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Cannabis sativa: A therapeutic medicinal plant-global marketing updates

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Abstract

Cannabis has been used for thousands of years for recreational, medicinal, or religious purposes and the therapeutic potential of medicinal Cannabis was demonstrated in various medical conditions. The legalization of Cannabis is an important source of economic growth as it contributes to the growing revenue tax, and the creation of new workplaces. The maturity of the Cannabis market varies across the globe mainly due to differing legal environments and public attitudes towards Cannabis. Some countries such as Canada and the United States have adopted fully regulated frameworks that allow the cultivation, consumption, and retail distribution of various Cannabis products. Uruguay became the first country in the world to legalize the production, distribution and consumption of cannabis in 2013. The Cannabis market in Canada and the USA is experiencing rapid growth due to the country's legalization of recreational use. Regulations can also differ regarding how cannabis is used. However, the use, cultivation, and marketing of Medical Cannabis sativa (drug or Marijuana type) is banned and prohibited in India due to the presence of high levels of psychoactive principle THC (Narcotic drug). On the other hand, Industrial Cannabis sativa (seed or fiber type) Hemp was legalized in 2021 by The Food Safety and Standards Authority of India (FSSAI), Government of India, New Delhi. In Azerbaijan, Cannabis is not available for medical or recreational use. Recreational Cannabis and medical marijuana are illegal in Azerbaijan. Marijuana is illegal for medical and recreational purposes in China. There is still a huge prejudice in society about medical Cannabis due to its recreational use. However, this scenario is changing, and the social resistance is decreasing for the medicinal use of Cannabis. The Cannabis (Hemp) market in India is predicted to experience a substantial revenue growth, with projections indicating that it will reach ₹US\$100.80m by 2024. The Cannabis market worldwide is projected to reach a revenue of US\$60.79bn in 2024. The global legal marijuana market size is expected to reach USD 73.6 billion by 2027 and is anticipated to expand at a CAGR of 18.1% during the forecast period.

Keywords: Azerbaijan; *Cannabis sativa*; Cannabidiol (CBD); Colombia; Global market; Hemp; India; A9 tetrahydrocannabinol (THC)

1. Introduction

In recent years, the medical application of medicinal Cannabis inflorescence gained widespread use, due to the beneficial pharmacological properties of its constituents [1-45]. The therapeutic potential of medicinal Cannabis was demonstrated in various medical conditions such as sleep disorders, nausea, anorexia, emesis, pain, inflammation,

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neurodegenerative diseases, epilepsy, and cancer [1-40]. Both Medical Cannabis (Marijuana or drug type) and Industrial Cannabis sativa hemp is used for controlling numerous diseases, such as cervical cancer, chronic pain, asthma, rheumatoid arthritis (RA), wound healing, constipation, multiple sclerosis (MS), cancer, inflammation, glaucoma, neurodegenerative disorders (Epilepsy-seizure disorder, Alzheimer's disease, Parkinson's disease), dengue viral disease, Huntington's disease, Tourette's syndrome, dystonia, Lennox-Gastaut Syndrome (LGS), Dravet Syndrome (DS), obesity, weight loss, anorexia, and emesis, osteoporosis, schizophrenia, cardiovascular disorders, sleep disorders, Traumatic brain injury (TBI), Post traumatic stress injury, drug addiction (Marijuana), AIDS Wasting syndrome, Amyotrophic lateral sclerosis (ALS), depression and anxiety, diabetes, migraine (headache disorder), Covid-19 (SARS-CoV-2), Leishmaniasis (Kala-Azar), and metabolic syndrome related disorders, to name just a few, are being treated or have the potential to be treated by Cannabinoid agonists/ antagonists/cannabinoid-related compounds [1-50]. According to recent studies, cannabis inflorescences are rich in secondary metabolites, comprised mainly of two major groups, namely cannabinoids and terpenes [1-50]. Cannabis-based products are widely used for various medicinal conditions. Currently, the most common method to identify and quantify cannabinoids are liquid chromatographic methods coupled to UV-VIS or mass spectrometric detectors [1-40].

Industrial hemp and marijuana share the same species, Cannabis sativa L, but represent different varieties [1-40] (Figure-1). As such, there are genetic differences that lead to different chemical characteristics, which, in turn, lead to different uses. Cannabis sativa L., is classified into two types as Industrial Cannabis sativa, hemp or Medical Cannabis sativa L. (drug or marijuana) based on its Δ^9 -tetrahydrocannabinol (THC) content [1-40] (Figure-1). Medical Cannabis sativa (drug or marijuana) contains very high levels of Δ^9 -tetrahydrocannabinol (THC) (above 0.3 to 38% of dry weight) and is grown inside the greenhouse- controlled conditions for the production of unfertilized female flowers [1-40] (Figure-1). These female flowers accumulate the psychoactive molecule THC and used for health disorders [1-50]. On the other hand Industrial Cannabis sativa L. (Hemp) contains very low levels of THC (0 to 0.3% of dry weight) grown outside in a large agriculture farms for the production of fibre, seeds and oil [1-45] (Figure-1). Hemp is used as a functional food and medicine since it contains Cannabidiol (CBD), and very low levels of THC [1-50] (Figure-1). In the following section, fluorescent-based detection, the present legal status of Cannabis in India and the global Cannabis marketing economy has been discussed.

2. Cannabinoids are Fluorescent Compounds

According to the study reported by Birenboim et al. (2022) [1], Cannabinoids are fluorescent compounds, fluorescent-based detection methods are gaining increasing interest [1-40]. The cannabinoids displayed a characteristic fluorescence excitation (225–400 nm)-emission (300–525 nm) signal [1-50]. Neutral and acid cannabinoids could be distinguished based on their characteristic excitation-emission spectrum, namely neutral cannabinoids exhibited maximal intensities at 280 nm excitation and 300 nm emission, while acidic cannabinoids displayed maximal intensity at 300 nm excitation and 400 nm emission [1-35]. Moreover, cannabinoids with overlapping UV spectrum (such as Δ^9 -trans-tetrahydrocannabinolic acid, Cannabidiolic acid and Cannabigerolic acid) were found to have overlapping fluorescence excitation-emission spectrum, due to the same number of conjugated double bonds and the presence or absence of a carboxylic group [1-40]. The UV spectra of the neutral cannabinoids (-)- Δ^9 -trans-tetrahydrocannabinol (THC), Cannabidiol (CBD) and Cannabigerol (CBG) and their corresponding acidic forms, namely (-)- Δ^9 -trans-tetrahydrocannabinolic acid (THCA), Cannabidiolic acid (CBDA) and Cannabigerolic acid (CBGA), have been reported to distinctively differ from each other [1-30]. Although Cannabinoids are fluorescent molecules, the application of fluorescent-based detectors for their identification and quantification is surprisingly scarce, especially in light of the fact that fluorescence is far more sensitive than UV and the emission and excitation spectrum might convey substantially more information about the underlying compounds of the sample [1-30]. Both acidic and neutral Cannabinoids displayed unique excitation-emission fluorescent spectra in the range of 225–400 nm for excitation and 300–525 nm for emission [1-30]. The spectral information provided in the present study by Birenboim et al. (2022) [1] could be of great value for fluorescence-based analytical method development [1-30]. Moreover, the spectral data reported by Birenboim et al. (2022) [1] could assist in developing a tool for initial screening of extracted samples for the presence of minor Cannabinoids, which are currently not commercially available as pure standards [1-30].

3. Use of Cannabis as Reintroduced Medicine

Cannabis was (re) introduced into British medical practice in the early 1840's by Irish physician Dr. William O'Shaughnessy, an army surgeon serving in Calcutta, India [1-2- 45]. In the Victorian period, Cannabis was widely used for a variety of ailments, including muscle spasms, menstrual cramps, rheumatism, the convulsions of tetanus, rabies, and epilepsy, and as a sedative [2-50]. Cannabis extracts were typically administered orally in the form of an alcoholic tincture and were commonly incorporated in proprietary medicines [2-50]. With the introduction of synthetic drugs,

herbal remedies were increasingly viewed as unpredictable and many of them, including cannabis extracts and tinctures, were removed from the British Pharmacopoeia of 1932 but retained in the British Pharmaceutical Codex of 1949 [2-50]. Under the Dangerous Drugs Act 1964, which implemented the 1961 UN Single Convention on Narcotic Drugs in the United Kingdom, the prescription of Cannabis tinctures continued to be permitted due to a “License of right” received under the Medicines Act 1968 [2-50]. In November, 2018, the UK’s Home Office (re) established a legal route for the prescription of Cannabis-based products for medicinal use in humans (CBPMs) through the amendment of both the Misuse of Drugs Regulations 2001 and Misuse of Drugs Order 2015, rescheduling CBPMs as Schedule 2 drugs [2-50]. CBPMs remain strictly regulated and include both Cannabis extracts for oral administration (“oils”) and dried Cannabis flowers for inhalation (“flos”) [2-50]. These products may only be prescribed by a specialist medical practitioner as “special” or “bespoke” medications following processes common to all unlicensed medications [2-50]. Additionally, the development of vaporizers and inhalers for flos, some of which have attained certification as medical devices, affords patients greater control over administration and dosing of the pharmacologically active molecules present in Cannabis, namely Cannabinoids Δ^9 -tetrahydrocannabinol (THC) and Cannabidiol (CBD), limiting the occurrence of side effects related to the central nervous system and the inhalation of toxic by-products of combustion [2-50]. Oral THC has been clinically approved for the treatment of several health conditions, such as chemotherapy-induced nausea and vomiting, wasting syndrome associated with AIDS and cancer, and spasticity in patients with multiple sclerosis, and its ability to treat other neurological conditions is under investigation [2-50]. A large body of scientific literature indicates that inhalation of chemotype I (THC-predominant) Cannabis flos can mitigate symptoms associated with chronic pain, increase relaxation, and facilitate resilience to cope with disability [2-50].

In November, 2018, the UK’s Home Office established a legal route for eligible patients to be prescribed Cannabis-based products for medicinal use in humans (CBPMs) as unlicensed medicines [2-50]. These include liquid Cannabis extracts for oral administration (“oils”) and dried flowers for inhalation (“flos”) [2-50]. Smoking of Cannabis-based products for medicinal use in humans (CBPMs) is expressly prohibited [2-50]. The experimental results of Moreno-Sanz et al., (2022) [2] concluded that controlled inhalation of pharmaceutical grade, THC-predominant Cannabis flos was associated with a robust improvement in patient-reported pain scores, general mood, anxiety, sleep, and overall HRQoL in a treatment-resistant clinical population [2-50]. The effect size, which was larger in patients diagnosed with anxiety disorders compared to chronic pain, appeared to be maximal at 3 months and sustained for at least 6 months [2-50]. Occurrence of side effects was minimal, probably due to the previous experience of participants with cannabis inhalation [2]. This evidence supports the notion that the administration of Cannabis flos in a medicalized environment under the supervision of a trained healthcare provider further improves the clinical outcomes of legally prescribed Cannabis-based products for medicinal use in humans (CBPMs) when compared to chronic patients self-medicating with illegal Cannabis [2-40].

4. *Cannabis sativa*: Current Legal status in India

Cannabis sativa L. belongs to the family Cannabaceae was used as a medicine before the Christian era in Asia, mainly in India, China, Bhutan, Nepal, Afghanistan, Pakistan, Azerbaijan, Iran, and Persians [3-50]. Cannabis has been used for thousands of years for recreational, medicinal, or religious purposes [3-53]. Cannabis is also a wild noxious weed with notorious psychoactive principle (THC) found growing in all the parts of India. Cannabis has a long history in India, recorded in legends and religion [3-50]. It was found in various habitats ranging from sea level to the temperate and alpine foothills of the Indian Himalaya Region from where it was probably spread over the last 10,000 years [3-50]. Many historians believed that Indian Himalayan Region was the centre of origin of *Cannabis sativa* L. and *Cannabis indica* L [3-50].

Cannabis is one of the oldest crops grown, traditionally held religious attachments in various cultures for its medicinal use much before its introduction to Western medicine [3-50]. In India, the sacred scripture “Atharva Veda” claimed Cannabis as an herb of happiness, as it elicited joy and pleasure, and hence used in ritualistic activities [3-50]. The Ayurvedic system of medicine also described the use of Cannabis for treating various gastrointestinal, respiratory, and urinary disorders [3-50]. The religious amalgam of cannabis was noticed in Tibetan practices and Buddhism together with Hinduism [3-50]. **Tantric** traditions also showed the unorthodox use of Cannabis for different ceremonial proceedings, upholding the history of Cannabis in India [3-50]. The increasing decriminalization of Cannabis internationally has increased awareness within the Indian Government [3-50]. Presently, Cannabis use in India is regulated in coherence with the Narcotic Drugs and Psychotropic Substances Act (NDPS), 1985, which prohibits the cultivation, possession, manufacturing, and sale of cannabis as Charas (resin), Hashish (liquid form), and Ganja (flowering or fruiting tops) excluding leaves or seed (Bhang) from the purview of the act [3-28-50]. However, provisions for cultivation exist but are strictly restricted for research purposes, excluding medical purposes owing to its limited proven use [3-28-50].

Therefore, the use, the cultivation and marketing of Medical Cannabis sativa (drug or Marijuana type) is banned and prohibited in India due to the presence of high levels of psychoactive principle (Narcotic drug) [3-28-50]. The concept of a Medical Cannabis sativa (drug or Marijuana type) program was already in progress when in 2016, BOHECO (Bombay Hemp Company) and the Council of Scientific and Industrial Research (CSIR) collaboratively organized ICARE (Indian Cannabis Analysis Research Education) to build awareness [3-28-50]. In the following year, the Government of India approved its first-ever license to Council of Scientific and Industrial Research–Indian Institute of Integrative Medicine (CSIR–IIIM) in collaboration with BOHECO to grow and formulate Cannabis-based medicines [3-28-50]. Till today, as of February 2024, India has not approved medicinal cannabis product to date [3-28-50]. However, in 2018, the Central Council for Research in Ayurvedic Sciences (CCRAS) reported the pioneer Cannabis clinical study where it reduced pain in cancer patients post chemotherapy and radiotherapy [3-28-40]. Presently, IIIM Jammu cultivates Cannabis and assesses the medicinal components for cancer, epilepsy, and sickle cell anemia, seeking approval for future clinical trials [3-28-50]. Moreover, recently, India, during the 63rd United Nations (UN) Commission on Narcotic Drugs (CND) session, voted in favor of removing Cannabis and its resin from the UN narcotic drug list [3-28-50]. The leniency in the decision from India in favor of cannabis legalization during the UN session indicated a future medicinal cannabis program in India [3-28-50].

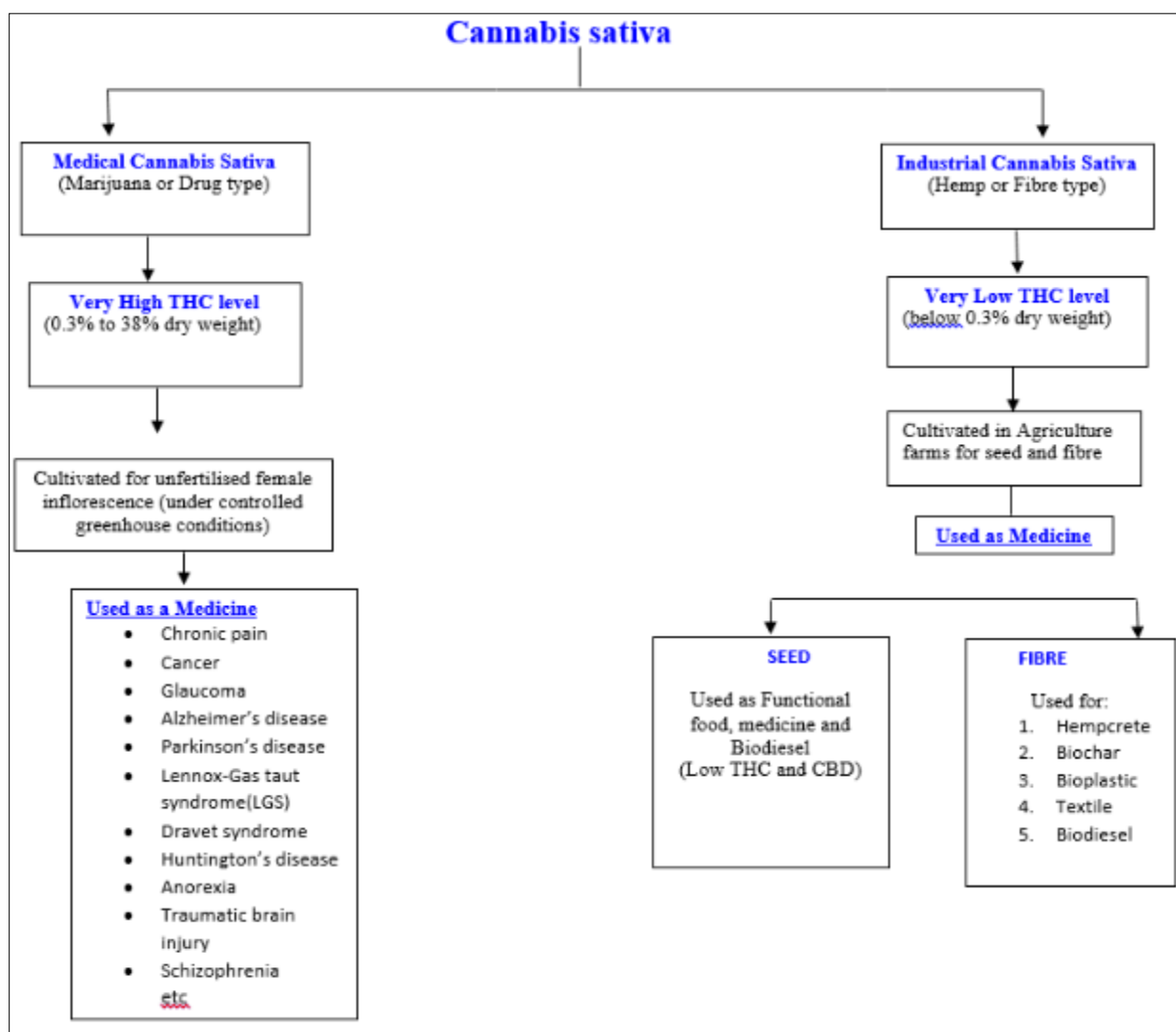


Figure 1 The difference between Industrial *Cannabis sativa*, hemp or Medical *Cannabis sativa* L.(drug or marijuana) based on its Δ^9 -tetrahydrocannabinol (THC) content

Cannabis sativa L., is classified into two types such as Industrial *Cannabis sativa*, hemp or Medical *Cannabis sativa* L. (drug or marijuana) based on its Δ^9 -tetrahydrocannabinol (THC) content [3-28-50](Figure-1). Industrial *Cannabis sativa* (hemp or fiber type) refers to non-intoxicating, low (Below 0.3% dry wt) of Δ^9 -tetrahydrocannabinol (Δ^9 -THC) cultivars of *Cannabis sativa* [3-28-40]. On the other hand Medical *Cannabis sativa* (drug or marijuana type) refers to

cultivars with high levels (above 0.3 to 38 % dry wt of Δ^9 -THC), the primary narcotic psychoactive Cannabinoid found in the plant and a federally controlled substance used for both recreational and therapeutic purposes [3-28-40]. Although marijuana and hemp belong to the same genus and species, they differ in terms of chemical and genetic composition, production practices, product uses, and regulatory status [3-28-40].

On the other hand, Industrial Cannabis sativa (seed or fibre type) was legalized on 15th November 2021 by FSSAI, Government of India [3-28-40]. The Food Safety and Standards Authority of India (FSSAI), Government of India recognized hemp seed and hemp seed products as functional food and license have been issued to the parties who are interested in growing hemp [3-28-50]. The notification regulates and allows for the sale of products derived from 'non-viable seeds of the Cannabis sativa/other indigenous cannabis species'. Further, the cultivation has to, as usual, comply with the Narcotic Drugs and Psychotropic Substance Act (NDPS), and state laws [3-28-40]. The Narcotic Drugs and Psychotropic Substance Act (NDPS), Act 1985 has been enacted by the government of India to combat the illicit trafficking of narcotic drugs, psychotropic substances, controlled chemicals as specified by the Government. It provides for prosecution of offenders, deterrent punishment and forfeiture of illicit property acquired from drug trafficking. There is a ray of hope that in the near future, hemp-based healthcare products will be in the market, and customer demand for hemp products is increasing [3-28-50]. There is also a need to perform more biological evaluation toward establishing therapeutic guidelines for Cannabis and Cannabinoids and to provide a strengthened pharmacological perspective about the prospects and challenges of Cannabis use in the future [3-28-50].

5. Global Cannabis Market Economy

The cultivation and use of cannabis is historically rooted in the Indian subcontinent and this rich heritage of cannabis use dates back to at least ten thousand years [3-28-40]. Cannabis remains an illicit substance in India despite its changing status globally with many countries legalizing cannabis use in recent years [2-28-50]. Despite the legal prohibitions, Cannabis remains the highest consumed and trafficked and frequently seized illicit substance in India [1-28-40]. The legalization of Cannabis is an important source of economic growth as it contributes to the growing revenue tax, increasing demands on the construction industry and to the creation of new workplaces [1-28-50]. In addition to economic benefits, legalization of Cannabis leads to more transparent tracking of its supply chain and therefore, reduces the counterfeiting activities and overall criminal rates [3-28-50]. The majority of consumers will shift from illicit markets to legal ones and potential users will be more eager to use Cannabis as it will not be subject to penalties [3-28-60]. Apart from benefits, there are however, potential negative consequences of the growing Cannabis market mainly for the environment [3-28-50]. In this regard, the governments have to take a lead in shaping the more sustainable production infrastructure [3-28-50].

The consumption of Cannabis derivatives, particularly bhang, has valuable religious and cultural connotations among Indians and thus remains widely accepted in Indian communities [3-28-40]. In line with the global trend toward decriminalizing Cannabis use, the support for legalizing Cannabis in India for medical and recreational purposes has been gradually growing [3-28-40]. The legislation for its medicinal and commercial use was also proposed in the Indian Parliament in 2016 [3-28-40]. Two Indian states of Uttarakhand and Madhya Pradesh permitted the cultivation of Cannabis for medicinal and industrial purposes in 2019 [3-28-40]. There have been efforts toward medicalizing cannabis, and the Central Government of India recently commissioned a council under the Ministry of Ayurveda, Yoga, Naturopathy, Unani, Sidha, and Homeopathy (AYUSH) to conduct scientific research on the efficacy of Cannabis for various medical conditions [3-28-40]. With increasing Cannabis legalization and decriminalization worldwide, India has joined the movement but the research on multiple facets of Cannabis use in India appears inadequate and with gaps in terms of providing key information for molding policies on Cannabis use [3-28-50].

The Cannabis (Hemp) market in India is predicted to experience a substantial growth in revenue, with projections indicating that it will reach ₹US\$100.80m by 2024 [3-28-49]. Furthermore, it is expected to exhibit a steady annual growth rate of 14.80% between 2024 and 2028, resulting in a market volume of ₹US\$175.10m by the end of the latter year [3-28-49]. There are many growing Indian companies (Bombay Hemp Company, Clean Green Biosystems or Clean Green Bio Research Foundation, BOHECO, Satliva, Hemp Fabric Lab, VEDI, Happy Hemp, SUI, Its Hemp, Bhu: Sattva's, Health Horizons, Hemis, Hemp Republic, Hempsters, B.E. Hemp, India Hemp Co., Inc, India Hemp Organics, Its Hemp, The Trost, and Gin Gin) involved in promoting the Indian hemp products, marketing, R & D research, cultivation, harvesting, processing, manufacturing, trading, wholesaling, retailing, innovating, advocating and motivating customers across India and around the world [3-28-49]. This will help to boost the Indian economy and increase the productivity of the Indian hemp (fiber type) [3-28-49]. When compared to other countries on a global scale, in the United States is anticipated to generate the highest revenue in the Cannabis market, with an estimated value of ₹US\$39,850.00m in 2024 [3-28-49]. In terms of per capita revenues, in India is predicted to generate ₹US\$0.07 per person in 2024 [3-28-49]. This

figure provides insight into the individual contribution towards the overall revenue generated in the Cannabis (hemp) market [3-28-49]. India's Cannabis (hemp) market is experiencing a surge in demand as more consumers are embracing the therapeutic and medicinal benefits of the plant [3-28-49]. The Cannabis market worldwide is projected to reach a revenue of US\$60.79bn in 2024 [3-28-49]. It is expected to show an annual growth rate (CAGR 2024-2028) of 14.06%, resulting in a market volume of US\$102.90bn by 2028 [3-28-49]. In terms of per person revenues, it is anticipated that in 2024, each individual worldwide will generate approximately US\$15.55 [3-28-49]. These numbers highlight the immense potential and growth within the Cannabis market [3-28-49].

Today, the cost of health care is constantly rising, and affecting people's ability to afford health coverage [3-28-49]. Drug-based medicines are being unaffordable for economically poor countries like India and problematic in the Western countries due to numerous side effects [3-28-49]. The drug should be the last rather than first mean of treatment, beginning with the natural healing method like Ayurveda [3-28-49]. One of the Ayurvedic treatment modalities such as Panchkarma can remove disease before its manifestation [3-28-49]. Having all the above beauties, Ayurveda is still lagging behind because of the lack of scientific evidence in many cases and poor research methodology [3-28-49]. There is a ray of hope that in near future, hemp based healthcare products will be in the market and customer demand for hemp products is increasing [3-28-49]. It is also a need to perform more biological evaluation towards establishing therapeutic guidelines of Cannabis and Cannabinoids and to provide a strengthened pharmacological perspective about the prospects and challenges of Cannabis use in the future [3-28-49].

The Cannabis market in Canada is experiencing rapid growth due to the country's legalization of recreational use [28-49]. Canada's Cannabis market is expected to experience significant growth in the coming years. According to projections, the revenue in this market is set to reach a staggering US\$4.70bn by 2024 [3-28-49]. Furthermore, a promising annual growth rate of 14.15% (CAGR 2024-2028) is anticipated, which will result in a market volume of US\$7.98bn by 2028 [3-28-49]. When comparing Canada's performance with other countries, it is noteworthy that in the United States is expected to generate the highest revenue in the Cannabis market, reaching an impressive US\$39,850.00m by 2024 [3-28-49]. This showcases the immense potential and profitability of the industry on a global scale [3-28-49]. In terms of per capita revenue, in Canada is projected to generate approximately US\$120.20 per person in 2024 [3-28-49]. This figure highlights the significant economic impact that the Cannabis market can have on the country's overall population [3-28-49]. Canada's legalization of recreational Cannabis has led to a booming market, with a wide range of products and a strong focus on regulatory compliance [3-28-49]. Canada is a leader in the global Cannabis market as it has established a fully legalized market for recreational, medical, and therapeutic use in 2018 [3-28-49]. Canadian economy is benefiting substantially from the legalization of cannabis with increased GDP, tax revenues and thousands of new work places [3-28-49]. As a result of this successful policy, licensed producers from Canada are the worlds' leading Cannabis players (e.g., Aphria, TerrAscend Corp., HEXO Corp, Canopy Growth, Aurora Cannabis, and Tilray) [3-28-49].

The maturity of the Cannabis market varies across the globe mainly due to differing legal environments and public attitudes towards cannabis [3-28-49]. Some countries such as Canada and the United States have adopted fully regulated frameworks that allowed cultivation, consumption, and retail distribution of various Cannabis products [3-28-49]. Regulations can also differ regarding how cannabis is used [3-28-49]. Some countries allowed the consumption of products that contain high tetrahydrocannabinol (THC) strictly for medical use, while there are other countries that also permit the consumption of high THC products for recreational use [3-28-49]. The Cannabis market is still in an emerging phase with considerable potential for growth as it can bring greater benefits to citizens, governments, and companies in the future [3-28-49]. The industry will evolve dramatically in the future with more and more individuals and revenues being involved in it [3-28-49].

Another report from Grandview Research, goes even further saying that the Global legal marijuana market size is expected to reach USD 73.6 billion by 2027 and is anticipated to expand at a CAGR of 18.1% during the forecast period [3-28-49]. It said that the increasing legalization of Cannabis for medical as well as adult-use is expected to promote growth [3-28-49]. Yet another report in Fortune Business insights projected that the Global Cannabis Market Size is predicted to reach \$97.35 Billion By End Of 2026 with A CAGR of 32.92% [3-28-49]. Grandview continued: "Based on product type, the legal marijuana buds segment accounted for the largest market share in terms of revenue and was valued at USD 9.1 billion in 2019 [3-28-49]. Buds are primary plant products and are readily available without any processing, which makes them relatively affordable for low-income patients [3-28-49]. Moreover, the rapid onset of action of smoking buds compared to other types is anticipated to further fuel the segment growth [3-28-49].

The global legal marijuana market size was valued at USD 21.0 billion in 2023 and is projected to grow at a compound annual growth rate (CAGR) of 25.7% from 2024 to 2030 [3-28-49]. Increasing demand for legal marijuana is a major

factor in growth of the market. Recently, many countries have legalized the use of **medical marijuana** for treating various conditions [3-28-49]. For instance, in June 2023, Luxembourg legalized possession and cultivation of Cannabis for recreational use and became second European Union member country to legalize it [3-28-49]. In addition, North America (the U.S. and Canada) has gone a step further and has sanctioned the use of recreational marijuana as well [3-28-49]. More than two-thirds of the U.S. states have legalized marijuana [3-28-49]. The industry is experiencing growth owing to growing awareness regarding various therapeutic benefits of the product, such as reducing eye pressure, appetite enhancement, and pain management [3-28-49].

In **Azerbaijan**, Cannabis is not available for medical or recreational use [50-54]. Recreational Cannabis and medical marijuana are illegal in Azerbaijan [50-53]. Those who violate the rules are subject to serious drug penalties [50-53]. The sale, use, and possession of Cannabis are illegal in Azerbaijan, despite the country's long history of medical marijuana use [50-53]. Those found possessing fewer than 10 grams are considered guilty of personal drug use and are often not prosecuted, instead referred to their families for potential drug addiction treatment [50-53]. Cannabis use is illegal in Azerbaijan, despite a centuries-long relationship with marijuana for medical use [50-53]. Researchers in Azerbaijan have documented evidence of medical marijuana in the country dating back to the Medieval period when healers used it to treat certain tumours, hysteria, and haemorrhoids [50-53]. In fact, the country's third-largest city is named Ganja, meaning "treasure," which is another term used to refer to Cannabis [50-53]. Today, Azerbaijan Cannabis laws restrict marijuana with a blanket ban [50-53]. Azerbaijan has a history as a transit country for illegal narcotics, including cocaine, heroin, and Cannabis [50-53]. Azerbaijan's Cannabis laws make no distinction between different cannabinoids, regardless of their intoxication [50-53]. As such, CBD is against the law, and those found possessing CBD products carry criminal liability in Azerbaijan [50-53]. Both medical and recreational marijuana are forbidden in Azerbaijan [50-53]. It is essential to be informed of local regulations and follow the law because breaking the rules might result in severe drug fines in Azerbaijan [50-53].

Asia is beginning to warm up to the use of Cannabis [3-28-49]. Thailand legalized marijuana cultivation at home in 2022, while South Korea, Japan and Malaysia are paving the way for pharmaceutical applications [3-28-49]. With the weed market estimated to be a \$100 billion industry, opens new tab by 2026, according to research firm Prohibition Partners, regional businesses are preparing for demand from Asian consumers [3-28-49]. South Korea was the first country in East Asia to legalize pharmaceutical Cannabis, and Japan, Malaysia and Taiwan are all considering similar moves [3-28-49]. The global legal marijuana market — including recreational use — was estimated to be worth \$13.8 billion last year and is projected to reach \$66.3 billion by the end of 2025, according to a 2018 report from California-based market research firm Grand View Research [3-28-49]. Today, the main goal is to direct economic policy to eliminate the results of the Covid-19 pandemic in Azerbaijan [66-67]. The importance of determining the economic indicators required to assess economic activity in Azerbaijan is considered appropriate [66-67]. Petroleum and natural gas, which are among the most used energy sources in the world, have a significant impact on financial markets and macroeconomic indicators as they are used as raw materials in many fields [66-67].

Marijuana is illegal for medical and recreational purposes in China [55-57]. Cannabis is not legal for medical use in China [55-57]. Marijuana is considered a narcotic drug the same as heroin or cocaine and possession for any reason is punishable by prison time or even the death penalty depending on the severity of the offense [55-57]. Non-psychoactive Cannabidiol (CBD) is not allowed for use in food and medicines despite it being produced in the country, China and exported to other countries [55-57]. The unauthorized cultivation of Cannabis for personal or medicinal use by Chinese citizens is illegal in China [55-57]. Since the People's Republic of China (PRC) established a government, they have taken a harsh anti-drug stance [55-57]. In 1985, China banned all hemp cultivation despite the ancient history of Cannabis cultivation in the Yunnan province, in the mountainous region bordering Myanmar, Vietnam, and Laos [55-57]. In the past, it was grown to make textiles such as rope and was used in traditional Chinese medicine [55-57]. However, in 2010 China began to allow the region to resume industrial hemp production. Since this ruling, China has become the world's leading producer of hemp fiber [55-57]. Cannabis is illegal in China except for industrial purposes (hemp) and some forms of medicine [55-57]. Historically, Cannabis has been used in China for fiber, seeds, as a traditional medicine, as well as for some ritual purposes within Taoism [55-57].

Cannabis in China is illegal, and generally negative perceptions surround both its medicinal and recreational usage, the country boasts a thriving industrial hemp industry that has seen it emerge as the number one producer of the plant across the globe [55-57]. However, despite its emergence as a significant player in the hemp and CBD industry, China Weed law ensures that its penalties for marijuana use, possession, and distribution are some of the stiffest anywhere in the world today [55-57]. Indeed, a digital campaign targeting Chinese youth was launched by the National Narcotics Control Commission in recent years [55-57]. This was part of a national effort to reduce marijuana use among young people in China [55-57].

China is the world's major Cannabis planting area, accounting for about half of the world's total area [55-57]. According to the statistics of the World Intellectual Property Organization, 306 of the 606 patents involving Cannabis in the world are from Chinese companies and individuals [55-57]. Two of China's 34 regions are leading a boom in cultivating Cannabis to produce Cannabidiol, or CBD, which has become a consumer health and beauty craze in the United States and beyond [55-57]. According to incomplete statistics, at least 190 companies in China include "industrial Cannabis" in their business scope [55-57]. There are more than 50 enterprises with industrial Cannabis planting licenses, but only 5 of them have been given a Yunnan Industrial Cannabis Leaf Processing License [55-57]. In China industrial Cannabis is not yet legal for medical applications and consequently, the market has not yet been developed, resulting in the low comprehensive utilization of industrial cannabis [55-57]. With the deepening of research in the field of Cannabis, the market space for extracts represented by CBD is increasing [55-57]. At the same time, the application of CBD in food, cosmetics, and health products will continue to expand. In the future, the CBD will become the focus of the development of the cannabis industry [55-57].

Despite the illegality of Cannabis in China, the country is actually one of the biggest producers of medicinal Cannabis [55-57]. Positioning itself at the forefront of the industry will likely enable the Chinese to cash in by exporting medicinal products to other countries where medicinal cannabis is both legal and highly sought after [55-57]. While cannabis's medical value has long been detailed in ancient Chinese literature, particularly concerning Cannabis seeds, legal medicinal Cannabis remains a distant and somewhat forlorn hope for Chinese citizens [55-57].

As mentioned earlier, China now has a vast industrial hemp industry and is, at present, by far the world's largest producer of industrial hemp and hemp products [55-57]. Having briefly banned the cultivation of hemp, the country once again began to export hemp (and hemp products) across the globe from 2010 onwards, with an ever-increased demand from North America and Europe [55-57]. This is largely a result of the hugely-increased usage of CBD products over the past decade [55-57]. Today, the country has several hemp plantations, which can be primarily found in the Yunnan and Shandong provinces [55-57]. A report published in 2018 revealed that China produces more than half the world's hemp supply [55-57]. Chinese hemp-fiber sales were estimated to be at a staggering \$1.2 billion in 2018 [55-57]. The same report also found that today China accounts for 11% of the now multi-billion dollar global CBD market that exists in both Europe and the United States [55-57].

Colombia, nicknamed the gateway to South America, is the fifth largest country in Latin America and is located at the tip of South America [58-61]. It is home to the second largest population of Spanish speakers in the entire world [58-61]. Colombia is one of the world's most biodiversity countries. It is home to a vast array of plant and animal species, with the highest number of bird species in the world [58-61]. The country has a rich musical heritage, and salsa music holds a special place in the country's culture [58-61]. Cannabis is legal for medical and scientific purposes in Colombia [58-61]. In 2017, Colombia legalized the cultivation, production, sale, and export of medical Cannabis products [58-61]. The country has established a comprehensive regulatory framework for the cultivation, processing, and distribution of medical cannabis [58-61]. Colombia is known for its favorable climate and ideal growing conditions, which has attracted significant investment in the Cannabis industry [58-61].

Cannabis in Colombia is fully legalized for medicinal purposes (since 2017) and for industrial purposes (since 2021) [58-61]. Cannabis for recreational purposes is partially legal: self-cultivation, possession and consumption have been legal (since 1994), but commercialization is illegal [58-61]. Colombia's Cannabis market is expected to reach a projected revenue of US\$140.10m in 2024 [58-61]. The market is projected to experience an annual growth rate (CAGR 2024-2028) of 16.09%, leading to a market volume of US\$254.50m by 2028 [58-61]. Colombia exported \$8.4 million worth of Cannabis, up 96% compared to the same period one year earlier, according to Pro-Colombia, a government agency in charge of promoting non traditional Colombian trade [58-61]. In 2022, over 90% of Colombia's Cannabis exports originated from the departments of Bogotá, Cundinamarca and Antioquia [58-61]. Recreational marijuana is illegal in Colombia, but medical marijuana has been legal since 2017 [58-61]. While Cannabis is not strictly legal for personal use in Colombia, possession of a limited quantity of all drugs, including Cannabis, has been decriminalized since 1994, meaning the government treats drug use and abuse as a public health issue, not a criminal one [58-61]. Decriminalization marked a stark shift in drug policy for the nation, which has taken steps to change its approach to drugs [58-61]. The ruling to decriminalize Cannabis allows citizens to possess up to 20 grams of Cannabis or grow 20 plants [58-61]. However, the sale or purchase of Cannabis is still illegal in Colombia [58-61]. In Colombia, personal consumption and possession of Cannabis have been decriminalized [58-61]. Individuals are allowed to possess up to 20 grams of Cannabis, cultivate up to 20 plants for personal use, and consume Cannabis in public settings [58-61]. It is worth noting that Colombia established a medical Cannabis program in 2015, which operates separately from the decriminalization of personal use and possession [58-61].

Hemp cultivation and production are legal in Colombia [58-61]. In 2017, Colombia implemented regulations to allow the cultivation, processing, and commercialization of hemp and hemp-derived products [58-61]. Hemp is defined as cannabis with a tetrahydrocannabinol (THC) content of less than 0.3 % and is primarily cultivated for industrial purposes, including the production of fiber, textiles, paper, and CBD (cannabidiol) extracts [58-61].

According to the regulations, both THC and CBD are allowed for specific purposes [58-61]. THC is exclusively permitted as an active ingredient in pharmaceutical products, while CBD can be utilized as an active ingredient in cosmetics, dietary supplements, and pharmaceutical products [58-61]. These guidelines distinguish the permitted applications of THC and CBD in Colombia [58-61]. CBD (Cannabidiol) is legal in Colombia [58-61]. The country allows the use of CBD as an active ingredient in various products, including cosmetics, dietary supplements, and pharmaceutical products [58-61]. CBD is derived from hemp, which is legal to cultivate and process in Colombia as long as it contains less than 0.3 % Δ -9 THC (Δ -9 tetrahydrocannabinol) [58-61]. The regulations in Colombia provide for the legal use of CBD in different industries, subject to compliance with the specific regulations and requirements outlined by the authorities [58-61]. According to Colombian law, citizens are allowed to cultivate cannabis for personal use in your own home [58-61]. The law permits individuals to grow up to 20 cannabis plants for personal consumption [58-61]. However, it's important to note that the cultivation must be strictly for personal use and not for commercial purposes [58-61]. Selling or distributing Cannabis is still illegal and can lead to legal consequences [58-61].

Growing, selling and importing Cannabis for medical use is allowed in Colombia [58-61]. There are several authorities involved in the authorisation processes. The ICA (the Colombian Agency for Agricultural and Animal Husbandry Products) will confirm that any kind of industrial crop farming has obtained certain phytosanitary and food safety approvals [58-61]. The Ministry of Justice authorizes the cultivation [58-61]. The Ministry of Health issues the authorisation to process the raw materials into processed ingredients, such as resins and oils that are not to be sold to the public [58-61]. INVIMA is the agency in Colombia that conducts market approval procedures for finished products [58-61]. As per these regulations, patients are not supposed to have access to raw Cannabis [58-61]. The regulations aim for patients to have access to pharmaceutical products [58-61]. If a patient prefers to use raw Cannabis, the regulations provide for the possibility of growth for personal consumption (up to 20 plants) [58-61]. No processing or commercialization is allowed for this personal consumption option [58-61]. Being a product with a very sensitive background in Colombia, and strong enforcement against recreational use, any breach that attempts to profit from commercialization of recreational use will be sanctioned as a criminal offence [58-61].

The recreational Cannabis remains illegal in Colombia [58-61]. Possessing quantities above 20 grams can be deemed as drug trafficking, carrying severe penalties that include lengthy imprisonment in Colombia [58-61]. Furthermore, engaging in any form of "commercial" cultivation, sale, or export of cannabis is strictly prohibited by law and can lead to prosecution [58-61]. Recreational use of Cannabis continues to be illegal and will be prosecuted as a criminal offence in Colombia [58-61]. Consumption is not punished but any commercial activity, import, export or production is prohibited and criminally prosecuted in Colombia [58-61]. On Dec. 22, 2016, President Juan Manuel Santos signed a bill into law to regulate the medical Cannabis industry in Colombia [58-64]. It is now fully legal to grow, process, import and export medical Cannabis and cannabis derivatives if you possess a federal license from the National Narcotics Council and/or the health ministry in Colombia [58-65].

The use of Cannabis for recreational purposes is prohibited in most countries. However, many have adopted a policy of decriminalization to make simple possession a non-criminal offense (often similar to a minor traffic violation) [58-65]. Others have much more severe penalties such as some Asian and Middle Eastern countries where possession of even small amounts is punished by imprisonment for several years [58-65]. Countries that have legalized recreational use of Cannabis are Canada, USA, Malawi, Malta, Georgia, Luxembourg, Malta, Mexico, South Africa, Brazil, Chile, Denmark, Finland, Germany, Panama, Peru, Poland, Portugal, Rwanda, Spain, Switzerland, UK, Zambia, Zimbabwe, Czech Republic, New Zealand, Norway, Thailand, and Uruguay, plus 24 states, 3 territories, and the District of Columbia in the United States and the Australian Capital Territory in Australia [62-65]. Commercial sale of recreational Cannabis is legalized nationwide in three countries (Canada, Thailand, and Uruguay) and in all sub-national U.S. jurisdictions that have legalized possession except Virginia and Washington, D.C [62-65]. A policy of limited enforcement has also been adopted in many countries, in particular the Netherlands where the sale of cannabis is tolerated at licensed coffee-shops [58-65].

Cannabis legalization is not exclusive to North America [62-64]. So far, more than 40 countries have legalized Cannabis fully or partially for medical and/or adult use [62-64]. Medical Cannabis has been legal in Chubut and Santa Fe Provinces since late 2016 [62-64]. In March, the Argentinian senate legalized Cannabidiol (CBD) oil for treatment of certain conditions, including epilepsy [62-64]. Chile legalized the cultivation of medical Cannabis in 2014 [62-64]. Cultivators

must get a license from the Chilean Agriculture Service [62-64]. Sale of medical Cannabis is only allowed through prescription at pharmacies [62-64]. Since 2013, MMJ has been legal in the Czech Republic [62-64]. In the first year of the program, federal authorities imported medical Cannabis products to sell at pharmacies [62-64]. Today, licensed cultivators grow Cannabis for the state [62-64]. Long a center for Cannabis research, Israel legalized medical marijuana in the 1990s [62-64]. In 2004, it began experimenting with THC as a treatment for PTSD in its military members [62-64]. There are currently eight licensed producers, and patients can get their prescriptions filled in company stores or medical centers [62-64]. Italy legalized Cannabis for medical use in 2013 [62-64]. Currently, production is limited to a military operation in Florence called the Military Pharmaceutical Plant [62-64]. The Army sends final medicine to pharmacies across the country, where patients with prescriptions can purchase medicine [62-64]. Legalized in 2016, medical marijuana in Macedonia is already attracting international investors [62-64]. A U.S.-based group, NYSK Holdings, has invested in a Cannabis oil-producing plant in the Balkan country [62-64]. Production is regulated by the federal authorities who issue licenses to select operators [62-64]. A recent law change saw Cannabis legalized for medical purposes in Mexico [62-64]. In April 2017, the Mexican Chamber of Deputies approved a Senate measure legalizing the plant for medical use [62-64]. Regulation and policies are being set by the country's Health Department [62-64]. Since then, the Supreme Court has ruled cannabis prohibition unconstitutional [62-64]. Legislators are drafting possible regulations for future legalization [62-64]. While Cannabis is still illegal in Poland, health authorities have been issuing reimbursements for the purchase of medical Cannabis [62-64]. Medical Cannabis products are imported from other countries [62-64]. Currently no laws regulate nor legalize the domestic production of Cannabis [62-64]. In 2018, South Africa legalized and decriminalized the adult use of cannabis, but a regulated system for the sale of Cannabis is not yet in place [62-64]. Turkey legalized Cannabis for medical uses in October 2016 [62-64]. Cultivation is allowed in select provinces, although any province can host a cultivation facility for scientific purposes if the federal authorities allow it [62-64]. Licenses are government-controlled and valid for three years [62-64].

Uruguay became the **first country in the world** to legalize the production, distribution and consumption of cannabis in 2013[62-64]. Uruguay legalized Cannabis in all forms in 2013 [62-64]. Consumers must be 18 years old or older, and residents of Uruguay and must be registered with federal authorities [62-64]. Cannabis sold in the country is produced by the federal government [62-64]. In 2018, Zimbabwe legalized medical Cannabis[62-64]. Significant investment has followed, and in May 2020 Zimbabwean farmers were granted 100% land ownership for turning their fields over to Cannabis [62-64]. Residents can buy up to 40 grams of weed a month from pharmacies, grow it themselves or join cannabis clubs where members tend the plants together[62-64].

The global cannabis market was valued at \$47.32 billion in 2022, and is projected to grow from \$57.18 billion in 2023 to \$444.34 billion by 2030 growing at a CAGR of 34% during the forecast period [62-64, 66, 67]. Marijuana legalization is gaining momentum around the globe, driven primarily by the increasing recognition that the product may have a range of legitimate medicinal benefits and therapeutic applications [1-62-64]. It is the most widely cultivated, trafficked, and consumed drug worldwide[1-62-64]. Cannabis legalization is a controversial and multi-faceted issue that has recently been the subject of serious debate around the world [62-65]. It may be difficult for physicians viewing Cannabis through the lens of addiction to see any silver lining from legalization, but the first and most immediate benefit is that patients who use weed for therapeutic purposes will no longer fear legal sanctions [62-65]. The most common therapeutic use of marijuana is for pain control, and while the drug is not strong enough for severe pain, it is quite effective for the chronic pain that plagues millions of people, especially as they age [62-65].

6. Conclusion

Cannabis-based medicines showed several therapeutic purposes, mainly to treat disorders such as constipation, some types of pain, epilepsy, anxiety and among others. In addition, the genus Cannabis exhibits great clinical relevance due to its Central Nervous System activities attributed to some phytochemicals compounds, as Cannabidiol and Δ^9 -tetrahydrocannabinol. The interest in the pharmacological properties of Cannabis is growing and several new studies are being carried out to prove its pharmacotherapeutic use which are important to design of novel drugs with different routes of administration and for multiple pathologies resistant to the conventional treatments. Although Cannabis sativa synthesizes a wide range of phytochemicals, much attention has been primarily given to two phytocannabinoids, Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD), due to their distinctive activities in humans. Currently, the most common method to identify and quantify cannabinoids are liquid chromatographic methods coupled to UV-VIS or mass spectrometric detectors. As cannabinoids are fluorescent compounds, fluorescent-based detection methods are gaining increasing interest. The cannabinoids displayed a characteristic fluorescence excitation (225–400 nm)-emission (300–525 nm) signal.

The use, cultivation and marketing of Medical Cannabis sativa (drug or Marijuana type) is banned and prohibited in India due to the presence of high levels of psychoactive principle (Narcotic drug). Recreational cannabis and medical marijuana are illegal and banned in Azerbaijan. Several researches have shown the potential medicinal activity of Cannabis and its chemical compounds. There is still a huge prejudice in society in relation to medical Cannabis due to its recreational use. However, this scenario is changing, and the social resistance is decreasing for the medicinal use of Cannabis. In this context, plant derivatives were identified, such as Δ^9 -tetrahydrocannabinol (Δ^9 -THC or THC) and cannabidiol (CBD), as well as, the endocannabinoid system, cannabinoid receptors type 1 and type 2 (CB1 and CB2, respectively). The Cannabis market in India is predicted to experience a substantial growth in revenue, with projections indicating that it will reach ₹US\$100.80m by 2024. In India, hemp is only legalized and FSSAI, Government of India approved as the functional food. The maturity of the Cannabis market varies across the globe mainly due to differing legal environments and public attitudes towards cannabis. Some countries such as Canada and the United States have adopted fully regulated frameworks that allow cultivation, consumption, and retail distribution of various cannabis products. Regulations can also differ regarding how cannabis is used. The global legal marijuana market size was valued at USD 21.0 billion in 2023 and is projected to grow at a compound annual growth rate (CAGR) of 25.7% from 2024 to 2030. Increasing demand for legal marijuana is a major factor in growth of the market.

The current medical access program for Cannabis has both strengths and limitations. Advantages of legalization of nonmedical Cannabis include reducing harms from criminalization of cannabis possession, regulating the distribution and content of product, and increasing government revenue through taxation. However, one of the most important limitations is that the Cannabis Act does not ensure medical cannabis patients will obtain any healthcare provider support as the act does not require this interaction. The Cannabis Act should provide mechanisms to support both patients and healthcare providers. Patients using cannabis for medical purposes require reliable sources of information and guidance from well-trained healthcare providers. Similarly, healthcare providers require ongoing support such as continuing education programs and appropriate documents for authorizing cannabis.

Compliance with ethical standards

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No conflict of interest to be disclosed.

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