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## The application of Delta-9-tetrahydrocannabinol (oral THC) against cannabis use disorder

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**Abstract:** *Cannabis sativa* is an Asian plant worldwide known as "marijuana", currently the drug most used among young and adults. It began to be studied from 1960, focusing on the compounds present in the drug, as well as its physiological effects. The use of its active constituents cannabidiol (CBD) and Delta-9-tetrahydrocannabinol (THC) has been discussed by science due to its therapeutic properties in the fight against diseases such as anxiety, depression, epilepsy, and psychoses. Also, THC has analgesic effects and has been widely used in post-chemotherapy medicine, immunosuppressive diseases and marijuana use disorder. The purpose of this present review is to discuss and question the viability and efficacy of Delta-9-tetrahydrocannabinol (THC) against marijuana drug dependence observed in users. Its functionality is not known for sporadic users. The application for the treatment of addiction taking advantage of one of its most abundant components, the THC, allows the user not to experience severely symptoms of abstinence. There are recent studies using Delta-9-tetrahydrocannabinol to combat the overuse of marijuana, by giving serial doses of THC associated or not with drugs, in order to induce less harmful effects of "pleasure" and decrease the number of implications of smoking the herb itself. It is known that abstinence to *Cannabis sativa* is due to the cannabinoid THC because of its various connections to the central nervous system, however, it only presents such symptoms when it is in the body in a concentration between or greater than 80-210 mg per day, thus, the purpose of the studies is to obtain the ideal dose for the treatment of individuals seeking to quit the use disorder.

**Keywords:** Abstinence; Cannabis sativa; THC; Treatment.

## 1. Introduction

Marijuana, scientifically known as *Cannabis sativa*, is an Asian plant that has a great adaptation for climate and soil. Regarding the chemical and pharmacological studies, marijuana began to be studied from the 1960s onwards, with research based on the identification of existing components in the herb (GONTIÈS, 2003). It is currently one of the most widely used drugs in the world (UNODC, 2007 apud BENYAMINA, 2008, p.1) and presents polemicized controversies regarding addiction and withdrawal effects, a maladaptive behavioral change when concentration declines in a physiologically high individual concentration for a chronic period, which may lead to reactions such as aggression, anorexia, irritability, among others (JURUENA, 2012). The active ingredients

## 2. Results and Discussion

The experiment carried out by Vandrey 2012 used standard procedures adopted for periodic administration, behavioral and cognitive observations, clinical manifestations and questionnaires answered by the volunteers. In the results of the study, it was possible to observe that individual doses of 120 mg/day of dronabinol significantly increased the symptoms of stomach pain, irritability, headaches, colds and total withdrawal when compared to the 60mg, 30mg and placebo (PBO); subjective improvement of sleep quality when compared to 30mg doses; and improvement in diarrhea, nausea, anger, and difficulty concentrating when compared to PBO. Doses of 60mg/day provided suppression of decreased appetite, difficulty in concentration, and discomfort of drug withdrawal when compared to the dose of 30mg/day and PBO. However, lower doses shown no differences observed between them.

Similar to latter, the Schilienz 2018 study used equivalent methodologies except for dronabinol dosages, with a minimum of 120mg/day and a maximum of 180-240mg/day

that stand out most from *Cannabis sp.* is the  $\Delta$ -9-tetrahydrocannabinol (THC) present abundantly and responsible for the psychoactive effects of the plant (VANDREY, 2012) and its potential addictive effect, and cannabidiol (CBD) known to be less toxic when compared to THC (GONÇALVEZ, 2014). However, THC has proven effects in patients with immunosuppressive diseases (HIV/AIDS) and post-chemotherapy treatments due to its analgesic effect (VOTH, 1997). In addition, the effects of dronabinol (synthetic oral THC) have shown potential in combating marijuana addiction, assisting to suppress withdrawal symptoms, depending on the dose given or associated compound (VANDREY, 2012).

with the addition of a post-treatment forced choice condition, where the participants had the option to choose between a *Cannabis sp.* active or money (drugs vs. money) in order to prove the efficacy of dronabinol. Individuals who underwent dronabinol treatment, when they responded the forced-choice test, opted for the value offered instead of the cigarette; in addition, responses to the use of different dosages of dronabinol were not discrepant, however, they considered that 120mg/day of the dronabinol is sufficient to achieve the reduction of withdrawal effects and consequently the attenuation of marijuana self-administration.

The research conducted by Levin 2012 was divergent from most studies, for the use of dronabinol in lower doses (13.1mg/day) associated with lofexidine (64mg/day) and was aimed at potentiating the action of dronabinol under the symptoms of dependence reducing the risk of relapse. However, there were unsatisfactory responses and adverse effects in patients dependent on marijuana such as dry mouth, hypotension and even cases of severe abdominal pain and intoxication. Thus, by

showing that the results of the application of placebo and the compound lofexidine-dronabinol were found in an analogy, it was argued that this

association has no therapeutic effect against abstinence.

### 3. Materials and Methods

The present study reflects a retrospective bibliographic survey of selected clinical data from three studies for reading and evaluation, published in the years of 2012, 2016 and 2018, in which they demonstrated different perspectives regarding

physiological and psycho-behavioral responses. They were attached to platforms such as: Scientific Electronic Library Online (SciELO) and PubMed, being found from the themes "THC", "marijuana", "addiction" and "combat".

### 4. Conclusions

The studies presented previously demonstrated that the potential of dronabinol in the fight against the chronic use of marijuana varies according to the administered dose and its drug associations. The lower doses of the compound when administered do not present changes of great significance, not demonstrating the expected effect to attenuate the symptoms of abstinence. However, higher doses may result in

more satisfactory effects, and the reactions in chronic users were considered tolerable and result in fewer side effects. The combination of dronabinol and loxefedine has not shown potential for use, as the effects did not differ from placebo. Furthermore, more clinical studies are needed to sediment the use of dronabinol to treat cannabis abstinence.

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