

A Handy List for Doctors and Patients

Which Conditions Might Cannabis Help Treat?

The medical marijuana initiative passed by California voters in 1996 authorizes physicians to approve the use of cannabis “in the treatment of cancer, anorexia, AIDS, chronic pain, spasticity, glaucoma, arthritis, migraine, or any other illness for which marijuana provides relief.” The voters’ understanding that cannabis is a remarkably versatile medicine has been confirmed in recent years by researchers who have identified the following conditions as likely targets for cannabis-based medicine.

AIDS Wasting Syndrome

AIDS (Acquired Immune Deficiency Syndrome) wasting syndrome was a very frequent complication of HIV infection prior to the advent of protease-inhibitor drugs (1), and has been associated with major weight loss and cachexia, serving to further debilitate its victims, already weakened by immune system failure and opportunistic infections. Cannabis has been a frequently employed alternative medicine for the condition, particularly in the USA (2), because of its reported benefits on appetite and amelioration of other AIDS symptoms. In the rest of the world, where such medications are seldom affordable, AIDS wasting remains a common problem to the extent that it is known in Africa as ‘slim disease’ (3).

In a randomized trial (4) in AIDS patients, 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. The possible benefit of cannabis in AIDS made it one of the lead indications for such treatment in the judgment of the American Institute of Medicine in their study (5).

A safety study was carried out in HIV positive patients to assess whether oral THC or smoked cannabis would produce immunological damage in patients on protease-inhibitor medication (6). No problems were noted with HIV viral loads or CD4 cell counts. The study was subsequently published in expanded form (7), and some weight gain was also observed in THC and cannabis-treated subjects as compared to controls.

It is likely that cannabis-based medicine extracts will have some considerable contribution to offer in future clinical trials in HIV/AIDS.

References

1. Bayer R. Medicinal uses of marijuana [letter; comment]. *Ann Intern Med* 1997;127(12):1134; discussion 1135.
2. Sidney S. Marijuana use in HIV-positive and AIDS patients: Results of an anonymous mail survey. *Journal of Cannabis Therapeutics* 2001;1(3-4):35-43r.
3. Russo EB. Cannabis therapeutics in HIV/AIDS. Binghamton, NY: Haworth Press; 2001.
4. Beal JE, Olson R, Laubenstein L, Morales JO, Bellman P, Yangco B, Lefkowitz L, Plasse T, Shepard KV (1995). Dronabinol as a treatment for anorexia associated with weight loss in patients with AIDS. *Journal of Pain & Symptom Management*, 10, 89-97
5. Joy JE, Watson SJ, Benson JA, Jr. Marijuana and medicine: Assessing the science base. Washington, DC: Institute of Medicine; 1999.
6. Bredt BM, Higuera-Alhino D, Shade SB, Hebert SJ, McCune JM, Abrams DI. Short-term effects of cannabinoids on immune phenotype and function in HIV-1-infected patients. *J Clin Pharmacol* 2002;42(11 Suppl):82S-89S.
7. Abrams DI, Hilton JF, Leiser RJ, Shade SB, Elbeik TA, Awecka FT, et al. Short-term effects of cannabinoids in patients with HIV-1 infection. A randomized, placebo-controlled clinical trial. *Ann Intern Med* 2003;139:258-266.

Arthritis

Arthritis refers to a large group of disorders that affect joints and soft tissues to produce chronic pain. The two most common forms are osteoarthritis (OA), a disease of aging and wear and tear) and rheumatoid arthritis (RA), a common autoimmune disorder producing joint pain, swelling and deformity. Cannabis may represent a new treatment option in both categories.

Cannabis has been employed to treat musculoskeletal pain for at least 4000 years, dating to the Ancient Assyrians (1). Marcandier’s 1758 work, *Traité du Chanvre* (2) is of particular interest because European cannabis of that time was fibre hemp that would be devoid of THC, but rich in cannabidiol (CBD).

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Very recently, the role of CBD as an anti-inflammatory and immunomodulatory agent potentially useful in treating autoimmune conditions has been of great interest. Malfait et al. (3) explored its effect in a mouse model of rheumatoid arthritis, and discovered that it arrested progression of the disease and protected joints against severe damage. CBD also blocked the release of tissue necrosis factor-alpha (TNF-a), a key target in modern approaches to RA treatment. These effects alongside anti-inflammatory and analgesic benefits of CBD and THC may represent a novel approach to this difficult clinical problem.

Clinical studies of GW’s cannabis based medicine extracts containing THC and CBD are currently in Phase II trials in RA patients.



References

1. Russo EB. Role of cannabis and cannabinoids in pain management. In: Weiner RS, editor. *Pain management: A practical guide for clinicians*. 6th ed. Boca Raton, FL: CRC Press; 2002. p. 357-375. http://www.montanorml.org/docs/Russo-AAPM_chapter.pdf
2. Marcandier M. *Treatise on hemp*. London: T. Becket and P.A. de Hondt; 1764.
3. Malfait AM, Gallily R, Sumariwalla PF, Malik AS, Andreacos E, Mechoulam R, et al. The nonpsychoactive cannabis constituent cannabidiol is an oral anti-arthritis therapeutic in murine collagen-induced arthritis. *Proc Natl Acad Sci U S A* 2000;97(17):9561-6.

Asthma

The use of cannabis in asthma dates to the traditional medicine of India (1), but was also rediscovered in Western medicine in the 19th century (2, 3).

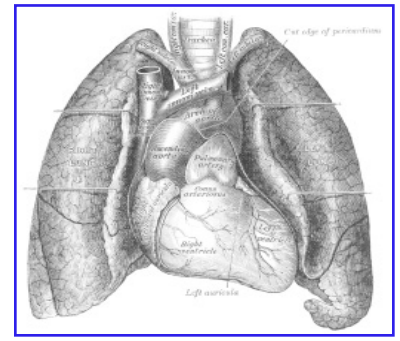
Although it may seem counter-intuitive, cannabis cigarettes such as those marketed by Grimault & Cie to treat asthma were popularly utilized for their bronchodilatory effects. Studies in the 1970s confirmed this benefit of cannabis (4), and in one study (5), inhaled THC produced an increase in FEV1 (forced expiratory volume in 1 second) after one hour that was equal to that of salbutamol. It has now been demonstrated that endocannabinoids regulate broncho-dilation and constriction (reviewed (6)).

Problems remain with the concept, however. Almost no modern authorities feel that asthmatics should smoke cannabis for asthma (7), although it seems that even chronic usage may not lead to emphysematous degeneration (8). Use of THC inhalation in isolation, however, has been proved to induce cough and lung irritation even without concomitant smoke.

Modern research has turned to alternative delivery systems. One, that of cannabis vapourisation, may be applicable (9-11), but to date, potential carcinogens in tobacco smoke have not been totally eliminated. The development of whole cannabis extract inhalers, as currently being researched by GW Pharmaceuticals (12-14) may offer advantages. Certainly, there is rationale behind inclusion of cannabis terpenoids, that have additional anti-inflammatory properties in their own right (15), especially pinene, that also demonstrates a bronchodilatory benefit (16). Further research is clearly required.

References

1. Nadkarni KM. *Indian materia medica*. 3rd ed. Bombay: Popular Prakashan; 1976.
2. McMeens RR. Report of the Ohio State Medical Committee on Cannabis indica . White Sulphur Springs, OH: Ohio State Medical Society; 1860 June12-14, 1860.
3. Mattison JB. Cannabis indica as an anodyne and hypnotic. *St. Louis Medical and Surgical Journal* 1891;61:265-271.
4. Tashkin DP, Shapiro BJ, Lee YE, Harper CE. Effects of smoked marijuana in experimentally induced asthma. *Am Rev Respir Dis* 1975;112(3):377-86.
5. Williams SJ, Hartley JP, Graham JD. Bronchodilator effect of delta1-tetrahydrocannabinol administered by aerosol of asthmatic patients. *Thorax* 1976;31(6):720-3.
6. Pertwee RG, Ross RA. Cannabinoid receptors and their ligands. *Prostaglandins Leukot Essent Fatty Acids* 2002;66(2-3):101-21.
7. Tashkin DP. Respiratory risks from marijuana smoking. In: Grotenhermen F, Russo E, editors. *Cannabis and cannabinoids: Pharmacology, toxicology and therapeutic potential*. Binghamton, NY: Haworth Press; 2001.
8. Tashkin DP, Simmons MS, Sherrill DL, Coulson AH. Heavy habitual marijuana smoking does not cause an accelerated decline in FEV1 with age. *Am J Respir Crit Care Med* 1997;155(1):141-8.
9. Gieringer D. Why marijuana smoke harm reduction? *Bulletin of the Multidisciplinary Association for Psychedelic Studies* 1996;6(64-66).
10. Gieringer DH. Cannabis “vaporization”: A promising strategy for smoke harm reduction. *Journal of Cannabis Therapeutics* 2001;1(3-4):in press.
11. Gieringer D, St. Laurent J, Goodrich S. Cannabis vaporizer combines efficient delivery of THC with effective suppression Of pyrolytic compounds. *Journal of Cannabis Therapeutics* 2004;4(1):In Press.
12. Whittle BA, Guy GW, Robson P. Prospects for new cannabis-based prescription



medicines. *Journal of Cannabis Therapeutics* 2001;1(3-4):183-205.

13. Whittle BA, Guy GW. Development of cannabis-based medicines; risk, benefit and serendipity. In: Whittle BA, Guy GW, Robson P, editors. *Medicinal uses of cannabis and cannabinoids*. London: Pharmaceutical Press; 2003.

14. Whittle BA, Guy GW, Robson P. *Cannabis and cannabinoids as medicines*. London: Pharmaceutical Press; 2003.

15. McPartland JM, Russo EB. Cannabis and cannabis extracts: Greater than the sum of their parts? *Journal of Cannabis Therapeutics* 2001;1(3-4):103-132.

www.montanorml.org/docs/McPartland-Russo-JCANT-1-3-4-2001.pdf

16. Falk AA, Hagberg MT, Lof AE, Wigaeus-Hjelm EM, Wang ZP. Uptake, distribution and elimination of alpha-pinene in man after exposure by inhalation. *Scand J Work Environ Health* 1990;16(5):372-8.

Crohn's Disease/ Inflammatory Bowel Disease

Crohn’s disease and ulcerative colitis are chronic, inflammatory conditions of the gastrointestinal tract of autoimmune origin. While ulcerative colitis preferentially affects the colon and lower small intestine, Crohn’s disease may affect any portion of the GI tract. Both are associated with tissue ulceration, bleeding, cramping, diarrhoea, weight loss, and the possibility of bowel obstruction with a resulting need for surgery. (1)

A recent epidemiological study (2) has examined the burden of gastrointestinal diseases in UK patients and found that both diseases are becoming more common. Prevalence of ulcerative colitis by age 30 for people born in 1970 is 30/10,000. The prevalence of Crohn’s disease by age 30 was 38/10,000. Both Crohn’s and ulcerative colitis are associated with considerable psychiatric comorbidity including depression, anxiety, somatisation, and decreased quality of life measures (3).

The long historical usage of cannabis for gastrointestinal complaints has been reviewed (4). Numerous studies in the 1970s indicated that THC slowed intestinal passage of a charcoal meal in rodents. Cannabidiol (CBD) had little effect of its own, but synergized the effects of THC (5). The most topical review of cannabinoid effects on the gastrointestinal tract is that of Pertwee (6). To summarise the major points:

1) The enteric nervous systems of mammals express CB1 and stimulation depresses gastrointestinal motility, especially through inhibition of contractile neurotransmitter release.

2) Observed effects include delayed gastric emptying, some decrease in peptic acid production, and slowed enteric motility, inhibition of stimulated acetylcholine release, peristalsis, and non-adrenergic non-cholinergic (NANC) contractions of smooth muscle, whether circular or longitudinal.

3) These effects are mediated at the brain level as well as in the GI tract

4) These effects are opposed by CB1

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