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CONSECUTIVE REVIEW ON PHYTOCHEMICAL, ANTIOXIDANT, ANTIMICROBIAL AND CLINICAL STUDIES ON SAINTLY HERB INDIAN HEMP (*CANNABIS SATIVA*)

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ABSTRACT

The Cannabaceae family includes Cannabis sativa. Carl Linneus made the initial discovery of the species in 1753. Cannabis sativa is an annual herbaceous flowering plant that is native to Eastern Asia but has since spread throughout the world due to widespread cultivation. Hashish and marijuana, two of the plant's phytochemical byproducts, are the most widely produced and consumed illegal drugs in Europe and India, where they have been used for centuries and are an essential part of Indian culture and religious practices. Although hemp is most well-known for its narcotic characteristics, pre-clinical studies on hemp derivatives have revealed potential for anti-oxidative, anti-inflammatory, anti-diabetic, anti-neuroinflammatory, anti-arthritic, anti-acne, and anti-microbial actions. In light of the numerous recent findings that are significant with regard to this plant, a comprehensive analysis of its phytoconstituents, antioxidants, antimicrobials, and clinical features are described in this paper. This plant has produced a large number of secondary metabolites that demonstrate an excessively wide spectrum of biological activity. The main chemical components of cannabis, delta-9 tetrahydrocannabinol (delta9-THC) and cannabidiol (CBD), are what give it its therapeutic effects. In summary, Cannabis sativa is a well-researched plant with therapeutic potential. With an eye toward the sociolegal context and perspectives for future research, this seeks to update the state of the art knowledge and evidence of using cannabis and its derivatives.

Keywords: *Cannabis sativa, Indian Hemp, Phytochemical, Antioxidant, Antimicrobial.*

1. INTRODUCTION:

Cannabis sativa was first discovered as Hemp, a high-growing industrial variety of the *Cannabis sativa* plant. Hemp is cultivated by humans for thousands of years, and can be used for textiles, food, fibre, building materials, paper, medical treatments, and can even be used as bio fuel. Hemp is grown specifically with THC levels less than 0.3%.

(www.thewellnesssoldier.com). *Cannabis sativa is a flowering, annual dioecious plant. Plants that are male (staminate) are often taller but weaker than female (pistillate) plants. Height is between 0.2 and 2.0 meters, and stems are upright. However, most plants only grow to a height of 1-3 m.* (Gigliano SG). When mankind discovered fire, we discovered a controlled method to burning herbs and incense for inhalation, this is when we discovered the hidden secrets of the *Cannabis sativa* plant. The term *Cannabis* (or marijuana) is used for describing a *Cannabis sativa* (HEMP) plant which is raised for its strong, sticky glands (known as trichomes), which contains higher amount of THC. THC is an acronym for tetrahydro-cannabinol. (www.thewellnesssoldier.com)

Recently, the molecular pharmacology of the seven most phytocannabinoids "(delta9-tetrahydrocannabivarin, cannabinol, cannabidiol, cannabidivarin, cannabigerol, and cannabichromene)" was investigated thoroughly, and 47 terpenoids, 14 cannabinoids, 7 flavonoids and 3 sterols have been profiled in *Cannabis* leaves, flowers, barks, stem and roots for the purposes medication. (Jin D, Dai K, Xie Z, Chen J).

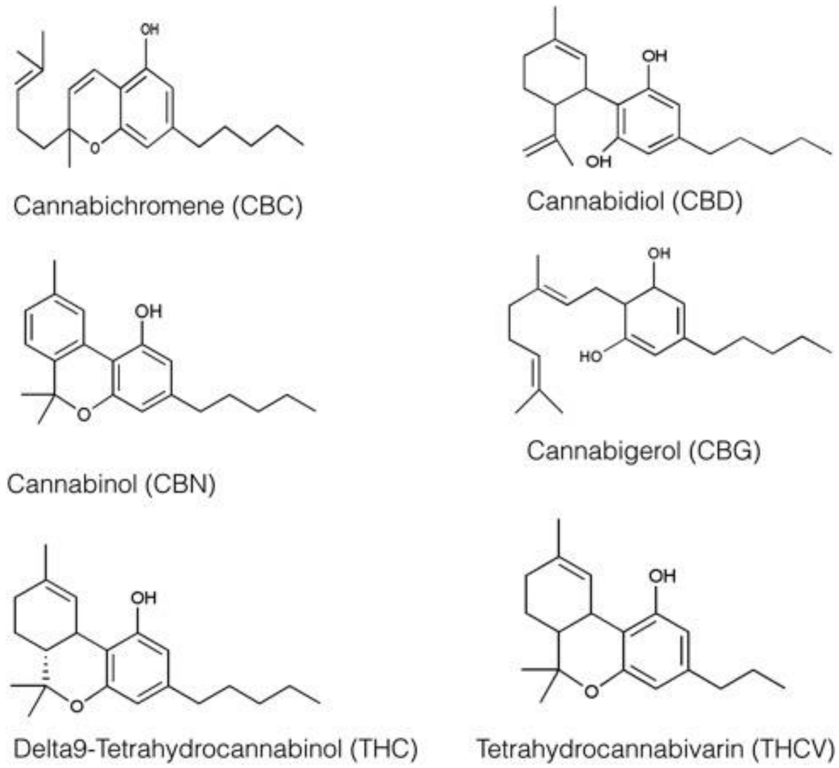

Fig. 1 Different derivatives of Cannabis phytochemicals

The primary psychoactive (mind-altering) substance in marijuana, THC, is what gives the drug its characteristic high. Resin made largely by the leaves and buds of the female Cannabis plant contains the THC molecule. More than 500 other chemicals are found in the cannabis plant, including more than 100 cannabinoids, which are chemically related to THC. Another popular cannabinoid is cannabidiol CBD, as it is non-psychoactive and has been found to affect the body, and produces a calming effect making it useful in the treatment of stress related disorders, pain related injuries, and sleep loss. Our body has what is known as an endocannabinoid system (ECS), which is a group of endogenous cannabinoid receptors located in your brain and throughout your central and peripheral nervous systems. So, when you eat, smoke, vaporize, or use *Cannabis* topically, the cannabinoids run through your endocannabinoid system to your cannabinoid receptors. (www.thewellnesssoldier.com).

2. CLASSIFICATION: (williams_spen/classification)

Kingdom	Plantae
Phylum	Magnoliophyta
Class	Magnoliopsida
Order	Rosales
Family	Cannabaceae
Genus	*Cannabis*
Species	*Cannabis sativa*

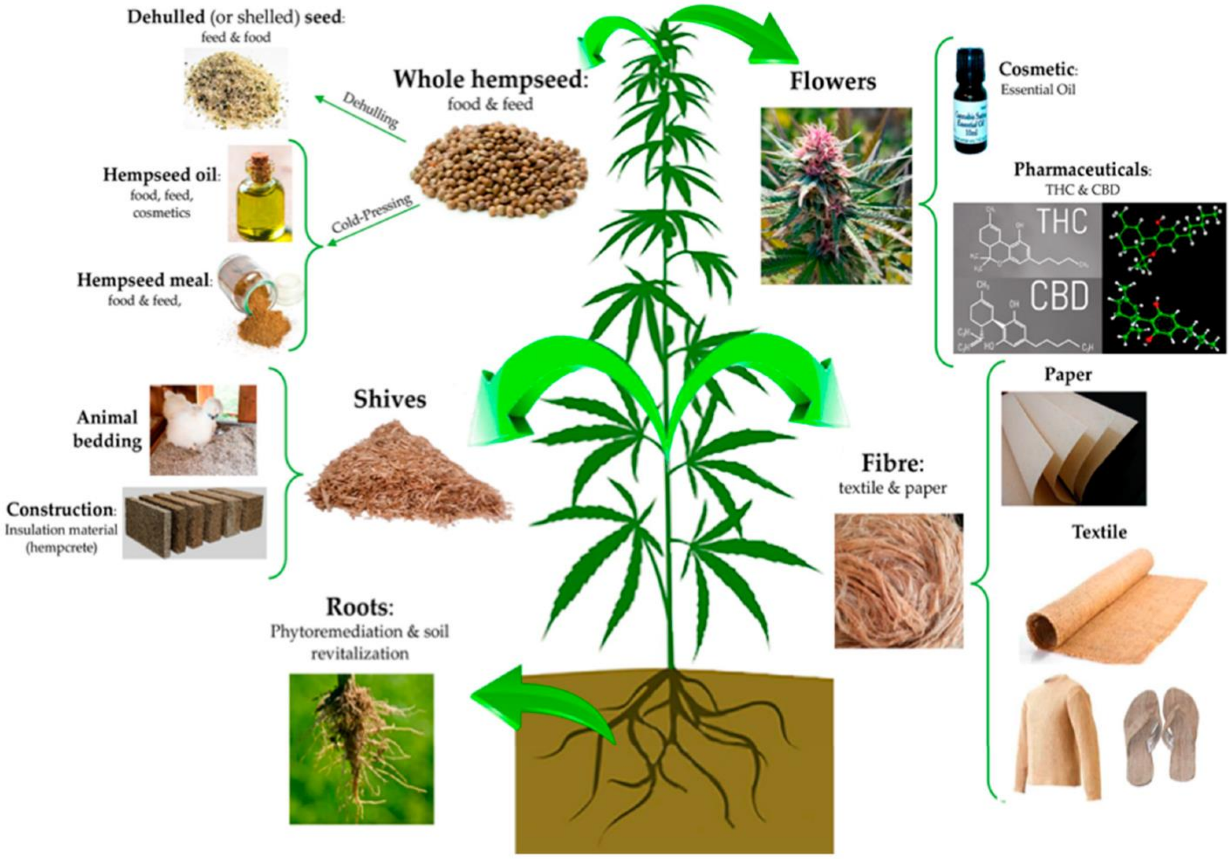

Fig 2. ***Cannabis sativa L.*** **plant parts with diversified applications**

3. ASPECTS OF *CANNABIS SATIVA*

A. Medical, ethnomedical & clinical aspects of *Cannabis sativa.*

Cannabis, sometimes known as cannabis, is one of the most well-known and demonized plant species in the world. However, substantial new research is beginning to show that Cannabis has the potential to develop secondary substances

that might provide a range of health benefits, transforming this unusual plant species from its status as an illegal narcotic into a true biopharmaceutical. This paper summarizes Cannabis' extensive history and describes the molecular mechanisms underlying the synthesis of significant secondary metabolites that may have therapeutic value. Additionally, we give a current overview of the molecular targets and possibilities of the largely unheard-of minor chemicals that the cannabis plant offers. We also go through the most recent developments in synthetic biology, cannabis medicine, and plant science. We continue by highlighting the similarities to earlier studies done on Papaver somniferum (opium poppies), another useful and therapeutically relevant plant, as a sign of the potential future course of Cannabis plant biology. This is because cannabis research is still very young. Overall, this review identifies new routes for cannabis research outside of the medical biology of its well-known chemical components and investigates new possibilities for enhancing the cannabis plant's therapeutic potential.
(Oultram, Jackson M. J. 2021et.al.).

Cannabis sativa application in biomedicine is gaining attention on a global scale. In Bangladesh, cannabis is used traditionally as a natural remedy, and it was grown commercially during the British Empire. Although folk medicine practitioners (FMPs) from various Bangladeshi districts have been employing Cannabis sativa, there haven't been any comprehensive research that focus specifically on this practice. Therefore, this review is an attempt to resurrect from existing ethnomedicinal studies the traditional use of Cannabis sativa as a phytomedicine. Data were searched by using keywords “ethnomedicinal Cannabis sativa and Bangladesh”; “Bangladesh cannabaceae and ethnomedicinal survey”; “ganja, bhang and folk medicine Bangladesh”; “tetrahydrocannabinol (THC), cannabinoid and therapeutic, clinical trial”; and “cannabis and pharmacological/biological” and repossessed from available ethnobotanical articles published on databases such as Science Direct, Scopus, PubMed and Google Scholar. To evaluate the effectiveness of the use of Cannabis sativa for ethnomedical purposes, a search of the pertinent scientific literature was also carried out. We discovered that FMPs of Bangladesh from 12 different districts used Cannabis sativa to treat a variety of cited illnesses, including sleep-related problems (n=5), neuropsychiatric and CNS problems (n=5), infections and respiratory problems (n=5), rheumatism, gastrointestinal, gynecological (n=4 each), cancer, sexual, and other ailments like hypertension, headache, itch, increases bile secretion, and abortifaci From the 11 out of 18 ethnomedicinal plant survey reports, a total of 15 formulations have been identified. The haighest part of the plant used as 53.8% was leaf, 23% was root, then 7.7% was seed and then flower, inflorescence, resin, and all parts were 3.8%. (Shakil, Shahriar S. M2021.et.al.).

The cannabis plant, Cannabis sativa L., has shown to be a valuable source of chemical compounds with a wide range of structures and pharmacological activity. Terpenes and phytocannabinoids are two of the most significant subgroups of chemicals. The cannabinoid receptors type 1 (CB1), type 2 (CB2), and the G protein-coupled receptor 55 (GPR55) are the receptors that these compounds are most likely to bind to, and they account for the majority of the pharmacological activity of cannabis that has been demonstrated thus far in conditions such as epilepsy, sclerosis multiplex, vomiting and nausea, pain, appetite loss, Parkinson's disease, Tourette's syndrome, schizophrenia, glaucoma Increased bioavailability and blood-brain barrier penetration are other signs of the synergistic impact of phytochemicals found in raw Cannabis sp. material. In light of the current understanding of the synergistic effects of the chemicals contained in cannabis extracts and the implications of their clinical usage in the treatment of specific disorders, this study gives an overview of the phytochemistry and pharmacology of the components. (Stasiłowicz, Anna, 2021 et.al.).

With more than 500,000 new cases reported each year among women in Sub-Saharan Africa, cervical cancer continues to be a problem for global health. Various treatment plans have been proposed in different parts of Africa, yet every year, over a quarter of a million women lose their lives to cervical cancer. Due to this, it is the most fatal malignancy in black women, necessitating immediate therapeutic approaches. In this work, we investigate the anti-proliferative effects of cannabis sativa crude extract and cannabidiol, the plant's primary chemical constituent, on various cervical cancer cell lines. Various procedures were used to accomplish our goal, including phytochemical screening, the MTT assay, cell growth analysis, flow cytometry, morphological analysis, the caspase 3/7 assay, and the ATP measurement assay. The findings show that at various doses, both cannabidiol and Cannabis sativa extracts were able to stop cell proliferation in all tested cell lines. They also demonstrated that cannabidiol caused apoptosis by increasing subG0/G1 and apoptosis via annexin V. The overexpression of p53, caspase 3, and bax demonstrated apoptosis. Further evidence for the triggering of apoptosis came from morphological modifications, an increase in caspase 3/7, and a drop in ATP levels. These findings imply that cannabidiol, as opposed to Cannabis sativa crude extracts, inhibits cell proliferation and induces cell death in cervical cancer cell lines. (Lukhele, Sindiswa T.2016, et.al.).

Cannabis is a contentious topic in every area of life, including politics, pharmacology, applied treatments, and even botanical classification. It has been disputed for more than 250 years whether or not Cannabis is a species. It seems unlikely that a clear winner between the "lumpers" and "splitters" in this taxonomical argument would emerge because all Cannabis kinds are eminently capable of cross-breeding to create fruitful progeny. The abundance of Cannabis strains offered on the criminal market and even on the growing legal market only serves to exacerbate this. Even though they are referred to as "strains" in everyday speech, Plantae do not accept the term "strains" when referring to bacteria or viruses but not among Plantae. Given the difficulty in defining terminology in Cannabis and the fact that traits like plant height and leaflet width do not distinguish one Cannabis plant from another, the only obvious course of action is to categorize them according to their biochemical/pharmacological properties. As a result, it is preferable to refer to cannabis variants as "chemovars," or chemical varieties. A flurry of study on alternate sources, particularly yeasts, and complicated systems for laboratory production have evolved in response to the current wave of interest in the cannabis industry, but these assume that single chemicals are a desirable endpoint. Instead, the "entourage effect" argument for

Cannabis synergy is currently strong enough to imply that one molecule is unlikely to equal the medical and even commercial potential of Cannabis alone as a phytochemical factory. Additionally, the astonishing versatility of the cannabis genome eliminates the necessity for genetic engineering techniques. (Russo, Ethan B.2018, et.al).

The skin is an organ that is frequently exposed to a variety of external elements that might have an impact on its composition and functionality. Numerous types of skin cells include various cannabinoid receptors, which allow cannabinoids to interact with them directly. The effect of two different cannabis sativa L. herb extracts on keratinocytes and fibroblasts was therefore evaluated as part of this experiment. It was determined how many biologically active substances were present, including phenols, flavonoids, chlorophylls, and cannabinoids. Using the DPPH radical, the H2DCFDA probe, and the detection of superoxide dismutase activity, the antioxidant capacity of the produced extracts was also evaluated. Through the use of the Alamar Blue, Neutral Red, and LDH tests, the cytotoxicity of hemp extracts was evaluated. It was determined whether the extracts could stop collagenase and elastase, two matrix metalloproteinases, from working. Model hydrogel preparations were made as well, and their impact on transepidermal water loss and skin hydration was assessed. According to the results, hemp extracts can be an important source of physiologically active compounds that lessen oxidative stress, thwart skin aging processes, and enhance skin cell viability. The investigation also revealed that cannabis-based hydrogels have a beneficial impact on skin moisture. (Zagórska-Dziok, Martyna2021 et.al.).

The development and consequences of neurodegenerative illnesses have been linked to decreased brain glucose uptake and utilization resulting from reduced glucose uptake and utilization. In isolated rat brains, tetrahydrocannabinol (THC)-rich Cannabis sativa L. extracts' capacity to promote brain glucose uptake and utilization as well as their modulatory impact on gluconeogenesis, antioxidative purinergic, and cholinergic activities were examined. Hexane and dichloromethane extracts of C. sativa leaves were obtained through successive extraction processes. Freshly harvested brains were treated with the extracts for two hours at 37°C while glucose was present. Brains without the extracts and glucose served as the typical control, whereas incubation without the extracts functioned as the control. Metformin served as the recommended medication. When compared to the controls, C. sativa extracts significantly (p 0.05) increased brain glucose absorption while also increasing glutathione levels, superoxide dismutase, catalase, and ecto-nucleoside triphosphate diphosphohydrolase activities. Malondialdehyde and nitric oxide levels, as well as the activities of acetylcholinesterase, butyrylcholinesterase, glucose 6-phosphatase, and fructose-1,6-biphosphatase, were all reduced during incubation with C. sativa extracts. THC was found in the extracts after being analyzed by GC-MS. THC was anticipated by in silico analysis to pass across the blood-brain barrier. Additionally, the oral LD50 and toxicity class values for THC were anticipated to be 482 mg/kg and 4, respectively. These findings show that C. sativa increases glucose uptake while simultaneously reducing oxidative stress, cholinergic dysfunction, and purinergic and gluconeogenic activity in brain regions. (Erukainure, Ochuko L.2020, et.al.).

Cannabis sativa, in contrast to other plants, is not governed by the United States Department of Agriculture (USDA). Unique Cannabis strains are excluded from registration, making them almost impossible to verify. Customers have been exposed to a flood of unique Cannabis products with numerous different names as Cannabis has become legal for both medical and recreational use in several jurisdictions. Despite there being more than 2000 named strains available to customers, there hasn't been any scientific research done to address concerns regarding the uniformity of commercially available strains. The necessity to offer customers reliable products grows more urgent as cannabis use and legality, both rise. In this study, we used genetic techniques to investigate commercially available, drug-type Cannabis strains to see if the distinctions that are frequently mentioned are valid and if samples with the same strain name are consistent when they are collected from different facilities. Using the "Purple Kush" genome, we created 10 new microsatellite markers to look into possible genetic variation among 30 strains received from dispensaries in three different states. In order to ascertain whether there is a genetic distinction between the commonly used terms Sativa, Indica, and Hybrid kinds as well as whether strain accessions obtained from various facilities have a consistent genetic identity, samples were analyzed. Within the samples of the same strain, significant genetic variations were found, suggesting that inconsistent items can be offered to customers. These variations could result in phenotypic variations and unanticipated effects, which might surprise recreational users but could have more serious repercussions for patients who depend on strains that treat particular medical problems. additional information on the internet: Supplemental information for this article can be found online at 10.1186/s42238-019-0001-1 for authorised users. (Schwabe, Anna L.2019, et.al).

B. Genomics, metabolomics & bioinformatics aspects of *Cannabis sativa.*

The two main chemical families that cannabis (Cannabis sativa L.) produces are cannabinoids and terpenoids. Cannabis is a complex, polymorphic plant species. However, the two main cannabinoids that have monopolized research interest are the psychoactive cannabinoid tetrahydrocannabinol (9-THC) and the non-psychoactive cannabinoid (CBD). Currently, there are more than 600 commercially accessible Cannabis types, giving consumers access to a wide range of strong extracts with intricate chemical makeups and completely unresolved genetics. Cannabis research and development (R&D) toward applications in the pharmaceutical, food, cosmetics, and agrochemical industries faces a big potential as well as a great problem as a result of recently introduced legislation legalizing cannabis growing in many countries. Metabolite composition of complicated matrices can be deconvoluted using metabolomics, which makes it a special bioanalytical tool that could substantially aid and speed up cannabis research and development. Cannabis metabolomics, also known as cannabinomics, can be used, among other things, in the taxonomy of Cannabis varieties in chemovars, the study of new sources of cannabis-based bioactivity in medicine, the creation of new food products, and the optimization of its cultivation with a view to increasing yield and potency. Although research on cannabis is still in its early stages, it is anticipated that using advanced metabolomics will yield information that could help the industry overcome the aforementioned difficulties. Here, the state-of-the-art and conceptual aspects of cannabomics are described in this context. (Aliferis, Konstantinos A. 2020, et.al.).

Dioecious, diploid (2n = 20), industrial hemp (Cannabis sativa L.) is grown for its fiber, seeds, and oil. Due to this crop's abundance of cannabinoids, terpenes, and other phenolic chemicals, interest in it has recently increased. In particular, hemp includes terpenophenolic elements including cannabidiol (CBD) and cannabigerol (CBG), which interact with cannabinoid receptors to positively control a range of physiological, immunological, and metabolic processes in humans. Due to CBD and CBG's impact on cytokine metabolism, cannabinoids are being investigated for their potential role in the treatment of viral illnesses like COVID-19. Numerous synthetic pathways of hemp secondary metabolite formation have been identified on the basis of genomic, transcriptomic, and metabolomic investigations. Despite the clear impact on the scientific and industrial sectors, there are few papers on hemp metabolic engineering. This article reviews the most recent developments and outlooks for hemp metabolic engineering. We discuss three different strategies for accelerating phytochemical production. Transgenic and transient gene delivery technologies, which are essential for efficient metabolic engineering of hemp, have received particular attention. With the development of new synthetic biology techniques, especially the CRISPR/Cas systems, it is now possible to use environmentally friendly metabolic engineering to boost the synthesis of useful hemp phytochemicals while removing the psychoactive ones, including tetrahydrocannabinol (THC). (Deguchi, Michihito 2020, et.al.).

Cannabis sativa was formerly only grown for commercial purposes in strains that produced high-quality fiber with little amounts of the psychotropic ingredient tetrahydrocannabinol (THC). Several jurisdictions have approved the production of cannabis with greater THC levels for medical and/or recreational purposes in recent years, and additional jurisdictions appear prepared to follow suit. As a result, it is anticipated that demand for cannabis with consistent cannabinoid profiles would rise on an industrial scale. In this paper, we emphasize that facility size—rather than yield per square meter—is currently used to predict yearly cannabis production. The primary factors influencing cannabis production per plant, per square meter, and per W of lighting energy were to be determined by this meta-analysis of cannabis yields reported in scientific literature. We suggest using the enormous quantity of genomic information already available for cannabis to better understand how genotype affects yield. Finally, we discuss potential diversification in cannabis producing systems and consider how plant-growth-promoting rhizobacteria (PGPR) might be used to promote growth, control THC production, and implement biocontrol. (Backer, Rachel.2019, et.al.).

A key concern in botany is how genetic diversity within a species impacts phytochemical composition. Tetrahydrocannabinol (THC) and cannabidiol (CBD), two specialized metabolites found in Cannabis sativa, can be divided into three major classes: THC-type, CBD-type, and intermediate type. We put to the test a genetic model linking these three groups to both functional and nonfunctional variants of the CBDAS gene. We evaluated the THC content and genotypes of more than 300 stray C. sativa plants in Minnesota, USA. We conducted a test cross to evaluate the inheritance of CBDAS. Twelve Canadian-certified grain cultivars and twenty clinical cultivars obtained blindly from the National Institute on Drug Abuse were also investigated. There were 0.88, 0.11, and 0.01 feral plants that were of the CBD, intermediate, and THC types, respectively. Despite the large variation in overall cannabis concentration, the three categories had a perfect correlation to CBDAS genotypes. The test cross's genotype frequencies supported the codominant Mendelian inheritance of the THC:CBD ratio. CBDAS genotypes were able to predict the THC: CBD ratio across clinical cultivars despite considerable mean differences in total cannabinoid concentration, and the same was true for industrial grain cultivars when plants showed >0.5% total cannabis content. Our findings show that the THC:CBD ratio can be predicted using CBDAS genotyping in a number of real-world scenarios, extending the universality of the inheritance model for THC:CBD to a range of C. sativa accessions. Feral C. sativa populations may be useful experimental systems and sources of genetic material, according to cannabinoid levels and associated CBDAS segregation patterns. (Wenger, Jonathan P.2020, et.al.).

One of the plants that produces illegal drugs is Cannabis sativa L. The most common narcotics in the world that are trafficked are cannabis products. The continent of Africa is where cannabis is produced at the highest levels worldwide. Rural Ethiopia produces a modest amount of cannabis, most of which is used domestically with a little amount exported to neighboring nations. The review of the literature found no reports on the metal content of cannabis grown in Ethiopia. The main goal of this study is to ascertain the concentration of certain metals in Ethiopian-grown Cannabis sativa L. leaves. Samples of Cannabis sativa L. were gathered in the Ethiopian regions of Metema (Amhara), Mekelle (Tigray), Sheshemene (Oromia), and Butajira (South Nations Nationality and Peoples, or SNNP). The amounts of metals were evaluated by flame atomic absorption spectrometry utilizing the optimum circumstances after correct sample pretreatment, reagent volume usage, digestion temperature, and digestion duration optimization. By examining the digest of the samples that had been spiked with standard solution, the accuracy of the optimized process was assessed. The percentage recoveries ranged from 88 to 103%. The levels of metals determined (µg/g dry weight) were in the ranges Ca (657–1,511), Zn (321–380), Ni (124–172), Cu (122–176), Cd (3–10), Pb (8–10), and Cr (4–8). Among trace metals, Zn had the highest concentration. With the exception of Pb, a statistical analysis of variance (ANOVA) revealed a significant difference in the levels of all the metals between the four sample averages. The findings show that the levels of Pb and Cd in medicinal plants that serve as the raw materials for completed goods surpass those specified by the World Health Organization (WHO). (Zerihun, Agalu 2015,et.al.).

The systematics of cannabis, including phylogenetics and nomenclature, is reviewed. Eight genera that were once in the Celtidaceae and Cannabis are now members of the family Cannabaceae. Actually, the combination of Cannabis, Humulus, and Celtis dates back 250 years. Cannabis likely lost a sibling around 20 million years ago (mya) according to a print fossil of the extinct species Dorofeevia (=Humularia). Since there are only three cannabis print fossils in the entire world, it is challenging to pinpoint her time and place of evolution. Chloroplast DNA (cpDNA) molecular clock study indicates that Cannabis and Humulus diverged 27.8 mya. The northern Tibetan Plateau appears to be the location of origin according to microfossil (fossil pollen) data. According to fossil pollen, cannabis reached Europe between 1.8 and 1.2 mya. Pollen distribution patterns throughout time indicate that the population of European Cannabis experienced genetic bottlenecks repeatedly as its range contracted. Allopatric variations between Asian Cannabis indica (THC>CBD) and European Cannabis sativa (CBD>Δ9-tetrahydrocannabinol [THC]) are presumably the result of genetic drift in this group. The distinction between these taxa at the subspecies level, as well as the formal recognition of C. sativa subsp. sativa and C. sativa subsp. indica, are supported by DNA barcode analysis. Field botanists during the 18th and 20th centuries gave these names to their collections in a very arbitrary manner, as shown by herbarium specimens. This might have influenced Vavilov and Schultes' taxonomic conclusions, leading to the emergence of the terms "Sativa" and "Indica" in today's vernacular taxonomy, which completely misaligns with the formal classifications of Cannabis sativa and Cannabis indica. The terms "Sativa" and "Indica" have been interchanged and hybridized so frequently that they are now essentially meaningless. (McPartland, John M. 2018, et.al.).

C. Biochemical, phytochemical & antimicrobial aspects of *Cannabis sativa.*

Hemp, or Cannabis sativa L., is an adaptable plant that can grow in a variety of environments. High-quality lipids, primarily in the form of polyunsaturated acids, and highly digestible proteins containing necessary aminoacids are both found in hempseeds. The genotype of the plant can affect the composition of hempseed, but other elements including agronomic practices and climatic circumstances might impact the existence of nutraceutical chemicals. In this study, seeds from two C. sativa cultivars—Futura 75 and Finola—that were raised in the Italian Alps' mountainous terrain were examined. This study used two protein extraction techniques (sequential and total proteins), two analytical techniques (SDS-PAGE and 2D-gel electrophoresis), and protein identification by mass spectrometry to examine changes in the protein profile of seeds obtained from such environments. Carotenoids concentration and the profile of fatty acids were also examined. Specifically, fatty acid and protein compositions of Finola seeds were impacted by mountain settings. The lone comparison of certified seeds from the Futura 75 and Finola cultivars did not foresee these modifications. While the protein analysis of Finola seeds from the experimental fields demonstrated a decrease in the protein content, the fatty acid profile verified a high PUFA content in both cultivars from the mountain region. (Cattaneo, Chiara 2021, et.al.).

Cannabis sativa L. is grown for its secondary metabolites, the cannabinoids in particular, which have proven health advantages and expanding medicinal potential. The recent legalization of cannabis cultivation in North America and Europe has been accompanied by a surge in research discoveries for cannabinoid production optimization. Cannabis cultivation with different lighting spectra indicates differential production and accumulation of medically important cannabinoids, including 9-tetrahydrocannabinol (Δ9-THC), cannabidiol (CBD), and cannabigerol (CBG), as well as terpenes and flavonoids, among the many environmental cues that can be manipulated during plant growth in controlled environments. In cannabis trichomes, ultraviolet (UV) radiation has the ability to stimulate the production of cannabinoids, therefore pre- or post-harvest UV therapy merits additional investigation to see if plant secondary metabolite accumulation could be boosted in this manner. THC and terpene buildup can be accelerated by visible LED light, but not CBD. It will be possible to learn more about the light-dependent regulatory and molecular processes in cannabis through well-designed research using light wavelengths other than blue and red light. At various developmental phases, lighting techniques including subcanopy lighting and a variety of light spectra can reduce energy use and maximize cannabis PSM output. There are still many unanswered concerns regarding cannabinoid production pathways in this rapidly expanding business, despite the fact that data suggests that secondary metabolites in cannabis may be controlled by the light spectrum like other plant species. Future study directions are offered after a summary of current findings on cannabis' light spectrum and secondary metabolites, as well as relevant light reactions in model plant species. (Desaulniers Brousseau, Vincent2021, et.al.).

Tetrahydrocannabinol (Δ9-THC), the primary psychoactive component of cannabis, and the G-protein-coupled cannabinoid receptors (CBR) type-1 (CB1R) and type-2 (CB2R), which are both components of the now-known endocannabinoid system (ECS), were both discovered as a result of the long history of medicinal use of Cannabis sativa L. The name "cannabinoids" encompasses a wide range of substances that might influence the CBR and ECS. These substances have been classified into three groups: (i) endogenous, (ii) synthetic, and (iii) phytocannabinoids. Specifically, phytocannabinoids are terpenoids or phenolic substances that are naturally derived from Cannabis sativa. The terpenoids and phenolic chemicals that cause these cannabinoid-like effects can, however, also come from non-cannabinoids found in other plants. In addition to being able to play a role in immune-mediated inflammatory and infectious diseases, neuroinflammatory, neurological, and neurodegenerative diseases, as well as cancer and autoimmunity alone, cannabimimetic ligands outside of the Cannabis plant can act as CBR agonists or antagonists, or as ECS enzyme inhibitors. We consolidate and critically emphasize past, current, and upcoming developments in the knowledge of the function of cannabinoid-like chemicals, primarily terpenes, as potential treatments for various pathological disorders in this review. (Gonçalves, Elaine C.2020, et.al.).

The emergence of germs that are multidrug resistant has highlighted the need for fresh antibacterial substances. Preparations of cannabis sativa have a long history of use in medicine, including the management of infectious disorders. This study gathers data on the effectiveness of C. sativa extracts and their primary constituents (cannabinoids and terpenes) against harmful bacteria and fungi in order to evaluate their potential as antibacterial agents.

OAB - Publisher: Abstract available from the publisher. (Schofs, Laureano .2021, et.al.). There are thought to be 545 separate biogenetic classes of chemical compounds produced by the cannabis plant (Cannabis sativa L.). Many of these phytochemicals have medical and physiological activities in addition to commercial utility. The plant is most well-known for its two most famous and extensively researched secondary metabolites, cannabidiol (CBD) and Δ9-tetrahydrocannabinol (Δ9-THC). Both Δ9-THC and CBD belong to a group of secondary metabolites called cannabinoids, of which there are thought to be over 104. Cannabinoids have a broad therapeutic range across a variety of diseases. This review will concentrate on Cannabis sativa non-cannabinoid metabolites that also have therapeutic potential and some of which have similar medical effects to cannabinoids. Terpenes and flavonoids stand out among these non-cannabinoid phytochemicals. We'll also talk about potential future possibilities for cannabis research and the creation of cannabis-based medicines. One of the most promising non-cannabinoids that is being advanced into clinical trials is caflanone, a flavonoid compound with specific activity against human viruses including the coronavirus OC43 (HCov-OC43) that is responsible for COVID-19 and certain malignancies. There is a wealth of anecdotal evidence supporting the medical benefits of cannabis, which is supported by thousands of years of the plant's use. The several phytochemicals in this plant, including non-cannabinoids, are thought to be responsible for these advantages. We talk about the non-cannabinoids that show the greatest promise for reducing the burden of sickness worldwide. (Lowe, Henry.2021, et.al.).

One of the oldest known medicinal herbs is Cannabis sativa. At the beginning of the 19th century, it was introduced into western medicine. It includes cannabinoids and non-cannabinoid-type substances in a complex mixture of secondary metabolites. There have been more than 500 reported chemicals from C. sativa, 125 of which have been isolated and/or recognized as cannabinoids. The C21 terpeno-phenolic chemicals known as cannabinoids are unique to Cannabis. Non-cannabinoid phenols, flavonoids, terpenes, alkaloids, and other substances are among the non-cannabinoid components. With a focus on their chemical structures, techniques of isolation, and identification, this paper addresses the chemistry of the principal non-cannabinoid ingredients (terpenes, non-cannabinoid phenolics, and alkaloids) as well as cannabinoids. (Radwan, Mohamed M.2021, et.al.).

Cannabis sativa L., a significant herbaceous species with origins in Central Asia, has long been valued for its use in traditional medicine and as a source of textile fiber. Due to its several uses, this quickly growing plant has recently attracted renewed interest. It is a veritable goldmine of phytochemicals and a plentiful supply of both cellulosic and woody fibers. The pharmaceutical and construction industries are both very interested in this plant because its metabolites have powerful biological effects on human health and because its outer and inner stem tissues can be used to produce bioplastics and concrete-like materials, respectively. In this review, the wide range of hemp phytochemicals is examined with a focus on molecules with industrial applications, such as cannabinoids, terpenes, and phenolic compounds, as well as the biochemical pathways for these molecules. Cannabinoids are the most researched class of chemicals, mostly because of the vast range of medicinal effects they have on people, including psychoactive properties. In light of the most recent literature evidence, the therapeutic and economic interests of various terpenes and phenolic compounds, particularly stilbenoids and lignans, are also highlighted. By examining the potential of plant genetic engineering and tissue culture, biotechnological avenues to improve the production and bioactivity of hemp secondary metabolites are suggested. Two approaches in particular—cell suspension and hairy root cultures—are examined. Additionally, due to the significance of hemp trichomes as phytochemical factories, a whole section is devoted to them. Finally, potential advantages of using -omics technologies, such as metabolomics and transcriptomics, to quickly identify and produce lead agents in high quantities from bioengineered Cannabis cell culture are discussed. (Andre, Christelle M.2016,et.al.).

Novel antimicrobial medications are urgently required to combat the rise of bacterial resistance. Since ancient times, several ailments have been treated with Cannabis sativa extracts. The majority of its phytocannabinoid contents, however, are linked to psychotropic effects and have a wide range of medical uses outside of the treatment of infections. Numerous cannabinoids have been shown to have strong antibacterial effects, particularly against Gram-positive bacteria like methicillin-resistant Staphylococcus aureus (MRSA). It's time to debate whether cannabis are promising antimicrobial medication prospects or overhyped intoxicants with advantages now that the first in vivo efficacy has been shown. (Klahn, Philipp.2020, et.al.).

Plants of the cannabis (Cannabis sativa) genus create and store a resin that is high in terpenes in glandular trichomes, which are many on the female inflorescence's surface. Cannabis resin contains bouquets of various monoterpenes and sesquiterpenes, which define some of the distinctive organoleptic features and may also affect the medical effects of various cannabis strains and kinds. Sequences of each stage of terpene production were identified through transcriptome sequencing of the trichomes of the Finola cannabis hemp strain. In the TPS- and TPS-b subfamilies, nine cannabis terpene synthases (CsTPS) have been discovered. The majority of the terpenes in "Finola" resin, including important compounds like "-myrcene," "(E)-ocimene," "(-)-limonene," "(+)-pinene," "(-)-caryophyllene," and "(-)-humulene," are found in mono- and sesqui-TPS, which were identified through functional characterisation. In comparison to tissues that don't produce resin, trichomes have higher expression levels of the transcripts involved in terpene production. Understanding the CsTPS gene family may present chances for choosing and enhancing particular terpene profiles in various cannabis strains and kinds. (Booth, Judith K. 2017, et.al.).

The creation of peripheral system-acting cannabinoid analgesics depends on the selective targeting of the cannabinoid receptor 2 (CB2). This research sought to identify potential CB2-selective molecules among the Cannabis sativa ingredients using computer assistance. ChEMBL was used to gather the molecular structures and associated CB1 and CB2 receptor binding affinities. From a phytochemical database, the molecular compositions of Cannabis sativa's components were gathered. In order to create quantitative structure-activity relationship (QSAR) models using a machine learning strategy, the collected records were filtered and put to use. The affinities of the components of Cannabis sativa were predicted by the verified models. From the Protein Data Bank (PDB), four CB2 structures were obtained. Two sets of decoys and CB2-selective ligands were tested for their capacity to distinguish amongst one another. The Q2 5-CV > 0.62 result indicates that the QSAR model we developed was successful. Three potential CB2-selective ligands that differ from previously investigated compounds were discovered with the aid of the QSAR models. The agonist-bound Cryogenic Electron Microscopy structure of CB2 had the highest statistical performance in differentiating between CB2-active and non-active ligands in a complementary structure-based virtual screening investigation that employed known PDB structures of CB2. Additionally, the same structure excelled at differentiating between CB2-selective and non-selective ligands. (Mizera, Mikołaj. 2020, et.al.).

Cannabis sativa L., also known as hemp, is a multipurpose plant that can quickly adapt to its surroundings. During the 2018 growing season, a monoecious cultivar (Futura 75) and a dioecious one (Finola) were evaluated in a mountainous region in Valsaviore, Italy's Rhaetian Alps (1,100 m a.s.l.). To acquire a comprehensive profile of two varieties grown at altitude, phytochemical behavior was assessed using a variety of analytical techniques, including HS-SPME GC-MS, SDS-PAGE LC-MS/MS, GC-FID, and HPLC-high-resolution mass spectrometry. Both genotypes are mostly competitors, according to the CSR functional approach employed for ecological evaluation, however Finola is more stress tolerator than Futura (C:S:R = 57:26:17%). Higher levels of -ocimene and -terpinolene were detected in Finola inflorescences, whereas - and ß-pinene were found to be more prevalent in Futura along with very high levels of ß-myrcene. Both types included a high concentration of sesquiterpenes (45 identified ones), the most prevalent of which were trans-caryophyllene and -humulene. Tetrahydrocannabinol in its whole was less than 0.1%, while cannabidiolic acid (CBDA), which was identified in Finola at 2.3% and Futura at 2.7%, was the most prevalent cannabinoid. The amount of cannabidiol, the comparable neutral form, varied greatly: 0.27% (Finola) vs. 0.056% (Futura). Edestin, heat shock protein 70, ß-conglycinin, and vicilin were the most prevalent proteins. An extensive phytochemical and ecological analysis of two fiber-type cultivars grown in the Italian Alps revealed a specific, safe, and legal cannabis profile, followed by a specific terpene composition, a high concentration of polyunsaturated fatty acids, and an advantageous protein profile. This hypothesis states that while choosing a type of hemp that would be acceptable for a particular end-use nutraceutical application, geographic provenience of the plant should be taken into account. (Pavlovic, Radmila. 2019, et.al.).

We presented a multi-methodological strategy to investigate the chemical and biological makeup of both the essential oil and the aromatic water of the Italian Cannabis sativa L. in light of the resurgence in interest in its cultivation and production. In terms of cannabis content, volatile component, phenolic and flavonoid pattern, and color features, we reported the chemical composition. Then, we demonstrated the ethnopharmacological relevance of this plant cultivated in Italy as a source of antioxidant compounds toward a large panel of enzymes (pancreatic lipase, α-amylase, α-glucosidase, and cholinesterases) and selected clinically relevant, multidrug-sensible, and multidrug-resistant microbial strains (Staphylococcus aureus, Helicobacter pylori, Candida, and Malassezia spp.), evaluating the cytotoxic effects against normal and malignant cell lines. On Galleria mellonella larvae, preliminary in vivo cytotoxicity tests were also carried out. The findings support the utilization of this natural product as a rich source of significant physiologically active compounds, with a focus on the function played by naringenin, one of the most significant secondary metabolites. (Zengin, Gokhan.2018, et.al.).

There are very few, if any, existing natural populations of the primarily diecious, phenotypically variable domesticated genus Cannabis. Cannabis genetic resource collections cannot be created, described, or used without complying with international drug treaties and related laws. This has limited the integration of secondary genepools linked to Green Revolution genetic improvement methodologies and led to the underutilization of genepool variability in cultivar development. The genetic advancement of Cannabis is anticipated to be facilitated by the organized screening of ex situ germplasm and the exploitation of locally-adapted intraspecific characteristics. To determine the full breadth of genetic resources accessible for pre-breeding, however, only a few attempts have been performed. We give a complete examination of the genetic resources of Cannabis grown ex situ and explore suggestions for their preservation as well as suggestions for pre-breeding characterization and genetic analysis that will support the production of new cultivars. Based on the extensive historical cultivation of cannabis in this area spanning a variety of latitudes, the apparent high levels of genetic diversity, and the comparatively limited representation in published genetic resource collections, we view East Asian germplasm as a priority for conservation. By minimizing hybridization and genetic drift that may take place during Cannabis germplasm regeneration, seed cryopreservation could enhance conservation. We suggest creating a global virtual core collection based on the collecting of consistent and extensive provenance meta-data and the use of high-throughput DNA sequencing technology in light of the special legal position of cannabis. This would make it possible to employ representative core samples for systematic phenotyping and support breeding plans for Cannabis genetic improvement. (Welling, Matthew T.2016, et.al.).

Four monoecious cultivars of Cannabis sativa L. (Ferimon, Uso-31, Felina 32, and Fedora 17) were recently introduced in the Lazio Region. Their chemical composition of the inflorescences was observed from June to September, providing information on their sensorial, pharmaceutical/nutraceutical proprieties. For the purpose of identifying and quantifying chemicals belonging to several classes (sugars, organic acids, amino acids, cannabinoids, terpenoids, phenols, tannins, flavonoids, and biogenic amines), targeted and untargeted studies (GC/MS, UHPLC, HPLC-PDA/FD, and spectrophotometry) were performed. While generally THC content grew over the season, all cultivars in each harvesting period displayed a THC content that was below the legal limit in Italy. The largest concentrations of glucose, malic acid, and citric acid were present during the late blooming stage, although proline levels in all cultivars significantly declined after June. Alloaromadendrene and trans-cinnamic acid were only found in the Uso-31 cultivar, but neophytadiene, nerolidol, and chlorogenic acid were only quantified in the Felina 32 cultivar, which is also distinguished by a very high content of flavonoids. Only the Fedora 17 and Ferimon cultivars contained naringenin and naringin, respectively. Additionally, Ferimon had the highest levels of biogenic amines, particularly in the months of July and August. All cultivars contained cadaverine, although it was only active in September. These findings imply that cultivar and harvesting time affect the chemical makeup of Cannabis sativa L. inflorescences. This information can be used by producers as a guide to help them choose inflorescences with unusual chemical properties depending on the intended purpose. (Ingallina, Cinzia.2020, et.al.).

Recent excavations at the Yanghai Tombs near Turpan, in the Xinjiang-Uighur Autonomous Region of China, revealed a Caucasoid shaman's 2700-year-old grave, along with a sizable stash of cannabis that had been wonderfully kept by climatic and burial conditions. A multidisciplinary international team proved that this substance contained tetrahydrocannabinol, the psychoactive component of cannabis, as well as its oxidative degradation product, cannabinol, other metabolites, and its synthetic enzyme, tetrahydrocannabinolic acid synthase, through botanical examination, phytochemical investigation, and genetic deoxyribonucleic acid analysis by polymerase chain reaction. Cannabis was probably used by this civilization as a drug, a hallucinogenic substance, or as a divination tool. These investigations add to the medical and archaeological records of this pre-Silk Road culture and, to our knowledge, are the first records of cannabis being a pharmacologically active substance. (Russo, Ethan B.2008, et.al).

China has a long history of using Cannabis sativa L. (Cannabaceae) as a fiber and seed crop, and its achenes ("seeds") and other plant parts have been mentioned in Chinese medical books for close to 2000 years. While cannabinoids like cannabidiol (CBD) and Δ9-tetrahydrocannabinol (THC) are the focus of current research, the primary uses of cannabis in Chinese medicine revolve around the use of achenes, ancient indications for the female inflorescence, and other plant parts, which include conditions like pain and mental illness. The analysis of the Chinese medical literature in light of recent developments in the pharmacology and taxonomy of cannabis, however, has not received much prior research, and the majority of the pertinent Chinese historical documents have not yet been translated into Western languages to facilitate textual research. The precise correspondence between various traditional drug names and various plant parts, as well as the effects of long-term selection for fiber-rich cultivars on the medical applications of cannabis in Chinese medicine, are among the many important questions that remain unanswered in the Chinese literature. This article reviews significant historical uses of cannabis in Chinese medicine in chronological order and looks into references to cannabinoids like CBD and Δ9-THC that may be found in ancient Chinese writings. (Brand, E. Joseph.2017, et.al.).

D. Tissue culture, biotechnological & genetic engineering aspects of *Cannabis sativa.*

Cannabis sativa L. has recently been made legal in several areas, which has highlighted the necessity for efficient breeding and biotechnologies for the plant. Micropropagation offers researchers and producers ways to quickly multiply clonal plants free of insects, diseases, and viruses, conserve germplasm, and serves as the foundation for other biotechnologies. Despite this necessity, the lengthy history of bans and restrictions limits research in the field. Existing literature has a number of drawbacks: Studies using drug-type cultivars are typically optimized using a single cultivar; the majority of protocols have not been replicated by independent groups; and some attempts demonstrate a lack of reproducibility across genotypes. Despite the fact that it is well known that there is significant genotype specificity, hemp is frequently used as a stand-in for drug-type Cannabis in publications. The multiplication step of micropropagation (Stage 2) has not been fully established in many publications due to culture decrease and other issues. A brief overview of the history and botany of cannabis will be given in this review, along with a thorough and insightful analysis of cannabis tissue culture. Current research obstacles, the limitations of completed cannabis micropropagation studies, new advancements in cannabis tissue culture technology, and its potential future paths will all receive special consideration. (Monthony, Adrian S 2021, et.al.).

Cannabis sativa has been utilized both medically and commercially for a very long period. There is an urgent need to use novel biotechnological technologies to introduce new genotypes with favorable features and higher secondary metabolite synthesis due to its growing demand in medicine, recreation, and industry. Cannabis has been researched and employed in micropropagation, conservation, cell suspension culture, hairy root culture, polyploidy manipulation, and Agrobacterium-mediated gene transformation. The use of these methods in cannabis has been constrained by challenges like the slow pace of transgenic plant regeneration and the ineffectiveness of secondary metabolite production in hairy root culture and cell suspension culture. In the current review, promising methods such as hairy root culture, in vitro culture, genetic engineering methods in cannabis, morphogenic genes, new computational approaches, clustered regularly interspaced short palindromic repeats (CRISPR), CRISPR/Cas9-equipped Agrobacterium-mediated genome editing, and CRISPR/Cas9-equipped Agrobacterium-mediated genome editing have been highlighted. These methods can help improve gene transformation and plant regeneration and increase secondary metabolite production (Hesami, Mohsen, et al., 2021). In vitro regeneration of Cannabis sativa L., a species having medical qualities, resulted in the production of high cannabidiol (CBD) and cannabigerol (CBG) variants. After sterilization, healthy axillary buds and nodal explants were put in Murashige-Skoog (MS) growth media. In full- or half-strength MS media supplemented with various concentrations of 6-benzyl-amino-purine (BA) or thidiazuron (TDZ), the shoots that had developed after 30 days were subcultured. Analysis of the CBD+ cannabidiolic acid (CBDA) and CBG+ cannabigerolic acid (CBGA) contents in each variety in comparison to the mother plant revealed no statistically significant differences (p 0.05), confirming stability of their chemical profiles. (Ioannidis, Kostas.2020, et.al.).

E. Nutraceuticals & functional food based study of *Cannabis sativa.*

Cannabis sativa L., sometimes known as industrial hemp, is a long-cultivated plant that originated in Central Asia. It has historically been prized for its fiber, food, and medical properties. Its manufacturing and varied usage were documented by a number of eastern and Asian cultures. Since the growing of industrial hemp (fiber and grain) was outlawed in most nations due to its resemblance to the narcotic/medical variety of Cannabis, decades of knowledge and genetic resources were lost. The majority of nations have approved industrial hemp production during the past 20 years, which has sparked extensive study into the health advantages of hemp and hemp-derived products. The numerous health claims made by the several hemp products that are commercially accessible have not yet been proven by current research. With regard to its use as value-added functional food ingredients/nutraceuticals and its health benefits, this review aims to compile recent advances in the science of industrial hemp. It also identifies knowledge gaps and potential directions for future research on this highly valuable multipurpose plant for the global food chain. (Rupasinghe, H. P. Vasantha.2020, et.al.).

The edible fruits of the Cannabis sativa L. plant known as hempseeds were at first thought of as a by-product of the hemp technical fiber business. A increasing interest in the production of hempseeds has emerged in recent years as a result of the reinstatement of the cultivation of Cannabis sativa L. plants with a delta-9-tetrahydrocannabinol (THC) content of less than 0.3% or 0.2% (industrial hemp). This is due to the excellent nutritional value and practical qualities of hempseeds. This review's objective is to investigate the scientific literature on the dietary benefits and practical uses of hempseeds. In addition, we updated the research on the possible use of hempseeds and their derivatives as dietary supplements for the prevention and treatment of inflammatory and chronic degenerative illnesses in both animal models and people. We outline the genetic, biochemical, and legal facets of this plant in the first section of the book because we believe that knowledge of these elements is crucial to understanding the distinction between "industrial" and "drug-type" hemp. The use of hempseeds by the food industry as a supplement to livestock feed and as an ingredient to enhance or fortify daily foods has also been amended in the last section of the evaluation. Overall, the goal of this review is to stimulate further thorough research into the use of hempseeds in the realm of functional foods. (Farinon, Barbara.2020, et.al.).

Cannabis is an annual plant that has a long history of being used as narcotics, food, fiber, fuel, and medicine. Although it is aware of its inherent worth, it has not yet discovered its proper place. It is now our turn to market cannabis after a lengthy history of ups and downs. There are 600 known and numerous other unnamed possibly beneficial chemicals in cannabis. Among the secondary metabolites found in cannabis include alkaloids, terpenoids, phenolic chemicals, and cannabinoids. The most significant chemical substances in this plant, however, are phytocannabinoids (PCs), which can be found in abundance. Only cannabis glandular hairs synthesize more than one hundred 21–22–carbon chemicals, either through polyketide or DOXP/MEP routes (deoxyxylulose phosphate/methylerythritol phosphate). When discussing cannabis, trans-9-tetrahydrocannabinol (9-THC) and cannabidiol (CBD) are the first compounds that come to mind. Cannabinol (CBN), cannabigerol (CBG), cannabichromene (CBC), tetrahydrocannabivarin (THCV), cannabidivarin (CBDV), cannabinodiol (CBND), and cannabinidiol (CBDL) may still have some possible medical effects despite their low concentrations. PCs and endocannabinoids (ECs) primarily use CB1 and CB2 receptors to exert their effects. Nobody can ignore the use of cannabinoids as promising tonics, analgesics, antipyretics, antiemetic, anti-inflammatory, anti-epileptic, and anticancer agents, which are effective for pain relief, depression, anxiety, sleep disorders, nausea and vomiting, multiple sclerosis, cardiovascular disorders, and appetite stimulation. This is true despite all the negative connotations associated with cannabis. Hemp-specific cannabis is now widely recognized by the scientific community and the general public as being much more than just a recreational substance. In veterinary or human medicine, there is an increasing need for cannabinoids, primarily CBD, with a wide range of medicinal and dietary qualities. This review article's primary goal is to historically describe research on cannabinoids, namely THC and CBD, in order to incorporate these beneficial substances into food, feed, and health products as well as present and emerging trends in the consumption of cannabis-derived goods. (Salami, Seyed Alireza.2020, et.al.).

Known for its therapeutic benefits, industrial hemp (Cannabis sativa L., Family Cannabaceae) includes a large variety of bioactive substances, specifically polyphenols such flavonoids, phenolic acids, phenol amides, and lignanamides. Nowadays, a lot of products marketed as having health-promoting properties and including polyphenols from botanical extracts. The inflorescence of industrial hemp could be a novel source of bioactive ingredients for nutraceutical compositions in this context. The purpose of this study was to provide a thorough analysis of the polyphenolic fraction present in polar extracts of four different commercial hemp cultivars (Kompoti, Tiborszallasi, Antal, and Carmagnola Cs) using spectrophotometric (TPC, DPPH tests), as well as spectrometry measurement (UHPLC-Q-Orbitrap HRMS) techniques. Results showed a significant amount of cannflavin A and B, which appear to be unique to cannabis, in the inflorescence examined samples, with mean values of 61.8 and 84.5 mg/kg, or ten- to one-hundred times more than in other plant sections. The Carmagnola CS cultivar has a maximum quercetin-3-glucoside concentration of 285.9 mg/kg among flavonols. The most typical flavanols were catechin and epicatechin, with mean concentrations across all cultivars of 53.3 and 66.2 mg/kg, respectively. The total amount of polyphenols in inflorescence samples was calculated to be between 10.51 and 52.58 mg GAE/g, while the amount of trolox used to scavenge free radicals was between 27.5 and 77.6 mmol/kg. As a result, the inflorescence of C. sativa may represent a potentially new source of polyphenols for nutraceutical compositions. (Izzo, Luana. 2020, et.al.).

F. Miscellaneous aspects of *Cannabis sativa.*

Cannabis has regained much attention as a result of updated legislation authorizing many different uses and can be classified on the basis of the content of tetrahydrocannabinol (THC), a psychotropic substance for which there are legal limitations in many countries. For this purpose, accurate qualitative and quantitative determination is essential. The relationship between THC and cannabidiol (CBD) is also significant as the latter substance is endowed with many specific and non-psychoactive proprieties. For these reasons, it becomes increasingly important and urgent to utilize fast, easy, validated, and harmonized procedures for determination of cannabinoids. The procedure described herein allows rapid determination of 10 cannabinoids from the inflorescences of Cannabis sativa L. by extraction with organic solvents. Separation and subsequent detection are by RP-HPLC-UV. Quantification is performed by an external standard method through the construction of calibration curves using pure standard chromatographic reference compounds. The main cannabinoids dosed (g/100 g) in actual samples were cannabidiolic acid (CBDA), CBD, and Δ9-THC (Sample L11 CBDA 0.88 ± 0.04, CBD 0.48 ± 0.02, Δ9-THC 0.06 ± 0.00; Sample L5 CBDA 0.93 ± 0.06, CBD 0.45 ± 0.03, Δ9-THC 0.06 ± 0.00). The present validated RP-HPLC-UV method allows determination of the main cannabinoids in Cannabis sativa L. inflorescences and appropriate legal classification as hemp or drug-type. (Mandrioli, Mara.2019, et.al.). Plants, including cannabis (Cannabis sativa subsp. sativa), host distinct beneficial microbial communities on and inside their tissues and organs, including seeds. They contribute to plant growth, facilitating mineral nutrient uptake, inducing defense resistance against pathogens, and modulating the production of plant secondary metabolites. Understanding the microbial partnerships with cannabis has the potential to affect the agricultural practices by improving plant fitness and the yield of cannabinoids. Little is known about this beneficial cannabis-microbe partnership, and the complex relationship between the endogenous microbes associated with various tissues of the plant, and the role that cannabis may play in supporting or enhancing them. This review will consider cannabis microbiota studies and the effects of endophytes on the elicitation of secondary metabolite production in cannabis plants. The review aims to shed light on the importance of the cannabis microbiome and how cannabinoid compound concentrations can be stimulated through symbiotic and/or mutualistic relationships with endophytes. (Taghinasab, Meysam.2020, et.al.).

Two kinds of drug-type Cannabis gained layman's terms in the 1980s. "Sativa" had origins in South Asia (India), with early historical dissemination to Southeast Asia, Africa, and the Americas. "Indica" had origins in Central Asia (Afghanistan, Pakistan,Turkestan). We have assigned unambiguous taxonomic names to these varieties, after examining morphological characters in 1100 herbarium specimens, and analyzing phytochemical and genetic data from the literature in a meta-analysis. “Sativa” and “Indica” are recognized as C.sativa subsp.indica var.indica and C.sativasubsp.indicavar.afghanica, respectively. Their wild-growing relatives are C.sativasubsp.indicavar.himalayensis (in South Asia), and C.sativasubsp.indicavar.asperrima (in Central Asia). Natural selection initiated divergence, driven by climatic conditions in South and Central Asia. Subsequent domestication drove further phytochemical divergence. South and Central Asian domesticates can be distinguished by tetrahydrocannabinol and cannabidiol content (THC/CBD ratios, ≥7 or <7, respectively), terpenoid profiles (absence or presence of sesquiterpene alcohols), and a suite of morphological characters.The domesticates have undergone widespread introgressive hybridization in the past 50 years. This has obliterated differences between hybridized “Sativa” and “Indica” currently available. “Strains” alleged to represent “Sativa” and “Indica” are usually based on THC/CBD ratios of plants with undocumented hybrid backgrounds (with so-called “Indicas” often delimited simply on possession of more CBD than “Sativas”). The classification presented here circumscribes and names four taxa of Cannabis that represent critically endangered reservoirs of germplasm from which modern cannabinoid strains originated, and which are in urgent need of conservation. (McPartland, John M.2020, et.al.).

4. CONCLUSION:

A plant of phytochemical laboratories is Indian hemp. The plant has been utilized for thousands of years by people all over the world for its unique biological properties, and no reports of its toxicity in current clinical preparations have been made. Although use of Cannabis in India is illegal, still local and domestinc practitioner of medicine use and prescribe it widely for the treatment a vatiety of ailments and deseases mostly treating arthritis and pain (gout, rheumatism and arthritic pain); problems related to sound sleep (insomnia, induce sleep, soporific); issues related to sexual activities (erectile dysfunction, sex stimulation, low libido, pleasant sensation); gynecological problems and disorders (dysmenorrhea, menorrhagia, expedite delivery); neuropsychiatric and CNS (paralysis, psychosis, insanity); gastrointestinal issues (diarrhea, dyspepsia, strangulated hernia, poor digestion, dysentery); respiratory problems and infections (tetanus, wound, tuberculosis, cough, asthma); also cancer and other ailments including hypertension, headache, itching, increases bile secretion, abortifacient, dandruff, fever, and urinary problems. According to the literature review we conducted, there is substantial scientific evidence in favor of Cannabis sativa's use as a traditional phytomedicine by Indian folk medicine practitioners. In order to provide therapeutic guidelines for cannabis and cannabinoids and to provide a better pharmacological perspective on the opportunities and difficulties of cannabis usage in the future, it is also necessary to do more biological evaluation. Although the sale and cultivation of cannabis are currently prohibited in India, folk medicine practitioners there have long used Cannabis sativa as a natural phytomedicine, and this use has been supported by pertinent pharmacological evidence. Although Cannabis sativa has ethnomedicinal properties in Indian folk medicine, additional biological research is required to associate pharmacological justification with regard to the scenarios and difficulties of Cannabis and cannabinoids' use in India as safe biomedicine for impending.

REFERENCES

1. Adrian S. Monthony, Serena R. Page, Mohsen Hesami, Andrew Maxwell P. Jones, The Past, Present and Future of Cannabis sativa Tissue Culture Plants (Basel) 2021 Jan; 10(1): 185. Published online 2021 Jan 19. doi: 10.3390/plants10010185 PMCID: PMC7835777
2. Agalu Zerihun, Bhagwan Singh Chandravanshi, Ayalew Debebe, Bewketu Mehari Springerplus Levels of selected metals in leaves of Cannabis sativa L. cultivated in Ethiopia. 2015; 4: 359. Published online 2015 Jul 16. doi: 10.1186/s40064-015-1145-x PMCID: PMC4503701
3. Anna L. Schwabe, Mitchell E. McGlaughlin J Genetic tools weed out misconceptions of strain reliability in Cannabis sativa: implications for a budding industry, Cannabis Res. 2019; 1: 3. Published online 2019 Jun 7. doi: 10.1186/s42238-019-0001-1 PMCID: PMC7815053
4. Anna Stasiłowicz, Anna Tomala, Irma Podolak, Judyta Cielecka-Piontek Int J. Cannabis sativa L. as a Natural Drug Meeting the Criteria of a Multitarget Approach to Treatment, J Mol Sci. 2021 Jan; 22(2): 778. Published online 2021 Jan 14. doi: 10.3390/ijms22020778 PMCID: PMC7830475
5. Barbara Farinon, Romina Molinari, Lara Costantini, Nicolò Merendino, The Seed of Industrial Hemp (Cannabis sativa L.): Nutritional Quality and Potential Functionality for Human Health and Nutrition Nutrients. 2020 Jul; 12(7): 1935. Published online 2020 Jun 29. doi: 10.3390/nu12071935 PMCID: PMC7400098.
6. Chiara Cattaneo, Annalisa Givonetti, Valeria Leoni, Nicoletta Guerrieri, Marcello Manfredi, Annamaria Giorgi, Maria Cavaletto, Biochemical aspects of seeds from Cannabis sativa L. plants grown in a mountain environment .
7. Christelle M. Andre, Jean-Francois Hausman, Gea Guerriero, Cannabis sativa: The Plant of the Thousand and One Molecules,Front Plant Sci. 2016; 7: 19. Published online 2016 Feb 4. doi: 10.3389/fpls.2016.00019
8. Cinzia Ingallina, Anatoly P. Sobolev, Simone Circi, Mattia Spano, Caterina Fraschetti, Antonello Filippi, Antonella Di Sotto, Silvia Di Giacomo, Giulia Mazzoccanti, Francesco Gasparrini, Deborah Quaglio, Enio Campiglia, Simone Carradori, Marcello Locatelli, Giuliana Vinci, Mattia Rapa, Salvatore Ciano, Anna Maria Giusti, Bruno Botta, Francesca Ghirga, Donatella Capitani, Luisa Mannina, Cannabis sativa L. Inflorescences from Monoecious Cultivars Grown in Central Italy: An Untargeted Chemical Characterization from Early Flowering to Ripening, Molecules. 2020 Apr; 25(8): 1908. Published online 2020 Apr 20. doi: 10.3390/molecules25081908.
9. E. Joseph Brand, Zhongzhen Zhao, Cannabis in Chinese Medicine: Are Some Traditional Indications Referenced in Ancient Literature Related to Cannabinoids? Front Pharmacol. 2017; 8: 108. Published online 2017 Mar 10. doi: 10.3389/fphar.2017.00108 PMCID: PMC5345167.

10. Elaine C. D. Gonçalves, Gabriela M. Baldasso, Maíra A. Bicca, Rodrigo S. Paes, Raffaele Capasso, Rafael C. Dutra Terpenoids, Cannabimimetic Ligands, beyond the Cannabis Plant Molecules. 2020 Apr; 25(7): 1567. Published online 2020 Mar 29. doi: 10.3390/molecules25071567 PMCID: PMC7181184
11. Ethan B. Russo The Case for the Entourage Effect and Conventional Breeding of Clinical Cannabis: No "Strain," No Gain, Front Plant Sci. 2018; 9: 1969. Published online 2019 Jan 9. doi: 10.3389/fpls.2018.01969
12. Ethan B. Russo, Hong-En Jiang, Xiao Li, Alan Sutton, Andrea Carboni, Francesca del Bianco, Giuseppe Mandolino, David J. Potter, You-Xing Zhao, Subir Bera, Yong-Bing Zhang, En-Guo Lü, David K. Ferguson, Francis Hueber, Liang-Cheng Zhao, Chang-Jiang Liu, Yu-Fei Wang, Cheng-Sen Li J Phytochemical and genetic analyses of ancient cannabis from Central Asia, Exp Bot. 2008 Nov; 59(15): 4171–4182. doi: 10.1093/jxb/ern260
13. Gigliano SG, Cannabios sativa L. botanical problems and molecular approaches in forensic investigations, Forensic Sci Rev., 13, 2001, 1-17.
14. Gokhan Zengin, Luigi Menghini, Antonella Di Sotto, Romina Mancinelli, Francesca Sisto, Simone Carradori, Stefania Cesa, Caterina Fraschetti, Antonello Filippi, Letizia Angiolella, Marcello Locatelli, Luisa Mannina, Cinzia Ingallina, Valentina Puca, Marianna D'Antonio, Rossella Grande, Chromatographic Analyses, In Vitro Biological Activities, and Cytotoxicity of Cannabis sativa L. Essential Oil: A Multidisciplinary Study, Molecules. 2018 Dec; 23(12): 3266. Published online 2018 Dec 10. doi: 10.3390/molecules23123266 PMCID: PMC6320915
15. H. P. Vasantha Rupasinghe, Amy Davis, Shanthanu K. Kumar, Beth Murray, Valtcho D. Zheljazkov Industrial Hemp (Cannabis sativa subsp. sativa) as an Emerging Source for Value-Added Functional Food Ingredients and Nutraceuticals, Molecules. 2020 Sep; 25(18): 4078. Published online 2020 Sep 7. doi: 10.3390/molecules2518407 PMCID: PMC7571072.
16. Henry Lowe, Blair Steele, Joseph Bryant, Ngeh Toyang, Wilfred Ngwa, Non-Cannabinoid Metabolites of Cannabis sativa L. with Therapeutic Potential Plants (Basel) 2021 Feb; 10(2): 400. Published online 2021 Feb 20. doi: 10.3390/plants10020400 PMCID: PMC7923270
17. Jackson M. J. Oultram, Joseph L. Pegler, Timothy A. Bowser, Luke J. Ney, Andrew L. Eamens, Christopher P. L. Grof Biomedicines. Cannabis sativa: Interdisciplinary Strategies and Avenues for Medical and Commercial Progression Outside of CBD and THC. 2021 Mar; 9(3): 234. Published online 2021 Feb 26. doi: 10.3390/biomedicines9030234 PMCID: PMC7996784
18. Jin D, Dai K, Xie Z, Chen J. Secondary metabolites profiled in Cannabis inflorescences, leaves, stem barks, and roots for medicinal purposes. Sci Rep. 2020;10(1):3309. https://doi.org/10.1038/s41598-020-60172-6.
19. John M. McPartland Cannabis Systematics at the Levels of Family, Genus, and Species, Cannabis Cannabinoid Res. 2018; 3(1): 203–212. Published online 2018 Oct 1. doi: 10.1089/can.2018.0039 PMCID: PMC6225593
20. John M. McPartland, Ernest Small PhytoKeys A classification of endangered high-THC cannabis (Cannabis sativa subsp. indica) domesticates and their wild

relatives. 2020; 144: 81–112. Published online 2020 Apr 3. doi: 10.3897/phytokeys.144.46700 PMCID: PMC7148385

21. Jonathan P. Wenger, Clemon J. Dabney, III, Mahmoud A. ElSohly, Suman Chandra, Mohamed M. Radwan, Chandrani G. Majumdar, George D. Weiblen Am J Validating a predictive model of cannabinoid inheritance with feral, clinical, and industrial Cannabis sativa, Bot. 2020 Oct; 107(10): 1423–1432. Published online 2020 Oct 25. doi: 10.1002/ajb2.1550 PMCID: PMC7702092.
22. Judith K. Booth, Jonathan E. Page, Jörg Bohlmann Terpene synthases from Cannabis sativa PLoS One. 2017; 12(3): e0173911. Published online 2017 Mar 29. doi: 10.1371/journal.pone.0173911 PMCID: PMC5371325
23. Konstantinos A. Aliferis, David Bernard-Perron Cannabinomics: Application of Metabolomics in Cannabis (Cannabis sativa L.) Research and Development, Front Plant Sci. 2020; 11: 554. Published online 2020 May 8. doi: 10.3389/fpls.2020.00554 PMCID: PMC7225349
24. Kostas Ioannidis, Evangelos Dadiotis, Vangelis Mitsis, Eleni Melliou, Prokopios Magiatis, Biotechnological Approaches on Two High CBD and CBG Cannabis sativa L. (Cannabaceae) Varieties: In Vitro Regeneration and Phytochemical Consistency Evaluation of Micropropagated Plants Using Quantitative 1H-NMR, Molecules. 2020 Dec; 25(24): 5928. Published online 2020 Dec 15. doi: 10.3390/molecules25245928 PMCID: PMC7765244
25. Laureano Schofs, Mónica D. Sparo, Sergio F. Sánchez Bruni The antimicrobial effect behind Cannabis sativa
26. Luana Izzo, Luigi Castaldo, Alfonso Narváez, Giulia Graziani, Anna Gaspari, Yelko Rodríguez-Carrasco, Alberto Ritieni Analysis of Phenolic Compounds in Commercial Cannabis sativa L. Inflorescences Using UHPLC-Q-Orbitrap HRMS Molecules. 2020 Feb; 25(3): 631. Published online 2020 Jan 31. doi: 10.3390/molecules25030631 PMCID: PMC7037164
27. Mara Mandrioli, Matilde Tura, Stefano Scotti, Tullia Gallina Toschi, Fast Detection of 10 Cannabinoids by RP-HPLC-UV Method in Cannabis sativa L. Molecules. 2019 Jun; 24(11): 2113. Published online 2019 Jun 4. doi: 10.3390/molecules24112113 PMCID: PMC6600594
28. Martyna Zagórska-Dziok, Tomasz Bujak, Aleksandra Ziemlewska, Zofia Nizioł-Łukaszewska Positive Effect of Cannabis sativa L. Herb Extracts on Skin Cells and Assessment of Cannabinoid-Based Hydrogels Properties Molecules. 2021 Feb; 26(4): 802. Published online 2021 Feb 4. doi: 10.3390/molecules26040802 PMCID: PMC7913911
29. Matthew T. Welling, Tim Shapter, Terry J. Rose, Lei Liu, Rhia Stanger, Graham J. King, A Belated Green Revolution for Cannabis: Virtual Genetic Resources to Fast-Track Cultivar Development Front Plant Sci. 2016; 7: 1113. Published online 2016 Jul 29. doi: 10.3389/fpls.2016.01113 PMCID: PMC4965456
30. Meysam Taghinasab, Suha Jabaji, Cannabis Microbiome and the Role of Endophytes in Modulating the Production of Secondary Metabolites: An Overview Microorganisms. 2020 Mar; 8(3): 355. Published online 2020 Mar 2. doi: 10.3390/microorganisms8030355 PMCID: PMC7143057
31. Michihito Deguchi, Shriya Kane, Shobha Potlakayala, Hannah George, Renata Proano, Vijay Sheri, Wayne R. Curtis, Sairam Rudrabhatla Metabolic

Engineering Strategies of Industrial Hemp (Cannabis sativa L.): A Brief Review of the Advances and Challenges Front Plant Sci. 2020; 11: 580621. Published online 2020 Dec 8. doi: 10.3389/fpls.2020.580621 PMCID: PMC7752810

32. Mikołaj Mizera, Dorota Latek, Judyta Cielecka-Piontek Int J Virtual Screening of C. Sativa Constituents for the Identification of Selective Ligands for Cannabinoid Receptor 2, Mol Sci. 2020 Aug; 21(15): 5308. Published online 2020 Jul 26. doi: 10.3390/ijms21155308 PMCID: PMC7432466
33. Mohamed M. Radwan, Suman Chandra, Shahbaz Gul, Mahmoud A. ElSohly, Cannabinoids, Phenolics, Terpenes and Alkaloids of Cannabis, Molecules. 2021 May; 26(9): 2774. Published online 2021 May 8. doi: 10.3390/molecules26092774 PMCID: PMC8125862
34. Mohsen Hesami, Austin Baiton, Milad Alizadeh, Marco Pepe, Davoud Torkamaneh, Andrew Maxwell Phineas Jones Advances and Perspectives in Tissue Culture and Genetic Engineering of Cannabis, Int J Mol Sci. 2021 Jun; 22(11): 5671. Published online 2021 May 26. doi: 10.3390/ijms22115671 PMCID: PMC8197860
35. Ochuko L. Erukainure, Motlalepula G. Matsabisa, Veronica F. Salau, Md. Shahidul Islam Tetrahydrocannabinol-Rich Extracts From Cannabis Sativa L. Improve Glucose Consumption and Modulate Metabolic Complications Linked to Neurodegenerative Diseases in Isolated Rat Brains, Front Pharmacol. 2020; 11: 592981. Published online 2020 Nov 24. doi: 10.3389/fphar.2020.592981 PMCID: PMC7774498
36. Pharmacol Res Perspect. 2021 Apr; 9(2): e00761. Published online 2021 Apr 6. doi: 10.1002/prp2.761 PMCID: PMC8023331
37. Philipp Klahn, Cannabinoids-Promising Antimicrobial Drugs or Intoxicants with Benefits?Antibiotics (Basel) 2020 Jun; 9(6): 297. Published online 2020 Jun 2. doi: 10.3390/antibiotics9060297 PMCID: PMC7345649
38. Rachel Backer, Timothy Schwinghamer, Phillip Rosenbaum, Vincent McCarty, Samuel Eichhorn Bilodeau, Dongmei Lyu, Md Bulbul Ahmed, George Robinson, Mark Lefsrud, Olivia Wilkins, Donald L. Smith Closing the Yield Gap for Cannabis: A Meta-Analysis of Factors Determining Cannabis Yield, Front Plant Sci. 2019; 10: 495. Published online 2019 Apr 24. doi: 10.3389/fpls.2019.00495 PMCID: PMC6491815
39. Radmila Pavlovic, Sara Panseri, Luca Giupponi, Valeria Leoni, Cinzia Citti, Chiara Cattaneo, Maria Cavaletto, Annamaria Giorgi Phytochemical and Ecological Analysis of Two Varieties of Hemp (Cannabis sativa L.) Grown in a Mountain Environment of Italian Alps, Front Plant Sci. 2019; 10: 1265. Published online 2019 Oct 15. doi: 10.3389/fpls.2019.01265 PMCID: PMC6822994
40. Sci Rep. 2021; 11: 3927. Published online 2021 Feb 16. doi: 10.1038/s41598-021-83290-1 PMCID: PMC7887209
41. Seyed Alireza Salami, Federico Martinelli, Antonio Giovino, Ava Bachari, Neda Arad, Nitin Mantri It Is Our Turn to Get Cannabis High: Put Cannabinoids in Food and Health Baskets, Molecules. 2020 Sep; 25(18): 4036. Published online 2020 Sep 4. doi: 10.3390/molecules25184036 PMCID: PMC7571138

42. Shahriar S. M. Shakil, Matt Gowan, Kerry Hughes, Md. Nur Kabidul Azam, Md. Nasir Ahmed J. A narrative review of the ethnomedicinal usage of Cannabis sativa Linnaeus as traditional phytomedicine by folk medicine practitioners of Bangladesh. Cannabis Res. 2021; 3: 8. Published online 2021 Mar 19. doi: 10.1186/s42238-021-00063-3
43. Sindiswa T. Lukhele, Lesetja R. Motadi Cannabidiol rather than Cannabis sativa extracts inhibit cell growth and induce apoptosis in cervical cancer cells, BMC Complement Altern Med. 2016; 16(1): 335. Published online 2016 Sep 1. doi: 10.1186/s12906-016-1280-0 PMCID: PMC5009497
44. The antimicrobial effect behind Cannabis sativa, Pharmacol Res Perspect. 2021 Apr; 9(2): e00761. Published online 2021 Apr 6. doi: 10.1002/prp2.761 PMCID: PMC8023331
45. Vincent Desaulniers Brousseau, Bo-Sen Wu, Sarah MacPherson, Victorio Morello, Mark Lefsrud Cannabinoids and Terpenes: How Production of Photo-Protectants Can Be Manipulated to Enhance Cannabis sativa L. Phytochemistry, Front Plant Sci. 2021; 12: 620021. Published online 2021 May 31. doi: 10.3389/fpls.2021.62002.
46. williams_spen/classification http://bioweb.uwlax.edu/bio203/2011/classification.htm.
47. www.thewellnesssoldier.com