

## Chapter 3: Cannabis and Marinol Compared



In the year 2001, there are still many people who doubt or dismiss reports of Cannabis' medical utility and safety. Nevertheless, one quick glance at Dr. Tod Mikuriya's International Classification of Diseases, (ICD) table shows the vast number of medical conditions that have been treated with Cannabis. Some investigators and researchers

argue that including these conditions is not based on randomized and controlled clinical trials, but "self-reports" that are scientifically suspect.

The use of Cannabis as medicine has rarely been based on detailed clinical investigation of unique medical indications. It is, rather, a response by large numbers of people who gain significant symptomatic relief for a variety of sensory complaints by using Cannabis in many different forms. Suffering people, tired of using pharmaceuticals and medical treatments that not only bankrupt them but cause intolerable side effects, use Cannabis to assert a greater measure of control over their own lives.

The lack of investigation is largely the result of deliberate U.S. governmental policy that subtly controls what, if any, research is carried out. In this context, it is reasonable that the vast historical record carries more evidentiary weight than the meager (but increasing) clinical research body. It is also remarkable that millions of Americans continue to place themselves and their families at great personal risk to obtain and use Cannabis to treat their symptoms. They often do this against the advice of physicians who can not, or will not advise their patients to "do what they need to do". In this climate the risks to patients and family members attempting to secure Cannabis for medical use include arrest, prosecution and conviction by a legal system so blinded by law-and-order hyperbole that it will not see the destruction it causes to the lives of sick people. This continues all over America, even in states that have medical Cannabis legislation.

Patient reports of efficacy comprise the largest knowledge-base for physicians and nurses to use in evaluating Cannabis as a medical treatment. Patient experiences guide the treatment planning and provide the foundation for the "feedback loop" of reevaluation which medical professionals (should) continuously use. As nurses and doctors know, the patient is the expert about her/his particular symptoms and disease. Patients know when, how, where, and often why they suffer. No physician or nurse can appreciate this extraordinary level of knowledge based upon experience, unless they experience the condition.



**The use of Cannabis as medicine has rarely been based on detailed clinical investigation of unique medical indications.**



**Suffering people...use Cannabis to assert a greater measure of control over their own lives.**



**The clinical research base into the medical indications of Cannabis is steadily expanding.**

## Dr. Tod Mikuriya's International Classification of Diseases (ICD) Table



### Ailments Grouped by Body Systems Affected Benefited by Use of Cannabis



#### 1) Neurological

291.0 Delirium tremens  
295.xx schizophrenia  
300.5 Neurasthenia  
307.0 Stuttering  
307.23 Tourette's syndrome  
307.42 Persistent insomnia  
307.81 Tension headache  
310.8 Nonpsychotic organic brain syndrome  
340.0 Multiple Sclerosis  
343.9 Cerebral palsy  
345.x Epilepsies  
345.1 Grand Mal seizures  
345.41 Limbic rage syndrome  
345.5 Jacksonian epilepsy  
346.x Migraines  
350.1 Tic Dolorous  
357.x Neuropathy  
379.5 Nystagmus, Congenital  
780.52 Insomnia  
780.7 Tremor/involuntary movements  
782.0 Myofascial pain syndrome

#### 2) Musculoskeletal

138.0 Post polio syndrome  
335.2 Amyotrophic lateral sclerosis  
340.0 Multiple sclerosis  
344.0x Quadraplegia  
344.1x Paraplegia  
354.0 Carpal tunnel syndrome  
714.0 Arthritis, rheumatoid  
715.0 Arthritis, degenerative  
716.1 Arthritis, post traumatic  
716.9 Arthropathy, degenerative  
717.7 Patellar chondromalacia  
718.5 Ankylosis  
722.x Intervertebral disk disease  
724.x Lumbosacral back disease  
728.85 Muscle spasm  
738.4 spondylolisthesis  
754.21 Scoliosis

#### 3) Immunological

042 AIDS related illness  
070.52 Viral B hepatitis, chronic  
070.54 Viral C hepatitis, chronic  
199.0 Cancer  
710.0 Lupus  
710.1 Scleroderma  
710.5 Eosinophilia-Myalgia Syndrome  
729.11 Fibromyalgia  
780.7 Chronic fatigue syndrome  
571.4 Hepatitis (non-viral)  
571.5 Pancreatitis  
600.0 Prostatitis

#### 4) Gastrointestinal

306.4 Psychogenic pylorospasm  
346.x Migraine  
535.0 Acute gastritis  
535.5 Gastritis  
535.6 Peptic ulcer/Dyspepsia  
536.9 Colitis, ulcerative  
537.81 Pylorospasm, reflex  
555.2 Regional enteritis  
555.9 Crohn's disease  
558.9 Colitis  
564.1 Irritable bowel syndrome (spastic colon)  
786.8 Hiccough  
787.01 Vomiting  
787.02 Nausea  
787.91 Diarrhea  
799.4 Cachexia  
994.6 Motion sickness

#### 5) Dermatological

287.0 Henoch-Schoelei Purpura  
698.9 Pruritis (generalized itching)  
710.1 Scleroderma

#### 6) Cardiopulmonary

401.1 Hypertension  
427.0 Paroxysmal atrial tachycardia  
429.4 Post cardiectomy syndrome  
461.9 Acute sinusitis  
473.9 Chronic sinusitis  
493.9 Asthma (unspecified)  
518.89 Cystic Fibrosis  
786.2 Cough

#### 7) Psychological

290.0 Senile dementia  
295.x Schizophrenia  
295.7 Schizoaffective disorder  
296.0 Mania  
296.3 Major depression, recurrent  
296.6 Bipolar disorder  
3000.00 Anxiety disorder  
300.1 Panic disorder  
300.3 Obsessive compulsive disorder  
303.0 Alcoholism  
304.0 Opiate dependence  
304.1 Sedative dependence  
304.2 Cocaine dependence  
304.4 Amphetamine dependence  
305.0 Tobacco dependence  
309.81 Post traumatic stress disorder  
310.91 Intermittent explosive display  
316.0 Psychogenic PAT  
345.41 Limbic rage syndrome

#### 8) Endocrine

242.0 Graves disease  
245.x Thyroiditis  
250.6 Diabetic gastroparesis  
277.3 Amyloidosis  
300.4 Dysthymic disorder  
332.0 Parkinson's disease  
333.4 Huntington's disease  
345.41 Limbic rage syndrome  
571.5 Pancreatitis  
600.0 Prostatitis

#### 9) Chemo/Radiation therapy

199.0 Cancer  
V66.2 Chemotherapy  
E929.9 Radiation therapy  
296.3 Major depression, recurrent  
300.00 Anxiety disorder  
300.01 Panic disorder  
304.0 Opiate dependence  
304.1 Sedative dependence  
346.x Migraine  
535.0 Acute gastritis  
535.5 Gastritis  
535.6 Peptic ulcer/ Dyspepsia  
537.81 Pylorospasm  
781.0 Anorexia  
787.01 Vomiting  
787.02 Nausea  
787.91 Diarrhea  
799.4 Cachexia

#### 10) Ophthalmological

362.5 Macular degeneration  
365.23 Glaucoma  
368.0 Dyslexic Amblyopia  
368.55 Color blindness  
372.9 Conjunctivitis  
377.21 Drusen of optic nerve

#### 11) Gynecological

617.9 Endometriosis  
625.4 Premenstrual syndrome

*Courtesy of Dr. Tod Mikuriya*

Health care professionals, on the other hand, possess voluminous and detailed knowledge concerning the established patterns of *many* disease conditions and their treatments. This level of expertise about the clinical nature of disease provides physicians with the tools to cure, stop, or minimize the undesirable effects of disease. A collaborative approach will usually result in the greatest benefit for patients and doctors, with each person respecting the expertise of the other.


In order for patients, nurses or doctors to understand why any particular drug or treatment works, they need to know about the disease. Cannabis is no exception. The more common medical indications for Cannabis are: *pain (of many types), nausea, anorexia, elevated intraocular pressure, spasms, cramps and seizures, insomnia, anxiety, cancer and AIDS or HIV symptoms*. There are over 100 other symptomatic diseases in which Cannabis has provided clear symptomatic relief. These include *opiate or benzodiazepine withdrawal, lupus, scoliosis, amyotrophic lateral sclerosis (ALS), brain trauma, schizoaffective disorder, bipolar disorder, post traumatic stress disorder (PTSD), tobacco dependence, hypertension and menopausal symptoms*. The list is long.

### **Cannabis helps people feel better**


One underlying denominator, which underscores Cannabis' vast utility, is its antianxiety effect. Most people who suffer from disease suffer also from the accumulation of the *experience of suffering*. Coping strategies and finances deteriorate over time. This ongoing mental and emotional "weight" contributes to hopelessness and depression and, in turn, increases the severity of the disease process. Cannabis has the quality, similar to benzodiazepines like Xanax and Ativan, to compartmentalize the emotional strain of disease away from immediate perception. This shunting of the awareness of symptoms seems to allow patients to relax and even understand deeper meanings in the disease. Unlike benzodiazepines, Cannabis does not often lead to serious drug-dependence issues. Many patients report using Cannabis to counter the withdrawal effects of long-term benzodiazepine use.

This antianxiety effect originates in part from the human ability to regulate emotional and physical functions by the use of *intention* or desire. The brain and body are biochemically integrated. Humans use the brain, focused through emotions and thoughts, to alter many different regulatory systems of the body. The adrenal gland responds to emotionally distressing situations by releasing neurotransmitters, like adrenaline (epinephrine), to heighten "survival" functions. For example, in the "fight-or-flight" response, the brain tells the body that there is potential for serious injury or death. The heart rate increases, the brain becomes more alert and blood gets shunted to the heart from the extremities. Cannabis helps to tone down "fight-or-flight" responses that may result from the disease or the stress of trying to cope.


For *most* people, Cannabis allows calming thoughts and feelings to influence the perception of pain or nausea. Some individuals experience *paradoxical* reactions to Cannabis. A paradoxical reaction occurs when




...the patient is the expert about their particular symptoms and disease.




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the drug has the exact opposite effect than expected, such as when someone taking Ativan becomes *more* anxious rather than less.

With the exception of glaucoma, Cannabis seems to be a treatment mostly for *symptomatic relief* from many neurological functions including pain. It is not usually *curative*. Since pain accompanies most disease processes at some time during their course, pain accounts for probably the greatest single indication for Cannabis. Pain also increases anxiety. Now we are beginning to clearly understand why.

Still, many medical professionals and patients do not understand these clinical applications, or don't understand the differences between Cannabis and Marinol-the "government-approved" THC molecule.

### Marinol and Cannabis: What's the difference?

#### Marinol (dronabinol)

Marinol is the trade name given the artificially synthesized delta-9-tetrahydrocannabinol (THC) molecule. (In Europe, THC is marketed under the name Nabilone.) Marinol is marketed by Roxane Laboratories under a licensing agreement with Unimed Pharmaceuticals. Marinol is not marijuana. It is single molecule THC that does not contain any of the other cannabinoids found in herbal Cannabis. Marinol is manufactured in a sesame seed oil base and, like herbal Cannabis, is insoluble in water. <sup>1</sup>

The lipid soluble nature of Cannabis and Marinol allow it to pass through the blood-brain barrier. (The blood-brain barrier is a cellular membrane that protects the brain and central nervous system from infection by filtering out certain chemical compounds.) This accounts for some of the *cognitive* effects of Cannabis and THC. Marinol also contains extra chemicals *like gelatin, glycerin, methylparaben, propylparaben, yellow, red and blue dye, and titanium dioxide*. (Vegetarians should be aware that gelatin is an animal product.) Any patient who has an allergy towards any of these substances should avoid taking Marinol.

#### Dosage and metabolism

The dosage of Marinol varies depending on set, setting, and medical condition. Generally a *psychoactive* dose is 0.05mg/kg. This translates into around 3.5 mg for a 70-kg (144-lb.) person. Patients should differentiate a *psychoactive* dose from a *therapeutic* dose. They are often not the same. Marinol is taken only by the oral route, unlike smoked Cannabis. Marinol is metabolized by the liver much the same way as Cannabis brownies are. Ninety percent (90%) of the Marinol dose is absorbed in the GI tract because of its high lipid solubility. Also, blood circulating through the intestines goes directly to the liver via the Portal veins carrying with it the large dose of THC absorbed through the stomach and intestines. Only about 10-20% of the dose reaches *systemic circulation* because the liver rapidly metabolizes the dose, converting it into other chemical compounds. <sup>2</sup>

Marinol comes in three dosage forms: 2.5, 5 and 10 mg. It is approved by the Food and Drug Administration (FDA) for appetite stimulation in AIDS wasting syndrome, and nausea and vomiting in cancer chemotherapy, for patients who have not responded to more conventional treatments.

For *anti-emetic* use the usual dosage is 5 mg., three or four times per day, increasing the dosage carefully until the therapeutic benefit is obtained without serious side effects. This may be achieved by dividing doses in the morning and evening. Doses can also be given before or after meals. The important consideration is to achieve a stable blood level of the drug. Ten and fifteen milligram (mg.) doses are more psychoactive and do not increase the benefit.

For *appetite stimulation* Marinol is given in lower doses, usually around 5 milligrams per day. The dosage should be slowly titrated up to the effective dosage short of significant side effects. For naive users this process may take repeated trials of different doses at different times. Altering the dosage up or down should be done in consultation with the patient's medication prescriber. Patients should consider increasing the *frequency* of smaller doses before increasing the total dosage.

#### Side effects

Side effects with Marinol vary widely among different people. One person's experience will be different than another's. Psychoactive effects may be desirable or undesirable. Roxane Laboratories lists euphoria (feeling "high") as an "adverse reaction," but this is often not the case. One of the significant psychiatric uses of Cannabis, if not Marinol, is as an anti-anxiety agent. However, other potentially serious side effects and adverse reactions may occur. The most common effects are: heart palpitations, tachycardia (rapid sustained heart rate), postural hypotension (low blood pressure caused by standing up), conjunctivitis (eye irritation), abdominal pain, nausea, vomiting, diarrhea, anxiety, confusion, depersonalization, paranoid reactions (possibly worse among people suffering from schizophrenia), and somnolence (lethargy). Less-common effects include tinnitus (ringing in the ears), depression, nightmares, visual disturbances, sweating and chills.

If disturbing experiences occur, patients should evaluate the benefits derived from the use of the drug versus the disagreeable effects. This risk-benefit ratio is the same for all drugs; Marinol and Cannabis are no exception. If the problems associated with the use of *any* drug exceed the benefits derived, patients should consider stopping therapy. Again, this is a decision that should be made with the knowledge of the prescriber.

The therapeutic benefits and side effects of dronabinol are *reversible*, that is, the effects fade away after the Marinol is stopped. Since Marinol and Cannabis are fat-soluble this process takes time as the drug slowly moves out of the tissues. Missed doses are not a problem. Taking the next dose early, then following the previous schedule will minimize drops in the blood level of the drug.



Marinol is metabolized by the liver much the same way as Cannabis brownies are.



...only 10-20% of the dose reaches systemic circulation because the liver rapidly metabolizes the dose, converting it into other chemical compounds.



Marinol...is approved by the FDA for appetite stimulation in AIDS wasting syndrome, and nausea and vomiting in cancer chemotherapy, for patients who have not responded to more conventional treatments.



Roxane Laboratories lists euphoria (feeling fine) as an "adverse reaction," but this is often not the case.



...the most common effects [of Marinol] are: heart palpitations, tachycardia, postural hypotension, conjunctivitis, abdominal pain, nausea, vomiting, diarrhea, anxiety, confusion, depersonalization, paranoid reactions, and somnolence.



If disturbing experiences occur, patients should evaluate the benefits derived from the use of the drug versus the disagreeable effects.



As with Cannabis, there are few truly life-threatening reactions with Marinol. The most likely severe reaction is dysphoria or increased apprehension and fear without cause.



...combinations [of drugs] can be additive as one drug potentiates or increases the effects of another.

As with Cannabis, there are few truly life-threatening reactions with Marinol. The most likely severe reaction is *dysphoria* or increased apprehension and fear without cause. (*Euphoria* is the more common effect, a feeling of expansion and inner peace.) Persons suffering from severe liver or cardiac disease should use Marinol carefully. As is the case with Cannabis, the dosage-related mortality is extremely low. Simply put, there are no dosage-related deaths from using Marinol (or Cannabis) in medical literature.

Cannabis dependence syndrome is a psychiatric disease classification. Long-term heavy use of Cannabis can lead to a lack of ability to control use despite adverse consequences. Cannabis dependence syndrome is treated by abstinence.

#### Drug/drug interactions

Drug interactions can be either *metabolic* or *pharmacological*. Drugs interact because they share the same metabolic (chemical breakdown) pathways, or directly interact with each other chemically. The chemical interaction of drugs can create totally different compounds in the body and can be dangerous. Also, these chemical combinations can be *additive* as one drug potentiates or increases the effects of another. Marinol is no exception. It has several notable drug/drug interactions, though none life-threatening. Since Cannabis is chemically similar to Marinol it is reasonable to consider the following drug interactions in connection with Cannabis. Any person taking other pharmaceuticals along with Marinol or Cannabis should research interactions and consult with the prescriber.

*Phenothiazines* are a class of major tranquilizers including Compazine (prochlorperazine) and Thorazine (chlorpromazine). Use of phenothiazines in combination with Marinol may cause *synergistic* effects. (Synergistic actions are those where the effects of different drugs taken together result in greater action than either drug alone.)

*Sympathomimetic agents* are drugs that stimulate the sympathetic nervous system resulting in increased blood pressure and heightened excitement. Examples of sympathomimetic drugs include amphetamines, cocaine, and epinephrine. Use of Marinol or Cannabis with these drugs may result in cardiotoxicity, increasing hypertension (blood pressure), and tachycardia (rapid heart rate).

*Anticholinergic agents* are those that block or interfere with parasympathetic nerve impulses. Parasympathetic nerve fibers carry impulses that constrict the pupil, contract smooth muscle of gastrointestinal tract and slow heart rate, among other functions. Examples of anticholinergic medications include atropine, scopolamine and antihistamines. Marinol or Cannabis use with these drugs may cause additive effects, including rapid heart rate and drowsiness.

*Tricyclic antidepressant agents* are a chemical class of antidepressants that increase the amount of neurotransmitters in the brain by blocking the “reuptake” of the neurotransmitter at the synapse. Common

examples of tricyclic antidepressants include Elavil (amitriptyline), Anafranil (clomipramine), Sinequan (doxepin) and Pamelor (nortriptyline.) Use of Marinol or Cannabis with these drugs may lead to additive effects, hypertension or drowsiness.

*Benzodiazapines, barbiturates and opioids* are drugs that depress or decrease central nervous system function resulting in somnolence, lethargy, drowsiness, constipation and slow heart rate among other effects. Examples include Ativan (lorazepam) Xanax (alprazolam), alcohol, Serax (oxazepam), Valium (diazepam), heroin, morphine and methadone. Marinol or Cannabis use with these drugs may result in additive effects including drowsiness, dizziness or hypotension (low blood pressure.) These drugs may also metabolize more slowly because of competition for the same metabolic pathways.

*Theophylline* is a drug used to relieve bronchial spasms in diseases like emphysema and asthma by relaxing “smooth muscle” in the airway and interfering with enzyme production. Cannabis or Marinol used concurrently with theophylline may increase the metabolism of the theophylline yielding unpredictable results.

### **Marinol overdose and treatment**

The lethal dose of Marinol is 30 milligrams per kilogram (mg./kg.) This translates into 2100 mg. in a 70 kg. (144 lb.) person. This is an exceedingly high dose and reflects the relatively non-lethal nature of Marinol. Cannabis has an unobtainable lethal dosage because it does not overwhelm vital functions. Anyone attempting to overdose on Cannabis would probably fall asleep first.

Treatment of a life-threatening Marinol overdose consists of gastric lavage, intravenous fluid administration, vasopressors to stabilize blood pressure and perhaps intravenous Valium. If the person is responsive, treatment includes close monitoring of blood pressure and heart rate, reassurance, a quiet peaceful environment and hydration.

### **Herbal Cannabis**

Herbal Cannabis is *not* Marinol. Unlike Marinol, Cannabis is an herb that contains many chemicals in addition to THC. Cannabis is made up of more than 60 *cannabinoids*, chemicals of similar composition to THC but with subtle differences. Additionally, Cannabis is packed with other compounds because it is a plant and not a sterile product of human manipulation, like Marinol. These additional chemicals include: alcohols, ketones, simple and fatty acids, steroids, vitamins, pigments, hydrocarbons and enzymes, among others. In fact, Cannabis is literally packed with over 300 chemical compounds.<sup>3</sup> But the major chemical compounds of interest to patients (and recreational smokers) are the afore-mentioned cannabinoids. The major cannabinoids—ones in greatest quantity—are: Tetrahydrocannabinol (THC), Cannabidiol (CBD), and Cannabinol (CBN). Although there are a number of other cannabinoids, these three are thought to exert most of the *physiologic* effects that patients experience. The *metabolism*



*Phenothiazines...a class of major tranquilizers ...in combination with Marinol may cause synergistic effects.*



*Use of Marinol or Cannabis with [sympathomimetic agents] may result in cardiotoxicity, increasing hypertension and tachycardia...*



*Marinol or Cannabis use with [anticholinergic agents] may cause additive effects including rapid heart rate and drowsiness.*



*Marinol or Cannabis use with [Benzodiazapines, barbiturates and opioids] may result in additive affects including drowsiness, dizziness or hypotension. These drugs may also metabolize more slowly because of competition for the same metabolic pathways.*



The lethal dose of Marinol is 30 milligrams per kilogram (mg./kg.) ...2100 mg. in a 70kg. (144 il.) person ...is an exceedingly high dose and reflects the relatively non-lethal nature of Marinol.



Treatment of a life-threatening Marinol overdose would consist of gastric lavage, intravenous fluid administration, vasopressors to stabilize blood pressure and perhaps intravenous Valium.



Herbal Cannabis is not Marinol. Unlike Marinol, Cannabis is an herb that contains many chemicals in addition to THC.

of cannabinoids affects their chemical nature also, because they are broken down by the liver into other compounds. This is why the effects of smoking or eating the same variety of herbal Cannabis will result in a different effect. (Chapter 8 discusses the different effects of smoking or eating Cannabis.)

#### *Delta-9-Tetrahydrocannabinol (THC)*

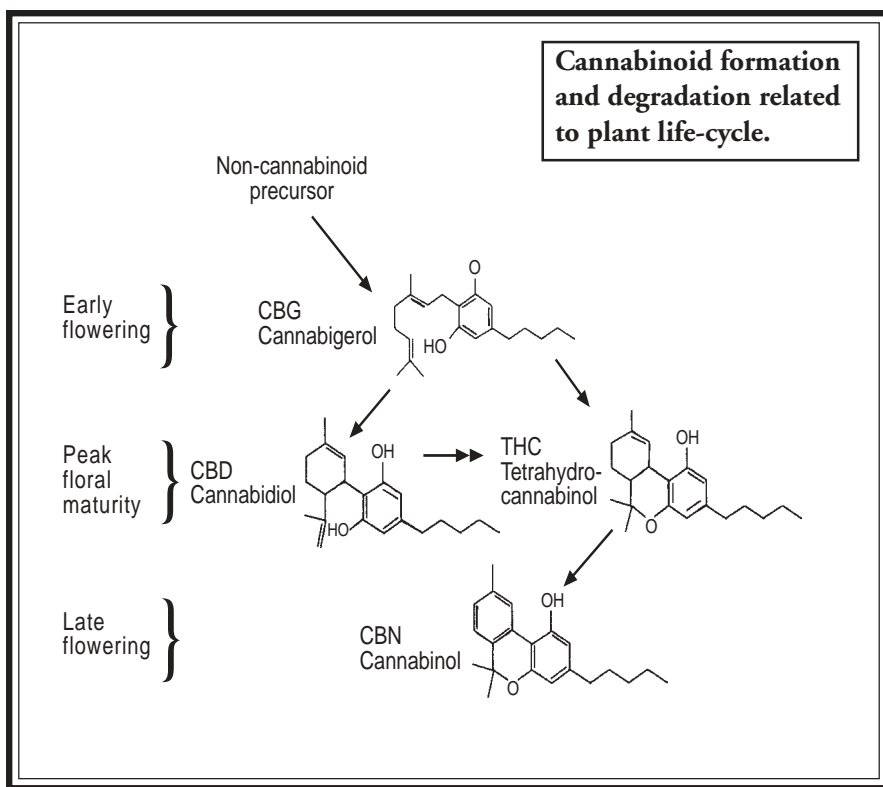
THC is the cannabinoid responsible for most of the effects of herbal Cannabis. Marinol is also pure THC. United States government Cannabis contains two to four percent THC. High-quality Cannabis contains ten percent and greater. (The world's record is 30%.) All the leaf surfaces produce THC but flowering tops are the highest source of THC on the plant. THC is indicated mostly for pain, spasticity, appetite stimulation and anti-nausea effects. Pure THC has a tendency to produce anxiety or even psychotic reactions in some vulnerable people. Other cannabinoids probably moderate or lessen the anxiety-producing qualities of pure THC. Tropical strains seem to have higher levels of THC than temperate strains. When THC is eaten in food, the drug passes through the liver (a process called "first-pass hepatic circulation"). Liver metabolism of THC creates a compound called "11-hydroxy-THC." This compound is more psychoactive than THC alone. For this reason, THC effects are *route-dependent*. Eating brownies or smoking the same strain will result in different effects.

#### *Cannabidiol (CBD)*

CBD is present in much smaller amounts than THC. It is called a *precursor* in the formation of THC—one of its chemical building blocks. Much less research has been done on CBD. CBD is present in higher amounts in northern climate plants like *C. ruderalis*, however CBD has no psychoactive effects. It does appear to have antipsychotic and possibly antispasmodic properties, and seems to moderate the effects of THC. It probably does this by interfering with, and decreasing THC metabolism in the liver. This can lead to higher sustained blood levels of THC. (This is one reason patients prefer Cannabis to Marinol.) CBD has also been shown to have an antidystonic effect. Dystonia is, among other causes, a side effect of *neuroleptic* (antipsychotic) drugs, and is defined as painful rhythmic muscular contractions of the face, neck, and body. CBD seems to increase cerebral (brain) blood flow and this may contribute to its reputed anti-psychotic effect. It also has *antioxidant* effects. Overall, there is a lack of research evidence describing exactly what CBD does. Most of the reports are from patients who find that CBD *attenuates* or moderates effects of THC.

#### *Cannabinol (CBN)*

Cannabinol is the third most common cannabinoid. Cannabinol is another link in the conversion of cannabinoids. CBN is formed from the *degradation*, or breakdown of THC. Like CBD, it is found in minute amounts in Cannabis preparations, but seems to have pharmacological and metabolic effects. CBN in laboratory animals lowered



The metabolism of cannabinoids affects their chemical nature ...because they are broken down by the liver into other compounds.

Delta-9-Tetrahydrocannabinol (THC) is the cannabinoid responsible for most of the effects of herbal Cannabis.

*Cannabinoid biosynthesis is the process that cannabinoids undergo as they chemically develop and degrade. CBG is an “early” cannabinoid molecule in the flowering process. As the plant matures, CBG is converted into CBD and then into THC. Delta-9-Tetrahydrocannabinol is the cannabinoid most responsible for pharmacological effects, and is present in highest concentration with peak floral maturity. Over time, as THC is exposed to oxygen, it degrades into CBN.*

body temperature and increased duration of sleep. CBN is formed as THC degrades. Cultivation experts report that after flowers have fully matured they begin the process of *oxidation* as they begin to degrade into CBN. Older flowers appear to have a sedative effect and this may be due to the higher percentages of CBN, especially if they are damaged, exposed to light or heat. There is little research demonstrating specific effects.

### The complexities of Cannabis: Making informed choices

Herbal Cannabis is a drug “cocktail” with many different constituents. Smoking or eating the same variety will result in different effects. Smoking Cannabis will also form many chemical substances, some of them harmful. For these reasons, patients should understand the complexities. Patients who expect to use Cannabis on a long-term basis have decisions to make about the amount, variety, frequency of dosing, procurement, metabolic interactions with other drugs, and work involved in procuring, growing, and storing the drug. Patients need to understand the basis of their disease and how Cannabis may help. Additionally, patients need to understand a whole host of legal and regulatory issues in their community. This is a daunting task.

Cannabidiol (CBD) ...has no psychoactive effects. It does appear to have anti-psychotic and possibly anti-spasmodic properties...

Cannabinol (CBN)... another link in the conversion of cannabinoids... seems to have pharmacological and metabolic effects.



...patients need to understand a whole host of legal and regulatory issues in their community. ...patients...are left to themselves to answer these questions... these barriers and obstructions will remain until Cannabis treatment is incorporated into the medical system instead of the legal system.



The field of cannabinoid research is wide open and quickly expanding. This is occurring as an outgrowth of understanding the biochemical actions of cannabinoids for several different conditions.



Today, the United Kingdom is perhaps the leader in researching cannabinoid therapeutics.

Unfortunately, patients can expect little help from physicians, nurses or governmental agencies who are either ignorant of it, or still entrenched in the War on Drugs. Thus, they are left to themselves to answer these questions, or rely on support from small, overworked networks. Fundamentally, these barriers and obstructions will remain until Cannabis treatment is incorporated into the medical system instead of the legal system. Until that day comes, patients who use Cannabis should expect to study the issues involved in order to understand how to safely use Cannabis and avail themselves of any laws or protections (like the Oregon Medical Marijuana Act), that exist.

### **Cannabinoid research today and tomorrow**

The field of cannabinoid research is wide open and quickly expanding. This is occurring as an outgrowth of understanding the biochemical actions of cannabinoids for several different conditions. Basic science has now charted the actions of cannabinoids on spastic disorders and analgesia. In the near future researchers will uncover the basic biochemical utilization of cannabinoids in glaucoma and immune function. This deeper understanding of cannabinoid physiology is profoundly altering the knowledge base and giving tremendous impetus to the design of new cannabinoid-based dosage forms. The future will show multiple delivery systems like transdermal patches, creams, and pills. Ironically, this explosion of knowledge is leading medical science *back in time* as new dosage forms remake the tinctures, lotions, pills and extracts that were widely manufactured and prescribed by physicians more than 50 years ago.

Today, the United Kingdom is perhaps the leader in researching cannabinoid therapeutics. GW Pharmaceuticals is conducting large clinical trials that meet FDA prescription drug-development protocols. By developing non-smoked cannabinoid-based medicines, GW Pharmaceuticals is rapidly expanding the therapeutic application of Cannabis. According to GW Pharmaceuticals:

*The key consideration when developing plant-based medicines is control of starting material so as to satisfy the “quality” criteria laid down by the medical regulatory authorities. All of GW’s Cannabis plant material comes from clones grown under computer-controlled conditions in a specialist cultivation facility in the UK.*

(GW Pharmaceutical written notes, First National Clinical Conference on Cannabis Therapeutics, April 6-8, 2000, Iowa City, Iowa, USA)

By controlling both genetics and environmental conditions it is possible to maintain high bud-to-bud and plant-to-plant consistency in terms of cannabinoid ratios and non-cannabinoid constituents. Such consistency is required for the development of pharmaceutical products. Additionally, GW is collaborating with other researchers and universities to conduct pre-clinical and clinical trials of their standard-

ized preparations. These steps will likely result in eventual approval of cannabinoid-based medicines by the U.S. Food and Drug Administration (FDA).

In the U.S., Larry Brooke and Cal C. Herrmann of General Hydroponics have completed the extensive patent application process, and received United States Patent # 6,113,940 for a “Cannabinoid patch and method of transdermal delivery” (Cannabis skin patch).

So, finally, the “cannabinoid is out of the bag.” Governmental interference and obstruction is giving way to an inevitable process of rediscovery. Cannabis clearly does not belong as a Schedule One substance of the *Controlled Substances Act*. It is doubtful that listing Cannabis is justified at all. Cannabinoids have been around for a long time as medicine and are here to stay. New dosage forms and new preparations will appear within the next decade. These welcome advances may lessen, but they will not preclude “old-fashioned” smoking as the preferred delivery route for many patients. Twenty-first century medicine will incorporate the best of 19th century medicine, but will not eliminate it.

#### **Marinol and Cannabis: Whats the difference? Notes**

**Marijuana and Medicine- Assessing the Science Base**, National Academy of Sciences, Institute of Medicine, 1998, pp.22-26, 33-37, 44-49, 109

**Marijuana Grower’s Guide**, Revised Color edition, M. Frank, Red Eye press, 1997, pp. 310-313.

**Marinol Drug Information Package Insert**, Roxane Laboratories, 1999.

#### **Cannabinoid research today and tomorrow Notes:**

*From illegal plant to prescription medicine*, D. Hadorn, **First Clinical Conference on Cannabis Therapeutics**, Iowa City, Iowa, 2000, written materials.

**Personal Communication**, Larry Brooke, 2000



**By controlling both genetics and environmental conditions it is possible to maintain high bud-to-bud and plant-to-plant consistency in terms of cannabinoid ratios and non-cannabinoid constituents.**



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## Footnotes

<sup>1</sup> Simply put, solubility is a measure of a chemical's ability to disperse and disintegrate in water. Fat or *lipid*-soluble chemicals do not readily dissolve in water. This property affects the way the chemical disperses throughout the body. Since cannabinoids are sticky and poorly soluble in water, they accumulate in tissues and require much longer time to be chemically broken down by the body. An entire drug-testing industry exploits this fact.

<sup>2</sup> This process is called “first-pass hepatic circulation.” The liver is an extremely vascular organ. It filters 1500 ml/min of the body's entire blood volume, mostly coming from the portal veins. It performs many complicated functions including; breaking down and metabolizing chemical compounds. This is also why taking a Marinol capsule is much different than smoking a joint.

<sup>3</sup> Cannabis a virtual factory for chemical compounds *and* nutritional ones. Cannabis contains many important nutritional supplements including GLA (gamma-linolenic acid) an essential fatty acid, high levels of protein and carbohydrates, and vitamins.