicinal use, recognizes "the right of patients to have safe access to therapeutic marijuana/cannabis," and calls for more research and education, as well as a rescheduling of marijuana for medical use.

Crohn's since 1995.

Erin Hildebrandt

My name is Erin Hildebrandt, and I'm a 34-year-old wife and stay-at-home mom to five kids, ages 3 to 9. I suffer from Crohn's Disease, a disease for which there is no known cure; therefore, symptom control is the goal of treatment. Marijuana is not a panacea, but it's the only medicine I've found that controls a large number of my most debilitating symptoms. Compared to the dozens of truly dangerous pharmaceuticals first given to me by doctors, the cannabis recommended by a friend, and subsequently endorsed by my doctor, is more effective and has fewer side-effects. For me, Crohn's Disease produces severe nausea, vomiting, diarrhea, intractable pain, cramping, fever, sweating, chills, bloating, and weight loss. I can only compare it to the worst case of food poisoning I can imagine, except that it doesn't just go away after a day or two. It comes back again and again, varying in both intensity and duration. During the worst attacks, proper nutrition and exercise are an often insurmountable challenge. However, through the use of marijuana, I feel well enough to function more normally. In addition, with consistent therapeutic use, the inflammation in my digestive tract stays under control, and I'm able to bring my disease into remission.

THE EXPERIENCE OF DOCTORS

Kate Scannell, M.D.

From working with AIDS and cancer patients, I repeatedly saw how marijuana could ameliorate a patient's debilitating fatigue, restore appetite, diminish pain, remedy nausea, cure vomiting and curtail down-to-the-bone weight loss. The federal obsession with a political agenda that keeps marijuana out of the hands of sick and dying people is appalling and irrational.

Kate Scannell, M.D. is Co-Director, Kaiser-Permanente, Northern California Ethics Department.

Marcus A. Conant, M.D.

Medical marijuana. . . stimulates the appetite and promotes weight gain, in turn strengthening the body, combating chronic fatigue, and providing the stamina and physical well-being necessary to endure or withstand both adverse side effects of ongoing treatment and other opportunistic infections. It has been shown effective in reducing nausea, neurological pain and anxiety, and in stimulating appetite. When these symptoms are associated with (or caused by) other therapies, marijuana has been useful in facilitating compliance with more traditional therapies. It may also allow individual patients to engage in normal social interactions and avoid the despair and isolation which frequently accompanies long-term discomfort and illness. . .

I was one of the principal investigators of an FDA-supervised trial conducted

by Unimed, Inc. on the safety and efficacy of Marinol as an appetite stimulant in HIV/AIDS patients suffering from wasting syndrome. Marinol is a form of THC, one of the key active components of marijuana; it is essentially a marijuana extract. It was approved by the FDA five years ago, and has been widely prescribed by physicians treating both AIDS and cancer

NEW ENGLAND JOURNAL OF MEDICINE

"A federal policy that prohibits physicians from alleviating suffering by prescribing marijuana to seriously ill patients is misguided, heavy-handed, and inhumane.... It is also hypocritical to forbid physicians to prescribe marijuana while permitting them to prescribe morphine and meperidine to relieve extreme dyspnea and pain...there is no risk of death from smoking marijuana.... To demand evidence of therapeutic efficacy is equally hypocritical"

**Jerome P. Kassirer, MD, editor
N Engl J Med 336:366-367, 1997**

patients. ...I am aware, however, that Marinol (like any medication) is not effective in treating all patients. In some cases, the reason is simple: Marinol is taken orally, in pill form. Patients suffering from severe nausea and retching cannot tolerate the pills and thus do not benefit from the drug. There are likely other reasons why smoked marijuana is sometimes more effective than Marinol. The body's absorption of the chemical may be faster or more complete when inhaled. Means of ingestion is often critical in

understanding treatment efficacy.

Dr. Marcus Conant has practiced medicine for 33 years. He is Professor at University of California San Francisco and is author of over 70 publications.

Neil M. Flynn, M.D., MPH

If I am unable to relieve the patient's nausea with [conventional] remedies, I next prescribe Marinol, a synthetic version of THC, one of the main active compounds found in marijuana. Marinol is also helpful in stimulating appetite in patients suffering from AIDS wasting, as are other drugs, Megace, anabolic steroids, and human growth hormone.

If Marinol does not provide adequate relief from nausea and/or wasting, I may suggest that the patient try a related remedy, marijuana. I firmly believe that medical marijuana is medically appropriate as a drug of last resort for a small number of seriously ill patients. Over 20 years of clinical experience persuade me of this fact. The anecdotal evidence is overwhelming. Almost every patient I have known to have tried marijuana achieved relief from symptoms with it. That success rate far surpasses that for Compazine.

Accordingly, as with any other medication that I consider potentially beneficial to my patients, I must discuss the option of medical marijuana in detail when appropriate. Anything less is malpractice. ... I have seen marijuana

restore patients' will to live by restoring their ability to eat, gain strength, and perform simple, daily activities free from crippling nausea or pain.

Dr. Neil M. Flynn is a Professor of Clinical Medicine at the University of California, Davis School of Medicine and is the author of numerous articles.

THE HISTORY OF CANNABIS AS MEDICINE

The history of the medical use of cannabis dates back to 2700 B.C. in the pharmacopoeia of Shen Nung, one of the fathers of Chinese medicine. In the west, it has been recognized as a valued, therapeutic herb for centuries. In 1823, Queen Victoria's personal physician, Sir Russell Reynolds, not only prescribed it to her for menstrual cramps but wrote in the first issue of *The Lancet*, "When pure and administered carefully, [it is] one of the of the most valuable medicines we possess." (*Lancet* 1; 1823).

The American Medical Association opposed the first federal law against cannabis with an article in its leading journal (108 *J.A.M.A.* 1543-44; 1937). Their representative, 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." Cannabis remained part of the American pharmacopoeia until 1942 and is currently available by prescription in the Netherlands and Canada.



Federal Policy is Contradictory

Federal policy on medical cannabis is filled with contradictions. Cannabis was widely prescribed until the turn of the century. Now cannabis is a Schedule I drug, classified 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. And the U.S. federal government grows and provides cannabis for a small number of patients today.

In 1976 the federal government created the Investigational New Drug (IND) compassionate access research program to allow patients to receive medical cannabis from the government. The application process was extremely complicated, and few physicians became involved. In the first twelve years the government accepted about a half dozen patients. The federal government approved the distribution of up to nine pounds of cannabis a year to these patients, all of whom report being substantially helped by it.

In 1989 the FDA was deluged with new applications from people 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, a few surviving patients still receive medical cannabis from the federal government, grown under a doctor's supervision at the University of Mississippi and paid for by federal tax dollars.

Despite this successful medical program and centuries of documented safe use, cannabis is still classified in America 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 so that it could be prescribed to patients.

The DEA stalled hearings for 16 years, but 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 classify cannabis as a substance with no medical use.

Widespread public support; state laws passed

Public opinion is clearly in favor of ending the prohibition of medical cannabis. According to a CNN/Time poll in November 2002, 80% of Americans support medical cannabis. The AARP, the national association whose 35 million members are over the age of fifty, released a national poll in December 2004 showing that nearly two-thirds of older Americans support legal access to medical marijuana. Support in the West, where most states that allow legal access are located, was strongest, at 82%, but at least 2 out of 3 everywhere agreed that "adults should be allowed to legally use marijuana for medical purposes if a physician recommends it."

The refusal of the federal government to act on this support has meant that patients have had to turn to the states for action. Since 1996, 15 states have removed criminal penalties for their citizens who use cannabis on the advice of a physician. Voters have passed medical cannabis ballot initiatives in 10 states plus the District of Columbia, while the legislatures in Hawaii, Maryland, New Jersey, New Mexico, Rhode Island, and Vermont have enacted similar bills. Approximately one third of the U.S. population resides in a state that permits medical use, and medical cannabis legislation is introduced in more states every year.

Currently, laws that effectively remove state-level criminal penalties for growing and/or possessing medical cannabis are in place in Alaska, Arizona, California, Colorado, Hawaii, Maine, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington, and the District of Columbia. Maryland has reduced the criminal penalty for medical use to a maximum \$100 fine. Thirty-six states have symbolic medical cannabis laws

(laws that support medical cannabis but do not provide patients with legal protection under state law).

2005 U.S. Supreme Court ruling

In June 2005, the U.S. Supreme Court overturned a decision by a U.S. appeals court (*Raich v. Ashcroft*) that had exempted medical cannabis from federal prohibition. The 2005 decision, now called *Gonzales v. Raich*, ruled that federal officials may prosecute medical cannabis patients for possessing, consuming, and cultivating medical cannabis. But according to numerous legal opinions, that ruling does not affect individual states' medical cannabis programs, and only applies to prosecution in federal, not state, court.

Petitions for legal prescriptions pending

The federal Department of Health and Human Services (HHS) and the FDA are currently reviewing two legal petitions with broad implications for medical cannabis. The first, brought by ASA under the Data Quality Act, says HHS must correct its statements that there is no medical use for cannabis to reflect the many studies which have found it helpful for many conditions. Acknowledging legitimate medical use would then force the agency to consider allowing the prescribing of cannabis as they do other drugs, based on its relative safety. A separate petition, of which ASA is a co-signer, asks the Drug Enforcement Administration for a full, formal re-evaluation of cannabis's medical benefits, based on hundreds of recent medical research studies and two thousand years of documented human use.

Legal Citations

1. See "The Administration's Response to the Passage of California Proposition 215 and Arizona Proposition 200" (Dec. 30, 1996).
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).

Research Citations

11. 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.
12. Joy JE, Watson SJ, Benson JA Jr, (1999). Marijuana and medicine: Assessing the science base. Washington, DC: Institute of Medicine.

13. Croci T et al (2003). Role of cannabinoid CB1 receptors and tumor necrosis factor-alpha in the gut and systemic anti-inflammatory activity of SR 141716 (rimonabant) in rodents. *Br J Pharmacol. Sep;140(1):115-22*. Epub 2003 Jul 29.
14. Izzo AA et al (2001). Cannabinoid CB1-receptor mediated regulation of gastrointestinal motility in mice in a model of intestinal inflammation. *Br J Pharmacol. Oct;134(3):563-70*.
15. Dajani EZ et al (1999). 1',1'-Dimethylheptyl-delta-8-tetrahydrocannabinol-11-oic acid: a novel, orally effective cannabinoid with analgesic and anti-inflammatory properties. *J Pharmacol Exp Ther. Oct;291(1):31-8*.
16. Kulkarni-Narla A, Brown DR (2000). Localization of CB1-cannabinoid receptor immunoreactivity in the porcine enteric nervous system. *Cell Tissue Res. Oct;302(1):73-80*.
17. Coutts AA et al (2002). Localisation of cannabinoid CB(1) receptor immunoreactivity in the guinea pig and rat myenteric plexus. *J Comp Neurol. Jul 8;448(4):410-22*.
18. Westfall RE et al (2006). Survey of medicinal cannabis use among childbearing women: patterns of its use in pregnancy and retroactive self-assessment of its efficacy against 'morning sickness'. *Complement Ther Clin Pract. Feb;12(1):27-33*. Epub 2005 Dec 22.
19. Gieringer D (1996). "Review of Human Studies on the Medical Use of Marijuana". www.canorml.org.
20. Beal JE et al (1995). Dronabinol as a treatment for anorexia associated with weight loss in patients with AIDS. *Journal of Pain & Symptom Management, 10, 89-97*.
21. Foltin R et al (1988). Effects of smoked marijuana on food intake and body weight of humans living in a residential laboratory, *Appetite 11: 1-14*.
22. Foltin R et al (1986). Behavioral analysis of marijuana effects on food intake in humans, *Pharmacology, Biochemistry and Behavior 25: 577-582*.
23. Gross H et al (1983). A double-blind trial of delta-9-THC in primary anorexia nervosa, *Journal of Clinical Psychopharmacology 3: 165-171*.
24. Hollister L (1971). Hunger and appetite after single doses of marihuana, alcohol, and dextroamphetamine. *Clinical Pharmacology and Therapeutics 12: 44-49*.
25. Greenberg I et al (1976). Effects of marihuana use on body weight and caloric intake in humans. *Journal of Psychopharmacology (Berlin) 49: 79-84*.
26. Gonzalez-Rosales F, Walsh D (1997). Intractable nausea and vomiting due to gastrointestinal mucosal metastases relieved by tetrahydrocannabinol (dronabinol). *J Pain Symptom Manage. Nov;14(5):311-4*.
27. Darmani NA (2002). The potent emetogenic effects of the endocannabinoid, 2-AG (2-arachidonoylglycerol) are blocked by delta(9)-tetrahydrocannabinol and other cannabinoids. *J Pharmacol Exp Ther. Jan;300(1):34-42*.
28. Van Sickle MD et al (2001). Cannabinoids inhibit emesis through CB1 receptors in the brainstem of the ferret. *Gastroenterology. Oct;121(4):767-74*.
29. Anderson PO, McGuire GG (1981). Delta-9-tetrahydrocannabinol as an antiemetic. *Am J Hosp Pharm. May;38(5):639-46*.
30. Coutts AA, Izzo AA (2004). The gastrointestinal pharmacology of cannabinoids: an update. *Curr Opin Pharmacol. Dec;4(6):572-9*.
31. Casu MA et al (2003). Differential distribution of functional cannabinoid CB1 receptors in the mouse gastroenteric tract. *Eur J Pharmacol. Jan 10;459(1):97-105*
32. Pinto L et al (2002). Endocannabinoids and the gut. *Prostaglandins Leukot Essent Fatty Acids. Feb-Mar;66(2-3):333-41*.
33. Manara L et al (2002). Functional assessment of neuronal cannabinoid receptors in the muscular layers of human ileum and colon. *Dig Liver Dis. Apr;34(4):262*.
34. Hillard CJ (2000). Biochemistry and pharmacology of the endocannabinoids arachidonylethanolamide and 2-arachidonylethanolamide. *Prostaglandins Other Lipid Mediat. Apr;61(1-2):3-18*.
35. Croci T et al (1998). In vitro functional evidence of neuronal cannabinoid CB1 receptors in human ileum. *Br J Pharmacol. Dec;125(7):1393-5*.
36. Grotenhermen F (2004). Pharmacology of cannabinoids. *Neuro Endocrinol Lett. Feb-Apr;25(1-2):14-23*.
37. Izzo AA, Mascolo N, Capasso F (2001). The gastrointestinal pharmacology of cannabinoids. *Curr Opin Pharmacol. Dec;1(6):597-603*.
38. Pertwee RG (2001). Cannabinoids and the gastrointestinal tract. *Gut. Jun;48(6):859-67*.
39. Capasso R et al. (2008) Cannabidiol, extracted from Cannabis sativa, selectively inhibits inflammatory hypermotility in mice. *Br J Pharmacol. 2008 Jul;154(5):1001-8*. 40. Borrelli F et al (2009) Cannabidiol, a safe and non-psychoactive ingredient of the marijuana plant Cannabis sativa, is

protective in a murine model of colitis. *Journal Molecular Medicine* Aug 20.

41. Mancinelli R et al (2001). Inhibition of peristaltic activity by cannabinoids in the isolated distal colon of mouse. *Life Sci.* May 25;69(1):101-11.
42. Mascolo N et al (2002). The endocannabinoid system and the molecular basis of paralytic ileus in mice. *FASEB J.* Dec;16(14):1973-5. Epub 2002 Oct 18.
43. Izzo AA et al (1999). The role of cannabinoid receptors in intestinal motility, defecation and diarrhoea in rats. *Eur J Pharmacol.* Nov 12;384(1):37-42.
44. Landi M et al (2002). Modulation of gastric emptying and gastrointestinal transit in rats through intestinal cannabinoid CB(1) receptors. *Eur J Pharmacol.* Aug 16;450(1):77-83.
45. Pinto L et al (2002). Endocannabinoids as physiological regulators of colonic propulsion in mice. *Gastroenterology.* Jul;123(1):227-34.
46. Krowicki ZK et al (1999). Delta9-tetrahydrocannabinol inhibits gastric motility in the rat through cannabinoid CB1 receptors. *Eur J Pharmacol.* Apr 29;371(2-3):187-96.
47. Heinemann A et al (1999). Cannabinoid inhibition of guinea-pig intestinal peristalsis via inhibition of excitatory and activation of inhibitory neural pathways. *Neuropharmacology.* Sep;38(9):1289-97.
48. Izzo AA et al (1999). Defaecation, intestinal fluid accumulation and motility in rodents: implications of cannabinoid CB1 receptors. *Naunyn Schmiedebergs Arch Pharmacol.* Jan;359(1):65-70.
49. Colombo G et al (1998). Cannabinoid modulation of intestinal propulsion in mice. *Eur J Pharmacol.* Feb 26;344(1):67-9.
50. Calignano A et al (1997). Inhibition of intestinal motility by anandamide, an endogenous cannabinoid. *Eur J Pharmacol.* Dec 11;340(2-3):R7-8.
51. Shook JE, Burks TF (1989). Psychoactive cannabinoids reduce gastrointestinal propulsion and motility in rodents. *J Pharmacol Exp Ther.* May;249(2):444-9.
52. Shook JE et al (1986). The central and peripheral effects of delta-9-tetrahydrocannabinol on gastrointestinal transit in mice. *NIDA Res Monogr.* 67:222-7.
53. Hornby PJ, Prouty SM (2004). Involvement of cannabinoid receptors in gut motility and visceral perception. *Br J Pharmacol.* Apr;141(8):1335-45.
54. Izzo AA et al (2000). Central and peripheral cannabinoid modulation of gastrointestinal transit in physiological states or during the diarrhoea induced by croton oil. *Br J Pharmacol.* Apr;129(8):1627-32.
55. Wright KL et al. (2008). Cannabinoid CB2 receptors in the gastrointestinal tract: a regulatory system in states of inflammation. *Br J Pharmacol.* Jan;153(2):263-70
56. Capasso R et al. (2008) Inhibitory effect of salvinorin A, from *Salvia divinorum*, on ileitis-induced hypermotility: cross-talk between kappa-opioid and cannabinoid CB(1) receptors. *Br J Pharmacol.* Nov;155(5):681-9
57. Russo EB (2004). Clinical endocannabinoid deficiency (CECD): can this concept explain therapeutic benefits of cannabis in migraine, fibromyalgia, irritable bowel syndrome and other treatment-resistant conditions? *Neuro Endocrinol Lett.* Feb-Apr;25(1-2):31-9.
58. Tonini M et al (2004). Progress with novel pharmacological strategies for gastro-oesophageal reflux disease. *Drugs.* 64(4):347-61.
59. Partosoedarso ER et al (2003). Cannabinoid1 receptor in the dorsal vagal complex modulates lower oesophageal sphincter relaxation in ferrets. *J Physiol.* May 16.
60. Lehmann A et al (2002). Cannabinoid receptor agonism inhibits transient lower esophageal sphincter relaxations and reflux in dogs. *Gastroenterology.* Oct;123(4):1129-34.
61. Russo. Op.Cit.
62. Di Carlo G, Izzo AA (2003). Cannabinoids for gastrointestinal diseases: potential therapeutic applications. *Expert Opin Investig Drugs.* 2003 Jan;12(1):39-49. Vigna SR. Cannabinoids and the gut. *Gastroenterology.* Sep;125(3):973-5.
63. Hunt RH, Tougas G (2002). Evolving concepts in functional gastrointestinal disorders: promising directions for novel pharmaceutical treatments. *Best Pract Res Clin Gastroenterol.* Dec;16(6):869-83.
64. Izzo AA, Mascolo N, Capasso F (2000). Forgotten target for marijuana: the endocannabinoid system in the gut. *Trends Pharmacol Sci.* Oct;21(10):372-3.
65. 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.
66. Tashkin D (2006). Marijuana Use and Lung Cancer: Results of a Case-Control Study. American Thoracic Society International Conference. May 23, 2006.
67. 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.

DEA CHIEF ADMINISTRATIVE LAW JUDGE

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 Honorable Francis L. Young,
Ruling on DEA rescheduling hearings, 1988

ADDITIONAL RESOURCES

Americans for Safe Access maintains a website with additional resources for doctors and patients. There you will find the latest information on legal and legislative developments, new medical research, and what you can do to help protect the rights of patients and doctors.

With more than 45,000 active members and chapters and affiliates in all 50 states, ASA is the largest national member-based organization of patients, medical professionals, scientists, and concerned citizens promoting safe and legal access to cannabis for therapeutic uses and research.



AmericansFor
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