



Utilization of Cannabis under 0.5% THC

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Abstract: Cannabis and hemp are both related to Cannabis sativa and have the psychoactive compounds tetrahydrocannabinol (THC). They are differentiated into diverse cultivar groups keeping in view the phytochemical constituents and functions. Hemp has a lower concentration of THC and a higher amount of cannabidiol (CBD) which is helpful for the assuage of stimulating the THC damages. Now-a-days hemp is progressively more permitted for cultivation all over the world. Hemp cultivars having cannabis under 0.5% THC are allowed to cultivate in the world for different purposes.

THC levels are also shifting, as breeding of different strains are yielding plants and resins with dramatic increases in THC content over the past decade, from ~ 3% to 12-16% or higher (w/w or percent THC weight/per dry weight of cannabis) and differing in different countries. This plant is widely known to be the major source of cannabinoids, including cannabidiol (CBD), tetrahydrocannabinol (THC), cannabichromene (CBC), cannabigerol (CBG), and cannabinol (CBN). Cannabinoids have shown strong remedial potential against inflammation, depression, nausea, epilepsy, and other effects of clinical relevance. Initial uses of cannabis date back to almost 5000 years in China. Industrial hemp will be utilized having Cannabis less than 0.5% THC. THC is the primary psychoactive compound, with CBD, a non-psychoactive compound, ranking second. Generally, THC is found at higher concentrations than CBD, unless the ratio is deliberately altered. The known chemical composition of Cannabis sativa is constantly changing. New non-cannabinoid and cannabinoid constituents in the plant are discovered frequently. Cannabinoids are basically derived from three sources: (a) Phytocannabinoids are cannabinoid compounds produced by plants Cannabis sativa or Cannabis indica; (b) Endocannabinoids are neurotransmitters produced in the brain or in peripheral tissues, and act on cannabinoid receptors; (c) Synthetic cannabinoids, synthesized in the laboratory, are structurally analogous to phytocannabinoids or endocannabinoids and act by similar biological mechanisms.

INTRODUCTION

Cannabinoids are basically derived from three sources: (a) Phytocannabinoids are cannabinoid compounds produced by plants Cannabis sativa or Cannabis indica; (b) Endocannabinoids are neurotransmitters produced in the brain or in peripheral tissues, and act on cannabinoid receptors; (c) Synthetic cannabinoids, synthesized in the laboratory, are structurally analogous to phytocannabinoids or endocannabinoids and act by similar biological mechanisms.

The evidence presented on potential medical uses and risks of cannabis in humans focuses on unprocessed, botanical cannabis and not isolated cannabinoids, some of which are medically approved. This is because it has been suggested that the cannabis plant contains chemicals that may be useful for treating illnesses or symptoms. Therefore, it has been advanced that whole plant cannabis could be used for medical purposes. The plant contains at least 750 chemicals, among which are some 104 different cannabinoids (Radwan *et al.*, 2015; Izzo *et al.*, 2009).

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The bioavailability of active cannabinoids in cannabis, delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) cannot be predicted because differences in smoking or vapor inhalation vary between users and types of delivery systems. In contrast, a fixed oral dose of a cannabinoid can be quantified in plasma or whole blood samples, yielding relatively predictable results;

THC is the primary psychoactive compound, with CBD, a non-psychoactive compound, ranking second. Generally, THC is found at higher concentrations than CBD, unless the ratio is deliberately altered. The known chemical composition of *Cannabis sativa* is constantly changing. New non-cannabinoid and cannabinoid constituents in the plant are discovered frequently. From 2005 to present, the number of cannabinoids identified in the whole plant increased from 70 to 104, and other known compounds in the plant increased from ~400 to ~650 (Radwan *et al.*, 2015; Elsohly and Slade, 2005; Ahmed *et al.*, 2008).

THC levels are also shifting, as breeding of different strains are yielding plants and resins with dramatic increases in THC content over the past decade, from ~ 3% to 12-16% or higher (w/w or percent THC weight/per dry weight of cannabis) and differing in different countries (Radwan *et al.*, 2008; Niesink *et al.*, 2005; Swift *et al.*, 2013; Zamengo *et al.*, 2014; Bruci *et al.*, 2012). In some cannabis preparations, THC levels have risen even more radically by using a concentrating process (butane hash oil) that yields levels approaching 80% THC (Stogner and Miller, 2015). In an unregulated environment, other factors such as soil quality, bacterial and fungal contamination, the use of herbicides, pesticides, insecticides, water, light, soil availability or quality, temperature, bacterial or viral contamination, animal waste, insects, toxic chemicals, active compounds, heavy metals, bear on cannabis quality (Tipparat *et al.*, 2012).

Lipophilicity of THC accounts for its accumulation after chronic repeated use (Hartman *et al.*, 2015; Grotenhermen, 2003). Metabolic elimination of THC from newly smoked

cannabis is much slower after years of heavy cannabis use. When a single 6.8% THC cannabis cigarette was administered to frequent and to occasional users, plasma THC concentrations were significantly higher in frequent smokers than in occasional smokers at most time points from 0.5 to 30 h. Median (range) time of last detection was 3.5 h (1.1 to .30 h) in frequent smokers and 1.0 h (0-2.1 h) in occasional smokers. In chronic heavy (daily) cannabis users, THC can be detected in blood during a month of sustained abstinence. These findings are consistent with THC lipophilicity and time course of persisting neurocognitive impairment reported in recent studies (Lee *et al.*, 2015; Bergamaschi *et al.*, 2013).

Endogenous and exogenous cannabinoids, including cannabis and THC, affect sleep patterns. There is poor quality evidence that cannabis or cannabinoids have therapeutic benefit in sleep disorders. The endogenous cannabinoid system inhibits seizure susceptibility. Therefore it is unsurprising that exogenous cannabis has antiseizure activity. However, if THC levels are high or cannabis is consumed by susceptible individuals, THC may promote seizures. CBD has therapeutic potential as antiepileptic drug without the psychoactive effects, or potential for pro-seizure activity of whole plant cannabis (Katona, 2015; Rosenberg *et al.*, 2015).

The endogenous cannabinoid system is also implicated in extinguishing learning of aversive situations. On the other hand, THC and cannabis decrease working memory, apparently by actions in the hippocampus, a brain region critical for learning and memory. The memory decrements induced by THC or cannabis resemble hippocampal lesions. These impairments may result from suppression of glutamate release in the hippocampus, which is responsible for the establishment of synaptic plasticity (Mechoulam and Parker, 2013; Zanettini *et al.*, 2011; Morena and Campolongo, 2014).

The induction of psychosis by cannabis was originally reviewed by Warnock in 1903 and substantiated



subsequently; (Wilkinson *et al.*, 2014; Semple *et al.*, 2005) (2) in those harboring a psychotic disorder, cannabis may exacerbate symptoms, trigger relapse, and have negative consequences on the course of the illness; (Manrique-Garcia *et al.*, 2014) (3) susceptible individuals in the general population develop a psychotic illness with heavy cannabis use, which is associated with age of onset of use, strength of THC in cannabis, frequency of use and duration of use; (Moore *et al.*, 2004). (Di Forti *et al.*, 2015) (4) cannabis use is associated with lowering the age of onset of schizophrenia (Di Forti *et al.*, 2014) .

The seed oil is known to be a rich source for unsaturated fatty acids. As a result of the ever increasing consumption of hemp seed products, particularly the oil, there have been some reports that ingestion of hemp seed oil could result in a positive drug test for marijuana use. Analysis of cannabis seeds by different investigators showed that the seeds do contain A9-THC in a wide range of concentrations, whereas others reported the absence of Ag-THC in ungerminated seeds.

This plant is widely known to be the major source of cannabinoids, including cannabidiol (CBD), tetrahydrocannabinol (THC), cannabichromene (CBC), cannabigerol (CBG), and cannabinol (CBN). Cannabinoids have shown strong remedial potential against inflammation, depression (Atalay *et al.*, 2019), nausea, epilepsy, and other effects of clinical relevance (Appendino *et al.*, 2008; Mechoulam and Parker, 2013). Initial uses of cannabis date back to almost 5000 years in China. Since then, hemp consumption has been spurred on by its wide range of properties and uses from one civilization to another through consecutive millennia.

The first-quality powder, which is called sigirma, is golden beige in colour, is produced through the reduction of the flowering tops and the inflorescences and is reputed to have a THC content of up to 20 per cent. The second quality, which is called hamda, also contains plant waste, giving it a greenish colour; more or less intensive sifting of

this powder yields products of varying quality, with a THC content of 2-10 per cent.

These are terpenophenols, classified in several groups according to their structure, the main ones being-9-THC and its acid, cannabidiol (CBD) and cannabinol (CBN). These compounds are accompanied by homologues with shorter side chains (propyl and methyl cannabinoids), precursors (cannabigerol (CBG)) and chromane derivatives (cannabicyclol and cannabichromene), among others.

In addition to the usual constituents of a great number of plants, such as flavonoids and terpenes, more than 60 cannabinoids have been found to be present in cannabis. The main cannabinoids having pharmacological effects on humans (Mura *et al.*, 2004) include: Δ -9-THC, the product; with the strongest psychoactive effect on humans; Δ -8-THC, which is less psychoactive than Δ -9-THC; CBD; CBN, which is not psychoactive but may have an anti-inflammatory effect; Δ -8-THC acid and Δ -9-THC acid (the latter is not active, but it is converted into Δ -9-THC when heated); CBG, which is not psychoactive but may have a bacteriological effect and Cannabichromene, cannabicyclol and their acids.

Plants of limited intoxicant ability, Δ 9 -THC usually comprising less than 0.3% (dry weight) of upper third of flowering plants (sometimes up to 1%) and usually less than half of cannabinoids of resin. Plants cultivated for fibre or oil or growing wild in regions where such cultivation has occurred.

Plants of considerable intoxicant ability, Δ 9-THC usually comprising more than 1% (dry weight) of upper third of flowering plants and frequently more than half of cannabinoids of resin. Plants cultivated for intoxicant properties or growing wild in regions where such cultivation has occurred.

One hundred and twenty phytocannabinoids have been recorded for *C. sativato* date and can be classified into 11 general types: (–)-trans- Δ 9-tetrahydrocannabinol (Δ 9-THC), (–)-trans- Δ 8-tetrahydrocannabinol (Δ 8-THC),



cannabigerol (CBG), cannabichromene (CBC), cannabidiol (CBD), cannabinodiol (CBND), cannabielsoin (CBE), cannabicyclol (CBL), cannabinol (CBN), cannabitriol (CBT), and miscellaneous types (Kinghorn *et al.*, 2017; Pertwee, 2014; Elsohly and Slade, 2005). Δ 9-THC and CBD are the most important plant cannabinoids. Δ 9-THC is the principal intoxicant constituent of *C. sativa* and CBD, which is not intoxicating, is the principal cannabinoid of non-intoxicating forms of *C. sativa*. The cannabis varieties selected for fibre and oilseed production are *C. sativa* subsp. *sativa* and the resin produced in the secretory glands usually has limited amounts of Δ 9-THC, but large amounts of CBD. In contrast, plants that have been selected for their intoxicating drug properties are generally high in Δ 9-THC and are placed in *C. sativa* subsp. *indica*. As reported by Small, “*sativa* type” cannabis varieties have little or no CBD, while “*indica* type” cannabis varieties frequently have substantial amounts of both Δ 9-THC and CBD (Small, 2017).

Although CBD and Δ 9-THC have such relevance when talking about cannabis, these molecules are not enzymatically synthesized in the plant, which instead produces cannabidiolic acid (CBDA) and tetrahydrocannabinolic acid (THCA). CBDA and THCA are the major components of the cannabis inflorescence. THCA is devoid of intoxicating properties and is not a scheduled substance. A chemical reaction triggered by heat leads to the decarboxylation of these compounds producing the corresponding decarboxylated species CBD and Δ 9-THC as occurs when marijuana is smoked or otherwise heated. Other minor cannabinoids are cannabichromenic acid (CBCA) and cannabigerolic acid (CBGA), which is the “stem cell” of the other carboxylated cannabinoid. These compounds, upon decarboxylation, lead to the derivatives cannabichromene (CBC) and cannabigerol (CBG), respectively. There are also different isomers of Δ 9-THC resulting from variations or isomerization in the position of the double bond in the

alicyclic carbon ring, like Δ 8-THC. It has been suggested that Δ 8-THC might be an isolation artefact since it is thermodynamically more stable than Δ 9-THC. Other minor phytocannabinoids are the propyl homologues of the C-3 n-pentyl side-chain of the different phytocannabinoids including Δ 9-THC, CBC, CBD and CBG; these are termed as Δ 9-tetrahydrocannabivarin (Δ 9-THCV), cannabichromevarin (CBCV), cannabidivarin (CBDV) and cannabigerovarin (CBGV), respectively. Moreover, cannabinol (CBN) can be recorded, which derives from the oxidation of Δ 9-THC. A schematic representation of the biosynthetic route of CBGA, THCA, CBDA and CBCA, their conversion into CBG, Δ 9-THC, CBD and CBC, respectively, and the oxidation of Δ 9-THC to CBN.

United Nations Office on Drugs and Crime (UNODC, 2009) verifies; 10–12% in pistillate flowers; 1–2% in leaves; 0.1–0.3% in stalks and < 0.03% in the roots.

Δ 9-THC concentration increases from the seedling to the flowering stage, then cannabinoids start to degrade. Determining the optimum harvesting stage is a critical step in cannabis cultivation since it significantly affects the yield of cannabinoids (Thomas and Elsohly, 2015). Resin production and Δ 9-THC content are affected by cultivation conditions such as plant density, supplies of essential factors including light, warmth, water, nutritional elements and carbon dioxide (CO₂) (Small, 2017).

According to Small, the qualitative variation in cannabinoid production seems to be much more influenced by genetics than by the environment (Small, 2017).

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