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The Origin, Domestication, and Global Spread of Cannabis (*Cannabis sativa*)

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Abstract This study systematically reviews the entire process of cannabis from its origins in Central Asia to its global spread. The research notes that cannabis originated in Central Asia and the Indian subcontinent and was initially domesticated in East Asia, then gradually spread globally due to its unique phytochemical properties and its uses in textiles and medicine. A case study of the "*Indica*" variety, *Cannabis sativa* subsp. *indica* var. afghanica, illustrates the specific adaptation processes driven by natural selection in response to local climatic conditions, as well as the impact of human migration and trade networks on the spread of this variety. By examining historical records and legal changes regarding cannabis in different regions, this study explores how cannabis adapts to different cultures and environments and analyzes the impact of various legal frameworks on the spread of cannabis. Furthermore, the study discusses how modern technologies like genetic editing and systematic breeding play roles in optimizing cannabis traits. This research not only reveals the complexity of cannabis as a plant but also reflects its significance as an economic and medicinal resource on a global scale.
Keywords Cannabis (*Cannabis sativa*); Origin; Domestication process; Natural selection; Global spread

1 Introduction

Cannabis, a genus of flowering plants in the family Cannabaceae, has a rich history that spans thousands of years. The genus includes three broadly recognized species: *Cannabis sativa*, *Cannabis indica*, and *Cannabis ruderalis*, all of which may be considered subspecies of *Cannabis sativa* (Lipman, 2017). The plant is indigenous to central Asia and the Indian subcontinent but has since spread globally. *Cannabis sativa*, in particular, has been an important source of fiber, oil, and medicinal compounds, with its psychoactive and non-psychoactive components, such as delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), being extensively studied for their pharmacological properties (Kopustinskiene et al., 2022). The plant's domestication history dates back to early Neolithic times in East Asia, with evidence suggesting that all current hemp and drug cultivars diverged from an ancestral gene pool in China (Ren et al., 2021).

Cannabis has played a significant role in various cultures throughout history. In ancient China, it was documented for medical use as early as the 28th century BC (Artiles et al., 2019). The plant was also integral to Hindu religious practices in India, where it was offered to the deity Shiva during ceremonies (Kuddus et al., 2013). In Africa, the use of cannabis has deep roots in the ancient cultures of the Zambezi Valley. African tribes have documented the use of cannabis in religious rituals and for medical and recreational purposes (Nikolaas, 2010).In the West, W.B.O Shanghnessy began using the current medical system to study the pharmacological mechanisms of cannabis (Russo, 2018).By the 19th century, Europe and the United States had published nearly 100 articles in medical journals about marijuana as a drug,cannabis was accepted as a mainstream medication, with numerous patented marijuana tinctures available for a range of medical conditions (Lipman, 2017). Despite its medicinal benefits, cannabis faced sociopolitical challenges, leading to its prohibition in many parts of the world by the early 20th century (Lipman, 2017). However, the illicit drug market has continued to involve the use of cannabis and scientific research,and as more countries have attempted to legalize marijuana for medical use in recent years, there has been a resurgence of legalization (Rupasinghe et al., 2020).

This study is to provide a comprehensive evaluation of the origin, domestication, and global spread of cannabis. It will synthesize current knowledge from various studies to offer a detailed understanding of the plant's historical significance, ethnopharmacological applications, and the genetic and biochemical factors that have influenced its domestication and cultivation. By examining the botanical, chemical, and pharmacological aspects of cannabis, this study expects to highlight its multifaceted nature and potential for future research and application in medicine, agriculture, and industry.

2 Historical Origin of Cannabis

2.1 Archaeological and genetic evidence tracing the earliest known uses

The historical origin of *Cannabis sativa* is a subject of extensive research, with evidence pointing to its use dating back to prehistoric times. Archaeological findings have revealed the presence of cannabis fibers, pollen, achenes, and imprints of achenes in various parts of Eurasia, suggesting a complex history of human interaction with the plant. Notably, cannabis records have been found in both Europe and East Asia, indicating a multiregional origin of human use (Long et al., 2017). The earliest known archaeological evidence of cannabis use dates back to around 10 000 BCE in Japan, followed by findings in China (McPartland et al., 2019). Additionally, fossil pollen studies have identified cannabis pollen in northwestern China dating back to 19.6 million years ago, further supporting the ancient presence of the plant in this region.

Genetic studies have also provided insights into the domestication history of cannabis. Whole-genome resequencing of 110 accessions from worldwide origins has shown that *Cannabis sativa* was first domesticated in early Neolithic times in East Asia. This research indicates that all current hemp and drug cultivars diverged from an ancestral gene pool currently represented by feral plants and landraces in China (Figure 1) (Ren et al., 2021). Furthermore, molecular evidence suggests that cannabis may have originated in low latitude regions, challenging the prevalent Central-Asia-Origin hypothesis (Zhang et al., 2018).

2.2 Geographical regions of initial cultivation

There are diverse hypotheses regarding the geographical areas where hemp was initially cultivated, which are associated with research approaches, inferential methods, or variety determinations. From the perspective of agricultural archaeologists, it is believed that hemp originated in Central Asia (i.e., the middle zone between Central West Asia, the Himalayas, and Siberia) or the Indian subcontinent. Among them, the most well-evidenced assertion is that of McPartland, who contends that the northeastern Tibetan Plateau near Qinghai Lake ought to be the origin center of hemp. This plant first spread westward to Europe and then eastward to eastern China. This region is also related to the development of the first grassland community in Asia, which might have played a role in the early cultivation and dissemination of hemp.

In Europe, cannabis cultivation is believed to have begun during the Copper or Bronze Age. Fossil pollen studies have shown the presence of wild-type *Cannabis ruderalis* in steppe and dry tundra landscapes throughout Europe during the early Holocene and Late Glacial periods. Cultivated hemp first appeared in the Pontic-Caspian steppe refugium, linked to the Copper Age Varna/Gumelnița culture and the Bronze Age Yamnaya and Terramara cultures (McPartland et al., 2018). The Scythians, an Iron Age steppe culture, are thought to have introduced hemp cultivation to Celtic and Proto-Slavic cultures (McPartland and Hegman, 2018).

In China, the antiquity of cannabis cultivation is well-documented, with historical accounts suggesting its presence in southern and central Russia, the south of the Caucasus, and other regions. The Hexi Corridor region in East Asia is highlighted as a hub for the spread of domesticated plants, animals, and cultural elements, including cannabis, originally from Southwest Asia and Europe (Long et al., 2017).

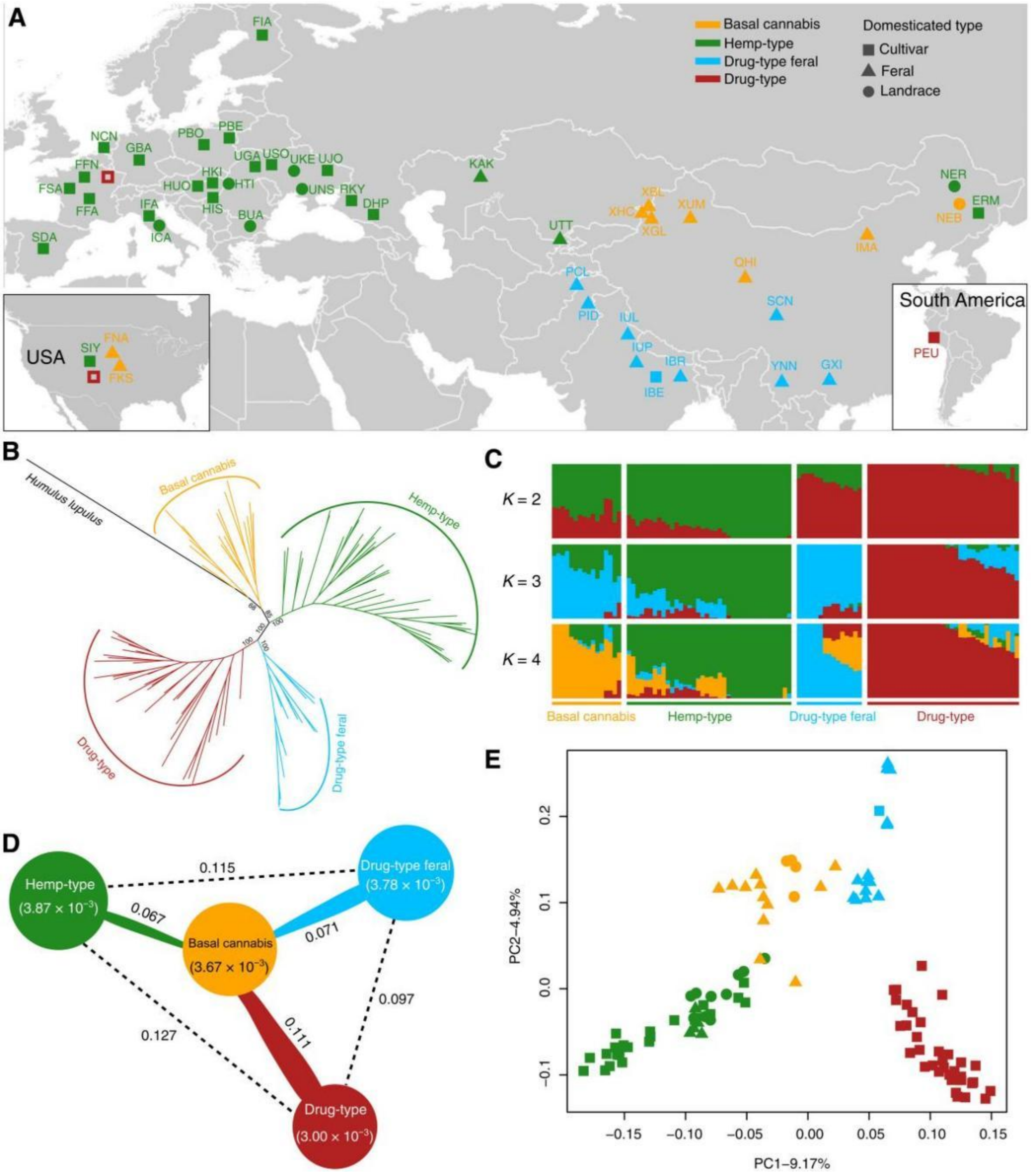

Figure 1 Population structure of *Cannabis* accessions (Adopted from Ren et al., 2021)

Image caption: (A) Geographic distribution (i.e., sampling sites of feral plants or country of origin of landraces and cultivars) of the samples analyzed in this study; Color codes correspond to the four groups obtained in the phylogenetic analysis and shapes indicate domestication types; The two empty red squares symbolize drug-type cultivars obtained from commercial stores located in Europe and the United States; For sample codes; (B) Maximum likelihood phylogenetic tree based on single-nucleotide polymorphisms (SNPs) at fourfold degenerate sites, using *H. lupulus* as outgroup; Bootstrap values for major clades are shown; (C) Bayesian model-based clustering analysis with different number of groups (K = 2 to 4). Each vertical bar represents one Cannabis accession, and the x axis shows the four groups; Each color represents one putative ancestral background, and the y axis quantifies ancestry membership. (D) Nucleotide diversity and population divergence across the four groups; Values in parentheses represent measures of nucleotide diversity (π) for the group, and values between pairs indicate population divergence (FST); (E) Principal component analysis (PCA) with the first two principal components, based on genome-wide SNP data. Colors correspond to the phylogenetic tree grouping (Adopted from Ren et al., 2021)

In China, the ancient nature of cannabis cultivation has been well documented. In the Chinese "Lu's Spring and Autumn Annals", hemp seeds are listed as one of the "five grains". This shows that at least in the Spring and Autumn Period of China, the local people have been very familiar with and understand the domestication of cannabis (Brand and Zhao, 2017). In "Erya", the cannabis plant is divided into Yin and Yang, indicating that the ancients had taken the male and female cannabis as a mark and skillfully mastered and used it. In other regions, historical accounts indicate that it also occurred in southern Russia, the southern Caucasus, and other regions. The

Hexi Corridor region of East Asia was highlighted as a hub for the spread of domesticated plants, animals, and cultural elements, including hemp originally from Southwest Asia and Europe (Long et al., 2017).

3 Process of Domestication

3.1 Changes in plant morphology and chemistry due to human cultivation

The domestication of Cannabis has led to significant changes in both its morphology and chemical composition. Human selection has driven the development of distinct varieties tailored for specific uses, such as fiber, seed, and drug production. For instance, the selection for fiber production has favored traits like increased stem length and reduced branching, while drug cultivars have been selected for higher concentrations of psychoactive compounds like tetrahydrocannabinol (THC) (Ren et al., 2021).

Moreover, the domestication process has resulted in the loss of function of certain genes involved in the synthesis of cannabinoids, leading to a divergence between hemp (low THC, high fiber) and drug (high THC) cultivars (Ren et al., 2021). The widespread use of single plant selections and inbreeding in modern breeding practices has further reduced genetic diversity, making many present-day cultivars more susceptible to pathogens and pests.

3.2 Comparison between wild varieties and domesticated strains

Wild varieties of Cannabis, often referred to as feral or ruderal populations, exhibit a broader genetic diversity compared to their domesticated counterparts. These wild populations are typically more resilient and adaptable to various environmental conditions due to their genetic variability (Small, 2015; Zhang et al., 2018). In contrast, domesticated strains have been selectively bred for specific traits, resulting in a narrower genetic pool and greater dependency on human cultivation for survival (Clarke and Merlin, 2016).

Morphologically, wild Cannabis plants tend to have more robust and variable growth patterns, while domesticated strains show more uniformity in traits such as plant height, leaf shape, and flowering time (McPartland and Small, 2020). Chemically, wild varieties often have a more balanced ratio of THC to cannabidiol (CBD), whereas domesticated drug strains are usually bred for higher THC content or CBD content, and fiber strains for lower THC and higher fiber yield (Ren et al., 2021).

The genetic exchange between wild and domesticated populations over thousands of years has blurred the lines between these groups, making it challenging to identify truly wild, unaltered populations (Small, 2017). This ongoing genetic exchange has also contributed to the development of hybrid strains that possess characteristics of both wild and domesticated varieties.

4 Cultural Significance and Historical Uses

4.1 Use of cannabis in traditional medicine, religious practices, and as a commodity in ancient trade

Cannabis has a rich history of use in traditional medicine, religious practices, and as a valuable commodity in ancient trade. Archaeological evidence suggests that cannabis was utilized by ancient civilizations for its medicinal properties as early as 12 000 years ago near the Altai Mountains in Central Asia (Crocq, 2020). The plant's seeds and inflorescences were employed to treat various physical ailments by ancient Oriental physicians, and its therapeutic applications have evolved over the centuries (Charitos et al., 2020).

According to traditional medicine, cannabis has the effect of dispelling wind, relieving pain and calming fright. Oriental classical medicine used cannabis for ventilation, arthralgia, insomnia, cough and other diseases.Oriental classical medicine used cannabis for ventilation, arthralgia, insomnia, cough and other diseases. In ancient Egyptian accounts, Ramses III Ramses-3 used cannabis to treat glaucoma, and later for menstrual cramps and enemas.In 70 AD, the Greek physician Pedanius Dioscorides, in his Medical Problems, documented the use of cannabis to treat earaches, edema, and other inflammatory diseases.The ancient Egyptians, Greeks and Romans, although they did not understand the psychoactive mechanism of cannabis, they all regarded cannabis as a medicine, and cannabis was effective in improving pain and inflammation (Raphael Mechoulam, 2016). Dating back to around 800 BCE, also document the use of cannabis for its anti-inflammatory, antiseptic, and anticonvulsant properties (Pisanti and Bifulco, 2018).

In religion, cannabis is widely used in the religious field because of its simple cultivation, psychoactive, and widely used to cure diseases and save lives.Religiously, cannabis played a role in burial rituals, as evidenced by the discovery of cannabinoid oils in wooden braziers at a cemetery on the Pamir Plateau, dating back to 500 BCE (Clauset and Post, 2019). This suggests that cannabis was used for its psychoactive effects in religious ceremonies.In 730 AD, Meng Shen, a Chinese physician, proposed in his book "Diet Medicine" that people who took cannabis for 100 days could pass through the mind of the gods. Taoist alchemist Tao Hongjing said in the book of Famous Doctors that if cannabis and ginseng are eaten together, it can give people magic powers to see the future. The most widespread use of religion is still in India, as evidenced by the Vedas in Hinduism. In Vedic times, monks used cannabis to enter a meditative and transcendental state. In Africa, tribal people in Congo, East Africa, Lake Additionally, the plant was a significant commodity in ancient trade, with its fibers being extensively used for textiles and its seeds for nutrition (Martinez et al., 2023).

4.2 Legal status and societal perceptions through the ages

The legal status and societal perceptions of cannabis have fluctuated significantly throughout history. In ancient times, cannabis was widely accepted and utilized for its medicinal and practical applications. However, its perception began to shift in the early 20th century when cannabis was banned in many countries as part of a broader movement to control addictive substances.

Despite its prohibition, cannabis remained a popular illicit drug, and its therapeutic potential continued to be recognized. The discovery of the endocannabinoid system in the late 20th century marked a turning point, providing a scientific basis for the medicinal use of cannabis and leading to a renewed interest in its therapeutic properties (Ren et al., 2021).

In recent years, there has been a significant shift in societal perceptions, with several countries legalizing cannabis for medical and recreational use. This change has been driven by accumulating evidence supporting its therapeutic benefits and a growing recognition of its potential to treat various medical conditions (Bonini et al., 2018). The legalization of cannabis in some jurisdictions has also spurred new research into its applications, further influencing public opinion and policy (Moon et al., 2023).

5 Global Spread from East to West

5.1 Routes of cannabis spread across continents

The spread of cannabis from its origins in Eurasia to other parts of the world is a complex process influenced by various factors, including human migration, trade, and cultural exchanges. Cannabis is believed to have been first domesticated in East Asia during the early Neolithic period, with evidence suggesting that all current hemp and drug cultivars diverged from an ancestral gene pool in China (Ren et al., 2021). The plant's spread across Eurasia is marked by its appearance in both Europe and East Asia around the same time, indicating a multiregional origin of human use (Long et al., 2017).

The Hexi Corridor region played a significant role as a hub for the spread of domesticated plants, animals, and cultural elements, including cannabis, from Southwest Asia and Europe to East Asia (Long et al., 2017). This trans-Eurasian exchange network facilitated the movement of cannabis across the continent, with a marked increase in cannabis achene records in East Asia between 5 000 and 4 000 years ago.

Cannabis seeds accompanied the migration of nomadic peoples, further aiding its spread. Historical records indicate the presence of cannabis in Central Asia around 12 000 years ago, and its medicinal use was documented in ancient China, Egypt, Greece, and later in the Roman Empire (Crocq, 2020). The plant's spread to Europe and the Iberian Peninsula is believed to have occurred during the European Copper/Bronze ages, with earlier signs of cultivation dating to the Early Medieval Ages (Figure 2) (Rull, 2021a; Rull, 2021b).

5.2 Influence of trade routes

Trade routes have significantly influenced the global spread of cannabis. The Silk Road, a network of trade routes connecting the East and West, played a crucial role in the dissemination of cannabis. The Hexi Corridor, part of the Silk Road, served as a major conduit for the movement of cannabis and other domesticated plants and animals. This facilitated the exchange of cannabis between different regions, contributing to its widespread cultivation and use.

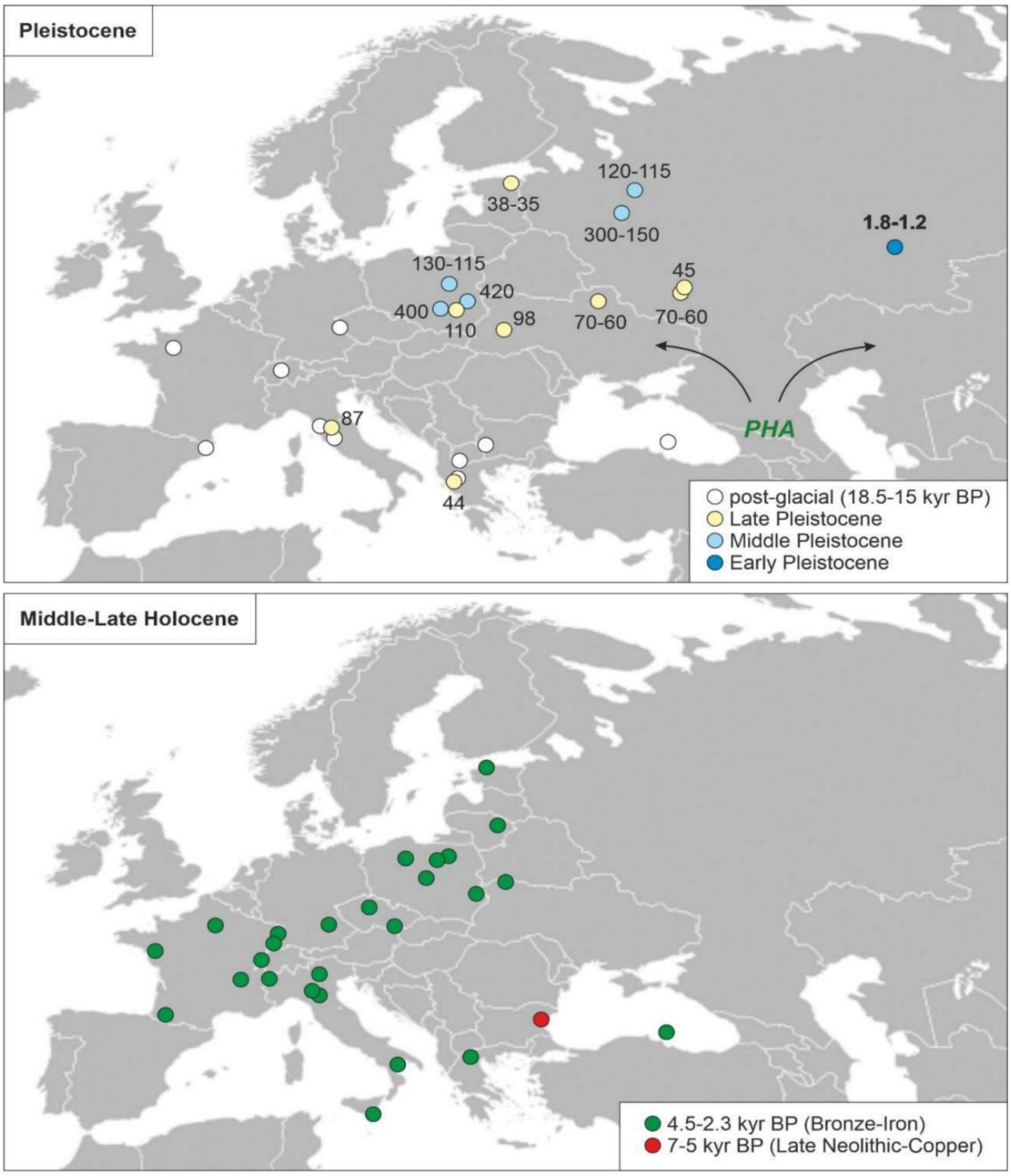

Figure 2 Pleistocene (upper panel) and Holocene (lower panel) European pollen records consistent with Cannabis, according to the assemblage identification approach (Adopted from Rull, 2021b)

Image caption: In the Pleistocene panel, post-glacial ages have been differentiated from the rest of late Pleistocene ages; PHA is the precursor of the European cannabis according to Clarke and Merlin (2013); Ages in million years before present (bold numbers) and in thousand years before present (normal numbers) (Adopted from Rull, 2021b)

In the modern era, the globalization of cannabis cultivation has been driven by the industrial utility of hemp and the recreational use of cannabis. The counter-culture movements of the 1960s and 1970s led to increased global demand for cannabis, prompting countries like Morocco and Mexico to become large-scale producers and major suppliers to European and American markets (Decorte and Potter, 2015). This period also saw the decentralization of cannabis production, with cultivation spreading to almost every country around the world.

The development of traditional landrace varieties, resulting from a combination of natural and farmer selection, further diversified cannabis cultivars as the plant spread to different regions with varying climatic and cultural conditions (Clarke and Merlin, 2016). The genetic diversity of cannabis has been shaped by these factors, with distinct phylogeographic structures observed in different regions (Zhang et al., 2018).

6 Modern Cultivation and Breeding Techniques

6.1 Advances in genetic modification and breeding for specific traits

Recent advancements in genetic modification and breeding techniques have significantly impacted the cultivation of *Cannabis sativa*, particularly in optimizing the content of key cannabinoids such as tetrahydrocannabinol (THC) and cannabidiol (CBD). Traditional breeding methods, while effective, are often time-consuming and costly due to the dioecious and highly heterogenic nature of cannabis (Ingvardsen and Brinch-Pedersen, 2023). Modern genome editing techniques, such as CRISPR/Cas9, offer a promising solution by allowing precise modifications to target genes responsible for cannabinoid biosynthesis. This approach can streamline the introduction of desirable traits without altering the overall cannabinoid profile.

Whole-genome resequencing has provided valuable insights into the domestication history and genetic diversity of cannabis, identifying candidate genes associated with traits differentiating hemp and drug cultivars. This genomic information is crucial for functional and molecular breeding research, enabling the development of cultivars with specific THC and CBD ratios tailored for medicinal or industrial purposes (Ren et al., 2021). Additionally, the characterization of physiological traits and the heritability of key parameters such as plant height and days to maturation can facilitate the selection of high-yielding genotypes, further enhancing breeding efficiency.

The use of tissue culture techniques, including micropropagation and genetic transformation, has also shown potential in cannabis breeding. These methods can produce disease-free, true-to-type plants and enable the development of novel phenotypes through gene expression modulation (Adhikary et al., 2021). The integration of these advanced techniques into breeding programs can accelerate the creation of elite cannabis strains with optimized cannabinoid content and other desirable traits.

6.2 Impact of technology on cultivation practices

Technological advancements have revolutionized cannabis cultivation practices, leading to more efficient and sustainable production methods. The adoption of precision agriculture techniques, such as controlled environment agriculture (CEA), allows for the optimization of growing conditions, resulting in higher yields and consistent quality (Spangenberg and Cogan, 2021). By monitoring and adjusting environmental parameters such as light, temperature, and humidity, growers can create ideal conditions for cannabis growth, reducing the risk of disease and pest infestations.

The use of high-throughput DNA sequencing technologies has enabled the establishment of virtual genetic resources, facilitating the systematic phenotyping and genetic analysis of cannabis germplasm (Welling et al., 2016). This approach can identify key genetic markers associated with desirable traits, supporting marker-assisted selection and the development of breeding programs that rely on less labor-intensive and time-consuming methods (Ranalli, 2004). The creation of a global virtual core collection of cannabis genetic resources can further enhance breeding strategies by providing a comprehensive database of genetic diversity and provenance meta-data.

Moreover, the characterization of cannabinoid accumulation, flowering time, and disease resistance in high-cannabinoid hemp cultivars has highlighted the importance of selecting cultivars with optimal performance for specific growing locations (Rose et al., 2021). By understanding the genetic and environmental factors influencing these traits, breeders can develop stable, uniform cultivars with improved disease resistance and flowering times tailored to different latitudes.

7 Case Study: Domestication and Dissemination of a Specific Strain

7.1 The origin, domestication process and spreading of the “*Indica*” variety

One notable strain of *Cannabis sativa* is the “*Indica*” variety, which has its origins in Central Asia, specifically in regions such as Afghanistan, Pakistan, and Turkestan (Figure 3). This strain, scientifically classified as *Cannabis sativa* subsp. *indica*, was initially domesticated in these areas due to the favorable climatic conditions that promoted its growth and unique phytochemical properties (McPartland and Small, 2020). The domestication process involved natural selection driven by the local climate, which led to the development of distinct morphological and chemical traits.

The spread of the *Indica* strain began with its early dissemination to Southeast Asia, Africa, and eventually the Americas. This spread was facilitated by human migration and trade routes, which allowed the strain to adapt to various environmental conditions and cultural practices (McPartland and Small, 2020). The popularity of *Indica* strains grew significantly in the 1980s, driven by their high tetrahydrocannabinol (THC) content and the psychoactive effects that were highly sought after for both recreational and medicinal purposes (McPartland and Small, 2020).

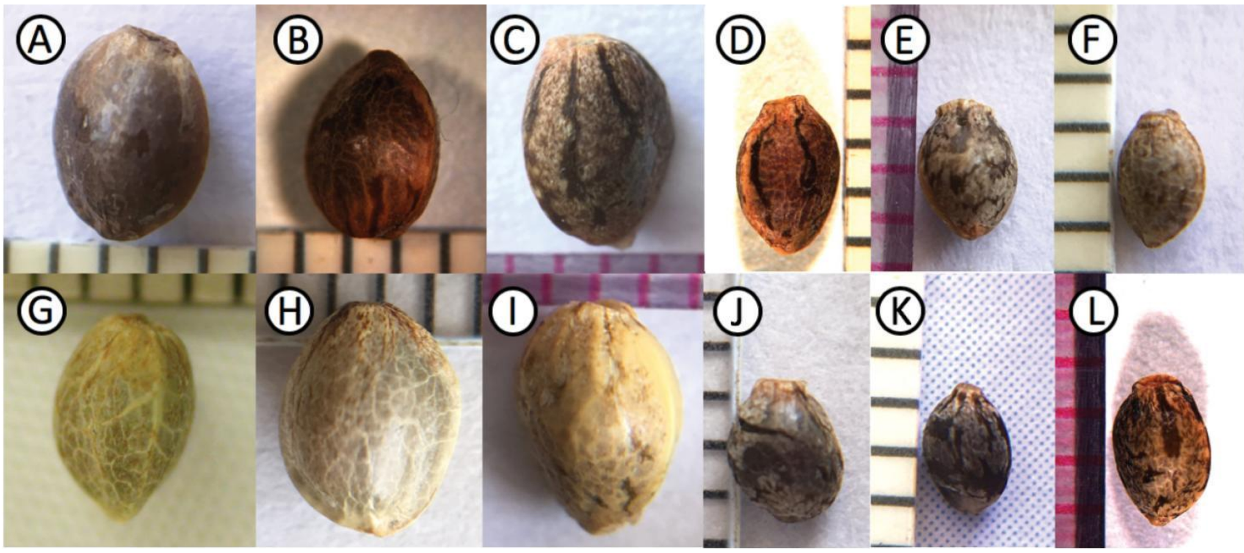

Figure 3 Representative achenes of four varieties (Adopted from McPartland and Small, 2020)
Image caption: (A) *indica*, Rajshahi (Bangladesh), *Clarke* 1877 (BM); (B) *indica*, Coimbatore (India), *Bircher* 1893 (K); (C) *indica*, South Africa, *Hillig* 1996; (IND); (D) *himalayensis* neotype; (E) *himalayensis*, Bareilly (India), *Roxburgh* 1796 (K); (F) *himalayensis*, East Bengal (Bangladesh) *Griffith* 1835 (GH); (G) *afghanica* neotype H *afghanica* epitype I *afghanica* Yarkant (Xīnjiāng), *Henderson* 1871 (LE); (J) *asperrima* lectotype K *asperrima* Nuristān (Afghanistan), *Street* 1965 (F); (L) Kailiyskiy Alatau (Kazakhstan), *Semenov-Tyan-Shansky* 1857 (LE) (Adopted from McPartland and Small, 2020)

7.2 Discuss the genetic improvements made and their impacts.

Genetic improvements in the *Indica* strain have been substantial, particularly through the process of polyploidization. This technique involves the induction of polyploidy, which has been shown to enhance certain desirable traits in cannabis plants. For instance, the development of tetraploid *Indica* lines has resulted in larger fan leaves, increased trichome density, and significant changes in the terpene profile. These genetic modifications have also led to a notable increase in cannabidiol (CBD) content, which is beneficial for medical applications (Parsons et al., 2019).

Moreover, the genetic diversity of *Indica* strains has been further enriched by cross-breeding with other cannabis varieties from different gene pools. This has resulted in hybrid strains that combine the high THC content of *Indica* with other beneficial traits such as improved yield and resistance to pests and diseases (Clarke and Merlin, 2016; Ren et al., 2021). The use of advanced genomic techniques, such as whole-genome resequencing, has provided deeper insights into the genetic makeup of *Indica* strains, enabling more targeted breeding strategies to enhance specific traits (Ren et al., 2021).

These genetic improvements have had significant impacts on both the medical and recreational cannabis markets. The increased CBD content and optimized terpene profiles have made *Indica* strains highly desirable for therapeutic uses, including pain relief, anxiety reduction, and anti-inflammatory effects. On the recreational side, the high THC content and unique flavor profiles have continued to drive the popularity of *Indica* strains among consumers (Parsons et al., 2019; Romero et al., 2020).

8 Legalization Movements Worldwide

8.1 Overview of global shifts in cannabis legislation

The global landscape of cannabis legislation has undergone significant transformations over the past decade. Countries around the world are increasingly adopting various forms of cannabis liberalization, including decriminalization, medicalization, and full legalization for recreational use. This shift is driven by a combination of economic, social, and medical factors, as well as a growing recognition of the failures of prohibitionist policies.

In North America, Canada and several U.S. states have been at the forefront of this movement. Canada legalized recreational cannabis in October 2018, aiming to minimize associated harms and redirect profits from criminal enterprises (Rotermann, 2020). Similarly, U.S. states like Colorado and Washington have established legal markets for non-medical cannabis, despite these actions contravening international drug conventions (Room, 2014). These pioneering efforts have set precedents that other jurisdictions are beginning to follow.

Internationally, Uruguay was the first country to fully legalize cannabis, and other nations are exploring similar paths. The evolving legal status of cannabis is not only a domestic issue but also has significant international implications, challenging existing drug control treaties and prompting discussions on the need for their revision (Room, 2014).

8.2 Economic, social, and medical drivers behind legalization

The push for cannabis legalization is multifaceted, with economic, social, and medical drivers playing crucial roles. Economically, the potential to generate substantial tax revenues and create new industries has been a significant motivator. For instance, proponents of legalization in Canada highlighted the potential to eradicate the black market, improve quality and safety control, and increase tax revenues (Bahji and Stephenson, 2019).

Socially, the movement towards legalization is often framed within the context of social justice. The historical enforcement of cannabis prohibition has disproportionately affected marginalized communities, leading to calls for reparative measures. Legalization efforts are seen as a way to address these injustices, although there is ongoing debate about whether current policies are sufficient to achieve true social equity (Koram, 2022).

Medically, the recognition of cannabis's therapeutic potential has been a major driver of legalization. Evidence suggests that cannabinoids can be effective for various medical conditions, prompting the adoption of medical cannabis laws in many jurisdictions (Hall et al., 2019). However, the public health implications of widespread cannabis use remain a concern, with studies highlighting both potential benefits and risks (Hall et al., 2019).

9 Current Challenges and Controversies

9.1 Legal, ethical, and health-related controversies surrounding cannabis use

The legalization and liberalization of cannabis laws have sparked significant debate and controversy across various domains, including legal, ethical, and health-related aspects. The rapid changes in cannabis regulations globally, with many countries moving towards decriminalization, medicalization, and even full legalization, have led to a complex landscape of cannabis use and its implications (Sevigny et al., 2023).

One of the primary legal and ethical concerns revolves around the regulation of cannabis production and sale. Different jurisdictions have adopted varied approaches, which have influenced both medicinal and recreational use. For instance, the regulation of medicinal cannabis has shown mixed results in terms of effectiveness and public health outcomes, with some studies indicating potential benefits while others highlight risks such as increased road crashes and other harms (Hall et al., 2019).

Health-related controversies are particularly prominent, as the long-term effects of cannabis use remain a subject of ongoing research. While some evidence suggests potential medicinal benefits, there are also significant concerns about adverse health effects, including dependency, mental health issues, and the impact on cognitive development, especially among younger users. The lack of robust, high-quality systematic research further complicates the understanding of these outcomes, highlighting the need for more comprehensive studies to inform policy and public health strategies (Sevigny et al., 2023).

9.2 Environmental impact of cannabis cultivation

The environmental impact of cannabis cultivation is another area of growing concern. The shift towards large-scale, commercial cannabis production has led to several environmental challenges, including the depletion of natural resources, pollution, and the introduction of invasive species. The intensive cultivation practices required for high-yield cannabis production often involve significant water usage, which can strain local water supplies, particularly in arid regions (Balthazar et al., 2022).

Moreover, the use of chemical fertilizers and pesticides in cannabis farming can lead to soil degradation and water contamination, posing risks to local ecosystems and biodiversity. The increased incidence of plant pathogens and diseases in large-scale cannabis cultivation further exacerbates these environmental issues, as the need for disease management often leads to the use of additional chemical treatments (Punja, 2021).

Sustainable cultivation practices, such as the use of beneficial *Pseudomonas* spp. bacteria as crop inoculants, have been proposed to mitigate some of these environmental impacts. These bacteria can enhance plant growth and stress tolerance, potentially reducing the need for chemical inputs and improving overall sustainability (Balthazar et al., 2022). However, the implementation of such practices faces challenges, including regulatory hurdles and the need for further research to optimize their efficacy and commercial viability.

10 Concluding Remarks

This study has systematically examined the extensive history and global diffusion of Cannabis, tracing its origins back to Central Asia and charting its spread across the globe. Key findings highlight Cannabis's significance not only as a psychoactive and medicinal plant but also as a commodity that influenced trade and cultures across continents. Its domestication in East Asia catalyzed a set of unique developments in plant morphology and chemical properties, adapted through natural selection to varied environmental and cultural contexts. The evolution of legal landscapes in the 20^{th} and 21^{st} centuries has further complexified its role, transitioning from widespread prohibition to a gradual, albeit contentious, acceptance.

Looking ahead, the future of Cannabis domestication and use appears poised for significant transformations influenced by scientific advancements and evolving societal norms. Technological improvements in genetics and cultivation could tailor plant strains to enhance desired traits such as yield, potency, or specific cannabinoid profiles, potentially reducing adverse environmental impacts. Legally, the global trajectory is veering towards more liberal policies, with increasing recognition of both the medical benefits and the economic potential of cannabis legalization. Socially, as public perception shifts further towards acceptance, cannabis may see integration in new therapeutic, recreational, and commercial domains.

As cannabis continues to be embraced more widely, there is an urgent need for an international consensus on regulation. This would help harmonize the legal, agricultural, and commercial frameworks across borders, facilitating better control of quality, potency, and safety standards. Additionally, as more regions legalize cannabis, there is a pressing requirement for comprehensive studies to explore its long-term impacts on public health, social structures, and economics. Collaborative international research efforts are essential to develop robust guidelines that ensure the safe integration of cannabis into society, balancing potential benefits against risks and mitigating any unintended consequences of its widespread use.

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