



MEDICAL MARIJUANA RESEARCH: WHAT DOES THE EVIDENCE SAY?

Cannabis (marijuana) is currently classified as a schedule I drug meaning it has a high potential for abuse and no accepted medical value. Other schedule I drugs include heroin, LSD and PCP.

However, more than 6,500 reports and journal articles from around the world support the medical value of marijuana. In addition, dozens of public health organizations have endorsed medical use of marijuana including the AIDS Action Council, the American Public Health Association, the American Academy of Family Physicians, the American Nurses Association, the Federation of American Scientists, Kaiser Permanente, the New England Journal of Medicine, the National Association for Public Health Policy, the California Medical Association, the Whitman-Walker Clinic, the Lymphoma Foundation of America, and many more.

Here is a sample of the latest research.

CANNABIS SMOKE DOES NO HARM

1. Cannabis Smoking Does Not Cause Cancer

Sources: Morgenstern H, et al. "Marijuana use and cancers of the lung and upper aerodigestive tract: results of a case-control study." Presentation at the ICRS Conference on Cannabinoids, 24-27 June, 2005, Clearwater, USA

According to Dr. Donald Tashkin and his colleagues at the University of California in Los Angeles results from a case-controlled study demonstrate that even heavy and long-term smoking of cannabis is not associated with lung cancer and other types of upper aerodigestive tract cancers.

The study included 1,209 residents of Los Angeles aged 18-59 with cancer (611 lung, 403 oral/pharyngeal, 90 laryngeal, and 108 esophageal). Interviewers collected lifetime histories of cannabis, tobacco, alcohol and other drug use, and data on other factors that may influence cancer risk, including diet, occupational exposures, and family history of cancer. Exposure to cannabis was measured in joint years (1 joint year = 365 joints). The cancer patients were compared to 1,040 cancer-free controls. Among the controls 46 per cent had never used cannabis, 31 per cent had used it for less than one joint year, 12 per cent for 10-30 joint years, 2 per cent for 30-60 joint years, and 3 per cent for more than 60 joint years.

Compared with subjects who had used less than one joint year, the risk for lung cancer was 0.78 for 1-10 joint years, 0.74 for 10-30 joint years, 0.85 for 30-60 joint years, and 0.81 for more than 60 joint years. A risk below 1.0 means that the risk for cannabis users was slightly lower than for non-users. Similar results were obtained for the other cancer sites. There was no dose-response relationship of cancer risk, which means that there was no increased risks for more intensive users.

2. Cannabis Does Not Accelerate HIV-infection

Sources: Abrams DI, Hilton JF, Leiser RJ, Shade SB, Elbeik TA, Aweeka FT, Benowitz NL, Bredt BM, Kosel B, Aberg JA, Deeks SG, Mitchell TF, Mulligan K, Bacchetti P, McCune JM, Schambelan M. "Short-term Effects of Cannabinoids in Patients with HIV-1 Infection: A Randomized, Placebo-controlled Clinical Trial." *Annals of Internal Medicine* 2003;139(4):258-266

According to a study led by Dr. Donald Abrams at the University of California in San Francisco, smoked cannabis and oral THC given over a course of 21 days did not adversely affect CD4+ cell counts or viral loads in HIV-infected patients. Instead, researchers found that there was a small non-significant positive effect of cannabis and THC on these laboratory parameters compared to placebo. Cannabis and THC also increased appetite and caused weight gain.

All of the patients had been receiving the same anti-HIV medication for at least 8 weeks before the study began. 67 patients with HIV-1 infection were randomly assigned to a 3.95%-tetrahydrocannabinol marijuana cigarette, a 2.5-mg dronabinol (delta-9-tetrahydrocannabinol) capsule, or a placebo capsule three times daily before meals. Although not statistically significant, compared with placebo use the application of marijuana and THC was associated with a slight drop in viral load of 15% and 8%, respectively.

CANNABIS PROVIDES SYMPTOMATIC RELIEF FOR HIV/AIDS, MS and LUNG DISEASE

1. Smoked Cannabis Reduces HIV-Related Painful Peripheral Neuropathy

Sources: Abrams DI, Jay CA, Vizoso H, Shade SB, Reda H, Press S, Kelly ME, Rowbotham M, Petersen K. "Smoked cannabis therapy for HIV-related painful peripheral neuropathy: results of a randomized, placebo-controlled clinical trial." Abstract, IACM 3rd Conference on Cannabinoids in Medicine, September 9-10, 2005, Leiden

The results of a randomized, placebo-controlled clinical trial demonstrates that smoked marijuana is effective in reducing HIV-related chronic ongoing neuropathic and acute pain. Neuropathy is a nerve disease, which often results in numbness, weakness, and spontaneous muscle twitching. Neuropathy is a serious medical problem with unsatisfactory treatment options.

In a clinical trial at the University of California, research participants smoked one marijuana cigarette containing 3.56% THC or a placebo three times daily for 5 days. Researchers concluded that smoked cannabis provided greater than a 30% reduction of pain in 13 of 25 randomized patients, who averaged 6 years of neuropathic pain.

2. Cannabis Reduces Neuropathic Pain In Multiple Sclerosis Patients

Sources: Rog DJ, Nurmikko TJ, Friede T, Young CA. "Randomized, controlled trial of cannabis-based medicine in central pain in multiple sclerosis". *Neurology* 2005;65(6):812-9;

Researchers for the Walton Centre for Neurology and Neurosurgery in Liverpool conducted a single-center, 5-week, randomized, placebo-controlled group trial on patients with MS of a whole-plant cannabis-based medicine delivered via an oral spray. Each spray delivered 2.7mg of THC and 2.5mg of CBD (THC and CBD are two active compounds produced naturally by the cannabis plant), and patients could gradually self-titrate to a maximum of 48 sprays in 24 hours.

The researchers concluded that the cannabis-based extract Sativex, manufactured by GW Pharmaceuticals, is effective in reducing central neuropathic pain and sleep disturbance in people with multiple sclerosis (MS).

Based on these study results, which were published now in the journal *Neurology*, Sativex was approved as a prescription medicine in Canada for the symptomatic relief of neuropathic pain in adults with MS and is available in pharmacies since 20 June 2005.

3. THC Is Effective in Appetite and Weight Loss in Severe Lung Disease

Source: Lecture by K-C Bergmann on 17 March 2005 at the Meeting of the German Society of Pulmonology in Berlin

Patients with the severe lung disease (COPD, chronic obstructive pulmonary disease) often suffer from appetite loss and cachexia (weight loss) resulting in reduced general well-being and early mortality. In an open clinical study at the Clinic for Allergies and Asthma in Bad Lippspringe, Germany, 18 COPD patients aged 49 to 81 years with a mean body weight of 48.5 kg received 3.3-4.2mg of THC two times daily for 16 days as oily drops delivered by THC Pharm, one-half an hour before breakfast and dinner. In the six months before entering the clinic 7 participants had a constant body weight and 11 lost 2.3 kg on average.

After 16 days of treatment, results indicated a considerable improvement of appetite, general well-being and functional performance (36 per cent mean increase in walking distance) and an average gain in body weight of 1.5 kg, which is significant given the short treatment period.

CANNABIS COMPOUNDS AND THE POTENTIAL FOR CURES

1. Cannabinoids Reduce the Progression of Alzheimer's Disease in Animals

Sources: Ramirez BG, et al. "Prevention of Alzheimer's disease pathology by cannabinoids: neuroprotection mediated by blockade of microglial activation." Journal of Neuroscience 2005;25(8):1904-13;

Research by scientists of Madrid's Complutense University and the Cajal Institute published in the *Journal of Neuroscience* has demonstrated that cannabinoids can reduce pathological processes associated with Alzheimer's disease. Researchers hope that cannabinoids may be used to develop new drug therapies against the disease.

They began by comparing the brain tissue of patients who died from Alzheimer's disease against the brain tissue of healthy people who had died at a similar age. The researchers found a dramatically reduced functioning of cannabinoid receptors in diseased brain tissue and markers of microglia activation. Microglia activate the brain's immune response and are found near the plaque deposits associated with Alzheimer's disease. When active, microglia cause inflammation. Nerve cells with cannabinoid-1 receptors (CB1), present in high numbers in control subjects, were greatly reduced in areas of microglial activation.

Next, rats were injected with amyloid-beta peptide. This protein plays an important role in Alzheimer's disease, since increased brain levels of amyloid-beta are supposed to result in aggregation of this protein to form plaques. Animals who also received different cannabinoids performed better in tests of their mental functioning. Analyses showed that cannabinoids had prevented microglial activation and thus had reduced inflammation. These effects were also mediated by cannabinoids that only bind to CB2 receptors. Researchers concluded: "Our results indicate that cannabinoid receptors are important in the pathology of AD and that cannabinoids succeed in preventing the neurodegenerative process occurring in the disease."

2. Derivatives of Cannabis May Unlock Anti-Cancer Treatment

Source: Kogan, N.M., Blaquez, C., Gallily, R., Guzman, M., and Mechoulam, R. "Quinone Type Cannabinoids as AntiCancer Compunds." Abstract, IACM 3rd Conference on Cannabinoids in Medicine, September 9-10, 2005, Leiden

Researchers at the Hebrew University in Israel have demonstrated that derivatives of the cannabis plant can be effective in arresting cancerous growths in laboratory and animal tests. Natalya Kogan, a Ph.D student working under the direction of Professors Raphael Mechoulam and Michael Schlesinger, has developed new compounds- known as quinonoid cannabinoids – that parallel a group of anti-cancer drugs, the best known which is daunomycin. However, whereas daunomycin is toxic to the heart the quinonoid compounds are significantly less toxic. The development of quinonoid compounds that display anticancer activity, but are less toxic is a major therapeutic goal.

Researchers are particularly interested in the cannabinoid quinone known as HU-331, which was very effective against human cancer cell lines in-vitro and also against in-vivo tumor grafts in nude mice. At 35 days after cancer cell injection, the tumors in the treated group were half the size of the tumors in the control group. Researchers conclude that HU-331 has a high potential as a new anti-cancer drug.

3. Cannabinoids May Promote the Development of New Brain Cells

Sources: Jiang W, Zhang Y, Xiao L, Van Cleemput J, Ji SP, Bai G, Zhang X. "Cannabinoids promote embryonic and adult hippocampus neurogenesis and produce anxiolytic- and antidepressant-like effects." Journal of Clinical Investigation. October, 2005

According to animal research at the University of Saskatchewan, Canada, cannabinoids that bind to the CB1 receptor promote the development of new nerve cells in the hippocampus, a brain region that is very important for memory and behavior. This cannabinoid effect may decrease anxiety and depression.

Scientists used the synthetic cannabinoid HU210 that acts similar to THC on CB1 receptors in the brain. Chronic, but not acute treatment with this cannabinoid promoted nerve cell proliferation in the hippocampus of adult rats and exerted anxiolytic- and antidepressant-like effects.

Other illegal and legal drugs, including opiates, alcohol, nicotine and cocaine, have been shown to suppress the formation of new brain cells when used chronically, but the effect of cannabis on that process was uncertain. Cannabis appears "to be the only illicit drug whose capacity to produce increased ... neurons is positively correlated with its (anti-anxiety) and anti-depressant-like effects," Dr. Xia Zhang and his colleagues wrote in an article for the November issue of the Journal of Clinical Investigation, of which an advance was posted online on 13 October 2005.