The Great Cannabis Debate: Decriminalization, Legalization or Depenalization?

Ahmed Yousif Ali*

Hayat Rehabilitation Center, Khartoum, Sudan

Marwan Ali

Hayat Rehabilitation Center, Khartoum, Sudan

ABSTRACT:

One of the biggest debates of our times involves cannabis decriminalization. Looking at the timeline of cannabis laws over the centuries, we see a clear pattern of unanimous outlawing and criminalization all over the world, the process taking decades. This picked up the pace in the last century and the world was unified by the 1961&1971 conventions in ratified criminalization. Fast forward a couple of decades later, many countries made a U- turn and started decriminalizing possession and use or legalizing medicinal use. Today the pattern is clear; more countries are legalizing its use, with no strings attached. Regardless of the moral arguments and legislative processes decriminalization camp seems to be gaining momentum and ground.

In this paper, we review the literature available on the plant, its chemistry, the potential benefits and perceived harms of its use and abuse. Finally, we hope to summarize the current views of the legalization and decriminalization camps.

KEYWORDS: Cannabis, Decriminalization, Legalization, United Nations Office on Drugs and Crime, Drug

INTRODUCTION

The World Drug Report 2022 by the United Nations Office on Drugs and Crime (UNODC) came out in June 2022 in "five separate booklets, providing an in-depth analysis of global drug markets and examining the nexus between drugs and the environment within the bigger picture of the Sustainable Development Goals (SDGs), climate change and environmental sustainability" (UNODC,2022).

Booklet 3, 'Drug market trends of Cannabis and Opioids', is a consensus document summarizing the best available evidence and knowledge in the scientific community regarding the effects and complications of cannabis use and legalization. The following are general highlights from the report:

- Non-medical drug use can endanger physical and mental health and is especially harmful in early adolescence. This is more pronounced in Western and Central Europe.

- Global drug challenges further complicate the post-COVID-19 world picture together with multiple conflicts, a continuing climate emergency and threat of recession, even as the multilateral order is showing troubling signs of strain and fatigue.

- As a general obligation, the international drug control conventions of 1961 and 1971 require state parties to establish measures to limit the production, manufacturing, export, import, distribution, and possession of controlled drugs, exclusively to medical and scientific purposes, subject to the provisions of those conventions. However, state parties are not required to establish criminal offences for drug use.

- The International Narcotics Bureau (INCB) has recently clarified that "measures to decriminalize the personal use and possession of small quantities of drugs are consistent with the provisions of the drug control conventions".

- As a substance subject to control under the 1961 Convention, provisions apply to cannabis. Accordingly, any of the above-mentioned activities conducted for non-medical and non-scientific purposes are inconsistent with the legal obligations of the State parties to the conventions.

Specific highlights pertaining to cannabis include:

- Near-universal cannabis cultivation, with growth in indoor seemingly outpacing growth in outdoor cultivation.

- A modest increase in the global prevalence of cannabis use.

- Illicit drug cultivation embeds underprivileged communities in impoverishment in the long run.

- Decreased perceptions of cannabis harms have decreased in areas where the drug has been legalized.

- A greater proportion of people with psychiatric disorders and suicides and hospitalizations associated with regular cannabis use has increased, together with the number of hospitalizations- Some 40 per cent of countries reported cannabis as the drug related to the greatest number of drug use disorders.

- The rising THC and falling CBD levels in cannabis amplify health risks.

- Trafficking trends in cannabis herb difficult to identify in some parts of the world.

PLANT ORIGIN, CHEMISTRY AND SHORT-TERM EFFECTS

THE PLANT ORIGIN: The main plant genus is cannabis, with 3 species: the main one, *cannabis sativa*, and two others, *cannabis indica* and *cannabis ruderalis*. *Cannabis sativa* has a higher THC concentration, whereas *cannabis indica* has a higher content of cannabidiol. What is known as hemp is the same species but is distinguished by its low THC content of less than 0.3%; a THC concentration of more than 0.3% legally classifies the plant as marijuana. Cannabis is a complex plant that has divided scientists, legislators, politicians and the public for decades.

CHEMISTRY: More than 500 chemical compounds are found in the sativa plant and just over 60 are cannabinoids. Of these 4 cannabinoids have been have been widely studied, namely:

1− *Δ-9-tetrahydrocannabinol (Δ-9-THC or delta-9 THC).*

2− *Δ -8-Tetrahydrocannabinol (Δ-9-THC or delta-8-THC).*

3− *Cannabidiol.*

4− *Cannabinol.*

(Atakan, 2012) (Figure 1)

Although cannabis has been used for thousands of years for medicinal and recreational purposes, it was only in 1964, in Israel, that Raphael Mechoulam first isolated Δ-9-tetrahydrocannabinol (Δ-9-THC) the active compound in the sativa plant. Once recognized, it was tested on monkeys, and found to only cause sedation. Then the research team tested it on humans, volunteering to use it on themselves, their friends and family. Their findings, that people differ in their response to the compound, still holds today and is corroborated by contemporary research.

In the mid-1980s, Ally Howlett discovered the endogenous cannabinoid receptor CB_1. Later a collaborating team from Aberdeen discovered anandamide, an endogenous cannabinoid compound, and discovered the existence of an endocannabinoid system in the body. It was later discovered that numerous minor cannabinoids work together, rather than a singular compound, to have the combined effect which was called the "entourage effect".

Cannabinol (CBN) is the product that results from heating THC and exposing it to oxygen. It is being marketed as sleep promoting agent, without any regulatory approvals. And like CBD and CBN, there is another hype involving another molecule called Tetrahydrocannabivarin or (THCV). It is dubbed "diet weed" or "weederall". It is being studied for its therapeutic potential in the treatment of diabetes and obesity.

SHORT-TERM EFFECTS: Smoking cannabis will lead to an almost immediate effect. This starts in 15 to 30 minutes and lasts for 4 hours depending on the dose. If consumed in food or beverages, the effect can start between 30 minutes to 3 hours after consumption, lasting up to 12 hours. However, less THC is delivered to the body through eating than smoking; eating means the THC must go through first pass metabolism, whereas smoking delivers the compound directly to the brain (Hua, 2021).

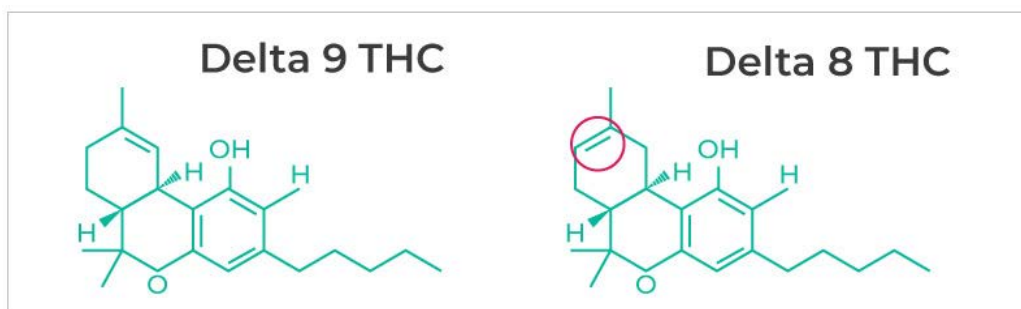The effects of cannabis on people differ from one person to the other, although children and adolescents will have

Figure 1. Δ-9 THC and Δ-8 THC.

more pronounced and more serious sequalae of cannabis consumption, especially on their developing nervous system. Pleasurable effects of cannabis include euphoria, relaxation, heightened sensory perception, laughter (the giggles), altered perception of time, and an increased appetite (the munchies).

Physiological effects of cannabis consumption include adrenergic-like effects, such as tachycardia, tachypnoea, increased respiratory rate, increased blood pressure, orthostatic hypotension, tremors, and conjunctival injection.

LONG TERM EFFECTS

- Dependence/addiction lifetime cumulative probability estimates indicate that 9.4% of cannabis-abusing individuals transition from abuse to dependence at some point in their lives. Half of the transitions occurred approximately 1.83 years after abuse onset. (Flórez-Salamanca L, 2013). The risk increases to 17% among those who begin use at an early age and to 25-50% among daily users. (Hasin et al, 2015). Compared to other drugs, lifetime cumulative probability estimates find a transition probability of 26.6% for alcohol and 15.6% for cocaine.

- Research on the effect of cannabis on brain development is conflicting. Some authors report regular cannabis use in adolescence is associated with altered connectivity and reduced volume of specific brain regions involved in executive functions such as memory, learning, and impulse control. This contradicts with other studies have not found significant differences (Filbey et al, 2014) (Pagliaccio et al, 2015).

- Neurocognitive effects include short term memory impairment, motor coordination, and judgement impairment – these effects may amalgamate and lead to taking unreasonable behavioral risks, such as driving under the influence (DUI). It is thought that delayed reaction time, delayed hand-eye coordination and altered time perception combine to make operating machinery and driving hazardous.

- The Dunedin study group reported in 2012 that those who used THC persistently had a decline of their Intelligence Quotient (IQ) by 6 to 8 points (Meier et al, 2012). This is a well reputed and robust longitudinal study that has tracked a cohort of a 1000 people born in the early 1970s in Dunedin New Zealand. Those who smoked the drug demonstrated a steady decline of IQ proportionate to the length of time how much they smoked. Other groups even claimed that those who never smoked Marijuana showed a slight increase in their IQs. Although longitudinal studies can demonstrate causation, which was true in this case, another strategy that analyzed results of two databases of longitudinal twin studies (southern California & Minnesota) failed to replicate and confirm this observation. Jackson and

Iacono, did exactly that by finding that IQ fell both in abstainers and users, when they analyzed data from the above two American cohort studies. Another study from UK also confirmed the American researchers' findings. The explanation seems to be the confounding effect of alcohol and other substance use in adolescence. It also seems that low IQ invites cannabis use and not vice versa. (Jackson et al, 2016). Other environmental factors could also explain the low IQ among users like behavioral traits of impulsivity and risk-taking behavior, delinquency, family factors, genetics etc.

- Psychiatric sequelae vary widely and depend on many factors, such as the potency of the cannabis ingested, regular or naïve user, genetic load and past psychiatric illness all contribute in the resulting effect of THC use. It is known that cannabinoids modify the modulatory activity of the endocannabinoid system. We need to think of the effects in the whole range from intoxication to withdrawals, some of which have been described in the corresponding sections. The experiences range from anxiety, euphoria, dysphoria, hallucinations, mystical thinking, transient paranoid thoughts, and acute psychotic experiences (used to be called "hemp insanity").

- Neurological effects of intoxication may include slurred speech, hyperkinesis, ataxia, nystagmus, seizures, coma and could be life threatening in young people. (Wang et al, 2013).

WITHDRAWAL PHENOMENA

In the past, the two most widely used classification systems, ICD 10 of the World Health Organization (WHO, 1992) and the DSM-1V of the American psychiatric association (Biederman DSM-1V, 1994) did not recognize Cannabis Withdrawal Syndrome as a diagnostic entity. Budney & Hughes proposed the existence of such a syndrome (CWS) in 2004 & (Budney, 2006).

In 2013, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (Anderson DSM-5, 2013) included the CWS in the list of diagnoses, officially recognizing it. It requires the presence of at least 3 of the following symptoms developing within 7 days of reduced cannabis use: Irritability, anger, or aggression, nervousness or anxiety, sleep disturbance, appetite or weight disturbance, restlessness, depressed mood, somatic symptoms, such as headaches, sweating, nausea, vomiting, or abdominal pain.

ICD 11 **also includes Cannabis Withdrawal Syndrome,** describing it as a clinically significant cluster of symptoms, behaviours and/or physiological features, varying in degree of severity and duration, that occurs upon cessation or reduction of use of cannabis in individuals who have developed Cannabis dependence or have used cannabis for a prolonged period or in large amounts. Presenting

features of Cannabis Withdrawal Syndrome may include irritability, anger or aggressive behaviour, shakiness, insomnia, restlessness, anxiety, depressed or dysphoric mood, decreased appetite and weight loss, headache, sweating or chills, abdominal cramps and muscle aches (World Health Organization, 2019).

A metanalysis by Bahji et al in JAMA, provided the strongest evidence so far for the existence of a withdrawal syndrome They found that 47% of individuals included in the studies experienced withdrawals, although these withdrawals were not akin in severity or life-threatening nature to opioid and alcohol withdrawal, respectively. (Bahji et al, 2020).

THE ENDOCANNABINOID SYSTEM

The Endocannabinoid system (ECS) is probably the most important neuromodulatory system in our body. It is an intricate and vast network of chemical signals and cellular receptors that play essential roles in the central nervous system (CNS) development, synaptic plasticity, and the response to endogenous and environmental insults. (Grinspoon, P, 2021). It is found in the whole animal kingdom except insects. It regulates and controls many bodily functions such as learning, memory, emotional processing, sleep, temperature control, pain control, inflammatory and immune responses, coordination and feeding behaviour. The ECS also functions as messenger system and contribute to homeostasis, some describe it as the switchboard of the communication system in our bodies.

The components of the system are: cannabinoid receptors, endogenous cannabinoids (endocannabinoids) and the enzymes responsible for the synthesis and degradation of the endocannabinoids.

THE CANNABINOID RECEPTORS: (Cannabinoid receptors type 1 &2 (CB$_1$, CB)$_2$, PPAR's and Transient Receptor Potential channels) (TRP). CB$_1$ *receptors* are abundant in the central nervous system (CNS), particularly in cortex, basal ganglia, hippocampus, and cerebellum. CB$_2$ *receptors* are much lower than CB$_1$ and are linked to an increased risk for schizophrenia and multiply by up to 100-fold following tissue injury or during inflammation. TRP channels, especially TRPV1, are activated by anandamide under certain conditions.

ENDOCANNABINOIDS (ENDOGENOUS CANNABINOIDS): (Anandamide &2-AG, virodhamine and 2-arachidonoyl glycerol ether**).** The most important Endocannabinoids are the first two (2-AG) and (anandamide). Anandamide's name comes from the Sanskrit word *ananda* meaning bliss).

As stated above, Endocannabinoids play a central role in many biological processes, and some even postulate that combinations of these compounds could explain the spectrum of human personalities. Research continues into other aspects like the hedonic effect of the system on the production of breast milk, osteoclasts, bone strength, and immunity. In animal testing, endocannabinoids have become a potential therapeutic target for research to halt the progression of certain diseases, such as motor neuron disease and amyotrophic lateral sclerosis. It has been shown that they can assist in shrinkage of tumors size, interfere with the process of apoptosis, and alleviate some symptoms of Alzheimer's disease.

THERAPEUTIC POTENTIAL & PHARMACOLOGICAL TREATMENTS

Cannabis has been used medicinally for thousands of years – examples of its use can be found as far back as the days of the pharaohs, Assyrians, Chinese, Arabs, and in traditional Indian medicine.

Medical text books in the early part of the 20th century contained an abundance of therapeutic uses of cannabis till 1937 when the United States banned cannabis on a federal level and the prohibitions phased out from medical use. Following the discovery of the endocannabinoid system in the 1990s, the potential medicinal use of cannabis extracts has been widely explored, with a focus on pharmaceutical products containing THC and other cannabinoids (Fraguas-Sánchez & Torres-Suárez, 2018). The range of disorders that cannabinoids have been found to attenuate is diverse; e.g., multiple sclerosis, cancer, neuropathic pain and nerve damage and glaucoma (Chandra, 2017). It has also been used to treat epilepsy, HIV/AIDS, weight loss, and specific types of inflammation (e.g., rheumatoid arthritis, Crohn's disease, ulcerative colitis). This not an exhaustive list, infact there are references of its use in dozens of ailments e.g., fibromyalgia, obstructive sleep apnoea, post-traumatic stress disorder (PTSD), etc.

It is very difficult at times to separate the anecdotal from hard science when talking about medicinal uses cannabinoids. There are accounts on the media about miraculous recovery experiences. One needs to be careful and disciplined when assessing the information and subject it to the necessary critical appraisal, as one does with any therapeutic intervention.

The main focus of therapeutic potential of cannabis is on cannabidiol or CBD. In general, cannabis products derived from *Cannabis sativa* exhibit a higher CBD/THC ratio than products derived from *Cannabis indica*. Different *Cannabis* strains have been bred either to maximize or, conversely, to reduce THC content and increase the concentration of CBD and other non-psychoactive ingredients, which is the desired end product to be used as a medicinal agent. The industry is estimated to reach 25 billion $ by 2025. The indications for its use are vast e.g.,

pain control, sleep promotion, depression, anxiety, PTSD, etc. It is even in food and beverages, lollipops and tooth picks.

The distinction made between THC being psychoactive and cannabidiol's effects, maybe not, is a matter for debate (De wit, 2019). The New York Times addressed some important questions about CBD where experts answered hot questions about it, like if it is a scam or not, does it really help with PTSD, sleep disorders, anxiety and depression or is it a placebo effect. (NYTimes, 2019). Many questions remain unanswered like cancer treatment, how much is needed? Why does one CBD product treat a certain cancer and not another (e.g., what works with prostate cancer may not work for ca colon and vice versa).

CBD is even being used to treat opioid addiction in some clinical trials.

Some pioneering work is going on in Israel at Technion labs where each crop is logged and given unique ID for every medicinal product from cannabis plants. Every time CBD is prescribed, researchers follow up the patients to know exactly where it came from and they can study its effect and reproduce the result. (Meiri, 2019).

The following is a list of cannabinoid-based pharmaceuticals approved in certain countries:

A-AGONISTS

- **Dronabinol**: Oral capsules or an oral solution containing synthetic THC. Dronabinol is indicated for anorexia, associated with weight loss in patients with HIV/AIDS, and nausea and vomiting associated with cancer chemotherapy - it is typically introduced after previous treatments have failed.

- **Nabilone:** Administered via oral capsules containing a synthetic cannabinoid similar to THC. Nabilone is used to treat nausea and vomiting associated with chemotherapy.

B-INVERSE AGONISTS

Rimonabant, withdrawn on an emergency basis due to increased cases of suicidality.

C-NABIXIMOLS (A.K.A SATIVEX)

A spray that is comprised of similar parts THC and CBD from two cannabis extracts. It is used to treat muscle spasticity resulting from multiple sclerosis.

D-EPIDIOLEX

Activation of CB_1 receptors reduces seizure severity. A plant-derived CBD oral solution indicated for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age or older. It was approved by the US Food & Drug Administration (Fraguas-Sánchez, 2018) and the remains the only cannabis extract approved so far. Further analysis is needed to ensure that this is not the result of drug interactions, especially with Clobazam. (Perucca, 2017).

`Finally, this article does not cover toxicology and lab tests but should warn about some CBD products being found to contain adulterants, some of which are addictive or can cause serious physical and mental health consequences, even fatalities. Some samples from users of CBD have led to positive drug tests as the products marketed contained more THC than indicated.

DECRIMINALIZATION, LEGALIZATION, DEPENAL-IZATION

This is a highly divisive and polarizing subject. At one end there are those who call for a liberal approach legalize cannabis possession and use and at the other end those who warn against it and call for at least continuation of the status quo and keep it as a controlled substance. The following are important definitions are taken directly from the 2022 World Drug Report of the UNODC:

DECRIMINALIZATION: Defined by the INCB (International Narcotics Control Bureau) as "the process through which an offence is reclassified from "criminal" to "non-criminal" through legislative action". While the behavior remains an offence, it may be addressed through other means than criminal law.

LEGALIZATION: Frequently associated with the regulation and commercialization of controlled drugs, such as cannabis, for non-medical and non-scientific purposes. Legalization entails no penalty (criminal, administrative, civil or otherwise) for production, manufacture, export, import and distribution of the drug. Decriminalization and legalization are quite distinct concepts, as decriminalization in the context of minor drug offices is within the provisions of the international drug conventions, legalization is not.

DEPENALIZATION: According to the INCB, a depenalization approach may include "police diversion practices, conditional sentences and the widening of prosecutorial discretion as an alternative to criminal prosecution". Depenalization differs from decriminalization in that it refers to a reduction in the use of existing criminal sanctions, although certain offences remain classified as "criminal". Moreover, in contrast to decriminalization, depenalization may not require changes to the existing legal framework.

The following table summarizes the current debate between those for and against the legalization of cannabis use, and the scientific opinion adopted by certain international organizations (Table 1):

Table 1.

The current debate between those for and against the legalization of cannabis use, and the scientific opinion adopted by certain international organizations.

Topic	For legalization	Against it	International consensus: AMA, AAP, WHO, ASAM, EMCDDA, NIDA.
Health effects	Harmless; endorse legalization.	Proven physical and psychological harm	Proven physical and psychological harm
Addiction potential & gateway drug	----------------------	1:10 get addicted & many transition.	addictive
Criminal offences	Lowers crime rate.	Increased violent crime &black-market activity.	Increased violent crime &black-market activity
Social gains	More jobs, more police resources.	Harm outweighs gains.	Harm outweighs gains.
Tax &revenue	Generates billions of dollars.	Cost outweighs benefits.	Cost outweighs benefits.
Legalization & regulation	Generally positive outlook.	Negative outlook.	Caution is advised.
Civil liberties	Hypocrisy when compared to alcohol and tobacco.	Not affected.	International treaties protect liberties.

Key: AMA: American Medical Association. AAP. American Academy of Pediatrics, ASAM American Society of Addiction Medicine, EMCDDA, European Monitoring Center for Drug and Drug Addiction, WHO: World Health Organization, NIDA, National Institute of Drug Abuse.

CONCLUSION

There is a unanimous agreement that the slogan "drug free society" is a myth and the war on drugs has failed. The prohibitions didn't really succeed in eradicating drug use and have a dark history of racial profiling and targeting certain races all over the world (in the US, cocaine prohibitions targeted people of color in the US, Marijuana targeted the Mexicans and opium the Chinese immigrants).

Public tolerance of cannabis decriminalization is a driving force at present and politician and governments can't ignore it. A good example comes from Thailand, country known for its harsh drug laws. Cannabis cultivation and possession was legalized in June 2022. A political candidate running for office promised to decriminalize Marijuana if he was elected and indeed, he was, and kept his promise. The physical and psychological impacts of its non-medical use and the consensus view of medical organizations to err on the side of caution are growingly disregarded.

It seems prudent to decriminalize cannabis use for therapeutic interventions, which is inevitable now considering the international trends, accommodating for the apparent health benefits. The needs of those dependent on it for rehabilitation and provision of support for users should not be overlooked. Measures to limit the cultivation and production of more potent and harmful products and regulate the industry as whole should be put in place. Support for farmers by catering for alternative means for their livelihood should not be overlooked.

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