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ORIGINAL PAPER



Pharmacological properties of Indian hemp- *Cannabis sativa*

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INTRODUCTION

The cannabis plant has a history of use dating back thousands of years across many ancient civilizations ranging from medicinal, recreational, and spiritual to its use as a potent poison. Its medicinal properties has a effect on physiological, psychological and endocannabinoid system due to presence of 400 different chemicals entities of which more than 60 of them are cannabinoid compounds like THC and CBD. It is surprising that we are deprived of this amazing plant from past three decades because of some misconceptions spread in our society. Its medicines are available in the form of oral tablets, cannabinoid oil, powder, and sometimes smoked. Some clinical trials has also proved its effectiveness against some neurological diseases (Epilepsy, Alzheimer's, etc.), psychological disorder (Bipolar disorder, ADHD, etc.) and physiological diseases (IBS, loss of appetite, Psoriasis, etc.). It also has some adverse effects if taken unprescribed. Industrially, the stalks of hemp plant are used as an excellent clothing material (also designated 'hemp fabric') which is not only economically feasible but again also have many medicinal properties like antibacterial, antifungal and anticancerous properties. It has immersed as a leading contender in the race to produce sustainable fuel alternatives. The cultivation of hemp plants also beneficial in many aspects. The hemp plant absorbs toxic metals such as copper, cadmium lead and mercury emitted by nuclear plants into the soil. In incidents of nuclear disaster these plants are used for phytoremediation. These plants are also naturally resistant to pest and weeds leading to reduction of air pollution and soil enrichment. There are many restrictions and laws imposed on the cultivation and use of the hemp plant which reduces the documentation and clinical trials to be processed although its fatalities are very rare. As more high-quality clinical trials will gather, there are high chances of establishment of marijuana as of therapeutic importance

and its therapeutic use may likely expand. Marijuana is an ancient medicinal herb famous with the name of Indian hemp, ganja. The scientific name of the plant is *Cannabis sativa*. It belongs to Cannabaceae family. It is known to be an annual herb with erect stem grows upto 3-10 feet or more than this and slightly branched with greyish green hair [planetayurveda.com/library/bhanga-cannabis-sativa/]

The use of marijuana has also not been hidden since time immemorial as its use has been cited in different Hindu texts. According to one description when the amrita (elixir of life) was produced from the churning of the ocean by the devas and the asuras, Shiva created cannabis from his own body to purify the elixir (whence, for cannabis, the epithet angaja or “body-born”). Another account suggests that when the drop of elixir was dropped on the ground. Thus, cannabis is used by sages due to association elixir and Shiva. Many Nepalese consume it during festivals like Shivaratri which the government tolerates to some extent and also for their personal uses and recreational purposes. Further in Nepal its seeds are also used in making pickles “Bhaang ko acchar”. Early Sikh military history was dominated by the Nihang, who are known for their victories where they were heavily outnumbered. Some Nihang group consumes cannabis to help in meditation. Sukhnidhaan or Sukhprasad is the term Nihang used to refer to it [hempvati.wordpress.com/medical-cannabis/]

Cannabis strains are either pure or hybrid varieties of the plant genus Cannabis, which encompasses the species *C.sativa*, *C.indica* and *C.ruderalis*. Cannabis sativa is found in equatorial climates such as in Thailand, South Africa and Mexico. It has tall and thin leaves. It is good for outdoor growth in warm climates. It helps in stimulating creativity, uplifting and energizing, reduces nausea, depression, increases appetite and sense of well-being. *C.indica*, mostly found in the Central Asia and the Indian subcontinent. It has short, bushy and wide leaves. It relieves pains and aches, aids sleep, anti-inflammatory, reduces stress and anxiety, help relief spasm and seizures.

Classification in the plant kingdom

<p>Kingdom: Plantae Division: Magnoliophyta Class: Magnoliopsida Order: Urticales Family: Cannabaceae Genus: Cannabis Species: <i>sativa</i>, <i>indica</i>, <i>ruderalis</i></p>
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Cannabis is a psychoactive plant that contains more than 500 components, of which 104 cannabinoids have presently been identified. Two of these have been subject of scientific investigation into their pharmacological properties; delta⁹-tetrahydrocannabinol (delta⁹-THC) and cannabidiol (CBD). Cannabis potency is primarily evaluated according a samples THC concentration. This is primary psychoactive cannabinoid in cannabis. The

adverse effects after acute or regular cannabis use are in direct relation to THC concentration in the product.

ENDOCANNABINOID SYSTEM

The endogenous cannabinoid system is an omnipresent lipid signaling pathway which performs and controls numerous physiological roles in the body and appeared early in its evolution. Cannabis like molecules or principal cannabinoid compounds is small functional molecule which has been isolated from arachidonic acid, a membrane layer, and has named anidamide and 2-arachinodoylglycerol. These molecules are directly linked to a class of G-protein coupled receptor. (De Fonseca et al., 2005) The cannabinoid receptors are mainly of 2 types, and belong to the superfamily of GPCR. The primary receptor, CB1, is majorly found in the peripheral and central cell terminus, glial cells, reproductive system, microcirculation and the major glands of human body. The cannabinoid CB2 receptor was initially found in multiple lymphoid organs and were highly expressed in the B- lymphocytes, moderately expressed in polymorphonuclear neutrophils and monocytes and were least expressed in the T-lymphocytes. The central nervous system has plentiful supply of CB1 receptors, particularly in the region of the cortex, basal ganglia, cerebellum and hippocampus. These receptors are particularly present on the axon terminal and the preterminal segments of the axon and spare the active zone on the neuron cell (Howlett, A.C., 2002)

THC is the psychoactive principle of cannabis, inducing the cannabis inebriation sought by many users. Its addictive potential and negative consequences are now well known. The effect of CBD are distinct and, in many cases, the opposite of THCs effects. CBD seems not to induce euphoria and seems to have antipsychotic, anxiolytic, antiepileptic and anti-inflammatory properties. [Rong, C. *et al.*, 2017)

Physiological Role of Endocannabinoid in Humans

1. **Gastrointestinal System** : The role of CB1 receptors was suggested in regulating the contractility in the gastrointestinal tract more than a decade before they were discovered (Sanger, G.J, 2007). The CB1 receptors prominently play a dominant role in the human gastrointestinal system compared to other compounds isolated from *Cannabis sativa* extract 2-AG was initially extracted from the intestine of canine in 1995 and sometimes later anandamide was also obtained from the tissue of mice small intestine with simultaneous presence of the FAAH enzyme (Massa *et al.*, 2005). The CB1 receptor was also found to be localized with immune reactive substance P in the neuron of the intestine, thereby indicating they can help or modulate reaction on the GIT tract on the humans and can alter the sensory motor function of intestine (Izzo & Camilleri, 2008)
2. **Cardiovascular System** : Cannabinoid affect cardiovascular system not only by cannabinoid receptor, but a variety of other receptors, located both in the nervous system and directly in the blood vessels and heart (Malinowska *et al.*, 2012). Stimulation of central CB1 receptor causes an increase in blood pressure, whereas

peripheral CB1 receptor located pre-synaptically at the endings of pre- and / or post ganglionic sympathetic neuron innervating the heart and vascular resistance are responsible for hypotensive effect of cannabinoid. Cannabinoid, in most cases, causes vasodilation in isolated blood vessels or perfused vascular beds, although vasoconstriction is also observed. This affects results from direct activation of CB1, TRP1, PPARs and the putative endothelial cannabinoid receptor.

3. **Immune System** : The endocannabinoid play significant role in controlling the functioning of the immune system and helps to maintain immune homeostasis. The receptors of endocannabinoid are highly expressed in immune B cells, followed by monocytes, natural killer cells and CD4 and CD8 lymphocytes (Rahaman & Ganguly, 2021)

Cannabis and Neurological Aspects

Marijuana consists of 85 phytocannabinoids, from which cannabidiol (CBD) and tetrahydrocannabinol (THC) are the main constituents. CBD and THC are responsible for the medicinal effects of marijuana (Babayeva, M., 2016). CBD is known psychoactive and is known to have Hypnotic, anxiolytic, antipsychotic, and neuroprotective effect (Suryadevara, *et al.*, 2017). THC is the main component responsible for psychotropic effects of cannabis, and it acts via two types of G-protein coupled receptors, known as cannabinoid type 1 (CB1) and type 2(CB2) (Pertwee, R.G., 2005). CB1 receptors are located mainly in the Central Nervous System (CNS) and CB2 receptors reside in organ and cell of immune system (Venderova D, 2004). While THC is psychoactive and partial agonist to CB1 and CB2 receptors, CBD is indirectly antagonistic to cannabinoid receptors. CBD inhibits the psychotropic effects of THC and improves its tolerability and therapeutic window, without being intoxicating. Endocannabinoid are produced in the body and help regulate memory, pleasure, concentration, thinking, movement, sensory and time perception, appetite and pain. The main endocannabinoid are anandamide and 2-arachidoyl glycerol.

1. Parkinson's Disease : PD arises as a result of the loss of dopaminergic neurons in the substantia nigra, resulting in the loss of control of voluntary movements, which manifest as tremor, rigidity and bradykinesia. Other non-motor symptoms are psychosis, cognitive impairment, depression and anxiety. Its exact cause is unknown, with genetic and environmental factors playing a role to some extent. Medical marijuana has been observed to improve both motor and non-motor symptoms including bradykinesia, rigidity, tremor, sleep and pain. A study demonstrated the effects on 85 individuals with PD. Most of them consumed a half a teaspoon of cannabis leaves, along with prescribed pharmacotherapy for PD. About 46% of these individuals reported relief of PD symptoms. Adverse effects of marijuana include temporary cognitive impairments. Chronic use results in dependence, cognitive impairment, depression and anxiety and increase risk for lung diseases.

2. Alzheimer's Disease : AD is a disease that is caused by gradual degeneration and death of cerebral cortical cells. The main symptoms include memory loss, cognitive

decline and behavioral disorders (Scuderi, C., 2014). In-vitro studies have showed that Cannabis protected PC12 cells from neurotoxicity and oxidation stress, increased cell survival, and inhibited AChE. Two in vivo studies using CBD treated the right dorsal hippocampus of mice with human A (beta) (1-42) to evaluate the effects of CBD on neurotoxicity and inflammation. The effects of CBD were confirmed with and without the antagonist of PPAR (gamma). The effects of CBD on neural damage and CBD stimulated the neurogenesis of the hippocampus through interactions (Giuseppe E, et al., 2011). Additionally, CBD+THC treatment to transgenic mice revealed that CBD+THC treatment was effective in memory and CBD+THC treatment was more effective than CBD alone or THC alone treatment (Seok Hee Kim, *et al.*, 2019)

3. Tourette syndrome : Tourette syndrome is a heterogeneous neurobehavioral disorder manifested by childhood-onset motor or phonic tics, often accompanied by a variety of behavioral comorbidities, including attention deficit and obsessive compulsive disorder (Billnitzer & Jankovic., 2020). Cannabis-based therapy has been explored in the past as a potential treatment option for TS. Patients given delta 9-tetrahydrocannabinol reported significant improvement in their tics and obsessive compulsive behavior 3 to 4 after treatment. Serum tetrahydrocannabinol (THC) concentrations were also measured during the study and correlated with improvement in tics as measured by the examiner (Muller-Vahl, K.R., 2002). In one cross-sectional survey of 42 patients with TS who were already undergoing treatment with medical cannabis, all patients interviewed reported some improvement with tics while taking medical cannabis in treating their symptoms. Adverse effects led to discontinuation of treatment in 10 patients, including one patient because of an episode of psychosis. Other patients who discontinued treatment has side effects that included hallucinations (4 patients), irritability and confusion (6 patients), and subjective cognitive decline (7 patients) (Thaler, *et al.*, 2019).

INDUSTRIAL APPLICATION

Industrial hemp was once a dominant crop on Indian and American landscape. This hardy and renewable resource was refined for various industrial application including paper, textiles and cordage. Over time, the use of industrial hemp was evolved into greater variety of products including health foods organic body care, clothing, construction material, biofuels, plastic composite and more than 25000 products can be made.

- I. **Textiles :** Hemp fabric is a type of textile that is made using fibre from stalk of Cannabis plan. This plant has been recognized as a source of extraordinarily tensile and durable textile fibre for millennia. Hemp is a lightweight fabric, which means that is highly breathable, and it also effectively facilitates the passage of moisture from the skin to the atmosphere, so it is ideal for hot climates. It is easy to dye this type of fabric, and it is highly resistant to mold, mildew and potentially harmful microbes. Hemp fabrics are used to produce shoes, socks, bags etc. [<https://sewport.com/fabrics-directory/hemp-fabric>]

- II. **Hemp seeds** : Hemp seeds are rich source of nutrients. Part of the hemp plant, these seeds are technically a nut that can be eaten raw or used to make milk, oil, cheese substitutes, or protein powder. Hemp seeds can be eaten raw, roasted or cooked, used as non-dairy hemp milk and hemp cheese. Hemp seeds are good source of iron, Vitamin E, Manganese, Magnesium, B-vitamins, Zinc, high levels of omega-3 and omega-6 essential fatty acids. Other products are also manufactured from Cannabis plant like Cannabinoid oil, Biofuels, etc.

CONCLUSION

With the growing popularity of Cannabis, it becomes extremely important to aware the people about its proven advantages and disadvantages. So, more and more research needs to be done on its active components like THC and CBD for its judicial use. However, because of the taboo attached, it becomes difficult to explore its properties as there is no board for its regulation. There are proven benefits of flower, roots, stalk and leaves of Cannabis in many fatal diseases like MS, Tourette syndrome, ASD, AIDS and cancer. The recreational use of cannabis especially in teenagers has shown retarded brain development. Use of marijuana in the form of smoke has been proven as carcinogenic in human body.

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