Review Article

Chemical Review and Letters
journal homepage: www.chemrevlett.com
ISSN (online): 2645-4947 (print) 2676-7279

Cannabis unveiled: From history to innovation, exploring the world of cannabis strains, chemistry, industry and economic impact

Amira Metouekel[1], Héritier Uwikunda Serondo[1], Chaimae El Koufi[2], Hamid EL Amri[3], Elmostafa El Fahime[4], Saïd El Kazzouli[1], Nabil El Brahmi[1,*]

[1]*Independent Researcher*
[2]*Department of Chemistry, Faculty of Science and Technology (FST), Sidi Mohamed Ben Abdellah University of Fez, Fez 30000, Morocco*
[3]*Institute of Genetic Analysis of the Royal Gendarmerie in Rabat (LRAM), Ibn Sina Av., Agdal, Rabat, Morocco*
[4]*National Center for Scientific and Technical Research (CNRST), Angle Avenues des FAR and Allal El Fassi, Hay Ryad, Rabat 10102, Morocco*

ARTICLE INFO

Article history:
Received 20 March 2024
Received in revised form 10 June 2024
Accepted 04 July 2024
Available online 04 July 2024

Keywords:
Cannabis, Patents, Economic Growth, Environmental Impact, Pharmaceutical Potential, Industrial Applications.

ABSTRACT

This article examines the diverse impacts of *Cannabis*, emphasizing its economic, environmental, and industrial aspects. In the realm of patents, we analyze the distribution of Cannabis-related patents, focusing on pharmaceutical applications with 73 patents. The global *Cannabis* market, both legal and illegal, is valued at $344.4 billion, with Africa contributing $37.7 billion, highlighting the industry's economic importance. Environmentally, hemp shows great promise for phytoremediation and CO_2 sequestration, absorbing up to 22 tons of CO_2 per hectare. The article also discusses factors affecting hemp growth, such as photoperiod sensitivity and optimal temperatures between 16°C and 27°C. Additionally, it explores the socio-economic benefits and the potential advantages of *Cannabis* legalization, including revenue generation and cost savings for various global locations.

1. Introduction

Cannabis is a plant that has been cultivated and used for many purposes for millennia. Its history is closely linked to human history. Cannabis has captivated people's attention through its use in the manufacture of fiber, its integration into culinary customs, and research into its potential medical benefits. The spread of Cannabis knowledge across different regions is a testament to its significance, including its introduction from India to Arab countries by early Arab travelers who recognized its therapeutic value. Over time, this knowledge extended further, reaching the Maghreb region from Egypt, thereby contributing to the cultural appreciation of Cannabis[1]. The Cannabis genus encompasses diverse species, such as Cannabis sativa, Cannabis indica, and Cannabis ruderalis, each characterized by their resin production through glandular trichomes, while excluding seeds and leaves unless accompanied by the tops[2].

In recent years, scientific understanding of Cannabis has undergone a transformative evolution, fueled by advancements in our comprehension of the complex endocannabinoid system within the human body, as well as the intricate chemical composition of Cannabis itself. This has led to an increasing utilization of Cannabis extracts and constituents for medicinal purposes. Researchers have particularly focused on exploring the properties of cannabinoids, flavones, and terpenes, which serve as key phytochemical compounds present in Cannabis[3].

The landscape of global Cannabis production has witnessed notable shifts, as evidenced by the transition of

* Corresponding author; n.elbrahmi@ueuromed.org
https://doi.org/10.22034/crl.2024.449414.1314
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hashish production dominance from Morocco to Afghanistan in the early 2000s, resulting in a significant decline in Moroccan hashish production during that period[4]. However, it is worth highlighting the unique characteristics of Moroccan hashish, often regarded as a distinctive terroir product[5].

The Rif region in northern Morocco has emerged as a prominent center for Cannabis cultivation, boasting a rich history dating back to the emergence of the hashish industry in the 1960s, followed by its subsequent expansion in the 1980s. The production process of hashish involves meticulous drying of female Cannabis plants to obtain resin and trichomes, which are then carefully separated from the plant material using techniques such as gentle beating or shaking over a fine nylon mesh. The remaining plant fragments are painstakingly removed, while the seeds are discarded[2].

The global Cannabis market has experienced remarkable growth, with an estimated value of USD 20.5 billion in 2020, and projections indicating its further expansion to reach USD 90.4 billion by 2026[6]. Key contributors to the global Cannabis industry include the USA, Morocco, Afghanistan, Mexico, Colombia, Paraguay, Jamaica, and Canada. However, it is crucial to acknowledge that legal restrictions on Cannabis cultivation have limited the availability of peer-reviewed research on pest and disease management, resulting in a scarcity of scientific literature in this particular area[7].

While several review articles focus on the nuclear and phytochemical genomic diversity of cannabis[8] and the varieties of legal cannabis edibles[9], his review aims to provide an indispensable resource for future researchers and investors, facilitating their exploration and understanding of the vast potential offered by Cannabis and determine its global value, especially on the economic level.

2. Methodology

Data collection involved a multi-faceted approach drawing upon an array of reputable scientific databases, including SciFinder, ScienceDirect, Google Scholar, Semantic Scholar, ResearchGate, PubMed Central, ChemSpider, CNKI, PubFacts, Wiley, Web of Science, ICRS, CMCR, Cannabis Clinical Trials, Cannabis Genome Browser. Historical data on Cannabis usage and cultivation were extracted from reputable archives, documents, and recognized sources. Chemical and genetic analysis relied on state-of-the-art laboratory procedures. Economic data was sourced from recognized industry reports, surveys, and statistical sources. The results encompass significant historical trends, detailed strain categorization, comprehensive chemical composition, and a robust economic impact assessment. Ethical considerations were paramount, and all research adhered to legal and ethical guidelines governing Cannabis-related studies, with necessary approvals obtained for data collection. The amassed articles underwent rigorous summarization and in-depth analysis, forming the bedrock of our research. Our approach ensured the inclusivity and comprehensiveness of the data, allowing for a robust examination of Cannabis-related phenomena across various domains.

3. Contextualization of *Cannabis*

3.1. Historical Exploration of *Cannabis*: Origins, Discoveries, and Medicinal Applications

3.1.1. Discovery

Cannabis, one of the oldest known plants, has a history going back thousands of years. Its exact discovery remains uncertain, but it was likely cultivated for its fibers and seeds. Over time, Cannabis was recognized for its pharmacological properties, leading to its religious and therapeutic use[1].

Moroccan cannabis may have been cultivated as early as the Arab conquest, which happened between 665 and 689 AD[10] and spawned the Arab Cannabis. This mingling of civilizations led to the discovery of Arab Cannabis. Since the discovery of hemp fibers in Greece in the third century, this substance has existed. However, Cannabis pollen was first introduced to Morocco during an Arab conquest that occurred between the seventh and the sixteenth century, and it wasn't until the eleventh century that it became widely accessible. All around Morocco, Cannabis was grown for local consumption as well as trade. Moroccans mostly smoked it with long pipes (sebsi), included it in their diet, or combined it into delicacies (maajouns).[11].

3.1.2. Origin

Cannabis has its roots in Central Asia, specifically in the Himalayan slopes of India[12] and then spreads outward in various ways [13]. It spread across the whole Indian subcontinent and into China as it moved east. It moved westward with the Scythians as they advanced into the Middle East and eventually arrived in the Nile Valley. Cannabis was first brought to the Maghreb countries by the Arab conquests. In addition, resin-based preparations were introduced to the West by the Crusaders' return from the East and the Arab conquests of Europe. Cannabis gained popularity over time among populations in western and southern Africa. After the Spanish conquest, it quickly spread to Central America, the Caribbean in the

early 19th century, and the United States in the early 20th century.

3.1.3. Historical Uses

Hemp was grown for its edible seeds, also called hemp seeds, and its fibers, which were used to make textiles[12]. Since the Neolithic era, when it was used to treat a variety of illnesses such as rheumatism, gout, female health problems, malaria, and beriberi, Cannabis has been known to have medical benefits. The various medical uses of Cannabis expanded throughout the Arab-Muslim globe during the Islamic Golden Age, from Persia to Spain. This information was extensively shared by Avicenna's well-known book, "The Canon of Medicine," which makes reference to the use of Cannabis for treating neurological diseases including epilepsy and migraines, as well as for alleviating dysmenorrhea and easing difficult births. Herbalists of the Middle Ages made a distinction between "wild hemp" (Ruderalis), which was empirically applied to nodules and tumors, and "cultivated hemp" (Sativa), which was used, for example, for coughs and jaundice.

Several medical writers from the Renaissance era, such as Paracelsus in the 16th century and John Parkinson in the 17th, wrote about the benefits of Cannabis. Professor J.A. Murray (18th century) recommended Cannabis as a gonorrhea and jaundice treatment, an analgesic, and an anesthetic in a work he dedicated twelve pages to the subject. By the end of the 1800s, doctors were frequently prescribing Cannabis indica as a sedative, analgesic, antispasmodic, antiemetic, antidepressant, and for diseases including psychoses, delirium tremens, and hysteria. The German pharmaceutical firm "Merck" introduced several Cannabis products to the market for the first time in 1882. However, cannabis use was outlawed and officially removed from pharmacopeias by European states in the mid-1900s due to hygienic concerns and pharmaceutical control over drugs. Cannabis was placed under the International Narcotics Control Board in 1961 after being classified by the United Nations Single Convention on Narcotic Drugs as one of the most hazardous drugs with no known medicinal benefit. This effectively ended medical studies on the drug. When two Israeli researchers, Yechiel Gaoni [14] and Raphael Mechoulam [15], determined the structure of tetrahydrocannabinol (THC) in 1964, the study cautiously picked back up, mostly to show the negative effects of cannabis use. Cannabis research did not take off until the end of the century, when the endocannabinoid system was discovered.

The scientific community worldwide now acknowledges the usefulness of Cannabis in medicine. There is currently a great deal of passion for research in this area; of the 20,000 articles published on cannabinoids, half were carried out in the last ten years.

3.2. Botanical Studies on the Genus *Cannabis*

Cannabaceae is a family of flowering plants that includes hemp, Cannabis, and hemp seed. This family is classified as belonging to the order Rosales within the Dicotyledons by the Angiosperms Phylogeny Group (APG III). It can be situated as follows:

→ *Phylum Spermatophytes (seed plants)*
→ *Subphylum Angiosperms (plants with ovaries)*
→ *Eudicots (embryo with two cotyledons)*
→ *Advanced Eudicots*
→ *Class Rosids*
→ *Subclass Eurosid I*
→ *Order Rosales*
→ *Family Cannabaceae*

It There are two varieties, with Cannabis (Cannabis L.) being one of them. The latter has grown since antiquity and is almost entirely subcosmopolitan. There has long been debate over the number of species in the Cannabis genus. According to certain sources, Cannabis is a polytype. However, it is generally accepted that there is just one highly polymorphic species, known as "Cannabis sativa Linnaeus,"[16] based on morphological, anatomical, photochemical, and genetic investigations [17].

3.2.1. Nomenclature and Taxonomy

A herbaceous annual plant, Cannabis sativa L. is categorized into various phenotypes that most botanists agree are subspecies and variations. These include ruderalis, or wild hemp, indica, or Indian hemp high in resin, and sativa, a kind used for its fibers[16]. Cannabis sativa and indica re both commercially significant and widely grown. Even though Cannabis ruderalis is more resilient, it is not often grown for medical purposes[18].

3.2.2. Anatomy and Morphology

Cannabis sativa L., commonly known as hemp, exhibits a diverse range of botanical and genetic characteristics, making it an annual upright herb that can attain heights ranging from one to four meters. Notably, hemp's root development plays a crucial role in its adaptation to arid environments, distinguishing it from other large-scale crops. Comprising less than 10% of the total biomass, the root system consists of a central pivot or primary root, extending secondary roots that vary in volume based on soil attributes, sexual phenotype, and cultivation practices. The primary function of the roots is

to absorb essential water and nutrients from the soil or growing mediums, underscoring their importance in supporting robust vegetative growth and ensuring a substantial harvest.

The stem of the hemp plant is characterized by a more or less hollow hexagonal cylinder, exhibiting diverse lengths and diameters influenced by environmental factors, varieties, and developmental stages. Composed of internodes, the stem further varies in length, with a diameter that increases toward the plant's base. Female plant stems are generally thicker than those of males but are shorter in stature.

A significant component constituting 30% of the total biomass, hemp's stipulate leaves are oppositely arranged and palmately compound. With five to seven unequal elongated and toothed segments, these leaves transition to alternate forms or ones with only three segments towards the stem's apex. Noteworthy are the characteristic hairs present on the leaves, including cystolith hairs, formed by a swollen cell accumulating carbonate crystals; tector hairs, unicellular and covering the epidermis; and glandular hairs, featuring a voluminous base secreting resin. This type of hair is abundant in resin-rich hemp, particularly on the bracts surrounding female flowers. The protrusion of these hairs forms trichomes, where the majority of cannabinoids and terpenes concentrate. Trichomes serve as a protective barrier against insects and molds, UV radiation, and extreme temperatures. They might also function as a defense mechanism for flowers and seeds

Naturally dioecious, hemp bears male and female flowers on separate plants, and occasionally a monoecious (hermaphrodite) phenotype. Male flowers cluster to form a panicle-type inflorescence. Female flowers form cymes at the stem apex, grouping multiple spikes at leaf junctions. Differentiating between the two can be challenging due to morphological similarities, but it may become possible during the flowering phase. Molecular techniques, however, can allow differentiation at an early stage.

The hemp fruit, referred to as "chenevis," emerges as the culmination of the seed-producing process in mature, pollinated female plants. Following successful fertilization, the blossoms undergo a metamorphosis into fruit, ultimately releasing chenevis. These seeds are smooth, and round, and come in a range of colors, from shiny gray to brown. Significantly, these seeds encapsulate the complete genetic blueprint necessary to initiate the growth of a new *Cannabis* plant. In the context of phytocannabinoid production, an emphasis is placed on the preference for seedless female plants, attributed to their capacity to yield higher quantities of secondary metabolites. This strategic preference involves the meticulous elimination of male plants as they emerge, a practice instrumental in preventing the pollination of female plants. The removal of male plants not only safeguards against unwanted pollination but also contributes to the preservation and amplification of secondary metabolites, notably cannabinoids. This meticulous approach ensures the maintenance of a desirable chemical profile, crucial for the consistency and potency required in medicinal and pharmaceutical production.

3.3. Legislation Advancements: *Cannabis* Regulations and Policies Worldwide

3.3.1. Globally

The global discourse on *Cannabis* consumption is marked by diverse legislative approaches, creating a complex legal landscape for both recreational and medical use. Recent years have witnessed a notable shift, with several jurisdictions worldwide opting for decriminalization and legalization of recreational *Cannabis*. Key milestones include Canada's legalization in October 2018, Mexico's move in June 2021, Malta's decision in December 2021, and South Africa's legalization in September 2018. In the United States, Washington and Colorado paved the way in 2012, with 22 states now fully legalizing *Cannabis* at the state level for both medicinal and recreational purposes, despite its federal illegality. The global prevalence of *Cannabis* use is underscored by estimates from the United Nations Office on Drugs and Crime[19], revealing that approximately 192 million individuals aged 15–64 used *Cannabis* in 2016 [20].

In areas where medical marijuana was legalized, the prevalence of serious mental illnesses like schizophrenia and bipolar disorder were significantly higher following legalization compared to the period before legalization; however, these studies were not able to distinguish between true epidemiological rises in prevalence from increasing rates of diagnosis.

Beyond usage statistics, the paragraph delves into the complex interplay between *Cannabis* legalization and mental health. Studies indicate a higher prevalence of serious mental illnesses, such as schizophrenia and bipolar disorder, in areas where medical marijuana has been legalized. Notably, the United Nations' Commission on Narcotic Drugs (CND) recently approved the reclassification of cannabis and its resin in international conventions. This decision, backed by a close vote during the 63rd session of the CND and aligned with World Health Organization (WHO) recommendations, signifies

a departure from the stringent categorization of *Cannabis* [21]. Previously considered under Annex IV of the Single Convention on Narcotic Drugs of 1961, a category for substances with little medical interest, *Cannabis* is now recognized for its therapeutic potential. The WHO's request in 2019, supported by scientific studies, paved the way for *Cannabis* to be used in the manufacturing of medicines, akin to opium or morphine, without facing UN prohibition. This shift highlights an evolving global perspective that acknowledges the medical utility of *Cannabis* and emphasizes a more nuanced approach to its regulation.

3.3.2. Canada

In 2017, Canada reported substantial *Cannabis* use, with 4.5 million individuals aged 15 or older engaging in past-year consumption. The landmark *Cannabis* Act [22], enacted on October 17, 2018, marked a significant turning point [23]. This legislation permitted certain previously prohibited activities, such as possessing small amounts of dried *Cannabis* in public or cultivating a limited number of plants at home. Simultaneously, it prohibited actions like selling *Cannabis* to young individuals or involving them in related offenses.

3.3.3. United States (US)

The historical journey of *Cannabis* legislation in the United States dates back to the 1600s when hemp cultivation was mandated in Virginia. The Marihuana Tax Act in the 1930s federally prohibited marijuana while allowing for medical use. The 1990s witnessed some states legalizing medical *Cannabis*, and by 2012, Washington and Colorado legalized recreational use. Despite federal illegality, 22 states now permit *Cannabis* for both medical and recreational purposes. The U.S. *Cannabis* market is poised for remarkable growth, projected to reach $30 billion in legal sales in 2022, with estimates ranging from $58 billion to $72 billion by the decade's end. Challenges [24] include the inability of California's marijuana farmers to bank with federal institutions and legal concerns about herbicide spraying on Cannabis plants[25].

3.3.4. Denmark - European Union (EU)

On January 1, 2018, Denmark took a progressive step in the realm of *Cannabis* legislation by legalizing certain industrially produced medicinal *Cannabis* products. This marked a significant development, allowing doctors in the country to prescribe specific *Cannabis*-based medications for patients facing conditions such as muscular sclerosis, spinal cord injuries, those undergoing chemotherapy, and individuals experiencing chronic pain[26]. The approval of Sativex products by the Danish Medicines Agency (Lagemiddelstyrelsen) broadened the options available for medical professionals to provide alternative treatments. However, the legislation imposed stringent conditions, requiring doctors to exhaust all conventional treatment options before considering medicinal *Cannabis* prescriptions. This cautious approach aimed to ensure responsible and informed medical use.

A distinctive feature of Denmark's approach is the allowance for both the importation and local cultivation of *Cannabis* for medicinal purposes. This strategic decision opened up new opportunities for companies interested in participating in the growing medicinal *Cannabis* market. By November 2017, 15 companies had already submitted applications to the Danish Medicines Agency for permission to cultivate *Cannabis*, indicating a burgeoning interest in this sector. Despite the potential economic benefits and the medical advancements associated with medicinal *Cannabis*, the trial encountered resistance from segments of the medical community. Some Danish doctors expressed concerns about the insufficient medical evidence available regarding the effects and potential side effects of medicinal *Cannabis*. These reservations contributed to a cautious stance and raised questions about the long-term impact of such medical interventions.

Furthermore, patient organizations warned of potential risks, emphasizing the need for careful monitoring and assessment to prevent patients from turning to the illegal *Cannabis* market due to any start-up difficulties or delays in the implementation of the new regulations. On a broader scale, the European Union (EU) witnessed a notable surge in hemp production. Between 2015 and 2019, the area dedicated to hemp cultivation grew by a substantial 75%, reaching 34,960 hectares in 2019 (Figure 2). However, despite this growth, the area under hemp in the EU remained constant in 2020 and experienced a slight decrease to 32,000 hectares in 2022.[27]. The EU's hemp production landscape is characterized by a diverse array of registered hemp varieties (cultivars), numbering 96 according to the EU Plant Variety Database. These cultivars, originating from various European countries including Hungary, Italy, France, Latvia, Lithuania, Romania, the Netherlands, Poland, Spain, Russia, Slovenia, Czech Republic, and Serbia, highlight the rich biodiversity and agricultural potential within the EU.

Denmark's intricate approach to medicinal *Cannabis* and the broader trends in EU hemp production illustrate the complex interplay between legal, medical, and

economic considerations shaping *Cannabis* legislation in European countries.

3.3.5. Morocco

In 2021, the Moroccan government identified specific regions, namely Al Hoceima, Chefchaouen, and Tetouan, as eligible areas for legal *Cannabis* cultivation. These areas were not only known for their historical association with illicit *Cannabis* production but also housed economically disadvantaged communities[29]. The legalization initiative aimed to address poverty in these regions and shift *Cannabis* production from the illicit to the legal economy, fostering economic development. Despite the noble intentions behind legalizing *Cannabis* cultivation, the implementation faced challenges, particularly in establishing the regulatory agency crucial for overseeing and enforcing the new laws. Delays in setting up this regulatory body raised concerns about the effective execution of the law and the potential for regulatory oversight.

Examining the historical context, regulations related to *Cannabis* cultivation in Morocco trace back to 1932. During this time, a Dahir was promulgated, prohibiting the cultivation of kif (a local term for *Cannabis*) in areas under the French protectorate. Subsequent Dahirs, such as the one on April 24, 1954, confirmed and reinforced these restrictions, accompanied by the implementation of taxes for *Cannabis* holders[31]. For instance, a decree issued on June 30, 1956, specified a tax of "4000 dirhams per kilogram." Further regulations in 1960 mandated a declaration filing deadline for *Cannabis* or kif holders within three months.The cultivation of *Cannabis* in the post-independence era saw additional regulations and laws. Notably, Dahir No. 1-2159, promulgated on July 14, 2021, marked a legislative milestone by outlining Law No. 13-21 on the lawful uses of *Cannabis*. This legislation stipulated specific conditions that must be met to obtain authorization for *Cannabis* cultivation, reflecting a more nuanced and regulated approach toward the plant[32]. The intricate history and recent legislative developments in Morocco underscore the complexities and multifaceted nature of *Cannabis* regulation, encompassing economic, historical, and regulatory considerations in its journey toward legalization and a regulated *Cannabis* industry.

Fig. 1. Illustration of cannabis plant parts.

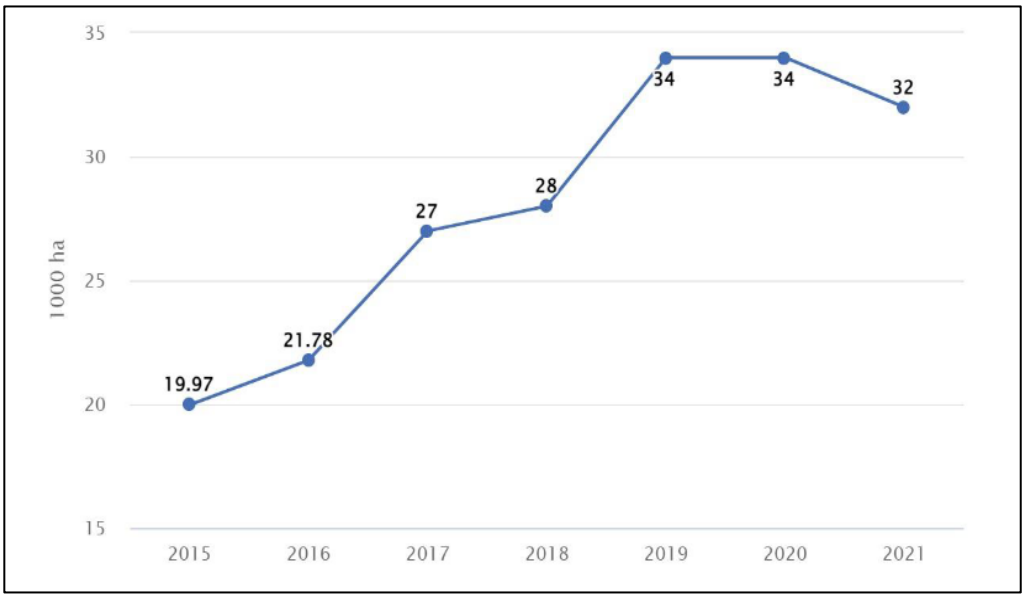

Fig. 2. EU Land area used for hemp cultivation[28].

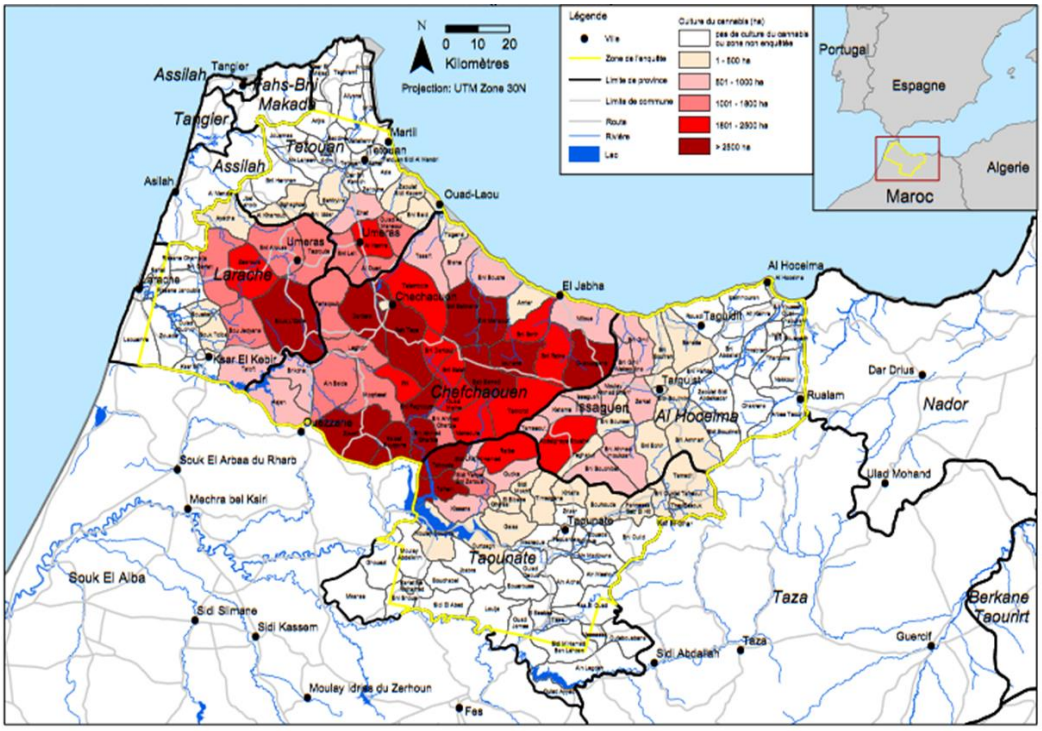

Fig. 3. *Cannabis* Cultivation Distribution in Morocco - Northern Province. Established in 2004[30].
Area framed by yellow highlighting: concentrated zone in Cannabis cultivation.
Source: United Nations Office on Drugs and Crime, Morocco: Cannabis Survey 2003 (December 2003)

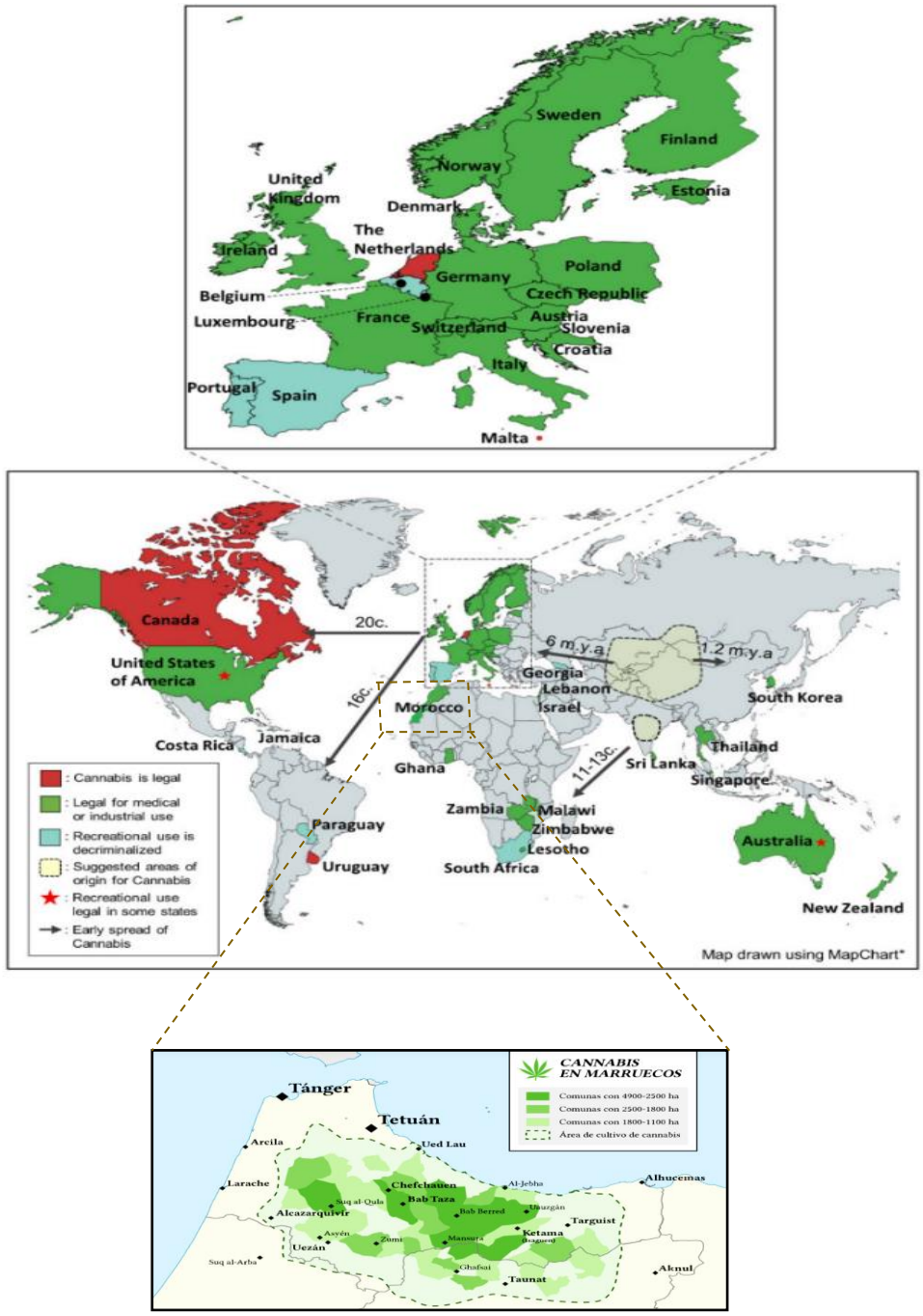

Fig. 4. Legal status and early spread of *Cannabis.* A close-up part of Europe and Morocco are shown in an insert map, 5.5× magnified. (c.: century, m.y.a.: million years ago)

4. Comprehensive Overview of *Cannabis* Global Distribution

Cannabis classified as an annual flowering plant, completes its life cycle in one year[33]. Its adaptability allows it to thrive in diverse climates. Originally from Central and Southern Asia, *Cannabis* has spread globally. While medical *Cannabis* is legally accepted in many countries, recreational use is either permitted or decriminalized in several nations, including Canada, The Netherlands, Malta, Uruguay, Portugal, Spain, Luxembourg, Belgium, Georgia, Costa Rica, Paraguay, Jamaica, South Africa, and specific US states and territories.

Cannabis plants do not have specific soil requirements [34], but soil pH, particularly close to neutral or slightly alkaline, is crucial [35].

Soil and climate conditions significantly influence metabolite content, with psychoactive THC and non-psychoactive CBD being key components. Varieties with low THC content are used for industrial purposes [36], while those with high THC content find applications in the pharmaceutical industry and medical *Cannabis* for conditions such as chronic pain [37].

4.1. Industrial *Cannabis*

Industrial *Cannabis* is characterized by relatively high levels of CBD[38]. Its Seed output per ha ranges from 1700 to 2000 kg and its physical properties are correlated[39]. It is primarily grown for its seeds and fiber. The seeds are rich in nutrients, proteins, fats, and minerals, making them valuable for various applications. Planting dates, fertilization, seeding rates, and watering significantly impact plant quality [40] and yield [41]. In moderate climates, late April or early May is considered the optimal sowing time[42].

4.2. Medicinal *Cannabis*

Medicinal *Cannabi*s, distinguished by a high content of THCA [43], is cultivated for its female flowers, known for therapeutic properties [44]. THCA concentration can range from 10% to 20-30% or even higher. Growth characteristics are influenced by plant density and seeding rates. A bushy growth habit with numerous side shoots is preferred. The optimum plant density [45] is around 20,000 plants per hectare [46].

5. *Cannabis* Uses: Medicinal, Recreational, and Industrial Applications

Cannabis's versatility extends across various industries, showcasing its potential in textiles, papermaking, construction, animal bedding, energy, cosmetics, and more.

5.1. *Cannabis* Use in Textiles

Hemp fibers have been utilized for a long time in fabricating durable textiles [47], including jeans, sportswear, bags, and various accessories[48]. Major consumer companies [48], such as Patagonia and Adidas [49], have incorporated hemp constituents in their product lines [50].

5.2. *Cannabis* Use in Papermaking

Hemp's strength, durability, and recyclability make it a preferred material for papermaking [51]. Its use contributes to environmental sustainability by reducing the need for deforestation [52].

5.3. *Cannabis* Use in Construction

Hemp-based biomaterials offer a range of benefits for construction. These materials are strong, lightweight, cost-effective, waterproof, fireproof, and exhibit excellent heating and cold tolerance [53]. They are also considered suitable for minimizing the impact of natural disasters [54].

5.4. *Cannabis* in Animal Bedding

Hemp-based bedding possesses hydrophilic characteristics, high water absorption capacity, and is dust-free. It is an excellent choice for various animals, including horses, chickens, and pets, providing comfort and reducing allergenic reactions[55].

5.5. *Cannabis* Biomass as a Source of Energy, Heat, and Fuel

Hemp biomass, when converted into pellets, can be burned directly to produce heat, contributing to renewable energy sources. Larger-scale applications involve transforming biomass into charcoal for power generation[56].

5.6. *Cannabis* Use as Mulch

*Cannabi*s mulch, is lightweight and effective at retaining moisture, reduces soil erosion, suppresses weeds, and acts as a screening layer to prevent seed germination [57]. Its water-absorbing capacity reduces the need for frequent watering, making it more effective than other types of mulch [48].

5.7. *Cannabis* for Body Care Products and Cosmetics

Hemp seed oil, with a high composition of unsaturated fatty acids, is a popular ingredient in body care and cosmetic products. Its properties make it suitable for manufacturing light body oils and lipid-rich lotions, contributing to the skin's health[58].

5.8. *Cannabis* in Industrial Grade Oil Uses

Hemp oil, known for its surface penetration and drying properties, has been used in various industrial applications, including inks, polishes, paints, sealers, cleaning agents, and lubricants. Studies also suggest potential benefits for livestock when hemp seed oil is added to diets. The multifaceted uses of *Cannabi*s [59] highlight its significance in various sectors, contributing to sustainable and eco-friendly practices. The plant's versatility continues to inspire innovation across

industries, promoting resource conservation and environmental well-being [60].

6. Unraveling Genetic Variability: *Cannabis* Strains and Cultivation Practices

Cultivating hemp grain involves navigating numerous factors that impact its growth and yield, with a critical focus on the delicate balance of water and nutrients within the soil. This discussion delves into the intricacies of nutrient management and water control, revealing their profound impact on hemp cultivation for grain.

6.1. Nitrogen

Nitrogen emerges as a pivotal nutrient, with the challenge of determining the optimal fertilization rate. *Cannabi*s, especially during the sensitive seedling stage, exhibits a low tolerance for fertilizers. It's crucial to carefully apply nitrogen fertilizers either before seeding or at a safe distance from the seed. Recommendations propose a total nitrogen range of 112 - 168 kg ha^{-1} for dry land and up to 224 kg ha^{-1} for irrigated hemp grain crops. Interestingly, fiber hemp [61] requires a more modest 56 kg ha^{-1} of nitrogen to maintain robust fiber quality[62].

6.2. Phosphorus

Studies [63] underscore the significance of managing phosphorus levels, revealing that hemp seed mortality increases notably when phosphorus applications exceed 22.4 kg ha^{-1} of actual phosphorus. Hemp [64] exhibits resilience by compensating for plant loss through enhanced branching. It is prudent to avoid exceeding 22.4 kg ha^{-1} of real P2O5 for seeding on specific soil types. Recommended phosphorus levels for both grain and fiber hemp crops are 56 kg ha^{-1} and 67 kg ha^{-1}, respectively [61].

6.3. Potassium

Hemp's substantial need for potassium is highlighted, with recommended levels of 336 kg ha^{-1} for grain/dual-purpose hemp and fiber crops [65]. Given potassium's soil mobility, a significant amount may leach into the soil, potentially resulting in nutrient loss over time [61].

6.4. Water Management

European research provides insights into hemp's water requirements, suggesting it needs 500–700 mm of available water, with 250–300 mm required during the crucial vegetative development period [66]. Studies on irrigation treatments indicate that hemp crops thrive with 66% of available water, corresponding to seasonal water usage of 410–460 mm [67]. The timing of seeding and water availability significantly influences hemp water consumption [68].

6.5. Diseases

Cannabis cultivation is susceptible to various diseases, with two significant threats being Sclerotinia sclerotiorum (white mold) and Botrytis cinerea (gray mold), both capable of adversely affecting hemp production[61].

Sclerotinia sclerotiorum: This fungus poses a considerable challenge as it can cause stem cankers or rot of seed-bearing buds. The presence of sclerotic produced by Sclerotinia in hemp seeds is particularly problematic, lowering the quality and overall value of the final product. Managing this disease involves meticulous control measures aimed at reducing the environmental conditions favorable to spore infection. Strategic planning, including precise planting timing and optimal plant density, is crucial to avoiding wetter conditions during the late stages of hemp maturation, where the risk of infection is higher.

Botrytis cinerea: Gray mold, caused by Botrytis cinerea, is another threat to hemp crops. This pathogen can lead to the development of mold on the flowers, compromising the quality of the harvested product. Similar to Sclerotinia sclerotiorum, controlling Botrytis involves environmental manipulation to hinder the conditions conducive to spore development. Proper ventilation, spacing of plants, and monitoring humidity levels are essential components of disease management.

Given the limited availability of registered fungicides for hemp, an integrated approach becomes paramount. Cultural practices, such as maintaining optimal plant density, avoiding excessive humidity, and strategic timing of planting, play a crucial role in preventing and managing these diseases. Additionally, exploring biological control methods, where beneficial organisms are employed to counteract pathogenic threats, becomes an increasingly important aspect of disease management in hemp cultivation. As the industry continues to evolve, ongoing research [68] and proactive disease prevention strategies will be integral to sustaining healthy and productive hemp crops [62].

7. Advancements in Cannabis Chemistry: Exploring Molecules of Industrial Interest and Tackling Instability

In the realm of cannabis, the versatile application of woody fibers, often referred to as "hurds" or "shivs," extends from high-absorption bedding for animals to the creation of concrete-like materials. The distinguished hemp bast fibers play a pivotal role in the bio-composite

sector, serving as a robust alternative to glass fibers. Noteworthy for their antibacterial properties, these fibers are not only utilized in the manufacturing of antibacterial agents but also find applications in the production of surgical devices and functionalized textiles.

Hemp bast fibers have a unique chemical composition. They are marked by the existence of both free and esterified sterols and triterpenes, among which β-sitosterol and β-amyrin exist. These compounds possess known antibacterial properties[69]. On the other hand, it also contains cannabinoids (2% of the total metabolite extract)[70]. More recently, hemp hurd powder showed antibacterial properties against Escherichia coli. Since the hurd has a higher lignin content than the bast fibers, its antibacterial property may be linked to lignin-related compounds such as phenolic compounds, as well as alkaloids and cannabinoids.

Numerous chemicals are produced in hemp through the secondary metabolism. They include cannabinoids, terpenes, and phenolic compounds.

7.1. *Cannabis* Trichomes: Small Factories of Phytochemicals

Cannabis stands out for its diverse trichomes, including capitate sessile, capitate stalked, and bulbous hemp trichomes. These microscopic structures act as secretory reservoirs for cannabinoids, with capitate-stalked trichomes boasting higher concentrations, notably of THCA. The terpenes found in hemp, including the rare nerolidol, exhibit antimalarial and anti-leishmanial effects, underscoring their pharmacological importance. There's a growing interest in exploring strategies to enhance secondary metabolism or increase trichome density in *Cannabis* [71], opening avenues for potential benefits in phytochemical production. (Figure 5: A–F) [72].

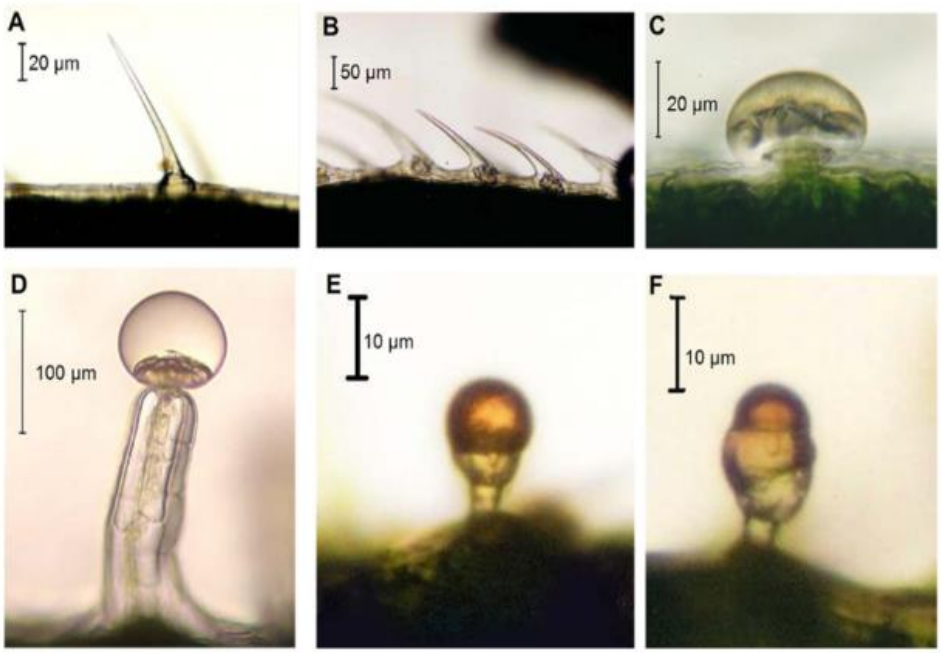

Fig. 5. Hemp Trichome types. (A) univellular non-glandular trichome; (B) cystolythic trichomes; (C) capitale sessile trichome; (D) capitate-stalked trichome; (E) simple bulbous trichome; (F) complex boulbous trichome[72].

7.2. Phytocannabinoids

The fascinating world of phytocannabinoids unfolds within *Cannabis*, comprising terpenophenolic compounds predominantly produced by the plant. Notable members of this compound family include THCA, CBDA, and CBCA, each with distinct roles dictated by their carboxylated forms. These compounds primarily accumulate in glandular trichomes, predominantly within female flowers, influencing various biological processes related to the endocannabinoid system. THC, a psychoactive cannabinoid, engages with CB1 and CB2 receptors, with CB1 receptors found throughout the body. CBD, another crucial phytocannabinoid, acts as an entourage compound, mitigating THC's side effects and

showcasing promising therapeutic potential across a spectrum of conditions. Adding to the repertoire of phytocannabinoids, CBC [73] exhibits a diverse array of properties, from anti-inflammatory and sedative to antibacterial and antifungal [74].

Terpenes, constituting the largest group of phytochemicals in *Cannabi*s, significantly contribute to the distinct odor and flavor profiles characterizing various strains. With over a hundred identified molecules, terpenes emerge as multifaceted compounds with pharmacological prowess. Their repertoire spans anti-bacterial, antifungal, anti-inflammatory, and anti-cancer effects, marking them as crucial contributors to the overall therapeutic profile of *Cannabi*s. [75].

7.3. Phenolic Compounds

In the intricate tapestry of *Cannabi*s s chemistry, phenolic compounds weave a story of potential health benefits. Demonstrating a correlation between dietary phenolic compound intake and a reduced incidence of chronic diseases, these compounds go beyond mere antioxidant properties. Flavones and flavonols found in *Cannabi*s showcase a spectrum of effects, including anti-inflammatory, anti-cancer, neuroprotective, anxiolytic, and estrogenic properties. The nuanced action of phenolic compounds involves up-regulation of endogenous antioxidant enzymes, offering a multifaceted approach to overall well-being. As our understanding of *Cannabi*s chemistry deepens [76], these compounds emerge as pivotal players in the intricate dance of therapeutic potential within the *Cannabi*s plant [77].

8. Ensuring Quality Control and Standardization in the *Cannabis* Industry

In the ever-evolving landscape of the *Cannabi*s industry, maintaining stringent quality control and establishing standardized practices is paramount. This is exemplified through two distinct cases that shed light on the rigorous testing and regulatory measures required to ensure the safe and effective utilization of *Cannabi*s-based products. Through these examples, we delve into a study concerning the impact of hemp seed cake on dairy cows and the utilization of hemp seed oil and essential oil as additives in human food and medicine. These instances illuminate the complex process of evaluating the effects of *Cannabis* products, both on livestock and human consumption, highlighting the significance of thorough research, regulation, and data-driven decision-making.

8.1. Experiment

To test the negative effects of *Cannabis* seed, a study was made. They fed hemp seed cake to dairy cows, and followed the results[78]. After providing hemp cake composed of leaves, flowers, and seeds (higher level of THC) it was noticeable that it reduced feed intake and milk production in dairy cows. Heart rate, respiratory rate, and animal behavior were all affected negatively. On the other hand, feeding cows reduced industrial hemp silage made from the entire hemp plant had no effect on their health or effectiveness. Other cannabinoids, particularly CBD, which was found in high concentrations in industrial hemp (and thus also in cow's milk after feeding), have insufficient data to evaluate potential health risks.

According to that, In March 2023, the United States had restricted the use of hemp and hemp-derived products in pet food or animal feed.

Food products are regulated by the FDA. The European Food Safety Authority (EFSA) states that hemp seed[79], hemp oil, hemp expeller, hemp flour, and hemp fiber can be used in various animal species' feed. This, however, depends on how much more food is consumed. The limit THC level was set at 0.2% in Commission Regulation (EU) 2017/1017 dated 15 June 2017.

8.2. Hemp Seed Oil and Essential Oil as Human Food Additives and Medicines:

Cannabis seed oil exposure to high temperatures causes the development of trans-fatty acids, which limit the beneficial components and cause the oil to taste bitter and spoiled. For this reason, hemp seed oil is not recommended for frying[80]. It is commonly used in salads and pasta sauces, as a margarine and butter alternative, and as a nutritional supplement[81]. And since hemp seeds are rich in important fatty acids, such as α-linolenic acid, hemp oil can be used to help with inflammatory diseases like arthritis, as well as to reduce blood pressure and cholesterol levels in the arteries[82], and if applied topically, it can be used to treat open wounds, scalding injuries, and irritations of the skin including psoriasis and neurodermatitis[83]. In addition, hemp contains gamma-linolenic acid, a popular substance with many health advantages. Hemp oil is expected to have a high market value and be used mostly in foods for humans and dietary supplementation. but more research is required to back up claims about hemp's effectiveness for a variety of illnesses, but more research is required to back up claims about hemp's effectiveness for variety of illnesses.

9. State of Art on Research and Innovation within the *Cannabis* Industry

9.1. Trends of *Cannabis* Research from 1783 to 2021

In the extensive archives of *Cannabi*s literature, notable patterns and trends emerge, providing insights into the evolution of research. *Cannabi*s research spanning from 1783 to 2021 can be summarized by monumental chronological milestones, encompassing the discovery of cannabinoids, cannabinoid receptors, and endocannabinoids. The vitality of ongoing research is underscored by the increasing number of articles since the year 2021. The dominant domains of *Cannabi*s research primarily include medical and medicinal sciences taking center stage, closely followed by pharmacology and pharmaceuticals, neurosciences and psychology, biochemistry and biotechnology, genetics and genomic sciences, agriculture and plant biology, and bioinformatics[84].

9.2. Patents For *Cannabis Sativa L.*

Within the intricate landscape of *Cannabis* Sativa L. patents, the collaboration with industrial partners assumes a pivotal role in steering research and development endeavors, particularly in the domains of medical science and biotechnology. These patents unfold across four distinct categories, delineating their multifaceted applications. The foremost among these is the pharmaceutical applications category, boasting an impressive tally of 73 registered patents. This category underscores the extensive exploration of *Cannabis* in medicinal contexts. The cannabinoid class, comprising patents related to cannabinoids as constituents, delves into three specific domains: isolation, extraction, and synthesis or biosynthesis. Notably, there are 6 patents each for cannabinoid isolation and extraction, while 12 patents focus on synthesis or biosynthesis[85].

The geographical distribution of these patents is noteworthy, with the United States holding a commanding share of 49.6%, underscoring the nation's prominence in *Cannabis* -related innovation. Following closely is Great Britain, contributing 11% to the global landscape of *Cannabis* patents. Beyond the pharmaceutical sphere, the patents extend their reach into diverse sectors, reflecting the versatility of *Cannabis* Sativa L. in various industries. Twenty-five patents cater to fibers and textiles, ten find applications in food products, five in the paper industry, three in architecture, one in biofuels, and three in plant breeding[86].

The legalization of *Cannabis* has propelled a surge in scientific research, particularly centering around cannabinoid compounds. However, a significant paradigm shift has been observed with the advent of advanced sequencing technologies. This shift redirects the focus towards the genetic genomics of fiber and drug-type plants. The confluence of substantial genomic data and the rapid evolution of artificial intelligence-based data analysis tools has ushered in a new era of exploration, enabling researchers to dissect *Cannabis* plants at the genetic and molecular levels. This integration of cutting-edge technologies not only amplifies the depth of understanding of *Cannabis* Sativa L. but also opens up avenues for innovative applications across diverse industries[85].

10. Economic Impact of *Cannabis*: Revenue, Employment, and Beyond

10.1. EU Drug Markets Report – 2019

10.1.1. Impacts and Drivers of Drug Markets

The Economic Impact of *Cannabis* is a multifaceted exploration, illuminated by insights from the EU Drug Markets Report of 2019. In this intricate ecosystem, organized crime groups (OCGs) find a substantial source of income through the illicit drug market, revealing a staggering valuation of €30 billion in 2017. Beyond affecting individual drug users, the profound impact of the drug market resonates across the entirety of society. The EU grapples with the persistent availability of high-purity, high-potency products at accessible prices, posing challenges and raising concerns[87].

Technological advancements and digitalization have ushered in a new era for OCGs, providing them with the means to exploit regulatory gaps and transform traditional methods of product movement. The landscape has evolved from large-volume shipments and postal services to a virtual marketplace, encompassing the surface web, darknet markets, social media, and apps. While this shift eliminates the need for conventional infrastructure, it concurrently introduces challenges for law enforcement and public health.

10.1.2. Responding to Drug Markets

Recognizing the complexity and adaptability of illicit drug markets, member states within the EU have orchestrated a range of policies and responses. Operational activities, strategic formulations, legislative initiatives, and bilateral arrangements collectively contribute to the response mechanisms. The overarching objective is to target serious OCGs engaged in the drug trade, acknowledging that the impact of the drug market extends beyond direct consequences such as health and security to encompass indirect repercussions like violence, safety, and environmental concerns.

This nuanced interplay necessitates a comprehensive examination of the intricate links between the illicit drug market and its far-reaching consequences across diverse policy areas. The call to action resonates: further scrutiny and understanding are essential to inform and integrate robust responses that navigate the multifaceted challenges posed by the illicit drug trade within the EU. Coordination among member states becomes paramount to devise strategies that effectively address the intricate web of impacts on health, security, violence, safety, and the environment [86].

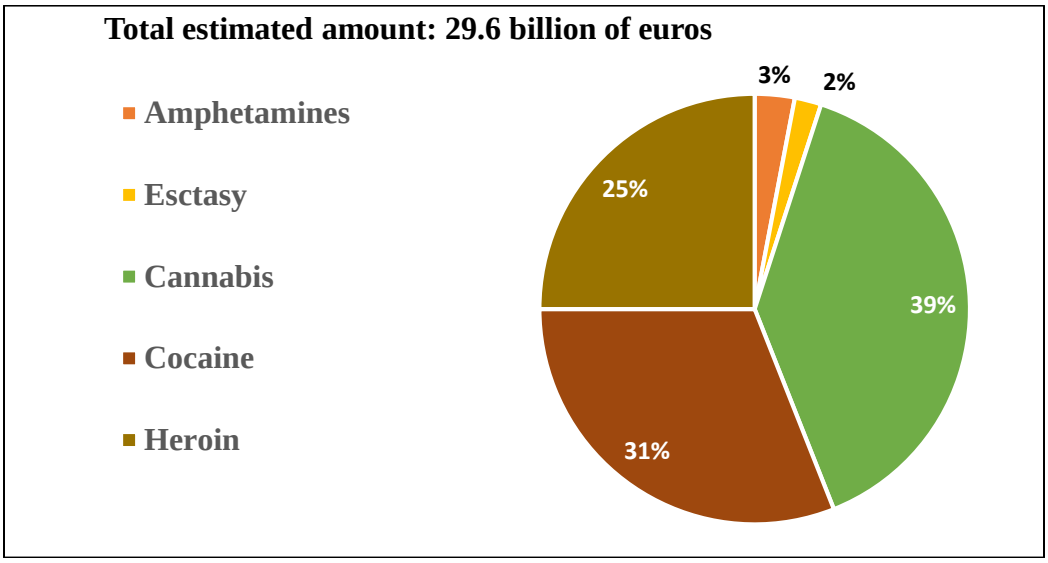

Fig. 6. Estimated retail value of the illicit market for the main drugs in the EU, From EU drug markets report, 2019[88].

11. Environmental Aspect of *Cannabis* Development

Cannabis stands as a beacon of environmental sustainability, offering unique characteristics that extend beyond its traditional uses. Its roots, adept at absorbing and storing toxic elements like lead, nickel, and cadmium, position hemp as an eco-friendly option for soil phytoremediation. This environmentally restorative quality allows *Cannabis* to play a vital role in detoxifying polluted soils, contributing to ecological balance.

The environmental prowess of *Cannabis* extends to its role as a CO_2 biomass converter. With a remarkable ability to absorb carbon dioxide, hemp surpasses conventional crops and even competes with the carbon-sequestering capacity of woodlands. Each hectare of hemp can absorb up to 22 tons of CO_2 annually, showcasing its potential as a powerful tool in mitigating climate change. The resulting biomass, in the form of biochar, serves as a valuable resource with fuel qualities comparable to, or even superior to, other solid biofuels.

Furthermore, the sustainable nature of hemp production goes beyond carbon sequestration. Hemp's rapid growth reduces the need for extensive pesticide use, making it an energy-efficient and environmentally friendly alternative. The cultivation of hemp yields over 13,000 kg of biochar per hectare annually, emphasizing its potential as a renewable and sustainable resource.

Understanding the nuances of hemp growth, particularly its photoperiod sensitivity, is crucial for optimizing its environmental benefits. This trait influences hemp's adaptation to specific regions, impacting both quantity and quality in terms of yield. Cultivators[89] can fully utilize hemp's potential for environmental regeneration by carefully managing the crop through all growth stages, from germination to maturity [87].

12. Economic, Socio-Economic Stability and the Impact of Recreational and Medicinal *Cannabis* Policies in Africa

Delving deeper into the economic and socio-economic implications of cannabis in Africa unveils a multifaceted landscape shaped by historical, political, and cultural nuances. Beyond the sheer market valuation of the global cannabis industry at USD$344.4 billion, Africa's share at 11% (USD$37.7 billion) reflects a significant economic opportunity, yet one entangled with intricate challenges. Nigeria emerges as a frontrunner in market potential, projecting USD$15.3 billion, followed closely by Ethiopia at USD$9.8 billion. However, these figures belie the complex socio-economic dynamics within individual African nations. South Africa, for instance, grapples with the aftermath of a war on *Cannabis* that cost taxpayers

over USD$223.7 million in 2014 and 2015. This financial toll emphasizes the economic implications of prohibitionist policies.

For certain regions, such as Lesotho, cannabis cultivation serves as more than an economic opportunity; it is a lifeline. High unemployment rates force communities to rely on *Cannabis* as the sole source of livelihood, bringing into sharp focus the socio-economic impact at the grassroots level. The Rif region in Morocco[90] echoes this sentiment, where *Cannabis* cultivation is not viewed as organized crime but as a means of economic stability[91]. The Rif region in Morocco stands out as a case study where *Cannabis* plays a pivotal role in maintaining socio-political stability. Profits generated from the *Cannabis* industry contribute to uncontrolled housing development, offering a unique lens into how *Cannabis* intersects with broader socio-economic dynamics. Northern Nigeria's wholesalers attribute financial successes to *Cannabis* 's profitability, showcasing its economic resilience even in the face of economic downturns.

The illegality of the cannabis trade, coupled with the need for secrecy, contributes to the creation of black markets and policy displacement. Communities are affected as enforcement resources are redirected, leading to shifts in drug production and supply. Moreover, the 'balloon effect,' where enforcement efforts in one area lead to the expansion of drug-related activities elsewhere, further complicates the socio-economic fabric[92].

Legalization emerges as a potential panacea, offering government gains and addressing various socio-economic challenges. In Morocco, with approximately 800,000 *Cannabis* growers, annual sales estimated at USD$10 billion could inject new life into the economy. The value chain opportunities, from industrialization to employment creation, present avenues for economic growth. Increased European demand for legal markets may result in a foreign currency influx, alleviating economic pressures.

However, the delicate balance lies in understanding that *Cannabis* policies are not one-size-fits-all. Stricter regulations may lead to unintended consequences, such as illegal immigration and community disruptions, hampering overall development. The *Cannabis* economy, thus, becomes a regulator of employment and emigration, influencing social dynamics and community well-being[93].

13. Conclusion: Key Insights and Future Prospects

This comprehensive literature review explores Cannabis's historical significance, regulatory landscapes, global distribution, and diverse applications in medicine, recreation, and industry. It highlights Cannabis's rich legacy, dating back thousands of years, and its increasing acceptance and legalization worldwide due to its medical and economic potential. Regulatory examples from Canada, the U.S., Europe, and Morocco illustrate the complexity of global Cannabis laws.

The review emphasizes the economic impact of *Cannabis*, noting its influence on local and global economies through employment and growth. It discusses the importance of genetic diversity and cultivation practices for quality yields, and the industrial potential of Cannabis-derived molecules like phytocannabinoids and terpenes, despite their instability. Quality control and standardization, particularly in contaminant and pesticide testing, are crucial for ensuring product safety.

The review concludes by advocating for balanced regulation and innovation, ongoing research, and a thoughtful approach to leveraging Cannabis's economic and therapeutic potential for future industry growth.

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