

## CANNABIDIOL – A CANNABIS SATIVA CONSTITUENT

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**ABSTRACT**

Most widely used illegal drug in world is Cannabis. Cannabis, more commonly called, *marijuana* refers to the several varieties of *Cannabis sativa*, or Indian hemp plant, that contains the psychoactive drug Delta-9-tetrahydrocannabinol[THC]. Others name are grass, pot, weed, tea, mary Jane, dagga, sinsemilla, herb, reefer, dope, shunk, boom, gangster, kif etc. The male and female plants are different. Female plant is tall about 16-18 feet and has darker and luxuriant foliage than the male. The word “cannabis” is used for the flowering and fruiting tops of the plant. It yields a sticky, amorphous resin called ‘cannabinone. The active principles in this resin are mainly cannabidiol, cannabinolic acid and many tetrahydrocannabinol isomers. It has been cultivated throughout recorded history, used as a source of industrial fiber, seed oil, food, recreation etc.

**KEYWORDS:** Cannabis, psychoactive drug, cannabinone, Indian Hemp plant.**INTRODUCTION**

In India's ancient Vedas texts, religious scholars described cannabis as “one of the five most sacred plants.” Cannabis has been a part of India's religious rituals and festivities for millennia. Ancient Indian Ayurvedic practices used cannabis as an ingredient in medicines, ranging from digestions problem to religious and spiritual moods and medicine. Nearly 191 formulations and more than 15 dosage forms have included as a key ingredient in Ayurvedic texts. The plant grows wild throughout India's Himalayan foothills and the adjoining plains, from Kashmir in the west to Assam in the east. Easy accessibility and abundance of cannabis provides India unique opportunity to harness the plant for economic growth. The plant *Cannabis indica* or *sativa* grows all over India that can be cultivate is restricted due to the monopoly of the state government. Despite the country's long history of cannabis use, the plants remain illegal except in government-authorised premises that produced and sell Bhang (which can either ground cannabis balls or a drink made by cannabis in milk), or for a research and medicinal purposes. Some powers are given to the state government to grant licences to cultivate cannabis under

certain circumstances (such as for research and medicinal uses), relatively few research organizations have obtained them. In fact, only the Uttar Pradesh and Uttarakhand regions, which are both in Northern India, received hemp cultivation licences.<sup>[1]</sup> The number of species in the genus *Cannabis* has been the subject of a long debate. Taxonomists have variously characterized the genus “*Cannabis*” based on its polytypic nature.<sup>[2-4]</sup> Schultes et al. divided this genus into three separate species: *Cannabis sativa*, *Cannabis indica*, and *Cannabis ruderalis*.<sup>[5]</sup> In contrast, several other researchers considered the genus to have two major species, *C. sativa* and *C. indica*.<sup>[6,7]</sup> The *sativa* and *indica* varieties are more economically important and widespread, whereas *ruderalis* is considered a hardier variety grown in the northern Himalayas and southern states of the former Soviet Union that is characterized by a sparse, “weedy” growth, and is rarely cultivated for its drug content. Compared to *sativa* for which the average plant height ranges from 2.5 to 3.5 m, plants of the *indica* variety are generally shorter (average height ca. 1.8 m) and bushier with broader and darker green leaves that mature early when cultivated outdoors.<sup>fig.1</sup><sup>[8]</sup> M.A. ElSohly et al.



It yields sticky amorphous resin, cannabinone, which consists of cannabinoids ( $C_6H_2O_2$ ), a colourless oily liquid, cannabidiol, cannabinolic acid and Tetrahydrocannabinol.<sup>[1]</sup>

Cannabis is classified under deliriant cerebral neurotic plant poison. It is also classified as mild hallucinogen or a sedative or a narcotic. In fact the drug is believed to produce all these effects in various individuals in a different way. However, presently it is considered as the most abused drug all over the world. Slang terms for cannabis include hash, grass, pot, ganja, spliff and refer.<sup>[9]</sup>

#### Botanical nomenclature<sup>[10]</sup>

Kingdom-Plantae (plants)  
 Sub-Kingdom-Tracheobionta (vascular plants)  
 Superdivison-Spermatophyta (seed plants)  
 Division-Magnoliophyta (flowering plants)  
 Class-Magnoliophyta (dicotyledons)  
 Subclass-Hamamelididae  
 Order-Urticales  
 Family-Cannabaceae  
 Genus-*Cannabis*  
 Species- *Sativa* L.

#### Constituents of *Cannabis sativa*

The two most abundant cannabinoids in *Cannabis sativa* are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). Different forms of cannabis vary in the relative proportions of THC and CBD and the risk of psychotic symptoms and impaired cognitive functioning.<sup>[11]</sup> Cannabidiol (CBD) has been traditionally used in Cannabis – based preparation, however historically, it has received far less interest as a single drug than the other drug components of Cannabis. Currently, CBD generates considerable interest due to beneficial neuro-protective, anti epileptic, anxiolytic, antipsychotic and its anti inflammatory properties.<sup>[12]</sup>

The mechanism of action of CBD is unclear, but it does not appear to involve the direct antagonism of dopamine receptors.<sup>[13]</sup> The first evidence that CBD might be useful in treating schizophrenia came from a case report in

which it was found to improve symptoms in a patient who had not responded to haloperidol.<sup>[14]</sup> CBD has also been reported to reduce psychotic symptoms in patients with Parkinson's disease.<sup>[15]</sup>

#### How does it work?

Cannabidiol has effects on the brain. The exact cause for these effects are not clear. However, cannabidiol seems to prevent the breakdown of a chemical in the brain that affects pain, mood, and mental function. Preventing the breakdown of this chemical and increasing its levels in the blood seems to reduce psychotic symptoms associated with conditions such as schizophrenia. Cannabidiol might also block some of the psychoactive effects of delta-9-tetra hydrocannabinol (THC). Cannabidiol seems to reduce pain and anxiety.<sup>[16]</sup> THC acts as a partial agonist at specific endogenous cannabinoid receptors, termed CB1 and CB2, both members of the G protein coupled receptor class.<sup>[17]</sup> The CB1 receptors are mainly expressed in the central nervous system, with a high density in the anterior cingulate, prefrontal cortex, medial temporal lobe and other areas<sup>[18]</sup> and are thought to mediate the majority of the effects of THC in the central nervous system. However, depending on the brain region, and whether the local CB1 receptors are expressed on neurons that release GABA or glutamate, THC can have either inhibitory or excitatory effects.<sup>[19]</sup> The acute administration of THC is associated with relaxation and enjoyment, but can also lead to unpleasant effects such as anxiety, psychotic symptoms, depression, apathy, and impairment of memory.<sup>[20]</sup> It has also been associated with impairments in learning, motor coordination, slowed reaction time, impaired concentration during complex tasks, deficits in some executive functions, and impairments in some aspects of verbal processing, such as verbal fluency.<sup>[21,22]</sup> THC administration can also produce an increase in heart rate and orthostatic hypotension. However, the acute effects of THC and their time of onset are subject to wide inter-individual variation and differences in route of administration, rate of absorption, metabolism and the subject's expectation of its effects.<sup>[23]</sup> In contrast, CBD has a low affinity for CB1 receptors.<sup>[24]</sup> Unlike THC, CBD does not have acute

effects on motor or cognitive performance,<sup>[25,26]</sup> nor does it have significant effects on pulse rate or blood pressure.<sup>[27,28]</sup> Functional neuro imaging studies have confirmed that neuro physiological effects of THC and CBD are distinct and opposite.<sup>[29-32]</sup> Moreover, co-administration of CBD and THC may alter the pharmacological effect of the THC, sometime CBD potentiates some of THC's desirable effects but attenuates some of its negative effects.<sup>[28,32-35]</sup> The therapeutic potential of CBD has been evaluated in cardiovascular, neurodegenerative, cancer, and metabolic diseases, which are usually accompanied by oxidative stress and inflammation.<sup>[36]</sup> One of the best uses of CBD

is for therapeutic effect in diabetes and its complications in animal and human studies.<sup>[37]</sup> CBD, by activating the cannabinoid receptor, CB2, has been shown to induce vasodilatation in type 2 diabetic rats,<sup>[38,39]</sup> and by activating 5-HTA<sub>1</sub> receptors, CBD showed a therapeutic effect in diabetic neuropathy.<sup>[40]</sup>

#### Medicinal chemistry of CBD<sup>[41]</sup>

Although there is considerable structural overlap between CBD and THC (Fig. 2), the conformational structures shown in Figure differ significantly.<sup>[42]</sup>

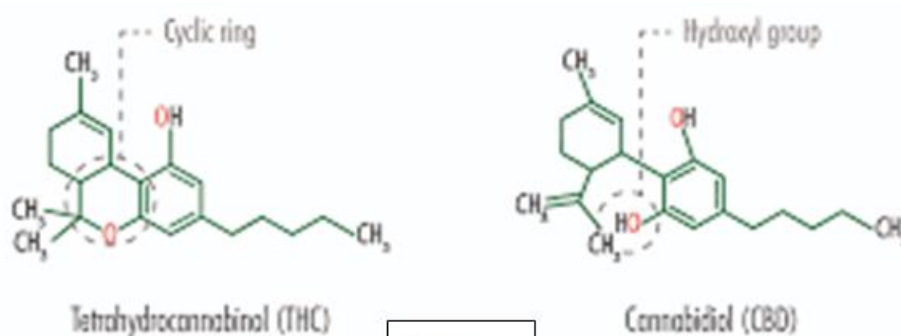


FIG.2

Whereas THC exists in an essentially planar conformation, CBD adopts a conformation in which the two rings are more or less at right angles to each other (Fig. 3). A result of this is the observation that CBD does not bind to or activate the CB<sub>1</sub> receptor an action that THC is capable of doing. This in turn leads to a complete

lack of psycho activity by CBD unlike THC, which is the psychoactive principle of Cannabis. The basis of this is a so called 'region of steric interference'<sup>[42]</sup> on the CB<sub>1</sub> receptor that allows THC to bind but interferes with CBD binding.

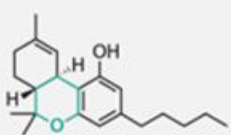
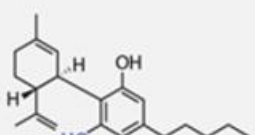
	THC	CBD
<b>SOURCE</b>	<i>Cannabis sativa</i>	<i>Cannabis sativa</i>
<b>MOLECULAR FORMULA</b>	$C_{21}H_{30}O_2$	$C_{21}H_{30}O_2$
<b>CHEMICAL STRUCTURE</b>		
	Contains <b>cyclic ring</b>	Contains <b>hydroxyl group</b>
<b>PSYCHOACTIVE EFFECTS</b>	Yes	No

FIG.3

**Anti-inflammatory actions of CBD.<sup>[41]</sup>**

Response	Model	Reference
Reduces immune response	Rats subjected to pneumococcal meningitis	[44]
Prevents experimental colitis	Murine model of colitis	[45]
Reduced iNOS and IL-1b	expression Mouse model of Alzheimer's disease	[46,47]
Reduces b-amyloid-induced neuroinflammation	Cultured astrocytes	[47]
TNF-a and IL-1b levels reduced	Murine collagen-induced arthritis	[48]
Decreases in PGE2 plasma levels	Carrageenan paw injection in the rat	[49]
Reduced the extent of colitis	TNB mouse model of colitis	[50]
Inhibition of neutrophil chemotaxis	Human neutrophil migration	[51]
Effects on NF-jB, MAPK, ICAM-1, VCAM-1, TNF-a	Mouse model of type I Diabetic cardiomyopathy	[52]
Enhanced IFN-c and IL-2 production	Mouse splenocytes	[53]
Exacerbates LPS-induced pulmonary inflammation	Pulmonary inflammation in C57BL/6 mice	[54]
Reduced the TNF-a level in the frontal cortex	Pneumococcal meningitis in rats	[55]
Decreases hepatic ischemia-reperfusion (I/R) injury	Mouse model of hepatic I/R	[56]
Reduced LPS-induced increase in TNFa and COX-2	Mouse model of sepsis-related encephalitis	[57]
Reduced effects of autoimmune encephalomyelitis	Immunized C57BL/6 mice	[58,59]
Reduces inflammation in acute lung injury (ALI)	Mouse model of lipopolysaccharide-induced ALI	[60,61]

**DISCUSSION**

CBD has become a major area of research only in recent years. In particular, its biological actions are a topic of many interesting reports that suggest possible therapeutic applications. Included are its anti inflammatory actions in a variety of preclinical models as shown in above table. Human studies suggest that CBD may have a protective role in  $\Delta$ 9-THC-induced cognitive impairments; however, there is limited human evidence for CBD treatment effects in pathological states (e.g. schizophrenia). Preclinical evidence suggests that overall CBD improves functioning in cognitive domains of learning and memory, in both  $\Delta$ 9-THC-induced and pathological states of cognitive impairment. In the context of the above data, CBD seems to be more preferred than other compounds from the phytocannabinoid group. CBD can reduce psychotic symptoms in schizophrenia,<sup>[11,13]</sup> in Parkinson's disease,<sup>[12]</sup> and in THC-induced psychosis, depression, apathy, and impairment of memory.<sup>[6]</sup>

**CONCLUSION**

Even though cannabis preparations are all banned in India and most of the countries of the world, the active principle (Tetrahydrocannabinol) does have, many medicinal uses. Its constituent THC and cannabidiol plays a very important role in all in pathological states. It is Anti emetic against nausea and vomiting induced by anti cancer drugs. THC in the form of a synthetic oral cannabinoid ("dronabiol") has been shown to be effective in controlling the nausea and diarrhoea

associated with AIDS. CBD has a possible role in treatment of convulsions, anxiety, pain and inflammation. Cannabis is commonly used an aphro – disiac agent. It is supposed to evoke the desire for sexual enjoyment and also increase the duration of sexual act. Phencyclidine may be intentionally combined with cannabis /marijuana ("super weed") to obtain a more intense hallucinogenic experience

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