

# ALTHEA

INVESTING IN THE FUTURE OF WELLNESS

**ARTICLE TITLE** CANNABIS AS MEDICINE

**AUTHOR** ANNABEL NOTH

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## CANNABIS AS MEDICINE

CONTROLLED SUBSTANCES ACT 1970

Schedule I: classification (DEA)

*Definition: Schedule I drugs, substances, or chemicals are defined as drugs with **no currently accepted medical use** and a high potential for abuse. Some examples of Schedule I drugs are: heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), 3,4-methylenedioxymethamphetamine (ecstasy), methaqualone, and peyote<sup>1</sup>*

Cannabis has been used for millennia as a fibre for making clothes, as a food source and as medicine. Its medicinal use was documented by the Greek historian Herodotus<sup>2</sup> in the fifth century B.C.E, but more recently, the first known instance of it being smoked was discovered by archaeologists at a burial site along the Silk Road in China over 2500 years ago.<sup>3</sup> More recently, the FDA itself has approved one cannabis-derived drug (Epidiolex, 2018) and three synthetic cannabis drugs (Marinol, 1985; Cesamet, 2006; Syndros, 2016). While the drug laws might still be telling us that the drug has no medical value, the States (36 as of November 2021), clinicians (67% of physicians and 82% of psychologists)<sup>4</sup>, and even the FDA seem to be saying otherwise. In fact, a patent for cannabinoids as an antioxidant and neuro-protectant is currently filed and owned by the US Department of Health and Human Services.<sup>5</sup>

So, what are cannabinoids and what do they do? To begin to understand, we must first look at the Endocannabinoid System.

### THE ENDOCANNABINOID SYSTEM

Discovered only in the 1980s, the Endocannabinoid System (ECS) is a biological regulatory system responsible for maintaining homeostasis, or equilibrium, throughout the body. The ECS operates similarly to the other transmitter systems in the body like the Sympathetic Nervous System, which controls our fight or flight response. The ECS modulates functions such as sleep, memory (and forgetting), appetite, stress, and inflammatory and immune responses.<sup>6</sup> It works like lock and key, whereby the cannabinoid receptors are the lock and the endocannabinoids are the key. Turning the response of the ECS on and off.

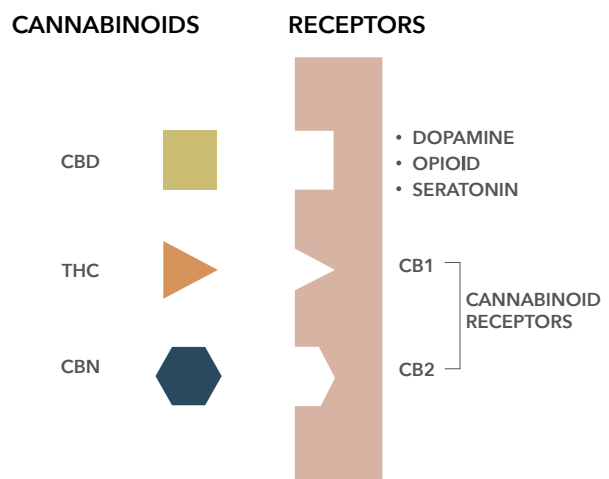


Figure 1 Cannabinoids and Receptors

<sup>1</sup> Drug Scheduling, DEA, <https://www.dea.gov/drug-information/drug-scheduling>

<sup>2</sup> Herodotus. *The Persian Wars, Volume I: Books 1-2*

<sup>3</sup> Ren, M. Tang, X. Wu, X. Spengler, R. Jiang, H. Yang, Y. Boivin, N. (2019). 'The origins of cannabis smoking: Chemical residue evidence from the first millennium BCE in the Pamirs', *Science Advances*, 5 (6).

<sup>4</sup> Frellick, Marcia (2018). 'Medical, Recreational Marijuana Should Be Legal, Most Clinicians Say', *Medscape*

<sup>5</sup> <https://patents.google.com/patent/US6630507>

<sup>6</sup> Grinspoon, Peter (2021). 'The endocannabinoid system: Essential and mysterious', *Harvard Health Publishing*.

There are two types of cannabinoid receptors, CB1 and CB2. CB1 is found in the central nervous system where it regulates things like sleep, appetite and memory. CB2 is generally found on the cells of the immune system where it influences pain and inflammation. There are further effects of cannabis which cannot be explained by the cannabinoid receptors and thus are thought to influence the dopamine, opioid and serotonin receptors.<sup>7</sup>

Much like opioids act on our endogenous opioid system to counteract pain, phytocannabinoids (cannabinoids produced by plants) are chemically similar to the endocannabinoids produced in our bodies and thus act on the ECS and have the power to modulate important homeostatic functions.

### CANNABIS: THE PLANT

One *Cannabis Sativa* can have over 550 phytochemicals including cannabinoids, terpenes and flavonoids. The most widely known cannabinoids found in the cannabis plant are THC (the stuff that gets you high) and CBD (the stuff that doesn't), but that is only the tip of the iceberg. To date, there are 144 known cannabinoids<sup>8</sup>, a list that keeps on growing. The 12 cannabinoids listed below

have 25 therapeutic uses among them, including pain management, anti-inflammation and immune system support. This is by no means an exhaustive list.

But cannabinoids aren't the whole story. It is believed that not only do cannabinoids work together, ie. CBD with THC Δ9, but also the other compounds found in the plant: terpenes and flavonoids. The cannabinoids, terpenes and possibly the flavonoids can create what is known as the "entourage effect<sup>9</sup>," where when taken together they may provide additional therapeutic benefits.

Many cannabis terpenes are also found in other substances of known therapeutic value, such as lavender and rosemary. Examples of the flavonoids found in cannabis are anthocyanins and quercetin, both powerful antioxidants found in every day food sources such as blueberries and red onion, respectively.

### CANNABIS AS MEDICINE

Beyond the funeral rites of the Scythians and the medicinal applications of the Greeks, cannabis first appeared in the *United States Pharmacopeia* in 1850<sup>10</sup>, and by the 20th century it was widely prescribed for a range of ailments such as menstrual cramps, insomnia and migraines. The compounds in cannabis are not water-soluble and cannot be injected, furthermore oral administration was slow and erratic. Along with quality control and supply issues, cannabis' own molecular structure led to cannabis treatments falling out of favor.<sup>11</sup> Opioids, a much pliable molecule, took over the role of herbal cannabis.

As of writing, a total of 36 states have legalized cannabis for medical use. In the state of Connecticut, the list of conditions approved for medical use continues to grow and currently stands at 40 for adults and 11 for patients under 18.

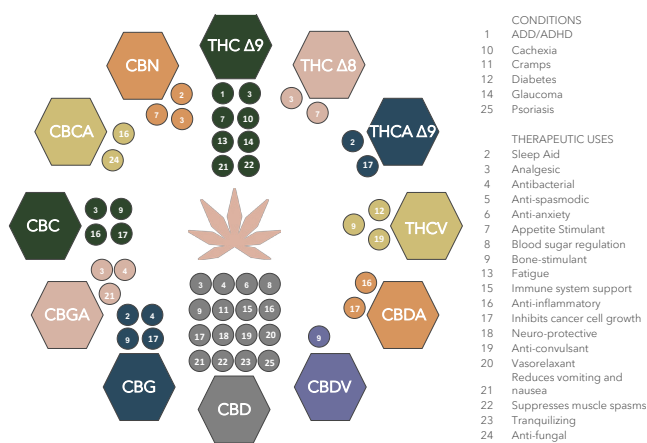


Figure 2 Cannabinoids - More than THC

7 Klumpers, Linda. Thacker, David. (2019). 'A Brief Background on Cannabis: From Plant to Medical Indications' Journal of AOAS International, 102 (2).

8 Berman, Paula et al., (2018) "A new ESI-LC/MS approach for comprehensive metabolic profiling of phytocannabinoids in Cannabis." Scientific reports vol. 8,1 14280.

9 Ferber, Sari Goldstein et al., (2020). 'The "Entourage Effect": Terpenes Coupled with Cannabinoids for the Treatment of Mood Disorders and Anxiety Disorders.' Current neuropharmacology vol. 18,2: 87-96.

and Therapeutic Potential', Haworth Integrative Healing Press.

10 Bridgeman, Mary Barna. Abazia, Daniel. (2017). 'Medicinal Cannabis: History, Pharmacology, and Implications for the Acute Care Setting', P&T, 42(3).

11 Grotenhermen, F., & Russo, E. (2002). 'Cannabis and Cannabinoids: Pharmacology,

Many of the earliest mainstream uses of cannabis as medicine were for the treatment of cancer and HIV patients, whether to mitigate nausea from allopathic (western or conventional medicine) or help with cachexia (extreme weight loss and muscle wasting). Now that list has expanded to include a myriad of diseases including Multiple Sclerosis, IBS, arthritis, chronic pain and Post-Traumatic Stress Disorder. Among all the ailments treated by cannabis, pain, in all its forms, is by far the most prevalent condition patients are using cannabis as the cure.

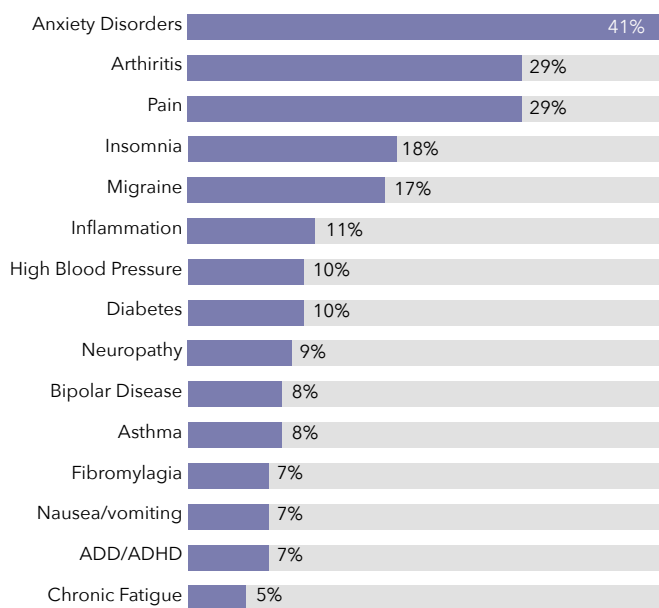


Figure 3 Medical Conditions Among Medical Cannabis Consumers

## PAIN

In July of 2021, the CDC published a report<sup>12</sup> saying that nearly 60% of Americans had experienced pain in the last 3 months. Of those 210 million people, 50 million (or 20% of the population) are said to suffer from chronic pain.<sup>13</sup> Many pain sufferers turn to cannabis after unsuccessful attempts to manage their pain through other pharmaceuticals, surgery and other therapies. Pain is mitigated either by binding with the opioid receptors primarily in the brain and central nervous system like heroin or morphine, or by inhibiting prostaglandin productions like Advil or Tylenol. Cannabinoids have been shown to work on both of those pathways.<sup>14</sup>

## ANXIETY/DEPRESSION

The neural pathways that drive stress, anxiety and fear are controlled by the Endocannabinoid System<sup>15</sup>. In fact, recent research has correlated depressive disorders with ECS dysregulation. Anxiety disorders are among the most common mental illnesses in the U.S., affecting over 40 million people per year. Depression has long been treated by cannabis; as early as 1621 cannabis extracts were prescribed for 'melancholia'<sup>16</sup>. It is suggested that physician guided cannabis treatment for anxiety and depression can often achieve better results than traditional psychiatric medications.

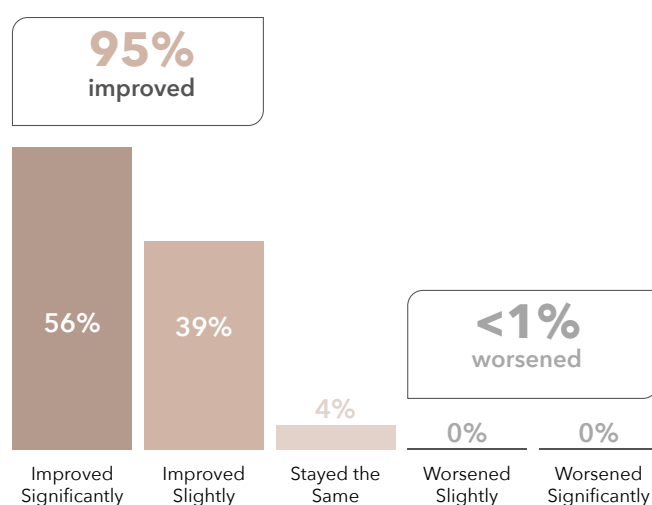


Figure 4 "What has been the impact of cannabis on your condition?"

Whatever the condition, what is clear is that for those who are using cannabis to treat their conditions, the lion's share believe it has made a positive impact in their lives. A recent study of medical cannabis users showed that 42% of them had stopped taking a pharmaceutical drug for their ailment and a further 38% used less of the pharmaceutical drug<sup>17</sup>. Additionally, a recent survey of physicians found that, given the dearth of clinical research, 64% of physicians said that anecdotal evidence from their patients was their main source of cannabis information, all the while, less than 40% of patients were telling their doctors about their cannabis use.<sup>18</sup>

<sup>12</sup> Lucas, Jacqueline, et al. (2021) Back, 'Lower Limb and Upper Limb Pain Among US Adults, 2019', NCHS Data Brief, 415.

<sup>13</sup> Yong, Robert J. et al. (2021). 'The prevalence of chronic pain among adults in the United States' Pain, 10.1097.

<sup>14</sup> Takeda, Shuso, et al., (2008). 'Cannabidiolic acid as a selective cyclooxygenase-2 inhibitory component in cannabis', Drug Metab Dispos, 1917 (21).

<sup>15</sup> Sharpe, Lara, et al., (2020) 'Cannabis, a cause for anxiety? A critical appraisal of the anxiogenic and anxiolytic properties,' Journal of Translational Medicine, 18 (374)

<sup>16</sup> Grinspoon, Lester (2005). 'History of Cannabis as Medicine,' DEA Administrative Law Judge Hearing.

<sup>17</sup> Kruger, Daniel, Kruger, Jessica, (2018). Medical Cannabis Users' Comparisons between Medical Cannabis and Mainstream Medicine', Journal of Psychoactive Drugs, 51 (1). Publishing.

<sup>18</sup> Anson, Pat (2021). 'Patients and Doctors Finally Talking about Medical Cannabis', Pain News Network.

Research into cannabis must be conducted under the watch of both the FDA and the DEA because of its Schedule I status which has stagnated scientific investigation<sup>19</sup>. Only recently (December 2021), NORML heralded 2021 as the year 3,800 research reports were published on PubMed about cannabis, eclipsing the previous record of 3,500 in 2020. Given there were only 3,000 papers published over the nearly 10-year period between 1990 and 1999, you can see why they are pointing to progress<sup>20</sup>. It is useful to point out, however, that in 2021 there were 5,800 papers published on NSAIDs (non-steroidal anti-inflammatory drugs), 10,400 on corticosteroids, and 11,000 on opioids. That is over 27,000 published papers on drugs that patients are using to replace cannabis.

## CONCLUSION

According to the State of Connecticut, cannabis has the potential to treat over 40 different conditions and that list keeps on growing. What is more, it treats diseases which typically confound Western medicine and are difficult to treat like Fibromyalgia (idiopathic widespread pain and extreme tiredness), Post-Traumatic Stress Disorder (PTSD) and rare forms of epilepsy.

The actual number of conditions treated by cannabis is, of course, yet unknown. Both clinical research and physician understanding lags demand and anecdotal evidence. Until Federal legalization occurs neither of the above are likely to change. A recent survey stated that 91% of Americans believe that at least medical cannabis should be legal<sup>21</sup>.

### Fewer than 10% of U.S adults say Marijuana should not be legal at all

% who say marijuana....

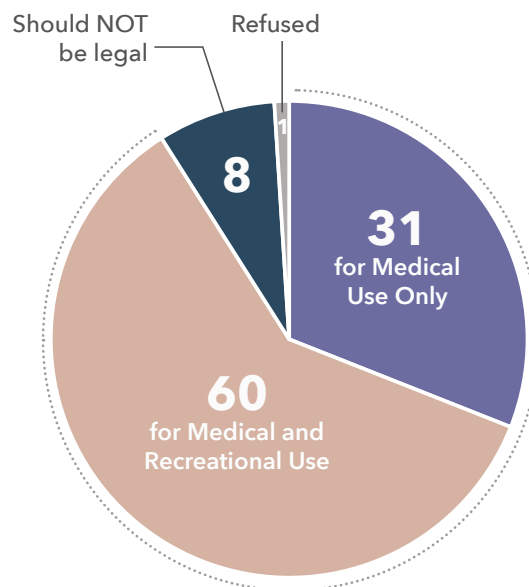


Figure 5 Cannabis and Legalization

Legalization, a politically driven topic and, despite public approval, the plethora of data and research momentum, will still take time. Unfortunately, the biggest losers are the millions of patients that could benefit from the increased understanding of this incredible medicinal plant.

## DISCLAIMER

*"This document is for general educational purposes only. The US Food and Drug Administration has not reviewed or advised on most health claims in the medical cannabis industry regarding general or specific benefits or treatment of a particular disease or condition."*

<sup>19</sup> Mead, Alice, (2019). 'Legal and Regulatory Issues Governing Cannabis and Cannabis-Derived Products in the United States', *Frontiers in Plant Science*.

<sup>20</sup> Record Number of Scientific Papers Published About Cannabis in 2021 - NORML

<sup>21</sup> <https://www.pewresearch.org/fact-tank/2021/04/16/americans-overwhelmingly-say-marijuana-should-be-legal-for-recreational-or-medical-use/>