

Cannabidiol (CBD) use in psychiatric disorders: A systematic review

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Abstract

Cannabidiol (CBD) and Δ^9 -tetrahydrocannabinol (THC) are the most represented phytocannabinoids in *Cannabis sativa* plants. However, CBD may present with a different activity compared with the psychotomimetic THC. Most typically, CBD is reported to be used in some medical conditions, including chronic pain. Conversely, the main aim of this systematic review is to assess and summarise the available body of evidence relating to both efficacy and safety of CBD as a treatment for psychiatric disorders, alone and/or in combination with other treatments. Eligible studies included randomized controlled trials (RCT) assessing the effect of CBD in a range of psychopathological conditions, such as substance use; psychosis, anxiety, mood disturbances, and other psychiatric (e.g., cognitive impairment; sleep; personality; eating; obsessive-compulsive; post-traumatic stress/PTSD; dissociative; and somatic) disorders. For data gathering purposes, the PRISMA guidelines were followed. The initial search strategy identified some $n = 1301$ papers; $n = 190$ studies were included after the abstract's screening and $n = 27$ articles met the inclusion criteria. There is currently limited evidence regarding the safety and efficacy of CBD for the treatment of psychiatric disorders. However, available trials reported potential therapeutic effects for specific psychopathological conditions, such as substance use disorders, chronic psychosis, and anxiety. Further large-scale RCTs are required to better evaluate the efficacy of CBD in both acute and chronic illnesses, special categories, as well as to exclude any possible abuse liability.

Section snippets

Background

Cannabidiol (CBD) and Δ^9 -tetrahydrocannabinol (THC) are the most represented phytocannabinoids in *Cannabis sativa* plants (Crippa et al., 2018; Corroon and Phillips, 2018; Ligresti et al., 2016). CBD was isolated from cannabis extracts in the 1940s (Adams et al., 1940) and, even though initially considered a non-active cannabinoid (Crippa et al., 2018; Zuardi, 2008), it was then recognised as presenting with a different activity compared with the psychotomimetic THC (Casajuana Köguel et al., 2018)

Search strategy

A systematic electronic search was performed on 31 st January 2019 on a range of international databases, including PubMed, Cochrane Controlled Register of Trials (CENTRAL), and Web of Science. The systematic review was structured in accordance with the PRISMA guidelines (Moher et al., 2009). The search terms “cannabidiol” and “CBD” were combined with “substance use disorders”, “psychotic disorders”, “anxiety disorders”, “mood disorders”, “cognitive disorders”, “sleep disorders”, “personality

Results

The initial search strategy yielded a total of $n = 1301$ articles that were screened by title and abstract for eligibility. A total of $n = 190$ studies passed the title/abstract screening and were considered for full-text screening. Of these studies, $n = 135$ were excluded, as either mostly referring to preclinical

models, or due to inappropriate study design/population. The remaining n = 55 were searched for duplicates, and secondary publications were aggregated in study-based units. Thus, n = 27

Background

The eCBS appears to be involved in both acquisition and maintenance of drug-seeking behaviour, possibly through its role in reward system and brain plasticity (National Academies of Sciences, Engineering, and Medicine, 2017). The dopaminergic pathway activation, linking the ventral tegmental area; the ventral striatum; and the nucleus accumbens, plays a central role in the reward circuit (Chye et al., 2019). In animal models, the CB1 receptor is identified in striatal output projection neurons

Background

The relationship between psychosis and cannabis use has been largely investigated. The acute use of cannabis could lead to the onset of a transient psychotic episode or heterogeneous psychotic-like symptoms (Favrat et al., 2005; Pierre et al., 2016; Thomas, 1996). Furthermore, cannabis has been proposed as a risk factor for the development of schizophrenia, with higher risk associated with younger age at first use, frequency, and duration of use (Casadio et al., 2011; Di Forti et al., 2015;

Background

The eCBS is involved in the regulation of several physiological functions, including the emotional behaviour, which is in turn associated with both learning and response to emotionally salient events (Blessing et al., 2015; Schiavon et al., 2016). The CB1 receptor is involved in the response of acute stress and fear/anxiety response (Blessing et al., 2015). In preclinical studies, reduction in CB1 receptor signaling mediates the anxiogenic effects of corticotropin-releasing hormone in the

Background

The eCBS is known to play a role in mood regulation. Several animal studies have reported depressive symptoms, such as anhedonic state, passive coping behaviour and cognitive deficits in both rat models and CB1 knock-out mice (Martin et al., 2002; Rubino et al., 2008, 2009). In a recent systematic review (Gibbs et al., 2015), it has been suggested the existence of an inverse relationship between cannabis use and clinical stability of bipolar disorder clients. Furthermore, antagonism at CB1

Background

CBD interest in neurocognitive disorders is due to its reported antioxidant, anti-inflammatory, anti-apoptotic and neuroprotective properties (da Silva et al., 2018d; Fernández-Ruiz et al., 2013; Martín - Moreno et al., 2011; Mori et al., 2017; Osborne et al., 2017; Schiavon et al., 2014). It has been proposed that these effects could be more related to the CBD structure and stereochemistry rather than to its CB-receptor binding affinity (Aso et al., 2016b; Wu et al., 2013). CBD

Discussion and conclusions

To the best of our knowledge, the present paper constitutes the most extensive and detailed systematic review specifically focussing on the evaluation of efficacy and safety of CBD in psychiatric populations. Recently, the therapeutic potential of drugs modulating the activity of endocannabinoid receptors has attracted significant interest (Chye et al., 2019; van der Flier et al., 2019v; Pretzsch et al., 2019). CBD use has been proposed for many medical issues for which it has not been studied (

Limitations and conclusions

Current work presents with some limitations. First, potentially eligible studies might have been missed. To minimise this risk, a wide search strategy was performed on three international databases, together with a backward search from the reference lists of included studies. Again, recruited participants in trials focusing on the same disease presented heterogenous characteristics

such as both stage (e.g. early-stage or chronic condition; low- and high-risk individuals), and state (i.e. acute

References (233)

A.J. Hill et al.

Phytocannabinoids as novel therapeutic agents in CNS disorders

Pharmacol. Ther.

(2012)

J.E.C. Hallak et al.

The interplay of cannabinoid and NMDA glutamate receptor systems in humans: preliminary evidence of interactive effects of cannabidiol and ketamine in healthy human subjects

Prog. Neuropsychopharmacol. Biol. Psychiatry

(2011)

A. Gururajan et al.

Does cannabidiol have a role in the treatment of schizophrenia?

Schizophr. Res.

(2016)

F.V. Gomes et al.

Decreased glial reactivity could be involved in the antipsychotic-like effect of cannabidiol

Schizophr. Res.

(2015)

M.V. Fogaça et al.

The anxiolytic effects of cannabidiol in chronically stressed mice are mediated by the endocannabinoid system: role of neurogenesis and dendritic remodeling

Neuropharmacology

(2018)

M.V. Fogaca et al.

Effects of intra-pretlimbic prefrontal cortex injection of cannabidiol on anxiety-like behavior: involvement of 5HT1A receptors and previous stressful experience

Eur. Neuropsychopharmacol.

(2014)

M. Fakhoury

Could cannabidiol be used as an alternative to antipsychotics?

J. Psychiatr. Res.

(2016)

M.W. Elmes et al.

Fatty acid-binding proteins (FABPs) are intracellular carriers for Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD)

J. Biol. Chem.

(2015)

A.T. El-Alfy et al.

Antidepressant-like effect of delta9-tetrahydrocannabinol and other cannabinoids isolated from Cannabis sativa L

Pharmacol. Biochem. Behav.

(2010)

M. Di Forti et al.

Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study

Lancet Psychiatry

(2015)

[View more references](#)

[Cited by \(72\)](#)

The use of cannabidiol as a novel treatment for oral stereotypic behaviour (crib-biting) in a horse
2023, Veterinary and Animal Science

Show abstract

Colombian Consensus of Treatment with Pure Cannabidiol (CBD) in Psychiatry

2023, Revista Colombiana de Psiquiatria

Show abstract

The association between cannabis use and facial emotion recognition in schizophrenia, siblings, and healthy controls: Results from the EUGEI study

2022, European Neuropsychopharmacology

Show abstract

Cannabinoids in movement disorders

2022, Parkinsonism and Related Disorders

Show abstract

Cannabidiol treatment prevents drug reinstatement and the molecular alterations evoked by amphetamine on receptors and enzymes from dopaminergic and endocannabinoid systems in rats

2022, Pharmacology Biochemistry and Behavior