

ROMAŃCZUK, Kuba Borys, KAMIŃSKA-OMASTA, Katarzyna, OMASTA, Bartosz, KRUPA, Olga, PIETRUKANIEC, Paulina Dorota, WÓJCIK, Zofia Martyna, FURTAK, Kinga, STOLARCZYK, Szymon Przemysław, CZERSKA, Magdalena Agata, and RYBAK, Daria. A Review of Human Studies Assessing the Efficacy of Cannabidiol for Anxiety Disorders. *Quality in Sport*. 2025;38:58231. eISSN 2450-3118.

<https://doi.org/10.12775/OS.2025.38.58231>

<https://apcz.umk.pl/OS/article/view/58231>

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.

Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).

Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.

Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

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The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 26.01.2025. Revised: 01.02.2025. Accepted: 05.02.2025 Published: 05.02.2025.

## **A Review of Human Studies Assessing the Efficacy of Cannabidiol for Anxiety Disorders**

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**ABSTRACT****Introduction**

Anxiety disorders are the most commonly diagnosed chronic mental health conditions worldwide, and their prevalence continues to rise, leading to significant social and economic burdens. Since psychotherapy and pharmacotherapy often prove insufficient in preventing symptom relapse, it is crucial to assess the effectiveness of cannabidiol (CBD) in the treatment of these disorders.

**Aim of the Study**

This systematic review assesses the current evidence on the efficacy of CBD in treating anxiety and related disorders, including post-traumatic stress disorder (PTSD), social anxiety disorder (SAD), and autism spectrum disorder (ASD). It provides a comprehensive analysis of CBD's therapeutic potential across diverse clinical populations.

**Materials and Methods**

A review of literature was conducted using the Google Scholar database to gather information on "cannabidiol," specifically focusing on its relationship with "anxiety," "social anxiety disorder", "post-traumatic stress disorder" and „human trials."

**Summary**

Anxiety disorders are the most commonly diagnosed mental disorders worldwide. Recent interest has focused on CBD as a potential treatment. Unlike open-label trials prone to placebo bias, this study reviews randomized, double-blind, placebo-controlled trials. Positive outcomes

were observed with 300 mg CBD doses, reducing anxiety in SAD patients, tremor in Parkinson's disease, and anxiety in ASD and opioid-dependent individuals. Minimal improvements were noted in PTSD patients with sexual trauma. Further research is needed to clarify CBD's therapeutic potential in diverse clinical contexts.

**Keywords:** anxiety, cannabidiol (CBD), post-traumatic stress disorder (PTSD), social anxiety disorder (SAD), human trials

## **Introduction**

In recent years, cannabidiol (CBD), one of the many naturally occurring phytocannabinoids, has attracted increasing interest from the scientific community, policymakers, and mainstream media. CBD is the second most abundant active compound found in the *Cannabis sativa* plant. Unlike  $\Delta^9$ -tetrahydrocannabinol (THC), the primary psychoactive component of this plant, CBD does not produce psychomimetic effects. Compared to THC, CBD has a very low affinity for cannabinoid receptors 1 and 2 (CB1, CB2) [1]. Furthermore, safety studies have shown that CBD is well-tolerated by patients, even at high doses, such as 6,000 mg per day when administered orally [2]. Scientific literature underscores the multifaceted effects of CBD on the human body, which include improvements in motor activity, neuropathic pain, and epilepsy, as well as anticancer and anti-inflammatory properties. Additionally, CBD may have beneficial metabolic effects, like enhancing lipid and glycemic parameters in individuals with type 2 diabetes [3]. Increasing attention is also being paid to the anxiolytic potential of CBD.

Anxiety is a natural emotional response to perceived threats; however, it becomes maladaptive when it occurs excessively in the absence of significant threats [4]. The "Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition" (DSM-5) classifies anxiety disorders such as generalized anxiety disorder (GAD), social anxiety disorder (SAD), specific phobias (SP), and separation anxiety as anxiety disorders. Obsessive-compulsive disorder (OCD) and post-traumatic stress disorder (PTSD) share similar symptoms of excessive anxiety, but they are discussed in separate chapters in the DSM-5, following the section on anxiety disorders [5]. Anxiety disorders are the most common mental disorders globally, affecting about 4% of the population [6]. Due to their chronic nature, these conditions impose significant social and economic burdens [7]. It is important to note that traditional treatment methods, such as

psychotherapy and pharmacotherapy, often prove inadequate in preventing symptom relapse [8].

Despite its low affinity for cannabinoid receptors, CBD can influence the endocannabinoid system, partly by inhibiting the breakdown of anandamide (AEA), an endogenous cannabinoid that activates CB1 receptors. The increase in AEA levels due to the inhibition of its breakdown may contribute to the anxiolytic effects of CBD. Other proposed mechanisms include the activation of transient receptor potential vanilloid type 1 (TRPV1) and serotonin 1A receptor (5-HT1A) receptors, which are located in brain regions involved in stress and anxiety regulation, such as the prefrontal cortex, hippocampus, amygdala, and periaqueductal gray matter [9]. This suggests that the anxiolytic effect of CBD may arise from its interaction with these receptors, making it a promising candidate for the treatment of anxiety disorders.

### **Literature overview**

In a randomized, double-blind, placebo-controlled study conducted by Bolsoni et al. (2022) among patients diagnosed with PTSD, 33 participants aged 18 to 60 years, including both genders, were enrolled. Participants were randomly assigned to two groups using a minimization method in a 1:1 ratio: one group received 300 mg of CBD (n=17), while the other received a placebo (n=16). The demographic and clinical characteristics, including gender, age, body mass index (BMI), and PTSD symptom severity measured by the PCL-5 checklist, did not differ significantly between the groups. Among the study participants, 14 experienced sexual trauma, and 19 experienced non-sexual trauma. In the sexual trauma subgroup, 7 participants received CBD, while 7 received a placebo. In the non-sexual trauma subgroup, 10 participants received CBD and 9 received a placebo [10].

The Portuguese version of the Visual Analog Mood Scale (VAMS) was utilized to assess the study's outcomes, focusing on four subjective factors: anxiety, sedation, cognitive impairment, and discomfort. Physiological measurements included systolic blood pressure (SBP) and diastolic blood pressure (DBP), heart rate (HR), and salivary cortisol levels [10].

The experimental protocol involved two sessions separated by one week. During the first session, participants recorded their traumatic experiences in audio format. In the second session, participants received either CBD or a placebo, and 90 minutes later, a trauma recall procedure was conducted, followed by the required measurements. Statistical analysis included t-tests for

continuous variables, Fisher's exact test for nominal data, and repeated-measures analysis of variance (ANOVA). Key factors considered in the analysis were treatment group (CBD vs. placebo), trauma type (sexual vs. non-sexual), and phase (pre- and post-trauma recall). A p-value of less than 0.05 was considered statistically significant [10].

The results indicated a significant increase in VAMS scores for all factors after the trauma recall. In the non-sexual trauma subgroup, the change in anxiety levels (VAMS) before and after trauma recall was significantly smaller in the CBD group compared to the placebo group (mean difference = -9.82;  $p = 0.033$ ; 95% CI: -18.74 to -0.91). No significant differences were noted between groups for sexual trauma (mean difference = 5.00;  $p = 0.497$ ; 95% CI: -10.56 to 20.57). Additionally, CBD resulted in a greater reduction in anxiety for non-sexual trauma compared to sexual trauma (mean difference = 11.40;  $p = 0.035$ ; 95% CI: 0.90–21.89). Regarding cognitive impairment, a significant reduction in VAMS scores was observed in the non-sexual trauma subgroup in the CBD group compared to the placebo group (mean difference = -8.21;  $p = 0.008$ ; 95% CI: -13.94 to -2.47). However, no significant differences were found in the sexual trauma subgroup (mean difference = -3.70;  $p = 0.524$ ; 95% CI: -16.00 to 8.60) [10].

No significant differences were identified between the placebo and CBD groups regarding sedation or discomfort, regardless of trauma type. Furthermore, a 300 mg dose of CBD did not affect physiological stress responses, as measured by changes in blood pressure (BP), HR, or salivary cortisol levels following trauma recall ( $p > 0.05$ ) [10].

In a randomized, double-blind, placebo-controlled experiment conducted by Linares et al. (2019), 57 healthy male participants were enrolled. The participants were randomly assigned to one of four groups: those receiving oral CBD at doses of 150 mg ( $n = 15$ ), 300 mg ( $n = 15$ ), 600 mg ( $n = 12$ ), or a placebo ( $n = 15$ ). The groups were comparable in terms of age (mean: 24.5 years), years of education, and socioeconomic status. None of the participants had any diagnosed mental health disorders [11].

The study included a Simulated Public Speaking Test (SPST), during which participants were tasked with delivering a short speech in front of an audience. Subjective anxiety levels were assessed using the VAMS scale, and physiological parameters such as SBP and DBP and HR were measured at six time points. Anticipatory anxiety was evaluated just before the speech.

Each participant delivered their speech in front of a camera while viewing their image on a television screen, and they were informed that their performance would be recorded and evaluated by psychologists [11].

The first measurements of anxiety (VAMS) and BP were taken 90 minutes after the administration of CBD or the placebo. Subsequent measurements were conducted mid-speech, followed by post-speech assessments immediately after the speech (F1) and 30 minutes later (F2) [11].

Statistical analyses were performed using Student's t-test for continuous variables and ANOVA via SPSS software (version 20.0). A p-value of less than 0.05 was considered statistically significant [11].

The ANOVA revealed a significant effect of phase ( $F(2,48) = 131.6$ ;  $p < 0.001$ ) and group ( $F(3,53) = 2.714$ ;  $p = 0.05$ ), with no significant interaction between group and phase ( $F(7,45) = 1.72$ ;  $p = 0.1$ ). Post hoc analyses indicated that the group receiving 300 mg of CBD experienced significantly lower anxiety levels during the speech phase compared to the placebo group ( $p = 0.042$ ). There were no significant differences in VAMS scores observed between the placebo group and those receiving 150 mg or 600 mg of CBD [11].

The VAMS results exhibited a dose-response pattern resembling an inverted "U" curve. The lowest dose (150 mg) and the highest dose (600 mg) of CBD produced minimal or no anxiolytic effects during the SPST, while the 300 mg dose was the most effective in reducing anxiety induced by public speaking [11].

Regardless of the dose, CBD did not affect physiological stress responses, as indicated by changes in BP and HR during the SPST ( $p > 0.05$ ) [11].

Bergamaschi et al. (2011) conducted a randomized, double-blind study to evaluate the therapeutic effects of CBD on individuals with SAD. The study involved 36 participants, including 24 individuals who met clinical criteria for SAD and 12 healthy participants serving as a control group. The participants with SAD were randomly assigned to receive either CBD

(600 mg, n = 12) or a placebo (n = 12), administered 1.5 hours before they took part in the SPST. The control group (n = 12) did not receive any substances prior to the SPST [12].

The study employed the Self-Statements During Public Speaking Scale (SSPS), which was translated into Portuguese and adapted to evaluate negative self-assessment (SSPS-N). Participants indicated their subjective feelings on a 100-mm line anchored by opposing mood descriptors. Additional tools included the Bodily Symptoms Scale (BSS), which measures physical symptoms potentially related to anxiety, and the VAMS scale, which assessed situational anxiety. Physiological parameters, such as BP, HR, and skin conductance, were also measured [12].

Baseline measurements were collected, followed by the administration of CBD, placebo, or no intervention for the control group. A second measurement was taken 80 minutes after substance administration. During the SPST, participants had 2 minutes to prepare a 4-minute speech on the topic of "the public transportation system in their city." Anxiety and physiological parameters were measured halfway through the speech, and final assessments were conducted 15 and 35 minutes after the test. The results were analyzed using ANOVA, with a significance level set at  $p < 0.05$  [12].

During the speech, the SAD-placebo group experienced significantly higher levels of anxiety ( $p = 0.007$ ), cognitive impairment ( $p = 0.001$ ), discomfort ( $p = 0.001$ ), and sedation ( $p = 0.005$ ) compared to the control group, as measured by VAMS scores. In contrast, the SAD-CBD group showed significant reductions in anxiety ( $p = 0.012$ ), cognitive impairment ( $p = 0.009$ ), discomfort ( $p = 0.029$ ), and sedation ( $p = 0.016$ ) compared to the SAD-placebo group following CBD administration [12].

Results from the SSPS-N also indicated significant differences between the SAD-placebo and SAD-CBD groups ( $p = 0.001$ ), as well as between the SAD-placebo group and the control group ( $p < 0.001$ ). Notably, no significant differences were observed between the SAD-CBD group and the control group regarding SSPS-N scores or VAMS components related to cognitive impairment, discomfort, and sedation [12].

De Faria et al. (2020) conducted a study to evaluate the effects of CBD on anxiety levels and tremors induced by the SPST in individuals with idiopathic Parkinson's disease (PD). This randomized, double-blind, crossover clinical trial involved 24 participants with PD who continued their standard antiparkinsonian treatments throughout the study [13].

Participants received a single dose of 300 mg CBD or a placebo before the SPST. Inclusion criteria ensured that participants had no significant cognitive impairments and were not using benzodiazepines or antidepressants during the study. Anxiety levels were assessed using the VAMS scale and the SSPS. Tremor frequency and amplitude were measured with an accelerometer, and motor symptoms were evaluated through a tapping test, which required participants to complete 10 cycles of tapping between two points 30 cm apart. Physiological parameters, including SBP, DBP, and HR, were recorded at designated time points [13].

The study consisted of two experimental sessions separated by 15 days, each lasting approximately three hours. Clinical assessments were conducted at baseline, immediately after the administration of CBD or placebo, and 90 minutes after administration. During the SPST, participants prepared for two minutes and then delivered a four-minute speech on topics related to urban infrastructure, such as transportation or water supply systems. The speeches were performed under socially stressful conditions: participants observed their images on a television screen and were informed that their performance would be recorded and evaluated by a psychologist [13].

Tremor measurements using the accelerometer were taken during the first minute of the speech, with additional measurements performed 10 minutes (F1) and 25 minutes (F2) after the SPST. Data were analyzed using ANOVA, with statistical significance set at  $p < 0.05$  [13].

The results showed that a single dose of 300 mg CBD significantly reduced subjective anxiety levels compared to the placebo, as measured by the VAMS ( $F(1,21) = 6.27$ ;  $p = 0.021$ ). CBD also significantly reduced peak tremor amplitude (PSA) as measured by the accelerometer ( $F(1,20) = 6.19$ ;  $p = 0.022$ ). However, no significant differences were observed between the groups regarding other VAMS factors such as sedation, discomfort, or cognitive impairment. Additionally, CBD did not have a significant effect on peak tremor frequency (PTF), power spectral entropy (PSE), or the time required to complete the tapping test [13].

A double-blind study conducted by Nobuo Masataka in 2019 involved 37 Japanese individuals aged 18 to 19 who were diagnosed with SAD. Participants, both male and female, had experienced anxiety disorders for at least six months. Over a four-week period, they received daily doses of hemp oil containing 300 mg of CBD (17 participants) or a placebo (20 participants) [14].

SAD symptoms were assessed at the beginning and end of the treatment period using the Fear of Negative Evaluation Questionnaire (FNE) and the Liebowitz Social Anxiety Scale (LSAS). A clinical psychologist, unaware of whether the participants received CBD or the placebo, visited their homes daily in the afternoon to administer 420 ml of the oil via a syringe throughout the four-week intervention. After the intervention, during a follow-up phase, the clinical psychologists monitored the participants' health and assessed any effects of the administered substance once a week for up to six months [14].

The average FNE score in the CBD group was significantly lower after the intervention compared to before ( $p = 0.02$ ), while no significant change was observed in the placebo group ( $p = 0.29$ ). Post-intervention FNE scores in the CBD group were significantly lower than those in the placebo group ( $p = 0.0002$ ). In contrast, pre-intervention differences between the groups were not statistically significant ( $p = 0.71$ ). Similarly, average LSAS scores in the CBD group were significantly reduced after the intervention compared to before ( $p = 0.03$ ), but no significant reduction in LSAS scores was found in the placebo group ( $p = 0.42$ ). Post-intervention LSAS scores in the CBD group were also significantly lower than those in the placebo group ( $p = 0.0018$ ), while pre-intervention differences between the two groups were not statistically significant ( $p = 0.66$ ) [14].

These findings provide evidence of the anxiolytic effects of repeated CBD administration in adolescents with SAD. [14].

A double-blind, randomized, placebo-controlled clinical trial conducted by Hurd et al. (2019) examined the effects of CBD on anxiety reduction in individuals with heroin addiction who had been abstinent for at least three months. The study involved 42 participants aged 21 to 65, who were randomly assigned to one of three groups: 400 mg of CBD (N=14), 800 mg of CBD

(N=13), or a placebo (N=15). Participants received their assigned substances daily for three consecutive days. Drug-related cues were presented immediately following the administration of CBD or placebo, as well as 24 hours and seven days after the final dose [15].

Before each test session, participants rated their anxiety levels using the Visual Analog Scale for Anxiety (VAS-A) and their opioid craving using the Visual Analog Scale for Craving (VAS-C). Post-administration measurements included VAS-A, VAS-C, the Positive and Negative Affect Schedule (PANAS), physiological parameters (skin temperature, BP, HR, respiratory rate, oxygen saturation), and salivary cortisol levels. Final assessments were conducted seven days after the last dose [15].

During all sessions, participants in the placebo group reported significantly higher anxiety levels after exposure to drug-related cues (mean increase: 0.97) compared to those in the CBD groups (400 mg: 0.48; 800 mg: 0.24). No significant differences were found between the 400 mg and 800 mg CBD groups. Acute CBD administration, unlike the placebo, significantly reduced cue-induced anxiety, with effects persisting up to seven days after the three-day administration period. CBD also decreased physiological stress markers, such as HR and salivary cortisol levels [15].

Data analysis employed a mixed-effects linear model with repeated measures using the MIXED procedure in SAS. The significance level was set at  $p < 0.05$ . CBD had a significant effect on opioid craving ( $F=5.74$ ,  $df=2$ ,  $78$ ,  $p=0.0047$ ) as measured by the VAS-C scale. Participants receiving the placebo reported higher cravings after cue exposure (mean increase: 0.93) compared to the CBD groups (800 mg: 0.23; 400 mg: 0.44). No significant differences were found between the 400 mg and 800 mg CBD groups, indicating that both doses were similarly effective in reducing cravings [15].

CBD also significantly reduced cue-induced anxiety ( $F=5.15$ ,  $df=2$ ,  $78$ ,  $p=0.0079$ ), as measured by the VAS-C. Participants in the placebo group experienced higher anxiety levels (mean increase: 0.97) compared to the CBD groups (400 mg: 0.48; 800 mg: 0.24). A significant main effect of the treatment group was observed ( $F=3.42$ ,  $df=2$ ,  $37$ ,  $p=0.0433$ ). Participants receiving the placebo exhibited the highest increase in negative affect (mean: 5.31), while those receiving 800 mg of CBD showed the lowest increase (mean: 0.79) [15].

The findings from the PANAS scale supported these observations ( $F=3.42$ ,  $df=2, 37$ ,  $p=0.0433$ ). The placebo group showed the highest increase in negative affect (mean: 5.31), while the 800 mg CBD group had the lowest increase (mean: 0.79) [15].

Participants in the placebo group demonstrated elevated HR and skin temperatures after cue exposure ( $F=1.629$ ,  $df=2, 35$ ,  $p=0.052$ ). Drug-related cues also significantly elevated cortisol levels in the placebo group compared to the 400 mg CBD group ( $p=0.049$ ). No significant differences were observed among groups for BP, respiratory rate, oxygen saturation, or cognitive test results ( $p > 0.05$ ) [15].

In a prospective, randomized, double-blind, phase 3 clinical trial conducted by Gundugurti et al. (2024), 178 participants with mild to moderate GAD, as assessed by the Depression Anxiety Stress Scale (DASS-21), were enrolled. During the 12-week treatment period, participants received either a nanodispersed oral solution of CBD at doses ranging from 300 to 600 mg daily or a placebo. The total duration of the study was 15 weeks. Anxiety severity was measured using the Hamilton Anxiety Rating Scale (HAM-A) and the Generalized Anxiety Disorder Scale (GAD-7) across 11 on-site visits and 4 teleconsultations. Statistical analysis was conducted using version 9.4 of the Statistical Analysis System (SAS), with a significance level set at  $p < 0.05$  [16].

The difference in GAD-7 scores from baseline to the end of treatment for the CBD group compared to the placebo group was  $-7.02$  (SE: 0.25, 95% CI:  $-7.52$  to  $-6.52$ ,  $p < 0.0001$ ). The difference in HAM-A scores was  $-11.9$  (SE: 0.33, 95% CI:  $-12.6$  to  $-11.3$ ,  $p < 0.0001$ ) [16].

In a randomized, double-blind, placebo-controlled clinical trial conducted by da Silva Junior et al. (2024), 60 children aged 5 to 11 years with autism spectrum disorder (ASD) were enrolled. Participants were assigned to receive either a CBD-rich cannabis extract or a placebo for a duration of 12 weeks, depending on their group assignment. The initial dosage of the CBD extract was six drops daily (three drops administered twice daily), with an option to increase the dosage by two drops per day, twice a week, up to a maximum of 70 drops daily [17].

To assess treatment efficacy, researchers used a semi-structured interview developed by the authors and the Autism Treatment Evaluation Checklist (ATEC), which caregivers completed before and after the study. Statistical analysis was conducted using ANOVA, with a significance level set at  $p < 0.05$  [17].

The results indicated statistically significant improvements in the CBD treatment group compared to the placebo group in several areas: social interactions ( $F_{1,116} = 14.13$ ,  $p = 0.0002$ ), anxiety ( $F_{1,116} = 5.99$ ,  $p = 0.016$ ), psychomotor agitation ( $F_{1,116} = 9.22$ ,  $p = 0.003$ ), daily meal frequency ( $F_{1,116} = 4.11$ ,  $p = 0.04$ ), and concentration ( $F_{1,48} = 6.75$ ,  $p = 0.01$ ). Notably, the improvement in concentration was significant only in cases of mild ASD. Adverse effects were reported in only three children in the treatment group (9.7%), which included dizziness, insomnia, colic, and weight gain. [17].

## Discussion

In summary, the results of the clinical trials discussed demonstrate the promising potential of CBD in reducing the severity of anxiety disorders. The key data is presented in the table below.

**Table 1. Summary and comparison of studies investigating the effects of CBD on anxiety disorders.**

Citation	Study design	Classification	Outcome Measures	Number of Participants	CBD Dosage Examined	Duration of active treatment	Effects of CBD on anxiety compared to Placebo	Impact of CBD on Physiological Parameters (BP, HR)
Bolsoni et al. (2022)	Randomized, parallel-group, double-blind, placebo-controlled trial	PTSD diagnosis	VAMS, physiological measures (BP, HR)	33	300mg	90 minutes	Improvement was observed in the non-sexual trauma group ( $p = 0.033$ for VAMS). No statistically significant difference was found in the sexual trauma group ( $p = 0.497$ on the VAMS scale).	There was no statistically significant difference ( $p > 0.05$ ).
Linares et al. (2019)	Double-blind, randomized, placebo-controlled trial	Response to anxiety in healthy volunteers.	VAMS, physiological measures (BP, HR)	57	150mg 300mg 600mg	120 minutes	Improvement was observed in the 300 mg CBD group ( $p = 0,042$ on the VAMS	There was no statistically significant difference ( $p > 0.05$ ).

							scale)	
Bergamaschi et al. (2011)	Double-blind, randomized, placebo-controlled trial	SAD diagnosis	VAMS, SSPS-N, BSS, physiological measures (BP, HR)	36	600mg	115 minutes	Improvement was observed in the 600 mg CBD group ( $p = 0,012$ on the VAMS scale) ( $p < 0,001$ on the SSPS-N scale) ( $p < 0,001$ on the BSS scale)	There was no statistically significant difference ( $p > 0.05$ ).
De Faria et al. (2020)	Randomised, double-blinded, placebo-controlled, crossover trial	Anxiety response in patients with PD	VAMS, SSPS, physiological measures (BP, HR)	24	300 mg	180 minutes	Improvement was observed in the 300 mg CBD group ( $p=0.021$ ) on the VAMS scale, No statistically significant difference on the SSPS scale	There was no statistically significant difference ( $p > 0.05$ ).
Masataka (2019)	Randomized, double-blind, placebo-controlled trial	Teenagers with SAD	LSAS, FNE	37	300 mg	4 weeks	Improvement was observed in the 300 mg CBD group ( $p = 0,0002$ on the FNE scale) ( $p = 0,0018$ on the LSAS scale)	N/A
Hurd et al. (2019)	Randomized, double-blind, placebo-controlled trial	Heroin users in abstinence.	VAS-A, VAS-C, PANAS, physiological measures (BP, HR, RR, SpO2)	42	400mg, 800mg	3 days	Improvement was observed in both 400 and 800 mg CBD group ( $p=0,0079$ on the VAS-A scale)	No statistically significant differences were found in BP, RR, SpO2 ( $p > 0.05$ ). Significant improvements were observed in HR, temperature, and salivary cortisol levels ( $p < 0.05$ ).
Gundugurti et al. (2024)	Prospective, randomized, double blind, parallel group,	Mild to moderate GAD	HAM-A, GAD-7	178	300-600mg	12 weeks	Improvement was observed in the CBD group ( $p < 0,0001$ on the	N/A

	placebo-controlled trial						GAD-7 and HAM-A scale)	
Da Silva Junior et al. (2024)	randomized, double-blind, and placebo-controlled clinical trial	Children aged 5 to 11 years old with an ASD diagnosis	Semi-structured author's questionnaire, ATEC	60	6-70 drops of CBD oil 5mg/ml	12 weeks	Improvement was observed in the CBD group (p = 0,016 on the author's questionnaire)	N/A

Source: Author's own compilation based on references [10–17].

The conducted meta-analysis provides evidence of the anxiolytic effects of CBD, showing statistically significant reductions in anxiety symptoms for both healthy individuals faced with stress-inducing situations and patients with conditions such as ASD, SAD, and PTSD. Notably, the analysis reveals differences in CBD efficacy based on specific anxiety disorder subtypes, indicating the necessity for a tailored therapeutic approach according to individual clinical profiles.

The findings demonstrate the notable effectiveness of CBD in alleviating subjective anxiety symptoms associated with SAD, with significant improvements observed in both short- and long-term usage (Masataka, 2019; Bergamaschi et al., 2011). Furthermore, CBD showed properties that help mitigate cognitive deficits related to the recall of traumatic events in PTSD patients, suggesting potential therapeutic benefits that extend beyond mere symptom reduction. However, it's important to note that in the subgroup of patients with sexual trauma, studies by Bolsoni et al. (2022) reported no significant differences compared to a placebo group.

Short-term studies on anxiety induced by public speaking (Linares et al., 2019; Bergamaschi et al., 2011; De Faria et al., 2020) demonstrated significant reductions in anxiety symptoms among participants receiving CBD compared to those given a placebo. Notably, patients with PD experienced not only reduced anxiety but also a decrease in tremor amplitude. These results align with previous reports indicating that anxiety can exacerbate tremors in such patients, highlighting CBD's potential as an adjunctive treatment, especially considering the adverse effects of conventional medications [18, 19].

Research by da Silva Junior et al. (2024) also underscores the beneficial impact of CBD on children with ASD, resulting in improvements in social interactions, reduced anxiety, and decreased hyperactivity. Further studies involving adults are crucial for a comprehensive evaluation of CBD's therapeutic potential in treating ASD.

The literature suggests optimal therapeutic doses of CBD, with dosages of 300–400 mg being most effective in reducing anxiety in stress-inducing situations like public speaking. However, a study by Hurd et al. (2019) found no difference in efficacy between 400 mg and 800 mg in opioid-dependent participants. Standardizing dosing and therapeutic outcome measurements is essential for making precise clinical recommendations.

Despite the promising results, most of the analyzed studies had small sample sizes, which limits their generalizability. Additionally, there is a notable lack of research exploring sex differences in CBD efficacy and side effects. Measuring plasma CBD levels and correlating these with outcomes would enhance understanding. Furthermore, many findings focus on short-term CBD use; data on chronic administration primarily come from open-label trials, which may be subject to placebo effect biases [20].

While CBD appears to have a favorable safety profile, potential interactions with drugs metabolized by CYP450 enzymes must be taken into account, as these interactions can alter plasma drug concentrations [21]. CBD is a strong inhibitor of CYP3A4 and CYP2D6, potentially increasing the levels of medications such as macrolides, calcium channel blockers, antidepressants, antipsychotics, and opioids [21]. It is essential to educate patients about these interactions. Other risks associated with CBD use may include dependency, cognitive impairment, and episodes of psychosis [22, 23, 24].

### **Conclusions:**

CBD shows promise as a therapeutic agent for treating anxiety disorders, with a relatively mild safety profile. Its efficacy in reducing anxiety symptoms has been confirmed in both healthy individuals and patients with SAD or PTSD. However, further research is required, particularly regarding the long-term use of CBD, its effects on patient health, and any sex-related differences in treatment response.

### **Disclosure**

#### **Author's contribution**

Conceptualization: Kuba Borys Romańczuk and Bartosz Omasta; Methodology: Katarzyna Kamińska – Omasta; Software: Olga Krupa; Check: Daria Rybak, Kinga Furtak and Zofia Martyna Wójcik; Formal analysis: Magdalena Agata Czerska; Investigation: Zofia Martyna Wójcik; Resources: Katarzyna Kamińska-Omasta; Data curation: Bartosz Omasta; Writing - through preparation: Szymon Przemysław Stolarczyk; Writing -review and editing: Kuba Borys

Romańczuk; Visualization: Szymon Przemysław Stolarczyk; Supervision: Paulina Dorota Pietrukaniec; Project administration: Daria Rybak; Receiving funding - no specific funding. All authors have read and agreed with the published version of the manuscript.

#### **Financing statement**

This research received no external funding.

#### **Institutional Review Board Statement**

Not applicable

#### **Informed Consent Statement**

Not applicable.

#### **Data Availability Statement**

Not applicable.

#### **Conflict of interest**

The authors deny any conflict of interest.

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