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Medical and Nonmedical Uses of Cannabis: Overview of Cannabis in Egypt

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Abstract: The medical use of cannabis is extending across many countries. Some of them legalize its use clearly and others require licensure systems to approve treatment for eligible patients. Despite this growing interest and utilization, there remains a lack of solid scientific evidence supporting its medical use, even though cannabis has been used therapeutically for thousands of years. The aim of the following conduct is to present updated data on the potential roles of cannabis-based treatments regulations globally including Egypt against various illness conditions. The information highlighted that incorporating cannabis into the therapeutic system may offer benefits. However, in many cases, despite encouraging perspectives and outcomes, the supporting evidence remains insufficient and requires further validation. Due to social and legal barriers, the conduct of such rigorous clinical trials has been hindered, limiting the availability of high-quality evidence to guide medical practice.

Keywords: Cannabis, Autoimmunity, Inflammation, Therapy, Recreation, Legalization.

INTRODUCTION

Cannabis genus belongs to the plant family Cannabaceae. Within this genus, there are several species, including Cannabis sativa, Cannabis indica, and Cannabis ruderalis. It was highly valued in ancient civilizations for its versatility, serving as a source of food (hemp seeds), fiber for textiles and rope, and as a medicinal and psychotropic agent [1,2]. It is also facing significant legal and social challenges over time [3-5].

Cannabis is a pharmacologically complex plant containing hundreds of organic compounds, including cannabinoids (also known as phytocannabinoids), terpenoids, flavonoids, polyphenols, phenolic acids, tocopherols, fatty acids, and other secondary metabolites. These constituents contribute to the diverse effects and therapeutic properties of cannabis, both individually and through their interactions [6-9].

Cannabinoids are unique to cannabis, with at least one hundred identified in the plant. The most studied and principal cannabinoids are Δ-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) [6-8, 10-14].

Cannabinoids, the active compounds in cannabis, have demonstrated immunosuppressive and immunomodulatory properties. They can suppress autoreactive lymphocytes and T cell functions induce functional regulatory T cell (Treg), and modulate inflammation through the endocannabinoid system (ECS) [15-18]. In animal models, CB2 agonists have enhanced Treg differentiation and suppressed disease activity in inflammatory bowel disease [15]. These properties have led to interest in cannabinoids as potential therapies for autoimmune diseases, with particular attention to their anti-inflammatory and analgesic effects [17, 18].

THC is the main psychoactive constituent, responsible for effects such as euphoria, relaxation, heightened sensory perception, laughter, and altered perception of time. It is also associated with adverse effects, including cognitive impairment, dependency, anxiety, psychosis-like symptoms, and exacerbation of psychiatric conditions, especially in adolescents. Its medical uses include reducing pain, spasticity, nausea, and increasing appetite in patients with anorexia or wasting syndrome in AIDS [7, 8, 10-13].

CBD is nonpsychoactive and has demonstrated anxiolytic, antipsychotic, antibacterial, antioxidant, anticancer, antiemetic, and anti-inflammatory properties. It may offset some of the negative effects of THC, such as anxiety and psychosis-like symptoms. It is often used for self-medication in anxiety and may have therapeutic effects in epilepsy and pain modulation [7, 8, 10, 13, 14]. Other cannabinoids under study include cannabinol, cannabichromene, and tetrahydrocannabivarin [8]. The ratio of THC to CBD varies among cannabis species and strains, with some strains (e.g., "skunk") being high in THC and low in CBD [7].

Terpenoids and flavonoids are significant secondary metabolites in cannabis. Terpenoids, such as beta-caryophyllene, have demonstrated pharmacological effects, including inhibition of gastric lesions in animal models. Terpenes can bind and activate cannabinoid receptors and may contribute to the overall effects of cannabis [8, 8, 19]. Flavonoids, including flavocannabiside, are also present and may contribute to the pharmacological profile of cannabis [9, 19].

MODE OF ACTION

Cannabis is consumed through various modes, including smoking (with or without tobacco), vaping/vaporizing, and oral ingestion via edibles or drinkable products [20-23]. The mode of administration can influence both the onset and intensity of effects, as well as health outcomes [21,23,24]. It exerts its effects primarily through interaction with cannabinoid receptors (CB1 and CB2) which are distributed throughout the body [25]. CB1 receptors are primarily located in the brain and spinal cord, where they play roles in pain relief, memory, movement, and the regulation of gut activity. In contrast, CB2 receptors are detected in many other tissues including the immune system and are less well understood. Both CB1 and CB2 receptors are expressed on immune cells, which can also synthesize, secrete, transport, and catabolize cannabinoids [26]. The discovery and cloning of these receptors in the brain clarified the mode of action of cannabis extracts and led to the identification of endogenous cannabinoids (endocannabinoids) such as anandamide (AEA) and 2-arachidonoylglycerol (2-AG). These compounds, along with phytocannabinoids from the plant, modulate various physiological processes [25, 27].

THC Acts mainly on CB1 and CB2 receptors, producing psychoactive effects and influencing pain, mood, appetite, and other functions [20,25]. It acts as a partial agonist on CB1 endocannabinoid receptors distributed across several brain regions. While CBD exact mechanism in epilepsy is unclear, it does not significantly affect CB1 or CB2 receptors. Suggested modes of action include antagonism of GPR55 in the thalamus, modulation of voltage-gated sodium and calcium channels, and agonism of serotonin (5-HT1A) receptors [28]. It has shown neuroprotective effects in animal models of Parkinson’s disease and can counteract oxidative stress [22].

METABOLISM OF CANNABIS

Cannabis metabolism is a multifaceted process involving absorption, distribution, hepatic metabolism, and excretion, with significant variability depending on the route of administration, frequency of use, and individual physiological and environmental factors. Its metabolism involves complex processes affecting various organs, primarily the liver, and is mediated by the endocannabinoid system (ECS), which includes neurotransmitters and receptors that respond to both endogenous and exogenous cannabinoids. The ECS plays a significant role in neurodevelopment, cognition, memory, motivation, arousal, sleep, pain, and immune processes, and is crucial for maintaining homeostasis by modulating neurotransmitter levels at the presynaptic nerve level [29-31].

The main metabolism of THC occurs in the liver, primarily via cytochrome P450 enzymes (CYP2C and CYP3A). THC undergoes Phase I metabolism, including hydroxylation to form active metabolites such as 11-hydroxy-THC (11-OH-THC) and 8-hydroxy-THC (8-β-OH-THC), followed by further oxidation to the inactive metabolite 11-carboxy-THC (THC-COOH) [32-35].

11-hydroxy-THC is more potent than THC and readily crosses the blood-brain barrier, potentially with greater brain penetrance than THC itself. In contrast, THC-COOH lacks cannabimimetic effects and is primarily excreted as a glucuronide conjugate [32, 34]. However, CBD metabolism is hydroxylated by CYP450 enzymes to the active metabolite 7-OH-CBD, which is further metabolized to the inactive 7-COOH-CBD. CBD also undergoes direct glucuronidation via UGTs [36].

THC is highly lipophilic, distributing rapidly to organs with high blood supply (brain, heart, liver) and later to adipose tissues. Chronic use leads to accumulation in fat-rich tissues, with gradual release and prolonged detectability in bio-samples [37].

Cannabis consumption leads to changes in perception and mood, increased heart rate, lowered blood pressure, and impairment of memory, psychomotor coordination, and concentration.

Long-term effects are less clear, and chronic use may result in toxic effects on organs such as the brain, heart, liver, and kidneys, as well as alterations in body mass index, redox balance, and glycemic status [38, 39]. There are slight discrepancies in reported excretion rates, with some sources stating 65% of the dose is eliminated in feces and 20% in urine, while others report 40% in feces and 30% in urine [32,40]. The number of metabolites identified after cannabis administration varies, with some sources mentioning about 20 metabolites and others stating almost 100 metabolites have been identified, especially after oral administration [34, 35].

In general, Cannabis pharmacokinetics is complex and highly variable, influenced by route of administration, formulation, individual factors, and genetic background. Both pharmacokinetic and pharmacodynamic drug–drug interactions are possible, primarily mediated by CYP450 enzymes and transporter proteins. There remain significant gaps in knowledge regarding the pharmacokinetics of many cannabis products, especially in special populations and with novel administration routes, underscoring the need for further research and individualized therapeutic approaches [41-43].

NONMEDICAL USES OF CANNABIS

The minimum amount of THC required for perceptible psychoactive effects is about 10 µg/kg body weight [38]. Nonmedical cannabis use is characterized by several main routes of administration, including smoking joints (with or without tobacco), using water pipes (with or without tobacco), and oral ingestion through food or tea. While joint smoking remains the most prevalent method, alternative routes such as water pipes and ingestion are increasingly popular among youth. Despite this trend, few studies have directly compared the health effects of different administration routes in nonmedical users, whereas such comparisons are more common in research on medical cannabis use. Additionally, cannabis use encompasses methods such as vaporizing and vaping, and individuals may use non-prescribed cannabis for reasons including pleasure-seeking, coping with difficult situations, self-medicating, and appetite control [44, 45].

Nonmedical cannabis use is often motivated by factors such as pleasure, coping with stress, self-medication, and appetite regulation. The distinction between medical and nonmedical use is sometimes blurred [46,47]. A long-term follow-up study found that Swedish males who consumed cannabis by age 18 were diagnosed with schizophrenia at a rate 2.4 times higher than non-users. Others reported adverse effects include anxiety, depression, psychosis, bronchitis, lung cancer, arrhythmia, and myocardial infarction. Acute complications are primarily cardiovascular and respiratory in nature [47]. However, in studies of the older general public, no significant beneficial physical or mental health outcomes were reported from adjusted analyses, except possibly reduced future incidence of head/neck and prostate cancers. Harmful outcomes were more prevalent than beneficial ones in randomized controlled trials and cohort studies. It is important to note that associations from cross-sectional and sequential studies do not establish causality, and cannabis use may be more common among individuals with pre-existing health conditions [46-48]. Cannabis for therapeutic purposes without formal medical authorization cases are classified as nonmedical when reports indicate recreational use or lack information about therapeutic indications [45, 49].

MEDICAL USES OF CANNABIS THERAPY

Medical cannabis (MC) is most commonly used for the management of chronic pain, but it is also employed in the treatment of other conditions such as mental health disorders (anxiety, depression, PTSD), sleep disorders, dementia, movement disorders (dystonia, dyskinesias, Tourette syndrome), multiple sclerosis spasticity, seizures (including Dravet syndrome and Lennox-Gastaut syndrome), glaucoma, cachexia, and appetite stimulation in patients suffering from anorexia and wasting syndromes 48, 50-53]. It has also been explored for the management of several autoimmune diseases, including multiple sclerosis (MS), rheumatoid arthritis (RA), inflammatory bowel disease (IBD), dermatomyositis, lupus, and Sjogren's syndrome [54-57]. Its use is primarily focused on symptom relief, such as spasticity, pain, and bladder dysfunction in MS, and quality-of-life improvements in IBD [15, 57,58].

As Multiple Sclerosis (MS) Therapy

MS is a persistent neuroinflammatory autoimmune disease that affects the human central nervous system and is driven by autoreactive T lymphocytes which attack myelin. This

inflammatory process results in the disruption of the blood-brain barrier leading to activation of macrophage and T cell, and increased production of cytokines and cytotoxic proteins, including metalloproteinases [59].

Cannabis use is common among people with multiple sclerosis (MS), with surveys indicating that over 40% to more than half of individuals with MS have used or are currently using cannabis, and nearly half have considered or tried it for symptom relief [60-63]. Many patients begin using cannabis after their MS diagnosis, often seeking relief from symptoms such as pain, spasticity, mood swings, and sleep disturbances [60,61]. However, only a small proportion of users (as low as 4% to 21%) receive medical cannabis prescriptions, with the majority using cannabis without professional guidance [61,63]. Cannabis use in MS is also associated with recreational drug experiences and tobacco smoking, and individuals with such backgrounds may be at greater risk of becoming dependent users [61,64].

MC are approved for treating spasticity in MS, with studies showing small but significant improvements in spasticity, pain, and bladder dysfunction [15,52,57,58]. Beyond spasticity, cognitive impairment is a critical concern in MS. Cognitive dysfunction already affects approximately 20 %–40 % of patients with relapsing-remitting MS and up to 70 %–80 % of those with secondary progressive MS [65,66]. Observational data indicates that MS patients who smoke MC show further deterioration in processing speed, memory, and executive functioning [67,68]. This reinforced concerns MC may adversely affect cognition in people with MS, who already suffer from high rates of cognitive dysfunction associated with the disease. It should be noted that there was heterogeneity in study design and outcomes, making definitive conclusions difficult.

Multiple studies, including randomized controlled trials and systematic reviews, have found that cannabis-based medicines may be effective in reducing chronic pain and spasticity in MS, with some evidence suggesting an effect magnitude comparable to standard pain medications [69-71]. Patients frequently report high efficacy of cannabis in relieving pain and spasticity, and some have reduced their use of prescription medications after starting cannabis [62, 63,70].

In general, cannabis is widely used among people with MS, primarily for symptom management of spasticity, pain, and bladder dysfunction, with many patients reporting subjective benefits [60, 61, 63]. However, chronic use is associated with cognitive risks and other adverse effects, and most users do not receive medical supervision [61, 68, 72]. The current evidence base is limited, and further high-quality, long-term studies are needed to clarify the benefits and risks of cannabis and cannabinoid products in MS [68, 73]. Result Set Now, submit each query to Google and record the first 50 results. This way, the result set of 10 queries become 500 results.

AS Inflammatory Bowel Disease (IBD) Therapy

IBD, immune-mediated inflammatory disease with rheumatologic manifestations, includes Crohn’s disease and ulcerative colitis, distinguished by specific clinical, radiological, endoscopic, and histological findings. The exact cause remains partially unclear, but it is believed to involve a multifactorial complex interplay of genetic predisposition, environmental factors, microbiota imbalance, and dysregulated immune responses.

Many studies have found connections between the ECS and IBD, but clinical trials report no significant benefit or adverse effects from MC for IBS symptoms [57, 58]. However, patients have reported improvements in quality-of-life scores, despite the lack of objective symptom improvement [57].

In addition, preclinical studies demonstrate that cannabinoid receptor agonists, particularly those targeting CB2, reduce inflammation, whereas receptor antagonism or genetic knockout in animal models is associated with increased inflammatory responses [74, 75]. This generated optimism regarding a potential role for MC in management of IBD, which includes both Crohn's and ulcerative colitis.

Significant resources have been invested in trying to realize the therapeutic potential of MC in managing IBD. Research in Clinical Gastroenterology and hepatology explored the mechanisms by which cannabinoids may modulate gut inflammation and detailed how cannabinoids can influence the gut microbiome and the immune system [76].

In-vivo studies have shown that activation of cannabinoid receptors can exert anti-inflammatory effects and may contribute to ameliorating colitis symptoms [77]. CB1 receptors, in particular, have been implicated in protecting against hyperstimulation of immune cells that occurs during IBD. Through this mechanism, THC may alleviate IBD symptoms, primarily diarrhea, and help control inflammation [76, 78]. Activation of CB2 receptors has been shown to induce apoptosis and reduce the proliferation of T cells. Additionally, it decreases the recruitment of neutrophils, T cells, and macrophages to the inflamed colon [79].

In summary, while MC appears to improve IBD symptoms, particularly pain and quality of life, objective evidence of anti-inflammatory or disease-modifying effects is lacking. Existing studies are small, short- term, or observational, with safety concerns emerging in long-term use. Larger, rigorously designed randomized controlled trials with robust clinical and endoscopic endpoints are necessary before cannabinoids can be recommended as standard therapy for IBD.

As Rheumatoid Arthritis (RA) Therapy

Cannabis-based medicines have been recognized for their potential in RA and other inflammatory diseases, though the supporting evidence remains insufficient and requires further validation [17, 18, 55, 56].

Rheumatoid arthritis (RA) is characterized by persistent synovial inflammation and progressive joint destruction, driven by proinflammatory cytokines (IL-1, TNF-α, IL-6), which promote matrix metalloproteinase activity and cartilage destruction [80]. It is among the most prevalent autoimmune rheumatic disorders and is a leading cause of disability globally.

Preclinical index supports a potential role for the endocannabinoid receptors (CB1/CB2) in modulating inflammation in RA. CB1 and CB2 receptors are expressed in synovial tissue, and their activation has been shown to downregulate proinflammatory cytokine release and fibroblast proliferation. Also, preclinical studies, including those evaluating selective CB2 agonists, have elucidated reductions in joint inflammation and tissue damage [81]. However, the ligands were detected in synovial fluid from RA and osteoarthritis patients but not in healthy controls, suggesting disease-specific dysregulation,

the synovial fluid of RA patients contains CB1, CB2 receptors, anandamide (AEA), and 2-arachidonoylglycerol (2-AG), which are absent in healthy individuals. It was also demonstrated that cannabinoid receptor stimulation led to the phosphorylation of the cellular kinases ERK-1 and ERK-2 in fibroblast- like cells from RA and osteoarthritis patients, this effect was inhibited when the cells were exposed to the CB1 antagonist [81, 82].

Further investigation and cultivation of synovial cells obtained from RA patients showed that CBD increased intracellular calcium levels, reduced cell viability and IL-6/IL-8/MMP-3 production by activating transient receptor potential ankyrin 1 channel and mitochondrial targets. This effect was enhanced by TNF-α suggesting CBD preferentially targets activated, pro-inflammatory rheumatoid arthritis synovial fibroblast [82].

In contrast to MS, clinical evidence for MC use in RA is even more limited. The only randomized controlled trial to date, conducted by Blake et al. (2006, n =58), evaluated MC over 5 weeks in RA patients with refractory pain. The study reported modest reductions in pain and improved sleep quality but no significant changes in disease activity scores [83]. In this context, systematic reviews of cannabinoids for pain, including in RA populations, have reached similar conclusions and found modest analgesic benefits with frequent, generally mild adverse effects such as dizziness and fatigue [84, 85].

In summary, MC may provide at times symptomatic relief and in preclinical model may provide anti-inflammatory effects, but translation into clinical benefit is unproven. Human data consist largely of small, short-term trials and uncontrolled surveys, making conclusions about efficacy, safety, and disease modification premature.

As Systemic Sclerosis (SSc) Therapy

Systemic sclerosis (SSc) is a multisystem autoimmune disease recognized by fibrosis of visceral organs and skin, as well as vascular damage. The disease is categorized into subtypes based on the extent of skin involvement. Complications in the heart, lungs, and kidneys are common, particularly in diffuse SSc, and these complications significantly contribute to increased morbidity and mortality [82].

Preclinical studies suggest potential antifibrotic effects. In murine models, cannabidiol (CBD) reduced skin and liver fibrosis and decreased immune cell infiltration [86]. (Similarly, the CB2 agonist JWH-133 reduced fibroblast proliferation, collagen accumulation, and pulmonary fibrosis in mice [87]. Emerging preclinical work has identified “compound 66”. This is a selective cannabinoid type-2 receptor agonist with potent anti-fibrotic activity. Designed through structure–activity relationship optimization of pyrazole-3-carboxamide derivatives, compound 66 was shown to reduce dermal inflammation, fibrosis, and profibrotic marker expression in bleomycin-induced skin fibrosis in mice [88]. While mechanistically compelling, these results derive entirely from animal models, which do not fully replicate the heterogeneity of human SSc.

Reviews have summarized potential benefits, particularly for pain relief and modulation of fibrotic processes [33]. The review highlighted potential symptomatic relief, particularly in pain reduction and modulation of fibrotic processes, but noted the lack of large-scale, high-quality clinical trials. In 2020, a review specifically on cannabidiol (CBD) concluded that while CBD may reduce inflammation and pain, clinical evidence remains limited [57]. However, these reviews consistently emphasize the lack of high- quality

clinical trials, underscoring that the majority of evidence remains preclinical. Translation of antifibrotic findings from animal models to human disease has historically been poor, and outcomes such as organ involvement, survival, or quality of life have never been systematically studied in cannabinoid trials for SSc. A 2021 preclinical study investigated cannabinoid therapy in fibrotic disease models, including SSc, and found that cannabinoids could reduce fibrosis and inflammation in animal models. It emphasized the need for human clinical trials to validate the findings [89].

Human evidence is extremely limited. A Phase II clinical trial evaluated lenabasum, a synthetic CB2 receptor agonist, not a THC/CBD extract, showing preliminary safety and efficacy signals in SSc [90]. The study was small, lacked long-term follow-up, and did not report robust endpoints such as organ function or survival, making conclusions tentative at best. Moreover, lenabasum is not MC but a synthetic CB2 receptor agonist.

In summary, while preclinical studies strongly suggest antifibrotic and anti-inflammatory effects, clinical evidence in SSc is scarce. Current human data are limited to small early-phase trials, insufficient to establish efficacy or safety. Until adequately powered randomized studies are conducted, cannabinoids in SSc should be considered experimental, with potential limited to symptomatic pain relief rather than disease modification.

As Fibromyalgia Therapy

The diagnosis of fibromyalgia comprises diffuse chronic pain, tender points at specific locations, uncomfortable sleep, fatigue and various cognitive difficulties and is only clinical as no objective biomarkers or imaging findings exist. These symptoms frequently overlap with other rheumatic, endocrinological, and psychiatric conditions, so the diagnosis is more challenging [91]. Given its strong correlation with pain, sleep disturbance, and fatigue, MC has gained attention as a potential therapeutic option [85]. A review by Albo and Amital through international prescription drug monitoring programs revealed marked increase in MC prescribing for chronic pain, particularly in fibromyalgia, reflecting both patient demand and physician willingness to consider MC as an alternative to opioids in complex pain syndromes [92]. Similarly, Singla et al. reported symptom improvement in 82 % of respondents, with remarkable effects on pain, anxiety, and sleep disturbances [93]. While valuable for capturing patient experience, such surveys are vulnerable to recall bias, lack control groups, and often recruit from self-selected populations of cannabis users, limiting generalizability.

Randomized evidence is emerging but remains limited. A Brazilian double-blind, placebo-controlled trial found significant improvement in Fibromyalgia Impact Questionnaire scores with THC-rich oil compared to placebo [94]. In contrast, a small, single-dose, randomized crossover trial by Van de Donk et al. (2019; n =20) showed limited short-term analgesia, highlighting the need for larger and longer trials [95].

Systematic reviews, including a 2018 meta analysis of 16 studies, found MC demonstrated moderate efficacy in for chronic pain conditions, including fibromyalgia [96]. It assessed both randomized controlled trials (RCTs) and observational studies. It concluded that while cannabinoids showed moderate efficacy in reducing pain intensity, the results were most significant for chronic pain conditions such as fibromyalgia. The conclusion was

based on the fact that MC did not consistently provide long-term benefits, and adverse effects such as dizziness and sedation were common.

A 2024 editorial by David et al. [97] emphasized the increasing interest in cannabinoids within rheumatology, particularly for chronic pain conditions such as fibromyalgia, while underscoring the need for more robust clinical evidence. These findings align with broader research suggesting that cannabinoids may provide relief for fibromyalgia-related symptoms, although larger controlled studies are still needed.

Overall, MC appears to provide symptomatic relief in subsets of fibromyalgia patients, particularly for pain and sleep disturbance. However, the current evidence base is limited by small sample sizes, short follow-up, reliance on patient-reported outcomes, and lack of standardized dosing or formulations. Robust, adequately powered RCTs are needed to establish long-term efficacy and safety.

As Diabetes Therapy

Previous studies have demonstrated that cannabis users have a modestly lower prevalence of both obesity and diabetes compared to matched controls, despite cannabis's appetite-stimulating effects and increased consumption of low-nutritional-value carbohydrates among users [98, 99]. However, these findings are subject to potential confounders such as the "well smoker effect," recall bias, relatively low cannabis exposure in survey populations and no dose-response effect has been demonstrated. In contrast, other studies have not consistently supported a protective association; for example, a Swedish prospective study found no change in diabetes incidence between cannabis smokers and non-smokers after adjusting for age [100].

Cannabinoids may influence diabetes and glucose control through several mechanisms. Stimulation of CB1 receptors in pancreatic beta cells can cause beta cell death, while activation in the brain and fat cells can increase appetite and promote adipogenesis and obesity, which are risk factors for glucose intolerance and type 2 diabetes [3, 101]. Human and animal studies have shown that cannabis use is associated with higher caloric intake, but paradoxically, users tend to have lower body mass index (BMI), lower prevalence of obesity, and reduced insulin resistance and fasting insulin levels [98, 99]. Also, its use is associated with higher glycated hemoglobin (HbA1c) and a greater incidence of diabetic ketoacidosis in type 1 diabetes, as well as evidence of poorer self-management during episodes of use [47, 102-104]. Some studies suggest that the beneficial impact of cannabis on insulin resistance may be mediated through its effect on lowering BMI rather than a direct metabolic effect [98]. While animal models have suggested a protective effect of cannabis against type 1 diabetes, these findings have not been replicated in humans [47].

Cannabis use among individuals with type 2 diabetes has increased, with a 34% rise in past-month use among U.S. adults with diabetes between 2021 and 2022 [102, 105]. There are also concerns about the joint effects of type 2 diabetes and cannabis use on mental health, including an elevated risk of suicide, which is paradoxical given the metabolic associations [105].

CBD and THC are the main cannabinoids in cannabis, and both may have anti-diabetic effects through their action on the endocannabinoid system [101, 106, 107]. However, detailed mechanisms remain unclear, and only one randomized controlled trial has

investigated CBD's efficacy on glycemic parameters in type 2 diabetes, finding no effect on lowering glycemic parameters despite some changes in other markers [106]. Preclinical studies in rodents have shown that CBD can arrest the onset and progression of diabetes and ameliorate some complications, but these findings have not been confirmed in humans [106, 107]. CBD's anti-inflammatory properties may be valuable in treating and delaying diabetes symptoms, as chronic inflammation is a risk factor and symptom of both type 1 and type 2 diabetes[107].

The literature on cannabis and diabetes is limited, with many studies being cross-sectional, based on self-report, or lacking in mechanistic detail [47, 106]. There are gaps in direct evidence linking cannabis use to improved or worsened outcomes in diabetes, and more high-quality research is needed to provide robust, evidence-informed guidance for patients and healthcare providers [104]. Current recommendations emphasize education, counseling, and caution regarding recreational cannabis use in people with diabetes, especially type 1 diabetes [102, 104].

As Mental Health Disorder Therapy

Medical cannabis is increasingly being used to manage a variety of mental health conditions, including anxiety, depression, post-traumatic stress disorder (PTSD), stress, insomnia, mood stabilization, and attention-deficit/hyperactivity disorder (ADHD) [57, 108-112]. While chronic pain remains the most common reason for medical cannabis use, mental health disorders are frequently cited as secondary or emerging indications [51, 57, 108, 109, 111, 112].

Anxiety is consistently reported as the most common mental health condition for which medical cannabis is used [57, 109, 111]. Depression and PTSD are also prominent reasons for medical cannabis authorization [57, 109, 112]. Other reported uses include management of stress, insomnia, mood stabilization, and ADHD [110, 112]. Both prescribed and self-administered cannabis are used for mental health symptom management, often alongside chronic pain and sleep disorders [51, 112, 113].

SAFETY PROFILE AND ADVERSE EFFECTS

Cannabinoids generally have a high safety profile for acute toxicity, but chronic use has been associated with negative effects on reproductive performance, including hypofertility [55].

Common side effects include dizziness, cognitive impairment, and nausea [58]. The psychoactive effects and addictive potential of Δ9-THC have historically limited clinical use, while CBD is well tolerated and lacks abuse liability [17].

While adverse effects associated with medical and recreational cannabis use include neural and psychiatric disorders, as well as increased risk of other conditions such as neoplasia [111, 113, 114]. There is a strong association between cannabis use and the onset or worsening of mental disorders such as schizophrenia, bipolar disorder, depression, anxiety attacks, panic disorders, and dependence [111, 113, 114].

LEGAL STATUS OF MEDICAL CANNABIS (MC)

MC authorization has been associated with an increased risk of emergency department visits or hospitalization for depressive disorders, highlighting the need for careful risk-benefit assessment, especially for patients seeking cannabis for depression [114]. Frequent cannabis users are more likely to have anxiety disorders, and patients with anxiety disorders have a higher risk of developing cannabis dependence [111]. In addition, the lack of rigorous clinical trials, small sample sizes, and legal/social barriers have hindered the accumulation of high-quality evidence [16, 57, 112]. However, the evidence supporting its efficacy is often described as limited, weak, or conflicting, with systematic reviews and clinical studies reporting mixed outcomes [16, 56, 57, 112].

Legal Status of cannabis for medical use varies significantly across countries and within countries, often creating a complex and sometimes contradictory regulatory environment. In the United States, cannabis is classified as a Schedule I substance under federal law, making its possession and use illegal at the federal level. However, many states have enacted their own laws permitting the use of cannabis for medical purposes, resulting in a patchwork of regulations. As of recent data, 36 to 38 states, several territories, and the District of Columbia have legalized cannabis for medical use, while 24 states and some territories have also legalized it for recreational use. Despite these state-level legalizations, federal law supersedes state law, and individuals may still face federal prosecution even in states where medical cannabis is legal [30, 50, 54, 115].

Other countries also display a range of legal frameworks. For example, Canada has legalized cannabis for both medical and recreational purposes, though there are restrictions such as minimum age requirements that vary by province. In the United Kingdom, medical cannabis can be prescribed by specialist consultants under specific conditions, but general practitioners are not permitted to prescribe it. Across the European Union, laws differ: some countries allow only cannabis-derived medications, while others have more permissive policies. In India, the legal status of cannabis varies by state, with some states allowing medical use under certain conditions and others maintaining strict prohibitions [46, 54, 115].

CANNABIS USES IN EGYPT

Historical Medical Use of Cannabis in Egypt

Evidence from ancient Egyptian medical papyri, such as the Ebers Papyrus (circa 1550 BCE), documents the use of cannabis for treating a variety of medical ailments, including inflammation, glaucoma, pain, eye diseases, and gynecologic disorders. Cannabis was also mentioned for topical application as an anti-inflammatory compound and as a remedy for depression and ophthalmic disorders in other ancient Egyptian texts, such as the Papyrus Ramesseum III (1700 BCE)[69, 116, 117]. Hemp threads have been found in Egyptian tombs, indicating its use as a source of fiber over 3300 years ago [116, 117].

However, there is conflicting information regarding the cultivation of cannabis in ancient Egypt, with one source stating that cannabis was neither cultivated nor known in Ancient Egypt [118].

while other sources suggest its presence and use [69, 116, 117].

Current Legal Status of Cannabis in Egypt

Cannabis is rigorously forbidden in Egypt, and its legal status is among the strictest in Africa. While some African countries have legalized or decriminalized cannabis for medical or traditional use, Egypt maintains strict prohibition [69]. Despite this, cannabis farming is partially authorized in Egypt, with cultivation occurring especially in the Sinai Peninsula and Upper Egypt. Hashish is commonly smuggled into the country, while herbal cannabis (bango) is increasingly cultivated domestically [118=120]. Cannabis is included in Schedule IV of the United Nations' Single Convention on Narcotic Drugs, which allows for medical and scientific use under a licensing system, but Egypt has not adopted such a system for medical cannabis [115].

Prevalence and Patterns of Use

Cannabis is the most abused drug in Egypt, with approximately 2.7%–4.9% of the population aged 15–64 years having used cannabis at least once in their lifetime. It is particularly prevalent among youth and drivers, often due to the belief that it is harmless [119, 121]. The main forms of cannabis abused in Egypt are bango (herbal cannabis) and hashish, with seizures of these substances increasing since 1998, possibly reflecting higher market demand or more effective law enforcement [118 119]. Drug abuse in Egypt is mainly a male problem between 20 and 30 years of age, although female abusers are increasing [121, 122].

Medical Use and Regulatory Framework

Currently, there is no legal framework for the medical use of cannabis in Egypt. Unlike countries such as Israel, the Netherlands, and several others where medical cannabis is regulated and available under prescription, Egypt has not legalized cannabis for medical purposes [69, 115]. The Egyptian government has focused on prevention and treatment of addiction, with clinics and treatment centers established for drug addicts, and educational programs aimed at young people [118]. The regulatory challenges in Egypt include strict prohibition, lack of product standardization, and absence of a system for medical cannabis access, contrasting with evolving frameworks in other countries [115, 123].

Comparison with Other Countries

Legalization and Regulation: Countries such as Israel, the Netherlands, the UK, and South Africa have legalized or regulated medical cannabis, with detailed criteria for licensure and prescription [53]. In contrast, Egypt maintains strict prohibition, with no legal access for medical use [69, 115, 118].

Cultivation and Market

While cannabis farming is partially authorized in Egypt, it is not regulated for medical use. Lebanon and Morocco, other Arab nations with high prevalence rates, have moved towards legalization for medical and industrial purposes, with Lebanon legalizing cannabis for medical use in 2020 [120]. Therapeutic Evidence: There is a strong consensus in the

literature supporting the therapeutic use of cannabis for conditions such as chronic pain, epilepsy, and cancer, which has led to re-evaluation of its legal status in many countries. However, Egypt has not adopted these changes [115, 123, 124].

CONCLUSION

Cannabis is one of the most widely used psychoactive substances globally, with over 192 million people reporting some level of usage in 2020, and nearly 1 in 10 individuals using it daily. Approximately the same proportion develops addictive symptomatology. Cannabis is the most commonly used drug worldwide, with particularly high use in North America, where 14.5% of the population reports use and 13.8 million adults are daily or near-daily users. As of 2020, 47 states in the US have medical cannabis programs, although cannabis remains a federally designated schedule I controlled substance. The World Health Organization estimates that about 2.5% (147 million) of the adult population worldwide uses cannabis for recreational or other reasons [125, 126, 127].

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