Review on Chemistry, Reproduction, Sex determination, Taxonomy and Medical uses of Cannabis Sativa

ISHA ARORA[1], KIRANJEET KAUR[2], CHAKSHU WALIA[3]

[1, 2, 3] *Assistant Professor at Chandigarh Pharmacy College, Jhanjeri*

Abstract— Cannabis is a genus of flowering plants in the family Cannabaceae. The number of species within the genus is disputed. The genus is widely accepted as being indigenous to and originating from Asia The plant is also known as hemp, although this term is often used to refer only to varieties of Cannabis cultivated for non-drug use. Cannabis has long been used for hemp <u>fibre</u>, hemp seeds and their oils, hemp leaves for use as vegetables and as juice, medicinal purposes, and as a recreational drug. Industrial hemp products are made from cannabis plants selected to produce an abundance of fibre. Various cannabis strains have been bred, often selectively to produce high or low levels of tetrahydrocannabinol (THC), a cannabinoid and the plant's principal psychoactive constituent. Compounds such as hashish and hash oil are extracted from the plant. Cannabis is commonly used as a recreational drug. People also commonly use cannabis for multiple sclerosis (MS) and nerve pain. It is also used for nausea, vomiting, migraine, and many other conditions, but there is no good scientific evidence to support these uses. Cannabis has various mental and physical effects, which include euphoria, altered states of mind and sense of time, difficulty concentrating, impaired short-term memory, impaired body movement (balance and fine psychomotor control), relaxation, and an increase in appetite

Index Terms- Cannabis sativa, chemistry, taxonomy, sex determination

I. INTRODUCTION

Cannabis also known as marijuana or weed among other names, is a psychoactive drug from the cannabis plant. Tetrahydrocannabinol (THC) is the main psychoactive component of cannabis, which is one of the 483 known compounds in the plant, including at least 65 other cannabinoids, such as cannabidiol (CBD). Cannabis can be used by smoking, vaporizing, within food, or as an extract. Cannabis has been one of the most used psychoactive drugs in the world since the late 20th century, following only tobacco and alcohol in popularity. According to Vera Rubin, the use of cannabis has been encompassed by two major cultural complexes over time: a continuous, traditional folk stream, and a more circumscribed, contemporary configuration. The former involves both sacred and secular use, and is usually based on small-scale cultivation: the use of the plant for cordage, clothing, medicine, food, and a "general use as an euphoriant and symbol of fellowship. The second stream of expansion of cannabis use encompasses "the use of hemp for commercial manufacturers utilizing large-scale cultivation primarily as a fiber for mercantile purposes"; but it is also linked to the search for psychedelic experiences (which can be traced back to the formation of the Parisian Club des Hashischins). As of 2022, Uruguay and Canada are the only countries that have fully legalized the cultivation, consumption and bartering of recreational cannabis nationwide.

Fig 1: Cannabis Sativa

In the United States, 24 states, 3 territories, and the District of Columbia have legalized the recreational use of cannabis – though the drug remains illegal at the federal level. Laws vary from state to state when it comes to the commercial sale. Court rulings in Georgia and South Africa have led to the legalization of cannabis consumption, but not legal sales. A policy of limited enforcement has also been adopted in many

countries, in particular Spain and the Netherlands where the sale of cannabis is tolerated at licensed establishments. Contrary to popular belief, cannabis is not legal in the Netherlands, but it has been decriminalized since the 1970s. In 2021, Malta was the first European Union member to legalize the use of cannabis for recreational purposes. In Estonia, it is only legal to sell cannabis products with a THC content of less than 0.2%, although products may contain more cannabidiol. Lebanon has recently become the first Arab country to legalize the plantation of cannabis for medical use. In some countries citizens can be punished if they have used the drug in another country, including Singapore and South Korea. A limited number of studies have examined the effects of cannabis smoking on the respiratory system.

Chronic heavy marijuana smoking is associated with respiratory infections, coughing, production of sputum, wheezing, and other symptoms of chronic bronchitis. The available evidence does not support a causal relationship between cannabis use and chronic obstructive pulmonary disease. Short-term use of cannabis is associated with bronchodilation. Other side effects of cannabis use include cannabinoid hyperemesis syndrome (CHS), a condition which involves recurrent nausea, cramping abdominal pain, and vomiting. Cannabis smoke contains thousands of organic and inorganic chemical compounds. Cannabis smoke is also inhaled more deeply than tobacco smoke. As of 2015, there is no consensus regarding whether cannabis smoking is associated with an increased risk of cancer. Light and moderate use of cannabis is not believed to increase risk of lung or upper airway cancer. Evidence for causing these cancers is mixed concerning heavy, long-term use. In general there are far lower risks of pulmonary complications for regular cannabis smokers when compared with those of tobacco.

A 2015 review found an association between cannabis use and the development of testicular germ cell tumors (TGCTs), particularly non-seminoma TGCTs. Another 2015 meta-analysis found no association between lifetime cannabis use and risk of head or neck cancer. Combustion products are not present when using a vaporizer, consuming THC in pill form, or consuming cannabis foods. There is

concern that cannabis may contribute to cardiovascular disease but as of 2018, evidence of this relationship was unclear. Research in these events is complicated because cannabis is often used in conjunction with tobacco, and drugs such as alcohol and cocaine that are known to have cardiovascular risk factors. Smoking cannabis has also been shown to increase the risk of myocardial infarction by 4.8 times for the 60 minutes after consumption. There is preliminary evidence that cannabis interferes with the anticoagulant properties of prescription drugs used for treating blood clots. As of 2019, the mechanisms for the anti-inflammatory and possible pain relieving effects of cannabis were not defined, and there were no governmental regulatory approvals or clinical practices for use of cannabis as a drug.

- Description:

Cannabis is an annual, dioeciously, flowering herb. The leaves are palmate compound or digitate, with serrate leaflets. The first pair of leaves usually have a single leaflet, the number gradually increasing up to a maximum of about thirteen leaflets per leaf (usually seven or nine), depending on variety and growing conditions. At the top of a flowering plant, this number again diminishes to a single leaflet per leaf. The lower leaf pairs usually occur in an opposite leaf arrangement and the upper leaf pairs in an alternate arrangement on the main stem of a mature plant.
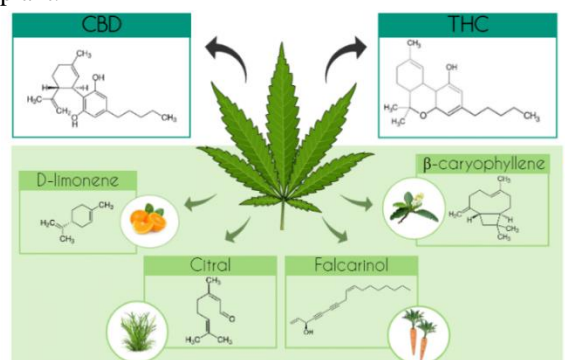

Fig 2: General description of Cannabis

The leaves have a peculiar and diagnostic venation pattern (which varies slightly among varieties) that allows for easy identification of cannabis leaves from unrelated species with similar leaves. As is common in serrated leaves, each serration

has a central vein extending to its tip, but in cannabis this originates from lower down the central vein of the leaflet, typically opposite to the position of the second notch down. This means that on its way from the midrib of the leaflet to the point of the serration, the vein serving the tip of the serration passes close by the intervening notch. Sometimes the vein will pass tangentially to the notch, but often will pass by at a small distance; when the latter happens a spur vein (or occasionally two) branches off and joins the leaf margin at the deepest point of the notch. Tiny samples of Cannabis also can be identified with precision by microscopic examination of leaf cells and similar features, requiring special equipment's and expertise.

• Reproduction:

Many monoecious varieties have also been described, in which individual plants bear both male and female flowers. (Although monoecious plants are often referred to as "hermaphrodites", true hermaphrodites – which are less common in Cannabis – bear staminate and pistillate structures together on individual flowers, whereas monoecious plants bear male and female flowers at different locations on the same plant.) Subdioecy (the occurrence of monoecious individuals and dioecious individuals within the same population) is widespread. Many populations have been described as sexually labile. As a result of intensive selection in cultivation, Cannabis exhibits many sexual phenotypes that can be described in terms of the ratio of female to male flowers occurring in the individual, or typical in the cultivar. Dioecious varieties are preferred for drug production, where the fruits (produced by female flowers) are used. Dioecious varieties are also preferred for textile fiber production, whereas monoecious varieties are preferred for pulp and paper production. It has been suggested that the presence of monoecy can be used to differentiate licit crops of monoecious hemp from illicit drug crops, but sativa strains often produce monoecious individuals, which is possibly as a result of inbreeding.

• Sex Determination

Since the 1920s, a number of sex determination models have been proposed for Cannabis. Ainsworth describes sex determination in the genus as using "an X/autosome dosage type". The question of whether heteromorphic sex chromosomes are indeed present is most conveniently answered if such chromosomes were clearly visible in a karyotype. Cannabis was one of the first plant species to be karyotyped; however, this was in a period when karyotype preparation was primitive by modern standards. Heteromorphic sex chromosomes were reported to occur in staminate individuals of dioecious "Kentucky" hemp, but were not found in pistillate individuals of the same variety. Dioecious "Kentucky" hemp was assumed to use an XY mechanism. Heterosomes were not observed in analyzed individuals of monoecious "Kentucky" hemp, nor in an unidentified German cultivar. These varieties were assumed to have sex chromosome composition XX. According to other researchers, no modern karyotype of Cannabis had been published as of 1996. Proponents of the XY system state that Y chromosome is slightly larger than the X, but difficult to differentiate cytologically. More recently, Sakamoto and various co-authors have used random amplification of polymorphic DNA (RAPD) to isolate several genetic marker sequences that they name Male-Associated DNA in Cannabis (MADC), and which they interpret as indirect evidence of a male chromosome.

Fig 3: Sex determination of Cannabis

It is not surprising that male-associated markers are relatively abundant. In Dioecious plants where sex chromosomes have not been identified, markers for maleness indicate either the presence of sex chromosomes which have not been distinguished by cytological methods or that the marker is tightly linked to a gene involved in sex determination. Environmental sex determination is known to occur in

a variety of species. Many researchers have suggested that sex in Cannabis is determined or strongly influenced by environmental factors. As in some reviews that treatment with auxin and ethylene have feminizing effects, and that treatment with cytokinins and gibberellins have masculinizing effects. It has been reported that sex can be reversed in Cannabis using chemical treatment.[40] A polymerase chain reaction-based method for the detection of female-associated DNA polymorphisms by genotyping has been developed.

• Chemistry

Cannabinoids, terpenes, terpenoids, and other compounds are secreted by glandular trichomes that occur most abundantly on the floral calyxes and bracts of female plants. Cannabis plants produce a large number of chemicals as part of their defence against herbivore. One group of these is called cannabinoids, which induce mental and physical effects when consumed.
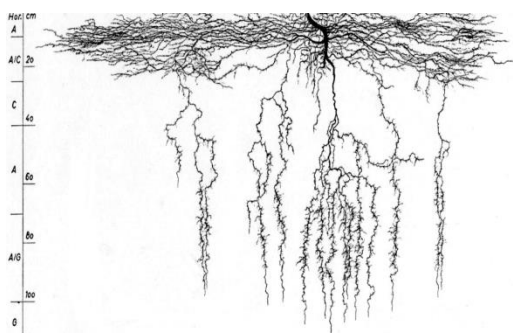

Fig 4: Root system side view

• Genetics

Cannabis, like many organisms, is diploid, having a chromosome complement of 2n=20, although polyploid individuals have been artificially produced. The first genome sequence of Cannabis, which is estimated to be 820 Mb in size, was published in 2011 by a team of Canadian scientists

• Taxonomy

The genus Cannabis was formerly placed in the nettle family (Urticaceae) or mulberry family (Moraceae), and later, along with the genus Humulus (hops), in a separate family, the hemp family (Cannabaceae sensu stricto).Recent phylogenetic studies based

on cpDNA restriction site analysis and gene sequencing strongly suggest that the Cannabaceae sensu stricto arose from within the former family Celtidaceae, and that the two families should be merged to form a single monophyletic family, the Cannabaceae sensu lato.

Various types of Cannabis have been described, and variously classified as species, subspecies, or varieties:

• Plants cultivated for fiber and seed production, described as low-intoxicant, non-drug, or fiber types.
• Plants cultivated for drug production, described as high-intoxicant or drug types.
• Escaped, hybridised, or wild forms of either of the above types.

Cannabis plants produce a unique family of terpeno-phenolic compounds called cannabinoids, some of which produce the "high" which may be experienced from consuming marijuana. There are 483 identifiable chemical constituents known to exist in the cannabis plant, and at least 85 different cannabinoids have been isolated from the plant. The two cannabinoids usually produced in greatest abundance are cannabidiol (CBD) and/or Δ^9-tetrahydrocannabinol (THC), but only THC is psychoactive. Since the early 1970s, Cannabis plants have been categorized by their chemical phenotype or "chemotype", based on the overall amount of THC produced, and on the ratio of THC to CBD. Although overall cannabinoid production is influenced by environmental factors, the THC/CBD ratio is genetically determined and remains fixed throughout the life of a plant. Non-drug plants produce relatively low levels of THC and high levels of CBD, while drug plants produce high levels of THC and low levels of CBD.

When plants of these two chemotypes cross-pollinate, the plants in the first filial (F_1) generation have an intermediate chemotype and produce intermediate amounts of CBD and THC. Female plants of this chemotype may produce enough THC to be utilized for drug production. Whether the drug and non-drug, cultivated and wild types of Cannabis constitute a single, highly variable species, or the genus is

polytypic with more than one species, has been a subject of debate for well over two centuries. This is a contentious issue because there is no universally accepted definition of a species. One widely applied criterion for species recognition is that species are "groups of actually or potentially interbreeding natural populations which are reproductively isolated from other such groups." Populations that are physiologically capable of interbreeding, but morphologically or genetically divergent and isolated by geography or ecology, are sometimes considered to be separate species. Physiological barriers to reproduction are not known to occur within Cannabis, and plants from widely divergent sources are interfertile. However, physical barriers to gene exchange (such as the Himalayan mountain range) might have enabled Cannabis gene pools to diverge before the onset of human intervention, resulting in speciation

- Medical Uses

Medical cannabis (or medical marijuana) refers to the use of cannabis and its constituent cannabinoids, in an effort to treat disease or improve symptoms. Cannabis is used to reduce nausea and vomiting during chemotherapy, to improve appetite in people with HIV/AIDS, and to treat chronic pain and muscle spasms. Cannabinoids are under preliminary research for their potential to affect stroke. Evidence is lacking for depression, anxiety, attention deficit hyperactivity disorder, Tourette syndrome, post-traumatic stress disorder, and psychosis. Two extracts of cannabis – dronabinol and nabilone – are approved by the FDA as medications in pill form for treating the side effects of chemotherapy and AIDS. Short-term use increases both minor and major adverse effects. Common side effects include dizziness, feeling tired, vomiting, and hallucinations. Long-term effects of cannabis are not clear. Concerns including memory and cognition problems, risk of addiction, schizophrenia in young people, and the risk of children taking it by accident

REFERENCES

[1] Merlin MD (2003) Archaeological evidence for the tradition of psychoactive plant use in the old world. Econ Bot 57:295

[2] Jiang HE, Li X, Zhao YX, Ferguson DK, Hueber F, Bera S, Wang YF, Zhao LC, Liu CJ, Li CS(2006) A new insight into Cannabis sativa (Cannabaceae) utilization from 2500-year-old Yanghai Tombs, Xinjiang, China. J Ethnopharmacol 108:414

[3] Kriese U, Schumann E, Weber WE, Beyer M, Br€ uhl L, Matthus B (2004) Oil content, tocopherol composition and fatty acid patterns of the seeds of 51 C. sativa L. genotypes. Euphytica 137:339

[4] Small E, Marcus D (2002) Hemp: a new crop with new uses for North America. In: Janick J, Whipkey A (eds) Trends in new crops and new uses. ASHS Press, Alexandria, VA, p 284

[5] Doyle E, Spence AA (1995) Cannabis as a medicine? Br J Anaesth 74:359

[6] Zuardi AW (2006) History of Cannabis as a medicine: a review. Braz J Psychiat 28:153

[7] Guindon J, Hohmann AG (2009) The endocannabinoid system and pain. Curr Drug Targets CNS Neurol Disord 8:403

[8] Jarvinen T, Pate DW, Laine K (2002) Cannabinoids in the treatment of glaucoma. Pharmacol Ther 95:203

[9] Slatkin NE (2007) Cannabinoids in the treatment of chemotherapy-induced nausea and vomiting: beyond prevention of acute emesis. J Support Oncol 5:1

[10] Viveros MP, Marco EM (2007) Cannabinoids, anxiety and depression. Recent Prog Med Plants 18:225

[11] Liang YC, Huang CC, Hsu KS (2004) Therapeutic potential of cannabinoids in trigeminal neuralgia. Curr Drug Targets CNS Neurol Disord 3:507

[12] Abrams DI, Jay CA, Shade SB, Vizoso H, Reda H, Press S, Kelly ME, Rowbotham MC, Petersen KL (2007) Cannabis in painful HIV-associated sensory neuropathy: a randomized placebo-controlled trial. Neurology 68:515

[13] Pryce G, Baker D (2005) Emerging properties of cannabinoid medicines in management of multiple sclerosis. Trends Neurosci 28:272

[14] Emboden WA (1974) Cannabis, a polytypic genus. Econ Bot 28:304

[15] Hillig KW (2004) A chemotaxonomic analysis of terpenoid variation in Cannabis. Biochem Syst Ecol 32:875

[16] Hillig KW (2005) Genetic evidence for speciation in Cannabis (Cannabaceae). Genet Resour Crop Evol 52:161

[17] Schultes RE, Klein WM, Plowman T, Lockwood TE (1974) Cannabis: an example of taxonomic neglect. Harv Univ Bot Mus Leafl 23:337

[18] Serebriakova TY, Sizov IA (1940) Cannabinaceae Lindl. In: Vavilov NI (ed) Kulturnaya Flora SSSR, vol 5. USSR, Moscow-Leningrad, p 1

[19] Vavilov NI, Bukinich DD (1929) Zemledel'cheskii Afghanistan. Trudy po Prikladnoi Botanike. Genetike i Selektsii 33:378

[20] Small E (1975) American law and the species problem in Cannabis: science and semantics. Bull Narc 27:1

[21] Small E (1975) Morphological variation of Cannabis. Can J Bot 53:978

[22] Small E, Cronquist A (1976) A practical and natural taxonomy for Cannabis. Taxon 25:405

[23] Gilmore S, Peakall R, Robertson J (2003) Short tandem repeat (STR) DNA markers are hypervariable and informative in Cannabis sativa: implications for forensic investigations. Forensic Sci Int 131:65

[24] Sakamoto K, Shimomura K, Komeda Y, Kamada H, Satoh S (1995) A male-associated DNA sequence in a dioecious plant, C. sativa L. Plant Cell Physiol 36:1549

[25] Mandolino G, Carboni A, Forapani S, Faeti V, Ranalli P (1999) Identification of DNA markers linked to the male sex in dioecious hemp (C. sativa L.). Theor Appl Genet 98:86

[26] Flachowsky H, Schuhmann E, Weber WE, Peil A (2001) Application of AFLP for the detection of sex-specific markers in hemp. Plant Breed 120:305

[27] T€ orje ́k O, Bucherna N, Kiss E, Homoki H, Finta-Korpelova ́ Z, Bo ́csa I, Nagy I, Heszky LE (2002) Novel male-specific molecular markers (MADC5, MADC6) in hemp. Euphytica 127:209

[28] Sakamoto K, Abe T, Matsuyama T, Yoshida S, Ohmido N, Fukui K, Satoh S (2005) RAPD markers encoding retrotransposable elements are linked to the male sex in C. sativa L. Genome 48:931

[29] Techen N, Chandra S, Lata H, ElSohly MA, Khan IA (2010) Genetic identification of female C. sativa plants at early developmental stage. Planta Med 16:1938

[30] U.S. Department of Justice, Drug Enforcement Agency, Office of Diversion Control. Title 21, United States Code (USC) Controlled Substances Act. http://www.deadiversion.usdoj.gov/21cfr/21usc/802.htm. Accessed 23 Jun 2016

[31] Chandra S, Lata H, Khan IA, ElSohly MA (2008) Photosynthetic response of C. sativa L. to variations in photosynthetic photon flux densities, temperature and CO_2 conditions. Physiol Mol Biol Plants 14:299

[32] Lata H, Chandra S, Khan IA, ElSohly MA (2009) Thidiazuron induced high frequency direct shoot organogenesis of Cannabis sativa L. In Vitro Cell Dev Biol Plant 45:12

[33] Lata H, Chandra S, Khan IA, ElSohly MA (2010) High frequency plant regeneration from leaf derived callus of high Δ9-tetrahydrocannabinol yielding C. sativa L. Planta Med 76:1629

[34] Faisal M, Anis M (2005) An efficient in vitro method for mass propagation of Tylophora indica. Biol Plant 49:257

[35] Agarwal V, Sardar PR (2006) In vitro propagation of Cassia angustifolia through leaflet and cotyledon derived calli. Biol Plant 50:118

[36] Zayova E, Ivanova RV, Kraptchev B, Stoeva D (2010) Somaclonal variations through indirect organogenesis in egg plant (Solanum melanogena L.). Biodivers Conserv 3:1

[37] Ducos JP, Alenton R, Reano JF, Kancnanomai C, Deshayesl A, Petiard V (2003) Agronomic performance of Coffea canephora P. trees derived from large-production in liquid medium. Euphytica 131:215

[38] Magioli C, Mansur E (2005) Eggplant (Solanum melongena L.): tissue culture, genetic

transformation and use as an alternative model plant. Acta Bot Bras 19:139

[39] Pospisilova J, Ticha I, Kadlecek P, Haisel D, Plzakova S (1999) Acclimatization of micropropagated plants to ex vitro conditions. Biol Plant 42:481

[40] Chandra S, Lata H, Mehmedic Z, Khan IA, ElSohly MA (2010) Assessment of cannabinoids content in micropropagated plants of Cannabis sativa L. and their comparison with conventionally propagated plants and mother plant during developmental stages of growth. Planta Med 76:743

[41] De Backer B, Debrus B, Lebrun P, Theunis L, Dubois N, Decock L, Verstraete A, Hubert P, Charlier C (2009) Innovative development and validation of an HPLC/DAD method for the qualitative and quantitative determination of major cannabinoids in Cannabis plant material. J Chromatogr B 877:4115

[42] Galal AM, Slade D, Gul W, El-Alfy AT, Ferreira D, ElSohly MA (2009) Naturally occurring and related synthetic cannabinoids and their potential therapeutic applications. Recent Pat CNS Drug Discov 4:112

[43] Bo ´csa I, Ma ´the´ P, Hangyel L (1997) Effect of nitrogen on tetrahydrocannabinol (THC) content in hemp (Cannabis sativa L.) leaves at different positions. J Int Hemp Assoc 4:80

[44] De Meijer EPM, Bagatta M, Carboni A, Crucitti P, Moliterni VMC, Ranalli P, Mandolino G (2003) The inheritance of chemical phenotype in C. sativa L. Genetics 163:335

[45] Sirikantaramas S, Taura F, Morimoto S, Shoyama Y (2007) Recent advances in Cannabis sativa research: biosynthetic studies and its potential in biotechnology. Curr Pharm Biotechnol 8:237