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Research Article

HEMP HELPS HUMAN HEALTH: ROLE OF PHYTOCANNABINOIDS

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ABSTRACT

Industrial Hemp, or Cannabis sativa L., belongs to Cannabiaceae family is an oleaginous, the oldest medicinal plant cultivated by humankind in India, China, Pakistan, Nepal, Bhutan, Afghanistan and Iran, Persians specifically for medicinal properties and non-edible fiber content. Initial uses of Cannabis date back to almost 5000 years in **India** which was well documented in A***yurveda.*** Cannabis sativa and Cannabis indica were native of **Indian origin** found as wild noxious weed in the Indian Himalayan Region. Since then, hemp consumption has been spurred on by its wide range of properties and uses from **Indian Himalayan civilization** to another through consecutive millennia. Cannabis research work remains years behind than other crops because of the long legacy of prohibition and stigmatization. Hemp has historically been attractive for its top-quality fiber and edible oil. **Hemp fibers** are used in paper, carpeting, home furnishing, construction materials, insulation materials, hempcrete, auto parts and composites. The **female inflorescence** is the main product of Medical Cannabis sativa (marijuana or drug type). Cannabis sativa has developed full of glandular type of **trichomes.** Phytocannabinoids are produced and stored in glandular trichomes, located all over the aerial part of the plant. Phytocannabinoids possess therapeutic, antibacterial, and antimicrobial properties. The nutritional value of hemp is attracting special attention since hemp seed protein and oil is used in treatment of several human diseases.

Keywords: Cannabis, Cannabidiol (CBD), Desi Vijaya, Fiber, Hemp, Himalayan Hemp, Indian Himalayan Region, India, Iran, Phytocannabinoids, ∆9 tetrahydrocannabinol (∆9-THC), Trichomes.

INTRODUCTION

Cannabis sativa L. is a potential source of fiber, food, oil, and protein (1-25). Cannabis has several varieties suitable for various purposes (1-35). **Cannabis sativa (Figure-1)** belongs to Cannabiaceae as a medicine was used before the **Christian era** in Asia**,** mainly **in India,** China, Bhutan, Nepal, Afghanistan, Pakistan and Iran, Persians (1-35). According to ***Ayuverda*** in India, the medicinal value of the Cannabis plants was well documented as **Vijaya** and often known **as Desi Vijaya** (1-35). This was the first Indian written evidence to support the medicinal value of **Cannabis plants which was well documented in** *Ayuverda* in India (1-25). It is 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 (1-40). Many historians believed that Indian Himalayan Region was the centre of origin of Cannabis sativa and Cannabis indica (1-20). Cannabis sativa has been widely used in industrial, ornamental, nutritional, recreational, and pharmaceutical applications and herbal medicine (1-45). Cannabis sativa L. that contain a large variety of secondary metabolites, including phytocannabinoids, terpenoids, and flavonoids, which are known for anti-microbial activities, anti-inflammatory, anti-oxidative, and neuromodulatory properties (1-55). Phytocannabinoids are classified into different subclasses according to their chemical structures, Cannabidiol (CBD), ∆9 -tetrahydrocannabinol (∆9-THC), Cannabigerol (CBG), ∆8-tetrahydrocannabinol (∆8 -THC), and Cannabinol (CBN) (1-55). However, Cannabis sativa particularly Medical Cannabis sativa (Marijuana type) was perceived as criminal and unacceptable to communities, since most consumers cannot differentiate between psychoactive Medical Cannabis sativa (Marijuana type) and non-psychoactive Industrial Cannabis sativa (hemp or fiber type) plants (1-45). Medical Cannabis sativa (Marijuana type) is also used for the treatment of any illness for which the drug provides relief for the individual (1-50).

In the past several decades, a lack of knowledge of hemp and marijuana has reduced the growth of Cannabis sativa plants (1-55). This is mainly due to the fact that Cannabis research work remains years behind than other crops because of the long legacy of prohibition and stigmatization (1-35). The use of Industrial Cannabis sativa (hemp or fiber type) plants with low levels of ∆9 -tetrahydrocannabinol (∆9-THC) in medicine and foods is based on various potentially beneficial Cannabinoid compounds including Cannabidiol (CBD) (1-57). Cannabidiol (CBD) has a wide spectrum of biological activity, such as antioxidant and anti-inflammatory activity (1-45). Therefore, Cannabidiol (CBD) can be used for the treatment of diseases associated with redox imbalance and inflammation (1-60). Cannabidiol (CBD) can be used for the treatment of **diabetes-related** cardiomyopathy, (including stroke, arrhythmia, and hypertension), cancer, anxiety, psychosis, epilepsy, neurodegenerative disease, musculoskeletal pain, and skin disease (1-55). A mixture of Cannabinoids may produce tattoo ink with a low risk of infection and inflammation (1-55, 60-65).

Cannabis sativa L (Figure-1) produces a wide array of secondary metabolites (1-55). This plant is best known for its production of Cannabinoids such as ∆9 tetrahydrocannabinol (∆9 THC), which has psychoactive properties, but it is also a prolific producer of **Volatile Organic Compounds** (VOCs) into the environment (4). About 200 scent compounds have been reported to make up the plants complex aroma (4). Some of the compounds that are typically found in high concentrations in Cannabis spp. Plants include β-myrcene, limonene, α-pinene, β-pinene, and terpineol (4). For example, one Medical Cannabis sativa (Marijuana type) cultivar has elevated levels of terpinolene and δ-limonene, giving the plant a

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woody citrus aroma, while one hybrid C. sativa × C. indica cultivar has a floral citrus aroma due to high amounts of **linalool** and **limonene** (4). **β-Myrcene** was the most abundant compound in most hemp cultivars (4). The main compounds driving the difference between cultivars and sexes were (Z)- and (E)-β-ocimene (4). Furthermore, the uses of Cannabis are economically significant, owing to the various food industry applications and the development of therapeutic and pharmacological applications of phytocannabinoids (1-40).

Figure-1: The robust growth of Cannabis sativa (hemp)

After the legalization of hemp in India in 2021, there are many efforts and hemp research work is slowly gaining interest and training programmes about hemp production, organic farming, promoting marketing hemp products are successful. Some of the Indian biotech companies are **A Bangalore**, Karnataka based **Namrata HempCo** Limited (**NHempCo**) was founded by Harshavardhan Reddy Sirupa and Narmrata Reddy Sirupa, **Cannasis Wellness**, Rajamahendravaram**, Andhra Pradesh (Keran Vankayala),** Pan India Medical Cannabis and Hemp Association (PIMCHA), Mumbai, Maharashtra state**, UKHI-Hemp Foundation, Bombay Hemp Company**, BOHECO, **Satliva, Himalayan Hemp, Hemp Fabric Lab**, Vedi Herbals, Happy Hemp, SUI, ItsHemp, **Bhu:Sattva's**, Health Horizons, Hemis, Hemp Republic, Hempsters, B.E. Hemp, India Hemp Co., Inc, India Hemp Organics, Health Horizons, Hemis, TheTrost, and Gin-Gin) involved in promoting the Indian hemp products marketing, research, cultivation, harvesting, processing, manufacturing, trading, wholesaling, retailing, innovating, advocating both across the nation and around the world.

CANNABIS SATIVA (HEMP) : INDUSTRIAL APPLICATIONS

Industrial Cannabis sativa (hemp or fiber type) has received a lot of special attention because of its multipurpose applications, short production cycle, low capital demand in cultivation, and as a carbon-negative material (1-35). Hemp offers super absorbency. Indian Himalayn hemp can produce an impressive amount of vegetative biomass depending on cultivar (1-40). Hemp biomass offers several components: fiber (found in the bark/outer skin) about 25 to 30 per cent of the stalk, hurd (woody inner portion of the hemp stalk) and dust (screenings/particulates) (1-30). Processing provides pure elements, as well as blends of these components. In comparison with other bast fibres (such as from flax, kenaf, jute or ramie), hemp fiber has excellent fiber length, strength, durability, absorbency, anti-mildew and anti-microbial properties (1-34). This quality is desirable for oil and gas cleanup, livestock bedding and personal hygiene markets. Hemp very high tensile strength, strength-to-weight ratio, flexural strength and ability to rebound are desired benefits in bio-composites for automotive parts, aerospace and packaging (1-50). The textile, paper and building markets have interest in some specialty applications due to hemp's durability, anti-microbial, acoustic and aesthetic properties (1-36). Generally, the demand for hemp products is expected to benefit from a growing demand for products that are healthy and environmentally sustainable. Organic and natural production by Indian Himalayan farmers can also provide growers with additional access to market channels, in particular, food, cosmetics and personal care, natural health products, textiles and in the future feed (1-30). Hemp maybe useful in carbon foot printing equations, as on average, it yields 4 times the biomass of an average forest in 90 days compared to 25 years in tree growth (1-35). Hemp is thought to provide a valuable break in a crop rotation for the purposes of disease and pest management. Hemp root system can break up compacted soil, it is thought to provide aeration (1-35). The roots may also help to control erosion. Hemp may contribute to pollution abatement through its ability to mitigate toxins from the ground through phytoremediation (decontaminating soil or water using plants and trees) (1-35).

The disadvantage of agricultural waste lignocellulosic materials is that they often have additional substances, such as waxes that may adversely affect the gluing process with conventional resins, and thus reduce the mechanical properties of the manufactured boards (65). One of the promising raw materials for the production of particleboard is Cannabis sativa (Hemp) (65). The development of hemp-based composites is an interesting alternative to protect the forests and the problems associated with the shortage of wood raw materials (1-40; 65-68). Cannabis sativa (Hemp) is a universal plant that is quite easy and environmentally friendly to grow (65). Currently, industrial hemp is grown primarily to obtain seeds for the production of oils and other nutritional supplements, which are very popular (1-35; 65). Additionally, hemp fiber is extremely strong and durable, which is why it is used in the production of ropes, fabrics, paper, fiberboards and insulation boards (1-45;65). Decortication of the stalks leads to three main fractions: long fibers, short fibers and woody core tissue (1-35; 65). The woody core part of the hemp stalk, which is called hurd (or shives when in the form of industrial particles), is considered waste in the hemp industry (1-68). Nevertheless, hemp shives are used as an energy raw material, as well as a raw material for the production of various types of composites (1-25; 65-68). There were also several works on the use of hemp shives as a raw material for the production of particleboards (65). Hence hemp shives can be successfully used in the production of particleboard as a substitute for wood in the core layers of the manufactured boards (65). Based on the research, it can be concluded that hemp shives can be used as a 10% and 25% substitute for raw wood material in the production of particleboards (65). It seems that particleboards with the best physical and mechanical properties have hemp shives added to the core layer or to the top and core layer but not only in the surface layers (65). Moreover, the share of hemp shives in particleboards has a positive effect on the moisture resistance of the manufactured particleboards, reducing their thickness swelling, which is a common problem when

using alternative lignocellulosic raw materials (65). This research points in the direction of using waste materials in the form of crop biomass in particleboard production, an inevitable alternative to wood resources (65).

The possibility of patenting hemp cultivars with high yields in the pharmaceutical industry has led to the cultivation of hemp in aerobic environments, exclusively for the pharmaceutical industry (1-45). Hemp products, Cannabidiol (CBD), and ∆9 tetrahydrocannabinol (∆9-THC) at lowest levels (0.2-0.3%) are the greatest wholesale potential markets and are highly attractive for their recreational and medicinal properties (1-50). Over 200 compounds with diverse biological activities, including flavonoids, terpenoids, and Cannabinoids, have been confirmed in hemp (1-56). Cannabis sativa produces a unique class of terpenophenolic compounds, called **Cannabinoids**, as well as non-Cannabinoid compounds (1-45). As of today, there are 70 countries including India, UK, USA, Netherlands, and Canada has permitted and supported the production of Hemp, Cannabis sativa (1-57). Edible usage of Hemp Cannabis sativa is classified into medicinal and recreational purposes (1-45). According to the Consumer market survey, a total hemp plant wholesale market was valued at more than 700 million dollars in the USA. The world market of industrial hemp production was estimated to be USD 4.13 billion in 2021 and is expected to grow by a 16.8% compound annual growth rate (CAGR) between 2022 and 2030 (1-35). Growing demand for industrial hemp from a wide variety of application industries drives the market (1-45). Despite the decline in the agriculture of Industrial Cannabis sativa (hemp or fiber type) owing to its existing legal restrictions, standard procedures have been established to encourage the natural production of fiber from hemp plant species (1-55). Hemp can be grown under a variety of agro-ecological conditions and has a capacity to grow quickly, especially after the first 4–5 weeks after emergence, making it an excellent candidate for **Carbon Sequestration** (1-56).

Industrial Cannabis sativa (hemp or fiber type) has been used as inexpensive, eco-friendly, biodegradable hemp plant raw materials to produce cellulose, biofuels, bioethanol, rope, textiles, clothing, biodegradable plastics, paint, insulation, food, animal feed, paper towels, paper plates, ready-made clothes, and even natural fiber shoes (1-60). Rural Indian Himalayan villages have increased the quantity and quality of indigenous Industrial (fiber type) hemp handloom products, such as shawls, stoles, accessories. Increasing production of **soaps, shampoos, bath gels, hand and body lotions, UV skin protectors, massage oils,** and a range of other hemp-based products is expected to have a positive impact on the market growth of Industrial Cannabis sativa (hemp or fiber type) (1-56).

Figure-3: The hemp fibre threads ready for the textile industries

Hemp fibers (Figure-3) are used in paper, carpeting, home furnishing, construction materials, insulation materials, auto parts and composites (1-45). Insulation materials and bio-composites consume a significant product amount on account of their low weight, superior strength, biodegradability, and thermodynamic properties (1-59). Hemp shivs cost half the value of fibres and have several applications in different industries, which is expected to drive the segment growth over the forecast period (1-57). These are majorly used in animal bedding materials on account of their high absorbance ability, which is around four times their own dry weigh (1-50). The high absorbency of hemp fiber is beneficial for livestock bedding, oil and gas cleanup, and personal hygiene applications. In addition, increasing product demand from the textile, paper, and building materials markets, owing to favorable acoustic and aesthetic properties, will support the hemp plant market growth. The products manufactured from hemp are eco-friendly, renewable, and associated with less harmful methods of preparation (1-56). **Paper produced from hemp fiber** requires **fewer chemicals** for processing as compared to paper produced from wood pulps. Hemp is a sustainable plant requiring less water or pesticides in cultivation compared to cotton (1-60). It has a short growth period and almost its whole plant body has versatile utility value (1-68).

Hemp also suppresses levels of fungi and nematodes in the soil and can be grown without fungicides or pesticides (1-35). Industrial Hemp (fiber type) is a natural **weed suppressor** and could be grown without herbicides (1-65). Industrial Cannabis sativa (hemp or fiber type) demonstrated capability for sustainable agricultural production, aiming to protect the soil and environment through lack of water consumption in the production of hemp fibers, and the ability to grow without the need for fertilizer and pesticides (1-45). Hemp contributes to the maintenance of soil quality by its anchored roots, which prevent soil erosion and nutrient leaching, may extract nutrients from deeper soil layers, and are effective for **phytoremediation** by absorbing heavy metal contaminants from the soil and storing them within the plant (1-60). **Industrial Hemp (fiber type)** fabric is **strong, hypo-allergic, and naturally resistant to UV light, mold, and mildew**, which represents an added advantage over other fabrics (1-68). In addition, it can be blended with cotton or linen, which adds stretch and strength to the fabric (1-45). As a fiber crop, hemp provides a high yield; it produces 250% more fiber than cotton and 600% more fiber than flax, from the same acreage (1-45). Industrial hemp is one of the most relevant substitutes for cotton because it requires less pesticides and water in cultivation (1-40). Hemp fiber is known as coarse and stiff. It also has poor spinnability in the ring spinning system (1-30). The blended use of cotton/hemp fibers for denim fabrics improved the thermo-physiological comfort as well as the soft-feeling nature. Moreover, higher air ventilation, higher water-absorbing property, and faster drying behaviour were observed in the mixed fabrics compared to a pure cotton fabric (1-45).

Hemp Biochar carbonized at 400–600^{o} C was classified as a lignocellulosic material with good potential for solid biofuel applications due to its high heating value (1-30). In contrast, hemp Biochar carbonized at 800–1000^{o}C developed a graphite-like microstructure and displayed interesting electrical conductivity, opening doors for its use in electrical purposes (1-45). Hydrothermal and mechanically generated hemp hurd nanofibers are utilized for sustainable barrier coatings/films (1-45). Hemp-based fiber is being applied even to the interior of high-end vehicles (1-34). Hemp-reinforced natural fibers have been used in the interior components of the **Mercedes-Benz E-Class** and body panels are manufactured using hemp fiber-reinforced polyester composite (1-50).

CANNABIS SATIVA (HEMP): BOTANY, FEMALE INFLORESCENCE AND TRICHOMES

Cannabis sativa L (Figure-1, 2) is naturally dioecious, with the staminate plants that are usually slender, taller, and that come to flower earlier that the pistillate ones (1-35). Hemp is a short-day plant, which means it requires a long period of darkness to form flowers (1-35). Short-day plants develop flowers only when the day length is less than about 12 hours (1-45). Hemp flowering is delayed by long days and hastened by short days (1-30). Shorter days then typically trigger flower development (1-30). Hemp is a short-day plant, which affects crop production. Once the flowering starts, the efficiency with which intercepted radiation is converted to dry matter drops rapidly (1-55). Hemp has been photo-period sensitive, meaning it tends to flower at the same calendar date no matter when it is planted (1-65). New varieties are available that are not photo-period sensitive (1-40). The differences in growth rate and development between male and female plants are large (1-49). Male plants tend to flower and senesce (deteriorate with age) earlier (1-30). This variation may limit yields, reduce the efficiency of resource use and may result in variable quality (1-45). Harvest of seed is approximately 100 to 120 days after sowing, depending on variety (1-50). Hemp shatters very easily and makes excellent birdseed. Harvest should begin soon after **birds are noticed in the field** (1-45). The quality and quantity of hemp fibre yield is affected by **retting**, the process of partially breaking down the gummy substances, especially pectin, that bind the fibres together in bundles and to the plant core (1-45). **Retting** can be done chemically or biologically (1-50).

Hemp is primarily dioecious, that is, the pollen-bearing parts are found in one plant and the seed-bearing flowers on another (1-40). Cannabis has a diploid genome (2n = 20). The male and female plants are not distinguishable before flowering (1-45). The male inflorescence can be identified by the development of round, pointed flower buds with five radial segments, while the female inflorescence can be identified by the presence of calyx (1-34). **Male plants die shortly after flowering.** The female plants live 3 to 5 weeks until seed is fully ripe (1-45). In a dioecious crop, the number of female plants is 10 per cent to 50 per cent higher than the number of male plants (1-45). There are a few monoecious cultivars now that have both male and female flowers on the same plant (1-45). **Hemp roots** can be harvested after the other plant parts are harvested. Dried cannabis roots have bioactive content and should be stored in consistent temperature and humidity to maintain quality (1-60).

Hemp is wind pollinated, and the male plants die after producing millions of pollen grains (1-30). A small percentage of monoecious plants can naturally occur, particularly in short-day conditions (1-36). Monoecious varieties have been selected in modern times to reduce the agronomic problems related to the sexual vegetative dimorphism present in dioecious varieties (1-45). Usually seeds in monoecious varieties are smaller than in dioecious ones (1-40). Cannabis sativa is wind pollinated. For the production of phytocannabinoids, female plants are preferred for several reasons (1-40). First, they produce higher amounts of Cannabinoids. Second, once pollinated, female plants produce seeds at maturity, whereas seed-free plants are preferred for their higher yield of secondary metabolites (1-40). Third, if several cannabis varieties are being grown together, cross-pollination would affect the quality (chemical profile) of the final product (1-45). To avoid this, **removing male plants** as they appear, screening female clones for higher metabolite content, conservation and multiplication using biotechnological tools ensures the consistency in chemical profile that is desirable for pharmaceuticals (1-34).

There is a misunderstanding that cross-pollination changes the chemotype of the plant (66). However, this change only appears in seeds resulting from cross-pollination and not in the pollinated plant (66). The problem with pollination occurring in crops intended for the production of phytocannabinoids is that the energy is shifted to seed production, not Cannabinoid production (66-68). Further pollination resulted in a significant decrease in the overall total phytocannabinoid concentration in inflorescences (66). The THC-rich chemovar female exhibited an average 75% decrease, while CBD-rich females showed a 60% decrease in phytocannabinoid content after fertilization (66). Pollination prevention stimulates the formation of new flowers, increasing phytocannabinoid production (66). Although male plants tend to be larger and bloom before female plants, it is difficult to distinguish them during the vegetative phase (66). The most common way to differentiate female plants from male plants is by analyzing the anatomy of the inflorescences, although some genotypes develop solitary internode flowers at early stages of development, making it possible for early sexual differentiation (66).

Figure-2: The female inflorescence is the main product of Medical Cannabis sativa (Marijuana or drug type)

The **female inflorescence** (Figure-2) is the main product of Medical Cannabis sativa (marijuana or drug type)(1-45). Cannabis sativa has devloped full of **trichomes** (1-37). Trichomes are collected from the protuberances, close to the leaves, flowers, seeds, and other important sections of Cannabis sativa plants (1-45). These trichomes are divided into various types of **glandular** and **non-glandular structures** (1-45). The secretory trichome's produce numerous biologically active compounds which take the form of protuberances and cover the plants leaves and stems (1-50). Phytocannabinoids are stored in glandular trichomes, located all over the aerial part of the plant (1-40). The root surface and root tissue do not produce phytocannabinoids (1-50). The main psychoactive constituent in Cannabis is THC, and the main non-psychoactive compound is CBD, which accumulates in glandular trichomes and is obtained from plant tissue, flowers, and a high density of plant constituents (1-50). Cannabis trichomes possess phytocannabinoid in large quantities (1-45). High temperatures or herbivory cause trichome rupture and the release of the phytocannabinoid content, which protects the plant from desiccation and high-temperature stress (1-50). It was also reported that phytocannabinoid production was enhanced in Cannabis flowers after UV-B-induced stress (1-45). Significantly, phytocannabinoids inside oil bodies provided tolerance against several abiotic stresses, such as cold temperature, heat, excessive light, and UV radiation (1-45).

Moreover, plants grown outdoors are exposed to a fair amount of ultraviolet UV-A and UV-B, and exposure to UV rays before harvest causes the plant to produce more THC compounds (1-60). In most cases, these UV-B-mediated induced physiological changes lead to the reinforcement of plant defenses (1-40).

CANNABIS SATIVA: PHYTOCANNABINOIDS

Phytocannabinoids are bioactive natural products found in some flowering plants, liverworts, and fungi that can be beneficial for the treatment of humans and animals and present potent antibiotic effects (1-50). Phytocannabinoids have been found in different plant species of Cannabis, including *Echinacea purpurea*, *Echinacea. angustifolia*, *Echinacea* pallida, *Acmella oleracea*, *Helichrysum umbraculigerum*, and *Radula marginata* (1-45). The most uses of phytocannabinoids are based on anti-inflammatory, neuroprotective, and anti-nociceptive activities (1-45). The biotechnological use of phytocannabinoids can be enhanced through agro-industrial approaches to understand their role in medication (1-50). Phytocannabinoids have a diverse roles in humans and exhibit antimicrobial and antibiotic activity (1-45). Phytocannabinoids exhibit antimicrobial activities against bacteria and fungi (1-35). A group of C21 and C22 carboxylated forms of terpenophenolic compounds exhibit binding affinity at Cannabinoid receptors (1-45). However, phytocannabinoid synthesis involves several structures of chemical compounds, such as THC, CBD, CBG, CBC, Cannabicyclol (CBL), and Cannabidiol type (CBND) (1-45). Cannabidiol (CBD) is the major non-psychoactive component isolated from Cannabis sativa and has been associated with multiple and potential biological activities, especially anxiolytic, antipsychotic, anti-inflammatory, analgesic, antioxidant, and neuroprotective properties (1-50). The potential uses of Cannabidiol (CBD) in antibacterial therapies has recently emerged (1-45). Many Cannabinoids are formed in correlation with increased moisture, heat, temperature, and abiotic stress conditions, as well as low soil moisture content (1-45).

The non-psychotropic phytocannabinoids are used in the treatment of seborrheic dermatitis, cancer, HIV/AIDS, multiple sclerosis, glaucoma, seizures/epilepsy, and pain are among the most recognized qualifying ailments (1-50). In addition, the Cannabis industry is expected to grow much faster than expected, reaching USD 57 billion by 2027 with North America (Canada) among the largest group of Cannabis buyers (1-45). The global market is expected to cover at least 67% of the expenditure, and medicinal marijuana the remaining 33% (1-45). Many developed countries are expected to contribute to the medicinal Cannabis market, thus making it the largest in the world (1-40).

Phytocannabinoids are naturally occurring cannabinoids found in the Cannabis plant (1-45). Phytocannabinoids are being investigated for their effect based on therapeutics in brain pathology (1-45). The phytocannabinoids have been valuable starting compounds for the development of drugs, including Nabiximols (marketed as Sativex oral spray (2.7 mg/mL THC and 2.5 mg/mL CBD) by GW Pharmaceutical, Cambridge, UK) (1-35). This drug has been approved in Canada, the USA, Europe, and several developing countries for treating muscle and neurological disorders, multiple sclerosis, and cancer. Several synthetic drugs, such as Cannabinoid-based drugs, have been approved for the relief of vomiting associated with cancer chemotherapy (**Marinol, (Dronabinol**), Solvay Pharmaceutical, and Cesamet) (1-40).

Phytocannabinoids have valuable efficacy in reducing the indicators of seizure, and several hypotheses dictate that Endocannabinoid system (ECS) modulators affect neurogenesis (1-35). Phytocannabinoids reflected in decreased agitation and aggression, increased appetite, sleep quality, objective mood, and pain control (1-45). Phytocannabinoids are promising candidates for treating symptoms of neurodegenerative and other diseases (1-40). Owing to the evidence that cannabinoids are more effective at reducing nausea, in combination with the U.S. Food and Drug Administration (FDA)'s approval of dronabinol, the latter is now used therapeutically in the USA and other developed countries as a vomiting and nausea-related cancer treatment drug (1-45). Phytocannabinoids have the ability to counteract anorexia, cachexia, and weight loss and act as an appetite stimulant in patients under chemotherapy (1-45). The potential of cannabinoids in different neurological disorders, including Parkinson's and **Alzheimer's disease**, anti-inflammatory, immunosuppressive, antioxidant, and neuroprotective properties, are due to the modulation of the endocannabinoid system. Cannabidiol (CBD) has exerted its protective effect over several signaling cascades involved with proteostasis, consequently reducing oxidative stress in cells (1-45).

Epidiolex (CBD) is in clinical trials for the treatment of resistance seizure disorders, such as Lennox-Gastaut and Dravet syndrome (1-45). Cannabis is capable of producing an impressive number of Cannabinoids exceeding 30% of the flower, bud, and dry weight (1-35). The physiological activity of cannabis has been largely restricted to ∆9-Tetrahydrocannabinol (∆9-THC) and Cannabidiol (CBD) compounds (1-40). However, some studies have reported that some of the effects arise from the other cannabinoids (1-35). Future research should focus on investigating these phytocannabinoids as a key to understanding their limitations (1-25). Finally the production of this plant, which is beneficial to animal health, has no negative impact on the environment (1-40).

HEMP HELPS HUMAN HEALTH: ROLE OF PHYTOCANNABINOIDS

Figure-4: The shelled Hemp Seeds ready for the consumption

Growing awareness regarding the dietary advantages of hempseed (**Figure-4, 5, 6**) and hempseed oil along with rising demand from the cosmetics and personal care industries will augment the hemp market growth (1-40). The nutritional value of hemp is attracting special attention. Hence, hemp are used in treatment of several human diseases, and these compounds can contribute to cold, heat, and UV radiation tolerance (1-45). Among Cannabis hemp products for skin care, Cannabidiol (CBD) oil with high therapeutic potential and without undesirable psychotropic effects has been extracted from leaves (1-45). The most important phytocannabinoids possess therapeutic, antibacterial, and **antimicrobial** properties (1-45). The stalks, seeds, and leaves of hemp are converted into various construction materials, textiles, paper, food, furniture, cosmetics, healthcare products (1-36). **Nutraceutical-** and health-product-based markets are about to grow in the coming years, owing to the increasing awareness about health among end-users (1-50). Several food manufacturing processes make use of hemp seeds and oil, which is expected to propel hemp market growth (1-45). Hemp seed is composed of a white kernel and brown hull (1-45). The kernel is rich in protein, unsaturated fatty acid, and dietary fibre (1-50). Hemp protein is considered as a novel emulsifier in food systems (1-45). The

high nutritional values and beneficial fatty acid and protein profile of industrial hemp (fibre type) are driving the demand for hemp products (1-45). Hemp plant shares a unique high-protein, low-carbohydrate nutritional composition with soybean, distinctively different from other functional food materials such as rice and wheat in the protein/carbohydrate (%, w/w) content (1-45). Hemp and soy are also rich in dietary fiber and unsaturated fatty acids. Hemp oil is popular and the hemp oil meal is a by-product of oil processing, and is utilized in many protein-rich foods as well as animal feeds (1-45).

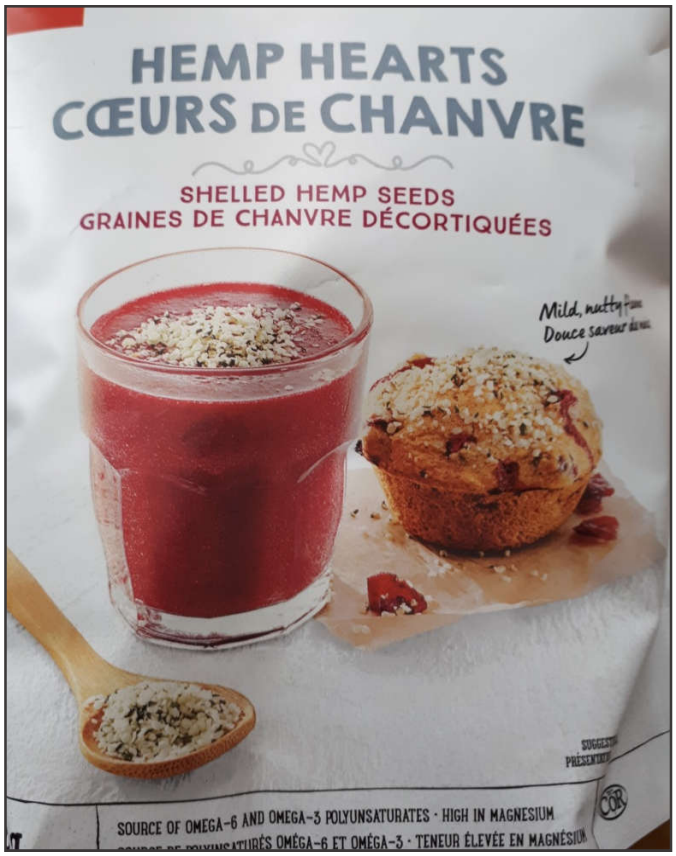

Figure-5: The shelled Hemp hearts ready for the consumption

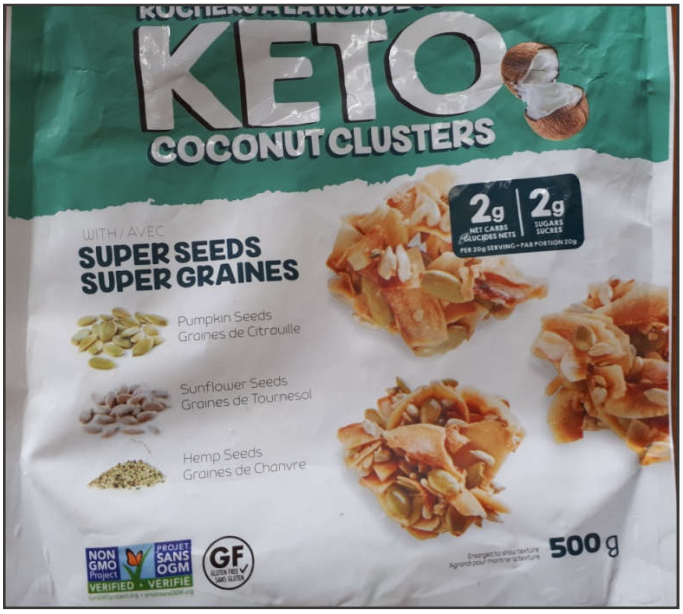

Figure-6: The combination of shelled Hemp seeds, pumpkin, and sunflower seeds ready for the consumption

Hemp seeds (**Figure-4, 5, 6**) are high in protein, low-carbohydrate, and rich in dietary fiber and unsaturated fatty acids (1-35). **Hemp seeds are rich in protein** content and majorly used as birdseed and animal feed (1-40). The bird and fish feed are important markets for hemp seeds in animal nutrition (1-39). **Fish and birds need fatty acids** with a high share of **Omega-3 and Omega-6** fatty acids for optimum development (1-45). Hemp seed is a balanced health product with bioactive components that have the capacity to aid health beyond that of basic nutrition (Grand View Research Inc., 201, San Franscico, CA, USA. Grand View Research Inc Report) (1-45).

The major protein in hemp kernel is **Edestin**, accounting for around 70% of hemp protein (1-45). Edestin is a hexamer of identical subunits and belongs to the globulin family (1-35). An Edestin subunit has five cysteine residues, two of which form a single intermolecular disulfide bond between basic and acidic subunits (1-45). **Edestin** is less soluble in water or buffer with neutral or acidic pH, but soluble in a basic buffer (1-35). Despite its less solubility, **Edestin** is known for its high digestibility (1-45). The second major hemp protein is **Albumin**, which has fewer disulfide bonds compared to Edestin (globulin), thus having a flexible structure with higher protein solubility and foaming capacity (1-35). It consists of two subunits made of 27 and 61 amino acid residues, respectively, which are held together by two intermolecular disulfide bonds (1-39). In vitro digestion tests demonstrated that hemp protein has a high degree of digestibility (1-45). Moreover, most hemp allergens, such as the major thaumatin-like protein and lipid transfer protein, were eliminated in the protein-isolation or digestion processes (1-45). Hemp protein is also usable as an ingredient for hypoallergenic foods (1-45). Hemp protein has a unique feature in view of the disulfide structure. It shows much higher free sulfhydryl content than soy protein (1-40). Thus, hemp protein with a high free SH content should have unexplored unique processing characteristics (1-45).

The major constituents of hemp seed include easily digestible protein (20–25%), **Polyunsaturated Fatty Acid (PUFA**), abundant lipids (25–35%), and carbohydrates (20–30%) high in insoluble fiber (1-45). Hemp seed protein is well-suited for human and animal consumption, consisting mainly of high-quality, easily digestible proteins **Edestin,** and **albumin**, which are abundant with essential amino acids (1-45). The rich source of **PUFA, Linoleic acid** (LA; Omega-6) and **Alpha-Linolenic Acid** (ALA; Omega-3), is favorable and regarded as balanced for human nutrition at a ratio of 3:1 (1-51). Nutritional recommendations indicated that 15–20% of daily caloric intake should come from fats, and approximately one-third of these fats should be essential fatty acids in a 3:1 ratio (1-51). It is estimated that this dietary goal can be met with three tablespoons of **hemp seed oil** (1-41). Numerous health benefits and potential therapies are reported for hemp seed. Hemp seed delivers a desirable ratio of **Omega-6 to Omega-3 PUFA**, which can improve **cardiovascular health, reduce osteoporosis symptoms, and diminish eczema** conditions (1-51). Cannabidiol (CBD) exerts pharmacological properties that make it a potential therapeutic agent for central nervous system diseases, such as epilepsy, neurodegenerative diseases, and multiple sclerosis (1-21). The **hemp seeds and sprouts** to be rich in beneficial bioactive compounds with both in vitro and ex vivo antioxidant activities (1-44). **Hemp fiber meal** can be used for isolation of essential amino acids, especially **Arginine**, by using food grade enzymes for polysaccharide digestion (1-50). The resulting polysaccharide fragments can be subjected to ultra-filtration and removed to concentrate the protein content, making it a superior isolate compared to other hemp protein products (1-45) The **rising concerns related to skin diseases and UV** protection are expected to drive the demand for hemp oil in the personal care industry in the region (1-24). In Europe, the product is majorly consumed in **automotive parts, construction materials, textiles, and fabrics** in the form of **fibers** (1-50).

The **hemp seeds** (Figure-4, 5, 6) **and sprouts** to be rich in beneficial bioactive compounds with both in vitro and ex vivo

antioxidant activities (1-54). Furthermore, these compounds exhibited an antimutagenic effect on Saccharomyces cerevisiae (1-45). The main polyphenols identified in hemp seeds and sprouts exhibiting antioxidant activities were **Cannabisin A, B, C**, and **Caffeoyltyramine** (1-50). The two primary compounds identified in sprouts that provide nutraceutical benefits were **Linoleic acid** and **Gluconic acids**, which act as intermediaries in the production of **vitamin C** (1-41). **Terpenes**, which are also found in hemp, have **anti-inflammatory** and some antiallergic properties, can treat pain, prevent the production of ROS, and act as potent antioxidants (1-51). Due to the presence of a wide variety of nutrients, including high levels of PUFA and essential amino acids, hemp seeds are praised for providing adequate quantities of different nutrients to satisfy human dietary requirements (1-50).

Cannabis sativa Hemp oil is widely used in the manufacturing of food and beverages on account of its high nutritional content, including fatty acids, proteins, and several other ingredients (1-45). **Hemp seed oil** contains **tocopherol isomers beta-tocopherol, gamma-tocopherol**, alpha-tocopherol, and delta-tocopherol, with the gamma-tocopherol derivative present in the highest quantity (1-50). **Tocopherols** are natural antioxidants that can reduce the risk of oxidative degeneration related disorders (1-35). In addition, terpenes and polyphenols have been detected, which contribute to the odor/flavor and intrinsic antioxidant activity, respectively (1-25). Among phenolic compounds, **flavonoids,** such as **flavanones**, flavonols, flavanols, and isoflavones were the most abundant (1-50).

Increasing demand for **plant-based milk** has enlarged its industry due to lactose intolerance, cow's milk allergy, and vegan lifestyles (1-40). **Hemp milk**, with its highly nutritional value and low allergenicity, looks to be an attractive alternative to dairy, soy, and nut milks (1-50). Comparison of milk products in the market reveals hemp milk as a better source of minerals than other dairy and plant milks (1-35). Hemp milk does not taste that different but has a "nuttier" flavor in comparison to soy or rice milk (1-47). High pressure homogenization following pH adjustment realized non- thermally processed hemp milk, which is remarkably stable, showing negligible phase separation in storage for 3 days at 4^{o}C (1-45). Hemp is one of the ideal food materials because of its high protein content, low content of saturated fats, and high content of unsaturated fatty acids such as ω3 and ω 6 (1-30). Addition of hemp protein concentrate significantly improved the nutritional value of the starch-based gluten-free bread (1-45). Hemp also changed the rheological characteristics of the gluten-free dough and reinforced the structure (1-45). Moreover, sensory acceptance on color and flavour was confirmed for the bread. Limited amylopectin recrystallization as well as limited hardening of the crumb were observed during storage (1-35). Demand for high quality vegan meat made of plant materials is increasing based on the shortage of animal stock due to the global increase of human population, as well as in view of animal welfare (1-45). Hemp cake, a residual material of oil expression from the hemp seed has long been utilized for livestock feeds (1-45). It is a highly nutritive as well as sustainable feed stuff for cows, quails, cockerels, pigs, and broilers. Now, research is in progress to utilize hemp protein "directly" as a material for plant meat (1-50).

Hemp is usable as both a fiber and food material (1-50, 66-68). Cotton is used mostly for fiber production, while soybean for food processing (1-30). As all seeds are available for oil expression, and the hemp residues are utilized as a highly nutritional food material (hemp and soybean) or for fiber production (hemp and cotton), they are all deemed sustainable (1-45). However, as hemp is more sustainable than cotton or soybean in view of cultivation and utility was marked only for hemp in the sustainability row (1-45). After the expression of oil from seeds, the residual mass is a useful protein-rich material for food processing (1-47). Moreover, hemp seed protein has distinctive characteristics suitable for developing new foods such as an emulsifier, plant-based meat, and gas-retaining membrane (1-45). The cysteine-rich protein feature realizes unique disulfide-mediated interactions with protein from other sources and is thus expected to facilitate development of new food materials (1-45). Meanwhile, hemp protein is reported to be less soluble, and a higher temperature is needed for processing compared to other plant protein (1-45). Therefore, suitable reaction conditions should be investigated for future application in the food industry. Further scientific understanding will facilitate expanded the use of this less-investigated protein compared to soy protein (1-46).

Industrial hemp (fiber type) seeds or oil contain an amino acid known as **Arginine** which is extremely **good for heart** as it dilates and relaxes blood vessels (1-45). Hemp oil fights **inflammation, lowers blood pressure**, and hence helps to prevent the formation of **blood clots** (1-57). Hemp seeds are a good source of **Gamma-linolenic acid** (GLA), which is known for its strong **anti-inflammatory** properties (1-35). Foods rich in **Gamma-linolenic acid** (GLA), are extensively used to fight inflammation in the joints (arthritis), **nerve damage**, and inflamed skin conditions such as **acne,** and **eczema** (1-45**).** Hemp seed oil is currently advertised primarily as a natural health product for body care purposes, as oil for **salad dressings**, or to be taken directly as a **dietary supplement** (1-50). The hemp seed oil has a strong susceptibility to rancidity with heat and prolonged storage, which reduces its use as cooking oil (1-45). Evidence suggests that phyto-, endo-, and synthetic cannabinoids contain properties that aid in the treatment of **the brain, prostate, breast, skin, pancreas**, and **colon cancer** (1-45). Furthermore, supplemented the human diet with 30 mL of hemp seed oil daily for four weeks has detected positive changes in the serum lipid profile (1-45). Cannabinoids have also been found to prevent the differentiation and proliferation of **glioma stem-like cells**, which may help to treat the difficult-to-eliminate nature of gliomas (1-45).

Of several natural Cannabinoids tested, a Cannabinoids (CBD) extract provided the most potent **cytotoxic effects** against breast cancer cells, with significantly lower damage to healthy cells (1-60). Cannabinoids (CBD) induced apoptosis in a breast cancer cell line via the activation of the overexpressed CB2 receptor (1-51). Other studies have explored **Cannabinoid therapy in skin, pancreas, and colon cancers** (1-61). In a traditional **Indian folk medicine**, hemp seed oil has been used to relieve chronic knee pain in patients with rheumatoid arthritis (RA) and improved blood circulation (1-45). Experimental evidences concluded that hemp seed oil promotes the production of **Reactive oxygen species** (ROS), storage of lipids, production of endoplasmic reticulum stress markers, which act as **anti-rheumatoid** factors in downstream processes, and improved blood circulation, providing additional relief to RA patients (1-55). A **Cannabinoids (CBD**)-based oil was used to treat another kind of Arhritis: **Steoarthritis** in **dog**s (1-61). Hemp seed oil can be an effective cure to eczema, as well as a host of other skin related ailments (1-41). Hemp seed oil is composed of more than **80% PUFA** (**polyunsaturated fatty acid**) and is rich in **tocopherols** (1-51). These constituents point to hemp seed oil's beneficial effects in reducing and eradicating skin diseases, including **eczema (1-50).**

CONCLUSION

Cannabis sativa (Hemp) is a multi-purpose crop, which is widely used for the production of biomaterials such as textile, paper, construction, and insulation materials, but also as functional foods, namely the oil and seeds, other applications including cosmetics, personal care products, and in the pharmaceutical industry. Cannabis sativa L., popularly known as Cannabis is classified as hemp or marijuana based on its THC content. Legal restrictions in the last decades in India and other parts of world have prevented the progress

of academic research involving Cannabis sativa L. (Hemp). These conditions have resulted in a scarcity of science based information on Cannabis sativa L. (Hemp). International narcotic conventions and associated legislation have constrained the establishment, characterization, and use of Cannabis genetic resource collections. This has resulted in the underutilization of genepool variability in cultivar development. Prohibitionist legislation has discouraged scientists from studying Cannabis production, the main factor responsible for the current lack of research on Cannabis. In several countries, legislation is changing due to recognition of the medicinal and agricultural value of Cannabis plants. Among hemp products, Cannabidiol (CBD) has the greatest market potential and is highly attractive for its recreational and medical potentials. The main characteristic of Cannabis sativa L. is the production of compounds of pharmaceutical interest known as phytocannabinoids.

Cannabis is a herbaceous, annual, dioecious species that can produce monoecious plants. Morphologically, the inflorescences of male dioecious plants are characterized by hanging panicles with few or no leaves, and inflorescences of female plants bear racemes with leafy bracts. Female plants have the highest phytocannabinoid production due to a higher density of glandular trichomes, where phytocannabinoid are synthesized and stored. In addition, male and hermaphroditic plants have reduced floral biomass and, thus, reduced phytocannabinoid yield. Additionally, the fibers produced by hemp plants grown for the production of phytocannabinoids can be used as raw material for several industries. Hemp plant shares a unique high-protein, low-carbohydrate nutritional composition with soybean, distinctively different from other functional food materials such as rice and wheat in the protein/carbohydrate (%, w/w) content. Hemp seeds are high in protein, low-carbohydrate, and rich in dietary fiber and unsaturated fatty acids. Conclusively, hemp is a suitable plant with versatile utility. The hemp seeds and the protein are expected to be promising food materials in the food industry.

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