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Hemp: A detailed ethnopharmacological review of a medicinal plant of great importance

Jihene Ben Ghnia[1], Huma Riaz[2], Rafia Rehman[2], Shafaq Nisar[2]* and Muhammad Idrees Jilani[2]

[1]Department of Biology, Faculty of Sciences, University of Tunis. E.I Manar Tunis and [2]Department of Chemistry, University of Agriculture, Faisalabad, Pakistan

Abstract

Hemp is an aromatic plant. Hemp essential oil is more remarkable oil in all essential oils. The oil of hemp is highly volatile. Monoterpenes, sesquiterpenes and other organic compounds are present in essential oil of hemp. In soaps, perfumes and candles, the essential oil of hemp can be used. For aromatization of food, hemp essential oil can be used. The components of essential oil of hemp like limonene and alpha pinene have repellent effect against insects. Hemp is used in insomnia, headaches, a whole host of gastrointestinal disorders, and pain. Cannabis is frequently used to relieve the pain of childbirth.

Key words: Cannabaceae, Sesquiterpenes, Insomnia, Cannabis, Cannabinoids

Full length article **Corresponding Author*, e-mail: shafaqnisar12@gmail.com, Tel: +923237628206

1. Introduction

Hemp (*Cannabis sativa* L.) is an annual and diocious plant belongs to family *Cannabaceae.* This family contains 170 species. Hemp is a plant which contains 70 active constituents which are called cannabinoids [1] . The use of cannabis in Pakistan is illegal. Indica, sativa and ruderalis are three species of cannabis. In many regions of Pakistan, cannabis can grow. Cannabis freely grows in large cities such as Lahore and Islamabad. For thousands of years, cannabis has been used for the treatment of various diseases such as dysentery, nausea, pain and sleep disturbance etc.[2]. Hemp consist of two main regions, (i) the woody core with woody fibers, vessels and ray cells (ii) the bast fibers which are bound by lamella and arrange in bundles. Hemp is a bery tall crop. The leaves of cannabis are digitate. The stems of cannabis are soft and covered with grandular hairs and become woody and faceted when mature. Hemp has a taproot. Single seed nut is a fruit of hemp. Mostly sexual reproduction can be used for reproduction of hemp. The seed produced by female plant are the result of pollination of seed by pollen from male flowers growing nearby. 20% of monoecious hemp undergoes self-pollination. Mostly cannabis is a wind pollinated [3]. Commonly, hemp is known as bhang and hashesh in Pakistan. The common names of cannabis are hash oil, blubbers, ganja, grass, bhang, hashesh, pot, charas, boom and weed[4]. In America it is called marijuana, charas, bhang and ganja in india, hashesh in Middle east, krori in Tunisia, Hakab in Turkey and dogga in South Africa [5]. Hemp is an aromatic plant. Hemp essential oil is more remarkable oil in all essential oils. The oil of hemp is highly volatile and generally analyzed by using GC-MS analysis [6-9]. Monoterpenes, sesquiterpenes and other organic compounds are present in essential oil of hemp. Essential oils can be used in pharmaceutical industries [10] due to its various properties such as antimicrobial [11] and antioxidant [7-12] etc. In soaps, perfumes and candles, the essential oil of hemp can be used. For aromatization of food, hemp essential oil can be used. The components of essential oil of hemp like limonene and alpha pinene have repellent effect against insects[13].

2. History/Origin

Cannabis is native to Central Asia (China, India, Pakistan, Russia and Iran) and Western Asia. In india, hemp is naturalized in sub Himalaya tract, where it grows in wasteland from Punjab to Bengal and Bihar. Cannabis grows wild in some regions of Potwar Plateau in, the NWFP (North West Frontier Province) and the northern areas of Pakistan. In Europe, China and Japan, the hemp also been cultivated commercially for its fiber [14]. In 1645, hemp was introduced to America and new England. Before recorded history, Cannabis has been entwined with the human racesince. Cannabis is used in herbal treatment. The origin of hemp was more specifically in Gobi desert and Turkmenistan. As an accepted medication in North America and Europe, cannabis became well established in early

twentieth century. The extract of cannabis as an antispasmodic, analgesic, and sedative were selling by Perke-Davis and Eli Lilly which are marketed by Griault and company. Marijuana became an accepted herbal remedy in many rural parts of United States.[15].

3. Demography/Location

Hemp is sun loving plant. If enough solar contact provided then hemp can easily grow to large heights. Hemp require lots of moisture. Hemp can survive daily as low temperatures as -0.5 degrees Celsius for 4-5 days after the third pair of leaves develop. The yield obviously depends on the type of seed and climate. Yield varies from 0.6 to 2.4 tons per hectare, depending on variety of legal industrial hemp seed. Industrial hemp is at least 5-7 times less productive for seed production than *Cannabis indica/Cannibis sativa* [16].

4. Botany, Morphology, Ecology

C. sativa L is an annual, usually dioecious, more rarely monoecious and wind-pollinated herb. It propagates from seed, grows vigorously in open sunny environments with well-drained soils, and has an abundant need for nutrients and water. It can reach up to 5m (16 ft) in height in a 4–6-month growing season. However, in modern breeding and cultivation of recreational Cannabis, the preferred way to propagate the plants is by cloning, using cuttings of the so-called mother plant. As this term indicates, female plants are used for this purpose, as they produce significantly higher amounts of psychoactive compounds than the male plants. The sexes of Cannabis are anatomically indistinguishable before they start flowering, but after that, the development of male and female plants varies greatly. Shorter days, or more accurately longer nights, induce the plant to start flowering. The female plant then produces several crowded clusters of individual flowers (flower tops); a large one at the top of the stem and several smaller ones on each branch, whereas the male flowers hang in loose clusters along a relatively leafless upright branch. The male plants finish shedding their pollen and die before the seeds in the female plants ripen, that is 4–8 weeks after being fertilized. [17].

5. Chemistry

Cannabis is very complex in its chemistry due to the vast number of its constituents and their possible interaction with one another. These compounds represent almost all of the chemical classes, e.g., mono- and sesquiterpenes, sugars, hydrocarbons, steroids, flavonoids, nitrogenous compounds and amino acids, among others. The best-known and the most specific class of Cannabis constituents is the C21 terpenophenolic cannabinoids, with (_)-D9-trans-(6aR,10aR)-tetrahydrocannabinol (D9-THC) being the most psychologically active constituent. The development of synthetic cannabinoids and the discovery of chemically different endogenous cannabinoid receptor ligands (endocannabinoids) have prompted the use of the term ‘‘phytocannabinoids’’ to describe these compounds. The total number of natural compounds identified in *C. sativa* L. in 1980 was 423 and in 1995 was 483.

5.1. Chemical composition

There are number of chemical classes present in marijuana: hydrocarbons, nitrogenous compounds, proteins, amino acids, enzymes, sugars, glycoproteins, simple alcohols, fatty acids, aldehydes, esters, ketones, acidslactones, terpenes, steroids, flavonoids and non-cannabinoid phenols etc. [18]. It was found that the whole seed of hemp plant have roughly 15% insoluble fiber, 25% protein, 30% carbohydrates, carotene, potassium, phosphrous, magnesium, calcium, sulphur, iron, zinc and various vitamins like E,C,B1,B2, B3, B6. [19]. However both type as well as % of chemical constituents depends on different seasons [6].

5.2. Phyto-chemistry

Hemp is a rich source of cellulosic as well as woody fibers. Both pharmaceutical and construction sectors are equally interested in hemp plant because of its remarkable bioactivities on human health and also the use of its outer and inner stem tissues in making bioplastics and concrete-like material.[20]. There were about nine oxygenated cannabinoids were isolated from the *Cannabis sativa* by some researchers. These minor compounds include one hydroxylated cannabinol, four tetrahydrocannabinols and four hexahydrocannabinols, and namely 1'S-hydroxycannabinol, Δ(9)-THC aldehyde A, 8-oxo-Δ(9)-THC, 9α-hydroxy-10-oxo-Δ(6a,10a)-THC, 10aα-hydroxy-10-oxo-Δ(8)-THC, 9α-hydroxyhexahydrocannabinol, 10α-hydroxyhexahydrocannabinol, 7-oxo-9α-hydroxyhexa-hydrocannabinol and 10aR-hydroxyhexahydrocannabinol,respectively [21].

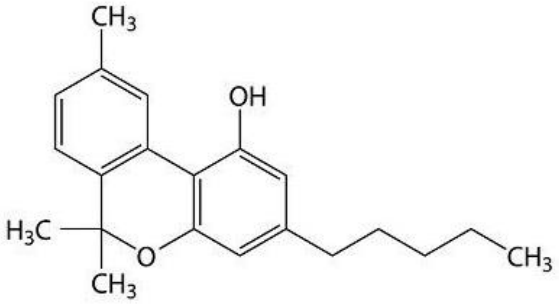

Fig.1. Structure of Cannabinol

6. Post-harvest technology

Hemp plant grows annually from the seed. It best grows on the land that provides high corn yields. The soil for proper growth of hemp plant should be well drained, non-acidic and rich in nitrogen. Hemp plant prefers a humid atmosphere, mild climate, and rainfall of at least 64-76 cm per year. Soil temperature should be 42-46°F before the plantation of seeds. Fiber hemp is generally ready to harvest in 70-90 days after seeding.

7. Processing

Hemp seeds should be cleaned as well as dried before the storing. Oil extraction from the seed is generally carried out by using mechanical expeller press under nitrogen atmosphere. Solvent extraction method can also be used for this purpose. In this method, hexane, ethanol, benzene or liquid carbon dioxide are used as solvent. Refining as well as deodorizing steps are required for the cosmetics manufacturers. Woody core is separated from the bast fiber by using sequence of rollers or hammermill. Next step is the cleaning of the bast fiber and then it is carded to the desired core content and fineness. After that, secondary steps are usually required. These include matting for non-woven mats and fleeces production, pulping, steam explosion, a chemical removal of natural binders for the production of wearable fiber. Complete processing lines for fiber hemp have outputs ranging from 2-8 short tons/hour.

8. Value addition

Hemp plant can be used in various field and industries at commercial level such as c in food, fuels, clothing and jewelry and among many other goods. Hence, hemp is considered to be as the most valuable plant known to human being, as well as the strongest and longest natural fiber.

9. Uses

Bhang (a cannabis drink) usually mixed with the milk and is used as anti-phlegmatic and anesthetic in India. "Marijuana proponents suggest that the recipe for the anointing oil passed from God to Moses included cannabis, or kaneh-bosm in Hebrew. They point to versions calling for fragrant cane, which they say was mistakenly changed to the plant calamus in the King James Version of the Bible." Cannabis was also used in Egypt in the twentieth century B.C for the treatment of sore eyes. Furthermore, it was also found to have applications in the treatment of various human ailments like wounds, burns, allergies, cuts, scabies, inflammation, leucoderma, leprosy, smallpox and sexually transmitted diseases [5].

9.1. General uses

Previous data available on the hemp plant confirms that due to the psychoactive properties of the plant it was used for the treatment of variety of ailment and illnesses. These included headaches, insomnia, gastrointestinal disorders. Cannabis was also commonly used for the relieve of childbirth pain [22]. Oil extracted from the hemp seed can be used in light cooking as well as in baking. Though, the flash point of hemp oil is low and it will start to smoke even at very low temperature. At too high temperature for example if used for the frying chicken oil may be hydrogenated. Thus, it is best to use hemp oil as “finishing oil”, used for salad dressing. Furthermore, hemp oil can be used as an alternative for other fats like butter on baked rice or potato. Hemp oil also be used as supplement and consumed 1-2 Tablespoons/day as required. There are various ways to use hemp or its oil in almost all food recipes in order to enjoy many hemp health benefits. Hemp was also tested for the insect control activity by some researcher and found that it has good insect control activity [23]." 6,000 BCE (Before Common Era), Cannabis oil and seeds were used for food in China and 4,000 BCE, in Turkestan and China used hemp in textile [24].

9.2. Pharmacological use

Hemp herb was found to have therapeutic effect, that is why it was used for this purposes for centuries. In Europe, it was used for the treatment of pain, asthma, spasms, sleep disorders, loss of appetite and depression at the end of nineteenth century. In 1964, (-)-trans-delta-9-tetrahydrocannabinol (THC, dronabinol), the major active cannabis chemical constituent, was stereochemically defined [25].

9.2.1. Antioxidant activities

Hemp seed oil was extracted with methyl alcohol and evaluated for radical scavenging activities against ABTS and DPPH, total phenolic contents (TPC), chelating activity and oxygen radical absorbing capacity (ORAC). It was found that extracted oils had significant antioxidant activities. Antioxidant properties of plant are due to the presence of phenolic or flavonoid components [12]. Obtained results suggested that cold-pressed hemp seed oils may serve as dietary sources of natural antioxidants for health promotion and also for disease prevention.

9.2.2. Antimicrobial activity of hemp

Antimicrobial activity of various varieties of hemp (Carmagnola, Fibranova and Futura) was evaluated from the extracted essential oils (EOs). These oils were compared to that of standard reagents on broad range microbial growth inhibition through minimum inhibitory concentration (MIC) assay. Microbial effect of these extracted oil were evaluated on different micooragnism i.e., gram (+) bacteria, gram (-) bacteria and yeasts. The obtained results showed that industrial hemp EOs can considerably inhibit microbial growth to an extent depending on the hemp variety. It was found that Futura have remarkable applications to control food-borne pathogens and also phytopathogens microorganisms [26].

9.2.3. Anti-inflammatory effects

Cannabinoids (group of compounds) mediated their effects via cannabinoid receptors. The Δ^9-tetrahydrocannabinol (THC) compound discovery as the major psychoactive major component in hemp, as well as the cannabinoid receptors identification and their endogenous ligands, has led to significant growth in research directed at understanding the cannabinoids physiological functions. Cannabinoid receptors include CB1 (present in brain) and CB2 (present in immune system). Various studies confirmed that THC administration into mice triggered the marked apoptosis in dendritic cells and T cells, resulting in immunosuppression. Furthermore, numerous studies revealed that cannabinoids down regulate

the production of chemokine and cytokine and, in some models, upregulate T-regulatory cells as a mechanism for the inflammatory responses suppression. Applications of cannabinoids in various experiments of autoimmune disorders like rheumatoid arthritis, multiple sclerosis, hepatitis and colitis have been revealed that it has ability to protect the host from the attack of pathogens via multiple anti-inflammatory induction pathways. Furthermore, cannabinoids may also be proved useful in various cancerous types which are triggered by the chronic inflammation. In these cases, cannabinoids can directly stop the growth of tumor, tumor angiogenesis and suppress inflammation. Further researches on revealed that another cannabinoid called as beta-caryophyllene or (E)-BCP has ability to fight with inflammation without affecting brain. However, (E)-BCP is already a part of daily diets of many people. Foods which have high quantity of this constituent include oregano, black pepper, lime, basil, celery, cinnamon and carrots [27].

9.2.4. Apoptotic effects

One major immunosupression mechanism by cannabinoids is apoptosis (induction of cell death) in immune cell populations. Apoptosis is required to maintain the homeostasis in cells and it involves morphological changes (membrane blebbing, nuclear fragmentation and cell shrinkage) as well as molecular changes (cytochrome c leakage and caspases induction). The apoptosis extrinsic pathway is initiated with the death receptors ligation (CD95) on surface of cell, leading to major caspases activation, like caspase 10, 8 and 3. The apoptosis intrinsic pathway is initiated through caspase 9 and nitochondria. Caspase 3 and cytochrome c are the principle constituents in the cell death induction.

9.2.5. Cannabis as a Medicine

Clinical potential of cannabinoids is large; some researchers suggested that it could be the ‘aspirin of the twenty-first century’. However, much of medicinal uses of cannabinoids evidences are anecdotal and now it has become very challenging to confirm these findings with the help of various clinical trials. Furthermore, it is frequently unknown that which chemical constituent of hemp herb is responsible for observed effect after the herbal extract administration. Due to the lack of suitable animal models or sample that has as complexity as human brain, the understanding of underlying biology between the chemical constituents of hemp herb and human system is slowly improving. Nevertheless despite these limitations, a various cannabinoids have been developed for clinical use. Now cannabis preparations have been used for the treatment of various diseases. The antiemetic, analgesic, muscle relaxant effects, appetite enhancing and its use in Tourette’s syndrome were all verified or confirmed by different researchers. The discovery of decrease in intraocular pressure with the administration of THC, (treatment of glaucoma) was made serendipitously during the examination of healthy Cannabis users The cannabis and the cannabinoids therapeutic potential is large [28].

9.2.6. Immunomodulatory activity

THC is the main psychoactive constituent present in the plant of marijuana. It was found that from various experiments that this compound exhibited good immunomodulatory properties. From the marijuana smokers, it was evaluated that they have impaired immunological functions (deficiency of blood leukocyte blastogenesis to mitogens). However, detailed studies or researches were carried on mice and concluded that animals given THC showed marked immunomodulation, including deficient production of cytokine, antibody formation suppression, etc. In recent studies, it was observed that lymphoid cells evince increased production or released IL1, but suppressed IL2 and production of interferon. Such lymphoid cells treated THC in vitro also showed suppression of blastogenesis to mitogens and antigens, suppression of NK activity, etc. In contrary, it has also evaluated that THC can increased the pro-inflammatory cytokines production or release. This includes these cytokines release from the macrophages (including augmented release of TNF IL6, alpha and IL1 activity).

9.2.7. Use of cannabis in HIV

In the present age, there is proper no cure available for the HIV or AIDS. However, significant improvements in the survival of individuals affected by HIV have been achieved. This survival of individuals has led to an enhancing individual’s prevalence with HIV infection, many on long-term treatment with the antiretroviral therapies combinations. This has increased the researcher focus on the chronic symptoms associated management with HIV as well as the side effects of antiretroviral medication. Cannabis was evaluated by some researchers in order to find out either it has proper applications in curing HIV infection or not. It was concluded that cannabis is appropriate for the treatment of some symptoms which are directly or indirectly related with the HIV infections and also to cure the side effects of antiretroviral drugs which are used for the treatment of this disease. These symptoms include weight loss, vomiting, nausea, pain, reduced appetite, diarrhea, headaches, constipation, depression and anxiety. Flu-like symptoms as well as severe myalgia can result directly from the seroconversion early in disease [29].

9.2.8. Neuropathic

Neuropathic pain is a disease of central nervous system (CNS) or peripheral nervous system (PNS) which is developed when spinal cord, a peripheral nerves or brain get injured or sensory system just fails to function in customary manner. In number of studies, it was found that Marijuana has ability to cure neuropathic pain and suggested that cannabis might hold promise for many sufferers of this malady. In a research, one patient with painful human

immunodeficiency virus (HIV) peripheral neuropathy was cure with cannabis and other was with placebo. Results showed that cannabis reduced the pain 46–52% while placebo reduced the pain 18–24% [30].

9.2.9. Cannabis side effects

There are number of side effects which are appeared due to the heavy and long term use of cannabis include: lungs irritation, risk of developing chronic bronchitis and risk of developing respiratory tract cancer cause cardiovascular disorders as it significantly increases the heart rate. Furthermore, it reduced short term memory, cause difficulty in learning and thinking and in some people it decreased sex drive. Its chronic use can decrease the sperm count in males while in females lead to irregular periods. Dependence on the cannabis compulsive need to use the drug, coupled with the problems related with the use of chronic drug.

10. Summary

Hemp is an aromatic plant. Hemp essential oil is more remarkable oil in all essential oils. The oil of hemp is highly volatile. Monoterpenes, sesquiterpenes and other organic compounds are present in essential oil of hemp. In soaps, perfumes and candles, the essential oil of hemp can be used. For aromatization of food, hemp essential oil can be used. The components of essential oil of hemp like limonene and alpha pinene have repellent effect against insects. Hemp is used in insomnia, headaches, a whole host of gastrointestinal disorders, and pain. Cannabis is frequently used to relieve the pain of childbirth.

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