Evidence for Use of Cannabinoids in Mood Disorders, Anxiety Disorders, and PTSD: A Systematic Review

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Objective: Two primary compounds of the cannabis plant (*Cannabis sativa*), delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), differentially and dose-dependently affect mood and anxiety. In this systematic review, the authors summarize the design and results of controlled trials assessing the effects of THC and CBD on affective disorders, anxiety disorders, and posttraumatic stress disorder (PTSD).

Methods: A keyword search of eight online literature databases identified eight randomized controlled trials of defined CBD or THC doses for the target populations.

Results: A 1-month trial of daily THC (up to 3 mg per day) for *DSM-II* anxiety disorder reduced anxiety symptoms, but symptoms were very low throughout the study. Another trial of sequential, single-day, low-dose THC in social anxiety disorder found no symptom changes. Two studies reported that single-dose CBD pretreatment reduced anxiety in laboratory paradigms among individuals with social anxiety disorder. A study of daily CBD for 4 weeks among adolescents with social anxiety disorder indicated modest symptom improvements. One crossover trial involving 10 patients with PTSD showed that THC added to standard pharmacotherapy reduced self-reported nightmares. Two small studies of THC for hospitalized patients with unipolar or bipolar depression found no improvement of depression; instead, anxiety and psychotic symptoms emerged in >50% of patients.

Conclusions: With only eight very small studies, insufficient evidence was found for efficacy of CBD and THC to manage affective disorders, anxiety disorders, or PTSD. Therefore, medical cannabis should not be recommended for treating patients with these disorders. Further research should investigate the safety and efficacy of managing psychiatric disorders with cannabinoids.

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Humans have utilized products from cannabis plant species for millennia—for example, ancient Chinese literature discussed the perceived medicinal values of cannabis several thousand years ago (1). Recreational use of cannabis species containing relatively high levels of delta-9-tetrahydrocannabinol (THC) became widespread in the western world in the 19th century and grew increasing popular in the United States later in the 20th century. In the 1970s, the U.S. Drug Enforcement Administration scheduled cannabis as a substance with high abuse potential and no known medicinal value (2), but illegal recreational use continued to be common. Since then, researchers have begun to explore whether cannabis has medicinal value, although this work has been slowed by strict regulations on studies that administer cannabis to humans.

As state efforts to legalize cannabis for medical and recreational purposes were increasingly successful over the past 10 years (3), public perceptions have shifted away from viewing cannabis as harmful. Almost half of the American public has endorsed the belief that cannabis may provide relief from anxiety and depression (4). Thus, in states where cannabis is legal for medical use, people approach their physicians to seek medical cannabis for symptoms of anxiety and depression, and over a third of people who use medical cannabis have reported using it to reduce anxiety (5). To date, 28 states list posttraumatic stress disorder (PTSD) as a

HIGHLIGHTS

- The authors conducted a systematic review of eight small studies on the efficacy of the cannabis compounds (cannabinoids) cannabidiol and delta-9-tetrahydrocannabinol (THC) for managing affective disorders, anxiety disorders, and PTSD.
- Research to date provides insufficient evidence for the efficacy of cannabinoids in treating patients with these disorders and indicates potential safety concerns associated with using THC for depression management.
- Medical cannabis should not be recommended for patients with these mental disorders, and further research should investigate the safety and efficacy of managing these three psychiatric disorders with cannabinoids.

potentially qualifiable condition for certification of cannabis purchase and use, one state lists anxiety, and one state lists refractory generalized anxiety disorder, but none specifically lists depressive disorders (6). Although effective pharmacotherapy and behavioral treatments for mood disorders, anxiety disorders, and PTSD are available, physicians feel compelled to respond to patients' requests for medical cannabis and thus need information regarding scientific evidence for whether cannabis is effective for managing these conditions.

When considering the efficacy of cannabis for a given condition, researchers must take into account the multiple cannabis components. The cannabis plant contains >500 constituents, including THC and cannabidiol (CBD) (7). THC is the most psychoactive component and responsible for intoxicating and neurocognitive effects that can lead to the development of cannabis use disorder and other adverse consequences (8) In contrast, CBD is not thought to be addictive (9). Additionally, cannabis contains other cannabinoids, including >100 terpenophenols that may have physiological activity in humans, and plant steroids, as well as fungi, bacteria, and pesticides (10), raising concerns over the potential impact of ingesting whole-plant materials and highlighting the complexity of conducting and interpreting studies with this plant. The type (or species) of cannabis plant, cultivation and harvesting techniques, environmental conditions, and other factors contribute to a wide variation in the concentrations of THC, CBD, and other cannabinoid components in a given plant (11). For correct interpretation and reproduction of research on the psychoactive effects of whole-plant "cannabis," the type, dose, and duration of administration of the constituents of the studied cannabis plant product must be specified (12, 13).

Neurobiological research involving humans and animals has begun to describe the functions and complexities of the endocannabinoid system (14), as well as its role in modulating fear, anxiety, and mood (14–16). Laboratory research involving healthy humans has assessed the impact of THC, and to a lesser extent CBD, on mood and anxiety. For example, THC administration increased anxiety, dysphoria, psychotic-like experiences, and sedation among 33% of healthy participants and engendered an overall feeling of intoxication. The impact of acute THC administration on anxiety is dose dependent, with low doses reducing anxiety and higher doses eliciting anxiety (17). CBD, on the other hand, does not cause these effects (18), and THC and CBD were shown in one study to have opposite effects on the amygdala during a fear-inducing task (19), suggesting biological plausibility for use of these agents in psychiatric disorders involving fear (i.e., PTSD and anxiety disorders). On its own, CBD has not been observed to function as an anxiolytic in healthy subjects (20, 21). Some studies, however, have reported that CBD-THC coadministration may reduce the anxiogenic effects of THC (17, 20), although the evidence is mixed (22–24). Thus, exogenous cannabinoids can differentially affect mood and anxiety, presumably via the endocannabinoid system.

Despite these observations, the National Academy of Sciences (NAS) recently summarized the preclinical, clinical, and epidemiological evidence related to cannabis without specifying the specific physiological roles of THC, CBD, or other cannabinoids. For example, rather than reporting evidence of efficacy, the NAS report concluded that a moderate level of evidence indicates that cannabis use is associated with increased incidence of social anxiety disorder among regular users, increased risk for developing depressive disorders, increased incidence of suicidal ideation and behavior (attempts as well as completion, particularly among heavy users), and increased symptoms of mania and hypomania among regular users with bipolar disorder. This report also indicated that limited evidence of statistical association between cannabis use and these conditions supports the conclusion that cannabis use increases the likelihood of developing bipolar disorders or any anxiety disorder, except social anxiety disorder; increases the severity of PTSD symptoms among those with a PTSD diagnosis; and increases symptoms of anxiety among daily users. Finally, the report conveyed that CBD use has limited evidence of efficacy in improving anxiety symptoms, as assessed by a public speaking test, among individuals with social anxiety disorder (25).

The goal of this review was to gather information in order to determine whether THC and CBD specifically influence clinical symptoms of anxiety and depression among individuals with psychiatric disorders. We conducted a systematic review of prospective, controlled studies testing the impact of cannabinoids on individuals with anxiety disorders, affective disorders, and PTSD.

METHODS

Data Sources

We searched PubMed/MEDLINE, PsycINFO, PsycARTICLES, CINAHL, EMBASE, Scopus, Cochrane, and Academic OneFile for English-language medical literature published between January 1, 1970, and February 5, 2020, by using the following search strategies and terms. "Cannabidiol AND PTSD," "cannabidiol AND post-traumatic stress*," "cannabidiol AND anxiety," "cannabidiol AND bipolar," "cannabidiol AND depress*," "cannabidiol AND mania," "cannabidiol AND schizo*," and "cannabidiol AND psycho*." "CBD AND PTSD," "CBD AND post-traumatic stress*," "CBD AND anxiety," "CBD AND bipolar," "CBD AND depress*," "CBD AND mania," "CBD AND schizo*," and "CBD AND psycho*." "Tetrahydrocannabinol AND PTSD," "tetrahydrocannabinol AND post-traumatic stress*," "tetrahydrocannabinol AND anxiety," "tetrahydrocannabinol AND bipolar," "tetrahydrocannabinol AND depress*," "tetrahydrocannabinol AND mania," "tetrahydrocannabinol AND schizo*," and "tetrahydrocannabinol AND psycho*." "THC AND PTSD," "THC AND post-traumatic stress*," "THC AND anxiety," "THC AND bipolar," "THC AND depress*," "THC AND mania," "THC AND schizo*," and "THC AND psycho*." The search results were

supplemented with references gleaned from recent reviews and citations in searched returns.

Inclusion and Exclusion Criteria

All studies reporting prospective, randomized, and controlled trials involving humans with specified doses of whole-plant cannabis or of CBD, THC, or both compounds compared with placebo were considered. Any commercially available or synthetic cannabinoid formulations were accepted. We included only studies involving individuals with a formal diagnosis of clinical disorders (anxiety, mood, or PTSD) as assessed by any version of the *DSM* (*DSM-I* through *DSM-5*). We excluded studies in which anxiety and mood disturbances were elicited among individuals without clinical disorders. The original search yielded 6,132 reports. Two authors (C.N.S. and N.T.) examined the title and abstract of each study. No disagreements arose about whether a report was eligible for the present study. Eight studies met our criteria for inclusion. (A flow diagram describing the study selection is presented in an online supplement to this article.)

RESULTS

Among the eight studies meeting our criteria, two included persons with *DSM-I* or *DSM-II* anxiety disorders (26, 27), three included individuals with social anxiety disorder (28–30), one included persons with PTSD (31), and two included persons with mood disorders during a depression episode (32, 33) (Table 1). Seven studies used a double-blind, randomized design with a placebo control (27–33), and one study used a single-blind Latin square design (26). Of the five anxiety disorder studies, two examined the role of single-dose CBD administration (N=34) (28, 29), one examined the role of daily CBD dosing for 4 weeks among individuals with social anxiety disorder (N=37) (30), and two examined the role of nabilone, a synthetic form of THC, either dosed weekly among individuals with generalized anxiety disorder (N=8) (26) or dosed daily for 28 days among individuals with diagnoses of low-grade anxiety disorders, according to the version of the *DSM* used before 1981 (N=20) (27). The PTSD study was performed with active duty Canadian military men (N=10) and mainly examined the impact of 7 weeks of daily nabilone administration on PTSD-related nightmares (31). The two studies involving individuals with bipolar and unipolar depression evaluated THC administration for 1 or 3 weeks and placebo or monitoring with no treatment for 1 or 3 weeks in an inpatient setting (N=21) (32, 33).

CBD and THC for Anxiety Disorders

Two small studies reported mixed findings on the impact of synthetic THC on various anxiety conditions (26, 27). Another two studies of single-dose CBD and one of daily-dosed CBD for 4 weeks among individuals with social anxiety disorders reported beneficial effects of CBD (28, 29). The details of these studies are summarized below.

The anxiolytic properties of nabilone were studied with a single-dosing paradigm (26). Eight symptomatic individuals with a diagnosis of either anxiety neurosis or generalized anxiety disorder received a single dose of 2 mg of nabilone or placebo and then once-a-week dosing of nabilone of various strengths, ranging from 0.5 mg to 5 mg, over 5 weeks. Nabilone was not associated with any improvements in anxiety symptoms. Adverse effects included increased heart rate and sedation; orthostatic hypotension was observed among 100% of people assigned to higher nabilone doses.

In contrast, a 1-month trial of daily nabilone for anxiety disorders reported statistically significant findings (27). In this double-blind trial, low-dose nabilone 1 mg three times per day or placebo was administered to 20 participants with a *DSM-II* diagnosis of psychoneurotic anxiety disorders over 28 days, followed by a 4-day washout. Anxiety symptoms improved in the nabilone group, compared with the placebo group. However, participants' total scores on the Hamilton Anxiety Rating Scale were very low to begin with. Scores on this scale can range from 0 to 56, with 18–24 indicating moderate anxiety levels. The mean total anxiety scores of participants in this study were in the very low range: 1.9 on the first treatment day and about 1.0 on day 28 in the nabilone group and 1.7 in the placebo group. Thus, inferences cannot be made regarding nabilone's efficacy among individuals with symptomatic anxiety disorders. Most participants continued to participate in the trial despite reports of mild to severe dry mouth among 18 of the 20 participants and drowsiness among three participants.

As for CBD trials, a blinded crossover functional MRI scanning study compared a single dose of 400 mg of oral CBD to placebo in 10 treatment-naïve men with a diagnosis of generalized social anxiety disorder (28). A significant decrease in anxiety was observed in the CBD-pretreated group upon exposure to an anxiety-provoking stimulus, without appreciable adverse effects. The mean±SD score on the anxiety factor of the Visual Analog Mood Scale (VAMS) decreased from 48.3±7.7 to 30.8±7.7 with CBD administration versus 46.9±7.6 to 42.1±10.3 with placebo. This was replicated in a subsequent study, in which 24 treatment-naïve undergraduates with a diagnosis of social anxiety disorder were randomly assigned to receive a single dose of 600 mg of oral CBD or placebo 90 minutes before a simulated public speaking test (29). In this study, those who received placebo experienced a 37-point worsening of the anxiety factor on the VAMS, compared with a 21-point worsening with CBD administration. Additionally, the CBD pretreatment also resulted in less cognitive impairment and less discomfort during both the anticipation and the speech phases of the test compared with placebo. Evaluation of adverse effects was not reported in the study.

In a recent double-blind, randomized controlled trial conducted with Japanese teenagers who had a *DSM-IV* diagnosis of social anxiety disorder, 300 mg of CBD oil was administered orally each day for 4 weeks (30). The 17 participants assigned to CBD experienced significant symptom

TABLE 1. Studies of cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC) to treat patients with mood and anxiety conditions[a]

Study	Clinical condition	Type of study[b]	Study population[c]	Intervention[d]	Results[e]
Masataka, 2019 (30)	Social anxiety disorder	Placebo-controlled, DB RCT	Japanese non–cannabis-using teenagers (N=37) in outpatient setting	CBD: 4 weeks of 300 mg qD vs. placebo	Decrease in anxiety: mean±SD FNE score improved more with CBD vs. placebo (24.4±2.7 to 19.1±2.1 vs. 23.5±2. to 23.3±2.9); mean LSAS score improved more with CBD vs. placebo (74.2±7.5 to 62.1±8.7 vs. 69.9±10.3 to 66.8±11.2). Adverse effects were not evaluated.
Bergamaschi et al., 2011 (29)	Social anxiety disorder	Placebo-controlled DB RCT	Portuguese undergraduate students (N=24) undergoing simulated public speaking test in outpatient setting	CBD: single dose of 600 mg vs. placebo	Decrease in anxiety: mean VAMS scores worsened less with CBD vs. placebo (21 vs. 37 points, respectively). Adverse effects were not evaluated.
Fabre and McLendon, 1981 (27)	Psychoneurotic anxiety disorder	Placebo-controlled DB RCT	Psychotropic-free adults (N=20) in private outpatient setting	Nabilone: 28 days of 1 mg TID vs. placebo	Decrease in anxiety: mean HAM-A improved more with nabilone vs. placebo (1.9 to 1.0 vs. 1.7 to 1.7). Adverse effects were common with nabilone (dry mouth, drowsiness).
Glass et al., 1981 (26)	Anxiety neurosis or generalized anxiety disorder	SB, placebo-controlled Latin square	Adults ages 23–30 years (N=8) in outpatient setting	Nabilone: once 2 mg, then weekly .5 –5 mg qD for 5 weeks vs. placebo	No improvement in anxiety as assessed with the POMS. Adverse effects were tachycardia, sedation, and orthostatic hypotension with higher nabilone doses; dizziness, dissociation, and time distortions at ≥4 mg/day.
Crippa et al., 2011 (28)	Social anxiety disorder	Placebo-controlled, DB RCT crossover	Treatment-naïve Portuguese adult men ages 20–33 years (N=10) undergoing anxiety-provoking stimuli in outpatient setting	CBD: single dose of 400 mg vs. placebo	Decrease in anxiety: mean VAMS worsened less with CBD vs. placebo (48.3±7.7 to 30.8±7.7 vs. 46.9±7.6 to 42.1±10.3). Adverse effects were not evaluated or reported.

continued

TABLE 1, *continued*

Study	Clinical condition	Type of study[b]	Study population[c]	Intervention[d]	Results[e]
Jetly et al., 2015 (31)	Nightmares among people with treated PTSD	Placebo-controlled, DB RCT crossover	Canadian male military personnel outpatients (N=10) with PTSD and nightmares refractory to prazosin and antidepressant treatment	Nabilone: 7 weeks of .5–3 mg qD vs. placebo	Improvement in nightmares: change in mean CAPS dream scores indicated greater improvement with nabilone vs. placebo (−3.6±2.4 vs. −1.0±2.1); CGI-C scores improved more with nabilone vs. placebo (1.9±1.1 vs. 3.2±11.2; p=.05). No PTSD scores were reported. Most participants experienced dry mouth and headache.
Ablon and Goodwin, 1974 (33)	Unipolar and bipolar major depression	Placebo-controlled, DB RCT	Adults (N=13) in inpatient setting (NIMH research unit)	THC: 7 days of .3 mg/kg BID vs. placebo	Clinical evaluation revealed no improvement in depressive symptoms. No standardized measures reported. Most participants experienced dysphoric reactions, including panic and psychotic disturbances, even after a single dose.
Kotin et al., 1973 (32)	Unipolar and bipolar major depression	Placebo-controlled, DB RCT crossover	Psychotropic-free adults (N=8) in inpatient setting (NIMH research unit)	THC: 7 days of 5 mg qD to 20 mg BID vs. placebo	Clinical evaluation and 15-item mood checklist (scores not reported) revealed no improvement in depressive symptoms. A 50% attrition rate was reported because of sedation, anxiety, and depersonalization, even after a single dose.

[a] Studies are ordered by mental health condition (anxiety, PTSD, and depression).
[b] DB, double blind; RCT, randomized controlled trial; SB, single blind.
[c] NIMH, National Institute of Mental Health.
[d] qD, once a day; TID, three times a day; BID, twice a day.
[e] CAPS, Clinician-Administered PTSD Scale (possible scores range from 0 to 4, with higher scores indicating more extreme or incapacitating symptoms); CGI-C, Clinical Global Impression of Change (possible scores range from 1 to 7, with higher scores indicating worse presentation); FNE, Fear of Negative Evaluation Questionnaire (possible scores range from 0 to 30, with higher scores indicating higher levels of social anxiety); HAM-A, Hamilton Anxiety Rating Scale (possible scores range from 0 to 56, with higher scores indicating more severe anxiety); LSAS, Liebowitz Social Anxiety Scale (possible scores range from 0 to 144, with higher scores indicating more severe social anxiety); POMS, Profile of Mood States; VAMS, Visual Analog Mood Scale (this scale has eight specific mood states: afraid, confused, sad, angry, energetic, tired, happy, and tense; possible scores range from 0 to 100 on these mood states, with higher scores indicating higher levels of a specific mood state).

improvement from baseline to 4 weeks, compared with the 20 participants assigned to placebo. Mean scores on the Liebowitz Social Anxiety Scale, on which possible scores range from 1 to 144 (higher scores indicated worse anxiety), improved from 74.2±7.5 to 62.1±8.7 in the CBD group versus 69.9±10.3 to 66.8±11.2 in the placebo group. Adverse effects were not systematically evaluated.

We did not find any prospective controlled trials of repeated or daily dosing of CBD or plant marijuana among individuals with other types of anxiety disorders in whom symptoms of these disorders were prospectively assessed. We also did not find any placebo-controlled studies of defined dose combinations of CBD and THC or plant marijuana involving persons with anxiety disorders.

THC and CBD for PTSD

One very small randomized, double-blind, and placebo-controlled crossover study investigated the effectiveness of nabilone for decreasing the frequency and intensity of trauma-related nightmares associated with PTSD (31). Ten military personnel with a PTSD diagnosis who continued to experience trauma-related nightmares despite treatment with prazosin and a standard antidepressant received either 0.5 mg of nabilone (titrated to an effective dose; the maximum was 3 mg and the mean dose 1.95±0.9 mg) or placebo. Participants were followed up for 7 weeks of treatment, underwent a 2-week washout, and then received the alternative treatment (nabilone or placebo). Nabilone treatment was associated with a statistically significant reduction in nightmare frequency and intensity and in scores on the Clinical Global Impression of Change (CGI-C) scale, compared with placebo (1.9±1.1 vs. 3.2±11.2, p=0.05). (Possible scores on the CGI-C range from 1 to 7, with higher scores indicating worse presentation.) Total PTSD scores were not reported. Dry mouth and headache were common adverse effects. We did not identify any prospective, placebo-controlled studies that examined the impact of CBD, THC-CBD combinations, or plant marijuana on individuals with PTSD.

THC and CBD for Affective Disorders

Two controlled trials in the 1970s evaluated THC for the treatment of patients with unipolar and bipolar depressive disorders (32, 33). Both trials failed to show significant antidepressant effects of THC and indicated that it has poor tolerability, as described below.

In one of the studies, eight psychotropic-free patients were hospitalized for moderate-to-severe depression (four with bipolar disorder and four with unipolar major depressive disorder) (32). Under double-blind conditions, they received 3 weeks of treatment: a 7-day course of placebo, followed by a 7-day course of twice-daily oral THC (0.3 mg per kg), and then another 7 days of placebo. No antidepressant effect of THC was found on subjective and objective measures of mood. Of the eight participants, only four could complete the THC treatment phase, even though they experienced some sedation. Four patients discontinued the drug because of adverse effects, two of whom experienced severe anxiety with depersonalization after a single dose. In the other study, 13 hospitalized patients (five with a bipolar disorder depression episode and eight with a unipolar major depression episode) underwent 3 weeks of observation, followed by treatment under double-blind conditions with oral THC, titrated from 5 mg daily up to 20 mg twice daily or placebo (33). Depression symptoms did not improve with this treatment. Seven of the 13 participants experienced dysphoric reactions (six of those with unipolar depression and one with bipolar depression); six could not complete the study because of panic reactions or psychotic disturbances after the first dose. The authors of the two articles did not report specific depression scale scores.

We did not find any prospective placebo-controlled studies of THC or plant marijuana for bipolar mania or the long-term treatment of persons with bipolar disorder. We did not identify any prospective placebo-controlled studies that examined the impact of CBD, defined combinations of CBD and THC, or plant marijuana on individuals with affective disorders.

DISCUSSION

Public interest in the use of medical cannabis has skyrocketed in the past few years (34). On the basis of existing studies that included control conditions, randomization, and prospective blinded assessments, we found that there is not enough research to adequately determine the efficacy of THC alone, CBD alone, defined CBD-THC combinations, or plant marijuana to treat individuals with anxiety disorders, affective disorders, or PTSD. In total, only 112 participants were studied across eight small trials, five of which included ≤13 participants. Furthermore, only two of these studies evaluated participants for a clinically relevant period (1 month), and none of the studies examined cannabinoid combinations or smoked whole plant. A recent meta-analysis that included studies of symptoms among patients given THC, CBD, or THC-CBD combinations for other conditions or disorders (e.g., pain or multiple sclerosis) similarly found insufficient evidence to confirm efficacy for these conditions and disorders (35).

In addition to the lack of evidence for efficacy in controlled prospective trials, careful epidemiologic research suggests that cannabis use can worsen the course of bipolar (36–38), depressive (39), and anxiety disorders (40). Furthermore, individuals with these disorders are at greater risk for developing substance use disorders, which are associated with several negative social, occupational, and health outcomes (41). Thus, given the current low level of evidence for the efficacy of THC and CBD for treating patients with these disorders and the availability of other effective, nonaddictive treatments approved by the Food and Drug Administration, cannabis (THC or CBD) is not indicated and should not be recommended for the treatment of persons with anxiety disorders, mood disorders, or PTSD. Clinicians and medical

cannabis programs should provide accurate information to their patients and strongly caution them about the use of cannabis products, particularly those that include psychoactive doses of THC.

The findings of this review indicate that the state of research regarding THC- and CBD-based treatment for persons with anxiety disorders, affective disorders, and PTSD is in a very early phase. Most of the studies reviewed were generally developmental: they recruited relevant clinical populations but used only a short treatment period to obtain a signal of efficacy and safety. The studies had tremendous heterogeneity in experimental design; designs were generally reasonable but often lacking in systematic symptom measurement and were usually underpowered. Additionally, the formulation, route of administration, and length of CBD and THC treatments varied widely, and the quality of the medications and plant products used was not reported. Other limitations included the lack of evidence that blinding of the interventions was effective; also, most studies did not evaluate whether past use of cannabis among participants could have affected the findings. The recent meta-analysis mentioned above also found that studies using THC, CBD, or a combination of both for treating symptoms of mental illness in broader populations generally had low quality (35).

Nevertheless, these small clinical studies provide very preliminary data on the potential value of cannabinoids for modulating the endocannabinoid system. Exploratory research should continue, including prospective controlled clinical trials, to test not just efficacy and safety but also dose, dosing regimen, route of administration, and other parameters prior to the proposal of any recommendations for or approval of cannabinoids for the management of any condition.

CONCLUSIONS

Currently, small and controlled clinical trials have provided only very limited data regarding the effects of cannabis in the management of mood disorders, anxiety disorders, and PTSD. Clinicians and medical cannabis programs should provide accurate information to their patients and caution them about the use of such products. Given the biological plausibility that cannabis compounds could have a positive impact on some conditions, high-quality, well-designed, and sufficiently powered studies should be undertaken to determine which, if any, anxiety- or trauma-related conditions could be managed with specific cannabinoids.

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