Medical Marijuana - What's It Good For?

Interest in medical marijuana is growing steadily, fanned by a large political movement that aims to increase its availability and legality. But what's it actually good for? Inaccurate, uncited memes claiming its efficacy in treating everything from cancer to epilepsy travel on social media like wildfire, but what does the science actually say?

Marijuana, or *Cannabis sativa*, is an annual plant originally from Central Asia that has been used for medicinal purposes for at least 3,000 years. The biologically active compounds found in the plant are called cannabinoids; at least 66 have been identified so far. These interact with two types of receptor; CB1 receptors which are found predominantly on cells in the brain and spinal cord, and CB2 which are found in various immune cells. The most potent cannabinoid is thought to be delta-9-tetrahydrocannabinol (THC).

It is thought that cannabinoids may be useful in treating a variety of ailments, namely glaucoma, pain, nausea, muscle spasms and loss of appetite. It is also being investigated in cancer patients as a way to alleviate the side effects of cancer therapy, but some laboratory tests are also investigating antitumor properties.

Stimulating Appetite

Cannabinoids such as THC have been shown in numerous animal studies to increase food consumption and some human trials have also shown positive results. For example, a study comparing THC with a placebo in cancer patients found that those taking THC had a better appetite and sense of taste, and although they didn't consume more calories they felt more relaxed and had a better quality of sleep compared to the placebo group. Another study investigating the FDA-approved synthetic cannabinoid (THC) drug dronabinol in HIV/AIDS patients presenting weight loss found that those taking THC ate more than controls and stopped losing weight. However, in a study comparing dronabinol with a standard drug (megestrol) in cancer patients presenting loss of appetite, researchers found that dronabinol was not as effective as megestrol in increasing appetite or weight gain.

How does it stimulate appetite? The CB1 receptor is active in numerous areas of the body that are known to stimulate eating behavior, such as the hypothalamus and limbic forebrain, and also certain areas in the stomach and intestine. THC can exert effects by mimicking endogenous substances (called endocannabinoids) that are naturally found in the body.

Nausea and Vomiting

There have been numerous studies investigating the ability of cannabinoids to reduce and nausea and vomiting associated with chemotherapy. A 2001 systematic review of 30 studies involving synthetic cannabinoids (dronabinol, nabilone or levonantradol) compared with a placebo or an active control (a non-cannabinoid drug) found that the cannabinoids were more effective than the active control or the placebo at reducing vomiting and nausea. Furthermore, patients demonstrated a preference for the cannabinoid drugs over the placebo and the active control drugs, and they presented limited side-effects.

How do they work? The endocannabinoid system (the name for the group of molecules and receptors such as CB1 and CB2 that are collectively involved in a variety of physiological processes and mediating the psychoactive effects of marijuana) is key to modulating numerous systems such as reward pathways, pain perception and emesis (vomiting). Areas of the brain involved in chemotherapy induced nausea and vomiting are higher cortical and limbic regions that can influence the stimulation or suppression of nausea and vomiting. CB1 receptors are found in high quantities in these areas, and drugs such as nabilone can agonize these receptors.

Pain Relief

While neither nabilone nor dronabinol are FDA approved for pain management, a few studies have shown that they may be beneficial. For example, a small 2010 study carried out by McGill University Health Centre investigated 21 adults with post-traumatic or postsurgical neuropathic pain. Participants were randomly assigned to receive cannabis at 4 potencies (0%, 2.5%, 6% or 9.4% THC) which was smoked at home three times a day. All participants used all four potencies, which were rotated throughout the duration of the study. Participants recorded pain intensity and also mood, sleep and quality of life. They found that cannabis smoked at a concentration of 9.4% THC moderately reduced pain and improved sleep, with few side-effects. Larger studies are needed to verify these results.

A 2007 study carried out by researchers from the University of California at San Francisco looked at HIV patients with peripheral neuropathy and found that a significantly higher number of patients receiving the treatment (smoking marijuana) experienced a reduction in pain compared with the placebo group.

Glaucoma

Glaucoma is a condition caused by an increase in pressure within the eye which can lead to blindness if left untreated. Cannabinoids effectively lower intraocular pressure (IOP), likely by increasing ocular blood flow through their vasorelaxant properties, and there have been a few studies since the 1970's investigating cannabis as a possible treatment for glaucoma. For example, an early and small trial in 1971 demonstrated that smoking marijuana reduced IOP but the effects only lasted 3-4 hours, limiting its usefulness when taken in this manner. However, studies have shown that while marijuana may temporarily reduce IOP, it also lowers blood pressure throughout the body, canceling out the beneficial effects.

A 1999 report by the Institute of Medicine concluded that despite the observed reduction in IOP by cannabinoids and marijuana, "…the effect is too short lived and required too high doses, and there are too many side effects to recommend lifelong use in the treatment of glaucoma. The potential harmful effects of chronic marijuana smoking outweigh its modest benefits in the treatment of glaucoma."

Epilepsy

Epilepsy, which is a neurological disorder characterized by episodic seizures, affects around 2.3 million Americans, almost half of whom live with uncontrolled seizures. The use of marijuana to treat epilepsy has a complex history. Some animal studies have demonstrated that THC can control seizures that are unresponsive to other treatments, whereas a few have also shown that it might trigger seizures. So far, there exists only one published human clinical trial demonstrating the effectiveness of marijuana in the treatment of epilepsy which was conducted in 1980 and involved only 16 participants. Half of the individuals receiving cannabidiol remained almost free of convulsions throughout the study, and a further 3 demonstrated some improvement in their condition. Only one of the placebo recipients improved.

Recent preclinical studies carried out by the University of Reading identified a particular marijuana compound that showed great promise in the treatment of epilepsy as it helped to reduce convulsions and was well-tolerated. To take this forward, a British pharmaceutical company called GW Pharmaceuticals announced last September that it would be initiating a Phase 1 Clinical Trial of a non-psychoactive cannabinoid called GWP42006 in the treatment of epilepsy.

Anecdotal evidence for the success of marijuana in controlling seizures from epilepsy sufferers also spurred a senator in the U.S. to put forward a bill allowing people in South Carolina to use CBD oil to treat epilepsy, which was passed into law two days ago.

Muscle Tension and Spasm

It has been suggested that marijuana may be able to help control both muscle stiffness and spasms, but the results are conflicting.

In 2001, a large placebo-controlled trial was initiated in Britain which set out to investigate marijuana in the treatment of multiple sclerosis. 630 people with different forms of MS were enrolled, and although the study found that oral derivatives or marijuana did not provide objective improvements in spasticity (as measured by physicians), the patients reported feeling improvements in spasticity and pain. Based on these results, a further study was initiated to investigate whether dronabinol slows the progression of MS. The study, which was published in *Lancet Neurology*, found that dronabinol did not positively affect (slow) disease progression.

However, a 2013 study led by the same researcher investigating 400 individuals with MS found that muscle stiffness improved by almost twofold in the cannabis group when compared with the placebo group.

Therefore, some inconsistencies remain in data and medics are currently unsure as to whether the benefits outweigh the side effects.

Autoimmune Diseases

A very recent study, published in *The Journal of Biological Chemistry*, has suggested that THC can suppress the immune system of rodents through epigenetic modifications (changes in gene expression that do not involve changes in DNA sequence), raising the possibility that it could be used to treat autoimmune diseases such as arthritis and multiple sclerosis. However, it is certainly early days yet and further investigation is warranted since the study left many questions unanswered, for example how long the effects of THC last for. Furthermore, their results also hinted that the infamous BRCA2 gene may be suppressed by THC. This tumor suppressor gene produces a protein involved in DNA repair, so we certainly don't want to be suppressing its activities as this can lead to cancer.

Antitumor Properties

There have been numerous laboratory and animal-based studies that have shown antitumor properties of cannabis, or more specifically THC. In particular, several studies have shown that cannabinoid administration can prevent the growth of cultured brain cancer cells and tumor xenografts (human tumor tissue transplanted into animals) in rodents, including gliomas (brain cancers derived from glial cells). One study investigating the most aggressive glioma, glioblastoma multiforme (GBM), which is also notoriously resistant to anticancer therapies, found that THC in combination with the conventional GBM therapy (temozolomide) exerted strong antitumor activities in mice with glioma xenografts. They also found that administering submaximal doses of THC and cannabidiol, another cannabinoid, together with temozolomide reduced the growth of both temozolomide-sensitive and temozolomide-resistant tumors in animal models.

Although no human studies (in the medical field) have yet been carried out on cancer and cannabis, the promising results gathered so far from cell culture and animal studies prompted researchers to initiate the *first human trials* using cannabis to treat GBM. The small pilot study will involve a double-blind, randomized placebo-controlled phase with 20 patients investigating cannabinoids in combination with temozolomide. Results have not yet been published.

A 2007 Harvard study investigating THC also found that non-toxic doses of the cannabinoid inhibited the growth and spread of lung tumor cell lines and also reduced tumor size in mice with human lung cancer xenografts when compared with a control group. However, the researchers cautioned that they did not know the exact mechanisms behind this and that further investigation is needed since some studies have actually shown that THC can *stimulate* some cancers. For example, a 2000 study published in the *Journal of Immunology* found that THC promoted lung tumor growth in mice by impeding the body's antitumor system.

There are many websites which state that "*cannabis cures cancer*"- it doesn't. As demonstrated, cannabis may have many potential applications in medicine, and laboratory and animal studies have yielded *some* promising results with

regards to cancer. But cancer is *not one single disease*, and saying it is a “cure” is wrong, especially due to conflicting results and the fact that studies so far regarding antitumor properties have not been conducted in humans.

If you'd like to find out more, check out this great review of cannabis studies conducted for a variety of medical conditions.

Marijuana is a fascinating plant, with a wide range of uses. Its use in medicine is currently being researched all around the world, and there are many situations in which it can be helpful. However, anything being touted as a "miracle" cure for *anything* should be treated with suspicion. There is no such thing as a miracle, and everything that has an effect also has side-effects. The positives and negatives to every treatment must be carefully weighed up. It is also important to not overstate the importance of laboratory and animal models - while useful and scientifically interesting, they do not prove anything with regards to human treatment. Long term, human trials are required before we can state definitively how useful medical marijuana is in treating each of these illnesses.