

## Research Article

### CANNABIS SATIVA: ETHNOBOTANY AND PHYTOCHEMISTRY

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#### ABSTRACT

This literature review paper is developed as a part of the awareness and to gather scientific information about the medicinal plant, Cannabis sativa. Several researches have shown the potential medicinal activity of Cannabis and its chemical compounds. Cannabis sativa L. is one of the medicinal plant known for fibre, medicinal, psychoactive agents and oil. There are two names of Cannabis sativa one is **Medical cannabis sativa (marijuana type)**, and another one is known **Industrial Cannabis sativa (fiber type)**. There is still a huge prejudice in society in relation to **Medical cannabis sativa (marijuana type)** due to its recreational use. In India, Cannabis sativa is also commonly known as Indian hemp, marijuana, **Bhang, Ganja**, and **Charas**, which are banned in India as an **illicit drug**. Sales and cultivation of **Medical cannabis (marijuana type)** are **illegal in India**. However, this scenario is changing, and the social resistance is decreasing for the medicinal use of Cannabis. The plant derivatives were identified as **psychoactive compound, Δ9-tetrahydrocannabinol (Δ9-THC or THC)** and **Cannabidiol (CBD)**, as well as, the endocannabinoid system, cannabinoid receptors type 1 and type 2 (CB1 and CB2, respectively). The plant has gained a lot of popularity in the last few decades for not only being an illicit drug but for its medicinal values from ancient times and a potential source for modern drugs to treat several targets for human wellness. Herein, our aim is to perform a literature overview about the plant, ethnobotany, and its chemical compounds of therapeutic interest.

**Keywords:** Bhang, Cannabidiol (CBD), Charas, Cannabis sativa, Ganja, Illicit drug, Psychoactive compound, hemp, marijuana, Δ9-Tetrahydrocannabinol-THC.

#### INTRODUCTION

**Cannabis sativa L.** (hemp) (**Medical cannabis- marijuana type; Industrial Cannabis sativa -fiber type**) is one of the oldest cultivated and non-cultivated (natural) medicinal plants in history (1-8,47). Cannabis sativa with proven applications, ranging from the textile, construction, paper industries, nutritional, pharmaceutical and cosmetic industries (1-13). Cannabis sativa L. ( $2n = 2x = 20$ ) is a dicotyledonous species belonging to **Cannabaceae** family under the order Rosales used for multiple purposes (fiber, oil, edible seeds, medicinal, drug) (1-10). Cannabis was originated in the **Himalaya Mountains** and is endemic to the **Indian landmass** and Asia (6-30). In India, Cannabis sativa is also commonly known as Indian hemp, marijuana, Bhang, Ganja, and Charas (8-29). As a plant, **Cannabis** is a highly variable species. Cannabis (**Cannabis sativa**, or hemp) and its constituents—in particular the cannabinoids—have been the focus of extensive chemical and biological research for almost half a century since the discovery of the chemical structure of its major active **psychoactive** constituent, **Δ9-tetrahydrocannabinol (Δ9-THC)** (1-30,47).

Cannabis contains hundreds of specialized metabolites with potential bioactivity, including cannabinoids, terpenes, and flavonoids, which are produced and accumulated in the glandular trichomes that are highly abundant mainly on **female inflorescences** (3-61). Bioplastics, Biofuels, and Biopesticides are some of the innovative applications of the plant (1-48). These compounds and derivatives thereof are involved in the treatment of disease conditions such as **cancer, Alzheimer's, multiple sclerosis, chronic pain and inflammation, glaucoma**, and many others (61). A recent study

revealed that **cannabinoids block** cellular entry of multiple **SARS-CoV-2 variants** and exhibited a potential to **prevent as well as treat SARS-CoV-2 infection** (61). Cannabis species have long been used as folk traditional medicine in different regions of India and the compounds from Cannabis are used against, reactive oxygen species (ROS), cancer and microbial infections including both bacterial and fungal strains (1-61). The global cannabis market value has been estimated at \$214–344 billion USD and legal markets are projected to expand in the next few years (61). Legalization or decriminalization of cannabis (**Cannabis sativa L.**) has been rapidly increasing worldwide over the past two decades (50-61). Further, over 70 countries have legalized some form of medical use of cannabis, while few countries including Canada, Uruguay, Mexico, The Netherlands, Spain, South Africa, and parts of the United States (24 US States) have legalized cannabis for adult use (61).

Cannabis sativa has been used by innumerable ethnic societies in Asia. **Uttaranchal (India)** is an ethnic region where the plant is a part of the local culture (8-29). **Industrial Cannabis sativa (fiber type)**, has been employed medicinally in Ireland since at least the Anglo-Saxon era, more than 1000 years ago (1-30). Its use came to the fore, however when **William B. O'Shaughnessy**, an Irish physician in India, became familiar with the versatility of Indian hemp in the treatment of rheumatic diseases, tetanus, cholera and epilepsy in 1838 (1-30). Majority of historians believe that the Hemp plant is indigenous to both Central Asia and the Indian subcontinent and is widely found in the **Himalayan mountain regions (Figure-1)** extending to India, Pakistan, China, Afghanistan, Nepal and even Bhutan and Myanmar (3-29). Scriptures like Vedas have estimated the plant to be at least 3400 years old and is even considered a sacred **Indian plant** (1-30).

#### Cannabis sativa: Difference between Hemp and Marijuana

Hemp (**Industrial Cannabis sativa-fiber type**), and marijuana (**Medical cannabis-marijuana type**) have different

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chemistry and characteristics. Hemp plants contain **low levels (0.3%) of the** intoxicating phytocannabinoid known as  **$\Delta$ -9 Tetrahydrocannabinol (THC)**(1-61). **Medical cannabis-marijuana type** does, however, contain high levels (**18-30%**) of the non-intoxicating phytocannabinoid  **$\Delta$ -9 Tetrahydrocannabinol (THC)** (30-61). There are two names of *Cannabis sativa*, one is **Medical cannabis (marijuana type)**, and another one is known as hemp (**Industrial Cannabis sativa-fiber type**). The major difference between hemp (**Industrial Cannabis sativa-fiber type**), and marijuana **Medical cannabis-marijuana type** is their psychoactive component:  **$\Delta$ -9 tetrahydrocannabinol, or THC. Hemp (Industrial Cannabis sativa-fiber type)**, has 0.3% or less THC, meaning hemp-derived products does not contain enough THC to create the “high” traditionally associated with marijuana. The main distinction between hemp and medical cannabis boils down to **tetrahydrocannabinol or THC concentration**. In general hemp (**Industrial Cannabis sativa-fiber type**), contains minimal amounts of THC (0.3% or less THC) and moderate to high amounts of CBD, when, in fact, **Medical cannabis-marijuana type** can contain up to 30% THC. Marijuana (**Medical cannabis-marijuana type**) plants are grown commercially for their psychoactive compounds, which are produced in the **trichomes** that develop on flower bracts in **female inflorescences** (3-61).

Hemp, or cannabis(**Industrial Cannabis sativa-fiber type**) with less than 0.3 percent THC, can also be grown to create other kinds of products, including: paper, **clothing, textiles, animal feed and plastic, food products, such as hemp seed, hemp milk, hemp protein powder, or hemp oil**. Because hemp(**Industrial Cannabis sativa-fiber type**) grows faster than trees and other crops, it's considered to be a more sustainable way of making products like paper and textiles. Hemp (**Industrial Cannabis sativa-fiber type**) seed is quite nutritious, as it's a complete protein that's also high in fiber. Hemp (**Industrial Cannabis sativa-fiber type**) is one of the most versatile plants in the world. The stalk of a hemp plant, for example, could be used for the manufacture of textiles or the development of biofuels (2-40). The seeds of hemp (**Industrial Cannabis sativa-fiber type**) are eaten or employed to create hemp seed oil, while the flowers can be used to extract CBD for use in a wide range of products, including skin care products like our Skin Therapy body butter and edibles like our beverage infusions (1-45, 60).

The cannabis plant produces marijuana (**Medical cannabis-marijuana type**) and **hashish** (cannabis resin) (1-47, 60). Cannabinoids are chemicals found in the cannabis plant or synthesized chemically. A few account for most of the known actions of cannabis on mental and bodily functions (1-60).  **$\Delta$ -9-tetrahydrocannabinol (THC)** is the cannabinoid with the greatest **psychoactive** effect, but **Cannabidiol (CBD)** shows considerable promise of usefulness for medical purposes (1-45, 46-60).

## CANNABIS SATIVA : ETHNOBOTANY

***Cannabis sativa* L. is one of the medicinal plant known for fibre, medicinal, psychoactive agents and oil (1-40).** Cannabis is popular for its medicinal and narcotic uses, which are attributed to its various secondary metabolites such as terpenoids, flavonoids, sterols and phytocannabinoids (46). **Industrial Cannabis sativa-(fiber type)** stems provide cellulosic and woody fibres of very high quality, the seeds are a rich source of fatty acids and proteins for the feed and food industries, the leaves and inflorescences are a gold-mine for secondary metabolites of several pharmaceutical applications (1-30). The inflorescence is the main product of **Medical cannabis- (marijuana type)**. Hundreds of specialized metabolites with potential bioactivity are produced and accumulated in the

glandular **trichomes** that are highly abundant mainly on **female inflorescences** (2-60).

Traditionally, stems, inflorescence and seeds were the most used plant parts. The term “Cannabis” is used to define the products (drugs and essential oils) that are prepared or obtained from the annual herb *Cannabis sativa* and its variants (1-30). The Hemp plant (*Cannabis*) belongs to the family of Cannabaceae has three species, ***Cannabis indica*, *Cannabis sativa*, and *Cannabis ruderalis*** that comprise the genus *Cannabis* (1-45). *Cannabis sativa* comprises short and neutral-day varieties. Among its different applications, its use in medicine, derived from its content in **Cannabinoids**, is raising an increasing interest (1-39). Cannabinoids are natural compounds found in the hemp (*Cannabis sativa*). The plant **Medical cannabis-(marijuana type)** has gained a lot of popularity in the last few decades for not only being **an illicit drug** but for its medicinal values from ancient times and a potential source for modern drugs to treat several targets for human wellness (1-38). The pharmacologic and therapeutic properties of preparations of ***Cannabis sativa* and  $\Delta$ -9-THC ( $\Delta$ 9-tetrahydrocannabinol)** its most **psychoactive** compound, have been extensively reviewed (1-40). An additional important cannabinoid in *Cannabis* of current interest is **Cannabidiol (CBD)** due to its reported activity as an **antiepileptic agent**, particularly its promise for the treatment of intractable pediatric epilepsy (1-39,42-48).

The plant produces a unique class of **terpenophenolic** compounds called **cannabinoids**. A total of **565** *Cannabis* constituents have been isolated from *Cannabis sativa* so far, out of which 120 are phytocannabinoids (1-45). Among cannabinoids,  **$\Delta$ -9-tetrahydrocannabinol (THC) and cannabidiol (CBD)** are generally the most abundant secondary metabolites in the plant, which are mainly present in the **flowers**, as well as the **leaves** of *Cannabis sativa* (1-30). Cannabinoids are primarily found in the **trichomes of female flower bracts** (5-30). Scientific interest in cannabinoids arose after the discovery of the major **psychoactive** component in **Industrial Cannabis sativa-(fiber type)  $\Delta$ -9-tetrahydrocannabinol (THC)** (1-40). The concentrations of cannabinoids are much lower in the root; shoot and leaf tissues and negligible amounts are found in the seed, seed oil, and pollen of the plant (5-28). In total, a broad spectrum of more than **566** phytochemicals has been identified from the leaves, flowers, bark, seeds, and roots (5-38). This includes numerous **cannabinoids, flavonoids, and terpenoids**, as well as sterols which are of industrial interest. The recent discoveries of the medicinal properties of cannabis and the cannabinoids in addition to their potential applications in the treatment of a number of serious illnesses, such as **glaucoma, depression, neuralgia, multiple sclerosis, Alzheimer's, and alleviation of symptoms of HIV/AIDS and cancer**, have given momentum to the quest for further understanding the chemistry, biology, and medicinal properties of this plant (1-45). **Terpenes** are volatile chemicals that give *Cannabis* its unique aroma and flavor. These compounds are widespread in the plant kingdom (2-40).

The narcotic principle (**Cannabinoids,  $\Delta$ -9-tetrahydrocannabinol (THC) and cannabidiol-CBD**) in the *Cannabis sativa* develops only when it matures, reaching its maximum at about **the time of flowering** and then gradually declining and beginning to disappear when the leaves and flowers turn yellow (1-40). For the manufacture of good bhang, in India therefore, the leaves should be separated when they are just mature and when there are no signs of decay or withering (9-29). The stalks, seeds, and leaves are converted into various construction materials, textiles, paper, food, furniture, cosmetics, healthcare products, and the list goes on (5-30).

The plant's behavioral and **psychotropic effects** are attributed to its content of this class of compounds, the cannabinoids, primarily  **$\Delta$ <sup>9</sup>-THC ( $\Delta$ 9-tetrahydrocannabinol)**, which is produced

mainly in the **leaves and flower buds** of the plant (2-40). Besides  $\Delta^9$ -THC, there are also non-psychoactive cannabinoids with several medicinal functions, such as cannabidiol (CBD), cannabichromene (CBC), and cannabigerol (CBG), along with other non-cannabinoid constituents belonging to diverse classes of natural products (2-40). As of today, more than **566 phytoconstituents** have been identified in cannabis (1-45).

Being a diversified one, Hemp or **Industrial Cannabis sativa-(fiber type)** can be a revolutionary plant for a better future and the upcoming generations (8-29). Due to its immense contributions, Industrial Hemp is emerging as a vital agricultural commodity and the appeal for its merchandise has increased steadily in the present century (2-40). It is an eco-friendly and worthwhile crop that complements a sustainable growth system. Growing Industrial hemp improves local states' economies and creates job possibilities, particularly in agriculture-dependent areas (4-30).

### Cannabis sativa: Classification as Industrial or Medical hemp

A generally accepted classification of cannabis plants is based on their primary agronomic purpose. The most widely cultivated group is "hemp" ("**fibres-type hemp**," "**industrial cannabis**"), which was once an important crop for the production of raw materials for textiles and ropes and which is currently experiencing a revival after a steady decrease in its acreage after World War II (9-37-42). It is grown for seeds and fibre, food and beverage production, substances for cosmetic use, animal feed, and other industrial uses (5-40). It can be cultivated as a field crop of registered varieties that contain no more than a legally defined, country specific threshold level of the psychoactive substance  $\Delta^9$ -tetrahydrocannabinol (THC) (9-37-42). In European countries, for example, the threshold is set at 0.2% or 0.3%  **$\Delta^9$ -THC ( $\Delta^9$ -tetrahydrocannabinol)**, in the upper third of the dried plant or in an upper 30 cm of dried plants shoots containing at least one female inflorescence(37-42).

Although hemp can also be used for pharmaceutical purposes, it contains small amounts of cannabinoids (37-42). Higher relative (in per cent of inflorescence dry weight, 30%) and absolute (in g per cultivated m<sup>2</sup>) amounts of cannabinoids can be produced in cannabis varieties popularly known as **Medical cannabis-(marijuana,** "**drug type cannabis**") (37-42). **Medical cannabis-(marijuana type)** varieties contain higher amounts of  **$\Delta^9$ -THC ( $\Delta^9$ -tetrahydrocannabinol)** than the legal national limits for hemp and can be grown indoors or outdoors only in compliance with strict national legal restrictions (37-42). **Medical cannabis-(marijuana type)** varieties contain high levels of plant cannabinoids, of which cannabidiol (CBD) and THC are the most abundant and pharmaceutically most important (37-42). Cannabis sativa L. is one of the oldest cultivated crops, used in medicine for millennia due to therapeutic characteristics of the phytocannabinoids it contains (37-42). Its medicinal properties are highly influenced by the chemotype, that is, the ratio of the two main cannabinoids cannabidiol (CBD) and  $\Delta^9$ -tetrahydrocannabinol (THC) (37-42). They contain high levels of plant cannabinoids, of which cannabidiol (CBD) and  $\Delta^9$ -tetrahydrocannabinol (THC) are the most abundant and pharmaceutically most important (1-37-42). They are produced in secretory cells within glandular trichomes as carboxylic acids cannabidiolic acid (CBD-A) and ( $\Delta^9$ -THC-A) that are decarboxylated to their corresponding neutral forms Cannabidiol (CBD) and  $\Delta^9$ -tetrahydrocannabinolic acid (THC), respectively, upon heating (37-42).

The relative abundance and ratio of Cannabidiol (CBD) and  $\Delta^9$ -tetrahydrocannabinolic acid (THC) has led to the second most widely used cannabis nomenclature, which divides cannabis plants into three discrete groups (1-45). "THC dominant" or "high THC" (CBD/THC ratio 0.00–0.05), "intermediate" (CBD/THC ratio 0.5–3), and "CBD dominant" or "high CBD" (CBD/THC ratio 15–25) (37-45). These three chemical phenotypes (chemotypes) have been named Type I (THC dominant), Type II (CBD/THC balanced) and Type III (CBD dominant) (37-42, 43-61).

Because of its complexity, the above classification has not been adopted for everyday use in the cannabis industry and recreational cultivation; therefore, the vernacular expressions "Sativa" and "Indica" have become accepted to describe cultivars with narrow leaflets and broad or wide leaflets, respectively (10-37-42). They were based on illustrations by Anderson, which differed from the original botanical nomenclature. "Sativa" plants produce much more THC than CBD, while "Indica" plants produce almost equal amounts of THC and CBD, with a CBD/THC ratio of around 1 (30-45). Significant morphological differences were found between plants and chemotypes (37-42).

Cannabidiol (CBD) has been shown to have therapeutic effects on humans and animals and no psychoactive effects; it even abolishes the psychoactivity and some adverse effects of THC, such as anxiety, tachycardia, and sedation (37-42). As a result, there has been a dramatic increase in Cannabidiol (CBD) containing supplements in the food and cosmetic industries in recent years, and even greater potential for its pharmaceutical use has been reported (10-37-45). This has encouraged breeding programmes aimed at developing new varieties of **Medical cannabis-(marijuana type)** with increased and stable Cannabidiol (CBD) content, as well as basic research into the inheritance of specific chemical profiles (1-37-45).

### CANNABIS SATIVA: MORHOLOGY

Cannabis sativa L. (**Medical cannabis-(marijuana type; Industrial Cannabis sativa-(fiber type)**) produces male and female inflorescences on different plants (dioecious) and therefore the plants are obligatory out-crossers. In commercial production, **Medical cannabis-(marijuana type)** plants are all genetically female; male plants are destroyed as seed formation reduces flower quality (3-61). Spontaneously occurring **hermaphroditic inflorescences**, in which pistillate flowers are accompanied by the formation of anthers, leads to undesired seed formation; the mechanism for this is poorly understood (3-61). Cannabis sativa L. (Cannabis, hemp or marijuana) is an erect annual herb of the Cannabaceae family (2-61). Cannabis predominantly is a **dioecious cross-pollinated** plant, and its **female flower** is richest in acidic form cannabinoids including  $\Delta^9$ -tetrahydrocannabinolic acid (THCa) and cannabidiolic acid (CBDa) (61). Cannabis is considered to be monotypic (occurs as a single species), but arguments for its polytypic nature also exist (46). There exist eight distinguishable characters between C. sativa and C. indica based on morphological characters like stalk length, branching habit, leaflets, and flowers (1-30). Domestication of Cannabis resulted from understanding of the benefits obtained from different parts of the plant. The multiple benefits of the plant, especially its use as a source of fibers, propelled the spread of the plant to other continents (1-46). Due to the nature of reproduction system in cannabis (dioecy, cross pollination), seed propagation is not commonly practiced as male plants have no commercial use and lack genetic uniformity among seedlings (61). Therefore, conventional methods of clonal propagation (stem cuttings) of cannabis became the primary method to maintain and propagate elite cultivars for industrial cultivation (61).



Cannabis sativa is an erect annual herb with palmate-shaped leaves and greenish-yellow colored small flowers (7-30). The herb may grow up to 4m tall, while leaves are grey-green up to 12 cm long. Flowers form spike like or branched clusters depending on the sex type. Spike like clusters grow on the pistillate plant while Branched clusters are formed on staminate plants (2-30, 40-61). Fruit is an achene that is small, dry, and thin-walled consisting of only one seed. The mode of pollination in the Hemp plant is **Anemophilous** whereby pollen is disseminated through the wind (34-61). Most of the species of Cannabis are generally short-day plants while Cannabis sativa subsp. sativa var. spontanea may be day-neutral (4-35). Flowering in Hemp plants is brought about by a dark period of approximately 12 hours while; the flowering is inhibited if the day length is longer. The photoperiodic fluctuations can be controlled if the plant is grown under protected conditions (2-36).

## CANNABIS SATIVA: LONG HISTORY IN INDIA

Cannabis sativa (**Medical cannabis-(marijuana type; Industrial Cannabis sativa-(fiber type)**) has a long history in India, recorded in legends and religion (8-42). Cannabis has been popular in India since the beginning of recorded history and is often taken as a drink (5-40). Nuts and spices, like almonds, pistachios, poppy seeds, pepper, ginger, and sugar are combined with cannabis and boiled with milk (5-40). The earliest mention of cannabis has been found in The Vedas, or sacred Indian Hindu texts (8-35). Much before the Irish physician Sir William Brooke O Shaughnessy (1808-1889) introduced cannabis (**Medical cannabis-(marijuana type; Industrial Cannabis sativa-(fiber type)**) into Western medicine sometime around the mid-nineteenth century (8-39). *Ganja* (hemp) had already been part of India's living culture as medicine and an intoxicating agent – even before 1000 B.C (8-29). These writings may have been compiled as early as 2000 to 1400 B.C. A reason for the popularity of Bhang in parts of north India was probably the scorching summer months (2-31). As a coolant, Bhang was the perfect 'summer drink (7-29). It was also relatively easy to prepare. The leaves of the hemp plant were pound along with spices and *gur* (molasses) and to swallow the paste. However, the most popular mode of consumption was the smoking of hemp along with tobacco in the chillum or the ubiquitous Hukka (3-40).

As per the literature survey, it was abundantly cultivated across the country from Kashmir to Kullu (Himachal Pradesh), across Gujarat, the Southern Maratha Country Agency, Central India, Bengal, Assam, Orissa and down to the Madras Presidency though the best variety of hemp, called the *baluchar* came from the Ganja Mahals of colonial Bengal (4-35). After the Ganja Mahals, the erstwhile tributary states of Orissa contained the most extensive cultivation of hemp (7-35). **Charas** and **Ganja** are the mostly smoked, while Bhang in India is always taken by mouth either in the form of a beverage or a confection. A number of preparations of Ganja for oral consumption are, however, also used in various parts of the India (6-29).

**Bhang**, the drink made of cannabis leaves, milk, sugar, and spices, has been part of 'India's living since time immemorial (8-35). It originates in the legends of the Shiva, designated as the 'Lord of Bhang' who planted the cannabis fields in the district of Kullu in Himachal Pradesh (5-39). Not without reason that hemp use has touched almost every major spiritual tradition on earth at some point in Indian history (6-39). The worship of the hemp plant in India thus emanates from this sacred lore, though it is intriguing that the worship rituals are shrouded in secrecy (3-36). The worship of the hemp plant was practised among the Kols of Kuamon region, and the Kunbis of western India. According to The Vedas, cannabis was one of five sacred plants and a guardian angel lived in its leaves (6-35). The Vedas call cannabis a source of happiness, joy-giver, liberator that

was compassionately given to humans to help us attain delight and lose fear (4-39). It releases us from anxiety (3-40). During the Middle Ages, soldiers often took a drink of bhang before entering battle, just as Westerners took a swig of whiskey (4-42). Bhang is also rolled and eaten in small balls (7-29). Bhang is about the strength of Western marijuana. Because milk contains fat, mixing cannabis with milk is an effective means of extracting **Δ9**-tetrahydrocannabinol (THC) but ingesting marijuana takes longer to feel the effects and is less consistent (4-39).

The cannabis drugs are used in India in three main forms - **Bhang, Ganja and Charas** (3-40). Bhang is composed of the matured leaves and, in some parts of India, also the fruit of the cannabis plant (8-27). Bhang consists of the dried matured leaves and flowering shoots of both female and male plants, wild or cultivated (8-40).

**Ganja** is derived from the **flowering tops of female plants** and twigs, which are covered with **resinous** exudation (8-42). Ganja consists of the dried flowering tops of the cultivated **female** cannabis plant, which become coated with a resinous exudation, chiefly from the glandular hairs, in consequence of being deprived of the opportunity of setting seed (8-28). As the female plants begin to form **flowers**, all the large leaves on the stem and branches are also removed (5-30). The smaller leaves and the bracts of inflorescence become agglutinated into a mass called **Ganja** (9-29). Fresh excise ganja has a rust-green colour with a characteristic odour. The material thus collected is further treated to form the Ganja of commerce which appears in two forms : **Flat Ganja** and **Round Ganja** (3-29).

**Charas** is the **resinous exudation** secreted by the leaves, young twigs, bark of stem and even the young fruit of the female cannabis plant (6-30). Charas is the resinous matter collected from the leaves and flowering tops and constitutes the active principle of the plant. Charas is a greenish mass with a peculiar characteristic odour. When kept for some time it turns to a brownish-grey colour, becomes hard and friable and loses most of its **narcotic activity**. Although the cannabis plant when cultivated in tropical regions such as India, Nepal, Pakistan, Afghanistan, Africa and Malaya, is rich in narcotic principles, it seldom yields sufficient resin to be collected as Charas (4-45). **Charas** is sometimes collected on the plateaus of central Asia and the southern Himalayas (Nepal), but both the yield and the quality are poor (6-37). The highest yield and best quality of Charas resin are obtained from plants grown in Yark and in Chinese Turkistan in central Asia. **This, however, is no longer the case, as the import of charas into India was entirely prohibited by the Government of India nearly two decades ago. The consumption of cannabis resin (Charas) is prohibited everywhere in India (9-30).**

Other preparations of cannabis in India include Ganja and Charas. Stronger than bhang, Ganja is made from the flowers and upper leaves of the **female plant**, Cannabis sativa (4-36). **Charas** is the strongest preparation and is made from blooming **flowers of Cannabis sativa** (1-45). Similar in strength to hashish, Charas contains a lot of resin. Both are smoked in an earthenware pipe called a Chillum (8-39). The pipe is also called as Hukka is usually shared among two to five people, making smoking a communal activity (4-38). The British found the use of cannabis so extensive in colonial India that they commissioned a large scale study in the late 1890s (4-37). They were concerned that the abuse of cannabis was endangering the health of the native people and driving them insane (4-36). Cannabis continues to be available in India of the 20th and 21st centuries. In their review in the mid-fifties, **Chopra and Chopra (1957)** found little changed since the Indian Hemp Drugs Commission Report of 1894 (5-38). Construction workers use bhang to feel refreshed at the end of the day and to fight fatigue (6-36). Hindus use bhang for religious ceremonies like Holi and ascetics use it to seek

divinity (8-37). Sadhus are Indian ascetics who have shunned material life and use cannabis to seek spiritual freedom (2-43). The herbal plant, cannabis, has a long and continuous history in India. It has lived for thousands of years in stories of gods and warriors and it continues to live today in religious ceremonies and street stands (5-38).

**Industrial Cannabis sativa-(fiber type)** is a derivative of cannabis, and is primarily cultivated for industrial use (6-38). Under colonial rule, where other substances like opium were illegal, cannabis derivatives were not banned outrightly (3-41). The British government deliberated that a ban was likely to cause social unrest, and decided to tax it instead (6-36). Cannabis also finds mentions in **Ayurveda** text as '**Vijaya**' and has been recommended for its medicinal properties (4-39). *Ayurveda* literature like Charaka Samhita mentions properties of Vijaya as digestive and intoxicating which makes the cultivation and usage of the plant a religious and cultural phenomenon (4-38).

The collection of bhang from wild or self-grown plants by wholesale and retail vendors for the purpose of sale was only permitted under licence in Punjab and Uttar Pradesh and the transport of bhang so collected was carefully regulated and restricted by the Government of India (4-38). Even for the production of hemp, **Industrial Cannabis sativa-(fiber type)**, fibre and hemp seed, the cultivation of the cannabis plant is strictly limited to the Uttarakhand state, Punjab, Uttar Pradesh (especially districts of Almora, Garhwal and Nainital) and Jammu and Kashmir (4-38).

In 2017, the **FSSAI (FOOD SAFETY AND STANDARDS AUTHORITY OF INDIA)** issued notices to hemp manufacturers, highlighting that the sale of such products under the FSSAI label is **illegal**. But 4 years and a couple of successful hemp businesses later, it has come around. **On 15th November 2021** FSSAI, recognized hemp seed (**Industrial Cannabis sativa-(fiber type)**) products as food (10-29). The notification regulates and allows for sale of products derived from 'non-viable seeds of the cannabis sativa/other indigenous cannabis species' (10-29). And the cultivation has to, as usual, comply with the NDPS and state laws (9-30).

Presently, there are a few hemp (**Industrial Cannabis sativa-(fiber type)**), companies that operate with an **AYUSH license**, regulated by the DCA, some of which are also recognized by the Department for Promotion of Industry and Internal Trade (10-35). However, with the existing regulatory uncertainty and overlap, policy deliberations are at the core of this industry. Industrial hemp, as a diverse plant, can be a revolutionary crop for a better future and for upcoming generations (9-34). It is an eco-friendly and worthwhile crop that complements sustainable growth system. Industrial hemp farming has the potential to dramatically minimize the amount of carbon impact on the environment and can be cultivated with little or no usage of chemical pesticides or fertilizers (10-30) The benefits of Industrial hemp production will improve farmers' socio-economic status around the world and may potentially contribute to a significant increase in countries' GDP per capita (5-40).

## Cannabis sativa: Wild distribution and growth in India



**Figure-1:** The wild growth of Cannabis sativa in Himalayan region

The cannabis drugs commonly used in India are derived from the flowers, leaves (and the resinous matter derived there from), fruit, young twigs and bark of the stem of the plant *Cannabis sativa* Linn. of the family *Cannabinaceae*. In India, the plant is found growing wild throughout the **Himalayan foothills (Figure-1)** and the adjoining plains, from Kashmir in the west to Assam in the east (4-45). It has become acclimatized to the plains of India and grows even in the warm climate of southern India, producing its narcotic principles (8-30). On the mountain tracts of upper India, the cannabis plant yields a fairly good fibre, but in Kashmir and Ladakh, its narcotic principles become much more predominant (7-35). When the plant is cultivated in the plains of India, the **cannabis resin** which constitutes **Charas** is not generally secreted; but the young female flowers and shoots show a tendency to develop the narcotic principle instead, and these constitute the Ganja of India. In other parts of India again, the narcotic property is often not developed in the cannabis plant until the fruits are mature (8-30).

The plant grows wild in the following states: Assam, Bihar, Tamil Nadu, Uttar Pradesh, Punjab, West Bengal, Jammu & Kashmir, Patiala and Punjab, Rajasthan. Kerala, Himachal Pradesh, Manipur and Tripura (5-38). The states where there is no wild growth include Maharashtra, Gujarat, Madhya Pradesh, Orissa, Telangana, Karnataka, Rajasthan, Ajmer, Coorg, Delhi, Andhra, Bhopal, Vindhya Pradesh and the Andaman and Nicobar Islands (5-39). It is the most luxuriant along the southern slopes of the Himalayas and along the eastern border of Assam up to an altitude of 10,000 feet above sea level (4-39).



## Cannabis sativa (Marijuana): Harmful Adverse Effects

Acute and chronic side effects related to *Cannabis* sp (Medical cannabis-(marijuana type) are gastrointestinal disorders, fatigue, hypotension, nausea, paranoia, psychiatric symptoms, dizziness, impaired neurocognitive and psychomotor performances, attention and memory deficits, increase of psychiatric disorders, risk for addiction, airway trauma and lung diseases (52-59). Regarding the **synthetic cannabinoids, acute adverse events are tachycardia, acute myocardial infarction, acute kidney injury, seizure, sedation, confusion and impaired motor skills, while the prolonged use is associated with withdrawal symptoms, including restlessness, anxiety and mood swings** (52-59). Considering the several adverse effects, the treatment with *Cannabis* sp. is contraindicated in patients with psychiatric, cardiovascular, renal or liver diseases (52--59). In addition, cannabinoids cross the placenta even at lower doses and are carried to breast milk, thus they are not recommended for pregnant and lactating women, as they can cause newborn weight-loss and neurobehavioral disorders (51-59).

The impairments in brain connectivity is associated with exposure to marijuana in adolescence are consistent with preclinical findings indicating that the cannabinoid system plays a prominent role in synapse formation during brain development (51-59). Regular marijuana use is associated with an increased risk of anxiety and depression, but causality has not been established(51-59). Marijuana is also linked with psychoses (including those associated with schizophrenia), especially among people with a preexisting genetic vulnerability, and exacerbates the course of illness in patients with schizophrenia (51-59).

**Marijuana smoking** is also associated with inflammation of the large airways, increased airway resistance, and lung hyperinflation, associations that are consistent with the fact that regular marijuana smokers are more likely to report symptoms of chronic bronchitis than are non-smoker (51-59).

**Marijuana** use has been associated with substantial adverse effects, some of which have been determined with a high level of confidence (51-59). Marijuana, like other drugs of abuse, can result in addiction. During intoxication, marijuana can interfere with cognitive function (e.g., memory and perception of time) and motor function (e.g., coordination), and these effects can have detrimental consequences (e.g., motor-vehicle accidents) (51-59). Repeated marijuana use during adolescence may result in long-lasting changes in brain function that can jeopardize educational, professional, and social achievements. However, the effects of a drug (legal or illegal) on individual health are determined not only by its pharmacologic properties but also by its availability and social acceptability (51-59).

## CANNABIS SATIVA: PHYTOCHEMISTRY

The plant *Cannabis sativa* has been widely used by humans over many centuries as a source of fibre, for medicinal purposes, for religious ceremonies and as a recreational drug (1-45). *Cannabis sativa* L. (*C. sativa*) is an annual dioecious plant, which shares its origins with the inception of the first agricultural human societies in Asia. The abundant phytocannabinoids produced by Cannabis, has been used as medicine for centuries (30-48). On the other hand, its narcotic effects caused the plant to be subjected to many decades of worldwide strict regulations (1-48). Over the course of time different parts of the plant have been utilized for therapeutic and recreational purposes, for instance, extraction of **healing oils** from seed, or the use of inflorescences for their **psychoactive** effects (3-40). The key psychoactive constituent in Cannabis sativa is called  **$\Delta$ -9-tetrahydrocannabinol** ( $\Delta$ -9-THC).

Amongst these compounds are the terpenes (volatile organic compounds also found in the essential oils of many plants) and the cannabinoids (or phytocannabinoids) that have pharmaceutical effects in humans (2-45). Cannabis terpenes and cannabinoids are manufactured in the secretory cavity of specialized structures on the surface of the plant, called glandular trichomes (1-45). These crystal-like outgrowths are densely concentrated on female flowers and in other aerial parts of *Cannabis* (3-45).  **$\Delta$ -9-tetrahydrocannabinol (THC)** was the first cannabinoid to be isolated from *Cannabis* and is highly concentrated (in its carboxylated form) in modern *Cannabis* drug chemotypes (3-45). In addition to its well-known psychoactive effects,  **$\Delta$ -9-tetrahydrocannabinol (THC)** potentially exerts a variety of therapeutic activities including analgesic (pain-relieving), anti-inflammatory, and possibly anticancer properties (4-40). Cannabinoids are isolated from leaves, flowers, stems, roots and seeds, but the main source of phytocannabinoids are trichomes of unfertilized female flowers, which secrete a resin loaded of phytocannabinoids, as the THC (1-48).

Since the discovery of its **main psychoactive** ingredient,  **$\Delta$ -9-tetrahydrocannabinol (THC)**, significant progress has been made towards the understanding of the in vitro and in vivo pharmacology both of  $\Delta$ -9-tetrahydrocannabinol (THC) and of certain other cannabis-derived compounds (2-40). The potential and actual uses of these "phytocannabinoids" as medicines has long been reported (3-40). Among Cannabinoids,  **$\Delta$ -9-Tetrahydrocannabinol (THC)** and **Cannabidiol (CBD)** are generally the most abundant in the plant (1-45). The utilization of this multipurpose plant has been restrained for a long time because of the **psychoactive effects** of a specific cannabinoid ( **$\Delta$ -9-Tetrahydrocannabinol; (C<sub>21</sub>H<sub>30</sub>O<sub>2</sub>)**) (2-40, 60). Subsequent studies detected the receptors in the brain subject to the actions of this compound, along with ligands for these receptors, i.e., endogenous cannabinoids (EC), which make up, along with the enzymes synthesizing, transporting, and degrading them, the endocannabinoid system (ECS) (3-45). Interest in endogenous cannabinoids (EC) has consistently increased in recent years, especially after their important role in cognitive functions was discovered (4-45, 60). They are regulators of synaptic transmission in the brain, mediate numerous forms of plasticity, and control neuron energy metabolism. (3-45).

When plant cannabinoids enter the human body, they act on the **receptors of the endocannabinoid system**, but more strongly and for a much longer time than the human produced endocannabinoids do (60). Plant cannabinoids can lead to sustained alterations that can produce both therapeutic effects and unwanted side-effects. Since the endocannabinoid system is so widely distributed throughout the body, cannabinoids can cause a number of changes in body functions (60). Therefore, the use of cannabinoids for therapeutic action is almost always accompanied to some degree by side-effects (60). The endocannabinoid system seems to be phylogenetically ancient, as it was present in the most primitive vertebrates with a neuronal network (2-40). N-arachidonylethanolamine (AEA) and 2-arachidonoyl glycerol (2-AG) are the main **endocannabinoids** ligands present in the animal kingdom, and the main endocannabinoid receptors are **cannabinoid type-1 (CB1) receptor** and **cannabinoid type-2 (CB2) receptor** (3-45, 60).

**Endocannabinoid system (EC)** exert influences using a series of mechanisms and interactions with neuromediators, neurotrophic factors, and neuropeptides (4-40). The main functions of Endocannabinoid system (EC) in the brain involved in synaptic signaling and neuromodulation, which maintain cellular homeostasis (5-40, 60). Information on the influences of cannabinoid drugs on cognitive functions is very contradictory (4-45, 60). It was strongly prohibited in the twentieth century, and was removed from the British pharmacopeia (3-40). The plant was demonized due to its high abuse

liability and supposedly insufficient health benefits (2-48). The resinous substance contained in cannabis is therefore, considered the principle responsible for its physiological activity (1-45). The resin probably contains a number of compounds, one of which is cannabidiol (Cahn) which is probably the active principle (2-40). Cannabidiol (**CBD**) and  $\Delta$ -9 tetrahydrocannabinol (**THC**) are the two important chemicals found in cannabis (3-40). There's a biological pathway in human body called the **endocannabinoid system** that helps to regulate mood, appetite, sleep, memory and pain sensation (2-45). Both  $\Delta$ -9 tetrahydrocannabinol (**THC**) and Cannabidiol (**CBD**) hijack this system, but in different ways (3-48). THC initiates a psychological response in brain and has 'psychotropic' effects (2-40). Cannabidiol (**CBD**) the non-psychoactive component, may have an effect on human body instead. So, between the two, it is  $\Delta$ -9 tetrahydrocannabinol (**THC**) that can make you 'high' in the conventional sense (3-48).

Another phytocannabinoid, cannabigerolic acid, was recently shown to be the primary precursor in the biosynthesis of the carboxylated forms of all the cannabinoids discussed above (THC, CBD, and CBC) (3-45). Therefore, it is often found at lower concentrations in *Cannabis* (3-40). In its neutral form, Cannabigerol (CBG) has been shown to exhibit analgesic and anti-erythemic (redness or irritation of the skin) effects (5-45). Lastly, Cannabinol (CBN) is an oxidative degradation product of  $\Delta$ -9 tetrahydrocannabinol (**THC**), and therefore, is found in higher concentrations in aged *Cannabis*. Cannabinol (CBN) potentially exhibits anticonvulsant and anti-inflammatory activities (3-48, 60).

Besides leaves and inflorescences, hemp root is an interesting target for phytochemical exploitation, which provides added value to the growers. In total 20 secondary metabolites were identified, which includes the firstly described  $\beta$ -amyron, glutinol, fucosterol, stigmastanol, stigmasta-3,5-diene, stigmasta-3,5,22-triene, and oleamide in hemp roots (49).

*Cannabis* contains a wide range of compounds, including fatty acids (protect cell membranes), cannabinoids (**active in CB1 or CB2 receptors**), flavonoids (plant pigments and control of cell growth), phenols (as THC), terpenes (confer smell), and other secondary metabolites are still under investigation (1-48). Furthermore, in *Cannabis* are found substances beneficial to health with nutritional value, such as: vegetable oils between 19-38%, protein around 20-30%, fiber ranging from 27-36%, minerals between 4-6%, besides tocopherol, carotenes and other phenolic compounds (1-48). There are around **556 chemical** constituents identified in the *Cannabis sativa*, being 113 phytocannabinoids and 120 terpenes, though only 90 components were purified and characterized (1-48).

## CONCLUSION

This literature review paper highlights about the medicinal plant, *Cannabis sativa*. On the basis of Google search, PubMed research articles and scientific literature survey was carried out in order to develop this literature review paper. *Cannabis sativa* (**Medical cannabis-(marijuana type)**; **Industrial Cannabis sativa-(fiber type)**) is also commonly known as Indian hemp, marijuana, Bhang, Ganja, and Charas, which are banned in India as **an illicit drug**. Sales and cultivation of *Cannabis* are **illegal** in India. Cannabis-based medicine is a rapidly emerging field of study, with implications for both healthcare practitioners and patients. There is a need for education for healthcare practitioners to enhance their capacity to support patients who require cannabis for medical purposes. In particular, healthcare practitioners need more information on potential risks, relative safety and precautions for patients who use medical cannabis. Research supports the medical use of cannabis to relieve nausea, vomiting and chronic pain, and to stimulate appetite, but the research is still emerging in its application

to other disease conditions. Cannabis and cannabinoids are also approved for stimulation of **appetite in AIDS patients** with a severe loss of body weight. Future development is likely to be focused on exploiting CBD and possibly other cannabinoids without psychoactivity, and improving the specificity of synthetic cannabinoids and their delivery by safer methods than smoking.

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