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MEDICINAL CANNABIS AND CHALLENGES OF LEGISLATION IN MOROCCO

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ABSTRACT: Cannabis is one of Morocco's top industries, and Morocco is one of the world's top Cannabis providers, however, the growth, the development, deal, and utilization of Cannabis is especially unlawful under the present legislation. Morocco has one of the most stringent law enforcement systems, but it has not legalized, there are 3 possibilities. The first is a continuation of the present ambiguity; the second to legalize; and the third is to completely authorize the present laws, ending in elimination of the culture each of these ways would impact affect Morocco, both financially and socially The purpose of this article is to update the current regulations on the utilization of Cannabis for medical purposes in Europe and Morocco. Thus, the botanical aspect, the chemical composition of *Cannabis sativa* is approached. This article will not discuss the recreational use of Cannabis. The review is based on information gathered from previous reports and government websites.

INTRODUCTION: The first evidence of the use of Cannabis dates back more than five thousand years before our era [1]. The introduction of Cannabis in Morocco goes back to a period between the 7th and the 15th century, following the successive Arab conquests in North Africa at that time [2]. Morocco remains the main source of Cannabis resin (hashish), supplying the European market in particular. The northern region of Morocco, where Cannabis is concentrated, covers about 20,000 km², distributed among five provinces. The psychotropic properties of this plant were only recognized in the twelfth century in Europe. In the principal half of the twentieth-century researchers were not able to build up the chemical structure of the elements of Cannabis plant [3].

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It was only in 1964 that trans–delta–9 tetrahydrocannabinol (THC, dronabinol), the main active ingredient of Cannabis, has been defined stereochemically [4]. Cannabis is the most generally used drug in the world for its psychoactive effects. However, this plant, composed of different cannabinoids also has many therapeutic properties. The legislation has been adapting in countries since the middle of the 20th century in order to exploit Cannabis therapeutically [1].

Cannabis sativa is an annual herb whose cycle is punctuated by the seasons. This plant is 1 to 2 meters high (extremely variable depending on the variety) and has a strong characteristic odor, characterized by the presence of trichomes (hairs) in which the cannabinoids are produced. The stem is straight, erect, fluted, and more or less branched, implanting itself on the ground by a strong pivot root and a radical system developed [6]. The leaves of the base are opposite and 5-7 segmented while those of the top are alternate, single or 3 segmented; the segments are lanceolate and dentate.

This is a naturally dioecious species; the male flowers are gathered in panicles; the perianth is divided into 5 equal parts each containing a pendent stamen with short filaments and terminal anthers, while the female flowers are grouped into compact cymes, mixed with leafy bracts. The fruit is a smooth ovoid achene about 3 mm in diameter [7].

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Taxonomy:

The Classification of Cannabis (APG IV): [5]

Category	:	Botanical Nomenclature
Branching	:	Spermatophyta - Seed plants
Division	:	Magnoliophyta - Flowering plants
Class	:	Eudicots
Subclass	:	Rosids
Order	:	Rosales
Family	:	Cannabaceae
Genus	:	Cannabis
Species	:	*Cannabis sativa* L.

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Endocannabinoid System:

Cannabinoid Receptors: To date, two cannabinoid receptors have been identified: CB1, cloned in 1990, CB2 cloned in 1993 [8]. A third suppurative receptor is being identified (GPR55) [9]. These are receptors with 7 transmembrane domains coupled to Gi / Go type G proteins [10]. CB2 has the same macrostructure as the CB1 receptor but with shorter N-termini and C-termini [11]. The CB1 receptor is basically expressed in the central and peripheral nervous system, both in nerve cells and in glial cells. CB2, then again, is expressed principally in the cells of the immune system as well as in other tissues [8]. This distribution explains that CB1 is rather involved in the psychotropic effects of cannabinoids, whereas CB2 is involved in their immunomodulatory effects [12].

Phytocannabinoids: Phytocannabinoïds represent a group of C21 or C22 (for the carboxylated forms) terpene phenolic compounds predominantly produced in *Cannabis*, *beside* the classic constituents of *Cannabis sativa*, more natural compounds *Flavonoids, terpenes, etc.*

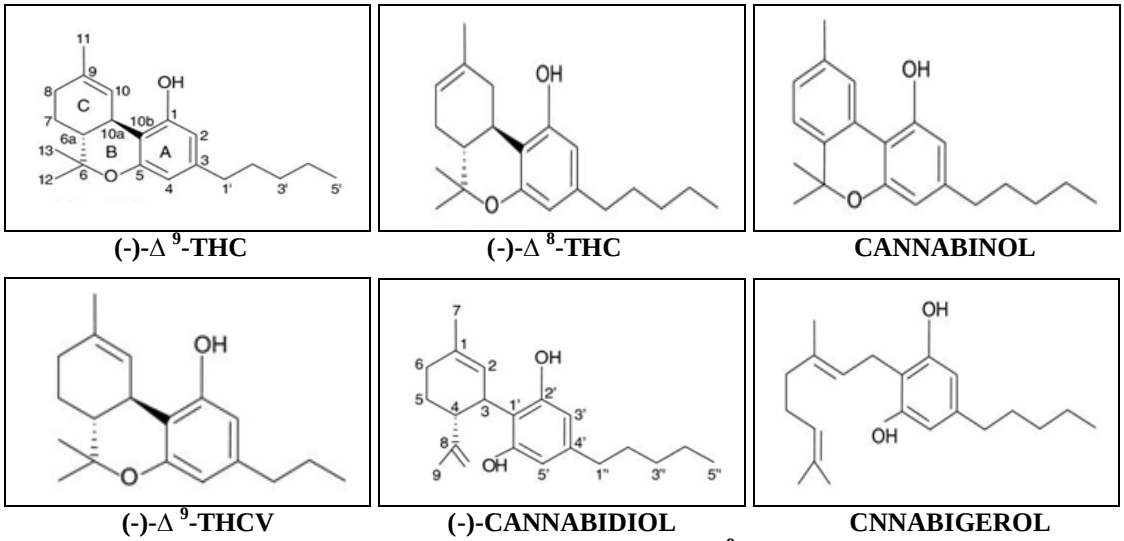

FIG. 1: THE STRUCTURES OF THE PHYTOCANNABINOIDS, (−) - Δ 9-TETRAHYDROCANNABINOL (Δ 9-THC), (−) - Δ 8 TETRAHYDROCANNABINOL (Δ 8-THC), CANNABINOL, (−) - Δ 9-TETRAHYDROCANNABIVARIN (Δ 9-THCV), (−) CANNABIDIOL (CBD) AND CANNABIGEROL [14]

To date, more than 60 Cannabinoids have accumulated in trichomes (resin bubble) and are concentrated mainly on the bracts of uncontaminated female flowers. The main Cannabinoids present in the plant and leading to pharmacological effects in humans include [13].

- Δ^{9}-tétrahydrocannabinol (THC), the main psychoactive product in humans.
- Cannabidiol (CBD).
- Δ^{8}-tétrahydrocannabinol, less psychoactive than THC.
- Cannabinol (CBN), non-psychoactive but which has anti-inflammatory activity.
- Δ^{8} and Δ^{9}-Tetrahydrocannabinolic acids. The latter is not active but is transformed into THC during its combustion.
- Cannabigerol (CBG) non-psychoactive but with bacteriostatic activity.

The levels of THC and CBD (percent dry weight) in the plant can be used to differentiate the chemotypes of *Cannabis sativa* [15] **Table 1**, in order to avoid any use for psychotropic purposes, the European Union allows a maximum THC level of 0.2%.

TABLE 1: MAIN CHEMOTYPES OF *CANNABIS SATIVA* ACCORDING TO THE PERCENTAGE OF CANNABINOIDS

Chimiotypes % Cannabinoid	"Drug"	"Intermediate"	"Fiber"
Δ^{9}-THC	> 2	>0,5	<0.3
CBD	0	>0.5	>0.5
Δ^{9}-THC/CBD	-	>0.5	<0.1

Endocannabinoids: Endocannabinoids were demonstrated later than Phytocannabinoids (1992) [16] are part of the family of neurotransmitters but are synthesized in neurons and astrocytes to be released and used immediately without the possibility of storage [17]. These ligands, derived from arachidonic acid, all have a very short half-life. Currently, five endocannabinoids have been identified [18].

- Three fatty acid amides
- 20:4, n-6, Anandamide N-arachidonoyl ethanolamine;
- 22:4, n-6, docosatetraenoylethanolamide;
- 20:3, n-6, homo-linolenylethanolamide;
- One fatty acid ester
- 2-arachidonoylglycerol(2-AG);
- One fatty acid ether
- Noladin ether (2-AGE, 2-arachidonyl glycerol ether).

Medical use of Approved Cannabinoids: The Governments of a few States (for the most part in Europe and North America) have passed enactment permitting patients suffering from certain health conditions (such as terminal cancer, epilepsy, and neurological illnesses) to utilize cannabinoids and cannabis to treat the indications of their diseases see **Table 1.** The United States Food and Drug Administration, for example, has approved several Cannabinoids for medical use. In 1985, it approved a synthetic THC, dronabinol (Marinol), for use as an antiemetic drug in cancer patients undergoing chemotherapy. Nabilone (Cesamet), a synthetic cannabinoid (with similar effects to THC), was approved in 1992 in capsule form as an appetite stimulant in patients with AIDS-related wasting [34]. In June 2018, the Food and Drug Administration approved the use of a CBD product (Epidiolex) to treat patients aged 2 years and older with Lennox-Gastaut and Dravet syndromes.

TABLE 2: PHARMACEUTICAL CANNABINOIDS THAT HAVE BEEN APPROVED FOR MEDICINAL USE

Cannabinoid	Composition	Trade name	Route	Indication
Dronabinol	Synthetic delta – 9 - THC	Marinol	Oral capsule	Nausea and vomiting associated with cancer chemotherapy [19]
Nabilone	Synthetic cannabinoid that mimics the effects of THC	Cesamet	Oral capsule	Nausea and vomiting; appetite stimulation [20]
Nabiximols	Cannabis extract with equal doses of THC and CBD	Sativex	Oral mucosal spray	Muscle spasticity and pain in multiple sclerosis [21]
CBD	CBD extracted from cannabis plants	Epidiolex	Oil for oral use	Epilepsy in Lennox-Gastaut and Dravetd syndromes for patients aged 2 years and older

Regulation of Cannabis for Medical use: There is a unique document that defines the international regulatory framework on narcotic drugs: the single convention on narcotic drugs, which was released

by the United Nations in 1961 and amended in 1972 [22]. The requirements of a system of control for cultivating the Cannabis plant for the production of Cannabis or Cannabis resin are addressed in article [28].

Control of Cannabis:

- If a Party permits the cultivation of the Cannabis plant for the production of cannabis or cannabis resin, it shall apply thereto the system of controls as provided in article [23] respecting the control of the opium poppy.
- This Convention does not have any significance to the cultivation of the Cannabis plant exclusively for industrial purposes (fiber and seed) or horticultural purposes.
- The Parties adopt such measures as might be important to counteract the abuse of, and unlawful traffic in, the leaves of the Cannabis plant.

In Morocco: The history of Morocco's drug policy, like that of criminal policy in general, is linked to the presence of France in our country for almost half a century under the protectorate imposed on the country from 1912 to 1956. Moroccan legislation under the French protectorate for cannabis, locally known as kif, remains a subtle mix of prohibition and tolerance.

Indeed, the Dahir of 3 November 1919 regulating the cultivation of hemp to kif had implemented measures allowing people interested in growing hemp to kif to do so under certain conditions, in particular, the prior obtaining of a cultivation permit that was to be issued by the tobacco control board. The same text was to fix the conditions and methods of exploitation of cultivated areas, as well as all the obligations relating to the delivery of the crops to the concerned authority. Finally, as in all legislative texts, criminal sanctions have been put in place to reinforce the binding nature of its provisions. The Dahir of April 24, 1954, relating to the prohibition of hemp to kif came to repeal all the laws and regulations governing the cultivation of hemp by imposing and explicitly prohibiting to all people to proceed to the cultivation, harvesting, manufacturing, processing, extraction, preparation, holding, supply, distribution, brokerage, purchase, sale, transportation, import, export, the consumption, in any form whatsoever, from Indian hemp or hemp to kif, preparations containing it or its active ingredients and in general, all agricultural, industrial or commercial operations relating to this plant, whole or not, to its preparations, to its active principles as well as to utensils and articles specially intended for its preparation and consumption.

This legislation remained unchanged for about 20 years after independence. It was not until Morocco ratified the single convention on narcotic drugs in New York in 1961 that cannabis was classified as a narcotic according to the provisions of the Dahir of 21 May 1974 relating to the repression of drug addiction and the prevention of drug abuse addicts.

The Dahir of 3 April 2002, which published the protocol amending the single convention on narcotic drugs of 1961, done at Geneva on 25 March 1972, still maintains this ban on the cultivation of cannabis except for "small quantities necessary for research purposes.

In Europe: In Europe, the situation is complex, since each country has its own laws governing narcotics, and therefore Cannabis. As a result, all European countries except the Netherlands and Spain, have adopted a prohibitionist policy prohibiting not only the use but also the import and cultivation of Cannabis. Despite this ban, some countries have allowed the medical use of Cannabis a large number of European countries allow the use of Cannabinoid - based medicinal products such as Sativex ®; now available in more than 17 European countries. Other European countries also allow dried cannabis in a therapeutic setting [23].

In the 28 countries of the European Union, there are 3 different types of sanctions for the use of Cannabis. France, Greece, Sweden, Finland, and Cyprus consider the use of Cannabis as a criminal offense. Portugal, Spain, Luxembourg, Bulgaria, Estonia, Latvia, Lithuania and Croatia consider the use of Cannabis as an administrative offense. The remaining 15 European Union countries do not prohibit the use of cannabis as such. However, possession of Cannabis is a criminal or administrative offense.

Eight countries in the European Union permit the utilization of Cannabis for therapeutic purposes. This is the case of Italy, France, the Netherlands, Belgium, Germany, Spain, the United Kingdom, and the Czech Republic [24].

In Canada: Canada is one of the few countries in the world (with Israel and the Netherlands) to have formalized and legislated access to cannabis at the federal level. Patients with a medical prescription can obtain cannabinoid-based medicinal products in the pharmacy (Sativex®, Nabilone®, Dronabinol®) [25]. Thus, the consumption and cultivation of Cannabis have been legal in Canada since October 17, 2018. Canada is the first G7 country to allow this drug for recreational purposes, and the second in the world after Uruguay.

The Impact of Legalization of Medical Cannabis in Morocco: The cannabis culture is one of incredible significance and benefits in Morocco, particularly within the Northern Rif region. Nonetheless, since the's first experience with the nation in the sixteenth century, its job and legitimateness have never been perfectly clear. Through exonerations, gifts, unfriendly grounds, and expanding joblessness, the industry has survived, as have the industry's workers. However, mere survival for the approximate 760,000 Moroccans depends on their livelihoods on cannabis culture [26]. Other observers estimate that 140,000 growers are engaged in cannabis cultivation and if their families are included, more than one million individuals rely upon the unlawful economy.

Economic and Social Impact:

Continuation: Morocco's Cannabis culture is estimated to make up the vast majority of the informal economy, and contributes between 30 and 40 billion dollars, meaning it alone makes up nearly 30% of the official GDP 90% of the product is exported to surrounding nations, centrally Spain from which it continues on through much of Europe (estimated that 70% of Europe's hashish came from Morocco in 2003 (Cannabis: World drug report, 2016). However, that about 180,000 tons of Cannabis cross Spain's border every year, and the received payment makes up the vast majority of these 40 billion dollars. Additionally, Morocco has been received mass sums of money from the European Union (estimated at 50 million annually) for an alternate crop project. So, the current situation is profitable for the nation and will likely continue to be profitable. The unregulated cannabis advertises in Morocco has negative social outcomes. Somewhere in the range of 48,000 cultivators have capture warrants hanging over their heads, which is a source of corruption and repression. An acquittal and decriminalization could be compelling measures to reduce negative social results and open the discussion about regulation.

Economic and Social Impact: Legalization: The production of Cannabis is without a doubt an income-generating activity, said a representative from the Ministry of Health Legitimizing its generation and utilization will add to the Moroccan GDP by more than 4.5% points per year. Then again, Morocco could possibly legally export medical and recreational Cannabis of high quality in countries where it is legal, which would generate employment and substantial income for the State.

Economic and Social Impact: Elimination: A complete elimination of the cannabis culture would leave Morocco's economy and people in a rather dire situation, the land in the Rif region is and always has been incapable of producing crops other than Cannabis and proposed solutions such as the European Union's alternate cultivation project will provide neither jobs nor significant GDP contribution. Both Morocco's government and its growers will not turn away from the cannabis culture until another more profitable alternative is thought of.

CONCLUSION: Many studies have been conducted worldwide on the possible utility of medical Cannabis since the end of the 1980s, leading more and more countries to legalize its use under conditions and in certain indications. As opposed to herbal Cannabis, Cannabinoid - based medications are approved by the FDA and by the vast majority of the nations in Europe.

Numerous nations have changed their enactments about medicinal Cannabis in the previous quite a long while and all things considered, the regulations will keep on changing in the up and coming years. Morocco's cannabis culture has been

a significant part of the country's economy and social makeup for centuries, but can no longer continue in the informal, underground manner it historically has. The political parties introduce the debate on the legalization of Cannabis in parliament, this initiative is the first step towards the introduction of a bill intended to legalize the cultivation of Cannabis very widely used. The race between pharmaceutical companies to penetrate this new segment with high growth potential has already started and Morocco as much as the largest cannabis producer on the African continent and one of the first in the world is called to position it today, so it's only a matter of time.

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