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"We change laws."

Medical Marijuana Research

MPP's model medical marijuana bill allows patients to obtain a medical marijuana card if they have a qualifying medical condition and a licensed physician believes they are likely to receive therapeutic or palliative benefit from the use of medical marijuana. The qualifying medical conditions listed in the bill are as follows (the state department of health can add others):

1. Cancer, glaucoma, positive status for human immunodeficiency virus, acquired immune deficiency syndrome, hepatitis C, amyotrophic lateral sclerosis, Crohn's disease, agitation of Alzheimer's disease, post-traumatic stress disorder, or the treatment of these conditions; and

2. A chronic or debilitating disease or medical condition or its treatment that produces one or more of the following: cachexia or wasting syndrome; severe, debilitating pain; severe nausea; seizures; or severe and persistent muscle spasms, including but not limited to those characteristic of multiple sclerosis.

Key medical references addressing marijuana's ability to alleviate these conditions are below, with related items/ subjects grouped together.

Nausea, Vomiting, Appetite Loss, Cachexia

In its 1999 report "Marijuana and Medicine: Assessing the Science Base," the Institute of Medicine concluded, "Nausea, appetite loss, pain and anxiety are all afflictions of wasting, and all can be mitigated by marijuana." Marijuana's active components (cannabinoids) can both stimulate appetite and reduce the nausea, vomiting, and weight loss experienced by patients in many circumstances, including the side effects of drug therapies given for cancer, HIV infection, and hepatitis C. Observational studies suggest this may improve treatment adherence among patients experiencing gastrointestinal toxicity from drug therapy.

Cancer References

(1) Vincent Vinciguerra, et al., "Inhalation Marijuana as an Antiemetic for Cancer Chemotherapy," *New York State Journal of Medicine* (October 1988).

In this clinical trial sponsored by the state of New York, "Fifty-six patients who had no improvement with standard antiemetic agents were treated and 78% demonstrated a positive response to marijuana ... inhalation marijuana is an effective therapy for the treatment of nausea and vomiting due to cancer chemotherapy."

(2) Richard Musty and Rita Rossi, "Effects of Smoked Cannabis and Oral Δ9-Tetrahydrocannabinol on Nausea and Emesis After Cancer Chemotherapy: A Review of State Clinical Trials," *Journal of Cannabis Therapeutics* 1, no. 1 (2001): 43-56.

Musty and Rossi reviewed data from a series of state-sponsored clinical trials of marijuana for relief of nausea and vomiting caused by cancer chemotherapy conducted in the 1970s and 1980s, concluding, "Patients who smoked marijuana experienced 70-100% relief from nausea and vomiting, while those who used the THC capsule experienced 76-88% relief."

(3) Manuel Guzman, "Cannabinoids: Potential Anticancer Agents," *Nature Reviews* 3 (2003): 745-766.

In this review article, Dr. Guzman, a leading cancer researcher, examined the data regarding use of marijuana and cannabinoids in cancer treatment. He concluded that marijuana/cannabinoids can be useful in preventing or treating "chemotherapy-induced nausea and vomiting." He also noted that cannabinoids have potential as antitumor agents: "Regarding effectiveness, cannabinoids exert a notable antitumour activity... Regarding toxicity, cannabinoids not only show a good safety profile but also have palliative effects in patients with cancer, indicating that clinical trials with cannabinoids in cancer therapy are feasible."

(4) K. Nelson, et al., "A Phase II Study of Delta-9-Tetrahydrocannabinol for Appetite Stimulation in Cancer-Associated Anorexia," *Journal of Palliative Care* 10, no. 1 (1994): 14-8.

In this study of patients with anorexia due to advanced cancer, the researchers concluded, "THC is an effective appetite stimulant in patients with advanced cancer. It is well tolerated at low doses."

(5) Marta Duran, et al., "Preliminary efficacy and safety of an oromucosal standardized cannabis extract in chemotherapy-induced nausea and vomiting," *Journal of Clinical Pharmacology* 70, no. 4 (2010): 656-63.

The researchers who conducted this double-blind, placebo-controlled clinical trial concluded that compared to the placebo, the whole plant cannabis (marijuana) medicine "added to standard antiemetic therapy was well tolerated and provided better protection against delayed CINV [chemotherapy-induced nausea and vomiting]."

HIV/AIDS References

1) Donald Abrams, et al., "Short-Term Effects of Cannabinoids on Patients With HIV-1 Infection: A Randomized, Placebo-Controlled Clinical Trial," *Annals of Internal Medicine* 139, no. 4 (2003): 258-266.

This preliminary, short-term clinical trial conducted over 21 days using 62 HIV-infected patients was designed to examine the short-term safety of smoked marijuana and oral THC on HIV-infected patients, including potential interactions with HIV protease inhibitors, viral load,

and CD4 and CD8 counts. Secondary endpoints included weight, caloric intake, and appetite. No safety concerns emerged with either treatment, and the authors concluded, "Our short-duration clinical trial suggests acceptable safety in a vulnerable immune-compromised patient population." Both the marijuana and oral THC groups gained significantly more weight than the placebo group.

2) B.D. de Jong, et al., "Marijuana Use and Its Association With Adherence to Antiretroviral Therapy Among HIV-Infected Persons With Moderate to Severe Nausea," *Journal of Acquired Immune Deficiency Syndromes* 38, no. 1 (2005): 43-6.

Use of illicit drugs is typically associated with poor adherence to medication regimens. This observational study sought to determine whether this common assumption applies to HIV/AIDS persons on antiretroviral therapy (ART). Marijuana-using patients who suffered moderate to severe nausea were far more likely to be adherent to ART than those suffering nausea who did not use marijuana (OR = 3.3). The authors concluded, "These data suggest that medicinal use of marijuana may facilitate, rather than impede, ART adherence for patients with nausea, in contrast of other illicit substances," particularly in the case of "use of smoked marijuana specifically for amelioration of nausea."

(3) M. Haney, et al., "Dronabinol and Marijuana in HIV-Positive Marijuana Smokers. Caloric Intake, Mood, and Sleep," *Journal of Acquired Immune Deficiency Syndromes* 45, no. 5 (2007): 545-54.

In this controlled clinical trial, both marijuana and oral THC (dronabinol) use resulted in increased caloric intake and body weight. Strikingly, a dronabinol dose "eight times current recommendations" was required to approximate the effect of relatively low-potency (3.9% THC) marijuana, and only the marijuana improved ratings of sleep. While both drugs produced some intoxication, researchers reported "little evidence of discomfort and no impairment of cognitive performance."

(See the section on chronic pain below for studies of marijuana for HIV-associated peripheral neuropathy.)

<u>Hepatitis C References</u>

1) D.L. Sylvestre, B.J. Clements, and Y. Malibu, "Cannabis Use Improves Retention and Virological Outcomes in Patients Treated For Hepatitis C," *European Journal of Gastroenterology and Hepatology* 18 (2006): 1057-63.

A prospective observational study was conducted on 71 patients to define the impact of cannabis use during interferon/ribavirin treatment for the hepatitis C virus. Compared to non-users, marijuana users had three times the rate of sustained virological response, apparently due to better treatment adherence. The researchers stated, "[T] he use of cannabis during HCV treatment can improve adherence by increasing the duration of time that patients remain on therapy; this translates to reduced rates of post-treatment virological relapse."

(2) B. Fischer, et al., "Treatment For Hepatitis C Virus and Cannabis Use in Illicit Drug User Patients: Implications and Questions," *European Journal of Gastroenterology and Hepatology* 18 (2006): 1039-42.

This commentary, published alongside the above study, placed the results in context, explaining how marijuana "may help address key challenges faced by drug users in HCV treatment (e.g. nausea, depression)."

Other References

(1) Richard W. Foltin, Marian W. Fischman, and Maryanne F. Byrne, "Effects of Smoked Marijuana on Food Intake and Body Weight of Humans Living in a Residential Laboratory," *Appetite* 11 (1988): 1-14.

This study, involving healthy volunteers living in a residential laboratory, documented marijuana's efficacy as an appetite stimulant. Compared to placebo, relatively weak marijuana cigarettes (2.3% THC) smoked at scheduled intervals resulted in a 40% increase in daily caloric intake.

(2) R. Layeeque, et al., "Prevention of Nausea and Vomiting Following Breast Surgery," *American Journal of Surgery* 191, no. 6 (2006): 767-72.

This retrospective review found that a prophylactic regimen combining oral THC with rectal prochlorperazine "significantly reduced the number and severity of episodes" of post-operative nausea and vomiting in breast surgical patients.

Severe, Debilitating Pain

Studies have shown that marijuana is especially effective in treating neuropathic pain, commonly seen in multiple sclerosis, HIV/AIDS, and other ailments. Neuropathic pain is notoriously resistant to treatment with conventional pain drugs, including opiates. Research also suggests that marijuana use may allow reduced opioid doses when given in combination.

References

(1) Barth Wilsey, et al., "Low-Dose Vaporized Cannabis Significantly Improves Neuropathic Pain," *The Journal of Pain* (2012): 136-148.

This double-blind, placebo-controlled study on 30 human subjects found that even low doses of vaporized marijuana were effective at alleviating treatment-resistant neuropathic pain. "Psychoactive effects were minimal and well tolerated, and neuropsychological effects were of limited duration and readily reversible within 1 to 2 hours."

(2) Donald Abrams, et al., "Cannabiniod-opioid interaction in chronic pain," *Clinical Pharmacology & Therapeutics* (2011): 844-851.

This clinical trial involved 21 individuals with severe pain who were taking sustained-release morphine or oxycodone. It found that vaporized marijuana augmented the analgesic effects of opioids. The authors reported that adding vaporized marijuana "may allow for opioid treatment at lower doses with fewer side effects."

(3) Mark Ware, et al., "Smoked cannabis for chronic neuropathic pain: a randomized controlled trial," *Canadian Medical Association Journal* (2010): 694-701.

This trial found that "a single inhalation of 25 mg of 9.4% tetrahydrocannabinol herbal cannabis three times daily for five days reduced the intensity of pain, improved sleep and was well tolerated."

(4) Donald Abrams, et al., "Cannabis in Painful HIV-Associated Sensory Neuropathy: a Randomized Placebo-Controlled Trial," *Neurology* 68, no. 7 (2007): 515-21.

This clinical trial involved HIV/AIDS patients suffering from HIV-associated sensory neuropathy, a painful condition estimated to eventually afflict up to one third of HIV-infected persons. There are presently no FDA-approved treatments for this indication. Donald Abrams and his colleagues tested the efficacy of smoked marijuana on both HIV neuropathy and a type of laboratory-induced pain. Smoked marijuana produced an average 34% reduction in pain and was well tolerated.

(5) R.J. Ellis, et al., "Smoked Medicinal Cannabis For Neuropathic Pain in HIV: a Randomized, Crossover Clinical Trial," *Neuropsychopharmacology* 34, no. 3 (2009): 672-80.

This trial focused on patients with HIV-associated neuropathy refractory to at least two previous analgesic classes. Ellis and colleagues reported, "In the present experiment, cannabis reduced pain intensity and unpleasantness equally. Thus, as with opioids, cannabis does not rely on a relaxing or tranquilizing effect (e.g. anxiolysis), but rather reduces both the core component of nociception and the emotional aspect of the pain experience to an equal degree. ... In general, side effects and changes in mood were inconsequential."

(6) B. Wilsey, et al., "A Randomized, Placebo-Controlled, Crossover Trial of Cannabis Cigarettes in Neuropathic Pain," *Journal of Pain* 9, no. 6 (2008):506-21.

This study investigated the efficacy of smoked marijuana in patients suffering from neuropathic pain related to a variety of conditions, including multiple sclerosis, spinal cord injury, diabetes, and complex regional pain syndrome. Wilsey and colleagues concluded, "This study adds to a growing body of evidence that cannabis may be effective at ameliorating neuropathic pain, and may be an alternative for patients who do not respond to, or cannot tolerate, other drugs."

(7) David Baker, et al., "The Therapeutic Potential of Cannabis," *The Lancet Neurology* 2, no. 5 (2003): 291-8.

This review, written prior to publication of the clinical trials described above, discussed in detail the biochemical basis for marijuana's analgesic effects. It also discussed the drawbacks of oral dosing (taking a pill with cannabinoids), explaining that "oral administration is probably the least satisfactory route for cannabis owing to sequestration of cannabinoids into fat from which there is slow and variable release into plasma. In addition, significant first-pass metabolism in the liver, which degrades THC, contributes to the variability of circulating concentrations of orally administered cannabinoids, which makes dose titration more difficult and therefore increases the potential for adverse psychoactive effects. Smoking has been the route of choice for many cannabis users because it delivers a more rapid 'hit' and allows more accurate dose-titration."

(8) M.E. Lynch, J. Young, A.J. Clark, "A Case Series of Patients Using Medicinal Marihuana for Management of Chronic Pain Under the Canadian Marihuana Medical Access Regulations," *Journal of Pain and Symptom Management* 32, no. 5 (2006): 497-501.

This case series is based on 30 patients qualified to use medical marijuana under Canadian regulations, seen at a pain management center in Nova Scotia. All suffered from chronic, severe pain that had not responded to conventional approaches. On an 11-point scale, 93% reported pain relief equal to six or greater, and many reported relief of other symptoms such as spasticity, poor sleep, nausea, and vomiting. 70% reported being "able to decrease use of other medications that had been causing side effects (e.g., NSAIDs, opioids, and antidepressants)."

Glaucoma

Glaucoma is a leading cause of blindness, damaging the optic nerve, which is responsible for carrying images from the eye to the brain. High pressure within the eye is one of the main risk factors for this optic nerve damage. There currently is no cure for glaucoma. Marijuana helps relieve the pressure within the eye, thus preventing damage.

Although other drugs are considered first-line glaucoma treatments, some patients and physicians have found marijuana useful when conventional drugs fail. One of the three patients who still receive medical marijuana from the federal government – Elvy Musikka – is a glaucoma patient, who also successfully argued in a Florida court case that marijuana was medically necessary to maintaining her vision.

References

(1) J.E. Joy, S.J. Watson, and J.A. Benson, "Marijuana and Medicine: Assessing the Science Base" (National Academy Press, 1999).

"In a number of studies of healthy adults and glaucoma pressure, IOP (intra-ocular pressure) was reduced by an average of 25% after smoking a marijuana cigarette that contained approximately 2% THC — a reduction as good as that observed with most other medications available today."

Amyotrophic lateral sclerosis

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's Disease, is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord, progressively reducing the ability of the brain to initiate and control muscle movement. Some research has shown that cannabinoids can delay the progression of ALS. Some ALS patients have indicated that medical marijuana has helped alleviate their symptoms, such as pain, appetite loss, depression, and drooling.

References

(1) Gregory T. Carter and Bill S. Rosen, "Marijuana in the Management of Amyotrophic Lateral Sclerosis," *American Journal of Hospice and Palliative Care* 18, no. 4 (2001): 264-69.

This review article, co-authored by a leading ALS and palliative medicine researcher from the University of Washington, concluded that marijuana may help with many symptoms of ALS, including pain, spasticity, drooling, dysautonomia, and wasting. The authors also discussed how marijuana's antioxidative and neuroprotective effects may prolong neuronal cell survival, and concluded, "In areas where it is legal to do so, marijuana should be considered in the pharmacological management of ALS."

(2) E. de Lago, J. Fernández-Ruiz, "Cannabinoids and Neuroprotection in Motor-Related Disorders," *CNS and Neurological Disorders — Drug Targets* 6, no. 6 (2007): 377-87.

This review explored in detail the mechanisms of cannabinoid neuroprotection related to a variety of disorders, including ALS.

(3) Dagmar Amtmann, et al., "Survey of Cannabis Use in Patients With Amyotrophic Lateral Sclerosis," *American Journal of Hospice and Palliative Medicine*, March-April 2004.

This anonymous survey of 131 people with ALS found that 10 percent had reported using marijuana in the past year, reporting relief of multiple symptoms. The authors concluded, "... results indicate that cannabis may be moderately effective at reducing symptoms of appetite loss, depression, pain, spasticity, and drooling."

Crohn's disease

Crohn's disease is marked by inflammation of the digestive tract, most commonly the lower part of the small intestine. It can cause severe abdominal pain, nausea, and weight loss – all symptoms that marijuana can help mitigate, as noted in other sections of this document. Preclinical research has demonstrated the role of the endocannabinoid system, the body's natural, marijuana-like chemicals, in protecting the GI tract, providing support for anecdotal reports of relief.

References

(1) J.E. Joy, S.J. Watson, and J.A. Benson, "Marijuana and Medicine: Assessing the Science Base" (National Academy Press, 1999).

"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."

(2) F. Massa, M. Storr, and B. Lutz, "The Endocannabinoid System in the Physiology and Pathophysiology of the Gastrointestinal Tract," *Journal of Molecular Medicine* 83, no. 12 (2005): 944-54.

This review article noted, "Under pathophysiological conditions induced experimentally in rodents, the endocannabinoid system conveys protection to the GI tract (e.g. from inflammation and abnormally high gastric and enteric secretions). Such protective activities are largely in agreement with anecdotal reports from folk medicine on the use of Cannabis sativa extracts by subjects suffering from various GI disorders."

Agitation of Alzheimer's disease

In preliminary research, THC has been shown to reduce agitation in severely demented Alzheimer's patients. Preclinical research also suggests that marijuana components may help retard the progression of Alzheimer's disease.

References

(1) S. Walther, et al., "Delta-9-Tetrahydrocannabinol for Nighttime Agitation in Severe Dementia," *Psychopharmacology* (Berl) 185, no. 4 (2006): 524-8.

This open-label pilot study reported, "Compared to baseline, dronabinol led to a reduction in nocturnal motor activity ($P=0.028$). These findings were corroborated by improvements in Neuropsychiatric Inventory total score ($P=0.027$) as well as in subscores for agitation, aberrant motor, and nighttime behaviors ($P<0.05$). No side effects were observed."

(2) G. Esposito, et al., "The Marijuana Component Cannabidiol Inhibits Beta-Amyloid-Induced Tau Protein Hyperphosphorylation Through Wnt/beta-catenin Pathway Rescue in PC12 Cells," *Journal of Molecular Medicine* 84, no. 3 (2006): 253-8.

"Here, we report that cannabidiol inhibits hyperphosphorylation of tau protein in Abeta-stimulated PC12 neuronal cells, which is one of the most representative hallmarks in AD. ... These results provide new molecular insight regarding the neuroprotective effect of cannabidiol and suggest its possible role in the pharmacological management of AD, especially in view of its low toxicity in humans."

Multiple sclerosis, seizures, muscle spasms

Clinical trials involving whole plant marijuana and various marijuana extracts have found that patients reported relief of muscle stiffness, pain,and spasticity.

Considerable data from animal models, as well as some human clinical evidence, suggest a role for marijuana in the treatment of seizure disorders such as epilepsy.

Multiple Sclerosis References

(1) Jody Corey-Bloom, et al., "Smoked cannabis for spasticity in multiple sclerosis: a randomized, placebo-controlled trial," *Canadian Medical Association Journal* 184, no. 10 (2012): 1143–1150.

This placebo-controlled, crossover trial of 37 participants with multiple sclerosis and spasticity found that smoked cannabis was superior to placebos in reducing pain and spasticity. The authors recommended that, "Future studies should examine whether different doses can result in similar beneficial effects with less cognitive impact." There were no serious adverse events during the trial.

(1) J. Zajicek, et al., "Multiple Sclerosis and Extract of Cannabis: results of the MUSEC trial," *Journal of Neurology, Neurosurgery & Psychiatry* 83: no 11 (2012): 1125-1132**.**

This double-blind, placebo-controlled, phase III clinical trial found that patients found almost twice as much relief from muscle stiffness from oral cannabis extract than from the placebo.

(2) A Novotna, et al., "A randomized, double-blind, placebo-controlled, parallel-group, enriched-design study of nabiximols* (Sativex(®)), as add-on therapy, in subjects with refractory spasticity caused by multiple sclerosis," *European Journal of Neurology* 18, no. 9 (2011): 1122-1131.

This phase III double-blind, placebo-controlled study on patients whose multiple sclerosis spasticity was not fully alleviated by other therapies found that more than 47% had their spasticity improve by at least 20% during the first four weeks of the trial. This trial involved Sativex, which is a cannabis extract that is approved for multiple sclerosis spasticity in several European countries, New Zealand, and Canada, but which is not legally available to patients in the United States.

(3) J. Zajicek, et al., "Cannabinoids for Treatment of Spasticity and Other Symptoms Related to Multiple Sclerosis (CAMS Study): Multicentre Randomised Placebo-Controlled Trial," *The Lancet* 362 (2003): 1517-26.

This trial, using an oral cannabis extract, reported "evidence of a treatment effect on patient-reported spasticity and pain (p=0·003), with improvement in spasticity reported in 61% (n=121, 95% CI 54·6–68·2), 60% (n=108, 52·5– 66·8), and 46% (n=91, 39·0–52·9) of participants on cannabis extract, 9-THC, and placebo, respectively."

(4) D.T. Wade, et al., "Long-Term Use of a Cannabis-Based Medicine in the Treatment of Spasticity and Other Symptoms in Multiple Sclerosis" *Multiple Sclerosis* 12 (2006): 639-45.

In this long-term follow-up of a clinical trial of a marijuana-based oral spray, patients were followed for as much as 82 weeks. The marijuana spray demonstrated long-term relief of spasticity, pain, and bladder issues related to MS, "without unacceptable adverse effects."

Epilepsy and Other References

(1) Alsasua del Valle, "Implication of Cannabinoids in Neurological Diseases," *Cellular and Molecular Neurobiology* 26, no. 4-6 (2006): 579-91

This wide-ranging review of the neurobiology of marijuana and its constituents in relation to neuroprotection and neurological disease noted, "It has been known for centuries that exogenous cannabinoids have anti-convulsant activity."

(2) K. Mortati, B. Dworetzky, and O. Devinsky, "Marijuana: an Effective Antiepileptic Treatment in Partial Epilepsy? A Case Report and Review of the Literature," *Reviews in Neurological Diseases* 4, no. 2 (2007): 103-6.

Mortati and colleagues reported the case of a 45-year-old male with cerebral palsy and epilepsy "who showed marked improvement with the use of marijuana." The authors reviewed the current literature and concluded, "Although more data are needed, animal studies and clinical experience suggest that marijuana or its active constituents may have a place in the treatment of partial epilepsy."

(3) D.W. Gross, et al., "Marijuana Use and Epilepsy: Prevalence in Patients of a Tertiary Care Epilepsy Center," *Neurology* 62, no. 11 (2004): 2095-7.

In this patient survey, of 28 epileptic patients who actively used marijuana, 68% reported that it improved severity of seizures, and 54% reported improvement of seizure frequency. None reported that it worsened these symptoms.

Nail-Patella Syndrome

Nail-patella syndrome is a rare genetic disorder involving the bones, joints, and connective tissue. Patients may have problems due to limitation of joint mobility, dislocation or both, especially at the elbow and knee where osteoarthritis may eventually occur. Nail-patella patients are also at increased risk for glaucoma and kidney problems. While there is a lack of controlled research on marijuana and nail-patella, one of the three patients who still receive medical marijuana from the federal government – George McMahon – suffers from the condition, and his case is described in the one study of these patients that has been published. This article notes: "On May 10, 2000, a letter to FDA noted the patient continued to do well on the therapy, smoking 8-10 cigarettes per day without other medication. He continued to function well using a cane and occasionally a wheelchair when bothered by spasms and nausea. At present, he utilizes about 7 grams a day or 1/4 ounce of NIDA material that is 3.75% THC ... He indicates that he has been short on his supply 3 times in 10 years, generally for 1-2 weeks, secondary to lack of

supply or paperwork problems. When this occurs he suffers more nausea and muscle spasms and is less active as a consequence."

References

(1) E. Russo, et al., "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, no. 1 (2002): 3-57.**

Post-Traumatic Stress Disorder

Post-traumatic stress disorder involves a person developing characteristic symptoms — such as flashbacks, numbing, and avoidance — after personally experiencing an extremely traumatic stressor. Available treatments are often not effective. About 3,700 of New Mexico's approximately 8,900 registered medical marijuana patients have a diagnosis of PTSD. Unfortunately, there has been limited research on whole plant marijuana and PTSD, including due to the U.S. federal government refusing to provide marijuana to an FDA-approved and institutional review board-approved study. However, there are clinical trials ongoing in Israel, where an open pilot study found marijuana effective at alleviating symptoms of combat veterans. In addition, other human and animal evidence supports the therapeutic potential of cannabis and cannabinoids in treating PTSD symptoms.

References

(1) Torsten Passie et al., "Mitigation of post-traumatic stress symptom by Cannabis resin: A review of the clinical and neurobiological evidence," ***Drug Testing and Analysis*** **(2012): 649-659**

This is a case report of a 19-year-old patient who had severe PTSD, including panic attacks and self-mutilation. He discovered that smoking cannabis resin dramatically reduced his major symptoms. As the abstract explains, "The major part of this review is concerned with the clinical and preclinical neurobiological evidence in order to offer a potential explanation of these effects on symptom reduction in PTSD." It noted, "Evidence is increasingly accumulating that cannabinoids might play a role in fear extinction and antidepressive effects."

(2) George Fraser, "The Use of a Synthetic Cannabinoid in the Management of Treatment-Resistant Nightmares in Posttraumatic Stress Disorder (PTSD)," ***CNS Neuroscience & Therapeutics*** **15, no 1. (2009): 84-88.**

This study involved administering a naboline — a prescription drug made of a synthetic cannabinoid (component of marijuana) to patients with treatment-resistant nightmares who had PTSD. They reported, "The majority of patients (72%) receiving nabilone experienced either cessation of nightmares or a significant reduction in nightmare intensity. Subjective improvement in sleep time, the quality of sleep, and the reduction of day-time flashbacks and nightsweats were also noted by some patients."

(3) Eti Ganon-Elaza and Irit Akirav, "Cannabinoids Prevent the Development of Behavioral and Endocrine Alterations in a Rat Model of Intense Stress," *Neuropsychopharmacology* (2012): 456–466.

In this study, synthetic marijuana was given to rats after a traumatic event. It was able to block symptoms of PTSD after the rodents were exposed to extreme stress. All of the rats experienced anxiety, but symptoms of PTSD disappeared in the group given marijuana within the 2 or 24 hour time-frame. The findings included that, "cannabinoids could serve as a pharmacological treatment of stress- and trauma-related disorder.

Vaporization as an Alternative to Smoking

One often-mentioned objection to medical use of marijuana is the respiratory risk associated with smoking. For this reason, the Institute of Medicine urged development of a "nonsmoked, rapid-onset cannabinoid delivery system." Published research suggests that vaporization — in which marijuana is heated to the point where cannabinoid vapors are released, but not to the point of combustion — represents a viable solution to this problem.

References

(1) A. Hazekamp, et al., "Evaluation of a Vaporizing Device (Volcano) for the Pulmonary Administration of Tetrahydrocannabinol," *Journal of Pharmaceutical Sciences* 95, no. 6 (2006): 1308-17.

This laboratory test of a commercially available vaporizer known as the Volcano used language strikingly similar to that of the Institute of Medicine, concluding, "Our results show that with the Volcano a safe and effective cannabinoid delivery system seems to be available to patients."

(2) D.I. Abrams, et al., "Vaporization as a Smokeless Cannabis Delivery System: A Pilot Study," *Clinical Pharmacology and Therapeutics* 282, no. 5 (2007): 572-8.

In this clinical trial, again using the Volcano vaporizer, volunteers were randomly assigned to either smoke or vaporize marijuana of three different strengths. Vaporization was comparable to smoking in terms of THC delivery, but dramatically reduced the amount of carbon monoxide, indicating "little or no exposure to gaseous combustion toxins." The researchers concluded that vaporization "therefore is expected to be much safer than smoking marijuana cigarettes."

(3) M. Earleywine and S.S. Barnwell, "Decreased Respiratory Symptoms in Cannabis Users Who Vaporize," *Harm Reduction Journal* 4, no. 11 (2007).

This Internet sample of nearly 7,000 participants compared self-reported respiratory symptoms among marijuana users whose primary method was smoking with those whose primary method was vaporization, reporting, "use of a vaporizer predicted fewer respiratory symptoms even when age, sex, cigarette smoking, and amount of cannabis used were taken into account."