Is the Cannabidiol Potentially Useful for the Treatment of Neuropsychiatric and Drug-Use Disorders?

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Commentary

Preclinical and clinical evidence collected over the past years suggests that Cannabidiol (CBD), one of the main compounds of the plant *Cannabis sativa*, presents potential therapeutic activity for the treatment of neuropsychiatric and drug-use disorders.

Studies carried out in animal models revealed that CBD presents anxiolytic-like effects in different paradigms such as the Vogel conflict test [1], the elevated plus maze test [2] and the fear conditioning test [3-6]. Antidepressant-like effects were reported in mice following acute or repeated CBD administration in the forced swim [7] and in the tail suspension tests [8]. In addition, CBD decreased defensive behaviors evoked by predator exposure, a proposed model of panic attacks and posttraumatic stress disorder (PTSD) [9,10]. Interestingly, CBD reversed the alteration of prepulse inhibition (PPI) observed in spontaneously hypertensive rats [11] and in a glutamate-based models of psychosis [12] and exhibited a similar profile compared with atypical antipsychotic drugs [13,14]. Indeed, CBD improved cognition in several preclinical models of cognitive impairment [15]. Recent evidences pointed out that CBD might be a potential treatment for drug-use disorders. CBD reduced heroin craving and relapse [16], and cocaine [17] and alcohol consumption mice [18].

In clinical studies, CBD reduced anxiety and the psychotic-like symptoms induced by Δ^9-tetrahydrocannabinol (Δ^9-THC) [19]. Indeed, CBD reduced anxiety in healthy volunteers [20-22], in treatment-naïve social phobic patients [23] and in posttraumatic stress disorder [24]. Also, CBD reduced the psychotic symptoms in schizophrenia [25,26] and in Parkinson´s disease [27,28].

In spite of the number of findings suggesting the potential therapeutic use of CBD, there is some controversy regarding its profile as a drug of abuse that significantly hampers further development of basic and clinical studies. CBD is currently classified in the Schedule 1 according to United Nations Single Convention on Narcotic Drugs of 1961 Comprehensive Drug Abuse Prevention and Control Act) of United States (US) [29]. A schedule I controlled substance is defined by the controlled substances act (CSA) as a substance presenting "no currently accepted medical use, a lack of accepted safety for the use under medical supervision, and a high potential for abuse". Furthermore, CBD is classified as a Schedule 2 drug according to the Controlled Drugs and Substances Act [29] also inferring "a high potential for abuse which may lead to severe psychological or physical dependence". However, there is no evidence that supports these considerations. On the other hand, CBD is not under any special restrictions in Europe. In contrast to THC, CBD did not induce euphoria or intoxication [30-32]. The lack of psychoactive activity appears to be related with its low affinity on CB1 receptors (100 fold less than THC) [33]. Interestingly, recent studies carried out in our laboratory demonstrated that CBD did not induce conditioned-place preference, withdrawal signs or oral self-administration suggesting lack of properties as a drug of abuse [34].

To date, no significant side effects have been observed in any of the preclinical and clinical studies carried out with CBD. Furthermore, CBD is present in Nabiximols (marketed as Sativex) currently approved for the treatment of spasticity in multiple sclerosis in several countries in Europe. Therefore, there is a large body of information regarding its safety and side effects.

Taken together, these results suggest that the classification of CBD in the Schedule I should be revised. The reconsideration of CBD as a drug lacking potential for drug abuse would allow the development of basic and clinical studies needed to elucidate its potential therapeutic use for the treatment of neuropsychiatric diseases.

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Conflict of Interest

Authors state that they have no biomedical financial interest or potential conflicts of interest.

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