

**NAT Pro Series:**

# **An Introduction to Medical Cannabis**

Course Notes

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## **Introduction**

The purpose of these video tutorials is to help you become more aware and informed about the basic aspects regarding cannabis, whether you're a patient with a chronic illness considering using cannabis as a part of your treatment, or a therapist looking to educate yourself in this field.

The cannabis plant has been linked to different therapeutic effects yet still "suffers" from a bad name and an association with different stigmas and stereotypes. These stigmas and stereotypes can be very destructive for patients considering using cannabis as a part of their treatment. The best way to address this is to help patients become more confident with their decisions i.e. help them become more educated.

Over the past twenty years the scientific literature available on medical cannabis has become extremely wide yet it is still relatively inaccessible. This course is an evidence-based summary of a collection of relevant literature regarding the medical aspects of cannabis.

Whatever your agenda is, I would like to empower you to make informed decisions regarding the use of medical cannabis.

## **Cannabis and it's Evolution**

Cannabis as a medicine was used before the Christian era in Asia, mainly in India. The introduction of cannabis in Western medicine occurred in the mid 19th century, reaching the climax in the last decade of that century, with the availability and usage of cannabis extracts.

In the first decades of the 20th century, the Western medical use of cannabis significantly decreased largely due to difficulties in obtaining consistent results from batches of plant material of different potencies.

From 1965, the identification of the chemical structure of cannabis components and the possibility of obtaining its pure constituents were related to a significant increase in scientific interest in the plant. This interest was renewed in the 1990's with the description of cannabinoid receptors and the identification of an endogenous cannabinoid system in the brain. A new and more consistent cycle of the use of cannabis derivatives as medication began, once treatment effectiveness and safety started to be scientifically proven.

The use of cannabis as a medicine by ancient Chinese was reported in the world's oldest pharmacopoeia, the Pen-ts'ao Ching which was compiled in the first century of this Era, but based on oral traditions passed down from the time of Emperor Shen-nung, who lived during the years 2.700 B.C.

Indications for the use of cannabis included: rheumatic pain, intestinal constipation, disorders of the female reproductive system, malaria, and others. In the beginning of the Christian Era, Hua T'o, the founder of Chinese surgery (A.D. 110 - 207), used a compound of the plant, taken with wine, to anesthetize patients during surgical operations.

As humans traveled and explored different continents, so the cannabis was able to move and change. In colder climates "hemp" evolved, although this term is often used to refer only to varieties of cannabis cultivated for non-drug use.

Cannabis has long been used for hemp fiber, for hemp oils, for medicinal purposes, and as a recreational drug. In the United States, the term "hemp" is used to describe a cannabis plant that produces no more than 0.3% THC, which is the molecule that causes the psychoactive effect associated with medicinal and adult-use cannabis.

Back in the day, hemp was the main cannabis type known in north America and Europe, but in warmer climates they had the psychoactive type which was higher in THC.

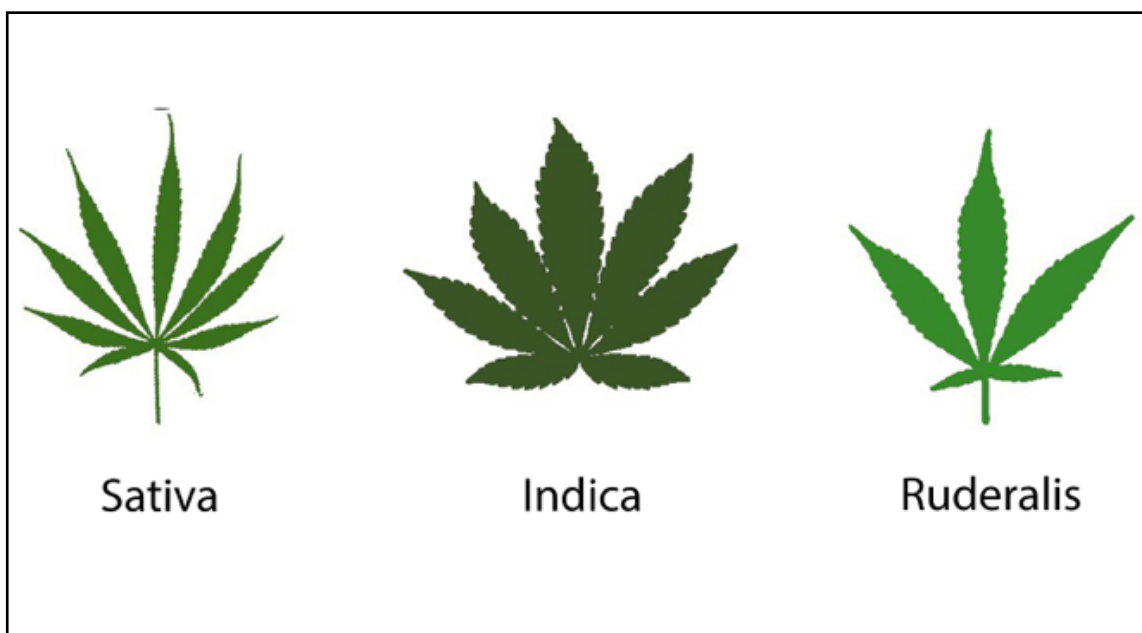
It spread to the Middle East as "Hashish", a paste made from cannabis resin which was actually used as an edible and not by smoking like we see today. From the Middle East it was spread to India and was used as a "holy drink", then to Africa as a medicine. Finally it was brought to America by transatlantic slave traders.



## What is Cannabis?

Hearing about cannabis has probably exposed you to an overwhelming cross section of terms and labels, both for the cannabis plant and its by-products. It takes a little while to understand the different terms so the confusion is understandable. The cannabis world has its own rich, frequently evolving language — making it hard to understand how everything fits together.

First of all, there are really only three types of cannabis: cannabis sativa, cannabis indica, and cannabis ruderalis.



Indica and sativa have been the foundation of the cannabis lexicon since the mid-1700s. In 1753, Swedish botanist Carl Linnaeus identified psychoactive cannabis plants as cannabis sativa. In his work *Species Plantarum*, the cannabis sativa plants grew tall and had light thin leaves. Thirty two years later, French biologist Jean-Baptiste Lamarck identified cannabis indica as a different species while observing the physical characteristics of India's cannabis plants. Lamarck saw that cannabis indica plants had dark green, wide leaves compared with cannabis sativa leaves, which are light and narrow.

The last type we're going to talk about is cannabis ruderalis, which is smaller than the other species and very short. Cannabis ruderalis was first discovered by Russian botanist D. E. Janischewsky in 1924 in Russia.

It reaches maturity much quicker than other species of cannabis, typically in a five to seven week period from seed. Unlike other species of cannabis, cannabis ruderalis enters the flowering stage based on the maturity of the plant, rather than its light cycle. It has less THC in its resin compared to other cannabis species, however, it is often high in cannabidiol (CBD).

Linnaeus also discovered something very interesting and important regarding the cannabis plant; some plants produce only seeds and others produce only pollen... implying the plant has a dioecious reproduction system – it has both female and male plants.

Once the female plants were isolated from the male plants they weren't fertilized and grew bigger psychoactive flowers. That is the key to understanding the strains we have today. The flowers contain most of the bioactive and psychoactive compounds known to us as Cannabinoids, Flavonoids and Terpenes.

These strains are nothing like the ancient sativa and indica we talked about, it's all pretty much hybrid. However, if you purchase cannabis you can see that the term indica and sativa is commonly used.

For the last 50 years of cannabis cultivation, crossbreeding has been the name of the game. As a result, there's virtually no such thing as a "pure" indica or sativa anymore. Every flower you've ever come in to contact with has most likely been a hybrid of some sort. Classifying a particular strain, as indica or sativa usually means that these strains were checked individually by someone and were classified by this person to have a "indica" or "sativa" characteristics. The "sativa" like effect is usually described as more energizing and uplifting, while "indica" ("in the couch") is described as more sedating and relaxing.

This classification is problematic since it doesn't rely on any actually scientific measurements - it is completely individual and inaccurate. Feeling confused? Well you have a good reason to be, but I assure you the answer isn't as vague.

The effects you experience while using different strains have a lot more to do with the concentrations of bioactive compounds within the plant known to us as Cannabinoids and Terpenes.

## **Introduction to the Endocannabinoid System (ECS)**

Before we jump into the specific science of the ECS think of it as an orchestra conductor responsible for indicating the right tempo. Now, this "conductor" also known as your ECS is affected by different levels of different cannabinoids that bind to it through different receptors.

The ECS doesn't exist because there's a plant somewhere out there, it plays a major role in survival by helping to maintain homeostasis in all mammals.

Pain, stress, appetite, energy, metabolism, cardiovascular function, reward and motivation, reproduction, and sleep are just a few of the functions the endogenous cannabinoid system is involved in. It is also involved in a protective mechanism against numerous cancers, neurological diseases, autoimmune diseases and more.

The scientific identification of the ECS in 1990 is a relatively recent development that stemmed from research into the cannabis plant, for which is named after.

The ECS consists of three main components: "messenger" molecules that our bodies synthesize that act as keys, the "receptors" these molecules bind to that act as locks, and the "enzymes" that break them down. This system is present throughout the entire body — on immune cells in our bloodstream, on our nerves throughout our extremities, on the entire axis of the spinal cord, and in virtually every cell in our entire brain. There are even cannabinoid receptors in our skin.

The "messenger" cannabinoid molecules naturally produced in our bodies are known as "anandamide" (The name is taken from the Sanskrit word ananda, which means "joy, bliss, delight") and 2-arachidonoylglycerol (2-AG).

These two bind to cannabinoid receptors CB1 and CB2 and also activate TRPV proteins which are responsible for the body's sensations of heat and cold.

CB1 receptors are largely found in the central nervous system, where they regulate a wide variety of brain functions. In fact, they are the most widely expressed protein of their kind in the brain. In the brain, the major role of the CB1 receptor is to regulate the release of other neurotransmitters, such as serotonin, dopamine, and glutamate.

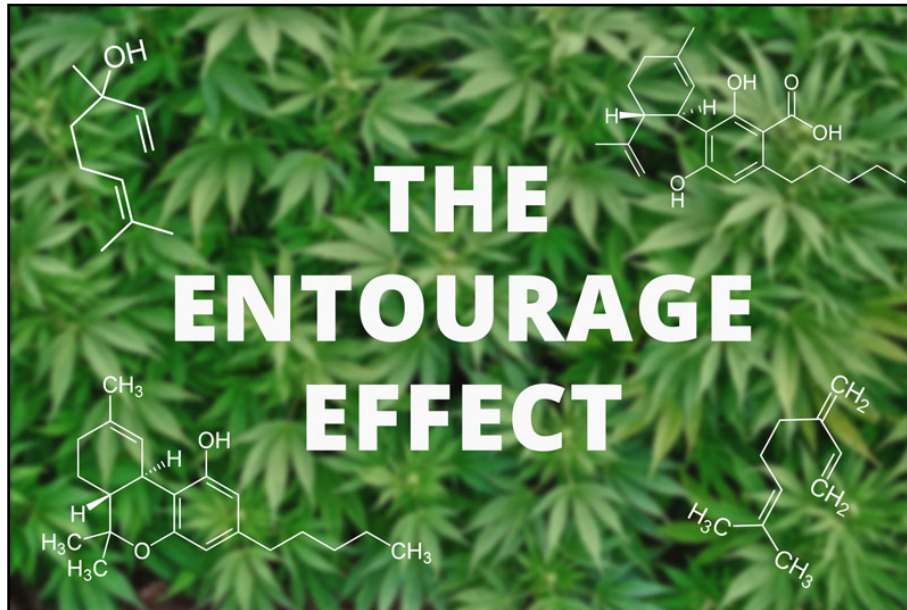
Although the CB1 receptor is responsible for the euphoric effects of cannabis, it's also critically involved in the brain's top-down control of pain.

CB2 receptors are mostly found on immune cells, which circulate throughout the body and brain via the bloodstream. They are also found on neurons in a few select brain regions. CB2 receptors are involved in pain relief, anti-inflammation and neuroprotection.

Endo (meaning; "inside") cannabinoids are produced by our body when needed. They are commonly referred to as "retrograde messengers" because they float backwards across the gap between two neurons, in the opposite direction of normal neuronal communication. After binding to their targets, the endocannabinoids are rapidly broken down by enzymes.

Because our bodies already use endocannabinoids molecules to regulate many functions, it is quite easy to understand why cannabinoids derived from cannabis are able to target so many functions.

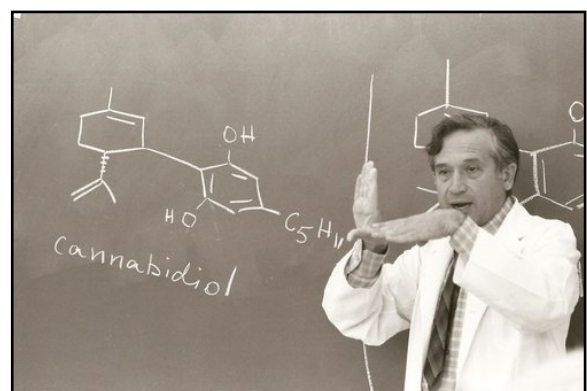
# Cannabinoids, Terpenes and the Entourage Effect



Now that we understand a little bit about our ECS and the different cannabis strains and their effects, it is time to look at the different compounds of this plant and how they synergistically act together.

The cannabis plant has more than 100 different cannabinoids known to man and the ratio between them is found to be responsible for varied effects. The main characters you have probably heard of are THC (tetrahydrocannabinol) and CBD (cannabidiol).

Understanding the mechanism of THC is possible thanks to the Israeli scientist Rafael Mechoulam who synthesized this molecule in 1965. THC has a psychoactive effect meaning it gets you "high". It activates the brain's reward pathway which makes us feel good and euphoric by binding to CB1 receptors in the brain.



CBD, the second cannabinoid I mentioned, does not appear to have the same psychoactive ("high") effects such as those caused by THC, but may have anti-anxiety and anti-psychotic effects.

CBD doesn't bind to CB1 receptors as well as THC. In fact, evidence suggests that it actually interferes with the activity of the CB1 receptor, especially in the presence of THC. When THC and CBD work together users tend to feel a more mellow, nuanced subjective high and have a much lower chance of experiencing paranoia compared to the effects felt when CBD is absent because having them both gives you a balancing effect.

While the full complexity of how CBD interacts with the body's ECS is yet to be fully revealed, a lot of studies have shown that CBD affects diseases of both the mind and the body, particularly neurological diseases, inflammatory illnesses, autoimmune diseases, and cancer.

CBD has been shown to have a clear and measurable therapeutic impact on inflammatory and anti-inflammatory regulation mechanisms such as in inflammatory bowel disease, arthritis and atherosclerosis.

Cannabis isn't just cannabinoids. There are over 400 active compounds that give each plant a different therapeutic profile. Some of those compounds belong to the Terpenes "family" which is responsible for the flavor and aroma, but terpenes do more than provide flavor and aroma. They also support other cannabis molecules in producing wanted effects by mediating the cannabinoids profile to what we call "the entourage effect".

Evidence suggests that whole-plant cannabis (that includes terpenes) is superior to isolated compounds from the plant. Cannabinoids like THC and CBD produce better outcomes when they are consumed alongside a supporting cast of terpenes.

There is a huge amount of research left to do in order for us to understand exactly how terpenes enhance the other health benefits of the cannabis plant, and exactly which constellations of molecules produce the different kinds of highs for which cannabis is known.

## Products



Cannabis products come in many different forms for many different experiences. Whether you prefer rolling a joint and smoking with friends, or you are a contemporary user who wants to maximize the therapeutic benefits without feeling high, cannabis in today's world means you can use it for a wide range of reasons, needs, and desires — it is just a matter of finding the right product.

If you want to consume flower or concentrates to feel relaxed, euphoric, stimulated, sedated, or "high," you can browse through a wide selection of flower and concentrates from cultivators and processors who are perfecting cannabinoid and terpene profiles to provide that exact experience. If you are looking for alternative ways to get the medical benefits of cannabis, you can choose from edibles, topicals, tinctures and more to avoid smoking or vaporizing. The options are vast and quickly growing to suit an array of preferences.

The important questions I would like you to take into consideration are; "what do I need?", "what do I want?" and "what is the best way I can achieve these, both mentally and health wise?". Be educated and learn to read the percentage of each ingredient.

You can find products that contain a large amount of THC that will probably make you extremely high, you can even find products with a greater amount of CBD and almost no THC.

Understanding how these different products affect you is important, because it can open a whole new approach for healing, both mentally and physically.



## **On-Going Research Today**

Some people use cannabis recreationally to create a sense of wellbeing or to alter the senses. It is either taken by mouth or smoked (inhaled).

Cannabis is also taken by mouth for medicinal purposes. Tetrahydrocannabinol (THC), is used in the prescription-only, FDA-approved product dronabinol (Marinol) for the treatment of weight loss or appetite loss due to AIDS, and for nausea and vomiting caused by cancer chemotherapy. Cannabinoids are at least as effective as some conventional medications for nausea, including prochlorperazine (Compazine), metoclopramide (Reglan), chlorpromazine (Compazine), and thiethylperazine (Torecan).

Cannabinoids from cannabis also appear to be similar to codeine for the treatment of pain. However, extreme sleepiness and other central nervous system effects make cannabinoids undesirable as painkillers. Other cannabinoids from cannabis have also been used by mouth to treat symptoms of multiple sclerosis (MS).

Cannabis is used for glaucoma, mucous membrane inflammation, leprosy, fever, dandruff, hemorrhoids, obesity, asthma, urinary tract infections, and coughing. It is also inhaled to weaken the immune system after kidney transplants to lessen the chance of a transplant rejection.

Medical cannabis refers to the use of cannabis or cannabinoids as medical therapy to treat disease or alleviate symptoms. Cannabinoids can be administered orally, sublingually, or topically; they can be smoked, inhaled, mixed with food, or made into tea. They can be taken in herbal form, extracted naturally from the plant, gained by isomerisation of cannabidiol, or manufactured synthetically. Prescribed cannabinoids include dronabinol capsules, nabilone capsules, and the oromucosal spray nabiximols.



Current research has shown that cannabis can be effective for different conditions;

**Glaucoma** It reduces pressure inside the eye in people with glaucoma. However, it also seems to decrease blood flow to the optic nerve. So far, it is not known if cannabis can improve sight.

**Eye** Cannabis and THC have been shown repeatedly to lower the intraocular pressure (IOP) by a mechanism that is not yet understood. This effect can be produced by systemic administration at doses that also produce the characteristic CNS effects, and rather inconsistently by local application to the eye.

**HIV/AIDS-related weight loss** Reports have indicated that smoked or ingested cannabis improves appetite and leads to weight gain and improved mood and quality of life among patients with AIDS. There was some evidence that Dronabinol (a pharmaceutical formulation of THC ) is associated with an increase in weight when compared with placebo. More limited evidence suggests that it may also be associated with increased appetite, greater percentage of body fat, reduced nausea, and improved functional status.

**Multiple sclerosis (MS)** When smoked or when used as a mouth spray, cannabis seems to be effective for the treatment of muscle tightness and

shakiness in people with MS. However, taking cannabis extract by mouth does not seem to consistently reduce shakiness in patients with MS.

**Nerve pain** Early research shows that smoking cannabis three times a day might reduce nerve pain caused by HIV and other conditions.

**Pain** Marijuana has been used to relieve pain for centuries. Studies have shown that cannabinoids acting through central CB1 receptors, and possibly peripheral CB1 and CB2 receptors, play important roles in modeling nociceptive responses in various models of pain. These findings are consistent with reports that cannabis may be effective in ameliorating neuropathic pain, even at very low levels of THC (1.29%). Both cannabis and Dronabinol, decrease pain, but dronabinol may lead to longer-lasting reductions in pain sensitivity and lower ratings of rewarding effects.

**Spasticity Due to MS or Paraplegia** Studies generally suggest that cannabinoids are associated with improvements in spasticity.

**Nausea and Vomiting due to Chemotherapy** Treatment of the nausea and vomiting associated with chemotherapy was one of the first medical uses of THC and other cannabinoids. THC is an effective antiemetic agent in patients undergoing chemotherapy, but patients often state that cannabis is more effective in suppressing nausea. Other, unidentified compounds in cannabis may enhance the effect of THC (as appears to be the case with THC and cannabidiol, which operate through different antiemetic mechanisms). Paradoxically, increased vomiting (hyperemesis) has been reported with repeated cannabis use.

**Sleep Disorder** Cannabis is also known to help with sleep disorders.

**Inflammation** Cannabinoids have substantial anti-inflammatory effects because of their ability to induce apoptosis, inhibit cell proliferation, and suppress cytokine production. CBD has attracted particular interest as an anti-inflammatory agent because of its lack of psychoactive effects. Animal models have shown that CBD is a promising candidate for the treatment of rheumatoid arthritis, for inflammatory diseases of the gastrointestinal tract (e.g., ulcerative colitis and Crohn's disease), and for different autoimmune diseases including type 1 diabetes, multiple sclerosis, psoriasis, rheumatoid arthritis and more.

**Epilepsy** In a recent small survey of parents who use cannabis with a high cannabidiol content to treat epileptic seizures in their children,<sup>72</sup> 11% (2 families out of the 19 that met the inclusion criteria) reported complete freedom from seizures, 42% (8 families) reported a reduction of more than 80% in seizure frequency, and 32% (6 families) reported a reduction of 25 to 60% in seizure frequency. In addition, there is increasing evidence of the role of CBD as an anti-epileptic agent in animal models.

## Side Effects of Cannabis:

The use of cannabis can cause dry mouth, nausea, vomiting, dry or red eyes, heart and blood pressure problems, lung problems, impaired mental functioning, headache, dizziness, numbness, panic reactions, hallucinations, flashbacks, depression, and sexual problems.

**Pregnancy** There is not enough research concerning the effect of cannabis on the fetus when taken by mouth or smoked during pregnancy. It is important to take into consideration that cannabinoids pass through the placenta and can slow the growth of the fetus.

**Breast-feeding** Using cannabis, either by mouth or by inhalation is **LIKELY UNSAFE** during breast-feeding. Some of the cannabinoids pass into breast milk and extensive cannabis use during breast-feeding may result in slowed development in the baby.

**Seizure disorders** Cannabis might make seizure disorders worse in some people; in others it may help to control seizures.

**Surgery** It affects the central nervous system. It might slow the central nervous system too much when combined with anesthesia and other medications during and after surgery.

Central nervous system: Cannabis acts essentially as a central nervous system (CNS) depressant; therefore, its main acute effects in many ways resemble those of alcohol. It produces drowsiness and decreased alertness, being synergistic with alcohol, barbiturates and other CNS depressants in this respect. Similarly, although THC has minimal respiratory depressant effect by itself, it may be synergistic with other depressants.

Cognitive effects include impairment of short term memory, slowed reactions, decreased accuracy of psychomotor task performance and decreased selectivity of attention (greater interference by extraneous stimuli). Motor coordination and muscle tone are also decreased, resulting in ataxia. As a result of all of these effects, it causes poorer performance in simulated driving or flying tasks. However, the risk for real life driving may be less than with equivalent levels of alcohol intoxication because the cannabis users appear to be more cautious and less aggressive.

Low doses of cannabis typically induce mild euphoria, relaxation, increased sociability and decreased anxiety. However, high doses often result in dysphoria, increased anxiety and panic reactions, especially in inexperienced users. Similarly, low doses tend to increase sensory acuity, often in a pleasurable way, whereas high doses may cause sensory distortion, hallucinations and even an acute toxic psychosis that is usually of short duration after the drug is discontinued.