Pak. J. Bot., 56(5): DOI: http://dx.doi.org/10.30848/PJB2024-5(30)

ETHNOPHARMACOLOGY, PHYTOCHEMISTRY AND PHARMACEUTICAL USES OF *CANNABIS SATIVA* L.

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Abstract

Cannabis sativa is an important medicinal plant that belongs to family Cannabaceae. Once considered native to Asian countries but now it is cultivated worldwide. This review article covers Ethnopharmacology, Phytochemistry and Pharmacology of *Cannabis sativa*. About 200 research and review articles were screened and date was taken from more than 50 research and review articles using Google Scholar, Pubmed, Research gate and Science direct. In ancient time, people use it to relieve stress but with the isolation of compounds many new uses of cannabis have been reported. Preparation from different parts of the plants have been used to treat vomiting, epilepsy and many other diseases. More than 500 compounds have been isolated from it. Cannabinoids are considered as major bioactive compounds responsible for medicinal use of *Cannabis sativa*. Terpenes form the second largest class of compounds along with phenols, alkaloids and flavonoids. Different methods have been used for the extraction, purification and identification of these bioactive compounds from different parts of the plant. These methods kept on improving with the passage of time. Due to large number of bioactive compounds, it has wide range of uses in traditional system of medicine. Plant has excellent antiepileptic, antiemetic, activities along with its usage for treatment of gastrointestinal problems.

Key words: Cannabinoids, Extraction methods, Pharmacological uses, Phytochemistry, Traditional uses.

Introduction

The use of plants as possible therapeutic agents by man extends back to antiquity and remains a significant source of medicine used to ease suffering from minor illnesses. The use of medicinal plants provided the pathway for discovery of modern medicines. People have been using plants as natural medicine since ancient times (Salmerón-Manzano *et al*., 2020: Shinwari *et al*., 2006). Plants have been a reliable supply of medicines since the dawn of time. Scientists from all over the world have been interested in plant-derived medicines for a long time because of their few side effects and beneficial impacts on human health (Shinwari & Nasim, 2014) Plants with a long history of use in ethnomedicine can be a rich source of medicines for the treatment of different infectious diseases in the pharmaceutical landscape. The vast majority of different kinds of bioactive compounds with a variety of therapeutic qualities are thought to be stored in medicinal plants (Shinwari & Ayaz, 2002) Anti-inflammatory, antiviral, antitumor, antimalarial, and analgesic properties are just a few of the numerous therapeutic benefits linked to medicinal plants (Aye *et al*., 2019: Shinwari *et al*., 2003). Anthropology, pharmacology, botany, zoology, medicine, chemistry, and statistics are just a few of the many fields that are incorporated into the study of ethnopharmacology as an interdisciplinary field of study. Ethnopharmacology primary areas of focus are the documentation and critical assessment of conventional empirical knowledge regarding the medicinal effects and therapeutic uses of plants and animals. (Bruhn & Rivier, 2019).

Cannabis sativa is one of earliest plants used by humans and cultivation of it started about 5000 to 6000 years ago. It belongs to genus *Cannabis* and family cannabaceae. *Cannabis sativa* is an annual wind pollinated herb both dioecious and rarely monoecious growing up to 3m in height. It is sun loving plant so if direct sunlight is provided it can grow to greater heights. *Cannabis sativa* was once considered to be native weed to Asian countries such as Pakistan, China, Afghanistan, Kazakhstan, India and Uzbekistan (Russo, 2007) but now it is cultivated in different parts of the world for its medicinal, recreational and industrial uses. In different parts of the world, it is known by different names such as in Bhutan it is known as "Ganza", in Bangladesh it is known as "Bhang", "Siddhi" and in Pakistan it is known as "Bhang" and "Hashish". It has long been used as folk medicine. Synonyms for cannabis are as *Cannabis chinensis*, *Cannabis erratica*, *Cannabis foetens*, *Cannabis gigantean* (McPartland, 2018).

Ethnopharmacological uses: Knowledge of ethnopharmacology is key element for discovery of drugs, for pharmacological and different phytochemicals. Medicinal use of *Cannabis sativa* dates back to 5000 years according to first Chinese Pharmacopeia and was reported for the treatment of rheumatism, malaria and fatigue. Different preparations of plant are reported to be used as anti-inflammatory, antimicrobial, and as sedative. In China, India and Egypt women use it to improve their moods and to reduce pain symptoms. In Romania and other European countries, seeds of *Cannabis sativa* are used for wound healing, for treatment of different skin disease such as scabies, impetigo, eczema and psoriasis, to increase hair growth, for treatment of leucorrhea as it is anti-infective. Traditional medicine practitioners in Zimbabwe used *Cannabis* as a whole to treat insomnia, anxiety, emesis, malaria, psychosis, psoriasis (Matowa *et al*., 2020: Gilca *et al*., 2018). People in Nawalparasi (central Nepal) dried and grind the seeds and leaves of *Cannabis*, drink them with water to treat indigestion problem and stomach

inflammation (Ghimire & Bastakoti, 2009). Traditional communities of Pakistan make decoction from leaves of plant and use it to cure fever, high blood pressure and other neurological disorders. "Thandai" is made from leaves of plant added into milk and other nuts to make it delicious. "Thandai" exerts cooling effects. It is an astringent used to cure leprosy and stomach pain (Ahmad *et al*., 2016). In Udhampur (India) paste of fresh leaves is applied on head to prevent hair loss, repair damaged scalp, to cure scorpion sting and for treatment of gastroenteritis. *Cannabis sativa* and *Terminalia chebula* leaves are crushed to make small tablets that are taken empty stomach with cow milk for treatment of piles. Roots of *Cannabis sativa* and leaves of *Chromolaena odorata* are macerated and taken orally to treat fever. Leaves of plant are dried, crushed and taken orally to treat arthritis, gout and different neurological disorder. Roots are crushed to make a paste along with twenty-five black pepper and given twice a day for insanity and tetanus, also used to relieve the pain of dysmenorrhea, menorrhagia, and phthisis. Seed oil is used in rheumatism, cancer chemotherapy and cancer pain (Hussain *et al*., 2010). Leaves make a good snuff for deterging the brain, juice removes dandruff. The resin called "Charas" is used to prevent and cure headaches and asthma. In Chamaba (India) paste of leaves along with urine of cow is applied on joints to reduce joint pain. The bark is use to make ropes (Savita, 2013). Ethnopharmacological uses of *Cannabis sativa* reported from different regions of the world have been presented in Table 1.

Extraction of bioactive compounds: First ever legal product of *Cannabis sativa* came in the market in 2018 after which research for extraction, purification and identification of bioactive compounds from *Cannabis sativa* accelerated (Koturbash & MacKay, 2020). Quantity of THC (Tetrahydrocannabinol) serve as a major barrier in the drug discovery from *Cannabis sativa*. Cannabinoids are main bioactive compounds isolated from and used in drugs. Major quantity of cannabinoids is found in trichrome. So the farms aiming for isolation of cannabinoids grew female plant in greater quantity. Seeds are mostly employed for extraction of oil. Major steps in extraction of bioactive active compounds from Cannabis sativa include harvesting of flower followed by trimming either manually or by machine then flowers are dried. Shredded flowers are then added to solvent (depending on method for extraction it might be modified) the co-extract is obtained that in addition to cannabinoids also contain polyphenols, phospholipids etc. that form a goosy gum (tar) that is further winterized (deep freezing for 24 h) followed by filtration. Solvent is then removed with the help of rotary evaporator and purified extract is obtained. To obtain a medical grade extract it needs to be further purified through chromatographic purification or through distillation method (House *et al*., 2010).

Phytochemistry of cannabis sativa: Terpenes, Steroids, Cannabinoids, Phenols and Flavonoids form major chemical constituents of *Cannabis sativa*.

Cannabinoids: Cannabinoids consist of 125 compounds that are further divided into eleven subclasses. Pure (-)-Δ^9-transtetrahydrocannbnoids was reported to be isolated from hexane extract hashish through column chromatography followed by alumina (Gaoni & Mechoulam, 1964). (-)-Δ^8-transtetrahydrocannbnoids was first isolated from benzene petroleum ether extract of flowers and leaves obtained from *Cannabis* grown in Maryland. Silicic acid Chromatography was used for its isolation. Cannabigerol was isolated from resins of *Cannabis sativa* through florisil Chromatography. Cannabidiol (CBD) was obtained from ethanol extract of wild hemp. Cannabinodiol (CBND) contain two compounds such as Cannabinodivirin isolated from hashish extract and CBND-C5 was isolated from Lebanese through silica gel column chromatography and structure was elucidated through 1H-NMR. Cannabielsoin was isolated from ethanolic extract of Lebanese hashish through GC-MS. Cannabichromene was obtained from hexane extract through column chromatography. Cannabitrol was isolated in 1966 from *Cannabis sativa* grown in japan but its structure was later on confirmed in 1976.

Table 1. Ethnopharmacological uses of *Cannabis sativa* reported from different regions of the world.

Country	Preparation	Reference
Turkey (Erzurum) Kenevir, kendir, çedene	Aerial part of the plant are crushed mix with goat oil and beeswax, waited in cold to treat infertility in women	Karakaya *et al*., 2019
Italy (Latium) Canapa	A decoction obtained from 2–3 branches was used for washing purposes ("it was to be cut under a waxing moon as then it produces strings")* To make girls' hair grow rapidly	Guarrera *et al*., 2005
	A warm strip applied, with oil, to the stomach*to treat Stomach-ache	
	Decoction of seeds is used to treat Pneumonia	
Nepal	Leaf is chewed and swallowed for cure of indigestion	Shrestha & Dhillion, 2003
Uganda Enjaga, Njaga	Leaves decoction to treat cough	Ssegawa and Kasenene, 2007
	Measles and body weakness	Tugume *et al*., 2016
Pakistan Bhang, Kabaly bhang. Bhang/ booti, Boang	Cough	Younis *et al*., 2018
	Seeds and shoots for insomnia, depression and loss of appetite.	Muhammad *et al*., 2021
	Leaves, roots, seeds, whole plant for constipation, diarrhea and as sedative	
	Leaves and seeds Decoction Chest pain, nerve tonic	Birjees *et al*., 2022
	Bark and poultice Decoction/ poultice Wound healing and burning	Shah *et al*., 2020
India Bhang, bijya, charas, ganga, bijya	Leaves and bark are used for treatment of Epilepsy and depression -	Sharma *et al*., 2022
	Leaves and seeds to treat cuts, burn, diabetes and dysentery	Kumar *et al*., 2009
	The seed oil is to be used to treat arthritic joint pain	
	Leaves decoction for depression, excessive urination, ear ache	Jan *et al*., 2021

Terpenes: Terpene form the second largest class of the compounds of *Cannabis sativa*. Terpenes are the compounds that give characteristic fragrance to the plant. About 120 terpenes have been reported in previous publications. These are divided into main classes as follows. Triterpene (2 compounds), Sesquiterpene (51 compounds), miscellaneous (4 compounds), Diterpenes (2 compounds) and monoterpenes (61 compounds). Monoterpenes can be both linear structure (myrecene) and cyclic structures (limonene). Compounds that were responsible for direct aroma of the plant are investigated through GC-MS. First Sesquiterpene was identified as α-caryophyllene through analysis of fraction of Egyptian hashish. There are only two Diterpenes, neophytadiene and phytol that were identified through GC-MS. Friedelin and epifriedolanol were identified from ethanolic extract of roots of *Cannabis sativa*. Vomifoliol and dihydrovmifoliol were isolated from Dutch hemp. β ionine and dihydroactinidiodile from volatile oil.

Lignans: *Cannabis*-related lignans can be split into two major categories: phenolic amides and lignanamides. Cannabisin A, grossamide, N-trans-coumaroyltyramine, N-trans-caffeoyltyramine, and N-trans-feruloyltyramine are phenolic compounds, N-(p-Hydroxyphenylethyl)-hydroxy-trans-cinnamamide was isolated from the ethanolic extract of cannabis roots. Amides have been discovered in *Cannabis* roots and fruits (Flores-Sanchez & Verpoorte, 2008). Contrarily, aqueous ethanolic extract of the fruit produced cannabisin A and grossamide.

Steroids: *Cannabis* roots contain stigmasterol, campesterol, and stigma sterol. *Cannabis* has been found to contain eleven phytosterols. The ergosterol, campesterol, stigmasterol, and sitosterol. The Indian cannabis strain produced a mixture of three sterols, including campesterol, stigmasterol, and -sitosterol. The three phytosterols were also found in *Cannabis* smoke. In addition, Radwan *et al*., (2009) successfully extracted -sitosterol-3-O-D glucopyranosyl-60 -acetate from cannabis for the first time. The extraction of sitosterol and sitosterol-D-glucoside was carried out using the plant's roots (Elhendawy *et al*., 2018). Sterol levels in inflorescences, leaves, roots, and stems increased with levels of campesterol, stigmasterol, and sitosterol. The chemical structure of some of the bioactive compounds from *Cannabis sativa* have been presented in Table 2.

Pharmacological uses

Antiemetic effect: Emesis can prevent digestion of harmful substances or sometimes it can be side effect of medication such as chemotherapeutic agent cisplatin in cancer patients. Cannabinoids can act to prevent emesis and nausea by blocking receptors located on DVC (dorsal vagal complex) interacting with CB1 and 5-HT3 receptors as blockage of 5- HT3 (5-hydroxytryptamine subtype) can suppress emesis. Cannabis plant was long used for treatment of vomiting and nausea and now in clinical trials it is also found to be an effective. Nabilone (synthetic analogue of D9-THC) is used as antiemetic agent for chemotherapeutic patients. *Cannabis sativa* was found to stimulate appetite as CBG (Cannabigerol) interact with endocannabinoids and non-endocannabinoids targets that can control energy and feeding balance by penetrating blood brain barrier. Dronabinol was investigated for wasting syndrome and malnutrition and was found effective by increasing 1% of body fat and increase food consumption by activating CB1 receptors located in hypothalamus (Breijyeh *et al*., 2021). A recent study conducted by Elgohary *et al*., (2022) reported antiemetic effect of cannabis in rats induced with cyclophosphamide. *Cannabis sativa* act as antiemetic agent by decreasing oxidative stress, serotonin (5-HT), dopamine and by increasing expression of CB1 receptors.

Alzheimer's diseases: Main reason of the disease is accumulation of beta amyloid peptide. One of the studies at university of Toronto suggested that synthetic compound (Nabilone) from *Cannabis sativa* was very effective in treating behavioral issue associated with Alzheimer's disease such as aggression. THC in medical *Cannabis* oil was also found to be effective in treating irritability, caregivers, distress, apathy, aggression, sleep (Shelef *et al*., 2016). As THC can repress the compound acetylcholinesterase that is responsible for amyloid beta peptide aggression. Night time delusion is a major symptom of presence of severe dementia. Treatment of some patients with dronabilone (pure isomer of THC) show that it can lessen the symptoms of the disease. Other drugs use for treatment of disease includes anandamide that shows effectiveness in a dose-dependent manner (Walther *et al*., 2006). According to the findings, CBD activated the Wnt/-catenin pathway, which in turn activated the Peroxisome Proliferator-Activated Receptor (P-PAR). As a result, it enhanced cell survival, decreased ROS production, decreased lipid peroxidation, prevented the hyperphosphorylation of tau protein, and inhibited AChE in PC12 cells, protecting them against neurotoxicity and oxidative stress (Vallee *et al*., 2017). A study conducted by Patil *et al*., (2022) shows that THCV and Cannabinol can inhibit Acetylcholinesterase and Butyrylcholinesterase much better than memantine (A drug used for the treatment of symptoms of disease). PC12 neuronal cells were the subject of in vitro research on CBD.

Antiepileptic effect: Epilepsy is a neurodegenerative disease common among people of all ages. Disease is characterized by unprovoked seizures. Use of cannabis against the disease started about four decades ago preclinical and clinical trial started in last decade. Treatment of patient with cannabis oil with CBD and THC in ratio of 20:1 can reduce the frequency of seizures (Tzadok *et al*., 2016) It can reduce formation of reactive oxygen species by acting as antioxidant, anti-inflammatory agent. CBD exert antiepileptic effect by reducing neurons excitability through activation of different receptors such as TRPV and Glutamate receptors or by effecting Calcium channels. It can block NMD receptors by binding to sigma subunit 1 of NMD thus act as reducing oxidative stress. An open-labeled single-arm research indicated the possible application of an enhanced formulation of extremely pure CBD from hemp embedded in seamless gelatine matrix beads for pediatric refractory epilepsy (Mitelpunkt *et al*., 2019).

Table 2. Chemical structure of some of the bioactive compounds from *Cannabis sativa*.

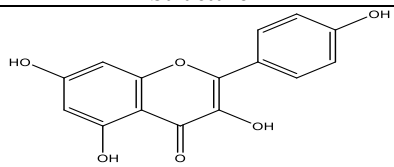
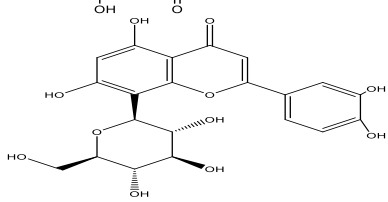
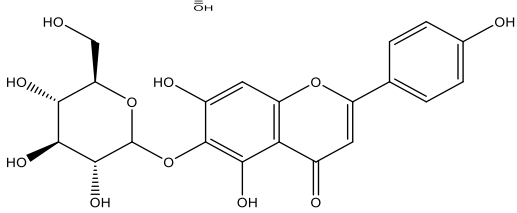
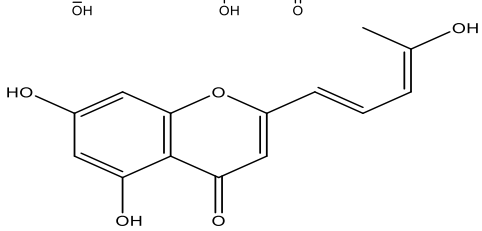
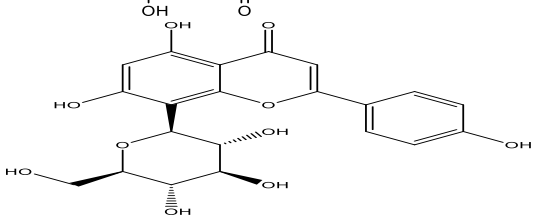
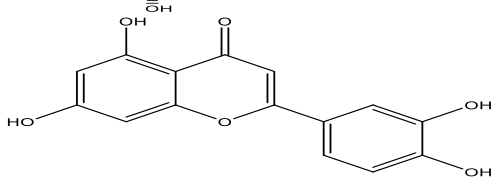
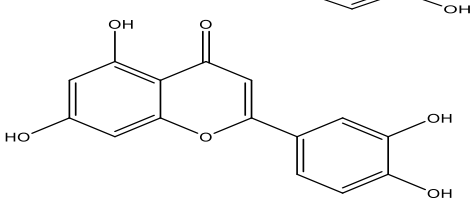
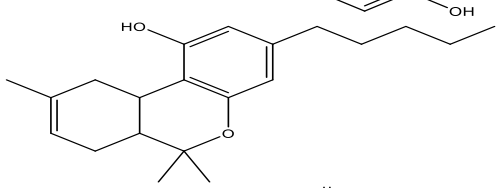
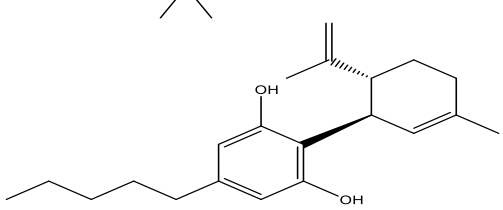
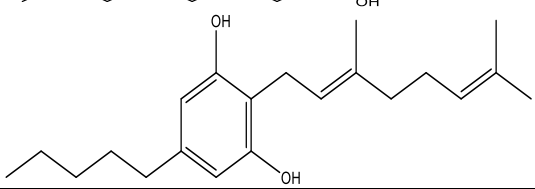
Class	Subclass	Structure	Reference
Flavonoids	Kaempferol		Ross *et al*., 2005
	Orientin		Clark & Bohm, 1979
	Isovitexin		Turner *et al*., 1980
	Apigenin		
	Vitexin		
	Luteolin		
	Quercetin		
Cannabinoids	(−)-Δ8-trans-tetrahydrocannabinol (Δ8-THC)		Hively *et al*., 1966
	Cannabidiol		Adams *et al*., 1940
	Cannabigerol		Turner *et al*., 1973

Table 2. (Cont'd.).

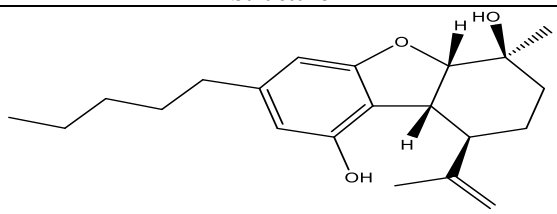
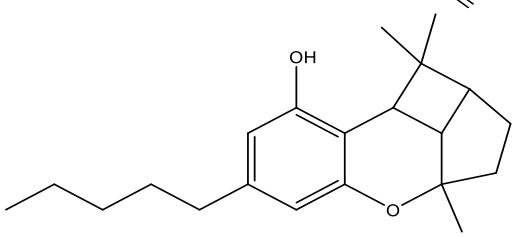
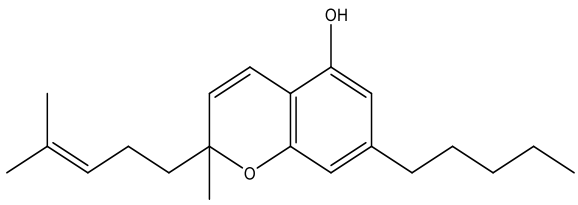
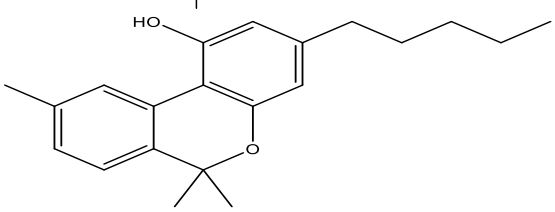
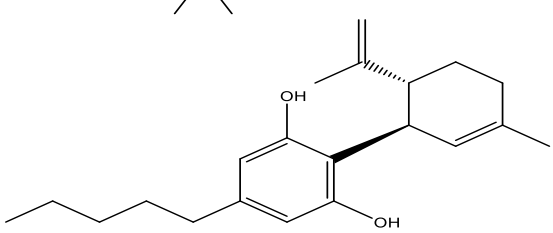
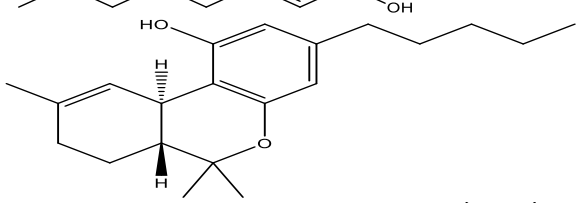
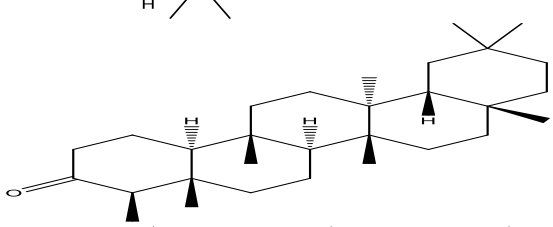
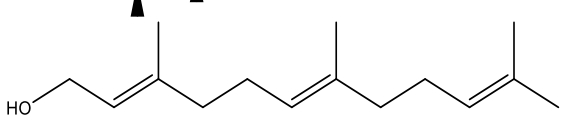
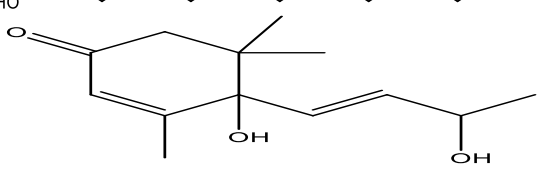
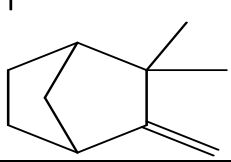
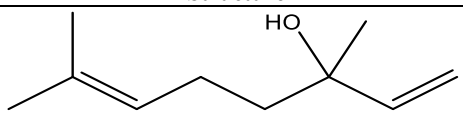
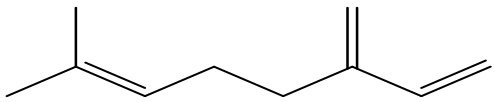
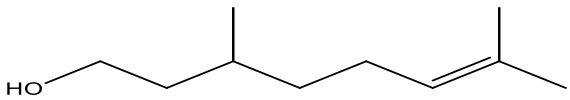
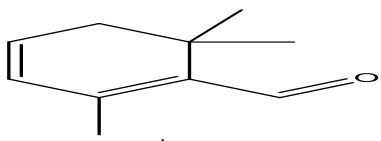
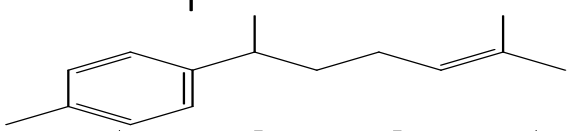
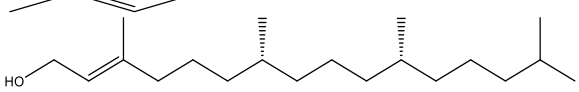
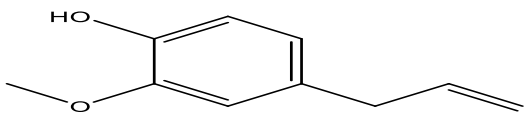
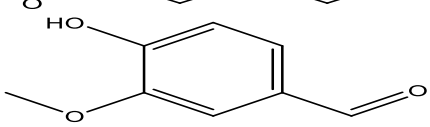
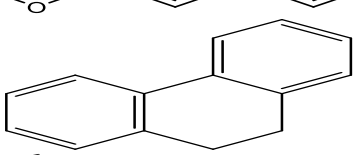
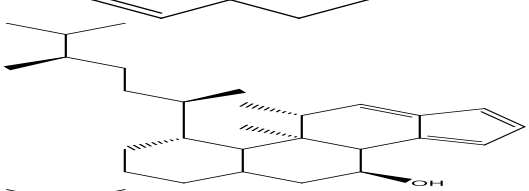
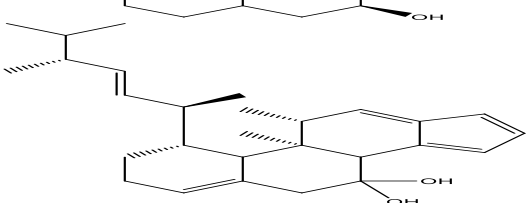
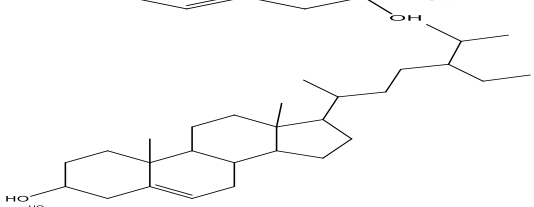
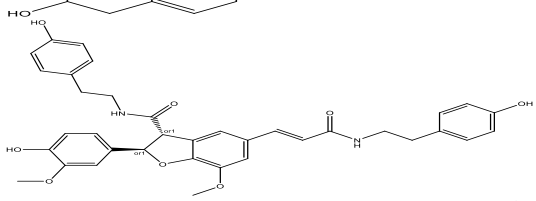
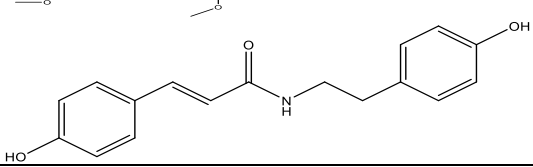
Class	Subclass	Structure	Reference
	Cannabielsoin		Bercht *et al*., 1973
	Cannabicyclol		Bercht *et al*., 1973
	Cannabichromene		Gaoni & Mechoulam, 1966
	Cannabinol		Gaoni & Mechoulam, 1966
	Cannabitrol		Gaoni & Mechoulam, 1966
	(−)-Δ 9 -Trans-Tetrahydrocannabinol		Gaoni & Mechoulam, 1966
Terpene	Friedelin		Slatkin *et al*., 1971
	Farnesol		Hendriks *et al*., 1978
	Vomifoliol		Hendriks *et al*., 1978
	Camphene		Nigam *et al*., 1965

Table 2. (Cont'd.).

Class	Subclass	Structure	Reference
	Linalool		Nigam *et al*., 1965
	Myrcene		Hendriks *et al*., 1978
	Citronellol		
	Safranal		Hendriks *et al*., 1978
	Curcumene		Ross & ElSohly, 1996
	Phytol		Hendriks *et al*., 1978
Phenol	Eugenol		Hendriks *et al*., 1978
	Vanillin		Hendriks *et al*., 1978
	Dihydrophenanthrene		Shoyama & Nishioka, 1978
Steroids	Campesterol		Radwan *et al*., 2009
	Ergosterol		Elhendawy *et al*., 2018
	Sitosterol		Elhendawy *et al*., 2018
Lignans	Grossamide		Flores-Sanchez & Verpoorte, 2008
	N-trans-coumaroyltyramine		Flores-Sanchez & Verpoorte, 2008

Amyotrophic lateral sclerosis: Amyotrophic lateral sclerosis damages the brain by selectively degenerating motor neurons in the brain and spinal cord. *Cannabis sativa* can be considered as a potential source of compounds for the treatment of disease as this disease involves cannabinoid receptors especially CB2. Cannabinoid receptors especially CB2 efficacy can increase the survival rate by 56% by slowing down the process of motor neuron degeneration thus it can open new pathways for the treatment of disease (Longinetti & Fang, 2019). A recent study conducted by Cavet *et al*., (2022) on SOD1-G93A murine ALS models shows that cannabidiol can slow the progression of the disease by acting as an anti-inflammatory agent and anti- spasticity agent.

Spasticity: Spasticity is muscular stiffness and is most common problem associated with multiple sclerosis. Different drugs used against it are either ineffective or limited by their side effects. Now the world is heading towards *Cannabis sativa* to reduce it and it is found to be very effective. Nabiximol were found to be very effective in reducing pain in MS patients that show no response to other drugs. However, some controversial results were also found as some authors reported its side effects such as psychosis, loss of memory, etc. So further research is required for it (Corey-Bloom *et al*., 2012). In response to the German authority's request, the first-line anti-spastic study was recently carried out using an enriched-design methodology as evidence that add-on Nabiximols were more effective than adjusting the anti-spasticity medication regimen alone in providing symptomatic relief of MS spasticity during a 4-week trial period compared to placebo. Oromucosal Nabixomol was used as an add-on therapy for treating MS spasticity in MS Patients (Haddad *et al*., 2022).

Sleep disorder: The Cannabis and cannabinoids are now extensively researched for sleep disorder. Chagas *et al*., (2013) observed an increase in the overall percentage of sleep in the rats, when rats received medium and high doses of CBD injections versus a placebo. Research reported by Gorelick *et al*., (2013) shows an overall decrease in the amount of nighttime sleep over time by administering synthetic THC, indicating a potential effect of tolerance. CBD is found to be useful in the treatment of insomnia and day sleepiness. But only adequate dose and prescribed time periods were found to be helpful. Overuse of D9-THC can impair sleep quality. Nabilone was found to be effective in reducing stress caused by nightmares and can improve sleep and reduce pain in patients (Kaul *et al*., 2021).

Gastrointestinal diseases: *Cannabis sativa* can be used for treatment of different gastrointestinal diseases. *Cannabis sativa* can be used to relieve different complication such as diarrhea and nausea, stomach pain etc. associated with Crohns disease also called irritable bowel syndrome. Endocannabinoids can be effective in the treatment of IBD (inflammatory bowel disease) by producing effector molecules against inflammation, diarrhea and nausea. Endocannabinoid system (arachidonoylethanolamine and 2-arachidonoylglycerol) can be activated by different lipid mediators, and enzymes (N-acyl phosphatidylethanolamine phospholipase D and diacylglycerol lipase) that can synthesize or degrade these lipid mediators. G protein coupled to Cannabinoids receptors that can also regulate endocannabinoids receptors. Endocannabinoids system can maintain homeostasis in intestine. Endocannabinoids can also reduce inflammation by inhibiting a range of proinflammatory mediators such as nitric acid, interleukin-1 beta (IL-1b), and TNF-α (Hasenoehrl *et al*., 2017).

Toxicity

Various studies conducted on humans indicated that smoking cannabis with THC level 0.5 and 2.9% w/w resulted in mild psychological changes with increase in heartbeat of 15 BPM and 57 BPM respectively. But when normalized to an administered THC dose per kilogram body weight e.g. 0.12mg/ kg oral or 0.05mg/kg mild mood changes, usually euphoria, as well as altered senses of time, visual, and auditory perception were reported (Spindle *et al*., 2019). Smoking high dose of THC e.g. 0.2 to 0.25mg/kg reported hallucination. After inhaling a single cigarette containing 3.55% THC, behavioral and physiological impacts show up quickly, correlating with 18ng/mL plasma amounts. According to some studies, the euphoric effects of THC at concentrations of 7 to 10 ng/mL can be compared to those of ethanol at 50 mg/dL or higher. THC blood levels in clinical case studies are uncommon. A 19-year-old male patient was discovered comatose, sweating, and with rigid muscles after reportedly smoking a substance. A thorough clinical investigation showed that a blood sample tested positive for THC and contained 180ng/mL (equivalent to a plasma concentration of 300ng/mL) according to radioimmunoassay analysis (Guidet *et al*., 2020). Overall, chronic cannabis users appear to be more susceptible to the dangers of adverse effects than nonusers. Early to mid-adolescent users who use regularly or who are dependent on the substance.

Conclusions

The review is based on critically analyzing data on traditional usage, Phytochemistry and Pharmacological uses of *Cannabis sativa*. *Cannabis sativa* is an important medicinal plant that has long being used by people for different purposes. Ethnomedicinal uses of the plant include its use for hair growth, to change mood, to reduce pain symptoms associated with different diseases, for treatment of indigestion and to relieve from stress. Research on compound isolation from it started in the last century but has been accelerated during last decade. Large number of compounds has been isolated from it which includes cannabinoids, terpenes, flavonoids, steroid compounds and Lignans. Still further research is going on to explore many new bioactive compounds from the plant. At first it was used as a sedative to relieve stress and improve sleep quality but now with the exploration of many new medicinal properties it has been as to treat Alzheimer, epilepsy, Vomiting, Gastrointestinal disorders, Spasticity and amyotrophic lateral sclerosis. Further research is required to study the mechanism of its action as antiepileptic agent, anti-Alzheimer's agent and for many other disease treatments. Exploration of the bioactivities of many compounds isolated from it, especially cannabinoids can pave the pathways for the discovery of many new drugs in the future.

Future perspectives: Legalizing cannabis would signal a significant shift in Pakistani policy because it would help to regulate the drug. Criminal offenses will occur less frequently, and the drug will be sold and bought in accordance with efficient regulatory guidelines. Patients with chronic conditions may be prescribed medicinal cannabis in Pakistan by doctors, enhancing their quality of life. A national patient register can be established to collect detailed information about the ailments for which patients use cannabis, enabling researchers to better understand usage patterns and the drug's potential benefits. The ease of obtaining the drug also makes it possible for researchers to perform observational and carefully monitored clinical trial studies on the security and effectiveness of medicinal cannabis therapies, which can open the door to new understandings. This is possible if Pakistan approves the legalization of cannabis use.

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(Received for publication 30 August 2023)