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HEMP SEED OIL FOR SKIN CARE (NON-DRUG CANNABIS SATIVA L.): A REVIEW

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ABSTRACT

Cannabis sativa L. is a quick growing, annual herb with a multitude of uses covering a range of products derived from fibre or oilseed that have been known throughout history. Cannabis sativa L. is a dioecious plant of the Cannabaceae family and it is widely distributed all over the world. The interest in hemp (non-drug Cannabis sativa L.) for skin care and cosmetic use is due to its high oil content, especially unsaturated fatty acids in seed with its therapeutic effects. The composition of fatty acid in hemp seed oil closely resembles the skin's natural lipids, so when applied topically it replenishes the skin, works as an anti-inflammatory and compensates partially for lower ceramide levels in the skin; thus increasing moisture retention and reducing the appearance of aging or skin inflamation. There are many essential fatty acids and nutrients present in Hempseed oil which help in the formation of keratin. Keratin is the key protein of hair and is responsible for its structural integrity. The high performance moisturizing emollients in hemp seed oil make it an ideal ingredient for both dryness and scalp conditions.

KEYWORDS: Cannabis, Hemp seed oil, CBD, THS, Flavonoids, Tannins.

INTRODUCTION

The term Hemp is used to classify varieties of Cannabis that contain 0.3% or less THC(delta-9-tetrahydrocannabinol).The term marijuana is used to classify varieties of Cannabis that contain more than 0.3% THC and can induce psychotropic or euphoric effects on the users. Hemp is legal, marijuana is not. In addition to its recreational use as a drug of abuse, the plant has widespread alternative uses including the production of food, cosmetics (hemp), textiles and medicinal applications.[1] Now a days the intrigue in hemp (non-drug category) for skin

care and cosmetic has gained popularity as people are getting aware of its restorative and curative effects. The high content of unsaturated fatty acids results in the therapeutic properties of hemp seed oil.[2]

Figure 1: Hemp seed oil.[3]

It is obtained from the seeds of Cannabis sativa L. and is known for its nutritive, health-enhancing properties and bioactivity.[4] Cannabis seed oil is a clear yellow liquid. The seeds contain approximately 29 per cent to 34 percent of oil by weight.[5]

History of hemp

The historical usage of Cannabis sativa L. has been controversial. Cannabis sativa can be classified into drug type (marijuana) and nondrug type (hemp). The former is generally applied for medicinal and recreational purposes, whereas the latter is important for food and fiber industries. Cultivation of hemp reached its peak between late 19th century and early 20th century, when it was utilized as a raw material for drying oil in painting industry, textile clothing, and fuel. Nevertheless, prohibition of all Cannabis varieties under the Marijuana Tax Act 1937 effectively halted cultivation of commercial hemp in most parts of the world. The U.S. government briefly lifted the sanction on hemp during the World War II. By then, hemp has been replaced by other oil seeds and synthetic materials, such as cotton and flaxseed, which dominated the markets i.e. textile and painting. Over the past 20 years, there is a resurrection of interest for hempseed due to its nutritional and pharmaceutical value. Australia, Canada, and most recently The United States have legalized the cultivation of hemp seed at low tetrahydrocannabinol (THC) levels (<0.3% w/w).[6]

Indian history

In India, Cannabis has a long history. The preliminary mention of Cannabis has been found in The Vedas, or sacred Hindu texts. In the late 1890s, a large scale study was commissioned by The Britishers who found the use of Cannabis so extensive in colonial India. They were concerned that the abuse of Cannabis was endangering the health of the native people and

driving them unstable. The British government asked the government of India to appoint a commission to look into the cultivation of the hemp plant, preparation of drugs from it and trade in those drugs. They were also asked to see the social and moral impact of its consumption, and possible prohibition.[7] In 1961, under America's pressure in a UN convention, it was declared and put into the synthetic drug category, and the Indian government banned it in America's pressure. But years later, the American government legalised Cannabis.[8] In India the central law that deals with Cannabis (marijuana or weed) is the Narcotic Drugs and Psychotropic Substances Act, 1985.[1] Nonetheless, different states have their own laws relating to consumption, possession, sale or purchase of weed or marijuana. Possession of these drugs is considered a criminal act in India, and can get you in serious legal trouble. But some states have their own rules and laws regarding to Cannabis. In Odisha, weed is legal and Uttarakhand has become the first state in India to allow commercial cultivation of Hemp.[9]

WHAT IS HEMP SEED OIL?

Hemp, (Cannabis sativa) also called as industrial hemp, is a plant of the family Cannabaceae. The non-drug hemp is cultivated for its fibre, consumer textile, industrial applications, food, medicines and personal care. Sometimes hemp is confused with the Cannabis plants that serve as sources of the drug marijuana and the drug preparation hashish. Although all three products—hemp, marijuana, and hashish—contain tetrahydrocannabinol (THC), a compound that produces psychoactive effects in humans, the variety of Cannabis cultivated for hemp has only small amounts of THC relative to that grown for the production of marijuana or hashish. [10] Hemp seed oil comes from extraction of the seeds of the plant Cannabis sativa. Hemp seed oil is a rich source of fatty acids, proteins, and other essential nutrients which are used in pharmacological as well as cosmeceutical preparations.[4]

Table 1: Difference between hemp seed oil and CBD oil.[11-15]

Hemp seed oil	CBD oil
Extracted only from hemp seeds	Extracted from whole hemp plant (leaves, stalks, buds, flowers)
No THC (tetrahydrocannabinol)	Low in THC (tetrahydrocannabinol) (>0.3% THC)
Non psychoactive effect	If exceeds 0.3% in quantity, psychoactive.
Cold press extraction	Supercritical, CO2 extraction.
Used for cooking, skin care	Primarily used for medicinal purpose

*CBD- responsible for many of the therapeutic effects.

*THC- responsible for the way your brain and body responds to Cannabis, including high intoxication.

Figure 2: Hemp leaves.[16]

Figure 3: Hemp seeds[17]

Table 2: Botanical description.[18][19]

Kingdom	Plantae
Sub-kingdom	Tracheobionta
Superdivision	Spermatophyta
Class	Magnoliophyta
Sub-class	Hamamelidae
Order	Urticales
Family	Cannabaceae
Genus	Cannabis
Species	Sativa
Synonyms	Cannabis Indica, Indian hemp, Weed, Ganja, Marijuana, Charas, Hashish etc.

GEOGRAPHICAL DISTRIBUTION

Originally, Cannabis sativa was a native of Western and Central Asia. It has been cultivated since ancient times in Asia and Europe. In India, cultivation of this plant is controlled and permitted only in the districts of Almora, Garhwal and Nainital (Uttarakhand) with small extent in Kashmir and Travancore.[18] The plant grows wild in the following states like Assam, Bihar, Uttar Pradesh, Punjab, West Bengal, Jammu & Kashmir, Rajasthan

Travancore-Cochin, Himachal Pradesh, Manipur and Tripura.[20] Industrial hemp flourishes in temperate climates and can be found in Europe, the Balkan countries including Turkey and Romania, China, Japan, Chile and Canada, Sweden and Australia.[21]

MORPHOLOGICAL CHARACTERISTICS

Cannabis sativa is an annual, dioecious (i.e., male and female flowers are found on separate plants) pollinated plants with strong taproot and erect stem. The stems are usually angular, furrowed, branched, with woody interior, sometimes hollow in the internodes, and vary from 1 to 6 m in height. The branching is either opposite or alternate.[22]

MACROSCOPICAL FEATURES

Roots- Advantageous, branched taproot, 30–60 cm deep, up to 2.5 m in loose soil, more branched in wet soils.[22]

Leaves- Green, palmate (seven lobes), size and shape of the leaflets differ markedly, (according to genetic origin), alternate/opposite/spiral arrangement, 6–11 cm length and 2–15 mm width.[22]

Fruits- One seeded, hard shell tightly covered by the thin wall of the ovary, ovate-lanceolate bract,[19] achene, ellipsoid seed, slightly compressed, smooth, about 2–5 mm long, generally brownish and mottled Seed.[22]

Inflorescences- Numerous flower heads, found on long leafy stems, five pale-green sepals on the staminates, about 2.5–4 mm long, five pendulous stamens, slender filaments and stamen, sessile pistillate in pairs.[22]

MICROSCOPICAL FEATURES

Cannabis trichomes comprise a diverse set of structures and different types of trichomes (e.g., glandular and non-glandular) on a single leaf, when viewed through a hand lens. Three types of glandular trichomes have been described on female plants, namely bulbous, sessile, and capitate stalked. Male plants have been found to exhibit a fourth type—the antherial glandular trichome, which has only been found on anthers. Glandular trichomes are made from a series of differentiated cells with different functional properties, namely the secretory cells, and stalk cells.[22]

CHARACTERISTICS

Odour: strong and characteristic[19] Taste: acrid and pungent[19] Appearance: Clear bright oily liquid[23] Acid value: ≤1.0 mg KOH/g[23] Peroxide Index: ≤10 meq O2/Kg oil[23] Refractive Index: 1.461-1.481[23] Solubility: insoluble in water, soluble in alcohol, ether, benzene and other organic solvents.[6]

Table 3: Chemical Constituents.[1, 6][24-33]

Chemical constituent	Examples	Percentage (%)	No. of constituents
Carbohydrates			
1.Monosacharides	1.Fructose, glucose, arabinose, mannose, rhamnose, galactose, etc.		13
2.Disacharides	2.Sucrose, maltose		2
3.Polysaccharides	3.Raffinose, cellulose, hemicellulose, pectin, xylan	20-30%	5
4.Sugar alcohol and cyclitols	4.Mannitol, sorbitol, glycerol, inositol, quebrachitol, ect.		12
5.Amino sugar	5.Galactosamine, flucosamine		2
Lipids		20-25%	
Proteins	Albumin Edestin Lysine Leucine Tryptophan	20-30%	Less than one, but higher than 0.5.
Flavonoids			
1.Flavones and flavonols	1.Apigenin, luteolin, quercetin, and kaempferol		
2. Flavonoid glycosides	2. Orientin, vitexin, luteolin-7-O-glucoside, apigenin-7-O-glucoside		20
3. Cannflavins A and B.			
Phenols			
1.Spiroindan type structure	1.Dannabispiran, isocannabispiran		9
2. Dihydro Stilbenes	2. Cannabis Stilbene -I, -II		9
3.Dihydrophenanthrene	3. Cannithrene-1, -2		3
4. Phenolic glycosides	4. Phloroglucinol glucoside		

Fatty acids 1.Saturated fatty acids	 Palmitic acid Stearic acid Arachidic acid Behenic acid	 6-9% 2-3.5% 1-3% 0.2%	
2.Unsaturated fatty acids	Linoleic acid (omega-6) alpha linolenic acid (0mega-3) Oleic acid (omega-9) γ-linolenic acid stearidonic acid	53-60% 15-25% 8.5-16% 1-4% 0.4-2%	
3. Monounsaturated Fatty Acids	Oleic acid Eicosenoic acid	11% 0.8%	
Ketones	Acetone, heptanone-2, 2methyl-2-hepten-6-one		13
Alcohol	Methanol ethanol 1-octene-3-ol		7
Aldehyde	Acetaldehyde, Isobutyraldehyde Pentanal		12
Tocopherols	Gamma tocopherol Delta tocopherol		
Tannins		1.36% – 2.14 %	
Cannabinoids	Cannabidiol (CBD) Tetrahydrocannabinol(THC) Cannabinol (CBN)	4.18 to 243.68 mg/Kg. 3.04 to 69.50 mg/Kg. 1.85 to 8.44 mg/Kg.	
Saponins		69.0 mg/Kg	
Terpenes	β-caryophyllene myrcene, Cycloartenol β-amyrin, Dammaradienol	3.0%- 5.0%	
Vitamins and minerals	Vitamin-E (Alphatocopherol) gamma tocopherol Thiamine Riboflavin Phosphorus	5% 85% 2-5.3%	90

	Potassium Magnesium Calcium Iron Sodium Manganese Zinc Copper Vitamin A Carotene		

EXTRACTION METHODS

Cold press method

Cold-pressed oil does not utilize an organic solvent nor heated to extract oil and therefore retains its beneficial bioactive compounds including natural antioxidants and being free of chemical contamination as what would occur with solvent extraction. The dark greenish colour of hemp seed oil is from the high chlorophyll content present. The presence of antioxidants and other molecules that stabilize cold-pressed oils give them a long shelf life stability. The oil recovered from the first fractions, or first press is called "Virgin oil" and is of the best quality.[34]

Steam Distillation

The technique of Steam distillation has been used for centuries to extract essential oil from plant material. It's a very simple concept that uses heat in the form of steam to separate the essential oil from the plant material. In this technique, a container with water is put on a burner. It will have an outlet that feeds into a plant material (hemp seed) flask. The flask which contains the plant material have an inlet and an outlet. As the steam rises from the container through the plant material i.e. the hemp seeds, essential oil vapours are released. The essential oil vapours are then collected in a condenser tube that condenses the vapours into a hydrosol. This hydrosol is a mixture of water and essential oil. Thereafter the oil is collected from the hydrosol.[35]

Solvent Extraction

The process of Solvent extraction is a step above steam distillation both in efficiency and complexity. Instead of using steam to extract the essential oils from the seeds, solvents are used. The solvents react with the seeds causing the essential oils to be removed from the plants and mix with the solvent. Traditionally, alcohol has been used to extract essential oils from plant materials. Hemp seeds are put in an alcohol mixture and allowed to extract. The hemp seed extract is then made into hemp seed oil by evaporating the alcohol.[36]

Soxhlet extraction

The seeds were placed in a paper thimble and placed in a Soxhlet apparatus with a round-bottom flask. Then methanol was added and used for 8 hour extraction at 90◦C. The temperature of the cooling bath used in the condenser is to be set at 15◦C. The extract was filtered and quantitatively adjusted after it is cooled.[37]

Hexane extraction

Hemp seed oil can also be extracted by hexane extraction, which is the most effective oil extracting agent. In this process the dried seeds were ground and soaked with three volumes of hexane for 24 hours while stirring. The extract was filtered and the extraction procedure was repeated twice with residue. Then the solvent was evaporated.[38]

Heat Reflux Extraction

The sample was placed in paper thimble in a round bottom flask and boiled at 90◦C for 4 h. The temperature of the cooling bath used in the condenser was set at 15 ◦C. After cooling, the extract was filtered and quantitatively adjusted accordingly.[37]

Supercritical Fluid Extraction

With CO2 extraction also known as Supercritical Fluid Extraction, the plant matter is added to a pressure chamber and filled with CO2. The CO2 pressure permeates the hemp plant and breaks down the inert plant material, leaving behind the cannabinoid-dense oil. The oil is then collected and the CO2 evaporates out of the chamber.[25] The CO2 extraction process starts with pure carbon dioxide being injected into a container with the plant material (hemp seed oil). As the pressure rises in the container, the carbon dioxide turns into a nearly liquid phase. This is called supercritical CO2. Some heat is then added at this point to help the liquefied carbon dioxide release the essential oils and aromatics from the plant material. As it is extracted, the vapours and aromatics are carried away to a separator phase. The separator separates the aromatics from the carbon dioxide solvent mixture. This essential oil is pure and is very high quality.[37]

PHARMACOLOGICAL USES

Antioxidant

Hemp seed oil is high in antioxidant constituents. Fatty acids like γ -linolenic acid (GLA), and vitamins A, C, and E are present in hemp seed oil. Skincare products containing

Antioxidants may help in giving your skin some protection against premature aging.[39] The endocannabinoid system is a key molecular system accountable for controlling homeostasis and is becoming an increasingly popular target of pharmacotherapy. The endocannabinoids are ester, ether, and amide derivatives of long chain polyunsaturated fatty acids (PUFAs), such as arachidonic acid, and they act mainly as cannabinoid receptor ligands. They belong to a large group of compounds with a similar structure and biological activity called cannabinoids. The Cannabinoids are chemical derivatives of dibenzopyrene or monoterpenoid. The most important of these are Δ9-tetrahydrocannabinol (Δ9-THC), Δ8-tetrahydrocannabinol (Δ8-THC), cannabinol (CBN), and cannabidiol (CBD), and they are members of a large group of biologically active compounds found in Cannabis sativa L.[40] The medical use of cannabinoids, in particular phytocannabinoids, has been one of the most interesting approaches to pharmacotherapy in recent years. One of the main pharmacologically active phytocannabinoids is CBD. It is non-psychoactive, but has many beneficial pharmacological effects, including anti-inflammatory and antioxidant effects.[41]

Antibacterial

Tannins present in Hemp oil are known to have antibacterial properties.[42] The antibacterial property is mainly contributed from Δ9-THC and CBD.[39] There are three source of cannabinoids of which, some are plant derived which are known as phytocannabinoids like CBD obtained from hemp plant, others are known as endocannabinoids which are endogenous cannabinoids which are produce in the body. Whereas there are other synthetic cannabinoids which can be developed in laboratory. Cannabinoids are basically the group of C21 compounds that are present in the hemp which are in the carboxylic acid form. These compounds are similar to Δ9 –THC, structurally or pharmacologically that can bind cannabinoids receptors. There are 86 known cannabinoids obtained from hemp plant and are classified into 11 structural type cannabidiol (CBD), cannabinol (CBN), Δ9 -THC, cannabigerol (CBG), cannabichromene (CBC), cannabinodiol (CBND), cannabicyclol (CBL), cannabielsoin (CBE), cannabitriol (CBT), Δ8 -THC, and others. Out of which, first three are most prevalent cannabinoids. Some of the cannabinoids from hemp extract have excellent antibacterial activity.[43]

Muscle tension and Pain relief

Many people use hemp oil as a form of natural pain relief. Rubbing a bit of hemp seed oil into tight muscles may help release tension and relax them.[44] α-Linolic acid is known to

soothe joint pain and ease stiffness to improve flexibility.[32] Cannabinoids are divided into three groups. First naturally occurring 21 carbon terpenophenolic compounds which are found in plant of Cannabis genus and are termed as phytocannabinoids and best known analgesic of these is THC.[45] The efficacy of transdermal CBD study was also done which showed the reduction in the inflammation associated symptoms in adjuvant induced monoarthritic animals, it showed the reduction in inflammation and also in secretions of pro inflammatory along with matrix degrading effector molecules by synovial cell connective tissue membrane lining joints which is important for rheumatoid arthritis.[46]

Psoriasis

The autoimmune inflammatory disorder Psoriasis can affect the skin and epidermal proliferation associated with it because of the dysregulation of immune system and pro inflammatory cytokines which also include the production of TNF-α, IL 12 and 23, along with this an inflammatory milieu is also developed and maintained with the cells like keratinocytes, T-helper cells 1 and 17, dendritic cells along with various types of immune cells. Study reveals that the Phytocannabinoids can be used in the positive treatment for the psoriasis as it is capable of inhibiting proliferation of keratinocytes and also able to modulate the inflammatory component associated with it.[47] Along with phytocannabionoids, Cannabinoids that are obtained from Cannabis (Cannabis Sativa) are known to have an anti-inflammatory properties and are known to have an inhibitory effect on various tumorigenic cell proliferation some of these are also known to mediated by cannabinoids receptors. As cannabinoids are known to inhibit keratinocyte proliferation, we can say that cannabinoids have the potential role in the treatment of psoriasis.[48] Thus, Hemp seed oil can help in treating psoriasis, according to several studies this might be largely due to the oil being made almost entirely of essential fatty acids, more than 75 percent omega-3 and omega-6.[49]

Lichen planus

Hemp seed oil constitutes Omega-3 which helps in treating Lichen planus. It is a condition in which the skin feels itchy and bumpy and causes swelling and irritation.[49] CBD can regulate the immune response as it works indirectly on the CB2 receptors and aids to alleviate skin flare- ups and various allergies. As CBD attaches to the CB2 receptors of the disturbed immune cells, it triggers an anti-inflammatory protein known as caspase which transmits a signal which initiates the process of cell death (apoptosis) of the immune cell. With the perishing of the immune cells through caspase stimulation, there occurs a lowering of the

inflammatory process as well as cytokines that are pro-inflammatory cells. This aids in controlling the skin rashes that are proliferated by the inflammation.[50]

COSMETIC USES

Moisturizing and Inflammation soothening

The biggest and most well-verified benefit that hemp seed oil can deliver is said to be moisturization. Hemp seed oil has emollient properties and leaves the skin feeling soft and supple.[39] One of the omega-6 fatty acids present in hemp oil is γ linolenic acid (GLA), which acts as a powerful anti-inflammatory agent while simultaneously encouraging new cell generation. This can help to calm inflammation and irritation on the skin, including acne and some conditions like psoriasis, while keeping the skin nourished and moisturized.[51] Hemp oil contains flavonoids that have anti-inflammatory properties, it may help relieve skin inflammation. Cannaflavin A found in Cannabis has beneficial effects for anti-inflammation.[52] Cannaflavin A and Cannaflavin B were isolated from the cannabinoid free ethanolic extract of Cannabis sativa L. effectively inhibited PEG-2, a prostaglandin responsible for inflammation.[53] Cannaflavin A, B and C have anti-inflammatory activity due the fact that they inhibit the prostaglandins inflammatory pathway. This mechanism is shared with other terpenoids which are present in the Cannabis plant, providing a better synergy and anti- inflammatory effect.[54]

Eczema or Atopic dermatitis

Application of hemp oil can help to treat skin conditions like atopic dermatitis. Vitamin E and Carotene helps in maintaining healthy skin.[55] Allergic contact dermatitis (ACD) is a type IV delayed hypersensitivity reaction developing as an immune response to an allergen, mediated by T cells and various cytokines and chemokines. CBD suppresses the inflammatory reaction of allergic contact dermatitis in vitro, without cytotoxic effects. Thus, CBD reduced inflammation in polyinosinic-polycytidylic acid-induced ACD in human keratinocyte (HaCaT) cells, by inhibiting the monocyte chemotactic protein-2 (MCP-2) chemokine and several pro- inflammatory cytokines, such as interleukins (ILs) 6 and 8, and TNF-α.[56] Part of what makes hemp seed oil so beneficial to the skin is that it’s rich in omega-6 and omega-3 fatty acids.[52]

Anti-aging properties

In addition to moisturizing and soothing of the skin, hemp seed oil also has anti-aging properties. Fine lines, wrinkles and other signs of aging can also be prevented by application

of hemp seed oil. The linoleic acid and oleic acids found in hemp oil can't be produced by the body but can play a crucial role in skin health and anti-aging.[51] Hemp oil showcases the largest supply of vitamins A, C and E3. These chemicals are crucial for preventing cell damage by radicals and reactive oxygen species. During skin disorders, discoloration of the skin is often seen. This is a result of excessive cell death. The antioxidants in hemp seed oil help accelerate cell growth and provide faster recovery of healthy looking skin. Hemp oil promotes the synthesis of collagen (protein which is responsible for maintaining smooth and elastic skin).[57]

Acne

The fatty acids present in hemp seed oil may help in balancing the skin and prevent inflammation that can result in acne. In other hand, the CBD oil may affect the sebum glands in people with chronic acne, leading to reduced sebum production and potentially helping clear the skin or prevent acne breakouts.[44] Inflammation of keratinocytes is caused by P. acne which is responsible for the TLRs activation and also the secretion of cytokines and chemokines like TNF-α, IL-1β, and IL-8 via the inflammatory enzymes expression. TLRs also activates MAPK signalling processes and NF-kB and enters the nucleus, which also include comprising of gene transcription involved in inflammatory responses. When the excess sebum is produced, P. acne can grow rapidly and in turn activate inflammation by increasing the level of inflammatory molecules like COX-2, iNOS, and proinflammatory cytokines. The hexane extract of hemp showed antimicrobial activity against P. acne.[38] Hemp seed hexane extracts used in the study contained high level polyunsaturated fatty acids which includes linoleic acid, cis-11-eicosenoic acid, oleic acid, and palmitic acid, γ-linolenic acid, palmitoleic acid, arachidic acid, and heneicosanoic acid in this investigation. Linoleic acid mostly known to be a significant constituent of the extracellular lipid matrix of stratum corneum. Thus, we can say Linoleic acid deficiency can increase the sebum content of acne-prone skin. Linoleic acid and γ-linolenic acid known to have anti-inflammatory and anti-microbial properties, and can inhibit inflammatory responses by inactivation of NFκB and AP-1 and thus we can say that the major components of HSHE, which includes linoleic acid and γ-linolenic acid, might be responsible for the improvement of acne vulgaris.[58] Cannabidiol (CBD) oil derived from Cannabis also known to prevent Pro-acne by elevating the TNF-α-expression, which is the main cytokine in the acne vulgaris pathogenesis. Study has also found that CBD possesses anti-inflammatory action on humane sebocytes by modeling both -ve negative and +ve positive infection by applying TLR4 activator LPS and

TLR2 activator LTA respectively and the results found that CBD prevents the elevating of TNF-α expression and also CBD normalized LPS- induced IL1B and IL6 expression. Thus we can say the sebostatic action is accompanied by anti-inflammatory effect which is helpful in treating acne vulgaris.[59]

Natural UV Protectant

Hemp seed oil has shown absorbance in the UV and UV-C ranges with an SPF rating of 6, demonstrating potential use as a low broad spectrum UV protectant. Because the plant is capable of developing its own UVR protection (like other plants do), its extracts form a natural protection from the sun. Importantly hemp seed oil helps deflect some of the UV rays without affecting the very important absorption of vitamin D, which is important as vitamin D plays a vital role in the human body.[60]

EFFECT OF ACTIVE CONSTITUENTS

Fatty acids

The long chains of lipid-carboxylic acid found in fats and oils and in cell membranes as a component of phospholipids and glycolipids (The Carboxylic acid is an organic acid containing the functional group -COOH.) Fatty acids come from animals and vegetable fats and oils. Fatty acids play important roles outside the body, they are used as lubricants, in cooking and food engineering, and in the production of soaps, detergents, and cosmetics.[32] In cosmetics, fatty acids are used in detergents and cleaners. They act as consistency regulators and co-emulsifiers and meet the various requirements for cosmetics and pharmaceutical products.[61] Hemp seed oil has a remarkable fatty acid profile which is of 35%. Hemp seed oil contains 50-70% linoleic acid (an omega-6-fatty acid) and 15-25% of α-linolenic acid (an omega-3-fatty acid). Hemp seed oil provides significant amount of higher fatty acids such as γ-linolenic acid (omega-6) and stearidonic acid. Oleic acid and saturated fatty acids mainly palmitic and stearic acid both make up about 10% of the oil.[62]

Cosmetic uses

Linoleic acid (Omega-6) promotes in hair growth and hair moisturization. It also helps in soothing acne and reduces chances of future outbreaks. Oleic acid (Omega-9) helps in maintaining softness and suppleness of skin and is effective in skin radiance. It helps in reducing wrinkles and fine lines. Shows antifungal properties and helps in eliminating dandruff and support hair growth. Palmitic acid has emollient properties. Softens hair without leaving hair greasy. Stearic acid shows cleansing properties that purge dirt, sebum and sweat

from hair and skin.[63]

Flavonoids

Flavonoids are polyphenolic compounds that are present in nature. Flavonoids are secondary plant metabolites which share the chromane ring with tocopherols, these compound show antioxidant activity. In this activity the major mechanism is to induce the direct scavenging of oxygen and nitrogen free radicals, inhibition of oxyradical producing enzymes, iron chelation and reduction of leukocyte adhesion to the blood vessel wall during tissue inflammation and reperfusion.[64] About 20 flavonoids have been identified in Cannabis, mainly belonging to the flavone and flavonol subclasses.[65] They approximately account for 10%, including the O- glycoside versions of the aglycones apigenin, luteolin, kaempferol and quercetin, as well as cannflavin A and cannflavin B, which are methylated isoprenoid flavones that are unique to Cannabis.[31]

Cosmetic use

Flavonoids have beneficial effects such as: anti-inflammatory, antioxidant, anti-fungal and anti-bacterial. Flavonoids are important for skin aging activity. Flavonoids like kaempferol delay skin aging by contrasting enzyme that break down the extracellular matrix, such as collagenase, elastases and hyaluronidases. Flavonoids provide the best antioxidant activity and protect the product from rancidity. Quercetin acts as an anti-oxidant. Cannaflavin A and Apigenin is uniquely found in Cannabis and has a strong anti-inflammatory property.[52]

Terpenes

Terpenes are common constitutes of flavour and fragrances. They are responsible for the aroma of Cannabis.[66] Terpenes are found in nature mainly in plant as constituents of essential oils.[67] Recent reports on analysis of their free radical scavenging capacity have suggested that they can act as antioxidant. Triterpenes are particularly useful compounds for dermatological conditions, triterpene used in cosmetic preparations for skin revitalization.[68] Cannabaceae plants Cannabis sativa L. comprise of terpenes as up to 3-5%.[69] The presence of several terpenes were confirmed in the seed oil, the most abundant of which were caryophyllene, include anti-inflammatory activities and myrcene, which exhibits antioxidant properties.[35]

Cosmetic use

Terpenes are used in cosmetic industries for generating flavours and fragrances due to their

pleasant scent.[68] β-amyrin shows anti-inflamatory activities.[70] Cycloartenol has activities like anti-inflamatory and anti-oxidant.[71]

Saponins

Saponins are bioactive compounds produced mainly by plants. Chemically, they occur as glycosides of steroids or polycyclic triterpenes. They are able to interact with cell membranes because of their lyobipolar properties and are also able to decrease the surface tension of an aqueous solution. This activity is the reason for the name "saponin", which is derived from the Latin word "sapo", which refers to the formation of a stable soap-like foam in aqueous solution.[72] Saponin presence in hemp seed oil is around 69.0 mg/Kg.[26] The presence of lipid-soluble aglycone and water-soluble sugar chain(s) in their structure (amphiphilic nature), make saponins surface active compounds with detergent, wetting, emulsifying, and foaming properties.[73]

Cosmetics uses

Saponins are known as natural surfactant, they form stable foam in aqueous solution such as soap. They are used in shampoo, liquid detergent and toothpaste as foaming agent. Saponins are also used as emulsifier and long lasting foaming agent.[74]

Tannins

Tannins are the heterogeneous group of high molecular weight polyphenolic compounds with alkaloids, polysaccharides, proteins, minerals, nucleic acids, etc.[75] Tannins are divided into four group on the basis of its structure- Gallotannins, Ellagitannins, complex tannins, condensed tannins.[76] Tannins are natural astringents which remove excess oil from skin pores and tighten them. They fight against bacteria which cause acne.[77] Tannins present in hemp seed oil ranges from 1.36% – 2.14 %g/kg.[27]

Cosmetics use

Tannins contain precipitate protein which are used for protection of inflamed surface of skin and treatment of burns. Tannins acts as astringent, antioxidant and also provide antibacterial activity.[43] Tannins helps to prevent aging of skin. Tannins also help to prevent hair loss.[78]

Phenols

Phenolic are hydroxyl group (-OH) containing class of chemical compounds where the (-OH) bonded directly with aromatic hydrocarbon group. The most important groups of phenolic are

flavonoids, polyphenols, and phenolic acids.[79] Phenolic compound are plant secondary metabolites, they have an important role as defence compounds. It acts as antioxidant, antibacterial, anti-inflammatory agents.[80] Total phenolic compounds determined for hemp oil is about 2.4 mg/100 g.[81]

Cosmetic use

Cosmetic preparation containing phenolic extract are sold with the claims of antiaging, wound healing and photo protection.[68] Phloroglucinol glucoside present in hemp seed oil claims to have combating skin aging.[82]

CONCLUSION

The clinical research on Cannabis was restricted for a long time due to its illegality, because of the burden of Cannabis prohibition, there has been very little development or innovation in hemp or hempseed production during the last 60-70 years. But the past two decades have seen renewed and concerned interest in the therapeutic potential of Cannabis sativa L. which represents many interesting properties. Although most people associate it with drugs, many scientific data exhibit that its medicinal features should not be neglected. Now a days, Cannabis sativa is used in Ayurvedic medications, and cosmetics due to its therapeutic properties and effective results. The main aspect of this article is to focus on the hemp seed oil which is highly nutritious and helpful especially for the skin. The profusion of fatty acids make the oil an excellent choice for nourishing the skin and protecting it from inflammation, oxidation and aging and also helps in keeping the skin healthy and free from breakouts. Topical application of hemp seed oil strengthens the skin and make it better and able to resist infection. The presence of phytochemical constituents like flavonoids, terpenes, phenols and tannins make hemp seed oil an ideal ingredient to be used in skin and hair care product and extremely useful for human skin. In conclusion, more studies related to hemp seed is being done by researchers for a better cannabis based cosmetics and skin care.

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REFERENCES

1. Paul R., Williams R., Hodson V., Peake C. Detection of cannabinoids in hair after cosmetic application of hemp oil. Sci Rep, 2019; 9(1): 2582.
2. Vogl, Christian Reinhard & Mölleken, Helga & Lissek-Wolf, Gunilla & Surböck, Andreas & Kobert, JÖRg. Hemp (Cannabis sativa L.) as a Resource for Green Cosmetics. Journal of Industrial Hemp, 2004; 9: 51-68.
3. https: //www.google.com/search?q=hemp+oil+and+seeds&safe=active&rlz=1C1CHBF_enIN853IN853&sxsrf=ALeKk03kYC5mIblJp0yrZX4tSay33NYj4Q:1589868880603&source=lnms&tbm=isch&sa=X&ved=2ahUKEwiunfiOo7_pAhXr8HMBHRVfBIYQ_AUoAnoECA8 QBA&biw=1536&bih=754#imgrc=1HMUT65v7FSDBM
4. Mikulcová V, Kašpárková V, Humpolíček P, Buňková L. Formulation, Characterization and Properties of Hemp Seed Oil and Its Emulsions. Molecules, 2017; 22(5): 700.
5. Laboratory and Scientific Section United nations office on drugs and crime Vienna Recommended Methods for the Identification and Analysis of Cannabis and Cannabis Products MANUAL FOR USE BY NATIONAL DRUG ANALYSIS LABORATORIES.
6. William Leonard Pangzhen Zhang Danyang Ying Zhongxiang Fang, Hempseed in food industry: Nutritional value, health benefits, and industrial applications, December 2019; 19(1).
7. History of Cannabis in India https: //www.psychologytoday.com/us/blog/the-teenage-mind/201106/history-cannabis-in- india.
8. The complete story behind why marijuana was banned in India. https: //www.mensxp.com/special-features/opinion/43897-the-complete-story-behind-why- marijuana-was-banned-in-india.html.
9. Is Weed or Marijuana Legal in India? https: //www.myadvo.in/blog/is-weed-or-marijuana- legal-in-india/.
10. Renée Johnson Specialist in Agricultural Policy, Hemp as an Agricultural Commodity, June 22, 2018.
11. D.W. Williams, Plant and Soil Sciences, and Rich Mundell, An Introduction to Industrial Hemp and Hemp Agronomy, Kentucky Tobacco Research and Development Center.
12. Hemp, Encyclopaedia Britannica, https: //www.britannica.com/plant/hemp.
13. VanDolah, Harrison J, Bauer, Brent A., Mauck, Karen F, Clinicians' Guide to Cannabidiol and Hemp Oils, 2019; 94(9): 1840-1851.

14. Cinzia Citti, Pasquale Linciano, and Giuseppe Cannazza, Cannabinoid Profiling of Hemp Seed Oil by Liquid Chromatography Coupled to High-Resolution Mass Spectrometry, Front. Plant Sci., 13 February 2019; 1-17.
15. CBD Oil vs. Hempseed Oil: How to Know What You're Paying For. https: //www.healthline.com/health/hemp-vs-cbd-oil#1.
16. https: //www.google.com/search?q=hemp HYPERLINK.
17. https: //www.google.com/search?q=hemp+ssed+oil HYPERLINK .
18. Kuddus, M., I. Ginawi, and A. Al-Hazimi. "CANNABIS SATIVA: AN ANCIENT WILD EDIBLE PLANT OF INDIA". Emirates Journal of Food and Agriculture, June 2013; 25(10): 736-45.
19. AMALA RAMAN, Department of Pharmacy, Kings College London, UK.The Cannabis Plant Botany Cultivation and Processing For, 12 Feb 2020.
20. Dr I. C. Chopra Pharmacologist, Col. Sir R. N. Chopra Director, Drug Research Laboratory, Jammu and Kashmir (India), Member of thc Expert Advisory Panel on Addiction- producing Drugs of the World Health Organization, The Use of the Cannabis Drugs in India1957/01/01.
21. Erin Michelle Young, LUMES, Revival of Industrial Hemp: A systematic analysis of the current global industry to determine limitations and identify future potentials within the concept of sustainability, December 9th, 2005.
22. Bonini SA, Premoli M, Tambaro S, et al. Cannabis sativa: A comprehensive ethnopharmacological review of a medicinal plant with a long history. J Ethnopharmacol, 2018; 227: 300-315.
23. Hempseed oil Brenntag https: //www.brenntag.com/media/documents/bsi/product_data_sheets/life_science/textron_natural_oils/hempseed_oil_refined_tx008087_pds.pdf.
24. Brenneisen R. (2007) Chemistry and Analysis of Phytocannabinoids and Other Cannabis Constituents. In: ElSohly M.A. (eds) Marijuana and the Cannabinoids. Forensic Science And Medicine. Humana Press.
25. Garcia, Agustin. Hemp: a Composition Review plus, 2017.
26. K. Aladić, a S. Jokić, b, T. Moslavac, b S. Tomas, b S. Vidović, c J. Vladić, c and D. Šubarićb, Cold Pressing and Supercritical CO2 Extraction of Hemp (Cannabis sativa) Seed Oil,
27. Paul, R., Williams, R., Hodson, V. et al. Detection of cannabinoids in hair after cosmetic application of hemp oil. Sci Rep, 2019; 9: 2582.

28. Christian R. Vogl, Helga Mölleken, Gunilla Lissek-Wolf, Andreas Surböck & JÖRg Kobert (2004) Hemp (Cannabis sativa L.) as a Resource for Green Cosmetics, Journal of Industrial Hemp, 2008; 9: 1: 51-68.
29. FedericaPellati, VittoriaBorgonetti, VirginiaBrighenti, MarcoBiagi, StefaniaBenvenuti, and LorenzoCorsi, Cannabis sativa L. and Nonpsychoactive Cannabinoids: Their Chemistry and Role against Oxidative Stress, Inflammation, and Cancer, 2018; 1-15.
30. Oomah, B. Dave, Muriel Busson, David V. Godfrey and John C. G. Drover. "Characteristics of hemp (Cannabis sativa L.) seed oil." (2002).
31. Christelle M. Andre, Jean-Francois Hausman and Gea Guerriero Cannabis sativa: The Plant of the Thousand and One Molecules, Front Plant Sci, 2016; 7: 19.
32. Deferne, J.L. and D. W. Pate, 1996. Hemp seed oil: A source of valuable essential fatty acids. Journal of the International Hemp Association, 3(1): 1, 4-7.
33. Cary Leizer BA, David Ribnicky PhD, Alexander Poulev PhD, Slavik Dushenkov PhD & Ilya Raskin PhD (2000) The Composition of Hemp Seed Oil and Its Potential as an Important Source of Nutrition, Journal of Nutraceuticals, Functional & Medical Foods, 2015; 2: 4, 35-53.
34. Garcia, Agustin G.M. Hemp: a composition review plus (2017). Senior project for B.S. Nutrition at Cal Poly San Luis Obispo. San Luis Obispo, CA.
35. The CBD extraction process.https: //cbdfx.com/cbd-extraction-process/
36. Hong, Sunghyun & Sowndhararajan, Kandhasamy & Joo, Taewoo & Lim, Chanmook & Cho, Haeme & Kim, Songmun & Kim, Gur-Yoo & Jhoo, Jin-Woo, Ethanol and supercritical fluid extracts of hemp seed (Cannabis sativa L.) increase gene expression of antioxidant enzymes in HepG2 cells. Asian Pacific Journal of Reproduction, 2015; 4(2): 147-152.
37. Chang CW, Yen CC, Wu MT, Hsu MC, Wu YT. Microwave-Assisted Extraction of Cannabinoids in Hemp Nut Using Response Surface Methodology: Optimization and Comparative Study. Molecules, 2017; 22(11): 1894. Published 2017 Nov 3.
38. Jin S., Lee M.-Y, The ameliorative effect of hemp seed hexane extracts on the Propionibacterium acnesinduced inflammation and lipogenesis in sebocytes PLoS ONE, 2018; 13(8).
39. How to use hemp oil for the skin, https: //www.verywellhealth.com/hemp-oil-for-skin-4588226
40. Morales, P.; Reggio, P.H.; Jagerovic, N. An Overview on Medicinal Chemistry of Synthetic and Natural Derivatives of Cannabidiol. Front. Pharmacol, 2017; 8: 422.

41. Atalay, S.; Jarocka-Karpowicz, I.; Skrzydlewska, E. Antioxidative and Anti-Inflammatory Properties of Cannabidiol. Antioxidants, 2020; 9: 21.
42. Himanshu Jaiswal, Om Ji Singh, Ankit Chauhan, Maneesh Kumar Sahu, Surya Prakash DV, A review on tannins, European Journal of Biotechnology and Bioscience, May 2018, Vol 6, pp. 16-17.
43. Khan, Belas & Warner, Philip & Wang, Hao. (2014). Antibacterial Properties of Hemp and Other Natural Fibre Plants: A Review. BioResources. 9. 10.15376/biores.9.2.3642-3659.
44. Hemp oil benefits list.https: //www.medicalnewstoday.com/articles/324450.
45. Russo E. B. (2008). Cannabinoids in the management of difficult to treat pain. Therapeutics and clinical risk management, Ther Clin Risk Manag, 2008 Feb; 4(1): 245–259.
46. Hammell, D. C., Zhang, L. P., Ma, F., Abshire, S. M., McIlwrath, S. L., Stinchcomb, A. L., & Westlund, K. N, Transdermal cannabidiol reduces inflammation and pain-related behaviours in a rat model of arthritis. European journal of pain (London, England), 2016; 20(6): 936–948.
47. Scheau C, Badarau IA, Mihai LG, et al. Cannabinoids in the Pathophysiology of Skin Inflammation. Molecules, 2020; 25(3): 652. Published 2020 Feb 4.
48. Wilkinson J.D., Williamson E.M, Cannabinoids inhibit human keratinocyte proliferation through a non-CB1/CB2 mechanism and have a potential therapeutic value in the treatment of psoriasis, Journal of Dermatological Science, 2007; 45(2): 87-92.
49. Can hemp oil cure my psoriasis? https: //www.healthline.com/health/hemp-oil-for-psoriasis
50. Heal Lichen planus the fast way with CBD.https: //hemp-oil.us/cbd-in-lichen-planus/
51. Hemp oil for skin.https: //www.healthline.com/health/hemp-oil-for-skin#benefits-for-your- skin.
52. What are flavonoids in cannabis? https: //www.cbdschool.com/what-are-flavonoids/
53. Barrett, M.L., Scutt, A.M. & Evans, F.J. Cannflavin A and B, prenylated flavones from Cannabis sativa L.. Experientia, 1986; 42: 452–453.
54. Flavonoids, https: //www.fundacion-canna.es/en/flavonoids
55. Jeong M, Cho J, Shin JI, et al. Hempseed oil induces reactive oxygen species- and C/EBP homologous protein-mediated apoptosis in MH7A human rheumatoid arthritis fibroblast-like synovial cells. J Ethnopharmacol. 2014; 154(3): 745-752.
56. Kaplan DH, Igyártó BZ, Gaspari AA. Early immune events in the induction of allergic

contact dermatitis. Nat Rev Immunol, 2012; 12(2): 114-124.

57. D Dutt (MSc. Biotech.), 11 ways hemp oil may benefit in skin disorders, https: //cbdnhemp.com/hemp/benefit/hemp-oil-benefit-skin-disorders/
58. Wang Y.-Y., Ryu A.-R., Jin S., Jeon Y.-M., Lee M.-Y, Chlorin e6-mediated Photodynamic therapy suppresses P. acnes-induced inflammatory response via NFκB and MAPKs signaling pathway, PLoS ONE, 2017; 1-14.
59. Oláh A, Tóth BI, Borbíró I, et al. Cannabidiol exerts sebostatic and antiinflammatory effects on human sebocytes. J Clin Invest, 2014; 124(9): 3713-3724.
60. Hemp seed oil and its incredible skin benefits, https: //www.hempme.com.au/hemp-seed-oil-skin-.
61. Fatty acids, https: //www.berg-schmidt.de/en/Cosmetic/c12_fatty_acid.php
62. Arno Hazekamp, Renee L. Ruhaak, Composition of hemp oil, Development & Modification of Bioactivity, Comprehensive Natural Products II, 2010.
63. REFINING & PROTECTIVE USES OF HEMP OIL https: //www.newdirectionsaromatics.com/blog/products/all-about-hemp-oil.html
64. AR Tapas, DM Sakarkar, and RB Kakde, Flavonoids as Nutraceuticals: A Review, Tropical Journal of Pharmaceutical Research, September 2008; 1089-1096.
65. Barrett M.L., Gordon D., Evans F.J, Isolation from cannabis sativa L. of cannflavin-a novel inhibitor of prostaglandin production, Biochemical Pharmacology, 1985, 34 (11) , pp. 2019- 2024.
66. Cannabinoids science, https: //www.medicaljane.com/category/cannabis-classroom/cannabis-science/#cannabinoids-101.
67. Cox-Georgian D, Ramadoss N, Dona C, Basu C. Therapeutic and Medicinal Uses of Terpenes. Medicinal Plants, 2019 Nov 12: 333–59..
68. Bruno Burlando, Luisella Verotta, Laura Cornara, and Elisa Bottini-Massa. Traditional Herbal Medicines for Modern Times. Herbal Principles in Cosmetics Properties and Mechanisms of Action by Taylor and Francis Group, LLC CRC Press is an imprint of Taylor & Francis Group, an Informa business, 2010; 9-26.
69. Nuutinen T. Medicinal properties of terpenes found in Cannabis sativa and Humulus lupulus. Eur J Med Chem, 2018; 157: 198-228.
70. Akihisa T, Kojima N, Kikuchi T, et al. Anti-inflammatory and chemopreventive effects of triterpene cinnamates and acetates from shea fat. J Oleo Sci, 2010; 59(6): 273-280.
71. Zhang ZL, Luo ZL, Shi HW, Zhang LX, Ma XJ. Zhongguo Zhong Yao Za Zhi, 2017; 42(3): 433-437.

72. Thakur, Melzig, Fuchs H, Weng A. Chemistry and pharmacology of saponins: special focus on cytotoxic properties. Botanics: Targets and Therapy, 2011; 1: 19-29.
73. Güçlü-Ustündağ O, Mazza G. Saponins: properties, applications and processing. Crit Rev Food Sci Nutr, 2007; 47(3): 231-258.
74. Dorota Kregiel, Joanna Berlowska, Izabela Witonska, Hubert Antolak, Charalampos Proestos, Mirko Babic, Ljiljana Babic and Bolin Zhang, Saponin-Based, Biological-Active Surfactants from Plants, Application and Characterization of Surfactants, 2017.
75. Mueller-Harvey I, Mcallan AB. Tannins: Their biochemistry and nutritional properties. Advances in plant cell biochemistry and biotechnology, Vol. 1 Morrison IM ed. JAI Press Ltd, London (UK), 1992; 151-217.
76. Mole S, Waterman PG. Tannic acid and proteolytic enzymes: enzyme inhibition or substrate deprivation. Phytochemistry, 1987; 26: 99-102.
77. Praveen Kumar Ashok, Kumud Upadhyaya, Tannins are Astringent, Journal of Pharmacognosy and Phytochemistry, 2013; 1(3): 45-50.
78. Vishakha Bagul, Sonal Dhabekar, Disha Sansarode, Sneha Dandekar , Wood Apple (Limonia Acidissima L.): A Multipurpose Herb In Cosmetics, July 2019 IJSDR, 172-181
79. Walton NJ, Mayer MJ, Narbad A. Molecules of Interest: Vanillin. Phytochemistry, 2003; 63: 505- 515.
80. Dai J, Mumper RJ. Plant phenolics: extraction, analysis and their antioxidant and anticancer properties. Molecules, 2010; 15(10): 7313-7352. Published 2010 Oct 21.
81. Alexander Siger, Malgorzata Nogala-Kalucka, Eleonora Lampart-Szczapa, The content and antioxidant activity of phenolic compounds in cold pressed plant oils, 23 April 2008.
82. Charles T.Hammond, Paul G.Mahlberg, Phloroglucinol glucoside as a natural constituent of Cannabis sativa, 1994; 37(3): 755-756.