An overview of the traditional applications, botanical features, chemical composition, and medicinal properties of *Cannabis sativa* L.

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Abstract.

Medicinal plants have been one of the most important sources of medicine since the dawn of human civilization. Indigenous communities have used products from this plant in different conditions throughout documented history. *Cannabis sativa* L. is one of the most widely employed herbaceous medicinal plants for textiles and fibers, in medicine, as a source of food, animal food, animal bedding, and agriculture for seeds. This paper highlights the traditional applications, botany, phytochemistry, and pharmacological properties of *Cannabis sativa* L. Extensive database retrieval, such as Google Scholar, Semantic Scholar, ResearchGate, Academia.edu, PubMed, SciFinder, ChemSpider, CNKI, PubFacts, etc., was performed by using the keywords "Hemp," "*Cannabis*," as well as the scientific name of this plant species (*Cannabis sativa* L). Besides, reviews of relevant textbooks, documents, and patents were also employed to collect sufficient information. This study revealed numerous pharmacological activities of *Cannabis sativa* L. that could help with several medical diseases. Besides that, more than 565 bioactive constituents have been isolated and identified from diverse parts of *Cannabis sativa* L. This could help discover potential therapeutic effects and develop new medications to benefit human health.

Graphical Abstract

Phytochemistry

565 compounds in *cannabis sativa* L. have been identified, including:

- 125 Phytocannabinoids (CBD, CBE, CBG, CBC, CBN, CBL, CBT, CBND, Δ^9-THC, Δ^8-THC, and miscellaneous type cannabinoids).

- More than 400 non cannabinoid compounds (Terpenes, Flavonoids, Phenols, and Alkaloids).

Systematic taxonomy of *Cannabis*

Kingdom:	Plantae (Plants)
Division:	Magnoliophyta (Flowering plants)
Class:	Magnoliopsida (Dicotyledons)
Order:	Rosales
Family:	Cannabaceae
Genus:	*Cannabis*
Species:	*Cannabis sativa* L.

Pharmacological activities

cannabis sativa L. and its phytochemical constituents have exhibited various interesting pharmacological properties, including: analgesic, anti-anxiety, anticonvulsant, antidepressant, antiemetic, antifungal, antihypertensive, anti-inflammatory, anti-melanogenesis, antimicrobial, antioxidant, antiproliferative, antipruritic, antispasmodic, antitumor, anxiolytic, cytotoxic, expectorant, gastroprotective, and numerous other pharmacological effects.

Traditional uses

Cannabis sativa L. is one of the most widely employed herbaceous plant species for agriculture, agrochemistry, beverages, bioenergy, biofuels, building materials, composites, cosmetology, environmental purposes, food industry, furniture, hygiene, medicine, paper, ropes, textiles and tech-textiles.

1. Introduction

Cannabis is a commonly used herbaceous medicinal plant in agriculture, agrochemistry, beverages, bioenergy, biofuels, building materials, composites, cosmetology, environmental purposes, food industry, furniture, hygiene, medicine, paper, ropes, textiles and tech-textiles [1–8]. Hemp is mainly used in healthcare to relieve pain and treat nervous system diseases [9]. It contains several chemically active compounds, such as cannabinoids, terpenoids, carbohydrates, amides, phenolic compounds, phytosterols, fatty acids and their esters, flavonoids, and alkaloids [10, 11]. *Cannabis sativa* L. is documented to be beneficial in the therapy of neuralgia, epilepsy, gout, liver, glaucoma, nausea, insanity, insomnia, pain, and rheumatism, among others, with activities virtually mainly on the upper nerve centers [12–14]. Several pertinent paleobotanical, archeological, and historical evidence of hemp, including seeds, pollen grains, carbonized remains, fibers, phytoliths, seed impressions, cannabinoid chemicals, and trichomes, has been recovered from dated archeological contexts [15]. One of the earliest Chinese medical literature, *Shennong pên Ts'ao Ching*, one of the earliest Chinese medical literature, explains *Cannabis sativa* L. roots as a pain treatment, dating back to 2700 BC [16].

Cannabis sativa L. is widely classed as a "narcotic," a legal term that is frequently applied arbitrarily. A narcotic is a drug or preparation often related to harsh punishments due to its actual or alleged

detrimental properties [17]. Since World War II, hemp has been illegal in Western countries since it is considered a leading substance abused. Almost all pharmacological and non-drug research and development have been forbidden [18]. In recent years, many countries (Canada, Colombia, Germany, Iran, Italy, Netherlands, Uruguay) have legalized the growing and processing of hemp varieties that contain relatively few psychoactive chemicals (industrial hemp). In Morocco, for example, law No. 13.21 was passed in 2021. This law (No. 13.21) legalizes the cultivation, transformation, and commercialization of cannabis for scientific and medical purposes while stressing the prohibition of its circulation and trafficking for entertainment, hallucinations, and smoking. Consequently, the United Nations Commission on Narcotic Drugs (CND) decided to withdraw *Cannabis sativa* L. from Schedule IV of the 1961 Single Convention on Narcotic Drugs in December 2020, acknowledging hemp's medical and therapeutic benefits [19]. This paper presents an overview of the results found about traditional uses, botany, phytochemical, and pharmacological activities of *Cannabis sativa* L.

2. Materials and Methods

2.1. *Taxonomic Hierarchy*

Cannabis sativa L. is a member of the Cannabaceae family, which includes 12 genera (*Aphananthe*, *Cannabis*, *Celtis*, *Gironniera*, *Humulus*, *Lozanella*, *Momisia*, *Parasponia*, *Pteroceltis*, *Sponia*, *Trema*, and *Ziziphus*). There are 636 scientific plant names for species ranked on the Plant List. There are 102 approved species names among them [20].

Kingdom: Plantae

Subkingdom: Tracheobionta

Superdivision: Spermatophyta

Division: Magnoliophyta

Class: Magnoliopsida

Order: Rosales

Family: Cannabaceae

Genus: *Cannabis*

Species: *Cannabis sativa* L.

2.2. *Botanical Description*

Cannabis sativa L. is a dioicous annual herbaceous plant of 1-2 meters, pubescent-harsh, with a strong odor whose phenotypic characteristics show considerable variability [21]. Leaves are opposite:

petiolate, palmate, with 5-7 lanceolate-acuminate segments, dentate, the upper ones often alternate, and 1-3 pieces. The stem is erect, stiff, and simple [17, 22]. The seeds (achenes) are round to nearly lens-shaped, with a round base. Flowers: green, dioecious, in a branching panicle, the females each providing a bract. Male perianth with five equal divisions, five pendulous stamens with terminal anthers and sharp filaments [22]. The female perianth is monosepalous, wrapped around the ovary. The fruit is sub-globose, smooth, grown in large, and sometimes sub-spontaneous in various countries [17].

2.3. Geographical distribution

Cannabis sativa L. is among the most commonly used industrial herbs in the world [23]. Researchers uncovered fruits in a culinary context, a kitchen midden, with a calibrated radiocarbon age of 8 000 cal BCE [24]. However, tracing the origins of *Cannabis sativa* L. to a single geographical place is challenging owing to the plant's many species, subspecies, and varieties. The source of *Cannabis sativa* L. can be found in many diverse areas, depending upon where we draw the line in the phylogenetic tree. Except for Antarctica, *Cannabis sativa L.* is found almost everywhere on the planet. The hemp plant is indigenous to Central Asia, most likely in the Himalayan foothills [3, 25]. *Cannabis sativa* L. was initially confined to this area; however, it has become more widespread due to man [3]. *Cannabis sativa* L. is found practically everywhere, bringing about the term "weed."

3. Results and Discussion

3.1. Traditional uses of Cannabis sativa L.

Cannabis sativa L. is among the first therapeutic, culinary, psychotropic, fiber, the textile, rope, and oil-yielding plants discovered since agricultural farming began some 10,000 years ago [4, 5, 26–30]. Hemp plants provide various benefits depending on the species, dose style, and volume. *Cannabis* uses is likewise largely reliant on the extraction procedure. It can be employed in multiple materials because each plant has different chemical components.

3.1. 1. Traditional medicine

Cannabis sativa L. is commonly used to treat nervous system diseases and pain [31–35]. It is documented to be helpful in the management of nausea, neuralgia, cachexia, gout, multiple sclerosis, seizures, cancer, Alzheimer's, rheumatism, insanity, insomnia, and Crohn's disease [4, 14, 36–50]. *Cannabis* extract has been employed in Arabic-Islamic medicine for its, anti-parasitic, anti-emetic, antipyretic, anti-tumor, anti-epileptic, anti-inflammatory, anti-bacterial, carminative, dermatic, vermifuge, and pain-killing effects [51, 52]. Cannabis can even be made into an oil or tincture and consumed. Remedies are mainly used in the pharmaceutical industry because of their high

concentration of active substances that produce healing results [4, 53, 54]. They also make dosage adjustments simple, lowering the likelihood of unwanted side effects.

3.1.2. *Alimentary use*

Alimentary use is separated into human and animal categories and food and drink. Traditional drinks containing *Cannabis*, which had healing, psychoactive, or spiritual benefits, were automatically added to the nutrient usage class [5]. *Cannabis* products are becoming more widely recognized as nutritious foods. Seeds are rich in lipids, magnesium, polyunsaturated fatty acids, carbs, insoluble fiber, and protein, making them a popular health food [55]. They can be used in smoothies, salads, and dairy-free milk alternatives [55]. *Cannabis* can be employed to manufacture an oil material to make paints, varnishes, soaps, and cooking oil. The oil derived from hemp seeds and derivatives is used in nutritional supplements, food processing, and animal feed. Furthermore, its nutritional value has been linked to improved health outcomes, such as decreased cholesterol and blood pressure [2, 4, 56].

3.1.3. *Hemp Fibers*

For thousands of years, *Cannabis* fiber has been used to make textiles, fabrics, ropes, yarns, rugs, and canvas. In comparison to other natural fibers such as cotton, nettle, and flax, hemp fiber is very durable. In the stems of *Cannabis*, there are two types of fiber: phloem in the outer stem and xylem in the inner stem. Plants have two vascular systems: phloem tissue, which distributes photosynthetic chemicals from the foliage to other parts of the plant, and xylem tissue, which moves water and solutes from the roots to other parts of the plant. Historically, phloem fiber was commonly used for cordage and textiles, whereas the woody core had little value. However, today, both types of wool are valued at [2, 6, 10, 57–59]. Hemp is also employed in plastics and composites by the automobile and aviation industries as a fiberglass substitute. Hemp fiber was cultivated largely for paper scrolls in ancient China [6]. Hemp paper outperformed tree-based paper in decomposition resistance, strength when wet, and resistance to yellowing [6–8]. Hemp fibers are used for insulation and composites in the automotive, fashion, and furniture sectors, where synthetic fibers are substituted with hemp fiber. Hemp hurdles are also utilized as horticultural mulch. *Cannabis* mulch, like traditional mulch, is often used as a cover application for parks with vegetables, flowers, and even container plants like shrubs.

3.1.4. *Other potential applications*

Other uses were divided into four subcategories: cosmetic, magico-religious, firewood, and miscellaneous usage, which were further divided into four subcategories: cosmetic, magico-religious, firewood, and various usages [2, 6–8]. Only human benefits are included in this category.

3.2. *Chemical composition of Cannabis sativa* L.

The overall number of natural chemicals isolated or discovered from *Cannabis sativa* L. has risen over several decades. So far, 565 chemicals in cannabis have been discovered, including 125 phytocannabinoids [10, 35, 60−65]. Cannabinoids are a class of chemicals distinguished by their C21 terpene phenolicbackbone [64]. This vocabulary can classify parent cannabinoids, derivatives of cannabinoids, and transformation products [10]. These cannabinoids are further divided into 11 sub-classes, which include: (−)-Δ^8-trans-tetrahydrocannabinol (Δ^8-THC), (−)-Δ^9-trans-tetrahydrocannabinol (Δ^9-THC), Cannabidiol (CBD), Cannabichromene (CBC), Cannabinol (CBN), Cannabielsoin (CBE), Cannabicyclol (CBL), Cannabitriol (CBT), Cannabigerol (CBG), Cannabinodiol (CBND), and miscellaneous-type cannabinoids. In addition to cannabinoids, More than 400 non-cannabinoid compounds have been extracted and determinated from the *Cannabis* plant [10, 66, 67]. These non-cannabinoids are classified into several chemical groups [64, 68−70]. The principal non-cannabinoid components are classified into four major classes: non-cannabinoid phenols, alkaloids, terpenes, and flavonoids (Table 1).

Table 1. Constituents of *Cannabis sativa* L. by chemical class

Cannabis constituents	Chemical class	References
Cannabinoid compounds (125 Compounds)	(-)-Δ^9-trans-Tetrahydrocannabinol (Δ^9-THC) Type (25 Cannabinoids)	[55, 56, 56, 58 – 70]
	(-)-Δ^8-trans-Tetrahydrocannabinol (Δ^8-THC) Type (5 Cannabinoids)	[61, 62, 62, 64–76]
	Cannabigerol (CBG) Type (16 Cannabinoids)	[61, 62, 62, 64–76]
	Cannabichromene (CBC) Type: (10 Cannabinoids)	[61, 62, 62, 64–76]
	Cannabidiol (CBD) Type: (2 Cannabinoids)	[61, 62, 62, 64–76]
	Cannabinodiol (CBND) Type: (5 compounds)	[61, 62, 62, 64–76]
	Cannabielsoin (CBE) Type: (3 compounds)	[61, 62, 62, 64–76]
	Cannabicyclol (CBL) Type: (9 compounds)	[61, 62, 62, 64–76]
	Cannabinol (CBN) Type: (11 compounds)	[61, 62, 62, 64–76]
	Cannabitriol (CBT) Type: (9 compounds)	[64]
	Miscellaneous Types: (30 compounds)	[61, 62, 62, 64–76]
	Phenols (42 compounds): Spiro-indans (16 compounds), Dihydrostilbenes (12 compounds), Dihydrophenanthrenes (7 compounds), and simple Phenols (7 compounds).	[64]
	Flavonoids (34 compounds): Apigenin, Canniflavin, Chrisoeriol, Cytisoside, Cytisoside glucoside, Geranyl flavone, Glycosides Iso-prenoid flavones, Isovitexin,	[61, 62, 62, 64–76]

Non-cannabinoid compounds (125 Compounds)	Kaempferol, Luteolin, Naringin, Orientin, Prenyl flavone, 6-Prenylapigenin, Rutin, Quercetin, Vitexin.	
	Terpenes (120 compounds): Monoterpenes (61 compounds), Sesquiterpenes (51 compounds), Diterpenes (2 compounds), Triterpenes (2 compounds), Miscellaneous Terpenes (4 compounds).	[61, 62, 62, 64–76]
	Alkaloids (2 compounds): Anhydrocannabisativine, Cannabisativine.	[61, 62, 62, 64–76]
	Lignans: (Phenolic amides and lignanamides)	[70, 71, 74–76]
	Steroids (11 compounds): Sitosterol, stigmasterol, β-sitosterol, campesterol, and ergosterol types	[70, 71, 74–76]

3.3. *Pharmacological activities of Cannabis sativa* **L.**

Cannabis sativa L., because of the number of secondary metabolites like cannabinoids, phenolic compounds, and terpenes, is one of the most researched plant species for phytochemistry. These phytochemical constituents have exhibited interesting pharmacological properties, including analgesic, anti-anxiety, anticonvulsant, antidepressant, antiemetic, antifungal, antihypertensive, anti-inflammatory, anti-melanogenesis, antimicrobial, antioxidant, antiproliferative, antipruritic, antispasmodic, antitumor, anxiolytic, cytotoxic, expectorant, gastroprotective, and numerous other pharmacological effects. The details about the pharmacological activities are recapitulated in Table 2.

Table 2. Phytochemical constituents of *Cannabis* and its pharmacological activities.

Pharmacological activities	Groups/Name of compounds	References
Analgesic	Δ^9-tetrahydrocannabinol (THC), cannabidiol (CBD).	[77]
	Delta-tetrahydrocannabinol (THC).	[78]
	Terpenes: β-caryophyllene, α-humulene, β-myrcene, linalool, monoterpenes, limonene, sesquiterpenes, α-pinene.	[79]
	Δ^9-tetrahydrocannabinol (THC), Terpenes (α-pinene, β-pinene, β-caryophyllene, linalool, α-terpineol, β-myrcene, limonene, terpinolene, α-humulene, caryophyllene oxide).	[80]
	Aspirin, cannabinol (CBN), δ^9-tetrahydrocannabinol (THC), morphine SO^4, cannabidiol (CBD), crude marihuana extract (CME)	[81]
	δ^9-tetrahydrocannabinol (δ^9-THC).	[82]
	$\underline{\Delta^9$-tetrahydrocannabinol}	[83]
	Aspirin, Petroleum extract, Ethanolic extract, Δ^1-THC, CBN,	[84]

	CBD, CBG, Olivetol, Cannflavon.	
Antianxiety	Cannabidiol (CBD)	[85–97]
Antibiofilm	*Cannabis sativa* L. seeds extract	[98]
Anticonvulsant	Cannabidiol (CBD)	[99–103]
	Cannabidivarin (CBDV)	[104]
	Δ^9-tetrahydrocannabinol	[101, 105, 106]
	Δ^8-tetrahydrocannabinol	[101]
	(–) and (+) Isomers of Cannabidiol (CBD)	[107]
Antidepressant	Cannabidiol (CBD)	[96, 97, 108–111]
	Ethanol extract	[112]
	Δ^9-tetrahydrocannabinol	[113]
Antiemitic	Δ^9-tetrahydrocannabinol	[52, 63]
Antifungal	Benzene, acetone, ethyl acetate, methanol, and chloroform extracts of different parts of *Cannabis*	[114]
	Leaf extract of *Cannabis*	[115]
	The n-hexane extracted volatile component of high-power *Cannabis*	[116]
Antihypertensive	*Cannabis* seed meal protein hydrolysate	[117]
	Δ^9-tetrahydrocannabinol	[118]
Antiinflammatory	Aspirin, Petroleum extract, Ethanolic extract, Δ^1-THC, CBN, CBD, CBG, Olivetol, Cannflavon	[84]
	Alkaloids (Cannabisative, anhydrocannabisativin)	[119]
	Δ^9-tetrahydrocannabinol	[120]
	Terpenoids	[121, 122]
	Steroids (Campesterol, stigmasterol, β-sitosterol)	[68]
	Cannabidiol (CBD)	[123]
	Combination of cannabidiol and moringin	[124]
Antimelanogenesis	Ethyl acetate fraction of defatted hemp	[125]
	Phenethyl Cinnamamide	[126]
	Essential Oils	[127, 128]
	Cannabidiol (CBD)	[129]
	Ethanolic extracts of *Cannabis*	[130, 131]
	Hydro-Alcoholic Extract of *Cannabis*	[132]
	Polyphenol contents	[133]
	Cannabis sativa L. seeds extract	[98]
	Δ^9-tetrahydrocannabinol	[134]

Antimicrobial	Cannabidiolic Acid and Cannabidiol	[135]
	Cannabinoids: CBGA, Δ^9-THC, CBD, CBG, CBN, CBC	[136]
	Petroleum ether, methanol extracts of the whole plant, and Oil of the seeds	[137]
Antioxidant	Δ^9-tetrahydrocannabinol	[134]
	Essential Oils	[128, 138, 139]
	Hemp protein isolates (HPIs)	[140]
	Cannabidiol and Cannabigerol	[141]
	Cannabidiol (CBD)	[142]
	Extracts obtained by using different solvents from *cannabis*	[143, 144]
	Combination of cannabidiol and moringin	[124]
	Lignanamides: 3,3′-dimethyl-heliotropamide, cannabisin N, cannabisin O, and cannabisin M	[145]
	Cannabis root extracts: stigmasta-3,5-diene, stigmasta-3,5,22-triene, oleamide, fucosterol, Glutinol, ß-amyrone, stigmastanol.	[146]
	Polar hemp extracts	[147, 148]
	Protein-derived from hemp seed	[117, 149]
Antiproliferative	Polar hemp extracts	[147]
	Δ^9-tetrahydrocannabinol	[150, 151]
	Cannabidiol (CBD	[152, 153]
Antipruritic	Cannabidiol (CBD)	[154]
	Cannabinoids	[155, 156]
Antitumor	(-)-delta-9-tetrahydrocannabinol (delta-9-THC)	[157, 158]
	Monoterpenes	[159]
	Cannabidiol (CBD)	[160–162]
	Cannabis flowers extracted	[163]
Anxiolytic	Cannabidiol (CBD)	[91, 92, 94–96, 164, 165]
Cytotoxic	Terpenoids, phytocannabinoids	[166, 167]
	Cannabidiol (CBD)	[153, 168]
	Flavonoids (Vitexin)	[169]
Neurodegenerative disease	Cannabidiol and Cannabigerol	[141, 170]
	Δ^9-tetrahydrocannabinol	[171–174]
	Cannabidiol (CBD)	[37, 172, 175–177]
	Phytocannabinoids	[174, 178, 179]

Sedative	Cannabidiol (CBD)	[180, 181]
	Δ^9-tetrahydrocannabinol	[181, 182]

4. **Conclusions**

Cannabis sativa L. has been grown throughout human civilization as a supply of textiles, fiber, oil, and food because of its anti-disease properties. Several pieces of this plant have been used to cure and prevent various illnesses, including glaucoma, insomnia, epilepsy, Alzheimer's disease, cancer, and pain. Phytocannabinoids such as Δ^9-tetrahydrocannabinol, cannabidiol, cannabinol, cannabicyclol, cannabitriol, and cannabinodiol are the main bioactive ingredients in the essential oils of this medicinal plant. This review has presented a comprehensive overview of the botany, phytochemistry, and pharmacological properties of *Cannabis* and its traditional uses. The molecular ingredients of *Cannabis* show high potential for offering new compounds that could significantly benefit the drug discovery approach to developing new medications. However, more bioactive components in *Cannabis* oils and extracts should be found utilizing bio-guided extraction techniques.

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