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Comprehensive Review of Phytochemical Studies and Legalization of Cannabis in Morocco

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ABSTRACT: Research on cannabis and its bioactive derivatives, including cannabinoids, non-cannabinoids, and extracts, has significantly increased in recent years due to their potential therapeutic applications as demonstrated by numerous published studies. Although there is evidence of the potential efficacy of cannabinoid and non-cannabinoid compounds from cannabis in the treatment of various diseases and syndromes, further research is required to mitigate the potential damage that could result from the excessive use of cannabinoid products, particularly tetrahydrocannabinol (THC), such as psychotropic effects, addiction, cognitive deficits, cardiovascular problems, and impacts on mental health. This review describes phytochemical and biological studies on cannabis grown in Morocco, utilizing databases such as SciFinder, ScienceDirect, Scopus, Google Scholar, and PubMed to provide updated data on cannabis in Morocco. The findings of this research aim to enable investors, economic operators, researchers, and policymakers to better understand the current state of cannabis in Morocco, thereby promoting industry growth and cannabis-related innovation. Additionally, this paper includes a brief discussion on the legalization of cannabis in Morocco, highlighting the new opportunities for investment in medical cannabis. This study also underscores that much remains to be explored regarding Moroccan cannabis, from the isolation of bioactive compounds and pre-clinical studies to clinical trials and the mass production of approved cannabis-based medicines. Furthermore, the findings are intended to inform key stakeholders about the current state of cannabis in Morocco, fostering industry growth and innovation.

1. INTRODUCTION

Cannabis, a medicinal plant with a history of domestication spanning thousands of years, has been utilized for various therapeutic purposes, including alleviating pain, reducing nausea and anxiety, enhancing appetite, relaxing muscles, and inducing euphoria (Crocq, 2020). Due to its healing properties, Arab travelers introduced cannabis from India to Arab nations. By the 9th to 12th centuries, the Arab world was already familiar with its psychoactive effects, leading to its spread from Egypt to the Maghreb region (Fatima et al., 2021). In Morocco, cannabis has a long tradition of use, particularly in the Rif region (North of Morocco), where it has been cultivated for centuries. People often combine cannabis with tobacco and smoke it, a cultural practice that stretches back to the 7th century (Blickman, 2017). Historically, cannabis has also had medicinal and religious applications (Stambouli et al., 2005). In traditional Moroccan pharmacopoeia, cannabis-based preparations are used for abortion, treating respiratory ailments, healing wounds, and managing diarrhea in infants, as well as in hair care, improving vision, and as anthelmintic and anti-vomiting agents (Merzouki & Mesa, 1999). The economic impact of cannabis cultivation in northern Morocco remains significant, with the industry contributing substantially to the region's economy. The cannabis market in Morocco is expected to see robust growth, with projections indicating a notable increase in market value in the coming years. This growth highlights a shift towards legalization, attracting international investment, and promoting economic development within the sector. Despite the United States leading in global revenue generation, Morocco's cannabis market is undergoing a significant transformation (I. Bouhlal et al., 2024)

Cannabis is classified into three species: *Cannabis sativa*, *Cannabis indica*, and *Cannabis ruderalis*, which are flowering plants that produce resin through glandular trichomes (Tongkasee et al., 2023). In recent years, a better understanding of our body's endocannabinoid system and

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the chemical composition of cannabis has led the scientific community to confirm the therapeutic potential of this plant and its derivatives (Dasram et al., 2022). Consequently, the use of cannabis extracts and components for medical purposes has expanded rapidly. The main phytochemicals found in cannabis are cannabinoids, flavones, and terpenes (Aazza, 2021). According to Chouvy and Afsahi, Morocco, which was previously considered as the top producer of hashish in 2003, has now been overtaken by Afghanistan. It is alleged that Moroccan hashish production decreased by 75% between 2003 and 2011, dropping from 3080 tons to 760 tons (Chouvy & Afsahi, 2014). Hashish of Moroccan origin can be considered a terroir product (Chouvy, 2022).

Since September 2021, the Moroccan government has legalized the cultivation, exportation, and importation of cannabis products for medical and industrial uses. This decision is expected to create jobs and stimulate the economy in rural areas, where thousands of families depend on cannabis cultivation for their livelihood. However, recreational use of cannabis remains illegal in Morocco (Kasraoui, 2023). In July 2024, Morocco legally exported cannabis produced on its soil to Switzerland for the first time in its history. This first export raises hopes for the future of cannabis-related industries (Bernard, 2024).

Cannabis is mainly cultivated in the Rif region of the north of Morocco, where it has been grown on a large scale since the emergence of the hashish industry in the 1960s and its expansion in the 1980s. To produce the golden-beige powder called “Hashish”, the traditional process involves drying the female plants, which makes the resin and trichomes dusty and brittle. These components are then separated from the plant material by beating or shaking them over a thin, stretched nylon veil. The remaining plant fragments are then separated from the seeds and discarded. In 2020, the global market size for cannabis was valued at USD 20.5 billion, and it is expected to grow (Rasera et al., 2021). The biggest producers of cannabis worldwide are: USA, Morocco, Afghanistan, Mexico, Columbia, Paraguay, Jamaica, and Canada (Chouvy, 2019). However, the limited number of countries where it is legally cultivated has resulted in a scarcity of peer-reviewed research on pest and disease management (Punja, 2021).

To our knowledge, there is no work summarizing all biological and chemical data of cannabis grown in Morocco, hence the originality of this study, which aims to inform investors, economic operators, researchers, and policymakers about the current state of cannabis in Morocco, promoting industry growth and innovation.

2. METHODOLOGY

Various scientific databases such as SciFinder, ScienceDirect, Scopus, Google Scholar, and PubMed were used to gather relevant information about cannabis in Morocco, using keywords such as: cannabis, biological properties of cannabis, phytochemical studies, traditional use of cannabis in Morocco, phytochemistry of cannabis, pharmacology of cannabis, and bioactivity of cannabis. All articles dealing with cannabis grown in Morocco were included, regardless of the date of publication. If two papers provided the same information, the more recent one was considered. Figure 1 below displays the documents that were found and indexed in Scopus.

3. BOTANICAL STUDIES ON THE GENUS CANNABIS

The classification of the Cannabis genus is outlined below (Chaachouay & Zidane, 2023):

Kingdom : Plantae (plants)
Subkingdom : Tracheobionta (vascular plants)
Superdivision : Spermatophyta (seed plants)
Division : Magnoliophyta (flowering plants)
Class : Magnoliopsida (dicotyledons)
Subclass : Hamamelididae
Order : Urticales
Family : Cannabaceae
Genus : *Cannabis*

The cannabis plant has been utilized across various cultures for numerous purposes. It is thought to have originated in Central Asia before spreading to Europe and the America. The plant is classified into three primary species: *Cannabis sativa* L., *Cannabis indica*, and *Cannabis ruderalis*, each exhibiting distinct characteristics (Hurgobin et al., 2021). However, due to extensive hybridization, the exact number of species and their classifications remain debated. Many experts consider that the cannabis genus is made up of a single species, *Cannabis sativa* L., with various subspecies and varieties. *Cannabis sativa* is a tall plant with long and narrow leaves that is less furcate. Its leaves are serrated and have a unique vein pattern that can vary among different varieties. In contrast, *Cannabis indica* is a highly branched plant with broader leaves that is short in height. Cannabis ruderalis is a short plant with small and thick leaves that has less branching. Cannabis is a plant species that has male and female flowers on separate plants. The active compounds for medicinal use are found in the inflorescences, which are mostly concentrated in the trichomes (Balant et al., 2021; Mcpartland & Small, 2020).

Currently, in Morocco, there are multiple varieties of cannabis available on the market. These varieties have been created through cross-breeding of the primary cannabis species, including *Cannabis sativa*, *Cannabis indica*, and *Cannabis ruderalis*, as well as the selection of specific seeds with elevated Δ^9-THC levels, such as those found in “feminized” or “autoflowering” strains. One of the cross-breeding experiments resulted in a hybrid that is 75% *sativa* and 25% *indica*, which has a fast growth cycle and produces high quantities of Δ^9-THC (Stambouli et al., 2016). Cannabis can be classified into two species based on their drug properties: broad-leaflet ”*Indica*” and narrow-leaflet ”*Sativa*”. The narrow-leaflet drug biotypes are from South Asia, while the broad-leaflet drug biotypes are from Central Asia. On the other hand, hemp-type cannabis, also known as *Cannabis sativa* ”hemp biotype” or narrow-leaf-hemp biotype refers to varieties with high CBD

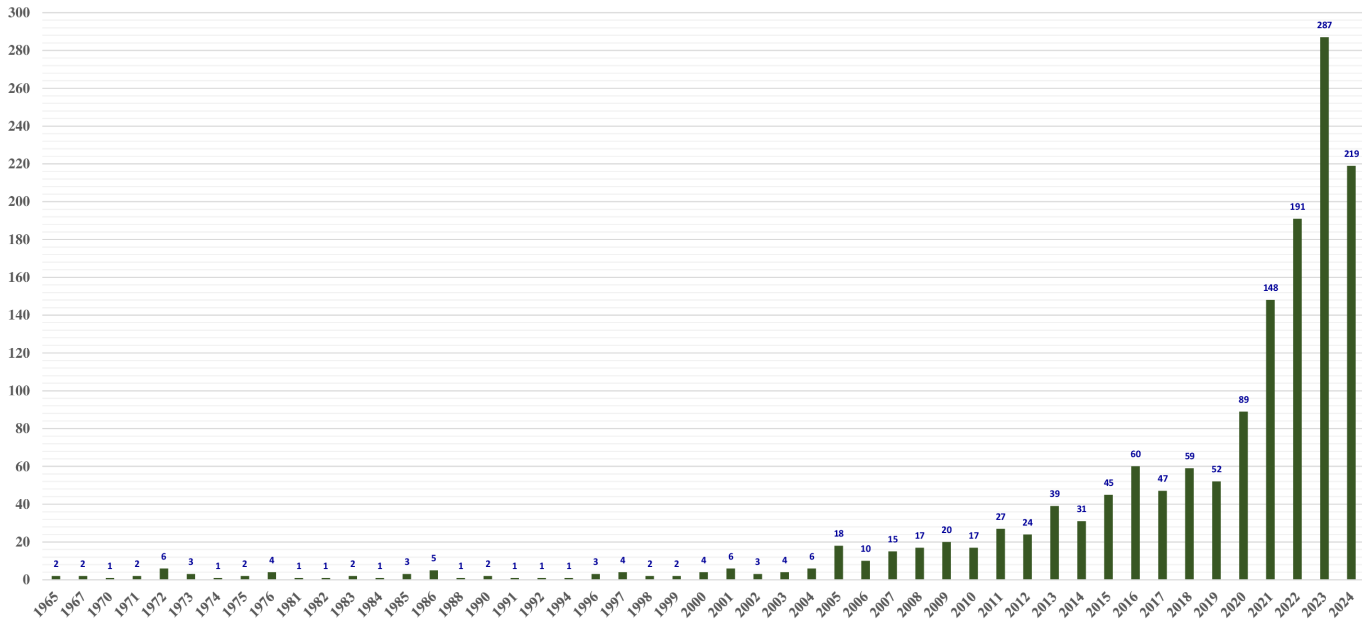

Figure 1. Distribution of published papers indexed in Scopus on cannabis grown in Morocco.

and low THC found in Europe that are used for seed and fiber production (Fatima et al., 2021).

El Alaoui and colleagues performed nucleic acid extraction and purification from eight hashish samples collected by the Moroccan Gendarmerie Royal's Forensic Sciences Laboratory. Using the Wagner CTAB method, they obtained DNA yields ranging from 15.3 to 373.8 ng/mL, which increased to approximately 40.88 to 303.4 ng/mL after an additional purification step. The modified CTAB method produced DNA yields between 24 and 424.2 ng/mL. Nucleic acid quality was assessed using the A260/A280 ratio, which varied from 1.49 to 1.88. The study demonstrated that PCR amplification of THCA synthase was effective with DNA extracted via the modified CTAB method, but not with DNA obtained through the Wagner protocol (Abdelaziz et al., 2016; Alaoui et al., 2013). On the other hand, complete sequences were obtained from mature *Cannabis sativa* inflorescences, revealing strain-specific differences in the conversion of CBGA into CBDA and/or THCA products. Comparative analysis of the expressed sequences identified various SNPs that were associated with the cannabinoid composition of the mature inflorescences, underscoring their functional relevance. The CBDAS sequence family exhibited more variability than the THCAS family, indicating that THCA-forming enzymes may have evolved more recently from the CBDAS group (Onofri et al., 2015). Genetic findings related to Moroccan cannabis are detailed in Tables 1 and 2 below.

4. TRADITIONAL USES OF CANNABIS IN MOROCCO

Historically, the term "hashish" has been used to describe various cannabis preparations (Charitos et al., 2021). Currently, it mainly refers to cannabis resin. Cannabis derivatives include (1) cannabis herb (Marihuana): this term generally refers to the dried flowers and leaves of the cannabis plant; (2) cannabis resin (hashish): this is the dried resinous secretion from the flowering tops of the cannabis plant, which can be brown or black in color; (3) cannabis oil: Also known as hash oil, this liquid is obtained by extracting cannabinoids from hashish or cannabis buds using solvents such as isopropyl alcohol. During flowering, the plant's trichomes produce a resinous sap rich in cannabinoids (Abdelaziz et al., 2016; Alaoui et al., 2013).

For centuries, cannabis has been utilized for both recreational and traditional medicinal purposes in Africa after being brought by Arab traders from India (Kakudidi et al., 2022). In Morocco, cannabis has many uses in traditional medicine, including the use of cannabis for abortion (Merzouki et al., 2001), dental pain, for anxiety, entero-gastric diseases, scarring injury, asthma, and stomach irritation, recreational drug (Ahmed et al., 2023; Mouna et al., 2020); for diabetes (Fouad et al., 2019; Mouna et al., 2020); eczema and fortify hair (Mostafa et al., 2021), as drug (Abdelmajid et al., 2011), as sedative, antiemetic, and stomachic (Abouri et al., 2012), cancer and hair care Benali et al. (2017) , (Fakir et al., 2019), cosmetics (T. Bouhlal et al., 2013), gastritis treatment and soothing pain (Merzouki et al., 2000; Mohamed et al., 2011), the management of diarrhea and

Table 1

Aligned sequences of polymorphic sites for THCA synthase gene of Moroccan *Cannabis sativa* L. Identical nucleotide for the simple with number AB212834_Mexico_DR are shown in (*). Nucleotide substitutions for the sample AB212834_Mexico_DR are represented by letters (Abdelaziz et al., 2016).

	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt	Nt
Nucleootide (NT) sites	46	64	79	92	117	118	121	129	136	137	151	154	187	198	221	229	268	269	282	285	287	292	294	300	312	355	366	383	385	399	409	412	418	424	494	505	612
AA Change	F16I	H22N	I27L	R31Q		K40E	H41Y		V46P	V46P	L51F	V52I	I63V		I74T	T77A	N90V	N90V			T96S					M119L		V128A	V129I		S137T	I138V	I140V	V142I	K165M	L169F	
AB212834_Mexico_DR	T	C	A	G	A	A	C	C	G	T	C	G	A	G	T	A	A	A	A	A	C	T	A	T	C	A	A	T	G	A	T	A	A	G	A	C	T
JQ437481_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	T	*	*	*	*	*	*	*	*	T	C
JQ437482_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	*	*	*	*	*	*	*	*	*	T	C
JQ437483_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	*	*	*	*	*	*	*	*	*	T	C
JQ437484_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	*	*	*	*	*	*	*	*	*	T	C
JQ437485_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	*	*	*	*	*	*	*	*	*	T	C
JQ437486_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	*	*	*	*	*	*	*	*	*	T	C
JQ437487_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	*	*	*	*	*	*	*	*	*	T	C
JQ437488_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	*	*	*	*	*	*	*	*	*	T	C
JQ437489_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	*	*	*	*	*	*	*	*	*	T	*
JQ437488_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	T	*	*	G	*	*	*	*	*	*	*
JQ437490_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	T	*	C	A	*	A	G	G	A	T	T	C
JQ437491_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	T	*	*	G	*	*	*	*	*	*	*
JQ437492_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	*	T	*	*	G	*	*	*	*	*	*	*
JQ437493_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	T	*	C	A	*	A	G	G	A	T	T	C
JQ437494_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	T	*	C	A	*	A	G	G	A	T	T	C
JQ437495_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	T	*	C	A	*	A	G	G	A	T	T	C
JQ437496_Morocco_DR	*	A	*	A	G	G	T	T	C	C	T	A	G	*	C	*	G	T	G	C	G	C	C	C	T	T	*	C	A	*	A	G	G	A	T	T	C

Table 2
SNPs in THCAS and CBDAS gene sequences expressed in the cannabis germplasm. All SNPs are defined in comparison with the GenBank accession Nr. E33090 and Nr. E55107 (Onofri et al., 2015).

SNPs in CBDAS gene sequences

Accession code	105	221	428	503	516	587	1032	1035	1095	1123	1278	1341	1420	1426	1465	1584	1616	1617	Seq.ID	CBD(V)A proportion
E55107	G	C	A	A	G	A	G	C	C	G	A	T	A	C	G	C	T	T	5/1	Unknown
2010.24a.35/C	T	C	A	A	G	A	G	C	C	G	A	T	A	C	G	C	T	T	6/2	77.3%
	T	C	A	A	G	A	G	C	C	G	A	T	A	C	G	C	T	A	6/3	

SNPs in THCAS gene sequences

Accession code	87	187	366	373	399	706	749	1179	1229	1395	1560	E	Seq.ID	THC(V)A proportion
E33090	T	A	A	G	A	G	C	A	A	G	T	G	1/1	Unknown
2010.24a.35/T	T	C	T	G	G	G	C	A	T	G	T	G		96.2 %

SNPs: single nucleotide polymorphisms; CBDAS: cannabidiolic acid-synthase; THCAS: tetrahydrocannabinolic acid-synthase.

to stimulate the appetite, as relaxing, anxiolytic, anticonvulsant, analgesic, antipyretic and antibacterial agents (Chouvy, 2008), hair lengthening, hair loss, against dandruff, strengthening hair and calming (Kharchoufa et al., 2021).

All over the world, the leaves of cannabis are used to treat more than 25 conditions in humans, including asthma, diabetes, tuberculosis, and cancer, as well as being used as an abortifacient (Shakil et al., 2021). Cannabis is also used in animals to manage over 15 ailments, including pneumonia, dysentery, and trypanosomiasis (Lima et al., 2022). Nevertheless, despite its many beneficial effects in traditional medicine, cannabis can cause some undesirable effects, such as intoxication (Elouardi et al., 2022; Kharchoufa et al., 2021). In addition, the consumption of cannabis and related products (hashish, kif) is associated with significant histological and molecular alterations in the bronchial epithelium, comparable to those observed in tobacco smokers, which explains the carcinogenicity of cannabis (Sasco et al., 2002).

5. CHEMOTYPES OF CANNABIS IN MOROCCO

Cannabis resin, also known in Morocco as hashish, is a concentrated form of cannabis. It is made from the resin of the cannabis plant, which contains high levels of THC, the main psychoactive compound in cannabis (Dujourdy & Besacier, 2017). There are two approaches to obtaining cannabis resin: (1) Hand Rubbing, the earliest method of collecting and preparing trichomes, involves gently rubbing dried plants until resin glands are secreted onto the hands and fingers. (2) Sieving, on the other hand, requires drying the plants first, rendering the resin and trichomes more brittle and dusty, which can then be isolated from the plant material through a sieve and percussive force (Abdelaziz et al., 2016; Alaoui et al., 2013).

In Morocco, the cannabis plant is widely grown in mountainous regions, particularly in the Rif, where the soil is rich in humus and there is access to water (Drioua et al., 2023). The presence of humus and access to water offer several advantages for plant growth and agriculture, such as nutrient-rich, improved water retention, sustainable agriculture, enhanced soil structure, greater crop yields, increased microbial activity, and erosion control (Bertola et al., 2021). The Maghreb region saw the introduction of the cannabis plant during the Arab invasions in the seventh century. Over the last four decades, cannabis cultivation has expanded from its traditional production zones to the west of Laarache and the south of Taounate (Chouvy, 2008). Mainly, the cultivation of cannabis takes place in the northern regions of Morocco, with three specific provinces contributing to over 75% of the total production. These provinces are Chefchaouen (50%), Al Hoceima (17%), and Larache (9%). While Chefchaouen and Al Hoceima are known for being traditional areas for growing cannabis (kif), the Larache region is a newer addition to this crop (Stambouli et al., 2005).

Cannabis can be categorized into three chemotypes based on the levels of THC and CBD. Chemotype I is predominantly THC, with a THC/CBD ratio greater than 1. Chemotype II contains high levels of both THC and CBD, with a THC/CBD ratio around 1. Chemotype III is primarily rich in CBD, with a THC/CBD ratio of less than 1. Strains high in THC are known for their psychoactive properties, while those rich in CBD are recognized for their potential therapeutic benefits. Knowing the chemotype of a cannabis strain allows users to select varieties that align with their desired effects and requirements, whether for recreational or medicinal use (Jin et al., 2021).

The GC-MS analysis of 180 samples of leaves of fresh female cannabis plants from three provinces: Chefchaouen, Al Hoceima, and Larache showed that the average of Δ^9-THC content ranged from 0.3 to 0.4% for the fresh female leaves and from 0.4 to 0.7% for the tops of the leaves of fresh female cannabis plants. In the case of fresh male cannabis plants, the same study showed that the overall average of Δ^9-THC content ranged from 0.3 to 0.4%. For dried female cannabis plants, the average of Δ^9-THC levels was 0.6-1.7% for the leaves and 2.8-4.1% for the buds. The determination of Δ^9-THC levels in cannabis powders showed the results of Δ^9-THC levels ranging from 5.5 to 11.3%. Powders from the Al Hoceima region, with an average Δ^9-THC content of 8.5%, were slightly richer than those from the Chefchaouen region, where the average of Δ^9-THC content was 8% (Alaoui et al., 2013).

The study of Δ^9-THC levels in 1,004 samples of resin seizures made by Morocco's Royal Gendarmerie over the period 2005-2014 demonstrated that Δ^9-THC levels increased from a range of 0.6-16.8% in 2005 to 0.5-25% in 2014. The maximum values recorded each year show exceptionally high levels in 2007 (28%), 2009 (29.6%), 2010 (31%), 2012 (33%), and 2013 (29.3%). The increase in Δ^9-THC in cannabis resin seizures in Morocco between 2005 and 2014 is thought to be linked to the emergence of international trade in cannabis varieties with high levels of Δ^9-THC and the introduction into the country of this type of seed of European origin (Stambouli et al., 2016). Samples collected from cannabis fields in Morocco resulted in a combination of 25% high-THC plants, 25% high-CBD plants, and 50% with mixed levels of both, resulting in a roughly equal amount of the two phytocannabinoids (Russo et al., 2008). The hashish, which is believed to have originated in Morocco, contains both THC and CBD, but it is often mixed with impurities like hair, dung, and petroleum distillates (Russo, 2007).

6. KIF PREPARATION SMOKED BY THE MOROCCAN POPULATION

Kif, the traditional way of smoking cannabis for its psychotropic effects, involves using female flowering tops that are harvested when the seeds are mature (Nahas et al., 1975). These tops are then dried and stored in plastic bags. Preparing kif is a meticulous process, typically done by experienced older men. It involves cleaning the plant branches, separating the leaves, and bracts from the shafts. The cannabis material is sliced finely with a knife and sifted to obtain vegetable material of about 1 mm in diameter. While cutting, the knife is cleaned regularly to remove the sticky resin that adheres to it. After completing the cutting process, tobacco is added to the cannabis. Cannabis leaves are never smoked alone as it is believed that without tobacco, it can cause brain damage, leading to dementia and madness. This preparation is known as kif Messouss, and the key ingredient in kif preparation, known as "salt," is wild tobacco called Tabba beldi (Merzouki & Mesa, 2002). The second step in the preparation of kif involves getting the tobacco ready. The leaves of Nicotiana rustica are dried in the shade and stored in plastic bags to keep them moist. They are then crushed, similar to the way cannabis is prepared. The ratio of tobacco to cannabis for kif preparation is one-third tobacco and two-thirds crushed cannabis (Merzouki et al., 2008). The smoking process of kif involves using sebsi pipes made from a thin wooden cane and a small terracotta bowl called "chkaf". These pipes are traditionally manufactured and are around 20-40 cm in length. The wood used to make the sebsi comes from Jasminum fruticans L., Nerium oleander L., or Viburnum tinus L. (Merzouki & Mesa, 2002).

Kif consumption involves a strict ritual where the first smoker fills the pipe and lights it, takes a puff, and then quickly passes it to the next person who smokes it completely (usually in 3-4 puffs) and removes the ash. After this, the empty pipe is returned to the first person, who repeats the process with the next smoker. This ritual is a daily practice for kif smokers. In small groups, each person brings their own bag of kif and sebsi to prove the quality of their product to others (Ounnir, 2011).

7. BIOLOGICAL ACTIVITIES OF CANNABIS GROWN IN MOROCCO

Cannabis is rich in biologically active secondary metabolites, particularly the phenolic compounds known as cannabinoids. These compounds, characterized by their low toxicity and diverse biological effects, show potential for treating a range of conditions. They may help manage severe chronic pain, diabetes, inflammation, neurodegenerative diseases, anxiety, mental health issues, nausea, and cancer. However, research suggests that cannabis and cannabinoids can be used alone or in their defined mixtures (Helcman & Šmejkal, 2022).

Mahou and colleagues investigated the vasorelaxant properties of the ethanolic fraction of the Moroccan *Cannabis sativa* threshing residues on the rat mesenteric arterial bed, particularly, examining the role of endothelium and muscarinic receptors. Their findings revealed that ethanol fraction caused a dose-dependent vasorelaxation on the mesenteric vascular bed. However, the addition of L-NAME, ODQ (a soluble guanylyl cyclase inhibitor), or potassium channel blockers reduced the decrease in perfusion pressure induced by ethanol fraction. Furthermore, the vasorelaxant effect of ethanol fraction was abolished by endothelial denudation or atropine, indicating the involvement of muscarinic receptors and endothelium-relaxing factors. The extract also stimulated nitric oxide release in aortic rings in a similar manner to acetylcholine, suggesting that the ethanolic fraction of the Moroccan *Cannabis sativa* threshing residues has an effect on both the muscarinic receptor and conductance arteries (Mahou et al., 2023).

Aazza studied the total polyphenol content (TPC), 2′2-dipheny-l-picrylhydrazyl (DPPH) radical scavenging activity, and ferric reducing antioxidant power (FRAP) of extracts from the waste of *Cannabis sativa* using one or a mixture of the following solvents: water, ethanol, methanol, and hexane. The results obtained showed that the minimum value of TPC was 5.17 $\pm$ 0.03 for the hexanic extract (100%) while the highest value was 21.03 $\pm$ 0.08 for the ethanol-water extract (1:1). The minimum value of DPPH was 25.03 $\pm$ 0.21 for the water extract (100%) while the highest value was 53.93 $\pm$ 0.15 for the ethanol-methanol-water extract (1:1:1), the minimum value of FRAP was 21.66 $\pm$ 0.36 for the hexanic extract (100%), while the highest value was 73.47 $\pm$ 0.38 for the methanolic extract (100 %) (Aazza, 2021). The GC-MS analysis of *Cannabis sativa* essential oil revealed that it mainly contains the (E)-caryophyllene (35.0%), α-humulene (12.8%), and caryophyllene oxide (10.6%) (Table 5). The antioxidant tests demonstrated that *Cannabis sativa* essential oil has moderate potency, with IC_{50} values of 1.6 $\pm$ 0.1 mg/mL for the DPPH assay, 1.8 $\pm$ 0.2 mg/mL for the β-carotene/linoleic acid assay, and 0.9 $\pm$ 0.1 mg/mL for the ferric reducing power

Table 3
Percentages of Δ^9-THC and CBD, and Δ^9-THC /CBD ratios of cannabis grown in Morocco.

Varieties	Parts	Solvents	% Δ^9-THC	% CBD	THC/CBD Ratios	References
	FL	Methanol	0.31	0.48	0.646	Davis et al. (1963)
VINP	FFGO[a]	Light petroleum	0.04	0.4	0.100	Ohlsson et al. (1971)
	FFGI[a]		0.04	0.1	0.400	
Santhica 27			From peak areas		0.000[b]	
Epsilon 68	AP	Hexane			0.056[b]	Taoufik et al. (2017)
Futura 75					0.039[b]	
Green plant	L		0.4[c]	-	-	Stambouli et al. (2005)
	I	Methanol-chloroform (9:1)	0.6[c]	-	-	
Dry plant	L		1.2[c]	-	-	
	I		2.9[c]	-	-	
Powdered plant	L and I		8.3[d]	-	-	
Resin seizures (2005-2006)			16.8	-	-	
Resin seizures (2007)			28.0	-	-	
Resin seizures (2008)			19.5	-	-	
Resin seizures (2009)	R[e] (Highest Δ^9-THC values)	Ethanol	29.6	-	-	Stambouli et al. (2016)
Resin seizures (2010)			31.0	-	-	
Resin seizures (2011)			21.0	-	-	
Resin seizures (2012)			33.0	-	-	
Resin seizures (2013)			29.0	-	-	
Resin seizures (2014)			25.0	-	-	

[a] Seeds of Moroccan origin were grown outdoors/indoors in a garden of Stockholm-Sweden and the flowering tops collected by the end of August 1969.
[b] These values are averages calculated for the 4 regions (Beni-Mellal, Agadir, Allal Tazi, Sefrou) for each variety.
[c, d] These values are averages calculated for the 3 regions: Chefchaouen, Al Hoceima, and Larache
[e] R: Cannabis resin seizures (2005-2014) determined by GC-FID analysis
AP: Arial parts; FL: Famale leaves, FFGO: Famale flowers grown outdoors; FFGI: Famale flowers grown indoors, L: Leaves; I: Inflorescences, VINP: Variety information not provided.

assay (Table 4). The antimicrobial assays showed that *Cannabis sativa* essential oil had noteworthy antimicrobial properties (Table 4). The tested extracts on microorganisms shown in Table 4 had minimum inhibitory concentration (MIC) values ranging from 1.2 to 37.8 mg/mL (Nafis et al., 2019).

The ethanolic fraction of threshing residues of *Cannabis sativa* induced an anticonvulsant effect (EC_{50} of 0.016 mg/mL) on an isolated rabbit jejunum, which was inhibited by atropine and verapamil. The effect of ethanolic fraction was significantly reduced (38.6 $\pm$3.34 %) under free calcium conditions. The acute toxicity test in female and male mice showed the ethanolic fraction to be a safe product (500, 1000, and 2000 mg/kg). Furthermore, like loperamide, the ethanolic fraction showed an antidiarrhoeal effect in mice and inhibited the secretion of intestinal fluid. In addition, ethanolic fraction showed a protective effect against ethanol-induced gastric ulcers in mice (85.71%) and exhibited antimicrobial properties against *Bacillus cereus* strains with a MIC of 2 mg/mL (Chda et al., 2023). The antioxidant power of seeds of two varieties (Beldia and Critical) of hemp grown in the north of Morocco using TAC, DPPH, ABTS, CUPRAC, and FRAP tests (Table 4) was (IC_{50} and EC_{50}) 1.83-4.14; 1.64-4.37; 2.45-6.02; 2.65-9.29, and 1.75-4.37 mg.mL^{-1} of extract for the TAC, DPPH, ABTS, CUPRAC, and FRAP tests, respectively (Benkirane et al., 2023).

8. PHYTOCHEMICAL STUDIES OF CANNABIS GROWN IN MOROCCO

The study of the phytochemistry of cannabis has received particular attention in recent years, as researchers seek to understand the complex chemical composition of this multi-faceted plant. Cannabis is rich in a variety of compounds, including cannabinoids, terpenes, and flavonoids, each of which can exert distinct effects on the human body. By examining these compounds and their interactions, scientists hope to elucidate the therapeutic potential of cannabis, as well as its possible risks and side effects. The main active compound in cannabis, Δ^9-tetrahydrocannabinol (Δ^9-THC), is known for its psychotropic effects and is found mainly in the plant's leaves and flower buds. In addition to Δ^9-THC, cannabis also contains non-psychoactive cannabinoids such as cannabidiol, cannabichromene, and cannabigerol, which have various therapeutic effects. To date, researchers have identified more than 560 components in cannabis (Salamone et al., 2022; Smith et al., 2022; Xie et al., 2022).

Research on the ethanolic fraction of *Cannabis sativa* grown in Morocco revealed several potential bioactive compounds, such as apigenin, luteolin derivatives, neophytadiene, squalene, and β-sitosterol (Mahou et al., 2023). In addition, El Bakali et al. studied the chemical profiles of the essential oils of

Table 4
Biological activities of cannabis grown in Morocco.

Types of samples	Varieties/ extracts	Place of harvest	Activities/Values	References
Seeds	Beldia	Jebha	TAC (EC_{50} = 1.83±0.05 mg.mL^{-1}) DPPH (IC_{50} = 1.83±0.03 mg.mL^{-1}) ABTS (IC_{50} = 2.45±0.06 mg.mL^{-1}) CUPRAC (EC_{50} = 2.65±0.02 mg.mL^{-1}) FRAP (EC_{50} = 2.38±0.02 mg.mL^{-1})	(Benkirane et al., 2023)
		Tamorot	TAC (EC_{50} = 2.98±0.04 mg.mL^{-1}) DPPH (IC_{50} = 2.21±0.03 mg.mL^{-1}) ABTS (IC_{50} = 3.10±0.19 mg.mL^{-1}) CUPRAC (EC_{50} = 4.16±0.11 mg.mL^{-1}) FRAP (EC_{50} = 2.70±0.10 mg.mL^{-1})	
		Ratba	TAC (EC_{50} = 5.59±0.05 mg.mL^{-1}) DPPH (IC_{50} = 4.82±0.31 mg.mL^{-1}) ABTS (IC_{50} = 5.62±0.22 mg.mL^{-1}) CUPRAC (EC_{50} = 7.64±0.27 mg.mL^{-1}) FRAP (EC_{50} = 4.37±0.11 mg.mL^{-1})	
		Galaz	TAC (EC_{50} = 3.12±0.13 mg.mL^{-1}) DPPH (IC_{50} = 2.19±0.06 mg.mL^{-1}) ABTS (IC_{50} = 3.21±0.10 mg.mL^{-1}) CUPRAC (EC_{50} = 3.38±0.13 mg.mL^{-1}) FRAP (EC_{50} = 2.20±0.09 mg.mL^{-1})	
	Critical	Jebha	TAC (EC_{50} = 2.62±0.13 mg.mL^{-1}) DPPH (IC_{50} = 1.64±0.06 mg.mL^{-1}) ABTS (IC_{50} = 2.45±0.03 mg.mL^{-1}) CUPRAC (EC_{50} = 2.79±0.12 mg.mL^{-1}) FRAP (EC_{50} = 1.75±0.09 mg.mL^{-1})	
		Tamorot	TAC (EC_{50} = 3.69±0.02 mg.mL^{-1}) DPPH (IC_{50} = 2.82±0.14 mg.0mL^{-1}) ABTS (IC_{50} = 4.07±0.12 mg.mL^{-1}) CUPRAC (EC_{50} = 5.21±0.11 mg.mL^{-1}) FRAP (EC_{50} = 2.91±0.09 mg.mL^{-1})	
		Ratba	TAC (EC_{50} = 4.14±0.08 mg.mL^{-1}) DPPH (IC_{50} = 4.37±0.18 mg.mL^{-1}) ABTS (IC_{50} = 6.02±0.13 mg.mL^{-1}) CUPRAC (EC_{50} = 9.29±0.25 mg.mL^{-1}) FRAP (EC_{50} = 3.69±0.19 mg.mL^{-1})	
Arial parts	Essential Oil	Rif region in northern Morocco	Antiescherichia coli (IZ=11.1±0.3, MIC=1.2 mg/mL) Antipseudomonas aeruginosa (IZ=12.6±0.2, MIC=1.2 mg/mL) Antiklebsiella pneumonia (IZ=8.5±0.2, MIC=37.8 mg/mL) Antibacillus subtilis (IZ=13.0±0.3, MIC=1.2 mg/mL) Antimicrococcus luteus (IZ=11.4±0.1mm, MIC=4.7 mg/mL) Antistaphylococcus aureus (IZ=13.0±0.2, MIC=4.7 mg/mL) Anticandida albicans (IZ=12.0±0.7, MIC=9.5 mg/mL) Anticandida glabrata (IZ=13.0±0.2, MIC=9.5 mg/mL) Anticandida krusei (IZ=12.5±0.2, MIC=9.5 mg/mL) Anticandida parapsilosis (IZ=15.0±0.3, MIC=9.5 mg/mL) DPPH (IC_{50} = 1.6 ± 0.1 mg/mL) Reducing power assay (IC_{50} = 1.8 ± 0.2 mg/mL) β-Carotene (IC_{50} = 0.9± 0.1 mg/mL)	(Nafis et al., 2019)

IZ: Diameter of inhibition zone in mm; MIC: Minimum Inhibitory Concentration in mg/mL, TAC: Total antioxidant capacity; DPPH: 2,2-diphenyl-1-picrylhydrazyl; ABTS: 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); CUPRAC: Cupric reducing antioxidant capacity; and FRAP: Ferric reducing antioxidant power.

three cultivars of *Cannabis sativa* L.: 'Beldia', 'Mexicana' and 'Critical Plus'. Essential oils were extracted from dried inflorescences by hydrodistillation and analyzed by GC-MS, with yields ranging from 0.330% to 0.688%, with the cultivar 'Critical Plus' providing the highest yield. The analysis showed a high concentration of terpenoids, reflecting significant phytochemical diversity (Table 4). The most abundant compounds in these essential oils were β-caryophyllene (13.39-25.32%), β-myrcene (10.03-20.09%), α-humulene (4.88-8.73%), caryophyllene oxide (1.46-6.07%), decane (1.41-4.46%), and α-pinene (1.91-3.66%). 'Beldia' had the highest concentrations of β-caryophyllene, caryophyllene oxide, and decane, while 'Mexicana' had the highest concentrations of β-myrcene, α-humulene, and α-pinene (Bakali et al., 2022).

The quantitative analyses of total polyphenols showed that the ethanolic and aqueous extracts were the richest in polyphenols, with 5.41 $\pm$ 0.04 μg EAG/mg for hexane extract, 27.66 $\pm$ 0.02 μg EAG/mg for dichloromethane extract, 32.03 $\pm$ 0.03 μg EAG/mg for aqueous extract, and 130 $\pm$ 0.08 μg EAG/mg for ethanolic extract. Several phytochemicals, including linoleic acid and 7-octadecenoic acid, were detected by GC-MS analysis (Table 5). In addition, the HPLC-UV analysis of the organic extracts and aqueous extract revealed several other phytocompounds presented in table 5, including catechin dihydrate, 6-hydroxy flavone, and sinapinic acid (Haddou et al., 2023). Benkirane et al. identified 31 phenolic compounds listed in Table 5, in seeds of two varieties (Beldia and Critical) of hemp grown in the north of Morocco using the HPLC-DAD/ESI-MS^2 technique (Benkirane et al., 2023).

The chemical composition of seed oils of three varieties, namely, Santhica 27, Futura 75, and Epsilon 68 of *Cannabis sativa* L. (hemp) showed the presence of linoleic acid (omega-6), α-linolenic acid, and other compounds listed in Table 5. These results indicate that hemp seeds grown in Morocco possess significant potential as a nutritious food source due to their exceptional nutritional value (Bouayoun et al., 2018). Another study showed that the hemp seeds of *Cannabis sativa* L. from two different varieties (Beldia and Critical) grown in the northern part of Morocco contain protein (19.25-24.18%), insoluble fiber (26.40-37.40%), ash (3.72-5.39%), total phenols (134.57-199.90 mg per 100g), flavonoids (39.40 to 69.54 mg per 100g), oil content (26.42 to 35.19 g per 100g of seeds), total tocopherol content (376.46 and 796.06 mg per kg of oil, with a predominance of γ-tocopherol), and fatty acids (87.30-88.96%, with the majority of unsaturated fatty acids like linoleic acid). In the same study, the triacylglycerols (TAGs) composition analysis indicated that trilinolein (14.34-22.62%), 1-oleoyl-2,3-dilinoleoyl-racglycerol (12.77-18.78%), and 1-oleoyl-2-linoleoyl-3-linolenoyl-rac-glycerol (12.32-18.59%) are dominant TAGs (Taaifi et al., 2021).

9. INDUSTRIAL STUDIES OF CANNABIS GROWN IN MOROCCO

Charai et al. developed one hundred local fibro-plasterboards by incorporating Moroccan Hemp fibers into local plaster at varying weight replacement ratios of 0, 2, 4, and 6%. The tests showed that Moroccan hemp stems are effective in improving the thermal transport properties of plaster, making it more thermally efficient. The addition of 6% by weight of hemp fibers in the plaster matrix significantly reduced the density, enhanced thermal insulation, and slowed the heat transfer rate by 24.5%, 31.3%, and 8.5%, respectively, when compared to plaster without fibers. The incorporation of 2% by the weight of hemp fibers resulted in the best thermal heat capacity (31.3%) (Charai et al., 2021).

Hempcrete outperformed other conventional wall systems in terms of embodied energy and overall environmental performance throughout its entire life cycle. It achieves significantly lower carbon emissions (484.42 tCO_2) compared to insulated double hollow clay brick and composite wall systems (546.27 tCO_2 and 546.55 tCO_2 for double hollow clay brick and composite wall, respectively) over a 100-year lifespan in the construction industry. This conclusion was drawn from a life-cycle assessment comparison of a residential house in Marrakech, Morocco. Using hempcrete instead of double hollow clay brick and composite wall for a single house can lead to significant savings of 61.85-62.13 tCO_2. These savings become even more substantial when applied to the national level of Moroccan homes. By utilizing Morocco's existing hemp biomass, it is possible to reduce overall Moroccan emissions by 1.91-1.92 $MtCO_2$, which is equivalent to 2.81-2.83% (Essaghouri et al., 2023).

Taaifi et al. investigated the effect of incorporating hemp seed on productive performance and egg quality traits. Ninety-six Lohmann Brown classic laying hens were randomly assigned to a control group and three feed treatments: hemp seed-10% group, hemp seed-20% group, and hemp seed-30% group. The sampling was taken after the 28-week rearing period, which is the peak egg-laying period. Throughout the experiment, the low incorporation rate (hemp seed-10%) showed no significant differences in egg-laying performance. However, the high incorporation rates (hemp seed-20% and hemp seed-30%) had a negative impact on egg-laying performance, with rates of 84-94% and 80-86%, respectively. Incorporating nonindustrial Moroccan cannabis seeds (ecotype Beldia) at a low rate in the diet of laying hens has no effect on egg laying performance or quality, according to the study. However, the inclusion and duration of heat stress significantly influenced the yolk color, with a decrease in yellow intensity observed with heat stress incorporation and aging. The albumen quality was also improved with hemp seed inclusion, resulting in higher haugh unit values ranging between 68.69-73.91 for the hemp seed - 30% groups (Taaifi et al., 2023).

Table 5
5: Identified compounds from cannabis grown in Morocco.

Types of samples	Types of varieties	Place of harvest	Compound names	Technics	References
Seeds	Beldia/Critical	Jebha, Tamorot, Ratba, and Galaz	Benzoic acid; p-coumaric acid; ferulic acid; N-trans-caffeoltyramine isomer; N-trans-caffeoyltyramine; cannabisin A; cannabisin B; N-trans-coumaroyltyramine; cannabisin B isomer 1; N-feruloyltyramine; cannabisin B isomer 2; demethylgrossamide; cannabisin C; cannabisin C isomer; cannabisin D; 3,3-didemethylgrossamide; tri-p-coumaroylspermidine; cannabisin E; grossamide K; cannabisin M; 3,3-demethylheliotropamide; cannabisin Q; cannabisin F; isocannabisin N; cannabisin O; dihydrocannabinol; cannabidiol; sinapic acid; cannabidiolic acid.	HPLC-DAD/ESI-MS^2	Benkirane et al. (2023)
Seeds	Santhica 27, Futura 75, and Epsilon 68	Beni Mellal, Sidi Alla, Sefrou and Afourer	Palmitic acid (C16:0), palmitoleic acid (C16:1), stearic acid (C18:0), oleic acid (C18:1), linoleic acid (Oméga-6: C18:2), linolenic acid (Oméga-3: C18:3), arachidic acid (C20:0)	GC-MS	Bouayoun et al. (2018); Taoufik et al. (2017)
Aerial parts (flowering tops)	Beldiya, Mexicana, and Critical Plus	Bab Taza (Central-northern Morocco)	Acetic acid, butyl ester; p-xylene, nonane; α-pinene; 1-ethyl-3-methylbenzene; 4-methylnonane; 4-methyl-1-decene; β-pinene; 1-ethyl-2-methylbenzene; β-myrcene; decane; 1,2,3-trimethylbenzene; D-limonene; eucalyptol; α-ocimene; p-mentha-1,4(8)-diene; linalool; undecane; β-caryophyllene; trans-α-bergamotene; α-humulene; alloaromadendrene; eudesma-4(14),11-diene; guaia-1(10),11-diene; guaia-3,9-diene; selina-3,7(11)-diene; cis-α-bisabolene; caryophyllene oxide; champacol; α-humulene epoxide II; cubedol	GC-MS	Bakali et al. (2022)
Leaves	-	Morocco	Cannabidiol acid, cannabidiol, cannabinol, tetrahydrocannabinol	GC-FID and PC	Davis et al. (1963)
Seeds	-	North of Morocco (Tangier-Tetouan-Al Hoceima/ Ketama)	Hesperidin acid, palmitic acid, linoleic acid, 7-octadecenoic, linolenic acid, stearic acid, heptacosanoic acid, 8-methoxyflavon, cinnamic acid, 6-hydroxyflavon, catechin acid dihydrate, ferulic acid, rutin, coumarin, catechin acid dihydrate, naringin, chlorogenic acid, o-dianisidine	GC-MS	Haddou et al. (2023)
Aerial parts	-	Rif region in northern Morocco	α-pinene; myrcene; mesitylene; β-pinene; limonene; 1,8-cineole; linalool; fenchol; ipsdienol; (E,E)-2,6-dimethyl-3,5,7-octatriene-2-ol; borneol; carveol; α-terpineol; coumaran; pulegone; (E)-caryophyllene; α-bergamotene; α-farnesene; α-humulene; aromadendrene; β-selinene; cis-α-bisabolene; caryophyllene oxide; humulene epoxide-II	GC-MS	Nafis et al. (2019)

Continued on next page

Table 5 continued

Whole plant	Khardala and Kif	Taounate region (Khlalfa, Tafrant, and Oudka)	Cannabichromene, cannabichromenic acid, cannabidiol, cannabidiolic acid, cannabinol, Δ^9-tetrahydrocannabinolic acid, tetrahydrocannabivarin	TLC	Mouna et al. (2015)
Leaves and I	-	Chefchaouen, Al Hoceima, and Larache	Trans-Δ^8- tetrahydrocannabinol, Δ^9-tetrahydrocannabinolic acid, cis-Δ^9-tetrahydrocannabinol, trans-Δ^9-tetrahydrocannabinol, methyl-tetrahydrocannabinol, cannabivarol, isomer cannabidiol, tetrahydrocannabivarin, butyl-tetrahydrocannabinol, cannabichromene, cannabidiol, cannabicoumaronone, hydroxy-tetrahydrocannabinol, cannabigerol, cannabinol, cannabidiolic acid, cannabinolic acid	GC-MS and HPLC-DAD	Stamboulі et al. (2005)
Seeds	Beldia and Critical	Northern of Morocco (Tamorot, Ratba, Jebha, and Galaz)	1-arachidoyl-2,3-dilinoleoyl-rac-glycerol; trilinolein; 1,2-dilinoleoyl-3-linolenoyl-rac-glycerol; 1,2-dilinoleoyl-3–linolenoyl-rac-glycerol; 1-linoleoyl-2- dilinolenoyl-rac-glycerol; 1-linoleoyl-2-linolenoyl-3–linolenoyl-rac-glycerol; 1-oleoyl-2,3-dilinoleoyl-rac-glycerol; 1-oleoyl-2-linoleoyl-3-linolenoyl-rac-glycerol;1,2-dioleoyl-3-linoleoyl-rac-glycerol; 1,2-dioleoyl-3-linolenoyl-rac-glycerol; triolein; 1-palmitoyl-2,3-linoleoyl-rac-glycerol; 1-palmitoyl-2-linoleoyl-3-linolenoyl-rac-glycerol; 1-palmitoyl-2,3-dilinolenoyl-rac-glycerol; 1-palmitoyl-2-oleoyl-3-linoleoyl-rac-glycerol; 1-stearoyl-2,3-linoleoyl-rac-glycerol; 1-stearoyl-2-linoleoyl-3-linolenoyl-rac-glycerol; 1-stearoyl-2-palmitoyl-3- linoleoyl-rac-glycerol	HPLC-RID	Taaifi et al. (2021)
Resin	Seizures	Morocco	Cannabidiol, cannabidiolic acid, cannabinol, cannabichromene, Δ^9-Tetrahydrocannabinolic acid, Δ^9-Tetrahydrocannabinol	HPLC-DAD	Baker et al. (1983)
Leaves and IFP	-	Tafrante in Morocco	Undecane, neophytadiene, palmitic acid methyl ester, digitoxin, methyl stearate, 17-pentatriacontene, heptacosane, squalene, β-sitosterol	GC-MS	Mahou et al. (2023)

GC-FID: Gas Chromatography-Flame Ionization; GC-MS: Gas Chromatography-Mass Spectrometry; HPLC-DAD/ESI-MS^2: High-Performance Liquid Chromatography with Diode Array Detection (HPLC-DAD) and Electrospray Ionization Tandem Mass Spectrometry (ESI-MS^2); HPLC-DAD: High-Performance Liquid Chromatography with Diode Array Detection; HPLC-RID: High-Performance Liquid Chromatography -Refractive Index Detector; I: inflorescences; IFP: Inflorescences of the Female Plant; PC: Paper Chromatography; TLC: Thin Layer Chromatography.

10. CURRENT STATE OF LEGAL CULTIVATION OF CANNABIS IN MOROCCO

The cultivation of cannabis has been a traditional practice for many farmers in the Rif Mountains region of Morocco, where the environment is well suited to its growth. The practice has been an integral part of the region's history and economy for centuries. In Morocco, cannabis is mainly used to produce hashish, a concentrated cannabis resin, but it has been illegal since the country's independence in 1956, with the total ban of drugs being reaffirmed in 1974. Despite this, cannabis cultivation has been somewhat tolerated (Sacchetti, 2012). Morocco ranks among the world's leading cannabis producers, with most production concentrated in the Rif mountains (Chouvy, 2016). Increasing European demand in the mid-1970s stimulated the expansion of cannabis cultivation beyond traditional areas. The 1980s saw significant improvements in the quality and quantity of cannabis grown in the central Rif. In the 2010s, modern cultivation techniques were widely adopted, improving the production of high-quality hashish (Chouvy & Macfarlane, 2018).

In order to meet the demand for hashish in the global market, particularly from Europe, traditional cultivation practices were gradually replaced with modern methods. The farmers started growing new imported strains of cannabis that are high in THC and yield more product. As a result, cannabis cultivation in Morocco has become more widespread than ever before, reaching a record high of 134,000 hectares (3,070 tons of hashish) in 2003, accounting for 1.48% of the country's cultivable land. However, between 2003 and 2013, the amount of land used for cannabis cultivation decreased by 65%, with only 47,500 hectares being used in 2011 (UNODC, 2011). Nevertheless, cannabis cultivation has declined, following the eradication of 15,160 hectares by the Moroccan authorities. Since the legalization of cannabis cultivation in 2021, production has begun to increase (UNODC, 2022). The yield increased significantly due to the introduction of new high-yielding hybrids, the modernization of agricultural practices, and the adoption of hashish production techniques that began in the mid-2000s and gained momentum after 2005 (UNODC, 2013). According to the United Nations Office on Drugs and Crime (UNODC), the area under cannabis resin cultivation in Morocco in 2017 was around 47,000 hectares (Figure 2), and in 2021, approximately 75,000 hectares of Moroccan farmland were dedicated to cannabis cultivation. Estimating the exact area under cannabis cultivation in Morocco is challenging due to the illicit nature of the crop and the mountainous terrain that makes it difficult to survey (Blickman, 2017; Chouvy, 2008; Dujourdy & Besacier, 2017). With the recent decriminalization of the cannabis sector in 2021, it is expected that exports of cannabis products will increase significantly.

In december 2020, the Commission on Narcotic Drugs (CND), the United Nations' main decision-making body on drug control, decided to remove cannabis from its list of the most dangerous drugs. This list also includes substances such as heroin and synthetic opioids. Previously, cannabis was classified under the 1961 Single Convention on Narcotic Drugs, which justified its prohibition on the basis of its "particularly dangerous properties". The decision to reclassify cannabis was supported by 27 countries, with 25 countries opposed. It is important to note that this reclassification does not mean a global legalization of cannabis, which remains classified as a "highly addictive substance subject to abuse".(WHO, 2020). The production and marketing of cannabis are restricted to scientific and medical purposes under international law (Dariš et al., 2019).

Morocco has brought up this matter at the Government Council level, and the Ministry of the Interior has proposed a law to legalize cannabis for medical, cosmetic, and industrial uses. Adopted in June 2021, this law will regulate all cannabis-related activities, including cultivation, production, manufacturing, transport, marketing, export, and import, under the authorization of National Agency for the Regulation of Cannabis Activities (Rammouz & Boujraf, 2022).

The legalization of cannabis for medical purposes allows for marketing and use in medical applications. Patients who need cannabis for medical reasons can legally access it through authorized channels, provided they have a medical prescription. This legal framework aims to ensure that patients can obtain cannabis for therapeutic purposes while maintaining strict control over its distribution and use. The legalization of cannabis for medical and industrial purposes presents significant economic opportunities for Morocco. Given the country's extensive experience in cannabis cultivation and its strategic location, the new legislation is seen as a potential catalyst for foreign direct investment and economic growth. The shift from an informal to a formal sector could also lead to improved working conditions and better integration of small and medium-sized enterprises. Despite the economic potential, the legalization of cannabis raises issues of social acceptance and cultural norms. Morocco, like many countries, has traditional views on cannabis consumption, which complicates the implementation of new laws. To ensure that legalization does not have a negative impact on public health, particularly among young people, careful monitoring and the development of effective prevention strategies are required (Rajkotwalla, 2023; Rammouz & Boujraf, 2022).

In 2022, the National Agency for the Regulation of Cannabis Activities issued the first 10 permits for industrial, medical, and export purposes. The agency indicated that farmers in northern mountain regions such as Al Houceima, Taounate, and Chefchaouen, who form cooperatives, will be progressively allowed to cultivate cannabis to satisfy the legal market's demands, with potential expansion to other provinces as the process becomes more settled (ISS, 2022).

For the Moroccan government, this decision presents an opportunity to address long-standing grievances among cannabis growers, who feel disconnected from the central government. These three regions (Al Houceima, Taounate, and Chefchaouen) account for the majority of cannabis

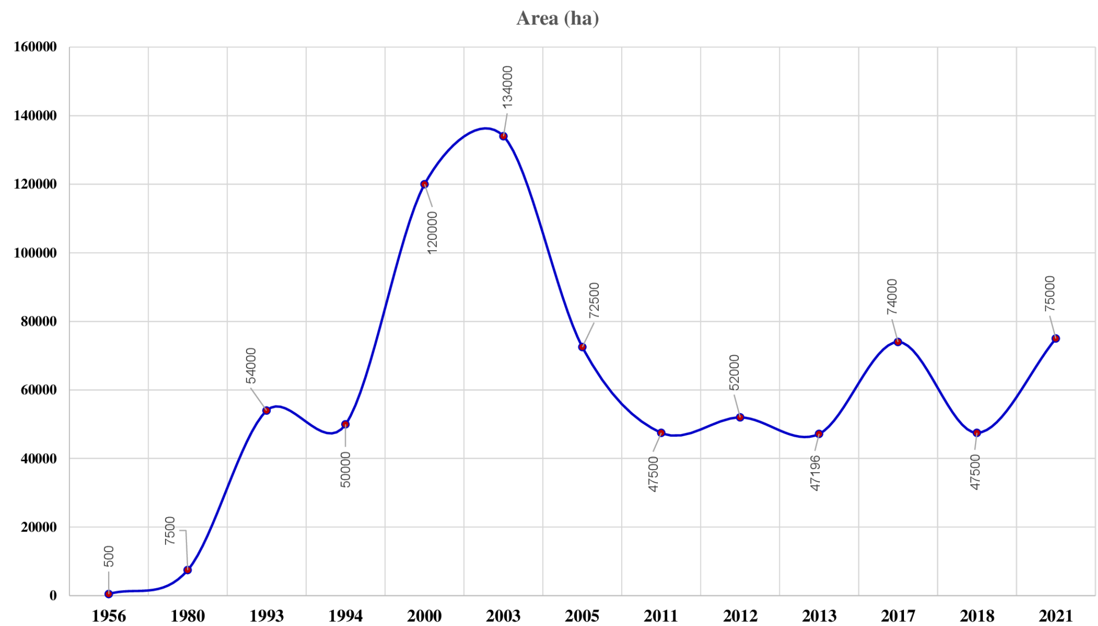

Figure 2. Area under cannabis cultivation in Morocco from 1956 to 2021.

production in Morocco, including illicit crops (Stambouli et al., 2005). Through this initiative, the government aims to reduce poverty by integrating cannabis production ino the legal economy.

The legalization of cannabis will lead to the creation of new jobs in the agricultural sector, spanning from cultivation to processing and distribution. This growth could be further supported by the establishment of nurseries and dispensaries for cannabis-based products, creating direct employment and stimulating economic activity. In addition, the legalization of cannabis opens up opportunities for the research and development of cannabis-based medical products. This research could lead to advances in the treatment of various pathologies, such as cancer, potentially offering new therapeutic options to patients (Mrinalini, 2024; Sevigny et al., 2023).

However, implementation of all the provisions related to the legalization of cannabis in Morocco remains slow. The delay is creating uncertainty, and a number of key questions unanswered. One of these questions is how far the future legal cannabis market in Morocco whether for export or domestic consumption can absorb the current level of production? At present, there is little information on the volume of cannabis that will be used on the Moroccan domestic market for therapeutic and pharmaceutical purposes, given that the Moroccan government continues to ban all production of cannabis for recreational use. This situation could lead to the coexistence of legal and illegal crops, complicating the application of the law and allowing traffickers to take advantage of this overlap to launder their income. The change underway in the process of legalizing Moroccan cannabis will have an impact on the Mediterranean region (North Africa, and Europe), potentially altering the landscape of this important production in Morocco (ENACT, 2022).

11. MARKET OF CANNABIS PRODUCTS

The cultivation of cannabis has long been a lucrative enterprise in Morocco, with the production of hashish offering substantial profitability. Morocco is part of a select but growing group of African countries seeking to participate in the growing international market for legal cannabis (Koehler & Lowther, 2022). In 2003, Morocco accounted for more than 70% of the hashish consumed in Europe, making it a significant source of income for Moroccans. The taxation of this substantial volume of cannabis derivatives presents a considerable opportunity for generating government revenue. Around the globe, approximately 192 million people consume cannabis annually, with various drug markets ranging from heavily regulated prohibitions to commercially legalized sales (Freeman et al., 2019). In Europe, the main sources of imported cannabis resin, also known as hashish, are Morocco, Lebanon and Afghanistan. This resin generally comes in the form of compacted blocks, usually brown in color (EMCDDA, 2016). The global cannabis market is valued at USD 344 billion, according to a 2019 report by New Frontier Data, with a regional breakdown of USD 132.9 billion for Asia, USD 85.6 billion for North America, USD 68.5 billion for Europe, USD 37.3 billion for Africa and USD

9.8 billion for Latin America. The legal marijuana market was valued at USD 17.5 billion in 2019 and is projected to reach USD 65.1 billion by 2027 (Dariš et al., 2019; Kitchen et al., 2022; Maroua, 2021).

A 2003-2004 United Nations study in Morocco estimated that cannabis cultivation covered approximately 134,000 hectares in 2003. During that period, the cannabis industry generated about USD 15 billion in 2003 and USD 13 billion in 2004. Morocco's total cannabis production was around 98,000 tons, with hashish production estimated at 2,760 tons, almost half of which came from the Chefchaouen region. However, these statistics have dropped drastically due to the "Cannabis Free Provinces" campaign that Morocco carried out in 2007, before it became again one of the world's largest producers of cannabis resin, with a market value of USD 9 billion in 2017. The illegal market is of course ahead of the legal market, but the process of legalization of cannabis and its products being undertaken by several countries around the world puts Morocco in an excellent position to take advantage of this legal market (Maroua, 2021).

However, it is crucial for Morocco not to solely rely on the local market's demand. Instead, efforts should be directed towards capitalizing on global markets and establishing robust export-oriented business models through partnerships with global pharmaceutical companies. Additionally, numerous countries are actively conducting extensive research on the medical applications of cannabis (Baron, 2015).

12. CONCLUSION

The analysis of the papers collected from various databases, such as SciFinder, ScienceDirect, Scopus, Google Scholar, and PubMed shows that much work remains to be done in the field of cannabis research in Morocco. This includes the isolation and characterization of cannabinoid and non-cannabinoid compounds, the determination of the THC/CBD ratio of all Moroccan-grown cannabis variants, and extensive studies of biological activities of cannabis products. This review highlights the importance of continued research in this area in order to understand the mechanisms of action and potential benefits of cannabis. Future research should prioritize the standardization of cannabis products and the conduct of rigorous clinical investigations. In light of these, we can advance the development of safe and effective cannabis-based therapies. Regarding the legalization of cannabis in Morocco, it is too early to estimate its impact, but it could have a positive effect in the pharmaceutical industry. Continued research on the efficacy of medical cannabis and evaluations its safety across a wide range of conditions are necessary to minimize the risks associated with its use.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest related to the publication of this review paper.

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