

USE OF CANNABIS IN INDIAN CLASSICAL FORMULATIONS

Abstract

Ayurveda is the world's oldest and most complete spiritual teachings, as well as the "oldest medicinal system" known to man. Ayurvedic treatments along with natural substances donot have any usual side effects as contemporary drugs. The cannabis plant has been used as a medicine for thousands of years to treat various illnesses including gastrointestinal disorders. THC and cannabidiol (CBD) are the most well-known and researched phytocannabinoids, with impressive therapeutic properties for a variety of neurological, gastrointestinal, ophthalmic, and skin problems. Cannabis and cannabinoids are beneficial in healing the sign and symptoms of several gastrointestinal diseases, according to research, in part because they interact with the digestive tracts endogenous cannabinoid receptors. This could help in relaxing pain and cramps, reducing discomfort, and improving motility. Many Indian classical formulations were found cannabis is used processing agent in pharmaceuticals. For the treatment of GI issues, there are some popular cannabis-based ayurveda or herbal formulations on the market. CBD levels are frequently higher in medical marijuana, while THC levels are lower. For certain people, the therapeutic CBD is desirable for medicinal purposes, but the psychoactive THC may be needless and undesired. There are numbers of traditional cannabis formulations on the market that lack standardised quality control parameters and methods of evaluation. So, there is a need to develop a standardization technique with special reference to CBD and THC content to include this system of medicine in the main stream of health science. Standardization of popular Ayurvedic or herbal formulations is essential in order to assess the quality, safety, efficacy of that.

Keywords: Ayurveda, Cannabis, cannabinoids, gastrointestinal disorders

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I. INTRODUCTION

Ayurveda is the world's oldest and most complete spiritual teachings, as well as the "oldest medicinal system" known to man. The principle of the "Five Great Elements" underpins the entire concept of ayurveda. Earth (prithvi), air (vayu), fire (agni), water (jal), and space (akash). Vata, pitta and kapha, are the three humours (or doshas) that result from the combination of each element. These doshas are thought to be in charge of a person's physical, mental, and emotional well-being.¹ Indian traditional medicines system are widely adopted to treat a variety of physical and psychological ailments, with a strong focus on the underlying cause of the illness like hypertension, obesity, arthritis, Gastrointestinal disorders, heart related disease, nervous disorder, anxiety, colds, colitis, constipation, asthma, skin problem, ulcer, acne, allergies, chronic fatigue syndrome, depression, diabetes, flu and immune problems. Our Traditional medicine tries to keep and restore the body's natural ability to maintain balance and combat disease. Use of medicine from natural sources has been an ancient practice and is an important component of the health care system in India.^{1,2} Any plant, animal, or mineral substances can be added in the ayurvedic pharmacopoeia, but only if its nomenclature, identity, qualities, and therapeutic applications are completely known. Ayurvedic and other traditional treatment systems depend heavily on plant-based medicines. In the Indian subcontinent, about more than 10,000 plants are being used for therapeutic purposes. In traditional and folk medicine in India, over 25,000 effective plant-based medicines are employed.³

II. CANNABIS: THE ANCIENT SACRED PLANT OF INDIA

In India, cannabis has a lengthy history that is veiled in stories and religion. The Vedas and other sacred Hindu literature include the first mentions of cannabis. The Hindus of India were the most prominent early consumers of Cannabis, and it was later spread outside of India with the Indo-Aryan culture⁴. The plant is known as Vijaya in Sanskrit and bhang in Hindi. Millions of individuals have used it to induce pleasure as well as ease pain since its discovery. *Cannabis sativa* commonly known as Hemp belongs to family Cannabaceae, a fast growing plant and is originated from central Asia, and long cultivated in Asia, Europe and China. It was used for fibre, food, oil, medicine, recreation, and spiritual purposes, among other things. It is commonly consumed as charas, hashish and bhang. In the 1930s, the British Government of India made it illegal to consume cannabis resin (charas) in India, which led to a decline in *C. sativa* cultivation and use. Bhang is made from the cannabis plant's leaves (and seeds). As a result, it is exempt from the NDPS Act of 1985, which prohibits the production; distribution and selling of cannabis flowers and derived resin while allowing the usage of its foliage and seeds. The National Policy on Narcotic Drugs and Psychotropic Substances allows cultivation of cannabis, with permit, only for research and not to be used for medical purposes. *Cannabis indica* or Indian hemp, is an annual herb of the family Cannabinaceae. It has been used by humans for at least 4,500 years as food, fiber and medicine and other purpose. It is a native to Central Asia, and long cultivated in Asia, Europe and China,^{5,6}

III. PHYTOCHEMICAL PROFILE OF CANNABIS PLANTS

Cannabis sativa is a chemically complex species based on its numerous reported natural secondary metabolite constituents. *C. sativa* possesses a complex and diverse chemical contents, like alkaloids, Cardiac glycosides, terpenes and terpenoids, β -

Caryophyllene, carbohydrates, fatty acids and their esters, amides, amines, phytosterols, aldehydes, proteins, glycoproteins, and enzymes, flavonoids elements, simple alcohols, pigments, vitamin K phenols, phenolic compounds, noncannabinoid, steroidsetc. The wild variety of cannabis found in India also possess almost same types of phytomolecule. The most pharmacologically active compounds known as **cannabinoids**. In 1964, (-)-trans-delta-9 tetrahydrocannabinol (Δ^9 -THC) was isolated for the first time. There are 489 compounds have been isolated from cannabis till 2005, out of 489 compounds, 70 were known as cannabinoid^{7,8,9}.

Cannabinoids: The isolated cannabinoids also known as phytocannabinoids can be divided into 11 different categories.: (-)- Δ^9 -trans-tetrahydrocannabinol (Δ^9 -THC), (-)- Δ^8 -trans-tetrahydrocannabinol (Δ^8 -THC), cannabidiol (CBD), cannabigerol (CBG), cannabichromene (CBC), cannabinodiol (CBND), cannabicyclol (CBL), cannabielsoin (CBE), cannabinol (CBN), cannabitol (CBT), and other additional types. THC is the most abundant cannabinoid found in drug-type plants while cannabinoidic acids like cannabidiolic acid (CBDA) and cannabigerolic acid (CBGA) are known to be abundant in fibre-type plants. After decarboxylated it transforms to compounds namely **cannabidiol (CBD)** and **cannabigerol (CBG)**. Cannabis' activities on the ECS (endocannabinoid system) have an impact on a variety of gastrointestinal processes^{10,11,12}

IV. ENDOCANNABINOID SYSTEM (ECS)

The Endocannabinoid System is a network of cannabinoid receptors, ligands, and enzymes that regulate the synthesis and degradation of cannabinoids. In general, our bodies produce endogenous cannabinoids, which are found in both the peripheral and central nervous systems. The ligands also known as endogenous cannabinoid are anandamide (AEA) and 2-arachydonilglycerol (2-AG). They activate presynaptic cannabinoid receptors known as CB1 and CB2 receptors and are synthesised on demand from membrane phospholipids. Diacylglycerol lipase and N-acylphosphatidylethanolamine specific phospholipase D (NAPE-PLD) are two enzymes that help in biosynthesis of endogenous endocannabinoids. In other hand the enzymes like fatty acid amide hydrolyse (FAAH) degrades AEA and Monoacylglycerol lipase (MAGL) hydrolyses 2-AG endocannabinoid in our body. In addition, cyclooxygenase 2 (COX-2) lipooxygenases and cytochrome P450 enzymes may also have role in the degradation of endocannabinoids and generates prostaglandins. Exogenous cannabis or other phytocannabinoids, as well as synthetic substances, can activate the ECS.^{13,14,15}

Table 1: Position of Different Cannabinoid Receptors and their Binding to Ligands

Sl. No	Cannabinoid receptors	Binding ligands	Position of receptors				
			CNS	Enteric nervous system of Alimentary canal (stomach, liver) pancreas, small and large intestines			Immune cells
1	CB1	AEA and 2AG	++	++	++	++	-
2	CB2	AEA and 2AG	+	+	++	++	++
3	TRPV1(transient receptor V1)	AEA		++	++	++	+

The two receptor mediators via which cannabinoids exert their effects on many organ systems, like the digestive, neurological, and immunological systems, are CB1 and CB2. The myenteric and submucosal plexes have higher concentrations of these two receptors. The phytocannabinoid, the psychoactive component THC is the most powerful whereas Cannabidiol (CBD), cannabigerol (CBG) and cannabichromene are some of the other natural cannabis compounds actively used for research purposes. CBD has proven its ability to act as an anti-inflammatory agent without causing psychotic symptoms.¹⁶ There are several functions of endocannabinoid system in the GI tract. The ECS influences gastrointestinal homeostasis through anti-inflammatory, antinociceptive and antisecretory effects. Some gastrointestinal disorders might therefore be treated with cannabinoids^{16,17}.

1. Mechanism of Action of Endocannabinoids: CB1 receptor activation causes anti-emetic and anti-motility effects by inhibiting adenylyl cyclase, resulting in reduced cAMP production and so preventing presynaptic neuron neurotransmitter release. CB2 receptors cause macrophage phagocytosis along with cytokine release. AEA facilitate the making of tumour necrosis factor (TNF)- α , interleukin (IL)-6, IL-12 and interferon- α through CB2 While functioning on T cells, AEA promotes IL-2 release, TNF generation, and triggered Th1 and Th17 responses via binding with CB2 receptor. It also raises anti-inflammatory cytokine levels¹⁸

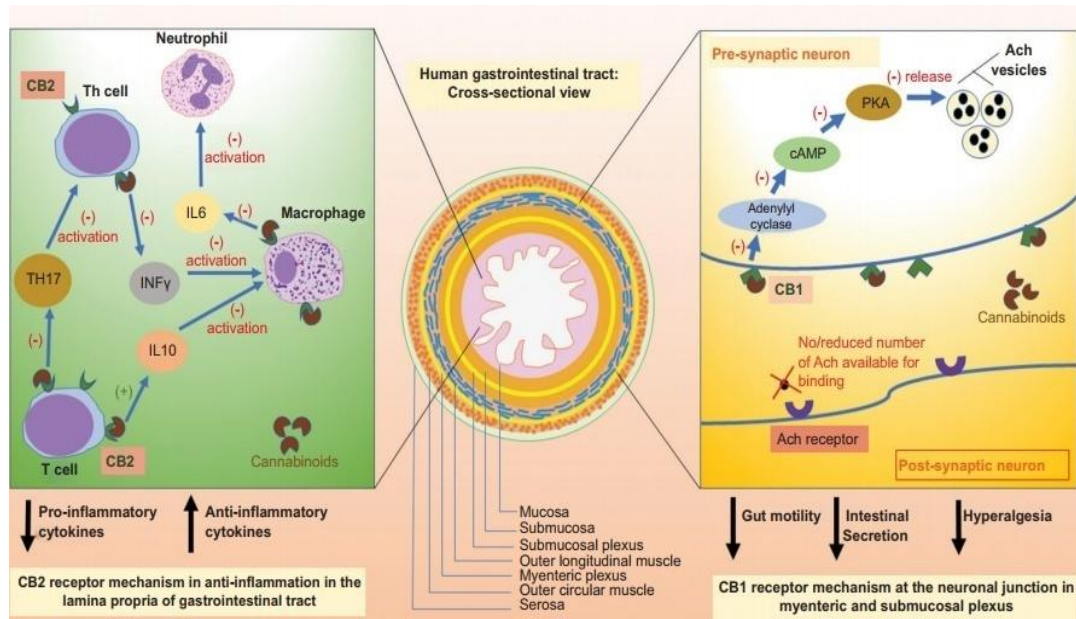


Figure 1: Mechanism of Action of Endocannabinoids.

2. Gastrointestinal Activity of Cannabinoids: Data from the literature indicate that cannabis prevent the release of gastric acid. This effect was mediated by CB1 receptors located on pre- and postganglionic cholinergic neurons.¹⁶ The activation of cannabinoid CB1 receptors by both psychoactive (THC) and non psychoactive (CBD)bring slow down the gastric emptying. Cannabinoids induce hyperphagia and increase appetite resulting in weight gain. Numerous studies have shown that cannabis have immunomodulatory, mostly immunosuppressive effects. Cannabinoids effectively reduce intestinal inflammation and several accompanying symptoms.¹⁷

V. CANNABIS IN THE AYURVEDIC MEDICINE

In India, the use of cannabis and cannabis leaves in medicines has caught public imagination. Contrary to popular perception, the use and consumption of cannabis and cannabis leaves is not entirely prohibited in India. It is permitted for medical and scientific purposes, subject to compliance with applicable laws. As per Ayurvedic practioners it pacifies Kapha and Vatadosaand, increases Pitta Dosa. It posses Dipana, Pachana, Ruchya, Madakiri action. Cannabis leaves are recommended as an antiphlegmatic, as a therapeutic for catarrh followed by diarrhoea, and as a cure for biliary fever in the *Susruta Samhita*, a well-known treatise on Hindu medicine. A full account of the cannabis plant and its medical virtues was given in *Rajanirghanta*, edited by Narahari Pandita. The drug has been described as astringent and relaxing, as well as having the ability to dissolve phlegm, relieve flatulence, reduce costiveness, sharpen memory, and stimulate hunger. The substance is listed as a general stimulant in the *SarangadharaSamhita*. It corrects derangements of humours and generates a healthy appetite, sharpens the wit, and acts as an aphrodisiac. Because of its strong narcotic qualities, ancient Indian and Chinese surgeons most likely employed it as an anaesthetic, often in combination with alcohol. The Hakims and Vaidyas acknowledge that cannabis has an aphrodisiac effect, and a number of formulations are mentioned in the texts of both systems for this reason.¹⁹.

The Gastrointestinal (GI) system, commonly known as the digestive system, consists of the organs of the human digestive tract from the mouth to the anal orifice, as well as the liver, pancreas, and gallbladder. Any disease in the GI system that affects the functioning of this system is called gastrointestinal disease. Ayurveda says the causes of gastric problem are due to inappropriate eating habits, poor physical work, overeating, wrong sitting postures, seasonal food intake, Intake of incompatible food, accompanied with certain poor lifestyle choices.²⁰ Traditional Systems have a long history of using herbs to treat sickness, thus their success rate in developing as a therapeutic strategy is significantly higher than that of the synthetic counterpart. Single or multiple herbs (polyherbal) are utilised for treatment in Ayurveda. Different literature emphasised the idea of polyherbalism as a means of enhancing therapeutic efficacy. Individual plants' active phytochemical components are insufficient to produce the desired therapeutic effects.^{21,22} The medicinal effects and toxicity are improved when different herbs are combined in a specific ratio. There are so many ayurvedic classical formulations are present in Ayurvedic text books such as Charak samhita, sushrutasamhita, Vaisjaratanbali etc. for different types of diseases²³. Here an attempt was made to search and compile the data of different types of classical formulation available for various gastrointestinal disorders with special reference to formulations containing cannabis.

Table 2: Classical Ayurvedic Formulations in Treatment of Different GI Disorders

Sl. No	Common Gastrointestinal Disorders	Some Popular Plants used in single or combined in Ayurveda for different GI disorder	Some popular Classical Formulations For different GI disorders		Ref.
			Single formulations	Compound formulation (Poly herbals)	
1	Constipation (Vibandha)	<i>Plantago Ovata</i> (Isabgol Husk) <i>Cassia aungustifolia</i> (Senna) <i>Terminalia chebula</i> (Haritaki) <i>Cassia angustifolia</i> (Indian Senna)	Trvrtchurna Eranda Taila	AvipattiChurnam Panchasakarchurna Trifalachurna Abhayarishta Kumarasva Chitrakadivati Vaiswanarachurna	24, 25, 26
2	Hyper acidity/Heartburn/GERD (Amlapita)	<i>Glycerhiza glabra</i> (Yastimadhu) <i>Phyllanthus embelica</i> (Amla) <i>Aspargusracemose</i> (Shtavari) <i>Zingiber officinale</i> (Sunthi)	Amlakiswarasa	Kamdudha Rasa PrawalPishti Shankh Bhasma Dhatri Lauha HingwastakChurna Triphalachurna Kshudha Vati Avipatrikachurna	24, 27, 28

3	Indigestion and Dyspepsia (Ajirna, Agnimandya)	<i>Myristica fragrans</i> (jatiphala) <i>Foeniculumvulgare</i> (swamp) <i>Phyllanthus emblica</i> (Amlaki) <i>Plumbago zeylanica</i> (Chitraka) <i>Terminalia chebula</i> (Pathya) <i>Piper longum</i> (Pippali) Rock salt (Saindhava lavana)		Agnitundi Vati Shivakshar Churan Avipattikar Churan Agnimukha Rasa II Kalashaka processed Lavanaabhaskarachurna Vijaya Rasa (RJ) Mahashankh Vati Bilwadi churn Hingsticchurna	24,29, 30,31
4	Diarrhoea(Atisara)	<i>Emblicoefficialis</i> (Amlaki) <i>Piper longum</i> (Pipali) <i>Aegle marmelos</i> (Bilba) <i>Woodfordiafruticosa</i> (Dhtaki) <i>Cannabis sativa</i> (Bhanga) <i>Myristica fragrans</i> (jatiphala) <i>Terminalia chebula</i> (Haritaki) <i>Santalum album</i> (Chandana) <i>Ageratum conyzoides</i> (Visadodi)	Nagakesharachurna Kutajaavaleha Kutajatwaka	JatiphaladiChurna Bilwdichurna JayakhandaChurna Aamkutha Rasa Dakshayani Rasa Bruhatdadimastakchurna. Laghu Gangadhar churna Kutajarista Karpura rasa	24,32,33,34
5	Irritable bowel syndrome (IBS) (Grahani/ Sangrahani)	<i>Aloe vera</i> (Ghirta kumara) <i>Mentha piperita</i> (Mint) <i>Plantago Ovata</i> (Isabgol Husk) <i>Cynara scolymus</i> <i>Cannabis sativa</i> (Bhanga) <i>Curcuma longa</i> (Haladi) <i>Zingiber officinale</i> (Sunthi) <i>Foeniculum Vulgare</i> (Fennel seed)	Takra(Butter Milk)	Bilvadileha Kutajarista Grahanigajakesari Rasa JatiphaladiChurna GangadharChurn(Bruhat) BilwadiChurna Lai Churna Kanaksundara Rasa CitrakadiGutika	24,21,35

				Jirakadi Modak Mustakarishtha	
6	Jaundice(Kamala)	<i>Swertia chirata</i> (Chireeta) <i>Boerhaaviadiffusa</i> (punnanava) <i>Phyllanthus niruri</i> (Bhumi amalaki)	Guduchi Kalka Trvrt	Lokanth rasa, SidhhaMakaradwja, Sarbeswar rasa Punarnavadikashayam Pratapa ravana Rasa Kumaryasava Triphalaswaras	36,24
7	Duodenal ulcer	<i>Aloe vera</i> (Ghritkumari) <i>Azadarchitaindica</i> (Neem) <i>Curcuma longa</i> (Haldi) <i>Terminalia Chebula</i> (Harida)	Sáambhuka Bhasma	Sutakeshara Rasa NarikelaKsara ShtavariMandura Narikela khanda Triphalaswaras	24
8	Dysentery(pravahika)	<i>Holarrhena antidysenterica</i> (Indrayava) <i>Aconitum heterophyllum</i> (Ativisha)	Musta kwatha Bilwadi churna Jatiphaladi churna	Bruhat Gangadhar churna Kutajaavaleha Kutajaarista Lokanatha Rasa BilwadiChurna	24,37

9	Inflammatory Bowel Disease (IBD) Ulcerative colitis (PittajGrahani) Crohn's Disease	<i>Boswellia serrate</i> (Shalaki) <i>Curcuruma longa</i> (Turmeric) <i>Tinospora cordifolia</i> (Guduchi) <i>Cyperus rotundus</i> (Mutha) Aegle marmelos(Bilba) <i>Pterocarpus santalinus</i> (Rakta chandana)		NagaradayaChurna BhunimbasyaChurna Kirtadayachurna Chandandayaghurta	38,24
10	Gastrointestinal cancer	<i>Allium sativum</i> (Lahsun) <i>Andrograpispaniculata</i> (BhiunNimba) <i>Cannabis sativa</i> (Bhanga) <i>Camelia sinensis</i> (Green tea) <i>Emblicaofficinalis</i> (Amlaki) <i>Ocimumsanctum</i> (Tulasi) <i>Curcuma longa</i> (Haladi) <i>Zingiber officinale</i> (Sunthi)	Shuddha Gandhaka Suvarna Bhasma	Tribhuvankirti Shwaskuthar Ras Kantakari powder Sitopaladichurna NavjeevanRasayan	39,40
11	Nausea and Vomiting (Chardi)	<i>Zingiber officinale</i> (Sunthi) <i>SyzygiumCumini</i> (jamun) Terminal chebula (Haritaki) <i>Citrus aurantium</i> (Mosumbi)	Mayurapaksa Bhasma	Khandkushmandavaleha KalyanakaGrita JivaneeyaGhrita Eladi churna Dadimastakachurna Vidangadichurna Dasmularista Guducyadikwatha	24

12	Helminthasis worm infestation (Kirmi)	<i>Adhatoda vasica</i> <i>Acrous calamus</i> <i>Allium sativum</i> <i>Curcuma longa</i> <i>.Artemesia pallens</i> <i>Martynia annua</i> <i>Pentanema indicum</i>	KrimikutharaRasa	Vidangadichurna Krimikutharras Krimighnardasheman	24,41,42,43
13	Haemorrhoids(Arsa)		HaritakiChurna Tamrabhasma Abhrakabhasma Kasisa bhasma Lohabhasma Trunakanta Yashada bhasma	ArsoghnaIepa Brhat surana Modak Kanakyan Modak Abhyaristra Arsakuthra Rasa KankayanaGutika	44,45

Cannabis in Various Gastro Intestinal Disorders: During various literature surveys it was found that there are a good number of formulations containing cannabis used for various gastro intestinal disorders. Cannabis-infused formulations have shown to be effective in the treatment of clinical gastro intestinal disorders like Agnimandya (digestive impairment), Ajeerna (indigestion), Grahani (malabsorption syndrome), Sangrahani (irritable bowel syndrome), Atisara (diarrhoea), Krimi (worm infestations) etc. Cannabis is used in more than 150 formulas recorded in the existing Rasa and Chikitsagrantha books. Levigation with Cannabis may be used to stimulate the endocannabinoid system's receptor-mediated endocannabinoid system in order to get the wide-ranging benefits of Cannabis. There are, however, some classical cannabis formulations that have been recommended by Ayurvedic physicians and Vaidyas for the treatment of gastrointestinal disorders.

Table 2: Classical Ayurvedic Formulations Containing Cannabis used for Different GI Disorders

Sl. no	Classical/Ayurvedic Formulations containing Cannabis	Types of dosage forms	Indications
1	Aamkutha Rasa	Rasa	Diarrhoea, (Atisara) Malabsorption syndrome /IBS(Grahani)
2	Abhra vatika	vatika	Diarrhoea with Fever (Jwaratisara), IBS
3	Agastisutraja rasa	Rasa	IBS(Irritable bowel syndrome)
4	Agnimukha Rasa II	Rasa	Digestive impairment (Agnimandya, IBS, pain(Shoola)
5	Ajeernari Rasa	Rasa	Indigestion(Ajeerna)
6	Atisaradalano Rasa II	Rasa	Diarrhoea,
7	Dakshayani Rasa	Rasa	Diarrhoea
8	Dugdahavati	Vati	IBS
9	Kutajaleha	Leha	Diarrhoea
10	Grahani-gajendra Rasa	Rasa	Diarrhoea with Fever
11	HansapottaliRasa	Rasa	Malabsorption syndrome
12	BilwadiChurna	churna	Diarrhoea and Dysentery
13	Lai churnaChurna	churna	Malabsorption syndrome
14	Kanakaprabha Gutika	pill	Malabsorption syndrome
15	Jatiphladichurna	churna	Chronic Dysentery &Chronic Colitis with Bloody Diarrhoea
16	Kshudha Vati	vati	(Hyperacidity) Amlapitta
17	Trailokya tilako Rasa	Rasa	Haemorrhoid (Arsha)

The most formulations are discovered to be recommended in malnutrition syndrome and irritable bowel syndrome, followed by diarrhoea and indigestion. Cannabis satisfies the criteria for a good and effective medication, as prescribed in Ayurvedic scriptures.^{46,47}

VI. CONCLUSION

The cannabis plant has been used as a medicine for thousands of years to treat various illnesses. It contains hundreds of different chemical compounds that operate on the endocannabinoid system in the human body to elicit pleasurable emotions, feelings of comfort, and health improvements in individuals suffering from various conditions. THC and cannabidiol (CBD) are the most well-known and researched phytocannabinoids, with impressive therapeutic properties for a variety of neurological, gastrointestinal, ophthalmic, and skin problems. Cannabis has psychotropic and additive effects. As a result, it has been considered as a narcotic, and its use without legal licence is prohibited. The manufacture and selling of cannabis resin and flowers, unlike its leaves and seeds, is prohibited under the NDPS Act of 1985. Marijuana's medical usage is much debated in modern medicine due to its recreational use. Cannabis is used for treating numerous disorders in 'traditional' or 'alternative' medicine, such as Persian, Siddha, Ayurvedic, and Unani medicine, in addition to modern therapeutic uses. It is one of the most popular medicinal herbs in India, as documented in numerous Ayurvedic literatures. Nearly about 157 Indian classical formulations were found where Bhang is used as a processing agent in pharmaceuticals. Cannabis and cannabinoids are beneficial in healing the signs and symptoms of several gastrointestinal diseases, according to research, in part because they interact with the digestive tract's endogenous cannabinoid receptors. This could help in relaxing pain and cramps, reducing discomfort, and improving motility. From this literature review it was found that there are ampoules of classical formulations containing cannabis that have been recommended for the treatment of GI issues. These formulations can be used to treat various gastrointestinal issues. However, standardization and quality control still remain grey areas for these available marketed formulations.⁴⁸ For certain people, the therapeutic CBD is desirable for medicinal purposes, but the psychoactive THC may be needless and undesired. The THC/CBD ratio is key information for medical professionals treating cannabis for medicinal purposes. Therefore, a complete standardization is often required to know the purity, quality, and safety of these available marketed formulations.

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