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Review Article on Role of *Bhanga* (Cannabis) in Pain Management.

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ABSTRACT:

Bhanga (Cannabis) has been an integral part of the Indian system of medicine and Indian culture from centuries. During *Holi* (the festival of colors) there is an increased availability and consumption of *Bhanga* and in *Maha-Shivratri Bhanga* is consumed because of its deliriant effect. However, since the consumption of *Bhanga* majorly falls under the category of recreational marijuana use, its exceptional medicinal values are not explored in-depth. However, during the last decade, interest in cannabis in medicinal use has been increasing. In many countries like the USA, UK etc. implementing their regulations in *Bhanga* (cannabis) based medicines. *Bhanga* is extracted from the buds, leaves, and flowers of the cannabis plant. *Bhanga* contains cannabinoids and is helpful in treating nausea and vomiting- mainly in the patients undergoing chemotherapy. One of the most well-known medicinal uses of cannabis products is pain reduction, especially CBD (Cannabidiol), which are quite effective in treating chronic pain. Cannabinoids can help in reducing chronic pain caused due to fibromyalgia and rheumatoid arthritis. Because of this reason research is increasing to explore the role of *Bhanga* (cannabis) in pain management.

Keywords: *Bhanga* (Cannabis), medicinal values, cannabinoids, Cannabidiol, pain management

INTRODUCTION

The cannabis plant has two main subspecies, Cannabis indica and Cannabis sativa, and they can be differentiated by their different physical characteristics. Indica-dominant strains are short plants with broad, dark green leaves and have higher cannabidiol content than the sativa plants in which THC content is higher. Sativa-dominant strains are usually taller and have thin leaves with a pale green color. Due to its higher THC content, Cannabis sativa is the preferred choice by users. [1] *Bhanga* has been an integral part of the Indian system of medicine and Indian culture from centuries. In *Holi* there is an increased availability and consumption of *Bhanga* and in *Maha-Shivratri Bhanga* is also freely consumed because of its association with Lord *Shiva*.[2,3]

Ayurvedic aspect of *Bhanga* (Cannabis)

Bhanga is described under *Mula Visha* (root poison) in *Susruta Samhita* as *Vijaya*[4] and decoction of its leaves are indicated as an external medication for rinsing the *Sushka*

Arsha (dry piles) in *Charak Samhita*.[5]

***Shodhana* (Purification) of *Bhanga*(Cannabis)**.

In *Ayurveda*, plants are primary source of medicine, number of compounds have been isolated from medicinal plants. However, most of these medicines have been withdrawn because of their toxicity or adverse effect. Various poisons plants, *like Bhanga (Cannabis sativa linn) Ahiphen (Papaver somnifera linn), Vatsnabha (Aconitus ferox), Kupilu (Strichnos nuxcomica linn), Dhatur (Dhatura metel linn),* and minerals like *Parad* (mercury), Arsenic have been used in *Ayurveda*. These have different phytochemicals so used after *Shodhana* (purification) process in crude form.[6] *Shodhana* (purification) of *visha dravya* (poisonous drugs) is also an important procedure which makes the toxic drug useful for there therapeutic use. [7] Also *Acharya Charka* mentioned that, any poison if processed or used properly is a potential medicine and any medicine if used improperly is a fatal poison [8] Many *Acharyas* have stated that not all medicinal plants are safe to use since they can bear many toxic and harmful phyto-constituents in them. There is a category of poisonous plants , called *Visha* and *Upvisha*. To reduce their toxic effect some *Shodhana* (purification) should be done to prevent the fatal effect of *visha dravya* (poisonous drugs). So it is important to understand the process of *Shodhana* (purification) of *Visha* and *Upvisha* mentioned in *Ayurvedic* text. The science of proficiency of *Visha Drvayas* (poisonous drugs) for their theuraptic use is known as *Shodhana* (purification). Various procedures of *Shodhana* (purification) are used for the purification of drugs like *Swedan* (fomentation), *Mardan (*triturated), *Prakshalan* (washing), *Dhalana*, *Nirvapan*, *Bharjana*, *Bhavana* (Levigation), *Nimajjana* (Dipping).

1st Method: The leaves are tied in a cloth and soaked with water. This procedure has to be continued until the greenish color stops discharge from the leaves. After this the leaves are dried under the shade, thereafter it should be fried in *Goghrita* (Cow's ghee) on a mild fire and used for therapeutic purposes.

2nd Method: *Swedana* (fomentation) in *Godugdha* (cow's milk) for 3 hours with mild heat then washed with water. After getting it dried, it is fired in *Goghrita* (Cow's ghee).

3rd Method: The *Bhanga*a leaves are to be fomented in decoction of *Babbul Tvak* (Bark of Acacia catechu) for 25-30 minutes with moderate heat and then subjected to drying under direct sunlight. Further they are triturated with *Godugdha* (cow's milk), dried and used. [9]

Ayurvedic properties of *Bhanga*: *Ras - Tikta, Guna - Laghu, Tikshna, and Vyavayi, Vipaka – Katu, Virya – Ushna*, Effect on *Tridoshas* – balanced *vata* and *kapha dosha*. Increase *pitta dosha*.[10]

Chemical Composition of *Bhanga*- Its plant contains about 426 chemical entities, of which more than 60 are cannabinoid compounds.[11] The four major compounds are d-9-THC (tetrahydrocannabinol), CBD (Cannabidiol), d-8-THC and cannabinol, which have been most researched.[12]

Legal Aspects-

1. According to the Narcotic Drugs and Psychotropic Substances (NDPS) Act of 1985:
   "cannabis (hemp)" means-
   (a) **Charas**, that is, the separated resin, in whatever form, whether crude or purified, obtained from the cannabis plant and also includes concentrated preparation and resin known as hashish oil or liquid hashish;
   (b) **Ganja**, that is, the flowering or fruiting tops of the cannabis plant (excluding the seeds and leaves when not accompanied by the tops), by whatever name they may be known or designated; and
   (c) Any mixture, with or without any neutral material, of any of the above forms of cannabis or any drink prepared therefrom.
   As *Bhanga* is prepared from the seeds and the leaves of the Cannabis plant, it is not banned under the NDPS Act of 1985. However, some states do regulate and ban the sale and consumption of *bhanga*. *Bhanga* can also be used in the form of medicine if the patient has a prescription from an *Ayurvedic* practitioner.[13]
2. The 1961 Single Convention on Narcotic Drugs was the first ever international treaty to have included cannabis (or marijuana) with other drugs and imposed a blanket ban on their production and supply except for medicinal and research purposes.[14] However, the Single Convention's definition of 'cannabis' does not include the leaves of the cannabis plant, thereby preserving the legality of *Bhanga* culture in India.[15]
3. An Italian law approved in 2015, authorizes the use of cannabis to treat chronic pain. The law allows for the utilization of cannabis not only for neuropathic pain but also for all chronic pain conditions. [16]
4. The medical use of marijuana is much debated in modern medicine. Medical marijuana refers to using the whole, unprocessed marijuana plant or its basic extracts. It is not yet approved by the US Food and Drug Administration (FDA) as a safe and effective drug for any indication, although many states in the United States have legalized

marijuana for medical purposes. However, the FDA has approved one medication, which contains the purified substance cannabidiol for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older.[17]

Pain Processes

Pain is a complex, biopsychosocial phenomenon that arises from the interaction of multiple neuroanatomic and neurochemical systems with a number of cognitive and affective processes. The International Association for the Study of Pain has offered the following definition of pain: "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.[18] The Neurochemistry of Pain explains that Nociception is mediated by the function of numerous intra- and extra-cellular molecular messengers involved in signal transduction in the peripheral and central nervous systems. In addition, inflammatory mediators are secreted at site of the original injury to stimulate nociceptor activation. This "inflammatory soup" is comprised of chemicals such as peptides (e.g., bradykinin), neurotransmitters (e.g., serotonin), lipids (e.g., prostaglandins), and neurotrophins (e.g., NGF). The presence of these molecules excites nociceptors or lowers their activation threshold, resulting in the transmission of afferent signals to the dorsal horn of the spinal cord as well as initiating neurogenic inflammation.[19]

Physiologically, pain occurs when sensory nerve endings called **nociceptors** (also referred to as pain receptors) come into contact with a painful or noxious stimulus. The resulting nerve impulse travels from the sensory nerve ending to the spinal cord, where the impulse is rapidly shunted to the brain via nerve tracts in the spinal cord and brainstem. The brain processes the pain sensation and quickly responds with a motor response in an attempt to cease the action causing the pain.

There are four major pain processes: transduction, transmission, modulation, and perception. Transduction refers to the processes by which tissue-damaging stimuli activate nerve endings. Transmission refers to the relay functions by which the message is carried from the site of tissue injury to the brain regions underlying perception. Modulation is a recently discovered neural process that acts specifically to reduce activity in the transmission system. Perception is the subjective awareness produced by sensory signals; it involves the integration of many sensory messages into a coherent and meaningful whole. Perception is a complex function of several processes, including attention, expectation, and interpretation.[20]

***Bhanga* (Cannabis) In Pain Management-**

The two major ascending pathways in mammals that are devoted to pain, the spinothalamic pathway and the spinoparabrachial pathway are responsible for the discriminatory and the affective aspect of pain, respectively. The descending control of pain can be inhibitory or facilitatory, originates in higher cortical region, amygdala and hypothalamus, and projects to the lower brain stem and the spinal cord.[21] The endocannabinoid system is expressed throughout the ascending and the descending pathway. The cannabinoid receptors 1 and 2 (CB1 and CB2) have been extensively studied as antinociceptive receptors , either singly or in combination. [22] The Bhanga (Cannabis) plant contains around 60 cannabinoids. Cannabinoids are endogenous or exogenous compounds that have activity on the cannabinoid receptors. [23]

Uses of Bhanga(Cannabis)-.

Starting with the Chinese around 2900 B.C., many civilizations have transcribed their use of cannabis for a variety of conditions, from joint pain and muscle spasms to conditions such as gout and malaria. [24]

Despite a paucity of standardized and controlled trial research to evaluate the short- and long-term health outcomes of cannabis use, all states are consistent in including chronic pain as one of the conditions for which cannabis is an approved pharmacotherapy. Indeed, pain relief is the most commonly cited reason for the medical use of cannabis. [25,26]

Medicinal cannabinoids, including medicinal cannabis and pharmaceutical cannabinoids and their synthetic derivatives, such as tetrahydrocannabinol (THC) and cannabidiol (CBD), have been suggested to have a therapeutic role in certain mental disorders. However, a recent review and meta-analysis analyzing the available evidence to ascertain the effectiveness and safety of all types of medicinal cannabinoids in treating symptoms of various mental disorders concluded that there is scarce evidence to suggest that cannabinoids improve depressive disorders and symptoms, anxiety disorders, attention-deficit hyperactivity disorder, Tourette syndrome, post-traumatic stress disorder or psychosis. [27]

Use of marijuana for chronic pain, neuropathic pain, and spasticity due to multiple sclerosis is supported by high-quality evidence. Six trials that included 325 patients

examined chronic pain, 6 trials that included 396 patients investigated neuropathic pain, and 12 trials that included 1600 patients focused on multiple sclerosis. Several of these trials had positive results, suggesting that marijuana or cannabinoids may be efficacious for these indications. [28] Cannabinoids studied included smoked cannabis, oromucosal extracts of cannabis based medicine, nabilone, dronabinol and a novel THC analogue. Chronic non-cancer pain conditions included neuropathic pain, fibromyalgia, rheumatoid arthritis, and mixed chronic pain. Overall the quality of trials was excellent. Fifteen of the eighteen trials that met the inclusion criteria demonstrated a significant analgesic effect of cannabinoid as compared with placebo and several reported significant improvements in sleep. There were no serious adverse effects. Adverse effects most commonly reported were generally well tolerated, mild to moderate in severity and led to withdrawal from the studies in only a few cases. Overall there is evidence that cannabinoids are safe and modestly effective in neuropathic pain with preliminary evidence of efficacy in fibromyalgia and rheumatoid arthritis. The context of the need for additional treatments for chronic pain is reviewed. Further large studies of longer duration examining specific cannabinoids in homogeneous populations are required.[29]

As only one of the six centers has extensively used cannabinoids for intractable chronic pain (614 patients of 659), only the population from Azienda Ospedaliero Universitaria Pisana (Pisa) was considered. Cannabis tea was the primary mode of delivery, and in almost all cases, it was used in association with all the other pain treatments. Initial and follow-up cannabinoid concentrations were found to vary considerably. At initial follow-up, 76.2% of patients continued the treatment, and <15% stopped the treatment due to side effects (none of which were severe).[30]

Risk in *Bhanga* (Cannabis) Use-

1. Use of *Bhanga* (Cannabis) during pregnancy may increase adverse outcomes for women and their neonates. [31]
2. Although much of the existing research investigating marijuana use in pregnancy is limited by study design and confounding factors, a growing accumulation of data suggests adverse outcomes. Studies have identified associations with decreased birth weight, increased spontaneous preterm birth, and impaired neurodevelopment among children and adults with in utero exposure. [32]
3. *Bhanga* (Cannabis) products may also increase your risk of certain disorders, such as depression and schizophrenia. [33]
4. It's mostly known for causing feelings of euphoria, but *Bhanga* (Cannabis) can also cause panic, fear, or depression in some people. [34, 35]

DISCUSSION

As depicted above, *Bhanga* (Cannabis) has various health benefits associated with it. Due to it being associated with recreational use, a majority of those consuming it are not aware of its medicinal properties. A medical practitioner should be consulted before consuming *Bhanga* (Cannabis) as a medicine, wherein the dosage to be administered would be specified.

Preclinical studies demonstrate a narrow therapeutic window for cannabis as pharmacotherapy for pain; the body of clinical evidence for this indication is not as extensive. A recent meta-analysis of clinical trials of cannabis and cannabinoids for pain found modest evidence supporting the use of cannabinoid pharmacotherapy for pain. Recent epidemiological studies have provided initial evidence for a possible reduction in opioid pharmacotherapy for pain as a result of increased implementation of medical cannabis regimens.

With increased use of medical *Bhanga* (Cannabis) as pharmacotherapy for pain comes a need for comprehensive risk-benefit discussions that take into account *Bhanga* (Cannabis) significant possible side effects like euphoria, unsafe in pregnancy, dizziness. As cannabis use increases in the context of medical and recreational *Bhanga* (Cannabis) policies, additional research to support or refute the current evidence base is essential to attempt to answer the questions that so many healthcare professionals and patients are asking.

An initial analysis of the Italian clinical practice of the use of cannabinoids for chronic pain syndromes in a reasonably large population is presented. Even with the heterogeneity of the sample size and the limited data available, it can be stated that the treatment seems to be effective and safe in the majority of patients, even though the safety and effectiveness data should be confirmed in a trial better designed to assess them. Nevertheless, additional data from a variety of types of trials are needed in order to better understand the benefits of cannabinoids to chronic pain sufferers. It is important for India and other Countries to more thoroughly investigate this topic in order to provide clearer and more useful guidelines, which will more adequately guide physicians in the use of this drug in the treatment of chronic pain.

CONCLUSION

Bhanga (Cannabis) has been used throughout decades by many civilizations. There were no formal processes or approval for its preparation and use. This is the time when scientific evaluation and research are needed to get evidence for the effectiveness and its safety on human beings in different illnesses. With increased use of medical *Bhanga* (Cannabis) as pharmacotherapy for pain comes a need for comprehensive risk-benefit discussions that take into account *Bhanga* (Cannabis) significant possible side effects. *Bhanga* (Cannabis) based medication appears to be safe having some risks like euphoria, unsafe in pregnancy, dizziness, depression and schizophrenia; however, there is need for research on their safety, mainly in vulnerable patients. Role of *Bhanga* (Cannabis) in pain management is a topic where ample research is needed to evaluate its uses and risks in patients. It is important for India and other Countries to more thoroughly investigate this topic in order to provide clearer and more useful guidelines, which will more adequately guide physicians in the use of this drug in the treatment of chronic pain.

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