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No. T-2030-13

Date DEC 22 2014
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Greffier **BETWEEN:**

FEDERAL COURT

NEIL ALLARD
TANYA BEEMISH
DAVID HEBERT
SHAWN DAVEY

PLAINTIFFS

AND:

HER MAJESTY THE QUEEN IN RIGHT OF CANADA

DEFENDANTS

AFFIDAVIT OF ROBERT C. CLARKE

I, ROBERT C. CLARKE, International Hemp Association, Postbus 75007, 1070AA, Amsterdam, The Netherlands, MAKE OATH AND SAY AS FOLLOWS, THAT:

1. My name is Robert C. Clarke and I make this affidavit of my own personal knowledge, information and belief. Where matters are stated to be on information and belief I so indicate and believe them to be true.
2. Now produced and marked as Exhibit "A" to this my Affidavit is my Rebuttal Expert Report.
3. Now produced and marked as Exhibit "B" to this my Affidavit is my signed Certificate Concerning Code of Conduct for Expert Witnesses.
4. I swear this Affidavit as an expert rebuttal witness on behalf of the Plaintiffs in this action.

December 20, 2014


ROBERT C. CLARKE

SERVICE OF A TRUE COPY
HEREOF ADMITTED

DEC. 22 2014

WILLIAM F. FENTNEY /
Solicitor for
A.G.C.



Sworn before me at La Crescenta, California, USA, this
20 day of December, 2014.


Andrew D. Turner, Calif. Bar No. 121694

This is Exhibit "A" referred to in the Affidavit of Robert C. Clarke sworn before me at La Crescenta, California, USA. this 20 day of December, 2014.


Andrew D. Turner, Calif. Bar No. 121694

EXPERT REPORT
ROBERT C. CLARKE

(a) A statement of the issues addressed in the report;

This report addresses in rebuttal various issues arising in the Defendant Expert Report of Dr. Harold Kalant of September 30th, 2014 and Mahmoud El Sohly, dated October 15th, 2014.

(b) A description of the qualifications of the expert on the issues addressed in the report;

Attached as Schedule "A" is a copy of my curriculum vitae and a list of publications. I am the author, along with Mark D. Merlin of *Cannabis: Evolution and Ethnobotany*, University of California Press, 2013, the details of which are annexed hereto as well as a copy of Chapter 8, entitled "Ethnobotanical History and Contemporary Context of Medicinal Cannabis". In 1981, I published *Marihuana Botany: An advanced study, the propagation and breeding of distinctive Cannabis*, Berkeley(CA), both of which are referenced in the American Herbal Pharmacopeia, "Cannabis Inflorescence, Standards of Identity, Analysis and Quality Control, Revision 2014". I am also familiar with the most recent publication of the "Handbook of Cannabis", Edited by Roger G. Pertwee of the Institute of Medical Sciences, University of Aberdeen, UK (2014), and believe that it contains the most up-to-date and current information on all aspects of cannabis, including in particular the science and state of our knowledge for its use for medicinal or medical purposes.

(c) The expert's current *curriculum vitae* attached to the report as a schedule;

Attached as Schedule "A"

(d) The facts and assumptions on which the opinions in the report are based; in that regard, a letter of instructions, if any, may be attached to the report as a schedule;

I was asked to review the Expert Reports of Dr. Harold Kalant, and Mahmoud El Sohly tendered on behalf of the Defendant Government of Canada in these proceedings, and to indicate and respond to any points contained in those opinions that in my opinion required some rebuttal by way of clarification, contradiction, amplification or otherwise.

(e) A summary of the opinions expressed;

In my opinion these witnesses' statements are in many respects not current and up-to-date. They focus on limitations and cautions in relation to the use of the plant, instead of accepting its many possibilities in light of current developments in medical science.

(f) In the case of a report that is provided in response to another expert's report, an indication of the points of agreement and of disagreement with the other expert's opinions;

With respect to Dr. Kalant's Report:

Page 4: While growing conditions can slightly alter the biochemical variation of compounds (e.g., cannabinoids and terpenoids) found in a *Cannabis* plant and possibly mildly help or markedly hurt it in relation to its medical efficacy; chemical profile is genetically, and not environmentally determined. This is the reason that medicinal patients need a consistent source of material that clinically suits their needs.

Page 5: His data on the tar content of cannabis appears to be based on old NIDA cannabis samples. Few if any medical marijuana patients smoke 0.5-1.0% THC cannabis as it will not produce desired effects. This was true in 1970 and it is still true today. More potent cannabis existed then, but it certainly is more prevalent now. Worries about the potency of cannabis arise each decade. In a medical context the more potent an herbal medicine is, the less a patient needs to consume to achieve medical efficacy, and the lower the chances of experiencing side effects.

Most medical cannabis users consume only enough of their cannabis medicine to achieve the desired effects, and no more, and they do not want to experience unpleasant side effects. Largely because of lingering prohibition mentality, commercially available medical cannabis remains well beyond the financial reach of many patients for whom it would be a welcome blessing.

Medical marijuana patients are generally quite sensitive about their general health and many use non-combustion vaporization devices or consume cannabis medicines orally.

Page 6: The sole active ingredient in Marinol[®] is pure THC. Marinol[®] is generally ineffective, and poorly tolerated because in its orally administered form THC passes through the liver and is changed into the liver metabolite 11-*hydroxy*-THC, which is much more potent than *delta*-9-THC and stays in the system much longer. Vaporized and sub-lingual administration allows THC to enter the bloodstream and have its medical effects before it slowly enters the liver and is converted to 11-*hydroxy*-THC at a measured pace. Patients generally prefer herbal cannabis and whole plant extracts because they offer greater efficacy with fewer side effects.

Page 7: Cannabis in one form or another may well be a drug of first choice. Cannabidiol (CBD) is effective for a wide variety of indications and is non-psychoactive. CBD and other non-psychoactive cannabinoids modify the effects of THC as well as having their own medicinal values.

Page 9: On pain, see this critical, but very supportive review [**reference 13 below**]. Sativex[®] is approved in Canada for central neuropathic pain in multiple sclerosis and cancer pain unresponsive to optimized opioids, and spasticity in

MS. For nausea, cannabis works when “modern” agents do not. He suggests that appetite stimulation is better with anabolic steroids than with cannabis; query him about which is more dangerous.

Page 10: For more recent data on the efficacy of Epidiolex[®] and cannabidiol (CBD) for epilepsy, see www.gwpharm.com web pages and presentations. His presentation on spasticity is woefully inadequate. Sativex[®] is approved for this indication in 27 countries, including Canada.

Page 11: He soft-pedals Blake **[reference 18 below]**. This study showed Sativex[®] notably helped rheumatoid arthritis in patients who failed conventional treatment. There is a USA patent filed by the National Institutes of Health on the neuroprotective benefits of cannabidiol (CBD). High doses of THC damaging neurons is unsubstantiated with a cited reference. THC is actually quite non-toxic in this regard. The dexamabinol study is not relevant; it employed a synthetic agent that has different effects than cannabis. A more recent study supports that cannabis and THC are neuroprotective in head injury.

Page 12: Data support benefit of cannabinoids in Parkinson disease after prolonged administration **[reference 22 below]**. There is extensive documentation of benefit in Tourette syndrome including controlled trial data **[references 24, 25, 26 below]**. His contention of no beneficial effect in movement disorders is patently false and misleading.

Page 13: The benefits of cannabinoids in cancer although yet to be substantiated in large trials are far more dramatic than portrayed, including case reports in two Canadian children whose brain tumors (pilocytic astrocytoma) disappeared as a result of treatment. Benefits of cannabidiol and other cannabinoids in psychosis are much more evident than claimed. Cannabis has a durable benefit in glaucoma.

Page 14: The best treatise on lung threats is here **[reference below 35]**. Cannabis may aid depression **[reference 36 below]**.

Page 15: Patients who vaporize herbal cannabis report less lung irritation. No one injects cannabis or THC except in government supported experiments that provoke florid psychotropic side effects.

Page 17: There are references to the therapeutic efficacy of unheated and undecarboxylated cannabinoid acids. There are many other surveys of cannabis usage. Overall, daily medicinal usage averages 1-3 grams.

Page 18: Emerging literature on cannabinoid synergy refutes the contention that strain or chemovar differences are not important therapeutically. This is quite clear from the positive results of Sativex[®] in opioid-resistant cancer pain where a high-THC extract without cannabidiol (CBD) failed to distinguish itself from the placebo.

Page 19: See Russo 2011 and McPartland 2014 above. Statements that there exist no studies showing differences between pure cannabinoids and extracts are

false. See above, plus **[reference 43 below]**.

Page 20: The literature on chronic cannabis usage is extensively reviewed here **[reference 1 below]**.

Page 21: Good up-to-date reviews on driving by Paul Armentano are available from the norml.org website. **[reference 46]**. For psychosis and mitigation by CBD, see **[references 32, 23, 34 below]**.

Page 22: On psychosis see Robson, Muller-Vahl, Leweke **[references 32, 23, 34 below]**. On cardiovascular risks, there is no epidemiological evidence whatsoever to support significant risk of cannabis use alone in higher rates of myocardial infarction **[references 53, 54 below]**. Most case reports are from Europe where cannabis is routinely smoked with tobacco, a known risk.

Page 23: Cannabis does not cause lung cancer when used alone **[references 55, 35 below]**. In fact, it is protective **[references 35, 55, 56 below]**. For psychiatric discussions see above, plus **[reference 37 below]**.

Page 25: Peter Fried spent a career trying to show damage to children from their mothers smoking cannabis in pregnancy. His results were paltry, at best, and easily explained by socioeconomic and/or nutritional factors. He never cites data from children with advanced development born to pure-cannabis-smoking alcohol-free Rastafarian mothers in Jamaica **[reference 58]**. Dependence figures from the USA are spurious. Fifty to sixty percent of people in cannabis treatment are there at the behest of the courts, not because they necessarily have a definable medical dependency.

His contraindications are all false and not absolute. Cannabis and cannabinoids may be indicated in pregnancy, particularly to treat hyperemesis gravidarum, a potentially fatal condition, the latter being a Canadian study **[references 59, 60, 61]**. Children are currently being treated with Sativex[®] for spasticity, and Epidiolex[®] for seizures. Psychosis is being treated with cannabidiol (CBD) as well. Cannabinoids have applications in treatment of various addictions, the latter two being Canadian studies **[references 62, 63 below]**.

Page 26: Tolerance to THC effects is totally avoidable by slow titration to affect symptoms, but not to produce psychoactivity. The lack of tolerance with Sativex[®] was not based on patient reports at all. It was objectively confirmed by usage rates and lack of dose escalation. There have been no Sativex[®] drug-drug interactions reported that I am aware of.

Page 27: He has no reference for increased manic episodes after cannabis. In fact, it can help improve psychological conditions **[references 65, 66 below]**. Cannabis has also been shown to mitigate damage from consuming Ecstasy **[reference 71 below]**.

Sativex[®] has been safely combined with opioids to treat resistant pain, see Johnson X2, Portenoy **[references 14, 15, 16 below]**.

Page 28: His data claiming increased cannabis usage in legal states are

misleading and probably wholly inaccurate. In fact, cannabis protects from opioid mortality [reference 67 below]. There absolutely are standardized preparations from cannabis (ex., Sativex[®] and Epidiolex[®]). These clearly indicate that others can and will follow. CCIC does an excellent job to educate physicians. Much literature and many educational symposia are available for those who actually seek substantive medical cannabis information.

Page 29: Data on insomnia [reference 70 below]. Novotna and others [reference 5 below] prove efficacy in spasticity and 27 countries including Canada agree.

Page 30: High doses of cannabinoids are needed for primary treatment of cancer. This has nothing to do with tolerance. That does develop **over time**, and helps people to cope with THC-related side effects. His contentions of lack of strain differences are absolutely false (see above). GW Pharmaceuticals has 30,000 patient-years of safety data on Sativex[®]. Could that be considered systematic study of adverse effects? His claim is erroneous.

Page 31: CNS effects of cannabis are reversible, even after long-term, chronic administration (see Pope, Grant [references 44, 45, 57]). His contraindications are false.

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With respect to Mahmoud El Sohly:

Dr. El Sohly describes the Good Agricultural Practices (GAP) that are required to produce government-approved cannabis crops. Queries should be made about Good Manufacturing Practice (GMP) and Good Laboratory Practice (GLP), and whether application of these approaches allow for the production of consistent extracts or concentrates of cannabis that could similarly be employed in Canada for use by patients or in clinical research. He should also be queried concerning the standards set by the American Herbal Pharmacopoeia in their monograph [reference 9 below] and the American Herbal Products Association both of which set standards for growing safely indoors and outdoors.

Page 5: A certificate of analysis should include quantitative assessment of cannabis terpenoids as well as cannabinoids. Responsible medical cannabis dispensaries often provide these data to patients so they may make more informed decisions concerning their choice of medicinal marijuana. Many analysis laboratories are available to growers and dispensaries who monitor various sorts of biological and chemical contamination. The medical cannabis industry is rapidly becoming self-regulating in quality control.

Dr. El Sohly is apt to be defensive about this. University of Mississippi cannabis is stored for as much as 10 years after it is grown before shipping to researchers or patients. While he has stated that the relatively low cannabinoid content is preserved, it has been demonstrated in a Canadian study that the terpenoid content of that material is as little as 1/8 that of street cannabis, the latter having a discussion of this fact [references 2 and 3 below]. He may also claim, as he has in previous testimony that photos of his cannabis have been "doctored" in the 2002 publication. This is false. The entire process of dissecting NIDA cannabis cigarettes was observed and photographed with many witnesses [reference 1 below]. Many scientists and consumers are recognizing the key therapeutic importance of terpenoids in modulating cannabinoid effects.

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(g) The reasons for each opinion expressed;

My reasons are expressed above after each reference.

(h) any literature or other materials specifically relied on in support of the opinions;

References also listed below each rebuttal in (f) above.

Clarke R., Merlin M. (2013) *Cannabis: Evolution and Ethnobotany*. **Attached as Schedule "B"**

Pertwee R (2014) *Handbook of Cannabis*. **Attached as Schedule "C"**

(i) a summary of the methodology used, including any examinations, tests or other investigations on which the expert has relied, including details of the qualifications of the person who carried them out, and whether a representative of any other party was present;

Not applicable

(j) any caveats or qualifications necessary to render the report complete and accurate, including those relating to any insufficiency of data or research and an indication of any matters that fall outside the expert's field of expertise; and

Not applicable

(k) particulars of any aspect of the expert's relationship with a party to the proceeding or the subject matter of his or her proposed evidence that might affect his or her duty to the Court.

I do not have any relationship with any party to the proceeding, and my relationship to the subject matter of my proposed evidence arises as a result of my experience and will not affect my duty to the court as an expert witness.

Schedule "A"

Robert C. Clarke

Academic affiliations:

Society for Economic Botany – Lifetime Member
International Hemp Association – Projects Manager
Textile Society of America – Member

Research interests:

Rob worked for HortaPharm in the Netherlands from 1993 through 2003 as a plant breeder, science consultant and liaison to the academic community. HortaPharm's primary goal was the development of single cannabinoid *Cannabis* varieties for use in medicines such as those produced by GW Pharmaceuticals in the United Kingdom amongst others. Other breeding interests included industrial hemp varieties suited for semi-tropical and equatorial conditions. During this time he also attended many international congresses presenting papers based on his field research.

Spanning the past three decades Rob traveled extensively throughout Eurasia documenting traditional *Cannabis* production and use. Field research focused primarily on the minority ethnic groups living in the highlands of Yunnan, Sichuan and Guizhou provinces of China as well as the neighboring regions of Laos, Thailand, Burma and Vietnam. Additional fieldwork was carried out in Eastern Europe, India, Japan, Korea and Nepal. During recent years field research and collecting have spread to Anatolia, the Balkans, and the Caucasus.

During the summers of 2004 through 2006 Rob began studies of traditional Japanese hemp textiles, living near Kyoto and regularly traveling the rail system to visit rural museums and private collectors. Much of this research centers on accessions in the vast holdings of the National Museum of Ethnology (MINPAKU) in Osaka, where Rob has completed an initial survey of the textile collection. Rob aims to resume research at MINPAKU, while searching for a Japanese colleague sharing similar interests, and to ultimately publish in both Japanese and English celebrating traditional Japanese hemp weaving culture. Rob's associated research interest is exploring the role of hemp in indigenous Japanese Shinto worship, and following an allied path into the ritual use of hemp in ancient Korean shamanistic traditions also still practiced today.

Publications:

In addition to "*Cannabis: Evolution and Ethnobotany*" Rob has written three books about *Cannabis* botany and culture – "*The Botany and Ecology of Cannabis*", "*Marijuana Botany*" and "*Hashish!*" and coauthored "*Hemp Diseases and Pests*" – several chapters in edited volumes concerning *Cannabis* breeding and medicinal applications, and numerous peer-reviewed articles.

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ROBERT C. CLARKE AND MARK D. MERLIN

SCHEDULE "B"

Cannabis

EVOLUTION AND ETHNOBOTANY

Cannabis

EVOLUTION AND ETHNOBOTANY

ROBERT C. CLARKE

AND

MARK D. MERLIN



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Ethnobotanical History and Contemporary Context of Medicinal *Cannabis*

Hemp, both because of its psychoactive properties and its mystical significance, became a popular and widely-utilized plant in the folk medicine of Europe and Asia. Since ancient times its soothing, tranquilizing action has been known.

(BENET 1975)

INTRODUCTION

EARLY EAST ASIAN MEDICINAL *CANNABIS* USE

SOUTH AND SOUTHEAST ASIAN MEDICAL TRADITIONS

EGYPTIAN MEDICINAL *CANNABIS* USE

CANNABIS IN EARLY MIDDLE EASTERN AND LATER ISLAMIC MEDICINE

AFRICAN AND SOUTH AMERICAN MEDICINAL *CANNABIS* USE

EUROPEAN MEDICINAL *CANNABIS* USE

PRESENT-DAY WESTERN MEDICINAL APPLICATIONS OF *CANNABIS*

SUMMARY AND CONCLUSIONS

Introduction

Earlier chapters in this book make it quite clear that *Cannabis* has a very long history as a multipurpose resource with particular uses differing from region to region (see Chapters 4 through 7). How *Cannabis* was first used remains unresolved, whether it was for fiber to produce cordage, seed for food, psychoactive resin for medicinal, ritual or spiritual applications, or a combination of these. In fact, it is often difficult to separate early medicinal, psychoactive, ritual, and even food uses of *Cannabis*, especially those involving mind-altering preparations utilized in any or all these contexts. This becomes particularly complex within the traditional interrelationships of religious belief, ritualistic practice, and medicinal use; the latter is the focus of this chapter. The archeological and historical records offer evidence that *Cannabis* plants provided a variety of important medicinal uses in antiquity, some of which persisted into modern times. Ancient medicinal texts (*materia medica*) of China and India, as well as Egypt, Greece, and Rome, refer to specific uses for *Cannabis*, and these are discussed later.

First it is important to recognize that awareness and use of food as medicine is an ancient tradition in various areas of the world and continues today (Etkin 2006). Chinese medical traditions, for example, hold that diet is the most important determinant of one's health, and there are often no distinct boundaries between foods and medicine. As Anderson (1988) explains, "Many things were purely medicines, but medicines often became food if people learned to like them; many foods became merely medicines when people stopped relishing them; and all foods were considered to have medicinal value,

positive or negative, with important effects on health." This concept of food as medicine applies to the traditional use of *Cannabis* in other parts of the world as well. In this chapter we investigate historical claims of *Cannabis*'s medicinal efficacy as they relate to absorption of cannabinoids (the physiologically active compounds found only in *Cannabis*) into the bloodstream via inhalation, swallowing, or absorption through skin or mucous membranes. (Ritual uses of psychoactive marijuana and hashish are discussed in Chapter 7, and ritual uses of nonpsychoactive stems, fiber, and seed are presented in Chapter 9.) The relationship between mind-altering and medicinal use in ritual contexts is also often assumed by the person(s) consuming *Cannabis* or celebrating its symbolic therapeutic potency. References to the use of *Cannabis* preparations as antibiotic and analgesic medicaments, most commonly for external use, can be found in folk medicine traditions and old herbals of the Middle East, East and South Asia, Europe, Africa, and the New World. Mechoulam (1986) provided a list of 20 medicinal applications of *Cannabis* by traditional societies.

Central and East Asia form a huge region to which we attribute the ethnobotanical origins of *Cannabis* use. Medicinal use of *Cannabis* has a lengthy history there, and much still remains to be gleaned from literary and potential archaeological records (e.g., see Chapter 7). Benet (1975, citing Antzyferov 1934) presented some examples. In Tashkent, the Central Asian capital city of present-day Uzbekistan, a confection consumed to induce a "happy mood," known as *guc-kand*, was made of *Cannabis* boiled in water, sieved, and then mashed together with sugar, saffron, and several egg whites. The paste was formed into small balls and then dried in the

TABLE II

For millennia *Cannabis* has been traditionally used around the world for relief from a wide variety of medical conditions.

Medical condition	Medicinal uses substantiated by modern research
Analgesic	X
Anesthetic	
Antiasthmatic	X
Antibiotic	X
Anticonvulsive	X
Antidepressive	
Antidiarrhoeal	X
Antimigraine	
Antiparasitic	X
Antirheumatic	X
Alleviation of memory loss	
Appetite promoter	X
Facilitation of childbirth	
Hypnotic	X
Reduction of fatigue	
Sedative	X

SOURCE: From Mechoulam 1986.

sun. The "candy," which is said to have been "popular among women," was given to children to "keep them from crying" and to boys before circumcision to "reduce pain." A mixture of lamb's fat with *nasha* (hashish) was "recommended for brides to use on their wedding night to reduce the pain of defloration." Apparently, the same formulation worked well for headache "when rubbed into the skin," and it was also eaten "spread on bread."

Early East Asian Medicinal Cannabis Use

The utilization of *Cannabis* for medical purposes is ancient in China where origins of therapeutic use can be traced through ancient legends and fables. For example, Abel (1980, citing Doolittle 1966) paraphrased a Chinese story about the mythical emperor Liu Chi-nu that explains connections between *Cannabis* and illnesses:

One day Liu was out in the fields cutting down some hemp, when he saw a snake. Taking no chances that it might bite him, he shot the serpent with an arrow. The next day he returned to the place and heard the sound of a mortar and pestle. Tracking down the noise he found two boys grinding marijuana leaves. When he asked them what they were doing, the boys told him they were preparing a medicine to give to their master who had been wounded by an arrow shot by Liu Chi-nu. Liu Chi-nu then asked what the boys would do to Liu Chi-nu if they ever found him. Surprisingly, the boys answered that they could not take revenge on him because Liu Chi-nu was destined to become the emperor of China. Liu berated the boys for their foolishness

and they ran away, leaving behind the medicine. Sometime later Liu himself was injured and he applied the crushed marijuana leaves to his wound. The medicine healed him and Liu subsequently announced his discovery to the people of China and they began using it for their injuries.

Another similar folk tale (Abel 1980, citing Wong and Lien-Teh 1936) tells us about a farmer who spotted a snake carrying leaves of *Cannabis* to put on the wound of another serpent. The following day the injured snake was cured. Inquisitive about the efficacy of the hemp remedy, the farmer experimented with *Cannabis* leaves on his own injury and was healed. These and other folk tales provide us with some insight about the notion that *Cannabis* possesses potency.

References to *Cannabis* in the oldest-known medical text, titled *Shen Nung Pen Ts'ao Ching*, or "Divine Husbandman's Materia Medica," are attributed to the legendary Chinese emperor Shen Nung, who probably lived sometime between 3494 and 2857 BCE (Chang 1962). Shen Nung is traditionally credited with inventing agriculture and introducing medicines to Chinese culture. The first known edition of Shen Nung's *Pen Ts'ao Ching* was published at the end of the Western Han dynasty (ca. 1800 BP) based on manuscripts possibly dating from as early as about 4700 BP. It contains descriptions of 365 medicines from natural sources, including the oldest written record of *Cannabis* use and demonstrates that the Chinese have been knowledgeable about medicinal herbs for several millennia (Li 1974a; Touw 1981). According to legend, Shen Nung had a transparent abdomen and intentionally ingested as many as 70 different plants per day so he could watch their effects and discover their various qualities. He was deified and acclaimed the "Father of Chinese Medicine." Based on his search for efficacious cures derived from prior shamanistic knowledge, and his documented medicinal use of many plants including tea (*Camellia sinensis*) and hemp, Shen Nung is considered the first Chinese medical researcher. Shen Nung is also known as the "Father of Agriculture" and credited with instructing the ancient Chinese people in the cultivation of hemp.

According to the *Pen Ts'ao Ching*, *Cannabis* is included among the drugs of the "first class," which is headed by ginseng. Drugs of the first class were not considered poisonous. In fact, no matter how much they were utilized they were believed to be harmless. Indeed these medicinal plants and their products were usually used to improve breathing and prolong life. *Má fěn* (麻粉), or "hemp powder," a preparation using the flowering tops of female *Cannabis* plants, including the resinous bracts surrounding the seeds, was thought by the ancient Chinese to contain the greatest amount of *yin* energy; *yin* is the receptive female dynamic attribute linked with *yang*, the creative male element in traditional Chinese philosophy and medicine. *Má fěn* was thus prescribed in cases of a loss of *yin*, such as in menstrual fatigue, rheumatism, malaria, beri-beri (Vitamin B₁ deficiency), constipation, and absentmindedness (Taylor 1963; Li 1975). On the other hand, the *Pen Ts'ao Ching* indicates that if too many hemp seeds were eaten, they could cause one to see demons, but if taken over a long time, they could enable one to communicate with spirits. Also, Li Shih-Chen's *Pen Ts'ao Kang Mu*, or "Great Herbal," of 1580 tells us that such consumption "makes one see devils" (Li 1974b; Anderson 1988). Both of these ancient references allude to the psychoactive effects of



FIGURE 45. Legendary Chinese Emperor Shen Nung allegedly wrote China's first pharmacopoeia and is said to have personally tested many potentially valuable medicinal herbs including *Cannabis* by swallowing them and observing their effects through his transparent abdomen.

Cannabis seeds, although the seeds contain no cannabinoids, and therefore these early authors were more likely referring to the bracts enveloping the seeds, which can contain large amounts mind-altering THC.

In China, during the second century CE, a new medical use was discovered for *Cannabis*, which is attributed to the famous Chinese surgeon Hua Tuo (lived 110 to 207 CE). According to the *Ho Han Shu*, or "History of the Later Han," the official history of the Eastern Han dynasty (25 to 221 CE) compiled by Fan Ye (died 445 CE), Hua Tuo performed complicated surgical procedures without causing pain, carrying out such amazing operations as incisions into the loin and chest, resectioning of the intestines, and organ grafts. His procedures involved an infusion-like anesthetic called *má yóu* (麻油), literally "hemp oil" but with the modern meaning: "sesame oil," which was thought to be made from *Cannabis* resin, *Datura*, and wine (Julien 1894). The character *má* (麻) means "numb" as well as "hemp" (see Chapter 7). A passage in a later work titled *Chêng Lei Pen Ts'ao*, or "Cheng Lei Herbal," written by Tang Shen-wei (1108 CE) and translated by Li (1974b), tells us that *má fên* has a spicy taste and is used for waste diseases and injuries, clears blood, and cools temperature; it relieves fluxes, undoes rheumatism, and discharges puss.

Wu Pu, a disciple of Hua Tuo, wrote the *Wu Pu Pen Ts'ao*, or "Wu Pu's Herbal" ca. 200 CE, in which he made a clear distinction between toxic hemp resin *má fên* and the non-poisonous seeds or kernels (Emboden 1972). Traditional Chinese medicine practitioners still prescribe hemp seed for the relief of digestive problems. This is due in part to their high roughage content and ability to nourish the elderly and others unable to ingest normal amounts of food, as they contain easily digestible edestin-type proteins and high levels of

essential fatty acids (EFAs). According to Shou-zhong (1997), hemp seeds are still widely used in modern clinical practice for hastening birth delivery and promoting lactation as well as facilitating urination and defecation; Perry and Metzger (1980) also referred to continued use of hemp seeds in China for aiding birth delivery as well as treating uterine prolapse, the slipping out of place of the uterus.

During the time of the Tang dynasty (618 to 907 CE), pulverized hemp mixed with rice wine was "recommended in various other materia medica against several ailments, ranging from constipation to hair loss" (Dikötter et al. 2004; also see Daihua 2002). The ancient Chinese text *Wu Lei Hsiang Kan Chih*, or "On the Mutual Responses of Things According to Their Categories," is believed to have been written by Lu Tsan-Ning (also known as Su Shih) in about 980 CE. In this text we are told that *Cannabis* is among plants that can drive away mosquitoes when its leaves are burnt, and this could have prevented the spread of mosquito-borne diseases and protected people from discomfort resulting from their bites (Needham et al. 1996).

Trade and communication between China, Korea, and Japan dwindled during the Chinese Qing dynasty (1644 to 1912 CE), the Korean Joseon dynasty (1392 to 1910 CE), and the Japanese Edo and early Meiji periods (1603 to 1912 CE) as each country followed its own introspective path. However, Korea and Japan continued to send scholars and students to learn medicine, agriculture, and science from the Chinese. In Japan, hemp (*tai ma asa*) is considered one of the *sanso*, or "Three Plants," along with red safflower (*benihana*, *Carthamus tinctorius*) and indigo (*ai*, *Indigofera tinctoria*), that symbolize long life (Shimamura 1991). Traditional Japanese doctors incorporated much of the ancient Chinese pharmacopoeia and utilized many *Cannabis* preparations (*asashijingan*) for a variety of indications, for example, as a mild laxative, to treat asthma, to relieve poisonous bites, to deworm domestic animals, to counteract skin ailments, and as a general tonic to promote vigor (Olson 1997).

South and Southeast Asian Medical Traditions

There appears to be no doubt that the cannabis plant was believed by the ancient Aryan settlers of India to possess sedative, cooling and febrifuge properties. (CHOPRA AND CHOPRA 1957)

The use of whole *Cannabis* plants for myriad medicinal treatments over the centuries is a testament to the general health value these plants and their products have had for people throughout the history of South Asia. Early references to the medicinal use of *Cannabis* can also be found in South Asian historical records and texts. The *Atharva Veda* (passage 11.6.15), thought to date from well before 500 CE and perhaps as far back as ca. 1600 BCE, refers to the sacred plant *bhangya* with indications that *Cannabis* helps "release us from anxiety" (e.g., see discussions regarding the *Report of the Indian Hemp Drugs Commission* in Campbell 1984 and Kaplan 1969). According to Sharma (1979), several later Vedic texts also make reference to the medicinal use of *Cannabis*. The *Susruta Samhita*, an ancient holy book of the traditional Indian Ayurvedic medical system (written by Punarvasu possibly as early as 800 BCE) listed hemp as a cure for mucus discharge accompanied by diarrhea and as a remedy for biliary fever (Chopra and Chopra 1957). The *Ashtadhyayi* by Panini and the *Vartika* by Katyayana indicate that *Cannabis* was known

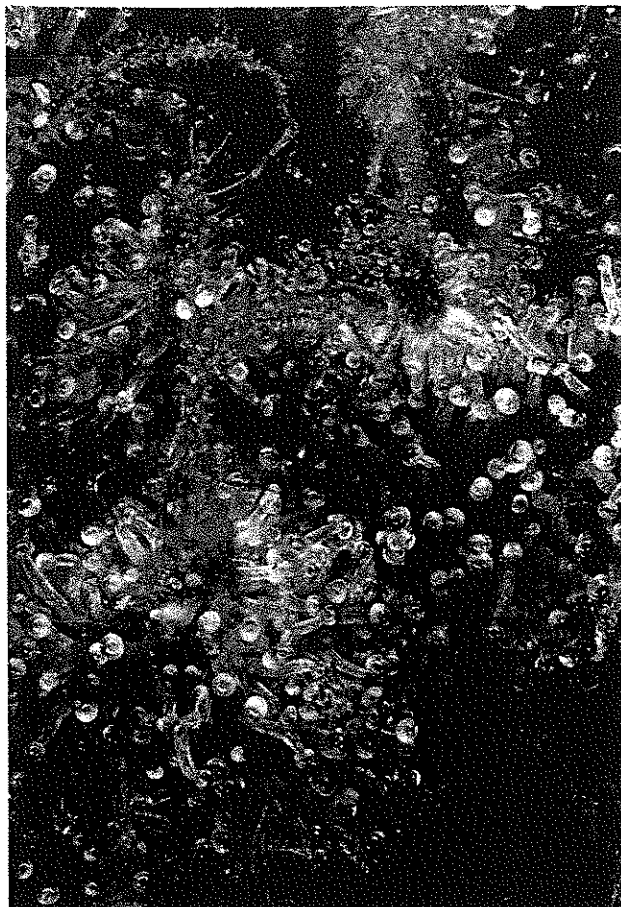


FIGURE 46. Glandular trichomes crowded together on the surface of the bracts and small leaflets, shown here in a seedless female *Cannabis* inflorescence, can secrete large amounts of aromatic and psychoactive resin that contains unique, medically valuable compounds (photo ©GrowMedicine.org).

in India as early as the fourth and third centuries BCE when it had already become part of traditional folk medicine (Dwarakanath 1965). Reliable Ayurvedic literary documents on materia medica such as *Rajanirghanta* (ca. 300 CE), *Dhanwantari nighantu* (eighth century CE), *Sharangadhara Samhita* (thirteenth century CE), *Madanapala nighantu* (1374 CE), *Rajanighantu* (1450 CE), *Dhurtasamagama* (ca. 1500 CE), and *Bhavaprakash* (ca. 1600 CE) describe various aspects of the medicinal use of *Cannabis*. In addition, *Cannabis* has been used as a veterinary therapeutic in India at least since the twelfth to thirteenth centuries CE and continues to this day (e.g., see Chopra and Chopra 1957; Jain 1999). Later Ayurvedic medical works reveal the increasing therapeutic significance of *Cannabis*, which is included in a large number of remedies (Dwarakanath 1965). *Cannabis* has long been prescribed to arouse appetite and as “a source of great staying-power under severe exercise or fatigue” (Nadkarni 1954), as well as for many other purposes including the following: *paphahari* to promote loosening, separation, and the elimination of phlegm; *grahini* to stimulate the retention and binding of the bowels; *pachani* to promote digestion; *ushna* to promote heat; *pitāla* to excite the flow of bile; *mada-var dhani* to encourage talkativeness; *moda-var dhani* to promote happiness; *vag-var dhani* to stimulate the digestion; *dipani* to



FIGURE 47. Terpenoid compounds, THC, and other medically valuable cannabinoids composing the resin are synthesized in and secreted by the head cells of glandular trichomes perched atop a stalked extension of the green leaf surface. The cluster of secretory cells is reflected inside the shiny surface of the gland head (photo ©Bubbleman).

encourage appetite; *ruchya* to stimulate taste; and *nidraprada* as a hypnotic (Chopra and Chopra 1957).

For centuries, Indian foot bearers transporting goods high into the Himalaya Mountains have relied on *Cannabis* to relieve fatigue. Potions containing juice from the *Cannabis* plant have been used to remove dandruff and vermin from hair, reduce pain from earaches, alleviate bowel complaints such as diarrhea and constipation, and check discharge from gonorrhea (e.g., see Knörzer 2000; Alt et al. 2003). Other significant applications include its use for relieving headaches, acute mania, whooping cough, asthma, and insomnia. In Ayurvedic medical practice, *bhāng* has been used to treat fevers, not directly or physically as an ordinary medicine but indirectly or spiritually, by soothing the “angry influences” causing the heats of fever. According to Indian legend, Lord Shiva, enraged by a slight from his father-in-law Daksha, “breathed from his nostrils the eight fevers that wither mankind.” If a person stricken with fever poured *bhāng* on a Shiva *lingum* (stylized phallus worshiped as a symbol of the god Shiva), “he was pleased, his breath cooled, and the portion of the breath in the body of the sufferer ceased to cause fever” (Campbell 1894; also see Mikuriya 1994). The seminal connections between religious ritual and medical cures strongly influenced traditional therapeutic use of *Cannabis* in India, and its utilization medicinally was not originally separated from religious belief: “The reference in the *Atharva Veda* to overcoming enemies and evil forces may, quite possibly, have included physical as well as spiritual ills. Once medicinal use became increasingly delimited from religious use, it remained distinct from other secular use and could, therefore, be freely and fully explored unhampered by secrecy or disreputability” (Touw 1981). *Cannabis* has long been considered a panacea

(cure-all) in India, used commonly in family remedies to treat numerous minor ailments, especially relief from physical pain and mental strain (Chopra and Chopra 1957). Indeed, it is not an overstatement to refer to *Cannabis* as “the penicillin of Ayurvedic medicine” (Sharma 1977a). Even the *Report of the Indian Hemp Drugs Commission* did not oppose the moderate use of *Cannabis* for social, ritual, and medicinal practices in the Indian subcontinent. Indeed, use of the *Cannabis*-based, traditional drink *bhang* was considered “the best of gifts” when consumed in moderation: “*Bhang* is a cordial, a bile absorber, an appetizer, a prolonger of life” (Campbell 1894). Indian Muslims also regard *Cannabis* (*bhang*) as both a holy and medicinal plant, and in Unani-Tibbi, the Arabic-Muslim system of medicine, practitioners use it for treating numerous diseases such as asthma, dandruff, and urinary disorders (e.g., Dwarakanth 1965; Lozano 2006).

Several other traditional medicinal uses for *Cannabis* have been recorded across South Asia. For example, in the uplands of Northwestern Pakistan, among tribal communities in the Hazar Nao forest of the Malakand district, the leaves are used to treat spasms by boiling them and tying them (while they are warm) “over the affected parts of the body” (Murad et al. 2011). East of Pakistan in Rajasthan, India, Singh and Pandey (1998) reported that the Meena and Garasia tribal groups apply a paste made of *Cannabis* leaves (*bhang*) on “bleeding and painful” hemorrhoids (also see Bajracharya 1979).

Throughout the Himalayan region a “widespread belief holds that a concoction of young *Cannabis* leaf powder and honey keeps youth, vitality and virility” and it is also applied to the hair to maintain color and texture (Sharma 1977a). In the northwestern Himalayan region, Sarin (1990) reported that a poultice of crushed female flower tops is used to treat prolapse of uterus and hydrocele, the excessive retention of fluid in the testicles that results from obstruction and inflammation of the lymphatic ducts draining the testicular region. In treating prolapse, a warm *Cannabis* poultice is “wrapped in a soft muslin cloth and kept inside the vagina at bed time,” and treatment of hydrocele consists of “wrapping the affected testicles with the warm pounded mass at bed time” with a reduction of swelling beginning “within a week or ten days.” In a pharmacological appraisal of traditional herbal medicine in far western Nepal, Kunwar et al. (2010) reported that *Cannabis* leaf juice is used to heal wounds, control bleeding, and relieve stomachaches (also see Watanabe et al. 2005), while leaves are smoked and taken internally to relieve discomfort and inflammation (Joshi 2006).

In Nepal, *Cannabis* has a long history of use as a sedative (Bajracharya 1979). According to Fisher (1975) mothers give *Cannabis* mixed with sweets to children as a mild tranquilizer: “by giving her child a small amount of *ganja*” a mother “keeps him less active and less likely to get into trouble while she is occupied in other ways.” La Barre (1977) compared use of *Cannabis* as a sedative to use of opium extracts to calm children: “The use of hashish is quite parallel to the use of opiates in soothing syrups given to fretful or teething babies in the nineteenth and twentieth centuries in America.”

In answer to the question of whether or not *Cannabis* and opium should be banned as medicines, Dwarakanath (1965) made a case for allowing continued traditional therapeutic use by Ayurvedic Hindu and Unani Muslim practitioners in India. He pointed out that the great majority of people in India reside in a half million villages, almost exclusively attended to by Ayurvedic physicians and Unani *hakims* with significant

responsibility for the health of these rural communities. Medical practitioners included *Cannabis* and opium in traditional formulations as important healing agents “especially in the treatment of such conditions as enteritis, dysentery, chronic diarrheas, including sprue syndrome [inability to absorb fats], painful states such as neuralgia, neuritis, rheumatism, insomnia, nervous disorders, etc.” Used as pain killers, hypnotics, antispasmodics, and so on, these *Cannabis*-based drugs still continue to play an important role in relieving physical and psychological stress (see Chopra and Chopra 1957 for a list of preparations containing *Cannabis* used in indigenous medicine during the middle of the last century). In sum, the breadth of evidence presented earlier highlights a long history of medicinal *Cannabis* use throughout much of South Asia, within both Hindu and Muslim medical traditions.

We also have evidence of medicinal *Cannabis* use in Southeast Asia, albeit much less than that for South Asia. For example, Martin (1975) studied ethnobotanical aspects of *Cannabis indica* use in this region, mainly in Cambodia and to a lesser extent in Thailand, Laos, and Vietnam. She assumed that the species was probably brought into Southeast Asia within the past 500 years or so from South Asia and pointed out that *ganja*, its Sanskrit name, is the widely used vernacular appellation for this plant in Southeast Asia where it is grown “on a family basis . . . around the house.” Besides its widespread use as a pain remedy (similar to opium products) in Southwest Asia, *C. indica* is also used to treat anorexia, dysentery, memory loss, asthma, coughing, lightheadedness, and convulsions, as well as suppressing polyps and calming nerves. It is also used to facilitate digestion and childbirth, stimulate lactation, purify blood, and clear bile, and it is believed to regulate function of the heart, liver, and lungs; eradicate intestinal parasites; induce decongestion; and effectively treat paralysis. A decoction is used in Southeast Asia to mitigate migraine pain and stiffness, and it is also said to be particularly effective in calming nerves when consumed with certain plants prior to bedtime and meals; this soothing effect is acknowledged “both by peasants and by the official pharmacopoeia of these countries.”

Martin (1975) pointed out that the medicinal effectiveness of *Cannabis* for many illnesses previously mentioned is not universally recognized through Southeast Asia today because many local folk medicines also include elements of magic. Martin also did refer to the rather broad medical “significance attached by the peasants to a plant which seems never to have been widespread in the region.” More than 300 years ago, Georg Eberhard Rumpf (also known as Rumphius), a German doctor serving the Dutch government in Indonesia, listed the local use of *Cannabis* root to treat gonorrhea in his famous botanical work, *Herbarium Amboinense*, first published in 1741. Rumphius also mentioned that “the green leaves of the female plant, cooked in water with nutmeg, [are given] to drink to folks who felt a great oppression in their breasts, along with stabs, as if they had Pleuritis too” (Rumpf and Beekman 1981, quoted in Russo 2002a; also see Rumpf and Beekman 1999).

Egyptian Medicinal *Cannabis* Use

Although it is probable that *Cannabis* and its medicinal use spread into Egypt from areas east of the Mediterranean Sea, the oldest references to such use in the Near Eastern region are associated with ancient Egypt; thus we continue with a

discussion of the Egyptian record. Nunn (1996), for example, cited several sources that believe the hieroglyphic word *shemshemet* refers to *Cannabis* and therefore indicates its medicinal use in ancient Egypt. Archeological evidence of ancient hemp fragments were reported from the tomb of Akhenaten (Amenophis IV), dated ca. 1350 BCE (see Manniche 1989), and *Cannabis* pollen was recovered from the tomb of Ramsés II (died 1224 BCE). This evidence supports the contention that *Cannabis* was present and presumably used in ancient Egypt (see Chapters 4 and 5 for further discussion of the history and strength of this conviction).

There are many references to the medical use of *shemshemet* inscribed on ancient Egyptian medical documents made of fibrous sheets of sedge (*Cyperus papyrus*) pith that date from the seventeenth through thirteenth centuries BCE. The earliest identification of the Egyptian word *shemshemet* comes from Fifth dynasty stone carvings dated to ca. 2350 BCE; these list *shemshemet* as a source of cordage. This increases the likelihood that ancient medical references to *shemshemet* in Egypt do refer to *Cannabis* since it is the only common fiber plant also widely employed as medicine. Based on historical research, Russo (2002a, citing Manniche 1989) tells us that in Egypt *Cannabis* “has remained in Egyptian pharmacopoeia since pharaonic times” and “was administered by mouth, rectum, vaginally, on the skin, in the eyes, and by fumigation.” Russo (2002b, quoting Ghalioungui 1987) referred to a passage (821) in the ancient *Ebers Papyrus* (dated to ca. 1550 BCE), which he believes is suggestive of nineteenth-century CE use of *Cannabis* to induce contractions during childbirth: “Another: *smsm-t* [*shemshemet*]; ground in honey; introduced into her vagina (*iwf*).” In addition, Russo (2002b) tells us that another passage (618) in the *Ebers Papyrus* “refers to treatment of a toenail with a bandage containing hemp resin.”

Manniche (1989) referred to a relevant passage from *Papyrus Ramesseum III* (dated to ca. 1700 BCE) that describes an eye treatment involving the use of “celery” and “hemp,” which were ground up and left overnight in the humid evening air; during the following morning, the patient’s eyes were then washed with the mixed celery and hemp potion. Russo (2002b) suggested that this remedy parallels modern use of *Cannabis* in treatment of glaucoma eye disease.

The Egyptian *Fayyum Medical Book* dating back more than 1,800 years and contemporaneous with early Greek medical treatises provides additional references to the use of *Cannabis* to control inflammations such as tumors and acute ear pain. Evidence of *Cannabis* use for medicinal purposes has not been identified for the period from about the third to the ninth or tenth centuries CE; however, by this time “Egyptian medicine had become Islamic medicine” (Russo 2007).

Cannabis in Early Middle Eastern and Later Islamic Medicine

If Thompson (1924, 1949) is correct in his interpretations of ancient manuscripts found in the archive of King Ashurbanipal dated to the seventh century BCE, *Cannabis* was present and used medicinally perhaps as far back as 4,000 years ago among people living in irrigated lowlands between the Tigris and Euphrates Rivers:

The earliest references to cannabis in female medical conditions probably originate in Ancient Mesopotamia. In the 7th century BCE, the Assyrian King Ashurbanipal assembled

a library of manuscripts of vast scale, including Sumerian and Akkadian medical stone tablets dating to 2000 BCE. Specifically according to Thompson, *azallû*, as hemp seeds were known, were mixed with other agents in beer for an unspecified female ailment (Thompson 1924). *Azallû* was also employed for difficult childbirth, and staying the menses when mixed with saffron and mint in beer (Thompson 1949). Usage of cannabis rectally and by fumigation was described for other indications. (RUSSO 2002a; also see RUSSO 2002b)

Other early records from the Middle East indicate medicinal use of *Cannabis* occurred before the rise of Islam. The Zoroastrian scriptures of ancient Persia, related to the Hindu *Vedas*, make reference to *bhang* for inducing miscarriage and producing euphoria. The *Zend-Avesta*, the holy Persian book of Zoroastrianism, which survives only in fragments dating from about the fourth to sixth centuries CE, alludes to the use of “*banga*” in a medical context; this word in the text is identified as *Cannabis* by the translator Darmesteter (1883). In the *XV Fargard* of the *Vendîdâd* (the first book of the *Zend-Avesta*), a compilation of religious laws and mythology, *Cannabis* is referred to as a stimulator of abortion, and thus “the damsel goes to the old woman and applies to her that she may procure her miscarriage, and the old woman brings her some *banga*, or *shalta* or *ghnana*, or *fraspata*, or some other of the drugs that produce miscarriage” (Darmesteter 1883).

The genesis of the ethnomedicinal knowledge and use of *Cannabis* in the Middle East region is not completely clear, but much of Egyptian understanding and application of this medical practice was adopted into Arabic Unani medicine and at least partially integrated into the Greek and Roman heritage. This is manifested in the writings of notable scholars of the time including Dioscorides, a renowned Greek physician and scholar from Cilicia in southern Asia Minor who became the personal physician of the Roman emperor Nero, Galen, a prominent second-century CE Roman physician and surgeon of Greek ancestry who was an accomplished medical researcher, and Pliny the Elder, a famous Roman naturalist and philosopher. Although the works of Dioscorides and Galen were translated into Arabic and had a major influence on development of the early Arabic medical system and to some degree on the use of *Cannabis*, it can be argued that much of this knowledge originated within the Egyptian medical system and that the transfer of medical information was largely from the East to the West. Arab and Greek physicians relied on *Cannabis* for much the same indications, and although many accepted Galen’s classification that it had both “desiccating and warming” powers, there were also contrary Arab opinions concerning the roots of its curative nature that may have originated directly from Egyptian concepts.

Awareness of *Cannabis*’s medicinal value shifted from Egyptian through Arabic and then to Greek and Roman medical traditions, but was this knowledge transfer accompanied by availability of *Cannabis* from a more medically effective gene pool? Pliny the Elder, in his *Historia Naturalis* (77 CE), tells us that “*Cannabis*, rather dark and rough in respect to its leaves, first grew in the forests.” Butrica (2006) points out that “Pliny’s description of the original plant as dark and rough of leaf resembles Dioscorides’ description of wild cannabis as having darker and rougher leaves than tame. Perhaps this reflects a belief that tame cannabis had been bred from wild cannabis (Herodotus already distinguishes between cultivated and wild varieties of the plant known to the Scythians); or perhaps—and not for the last time—Pliny confused

the two plants or carelessly ignored the distinction." Could it be that the Greek historians were noting botanical phenotypic differences between different biotypes of *Cannabis*—NLH versus NLD cultivars—rather than between stages in its domestication? Do historical accounts actually differentiate between *C. sativa* narrow-leaf hemp (NLH), the "tame" cultivated type with which the Greeks and Romans were very familiar, and *C. indica* narrow-leaf drug (NLD), the "wild" type that was described as being darker and rougher than the "tame." "Darker and rougher" describes accurately the psychoactive and medically potent *C. indica* biotypes originating to the east in southern Asia, which are characterized as darker green and more highly branched plants. Possibly the ancient Greeks and Romans were describing the differences between foreign and familiar or introduced and local varieties rather than between "wild" and "tame" stages of domestication.

By the first century CE the Greeks and Romans had extensive knowledge of their native NLH, commonly cultivated as a fiber and seed crop, but the content of cannabinoids, particularly psychoactive THC, in NLH biotypes would have been very low. However, if "wild" actually meant introduced NLD varieties from the east, they would have been more curatively potent than the local varieties and therefore worthy of denoting with a separate name, in this case "wild," O'Shaughnessy (1839) had the following to say regarding the difference in medicinal value of European hemp as compared to that of Middle Eastern and South Asian "hemp":

Much difference of opinion exists on the question, whether the Hemp so abundant in Europe, even in high northern latitudes, is identical in specific characters with the Hemp of Asia Minor and Hindustan. The extraordinary symptoms produced by the latter depend on a resinous secretion with which it abounds and which seems totally absent in the European kind. As the closest physical resemblance or even identity exists between both plants, difference of climate seems to me more than sufficient to account for the absence of the resinous secretion, and consequent want of narcotic [sic] power in that indigenous in colder climates.

The obvious difference in resin content noted by O'Shaughnessy is accurate but cannot be explained simply as a product of differing climate or nurture. Variations in resin content result from a coevolutionary blend of nature (the genetic programming of NLD biotypes to make THC and the adaptation of *C. indica* to warmer subtropical climates) and nurture (the growing of NLD cultivars at latitudes favoring resin and THC production). Egyptian and Arab physicians lived in much closer proximity to the home of potent NLD *Cannabis* and were likely familiar with it early on.

A prime example of *Cannabis* use in Arabic medicine involves hemp seed oil, which was commonly administered externally as ear drops. Arab medical treatises dating from the ninth to the thirteenth centuries CE also recommended using the juice expressed from fresh female inflorescences containing immature seeds in various ways. Recommendations included their use to treat ear discomforts and skin disease, kill intestinal worms, relieve flatulence, purge poisonous humors from many parts of the body, ease uterine contractions and hardening, sooth neurological pain, lower fevers, control vomiting, and kill lice (see Russo 2007; Lozano 2006; Hamarneh 1972; Lozano Cámara 1990).

Abubakr Muhammad Ibn Zakaria Razi (lived 865 to 925 CE), known in the West as Rhazes and regarded as "one of the greatest physicians Islam has ever produced" (Daghestani

1997), provided us with a detailed description of therapeutic *Cannabis* use. Medicinal use of *Cannabis* is also referred to in other ancient Arabic and Persian medical works such as *Firdous-usul-Hikmat* and *Mujardat Quanan* (Dwarakanath 1965; also see *Al-Mukhtar* by Muhadhahab Al-Deen Al-Baghdadi, lived 1117 to 1213 CE). Lozano (2006) in his recent study of *Cannabis* in Arabic medicine came to the conclusion that Arab scientists were centuries ahead of our current knowledge of its curative powers. By medieval times, medicinal potions containing *Cannabis* were apparently popular in Arabia, Persia, and Muslim India. According to Benet (1975, citing Dragendorff 1898), medieval Arab physicians referred to hemp as *schahdanach*, *schadabach*, or *kannab*, which they regarded as a "sacred medicine." *Cannabis* was used in Arabia and Persia during medieval times as a diuretic to increase urine flow, an emmenagogue to stimulate blood flow to the pelvis and uterus, and an anthelmintic to expel intestinal worms (Levey and Al-Khaledy 1967). Medieval Arabs also knew and used *Cannabis* for its antiemetic, antiepileptic, anti-inflammatory, and pain-killing effects, among others, and for this reason, Lozano (2006) recommended that information regarding medicinal efficacy of *Cannabis*, which may "be found in Arabic literature could be considered as a possible basis for future research on the therapeutic potential of cannabis and hemp seeds." According to Levey and Al-Khaledy (1967), in more recent Arabic medical practice, *Cannabis* is still considered to be useful as a retentive, anesthetic, and astringent, all curative powers not alluded to in the Greco-Arabic treatises.

Remarkable physical evidence for ancient medicinal *Cannabis* use in the Near East was found at the town of Beit Shemesh, Israel, between Jerusalem and Tel Aviv. Archeologists excavating a fourth-century CE late-Roman-period tomb uncovered the skeleton of a girl about 14 years old, which contained in its pelvic area the skeleton of a fetus of a size that would complicate delivery (Zias et al. 1993). A small amount (6.97 grams, or one-quarter ounce) of a dark-colored burnt substance was found in the abdominal area of the skeleton. Initially thought to have been incense, analysis by Israeli police and botanists at Hebrew University determined that the ancient material is a mixture of *Cannabis* resin (hashish), dried seeds, fruits, and a common reed (*Phragmites*). Direct evidence of ancient drugs themselves is rare because most organic compounds decay rapidly. However, this substance was preserved because it had been carbonized through burning, and thus the relatively stable cannabinoid Δ^8 -THC (Δ^6 -THC) could be identified (Zias et al. 1993). Archeologists who uncovered this evidence believe the *Cannabis* was used as an aid in childbirth since it increases the strength and rate of recurring contractions during labor. *Cannabis* was commonly used in deliveries well into the nineteenth century, after which newly developed drugs replaced it. However, others have disagreed with the strict medicinal use hypothesis (Pioreschi and Babin 1993), arguing that ritualistic use cannot be discounted. Again, we have evidence that may be explained by both *Cannabis*'s direct medicinal efficacy as well as its use in a ritual context.

It should be noted here that ethnobotanists working in the Rif Mountains, the northern zone of Morocco, have recorded the use of *Cannabis* in at least two separate herbal preparations associated with abortion applications (Merzouki et al. 2000). In addition to *Cannabis*, these preparations generally contain known toxic plants. Based on their methodical survey, Merzouki et al. (2000) indicated that such remedies "were commonly used to treat different

ailments because many communities and villagers live in remote areas where health facilities are not available." Their ethnomedicinal research in the Rif region since 1992 also documented customary *Cannabis* use to treat various ailments (e.g., see Merzouki et al. 1999; Merzouki and Molero Mesa 1999) but without any record that *Cannabis* has direct abortive effects. However, abortion could be provoked when preparations included one or more variably toxic plants, and since *Cannabis* does not induce uterine contractions, it was likely included for pain relief. Merzouki et al. (2000) also referred to Mathieu and Maneville (1952), who pointed out that in Casablanca a decoction including *Cannabis* leaves was administered orally to produce abortion.

African and South American Medicinal *Cannabis* Use

Although historical references to recreational and ritual *Cannabis* use in Africa are relatively sparse, and those concerning medical use are even more rare, it is likely that awareness of the medicinal values of *Cannabis* developed soon after it arrived in the region, and additional medicinal uses for *Cannabis* were discovered as it was disseminated across Africa and into the New World (see earlier discussion regarding medicinal use of *Cannabis* in Morocco, as well as Chapters 4 and 7). Hewat (1906) referred to a Sotho herbalist in South Africa who eased childbirth by "getting his patient stupefied by much smoking of *dagga* [*Cannabis*]," and Du Toit (1980) described similar facilitation of birthing, saying that "pregnant women were given *dagga* to make them brave" and avoid pain in the process (also see Watt 1961 and Russo 2002, 2006). According to Watt and Breyer-Branwijk (1932), women of the Sato tribe smoked *Cannabis* to numb themselves during childbirth, and the "Hottentots," more correctly known as the Khoikhoi ethnic group associated with a pastoral culture and language found across southern Africa, made a drink from *Cannabis* leaves to use as a strong laxative and for inducing abortion. *Cannabis* has also been used in South Africa to combat malaria, blackwater fever, blood poisoning, anthrax, and dysentery (cf. Du Toit 1980).

Remedies also developed after *Cannabis* was introduced to several areas in the New World (see Chapter 4). According to Forster (1996), medicinal use of "both hemp and marijuana varieties" of *Cannabis* occurs in Latin America with separate listings in regional ethnopharmacopoeias "indicating that they are considered to be distinct herbal entities" (from our perspective, these "entities" can be grouped into *C. sativa* narrow-leaf hemp, or NLH, and *C. indica* narrow-leaf drug, or NLD). In Chile, Forster (1996) referred to use of hemp (*cañamo*) roots as a purgative, and stems and seeds combined in an infusion used to induce sleep. He also reported that a drink prepared with a relatively small amount of *Cannabis* is used as an all-purpose pain reliever to curtail convulsions, reduce rheumatism, and treat urinary problems. People in Chile apply a plaster of ground up fresh *Cannabis* flowers to body parts experiencing "cold humors" as a blood purgative. The medicinal use of psychoactive *Cannabis* (*hierba*, *hierba mala*, *hierba buena*, or *marijuana*) was formally extensive, especially in tinctures produced by "mixing 20 grams [about three-quarter ounce] of dried flowering tops with 90 proof [45 percent] alcohol and soaking for 15 days," after which the liquid was filtered through a cloth or paper. The resulting tincture of *Cannabis* was diluted in water and soaked into

compresses applied to the body to reduce headaches and neuralgia. Because of the strong traditions of herbal healing in Latin America, Forster (1996) also indicated that many Chilean physicians "support its reappearance as an effective and socially acceptable medicine."

According to Kabelik et al. (1960), *Cannabis* has been used in Argentina to treat depression, tetanus, colic, stomachache, swelling of the liver, gonorrhoea, sterility, impotency, tuberculosis, and asthma. Colombians also use *Cannabis* for medicinal purposes. For example, Partridge (1975), in his study of a community located at the base of the western slopes of the Sierra Nevada de Santa Marta in Colombia, recorded the use of *Cannabis* soaked in "rum or *aguardiente*" and rubbed into the skin to relieve joint and muscle pain. Partridge also listed *Cannabis* smoking as a part of a "program of health maintenance," use of green hemp leaves "crushed and rubbed on the skin for treatment of pain," and feeding boiled water containing *Cannabis* and raw sugar "to infants for excessive crying."

In northeastern Brazil, an infusion of *Cannabis* leaves and water is consumed "to relieve rheumatism, female troubles, colic and other common complaints," and for toothache, parts of the plant are "packed into and around the aching tooth and left for a period of time, during which it supposedly performs an analgesic function" (Hutchinson 1975; de Pinho 1975). In Jamaica, many people "across socioeconomic lines" have used tonic drinks and pain-relieving salves containing *Cannabis* for "medicinal or prophylactic purposes" (Comitas 1975; see also Rubin and Comitas 1975).

European Medicinal *Cannabis* Use

Ritual Scythian *Cannabis* use was documented by the Greek historian Herodotus in the fifth century BCE, but there is no mention of hemp in the writings of Hippocrates and his followers, indicating that the medicinal use of *Cannabis* had not reached Greece by that time (Butrica 2006; Stefanis et al. 1975). However, by the first century CE, the Greek physician Dioscorides had referred to the medicinal uses of *Cannabis*. Dioscorides marshaled information dealing with medicinal herbs and compiled one of the earliest pharmacopoeias, the *Materia Medica*, published ca. 65 CE. Therapeutic *Cannabis* is among several hundred medicinal plants and their uses he described. Dioscorides listed *Kannabis emeros* (females) and *Kannabis agria* (males) as separate entities, indicating that *Kannabis emeros* could be used to relieve earaches and induce menstrual flow, and that *Kannabis agria* could be used to relieve muscular ailments.

The Roman scholar Pliny the Elder (lived 23 to 79 CE) provided informative accounts of the uses of many plants in his *Historia Naturalis*, completed in 77 CE and dedicated to Emperor Titus. He referred to a number of medicinal uses of *Cannabis*, informing us that the "seed is said to extinguish men's semen," that hemp seed oil "casts out ear-worms and whatever animal has entered," and that the root cooked in water "softens contracted joints, likewise gout and similar attacks" and "uncooked it is spread on burns" (Butrica 2006; also see Stefanis et al. 1975).

Galen, the famed second-century CE Roman physician of Greek ancestry, mentioned *Cannabis* in at least three passages, which are described and discussed by Arata (2004). In one passage (*De alimentorum facultatibus* 6: 549–50), Galen referred to the use of hemp seed as "difficult to digest and gives pain to the stomach and to the head and spoils

humours [certain allegedly important bodily fluids]." Galen also pointed out that seeds were eaten by some people for pleasure during a meal but claimed that eating too many will send heat to the head as well as induce "pharmaceutical fumes." This description of the effects of consuming *Cannabis* seeds is echoed by Oribasius (fourth century CE), a Greek author of medical literature and personal physician of the Roman emperor Julian, as well as by Aëtius Amidenus (late fifth to early sixth centuries CE). The latter was a Byzantine physician who referred to the use of *Cannabis* "fruit," putting less emphasis on the alimentary use of *Cannabis* but adding in this context "that it does not help the formation of gas." Oribasius and Aëtius studied in Alexandria, in what is now Egypt, and both also noted that *Cannabis* "is so desiccating that, if eaten in a rather large quantity, it dries male seed" (Arata 2004; also see Withington 1894), essentially repeating what Galen reported earlier in his *De simplicium medicamentorum temperamentis ac facultatibus*. Indeed Galen repeated the evaluations of Dioscorides and Pliny "that some people, pulling out the juice from it when it is not ripe, use it against ear pains due to an occlusion" (Arata 2004).

Hemp seed oil is expressed from mature seeds and does have medicinal properties of its own, especially in topical and dietary applications due to its high EFA contents. Cannabinoids are not produced in hemp seeds, but a series of ancient Greek and Roman remedies were based on a "juice" or infusion of the immature seeds along with the fresh female inflorescences. The infusion was made by chopping up fresh *Cannabis*, adding it to hot water, wine, and other liquids, and then steeping it for several days (Butrica 2006). This "juice" may have been rich in cannabinoids that could account for the efficacy of early *Cannabis* medicines. According to Arata (2004), the obvious conclusion based on the references to the attributes of "seeds" or "fruits" of *Cannabis* by Galen, Oribasius, and Aëtius, especially to their "desiccating power," is its effective use in treating certain ailments. For example, the ancient Greeks and Romans used *Cannabis* "to cure gonorrhoea and epistaxis" (the latter being an acute hemorrhage from the nostril, nasal cavity, or nasopharynx). Arata also listed a third condition that Galen attributed to *Cannabis* in his *De Victu Attenuante*, which states that eating too many hemp seeds will be "painful for the head" (*kephalalgês*), in other words, causing "cephalalgia." In sum, we suggest that despite the Roman's well-known familiarity with fiber hemp, there is little or no evidence to indicate that early Europeans had medicinal uses for *Cannabis* other than those few learned from the Egyptian medicinal tradition via Greeks and Romans.

Nevertheless, in parts of pre-Christian Europe, *Cannabis* apparently was used therapeutically before and perhaps to some extent after the spread of medicinal knowledge about hemp from early Mediterranean civilizations. Shimwell (2005, citing Rättsch 2001) claimed that *Cannabis* was used in some European regions during this period "for ear ailments, to induce an ecstatic state, for frostbite, herpes, nipple pains, stiffness, swelling and wounds." We can be more certain that *Cannabis* was part of Eastern European medical traditions. Benet (1975), for example, tells us that in Poland, Russia, and Lithuania, toothache was alleviated by inhaling the vapor from hemp seeds thrown on hot stones (see Biegeleisen 1929), much in the same fashion as the Scythians made their "vapor baths" more than two millennia ago. Benet (1975, 1936) provided other traditional uses of medicinal *Cannabis* in Eastern Europe such as its use to treat fevers

in Czechoslovakia, Moravia, and Poland; mixing hemp flowers with olive oil to dress wounds in Poland; and combining hemp flowers with hemp seed oil to treat jaundice and rheumatism in Russia. In addition, Benet (1975) referred to Simon Syrenius (lived 1540 to 1611 CE), a pre-Linnean Polish scholar interested in plants who published a huge botanical atlas (five volumes, 1,540 pages) describing 765 species. Syrenius noted that an ointment containing *Cannabis* resin could be used as an effective remedy for burns and indicated that ailing human joints could be cured with roots of hemp boiled in water. Furthermore, Benet (1975) tells us that during the sixteenth century CE, "Szyman of Lowic" provided a Polish prescription for removing "worms in the teeth." This involved boiling hemp seeds in a fresh pot by adding heated stones and then inhaling the vapors, which is similar to a Ukrainian folk medicine tradition based on belief that fumes of cooked hemp porridge will "intoxicate the worms and cause them to fall out" (see Chapter 9 for a lengthy discussion of the ritualistic traditions of *Cannabis* use, many of which are probably reflections of therapeutic use, especially in Eastern Europe).

Cannabis was probably brought into the British Isles during Roman times (Godwin 1967a/b). Although there is some evidence that it might have been introduced much earlier, hemp only became important as a principal fiber crop after the Romans invaded. In any case, *haenep* (Old English name for hemp) developed into a widely cultivated fiber crop subsequent to the arrival of the Roman legions and their colonial development of Britain. Exactly when medicinal preparations made from *Cannabis* came into use is unclear, but it is said to have become useful for therapeutic purposes in medieval times. For example, it is referred to as an anesthetic in an eleventh-century "Anglo Saxon Herbarium," and it is claimed that parts of the hemp plant, especially roots and seeds, were utilized in medieval Europe to treat pain associated with gout, weight loss, swelling of the head, urinary infections, and birthing problems (Frankhauser 2002; also see Shimwell 2005, citing Pollington 2000; Emerson 2002; Le Strange 1977). The roots of *Cannabis* "have received little research attention in recent decades" (Russo 2007); although we know they do not produce cannabinoids, they do generate terpenoids, sterols, and alkaloids (Sethi et al. 1977; ElSohly et al. 1978), which may explain their past and present use in some medicinal traditions.

In medieval Scotland, hemp cultivation for fiber and medicine was important in some areas, particularly near fishing communities where hemp fiber was used to make nets, ropes, and sails for fishing boats (e.g., see Dingwall 2003). Besides the old place names that reflect the former significance of hemp farming (e.g., Hemphill in Kilmarnock Parish, Aryshire; Hempland in Torthowald, Dumfriesshire; Hempriggs in Wick, Caithness; and Hemp Shot in Oldhanstocks, East Lothian), some record of use of *Cannabis* for fiber or medicine in medieval Scotland can be found in the history, archeology, and archaeobotany associated with the "religious hospitals" and monastic houses of the region (e.g., see Donaldson 1960). It appears that hemp was commonly grown around these ancient institutions for easy access to the plants for fiber and medicinal use (e.g., see Moffat and Fulton 1989 for evidence from the long-running excavation of the hospital at Soutra Mains in Scotland near the border with England and Whittingham and Edwards 1990, who discuss the archaeobotany and history of hemp farming and use of hemp in Scotland).

Among the more remarkable medieval Europeans to discuss the medicinal qualities of *Cannabis* was Hildegard von Bingen (lived 1098 to 1179 CE), the twelfth-century visionary Benedictine abbess of Rhineland, whose contributions to art, literature, linguistics, science, philosophy, poetry, music, herbalism, and medicine are testament to her considerable interest in many fields (von Bingen 2002 [English translation]; also see Hozeski 2001; Throop 1998; Strehlow and Hertzka 1988; Anderson 1977). One of her many works was called "Subtleties of the Diverse Qualities of Created Things," which was produced between 1151 and 1158, and later named *Physica*, or "Medicine" (also known as the "Book of Medicinal Simples"), in the 1533 edition. In *Physica*, von Bingen lists basic qualities of plants and their uses—in other words, are they "hot" or "cold," "dry" or "moist"—and asks if these dualities can be balanced to cure patients. She then expounds on the relative medicinal importance of each and explains how to concoct and apply the medical potion she recommends. Regarding the therapeutic use of *Cannabis* seeds, von Bingen comments at length:

Hemp (*hanf*) is hot, and it grows where the air is neither very hot nor very cold, and its nature is similar. Its seed is salubrious, and good as food for healthy people. It is gentle and profitable to the stomach, taking away a bit of its mucus. It is easy to digest, diminishes bad humors, and fortifies good humors. Nevertheless, if one who is weak in the head, and has a vacant brain eats hemp, it easily afflicts his head. It does not harm one who has a healthy head and full brain. In one who is very ill, it even afflicts his stomach a bit. Eating it does not harm one who is moderately ill. Let one who has cold stomach cook hemp in water and, when the water has been squeezed out, wrap it in a small cloth, and frequently place it, warm on his stomach. This strengthens and renews that area. Also, a cloth made from hemp is good for binding ulcers and wounds, since the heat it has been tempered. (Translation by THROOP 1998, following the Schott edition based on the 1533 original *Physica*)

The use of medical *Cannabis* was significantly affected following the Papal Bull of Innocent VIII in 1484 in which an association between herbal healers practicing "witchcraft" and *Cannabis* was asserted; this characterized hemp medicine as "an unholy sacrament of satanic rituals" (Frankhauser 2002) and consequently drove its use underground, only to be "resurrected under a pseudonym" in François Rabelais's *Gargantua et Pantagruelion* in the mid-sixteenth century (Booth 2003; Russo 2004).

In his seventeenth-century CE book on plants and their uses, *Theatrum Botanicum*, John Parkinson (1640) described a series of medicinal uses of "hempe," including how the Dutch made an emulsion of the seeds to alleviate several ailments including obstructions of the gall bladder, pains associated with colic, and bowel problems. Parkinson also referred to a decoction of the roots that was said to reduce inflammations in the head or other parts of the body, relieve pain from gout, help cure hard tumors and joint irritations, and lessen swellings of the "sinews" and the hips, and, if mixed with a little oil and butter, it served as a salve for burned skin.

Nicholas Culpeper (lived 1616 to 1654 CE) was a strong advocate of equal access to inexpensive medication. In 1649, Culpeper produced an unauthorized translation of the London College of Physicians' *Pharmacopoeia*, which made accessible a large amount of medical knowledge previously unavailable to the general public, including a good deal of

plant lore and herbal medicine. This medical compendium was published as a book in 1653 and later became known as *The Complete Herbal* (Wear 2000; Le Strange 1977), and *Cannabis* was one of several hundred medicinally useful plants that Culpeper listed. Although he did not provide a description of hemp, since he viewed it as "so common a plant, and so well known by almost every inhabitant of this kingdom, that a description of it would be altogether superfluous," his widely available herbal ensured that hemp would have "its place in folk medicine as an antiseptic, anti-inflammatory and anti-spasmodic" (Shimwell 2005). Specifically, Culpeper referred to *Cannabis* as therapeutically useful for inflammations, burns, dry coughs, jaundice, colic, bowel trouble, bleeding, eliminating "worms" and insects in the ear, and relief from many painful ailments.

According to Shimwell (2005, citing Holmstedt 1973), hashish was used not only for its visionary psychoactive powers (e.g., the Parisian "Le Club des Hashichins," or "The Hashish-Eaters' Club") but also as a medicinal product, largely because of a paper presented to the Institute of France in 1809 by Baron Sylvestre de Sacy (lived 1758 to 1838 CE), a notable French scholar of Arabic culture and history and professor at the École des Langues Orientales. Baron Sylvestre de Sacy found previously unknown eleventh- and twelfth-century CE chronicles in the Arabic manuscript collection held at the Bibliothèque Nationale and translated them into French. This work helped stimulate new interest in the psychoactive and medicinal potency of *Cannabis* (Booth 2003).

William Brooke O'Shaughnessy studied medicine in India and played a key role in the introduction of medicinal use of *Cannabis indica* or "Indian hemp" to Europe (Walton 1938; Mikuriya 1969). O'Shaughnessy presented his treatise *On the Preparations of the Indian Hemp, or Gunjah* at the Medical College of Calcutta in 1839, where he reported the efficacy of *Cannabis* extracts in patients suffering from rabies, cholera, tetanus, and infantile convulsions (Chopra and Chopra 1957). However, prior to his return from India with samples of potent *charas* (*Cannabis* resin) and knowledge of its medicinal use, some European physicians were using either wild *Cannabis* or cultivated NLH (*C. sativa*) growing in Europe, yet both of these sources were likely very low in cannabinoids. This could explain why hemp remedies in Europe employed since the Classical Age were quite limited in their scope and emphasized the use of hemp seed and seed oil rather than extracts of *Cannabis* flowers and resin favored in later preparations. Once there was a steady supply of potent NLD *Cannabis indica* from British India, its medicinal use in a wide range of packaged remedies increased significantly.

Previous to its relatively widespread introduction to Western Europe, stimulated by the work of Sylvestre de Sacy in France and O'Shaughnessy in Britain, one of the more common medicinal products of *Cannabis* was a "pharmaceutical preparation, or 'electuary' . . . taken in the form of a greenish paste" (Shimwell 2005 citing Holmstedt 1973) similar to Indian *majoon* (see Chapter 7). In England during the nineteenth century, medicinal *Cannabis* preparations became available in tinctures, pills, and extracts, which were utilized to reduce or soothe the pain by lessening the sensitivity of the brain or nervous system, as well as for relief from spasms and inflammations.

In 1899, the well-known British pharmacologist Walter Ernest Dixon (1899) published a paper on "the pharmacology of *Cannabis indica*," which described his extensive research; he concluded that *Cannabis* was pharmacologically useful as



FIGURE 48. Several *Cannabis* varieties were used in popular late nineteenth- and early twentieth-century medicines such as an Eli Lilly tincture made from American-grown narrow-leaf drug (NLD) *Cannabis* (right), a British Drug House tincture of Indian-grown NLD *Cannabis* (center top), and a Seabury's Corn Plaster (bottom left). Present-day prescription *Cannabis* drugs include Sativex sublingual spray (center), containing a blend of THC from a hybrid NLD/BLD drug cultivar and CBD from a narrow-leaf hemp (NLH) cultivar, both grown in the United Kingdom. Marinol capsules (bottom right), known as the "pot pill," contain synthetic THC in sesame oil. Chinese "Ma Ren Wan" pills (left) are made from broad-leaf hemp (BLH) seeds and stimulate digestion (from the collection of David Watson, HortaPharm BV, Netherlands).

a "food accessory." As Russo (2002) has pointed out, Dixon's insightful suggestion was a forerunner of the modern usage of *Cannabis* to alleviate symptoms of weight loss, muscle atrophy, fatigue, weakness, and significant appetite loss associated with cancer chemotherapy and HIV-positive patients. In addition, Dixon refocused attention on smoking medicinal *Cannabis*: "In cases where an immediate effect is desired the drug should be smoked, the fumes being drawn through water. In fits of depression, mental fatigue, nervous headache, and exhaustion a few inhalations produce an almost immediate effect, the sense of depression, headache, feeling of fatigue disappear and the subject is enabled to continue his work, feeling refreshed and soothed. I am further convinced that its results are marvelous in giving staying power and altering the feelings of muscular fatigue which follow hard physical labour [sic]" (quoted in Russo 2002b).

During the same year, Shoemaker (1899) reported on a large series of patients who were all effectively treated for painful conditions including "migraine, dental neuralgia, gastralgia, enteralgia, cerebral tumor and herpes zoster" (Russo 2002b).

Although some physicians emphasized the value of medicinal *Cannabis* during the middle of the nineteenth century, it does not appear to have been used extensively. Shimwell (2005) indicates that the use of medicinal *Cannabis* may not always have been looked upon favorably during this period: "Serious flaws, such as unreliability in strength and effect of the drug, the inability to obtain quality and regular supplies of the drug and the stigma that was associated with it were responsible for limited use." Nevertheless, in 1883, two letters to the *British Medical Journal* attested to benefits of an extract of *Cannabis indica* for treating menorrhagia, an abnormally heavy and prolonged menstrual period, with both the

associated pain and bleeding successfully reduced with a few doses (Batho 1883; Brown 1883; also Reynolds 1879).

A short, late nineteenth-century editorial titled "Cannabis Indica" from the *Medical and Surgical Reporter*, published in New York, informs us that

this drug, the most active of non-opiate anodynes or soporifics, which was very popular years ago, although little the fashion at present, is deserving of a large share of professional favor. The principal cause which led to its disuse was fear of its toxic power though there has never been a case of poisoning recorded from its use. Its effect on the system is most marvelous. It causes sleep, overcomes spasms, relieves pain and all nervous irritability, and that too within a few moments after administration. Its soothing and curative effects upon the nervous sympathetic system are great, and there is no one agent that will restore the equilibrium of nerve motion more quickly. The placidity of repose that is produced by this narcotic [sic] is rapid and to the point. Further, it does not check secretion or tend to constipation. It does relieve fatigue and arouse vital action, and can and should be given freely until the effect desired is apparent. (KYNETT 1895)

Throughout the latter half of the nineteenth century, a number of prominent physicians in Europe and North America advocated use of extracts of *Cannabis indica* for several ailments, and *Cannabis* was included in the mainstream pharmacopoeias of Britain and America. An example is common use of *Cannabis* in treatment of migraine headaches. In 1915, Sir William Osler, famous English physician and acknowledged father of modern medicine, referred to *Cannabis* as perhaps the best remedy for severe headache treatment. According to Russo (1998), this in turn stimulated physicians in Europe as well as North America to acknowledge efficacy of *Cannabis* in remedies for restlessness, insomnia, and pain, such as that produced by menstrual migraine: "*Cannabis*, or marijuana, has been used for centuries for both symptomatic and prophylactic treatment of migraine. It was highly esteemed as a headache remedy by the most prominent physicians of the age between 1874 and 1942, remaining part of the Western pharmacopoeia for this indication even into the mid-20th century."

Most contemporary doctors are not cognizant of the important former status of *Cannabis* drugs in medical practice; indeed most "remedies fall in and out of favor" with their popular use, rarely exceeding a few decades, and once they are replaced by more popular or easily available remedies, most "fail to re-attain a position of prominence" (Russo 1998). In the case of medicinal *Cannabis*, this remains to be seen. If the recent upsurge of its use is any indication of efficacy, growing acceptance of its valid therapeutic use will rise even more significantly.

Present-Day Western Medicinal Applications of *Cannabis*

To some it's the classic "gateway drug," to others it is a harmless way to relax, or provide relief from pain. (BOOTH 2003)

Cannabis medicines were prescribed for a variety of medical indications throughout the early twentieth century, though on a more limited level than during previous centuries. In 1937, the Marijuana Tax Act was enacted, and in 1941,

Cannabis preparations were dropped from the United States Pharmacopoeia. Two decades later, in the 1960s, an exponential increase in recreational use of marijuana moved *Cannabis* to the forefront of Western consciousness, eventually reaching a level of notoriety sufficient to discourage almost all legal medicinal use of this age-old and, for countless patients, venerable herb. However, medical research involving *Cannabis* resumed recently, stimulated by "anecdotal reports of patients who serendipitously discovered its benefits" (Russo 1998). In an attempt to dampen newly reinvigorated medicinal interest in herbal *Cannabis*, the US Supreme Court declared medical use of *Cannabis* illegal on the federal level in June 2005, although as of early 2013 its use had been allowed in 18 states and the national capital.

As we outlined earlier, medical use of *Cannabis* has a long association with humans and subjective evidence for its efficacy is plentiful; furthermore, interest in medicinal efficacy of *Cannabis* has been rekindled as commercial interest in plant-based natural medicines increases. During the last decade of the twentieth century public interest in benefits of medicinal *Cannabis* grew exponentially from the knowledge of a limited few to widespread use for largely illicit self-medication in both North America and Europe. As awareness of its medicinal values spread, many patients frustrated by the ineffectiveness of accepted medications tried *Cannabis* for the first time and felt immediate relief from their persistent symptoms. Many more began to realize that their satisfaction with recreational *Cannabis* use lay in part in its ability to mediate long-term psychological and physical conditions. It should be pointed out that although *Cannabis* is a powerful medicine, enabling patients to relieve a wide variety of discomforts and improve their quality of life, it has not as yet been shown to "cure" any medical condition. This situation proves important in the context of the modern pharmaceutical business where single compound "silver bullet cures" are more patentable, profitable, and fundable than whole herbs and plant extracts, although historically plants have proven effective in treating symptoms and improving the quality of life of the sick and dying.

At the federal level in the United States, the only legally available *Cannabis* medicine is synthetic THC called dronabinol in the oral dosage form, and trade-named Marinol. Although approved for sale in 1985, for many people Marinol is not patient-friendly, and it is not easy to titrate dosage as with smoked or vaporized *Cannabis*. Sales of Marinol and Nabilone (a synthetic compound that mimics the action of THC) exceeded US\$110 million in 1995 and have increased steadily each year since then. Total Marinol sales in the US were about \$190 million in 2008 (Par Pharmaceutical 2008), and worldwide sales of Nabilone in 2009 were nearly \$50 million (EvaluatePharma 2013). When humans consume *Cannabis*, Δ^9 -THC and its liver metabolite 11-*hydroxy*-THC activate cannabinoid (CB) receptors found throughout the brain and body, resulting in various physiological and psychological responses. For example, when Δ^9 -THC is inhaled, it passes from the lungs into the bloodstream, directly to the brain, and then slowly back through the circulatory system to the liver. The liver then converts Δ^9 -THC into 11-*hydroxy*-THC. On the other hand, when Δ^9 -THC is swallowed, it is absorbed by the gastrointestinal tract and makes a first pass through the liver, where it is converted to 11-*hydroxy*-THC, and then the 11-*hydroxy*-THC enters the bloodstream and is carried to the brain (see Chapter 7). 11-*hydroxy*-THC is considerably more potent and long lasting, and it produces

more unpleasant side effects than Δ^9 -THC. Since the potency and effects of Δ^9 -THC and 11-*hydroxy*-THC differ greatly, so do the clinical effects of the two routes of administration. As a result, the vast majority of medicinal *Cannabis* users in Europe and North America self-medicate by smoking illegally obtained, black market marijuana rather than pursuing legal relief through a pharmacy. In the United States, 17 states as well as Washington, DC, have, over the six years between 1996 and 2012, legalized or decriminalized medical *Cannabis* use. These are Alaska, Arizona, California, Colorado, Delaware, Hawai'i, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Virginia, and Washington. Several now allow the cultivation of limited amounts of *Cannabis* for medicinal use under a wide variety of localized restrictions.

Since the 1970s, modern North American and European hybrid drug *Cannabis* varieties have been developed, largely by clandestine breeders from crosses between South Asian NLD varieties (that spread early on throughout South and Southeast Asia, Africa, and eventually to the New World), and more recently Central Asian broad-leaf drug (BLD) hashish varieties have been spread widely (see Chapters 4 and 10). In Western societies, recreational *sinsemilla* varieties are commonly used with great efficacy as medicinal *Cannabis*. The primary cannabinoid contained in the vast majority of Western recreational and medicinal *Cannabis* varieties is THC. These varieties usually contain only small amounts of CBD, owing to their predominantly NLD heritage as well as selective breeding for psychoactive potency with increased levels of THC and reduced levels of CBD. In addition to THC and CBD, *Cannabis* produces a myriad of other secondary metabolites, including more than 60 minor cannabinoids and well over 100 terpenoids (Turner et al. 1980). Terpenoids are the primary ingredients in the essential oil of *Cannabis* and are largely responsible for the fragrances associated with different varieties. It is possible that the diverse chemical components in *Cannabis* account for the wide range of psychoactive and therapeutic effects produced by the consumption of various cultivars. In fact, *Cannabis* is considered to be a synergistic medicine by some herbalists, containing primary pharmaceutically active compounds (e.g., THC and CBD) along with many other secondary compounds (e.g., auxiliary cannabinoids and terpenoids) that both enhance the effects of a primary pharmaceutical compound and mitigate its side effects (e.g., see Russo 2011; McPartland and Russo 2001).

Cannabis consumers often associate individual varieties with particular mind and/or body effects as well as differing levels of medical efficacy for certain illnesses. Some medical users often consider varieties with a certain flavor to express similar medicinal effects (e.g., "skunky" smelling varieties are often sedative). These variations can likely be attributed to the auxiliary cannabinoids if present (e.g., CBD and CBN), some of the myriad terpenoids, and possibly other classes of secondary metabolites such as flavonoids. Comparative experiments with THC vaporized and inhaled alone and with the addition of various terpenes indicate that the synergistic effect of each terpene differs (David Watson, personal communication 2007). Several terpenoid and other trace compounds that modify the action of THC and/or CBD may cause the specific medicinal and/or recreational effects associated with each cultivar. Synergized therapeutic effects have also been elucidated using whole *Cannabis* extracts versus THC and THC + CBD versus THC. Cannabinoids act as partial agonists of CB receptors so that they produce more

subtle effects than full agonists and are also less likely to cause tolerance. Medical *Cannabis* users come to realize that they develop tolerance to its minor side effects while developing little if any tolerance to its therapeutic benefits (McPartland and Guy 2004a/b). More biochemical and pharmaceutical research is needed to address these issues.

CBD is nonpsychoactive but produces powerful anticonvulsant and anti-inflammatory effects. CBD has also been shown to attenuate and prolong the effects of THC (Musty 2004). Increased ratios of CBD to THC may prove clinically valuable in reducing anxiety and other unpleasant side effects occasionally experienced with THC while extending the effectiveness of each dose. Terpenoids have been shown to affect CB and other receptors. Terpenoids also alter cannabinoid pharmacokinetics by dilating bronchial capillaries and increasing blood-brain barrier permeability, allowing more THC to reach the brain more quickly (McPartland and Russo 2001; McPartland and Guy 2004a/b). The entire terpenophenolic biosynthesis mechanism (producing both cannabinoids and terpenoids) may have been under positive selection by humans because of two factors: first, terpenoid molecules are required as substrate for cannabinoid biosynthesis, and second, THC is much more effective in the presence of certain associated terpenoid compounds that are biosynthetically similar. Phytocannabinoids stimulate the central nervous system through the human CB1 receptor, but they also stimulate CB2 receptors throughout the body and modulate the immune system. THC also enhances the effects of the opioids, secondary metabolites of the opium poppy—another important medical plant with a long history (Merlin 1984; Russo 2004). Relief of glaucoma symptoms; control of vomiting; and protection of the brain, retina, and nervous system from toxic stresses have also been proven to be effected favorably by cannabinoids.

GW Pharmaceuticals Ltd. in the United Kingdom, continuing the pioneering work of HortaPharm BV in the Netherlands, is developing *Cannabis* varieties that produce only one of the four major cannabinoid compounds (e.g., THC, CBD, CBC, CBG, or their propyl homologs), as well as varieties with consistently uniform mixed cannabinoid and terpenoid profiles. In 1999, GW Pharmaceuticals began clinical trials of a *Cannabis*-based medicine aimed at relieving multiple sclerosis-associated neuropathic pain and spasticity. An oromucosal spray trade-named Sativex with a plant-derived combination of 50 percent THC and 50 percent CBD, has been approved for sale in Canada, the United Kingdom, and Spain and should be approved in the United States in the near future. In addition, plant preparations and extracts delivered through vaporizing or nebulizing (fine spray) devices often offer medicinal efficacy similar to that of smoking *Cannabis* without subjecting the patient to the potentially harmful products of combustion.

Continuing experimentation and medical trials with *Cannabis* extracts and isolated cannabinoid compounds as well as improved delivery systems should return *Cannabis* to the front line of remedies for a variety of indications. In the meantime, patients will largely continue to self-medicate with *Cannabis*, appreciative of the relief they receive, and well aware of the legal risks they often take. For a challenging discussion of the medical value of *Cannabis* in light of its largely illegal status, see Grinspoon and Bakalar (1997). Given the quite lengthy history of *Cannabis* use for pain relief and a wide variety of other medical problems, its future therapeutic utilization seems highly warranted (e.g., see Russo 2001,

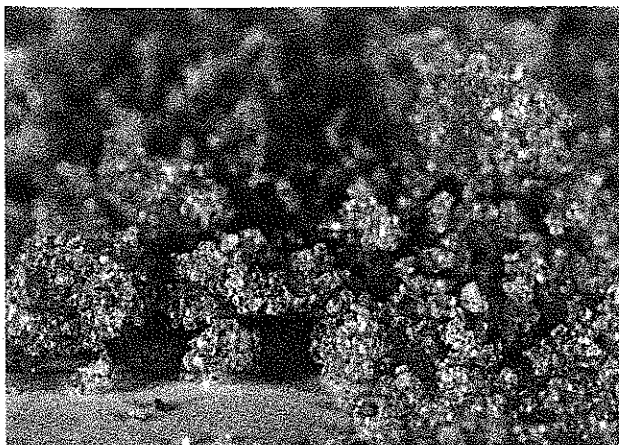


FIGURE 49. Resin glands can be collected from dried female flowers and mechanically isolated to make the purest natural medicinal and recreational *Cannabis* preparations. Each of the tiny transparent gland heads contains aromatic essential oil rich in cannabinoid compounds (photos ©Bubbleman).

2002a/b, 2004, 2011; Russo and Grotenhermen 2006; Guy et al. 2004). It will be difficult for modern pharmaceutical companies to improve on nature's tried and true herbal medicine, and until modern cannabinoid medicines become more available patients will continue to self-medicate with natural herbal *Cannabis*. As Dr. Lester Grinspoon (2007), an emeritus professor of psychiatry at Harvard Medical School, explains,

The pharmaceutical industry is scrambling to isolate cannabinoids and synthesize analogs and to package them in non-smokable forms. In time, companies will almost certainly come up with products and delivery systems that are more useful and less expensive than herbal marijuana. However, the analogs they have produced so far are more expensive than herbal marijuana, and none has shown any improvement over the plant nature gave us to take orally or to smoke. We live in an antismoking environment. But as a method of delivering certain medicinal compounds, smoking marijuana has some real advantages: The effect is almost instantaneous, allowing the patient to fine-tune his or her dose to get the needed relief without intoxication.

It should also be pointed out here that since the mid-twentieth century, hemp seed and its oil also become increasingly recognized as valuable in modern medicinal and nutraceutical applications. For example, in 1955, a Czechoslovakian nutrition study concluded that hemp seed was the "only food that can successfully treat the consumptive disease tuberculosis, in which the nutritive processes are impaired and the body wastes away" (Robinson 1996). Medical uses of hemp seed oil in various regions in the past can serve as models in contemporary societies to successfully treat ear, nose, and throat cases as well as burns and chronic eczema (e.g., see Grigoriev 2002). Modern body care products advertise the emollient effects of hemp seed oil in softening skin. For example, the Fushi Ltd. company based in England, which advertises itself as providing "holistic health and beauty solutions," refers to the polyunsaturated EFAs (linoleic and linolenic acids) in hemp seed oil as balancing dry skin: "It is a non-greasy, emollient and moisturizing compound with excellent anti-ageing and moisture balancing properties" (Fushi Ltd. 2007). EFAs not only help to restore wasting bodies and treat skin

conditions but also may improve damaged immune systems, and researchers are studying them in relation to treating immune system-attacking HIV and reducing the incidence of cancer (e.g., see Leson and Pless 2002).

Zuardi (2006) reviewed the history of medicinal *Cannabis* and pointed out that its relatively widespread use in Western medicine occurred in the middle of the nineteenth century and reached a peak during the last decade of that century with the availability and usage of *Cannabis* extracts or tinctures. Then in the first decades of the twentieth century, use of *Cannabis* in Western medicine decreased significantly mostly because it was difficult to obtain consistent results from plant material that characteristically had variable potencies; this was compounded significantly by the subsequent political and legal pressures against any use of *Cannabis* throughout much of the world. Russo (1998) articulated the situation succinctly: "Problems with quality control and an association with perceived dangerous effects sounded the death knell for *Cannabis* as a recognized Western therapy."

Russo also reminded us that some medicines that potentially produce much more damaging effects than *Cannabis* remain in our pharmacopoeias because of recognized medical efficacy; these include, for example, "opiates for pain control, amphetamines for narcolepsy and attention deficit hyperactivity disorder [ADHD], etc." However, since about 1965, research directed at identifying the chemical structure of *Cannabis*'s components and possibly obtaining its "pure constituents" produced an important boost in *Cannabis* interest among the scientific community. Attention was renewed and greatly accelerated in the late twentieth century with discovery of human cannabinoid receptors and identification of an endogenous cannabinoid system in the brain (e.g., see Devane et al. 1992; McPartland 2004, 2008; McPartland and Guy 2004a).

By 1995 the future of *Cannabis*-based medicines was brightening and cannabinoids were ready to be developed into pharmaceutical rather than political products. Since then there has been a large number of scientific studies to determine the therapeutic benefits and drawbacks of these medicines. Kalant (2001) summarized the history and status of medicinal *Cannabis* use, pointing out that THC and a number of analogs had been shown to offer significant therapeutic benefits in relief of nausea and vomiting, as well as stimulation of appetite in patients with wasting syndrome. He also noted that research "clearly demonstrates analgesic and antispasticity effects that will probably prove to be clinically useful." Kalant argued that "the anticonvulsant effect of cannabidiol [CBD] is sufficiently promising to warrant further properly designed clinical trials" but noted that "a major lack of long-term pharmacokinetic data, and information on drug interactions" remained to be rectified. He emphasized that although "pure cannabinoids, administered orally, rectally, or parenterally [into a vein], have been shown to be effective," smoking medicinal *Cannabis* "might be justified on compassionate grounds in terminally ill patients who are already accustomed to using cannabis in this manner." Kalant called for research that can "yield new synthetic analogs," and these novel products would provide "better separation of therapeutic effects from undesired psychoactivity and other side effects" while having "solubility properties that may permit topical administration in the eye, or aerosol inhalation for rapid systemic effect without the risks associated with smoke inhalation." Five years later, Zuardi (2006) pointed out that a "new and more consistent cycle of the use

TABLE 12

Cannabis produces unique cannabinoid compounds that exhibit a wide range of potentially beneficial psychological and physiological effects.

Phytocannabinoid	Description, occurrence, and effects
Δ^8 -Tetrahydrocannabinol or Δ^9 -THC (Δ^L -THC)	<ul style="list-style-type: none"> • Primary psychotropic ingredient of <i>Cannabis</i>. Primary cannabinoid in marijuana varieties. • Therapeutically used as an antiemetic and to boost appetite in AIDS patients. • A <i>Cannabis</i>-based extract with approx 1:1 ratio of Δ^9-THC and CBD (Sativex) is effective for the symptomatic relief of neuropathic pain in adults with multiple sclerosis and as an adjunctive analgesic treatment for adults with advanced cancer. • Plant-based Δ^9-THC is also used in the generic equivalent of Marinol used in treating AIDS-related anorexia and nausea and vomiting associated with cancer chemotherapy. • Antimicrobial and antifungal. Promising for the treatment of many medical indications.
Δ^8 -Tetrahydrocannabinol or Δ^8 -THC (Δ^6 -THC)	<ul style="list-style-type: none"> • Artifact resulting from isomerization of Δ^9-THC found only in trace amounts in <i>Cannabis</i>. • Pharmacology similar to Δ^9-THC. • Not used medically.
Cannabinol or CBN	<ul style="list-style-type: none"> • Product of Δ^9-THC degradative oxidization resulting largely from postharvest storage found only in trace amounts in fresh <i>Cannabis</i>. • Up to 10 percent of the potency of Δ^9-THC. Not used medically.
Cannabidiol or CBD	<ul style="list-style-type: none"> • Major nonpsychotropic cannabinoid. Commonly produced by hemp and hashish varieties but uncommon in hybrid <i>sinemilla</i> cultivars. • Anti-inflammatory, analgesic, antioxidant, antispasmodic, antiemetic, antipsychotic, antiepileptic, vasorelaxant, immunosuppressive, and neuroprotective actions. • Effective in anxiety, psychosis, and movement disorders and relieves neuropathic pain in patients with multiple sclerosis (in combination with Δ^9-THC as in Sativex). • Protects against diabetes-induced retinal damage. • Beneficial effects on bone formation and fracture healing. • Antimicrobial and antifungal. • Potential use in the treatment of chemotherapy-induced and anticipatory nausea. • Promising for cancer treatment
Δ^9 -Tetrahydrocannabivarin or Δ^9 -THCV	<ul style="list-style-type: none"> • Found in Pakistani hashish varieties. • Antagonizes Δ^9-THC effects in low doses. Antiepileptic and anorectic. • May reduce food intake. • Beneficial effects on bone formation and fracture healing.
Cannabigerol or CBG	<ul style="list-style-type: none"> • Nonpsychotropic. • Antiproliferative, antimicrobial, antifungal, and antibacterial activity. • Beneficial effects on bone formation and fracture healing. • Potential role in analgesia. Promising for cancer treatment.
Cannabidivarin or CBDV	<ul style="list-style-type: none"> • Nonpsychotropic. • Found in Pakistani hashish varieties. • Beneficial effects on bone formation and fracture healing. • Physiological effects poorly understood.
Cannabichromene or CBC	<ul style="list-style-type: none"> • Nonpsychotropic. Along with Δ^9-THC the major cannabinoid in marijuana. • Exerts anti-inflammatory, antimicrobial, antifungal, and modest analgesic activity. • Beneficial effects on bone formation and fracture healing. • Potential role in analgesia. Promising for cancer treatment.
Δ^9 -Tetrahydrocannabinolic acid or Δ^9 -THCA	<ul style="list-style-type: none"> • Naturally occurring form of Δ^9-THC in fresh plants. • Exerts antiproliferative and antispasmodic actions. • Potential role in analgesia and in the treatment of prostate carcinoma.
Cannabidiolic acid or CBDA	<ul style="list-style-type: none"> • Naturally occurring form of CBD in fresh plants. • Exerts antiproliferative action. • Potential role in analgesia, inflammation, and the treatment of prostate carcinoma.

NOTE: Adapted from Izzo et al. 2009.

of *Cannabis* derivatives as medication” had begun with the establishment of effective and safe treatment supported by progressive scientific research. Izzo et al. (2009) reviewed therapeutic opportunities for cannabinoids, concluding that

recent developments suggest that non-psychotropic phytocannabinoids exert a wide range of pharmacological effects, many of which are of potential therapeutic interest. The most studied among these compounds is CBD, the pharmacological effects of which might be explained, at least in part, by a combination of mechanisms of action. CBD has an extremely safe profile in humans, and it has been clinically evaluated (albeit in a preliminary fashion) for the treatment of anxiety, psychosis, and movement disorders. There is good pre-clinical evidence to warrant clinical studies into its use for the treatment of diabetes, ischemia and cancer.

Izzo and his colleagues also referred to a number of other neglected phytocannabinoids such as CBC and CBG, which should be explored for their potential use in pain management.

Russo continues to study the medical history and modern applications of *Cannabis* with some of his most recent research focusing on phytochemicals other than cannabinoids. In his recent review, Russo (2011) explores another stratum of phytotherapeutic *Cannabis* agents—the terpenoids (e.g., limonene, myrcene, α -pinene, linalool, β -caryophyllene, caryophyllene oxide, nerolidol, and phytol). Even though they are regarded as safe by the United States Food and Drug Administration (USFDA) and other regulatory agencies, terpenoids are quite powerful, affecting “animal and even human behavior when inhaled from ambient air at serum levels in the single digits (ng/mL).” Russo argues the *Cannabis* terpenoids can induce distinctive healing effects that could “contribute meaningfully to the entourage effects of cannabis-based medicinal extracts” and “could produce synergy with respect to treatment of pain, inflammation, depression, anxiety, addiction, epilepsy, cancer, fungal and bacterial infections.” He also discusses scientific evidence indicating that noncannabinoid plant components may act as antidotes to intoxicating effects of THC (which might improve its therapeutic value) and suggests a set of experimental methods to investigate the putative “entourage effects” of “phytocannabinoid-terpenoid synergy” in the future. If his thesis is confirmed, it would increase the probability that *Cannabis* will provide a broad array of new healing products: “Selective cross-breeding of high-terpenoid- and high phytocannabinoid-specific chemotypes has thus become a rational target that may lead to novel approaches to such disorders as treatment-resistant depression, anxiety, drug dependency, dementia and a panoply of dermatological disorders, as well as industrial applications as safer pesticides

and antiseptics. A better future via cannabis phytochemistry may be an achievable goal through further research of the entourage effect in this versatile plant that may help it fulfill its promise as a pharmacological treasure trove” (Russo 2011).

Summary and Conclusions

Medicinal *Cannabis* has a long and well documented history across Eurasia reaching back several millennia. *Cannabis* has not been found to cure any illness but is extremely effective in relieving the symptoms of a wide variety of medical conditions. Based largely on anecdotal accounts of its efficacy, *Cannabis* is slowly gaining interest from the pharmaceutical industry.

The original prohibition of cannabis arose from social pressure as much as safety concerns. It is heartening that the scientific evidence on which a rational reappraisal of cannabis as a prescription medicine can be made has been forthcoming. Patients with intractable disease will welcome this. They are often afflicted in their prime, and availability of an effective and safe prescription medicine will, in turn, lead to an improved quality of life. It is also refreshing to see that the derivation of the first prescription medicine based on whole cannabis represent a return to the roots of science—medicinal plants. (ALAN MACFARLANE, forward in Guy et al. 2004)

Lester Grinspoon (2007) recently summed up the medicinal marijuana situation succinctly: “It is a sad commentary on the state of modern medicine that we still need ‘proof’ of something that medicine has known for 5000 years. . . . If marijuana were a new discovery rather than a well-known substance carrying cultural and political baggage, it would be hailed as a wonder drug.”

While the Pharmaceutical industry fights for patient control of new, politically correct preparations and administration devices, the vast majority of medical use remains self-administered—either smoked or eaten herbal preparations—and illegal in most jurisdictions. Eighteen states in the United States have approved medical *Cannabis* use by popular referendum, yet the federal government has failed to recognize it as an effective medicine. Medical *Cannabis* use is here to stay and will likely become much more popular in the near future. For further, in-depth discussions of historical and modern medicinal uses of *Cannabis* and cannabinoids, see, for example, Russo (2011, 2008, 2006, 2004, 2002, 2001, 1998), Izzo et al. (2009), Guy et al. (2004), Earlywine (2002), Fankhauser (2002), Rättsch (2001), Aldrich (1997), and Mechoulam (1986).

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Edited by
Roger G. Pertwee

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Handbook of Cannabis

Edited by

Roger G. Pertwee
Institute of Medical Sciences
University of Aberdeen, UK

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PLAINTIFFS

AND:

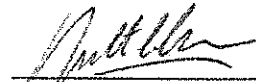
HER MAJESTY THE QUEEN IN RIGHT OF CANADA

DEFENDANTS

CERTIFICATE CONCERNING CODE OF CONDUCT FOR EXPERT WITNESSES


I, Robert C. Clarke, having been named as an expert witness by the Plaintiffs, certify that I have read the Code of Conduct for Expert Witnesses set out in the schedule to the Federal Courts Rules before the commissioning of my Affidavit and agree to be bound by it.

Dated: December 20, 2014



Robert C. Clarke
Expert Witness
International Hemp Association
Postbus 75007, 1070AA
Amsterdam, The Netherlands

This is Exhibit "B" referred to in the Affidavit of Robert C. Clarke sworn before me at La Crescenta, California, USA. this 20 day of December, 2014.



Andrew D. Turner, Calif. Bar No. 121694