

UNC SON **ECHO** ABC for MOUD

Addiction and Behavioral Clinic for Medication for Opioid Use Disorder Treatment

INTRODUCTION TO THE ENDOCANNABINOID SYSTEM AND CANNABINOIDS

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UNC
SCHOOL OF NURSING



University of North Carolina
at Chapel Hill
School of Nursing

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NO DISCLOSURES TO REPORT



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Objectives

The participant will be able to describe 2 historical aspects of the challenges to cannabis research and therapeutics.

The participant will be able to state the 2 naturally occurring cannabinoids in the endocannabinoid system

The participant will be able to identify 3 areas of health care that are seeing increasing research into the utilization of cannabinoids for optimizing health outcomes.

The participant will be able to state 3 common side effects of cannabinoids.

Historical Facts about Cannabis

Two archaeologists of the Chinese Academy of Sciences in Beijing, Yang Yimin and Ren Meng, reported clear physical evidence that mourners burned cannabis for its intoxicating fumes on a remote mountain plateau in Central Asia some 2500 years ago.

In 440 B.C.E., the Greek historian Herodotus wrote that the nomadic Scythians, who controlled vast areas from Siberia to Eastern Europe, made tents and heated rocks in order to inhale hemp vapors that made them "shout for joy."

As early as 1619, the first Virginia [House of Burgesses](#) passed an Act requiring all planters in Virginia to sow "both English and Indian" hemp on their plantations



Historical Facts about Cannabis (Continued)

The Marihuana Tax Act of 1937 effectively made possession or transfer of marijuana illegal throughout the United States under [federal law](#), excluding medical and industrial uses, through imposition of an [excise tax](#) on all sales of hemp.

Cannabis was dropped from the United States Pharmacopoeia in 1942.

Congress passed the [Controlled Substances Act](#) as Title II of the [Comprehensive Drug Abuse Prevention and Control Act of 1970](#), which repealed the Marijuana Tax Act. Under the CSA cannabis was assigned a Schedule I classification, deemed to have a high potential for abuse and no accepted medical use – thereby prohibiting even medical use of the drug.

In 2018, research on the potential harms of cannabis received more than 20 times more funding than research on cannabis therapeutics, according to an analysis of cannabis research grants from 50 public agency and charity funders. Up until recently research funding had to include “harm”. That changed in 2018. In 2021, 3,800 papers were published on cannabis.

Currently 36 states have medical marijuana laws and another 18 states have recreational marijuana laws and 13 states have decriminalized use.

Cannabis Therapeutics and Advancing Education

The National Council of State Boards of Nursing (NCSBN) released guidelines in July 2018. The JNR supplement covers:

Current Legislation, Scientific Literature Review, and Nursing Implications
Nursing Care of the Patient Using Medical Marijuana
Medical Marijuana Education in Pre-Licensure Nursing Programs
Medical Marijuana Education in APRN Nursing Programs
[NCSBN National Nursing Guidelines for Medical Marijuana](#)

What You Did Not Learn in Nursing School

Dr. Raphael Mechoulam published a paper in 1964, *Isolation, structure, & partial synthesis of an active constituent of Hashish*. Journal of the American Chemical Society 1964, and went on to identify Phytocannabinoids (CBD and THC); Endocannabinoids in humans (2-AG and Anandamide) and the signaling receptors- CB1 and CB2

In 1992, at the Hebrew University in Jerusalem, Dr. Lumir Hanus along with American researcher Dr. William Devane discovered the endocannabinoid anandamide. The discovery of these receptors resulted in the uncovering of naturally occurring neurotransmitters called endocannabinoids

The Endocannabinoid System is present in humans as well as all animals, including vertebrates (mammals, birds, reptiles, and fish) and invertebrates (sea urchins, leeches, mussels, nematodes, and others) that promotes homeostasis.

Unlike the CNS, the circulatory system, PNS, etc the endocannabinoid system is rarely addressed in medical and nursing education.



What You Did Not Learn in Nursing School

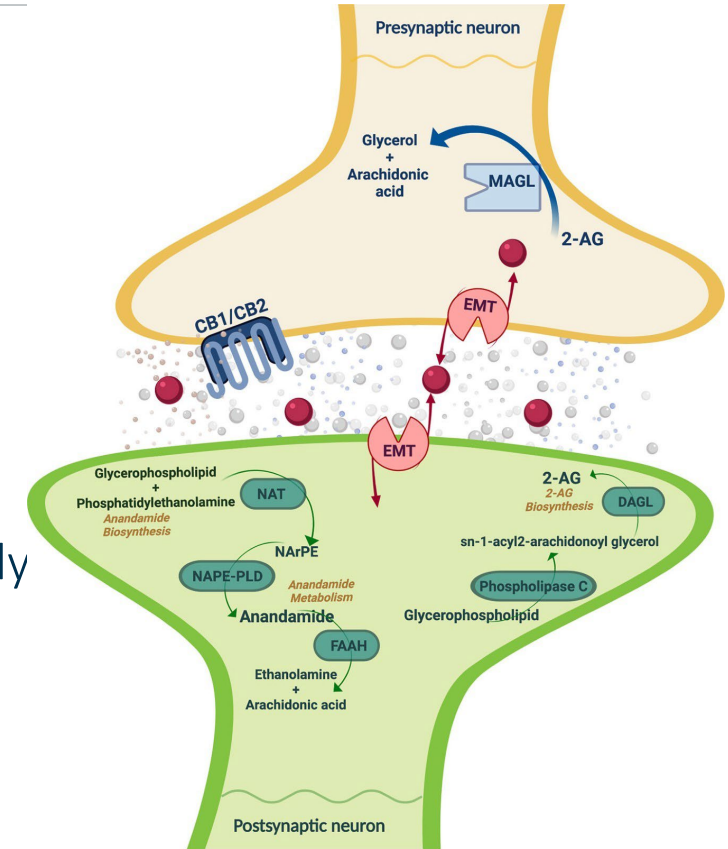
The endocannabinoid system is made up of CB receptors which are G-protein-coupled receptors. CB1 and CB2

It has been documented that ECS is directly involved with various roles in apoptosis, neurotransmitter levels, and homeostasis (Basavarajappa, Nixon, & Arancio, 2009).

CB1 receptors are located in the CNS, brain, spinal cord, nerves, organs. The highest densities of CB1 receptors appear in the hippocampus, cerebral cortex, cerebellum, amygdaloid nucleus, and basal ganglia.

CB2 receptors are located in the skin, immune system, peripheral tissues and organs. The homeostatic effect produced by CB2 stimulation is mostly the reduction of inflammation.

Cannabinoid receptors are possibly the most numerous of any other regulatory body system.



Cannabinoids

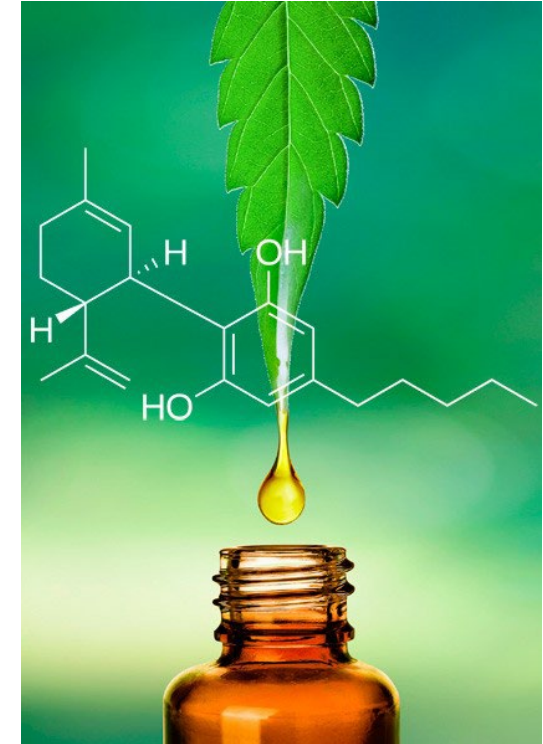
A cannabinoid is a chemical compound that influences cannabinoid receptors in cells to affect neurotransmitter release. It refers to any of the categories including endocannabinoids, phytocannabinoids, and synthetic cannabinoids.

Endocannabinoids-Naturally occurring in the body. Anandamide (AEA) and 2-arachidonoylglycerol (2-AG).

Phytocannabinoids-Cannabinoids found in plants. There are over 100 unique phytocannabinoids. Most studied are Tetrahydrocannabinol (THC) and Cannabidiol (CBD).

Synthetic-Cannabinoids that are isolated and reproduced. Prescription drugs include Dronabinol, Nabilone and Rimonabant (THC).

Epidiolex (CBD) is a full plant extract.



What is it good for?

ADD/ADHD

ALS

ANXIETY

ATAXIA

CACHEXIA

CANCER

DIABETES MELLITUS

GI DISORDERS

FIBROMYALGIA

MIGRAINE

MULTIPLE SCLEROSIS

SPASMS

NEUROPATHY

ALZHEIMER'S DISEASE

ANOREXIA

ASTHMA

CHRONIC FATIGUE

CRAMPS

CHRONIC PAIN

DEPRESSION

EPILEPSY/SEIZURES

HIV

PTSD

TOURETTE'S

RHEUMATOID ARTHRITIS

HYPERTENSION

Cannabinoids and Terpenes

There are several cannabinoids in addition to CBD (cannabidiol) and THC(tetrahydrocannabinol). Some of the more common ones are CBG (cannabigerol), CBN (cannabinol). Also CBDA and THCA-these are raw forms.

Terpenes are the chemical components that gives plants their smell and are abundant in cannabis. Common terpenes include linalool (Lavender), myrcene (mango), pinene (pine), beta carophyllene (clove, black pepper), limonene (citrus),alpha humulene (sage, ginger), terpinolene (sage, lilac, rosemary). There are numerous medicinal benefits to terpenes including anti-inflammatory, anti-anxiolytic, anti-cancer, analgesia, etc.



Cannabinoids and Terpenes (Continue)

Entourage Effect-when used together as found in the whole plant, there is synergistic enhancement- cannabinoids work better together than when isolated from one another.

In the practice of cannabis medicine, the practitioner may combine the phytocannabinoid and terpene for enhanced effects. For example:

THC + CBD + B-Myrcene + B-Caryophyllene = Pain Relief

CBD + CBN + Limonene + Linalool =Insomnia and Anxiety Relief



Side Effects of THC



INCREASED HEART RATE

SLEEPINESS/FATIGUE

DECREASE BLOOD PRESSURE

DRY MOUTH

DECREASED URINATION

FORGETFULNESS

ANXIETY

INCREASED APPETITE

DIZZINESS

DECREASED TEMPERATURE

DRY EYES

HALLUCINATION

PARANOIA

Side effects are dose dependent and more prevalent at higher doses.

Side Effects of CBD

DIZZINESS

ANXIETY

DECREASED APPETITE

JITTERINESS

DRUG INTERACTIONS

Side effects are dose dependent and more prevalent at higher doses.

LIGHTHEADEDNESS

INCREASED HEART RATE

DROWSINESS

DIARRHEA



Metabolism and Drug Interactions

In part this depends on the method of administration and whether the product is involved in first pass metabolism (edibles, oral forms) versus inhaled or topical forms.

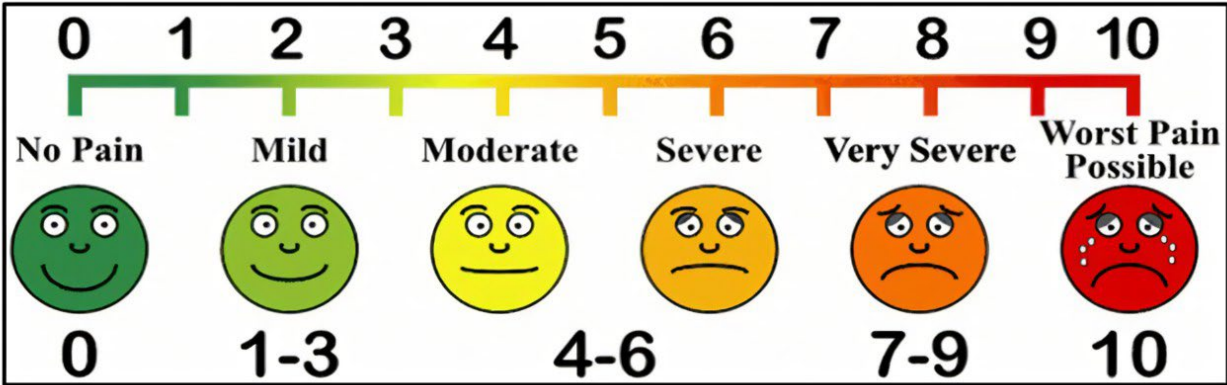
CBD is metabolized by CYP2C19, CYP3A4, and CYP2C9.

CBD is a potent inhibitor of CYP3A4 and CYP2D6 and therefore can increase serum concentrations of several medications including benzodiazepines, TCA, opioids, anti-psychotics, macrolides, statins and warfarin.

THC is metabolized by the liver by hydroxylation, oxidation and conjugation through CYP450 complex, specifically CYP2C9 and CYP3A.

Cannabis, Chronic Pain, Opioid Use and Abuse

Increasingly research suggests a potential role of cannabis as an adjunctive therapy with or without opioids to optimize pain control. Results demonstrate possibility of better pain control clinically with lower doses of opioids, improved pain related outcomes and reduced opioid related harm. (MacCallum, Eadie, Barr, Boivin and Lu, 2021).



Cannabis, Chronic Pain, Opioid Use and Abuse (Continued)

To fill the gap between efficacious OUD treatments and the widespread prevalence of misuse, relapse, and overdose, the development of novel, alternative, or adjunct OUD treatment therapies is highly warranted. In this article, we review emerging evidence that suggests that cannabis may play a role in ameliorating the impact of OUD. Herein, we highlight knowledge gaps and discuss cannabis' potential to prevent opioid misuse (as an analgesic alternative), alleviate opioid withdrawal symptoms, and decrease the likelihood of relapse. (Wiese and Wilson-Poe, 2018).

Cannabis, Chronic Pain, Opioid Use and Abuse (Continued)

Results provide evidence that MMLs may be effective at reducing opioid reliance as survey respondents living in states with medical cannabis legislation are much less apt to report using opioid analgesics than people living in states without such laws, net other factors. Results further indicate that the presence of medicinal cannabis legislation appears to have no influence over opioid misuse. (Flexon J, Stolzenberg L and D'Alessio S. (2019).

Cannabinoids and PTSD

Three biomarkers examined collectively—OMAR V_T , anandamide and cortisol—correctly classified nearly 85% of PTSD cases. These results suggest that abnormal CB_1 receptor-mediated anandamide signaling is implicated in the etiology of PTSD, and provide a promising neurobiological model to develop novel, evidence-based pharmacotherapies for this disorder. (Neumeister A, Normandin M, Pietrzak R, Piomelli D, et al (2013).

Federal Study Finds Cannabis Beneficial for PTSD Treatment

Over the course of a year, the study found that cannabis users reported a greater decrease in the severity of their PTSD symptoms. They also were more than 2.5 times as likely to no longer meet the diagnostic criteria for PTSD as those who did not use cannabis. Sep 21, 2021. <https://www.vfw.org/media-and-events/latest-releases/archives/2021/9/federal-study-finds-cannabis-beneficial-for-ptsd-treatment>

Cannabinoids and PTSD

[Use of Medicinal Cannabis and Synthetic Cannabinoids in Post-Traumatic Stress Disorder \(PTSD\): A Systematic Review.](#)

Orsolini L, Chiappini S, Volpe U, Berardis D, Latini R, Papanti GD, Corkery AJM. *Medicina (Kaunas)*. 2019 Aug 23;55(9):525. doi: 10.3390/medicina55090525. PMID: 31450833 Free PMC article.

[Marijuana and other cannabinoids as a treatment for posttraumatic stress disorder: A literature review.](#)

Steenkamp MM, Blessing EM, Galatzer-Levy IR, Hollahan LC, Anderson WT. *Depress Anxiety*. 2017 Mar;34(3):207-216. doi: 10.1002/da.22596. Epub 2017 Feb 28. PMID: 28245077 Review.

[Toward a translational approach to targeting the endocannabinoid system in posttraumatic stress disorder: a critical review of preclinical research.](#)

Papini S, Sullivan GM, Hien DA, Shvil E, Neria Y. *Biol Psychol*. 2015 Jan;104:8-18. doi: 10.1016/j.biopsycho.2014.10.010. Epub 2014 Nov 4. PMID: 25448242 Free PMC article. Review.

[Cannabinoids and post-traumatic stress disorder: clinical and preclinical evidence for treatment and prevention.](#)

Mizrachi Zer-Aviv T, Segev A, Akirav I. *Behav Pharmacol*. 2016 Oct;27(7):561-9. doi: 10.1097/FBP.0000000000000253. PMID: 27551883 Review.

[Integrating Endocannabinoid Signaling and Cannabinoids into the Biology and Treatment of Posttraumatic Stress Disorder.](#) Hill MN, Campolongo P, Yehuda R, Patel S. *Neuropsychopharmacology*. 2018 Jan;43(1):80-102. doi: 10.1038/npp.2017.162. Epub 2017 Jul 26. PMID: 28745306 Free PMC article. Review.

Cannabinoids and PTSD

[Cannabinoids and post-traumatic stress disorder: clinical and preclinical evidence for treatment and prevention.](#)

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[Cannabidiol and the corticoraphe circuit in post-traumatic stress disorder.](#)

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[Cannabis in the management of PTSD: a systematic review.](#)

Rehman Y, Saini A, Huang S, Sood E, Gill R, Yanikomeroğlu S. AIMS Neurosci. 2021 May 13;8(3):414-434. doi: 10.3934/Neuroscience.2021022. eCollection 2021. PMID: 34183989 Free PMC article. Review.

[Use of a synthetic cannabinoid in a correctional population for posttraumatic stress disorder-related insomnia and nightmares, chronic pain, harm reduction, and other indications: a retrospective evaluation.](#)

_Cameron C, Watson D, Robinson J. J Clin Psychopharmacol. 2014 Oct;34(5):559 -64. doi: 10.1097/JCP.0000000000000180. PMID: 24987795 Free PMC article.

[The efficacy of nabilone, a synthetic cannabinoid, in the treatment of PTSD-associated nightmares: A preliminary randomized, double-blind, placebo-controlled cross-over design study.](#)

_Jetly R, Heber A, Fraser G, Boisvert D. Psychoneuroendocrinology. 2015 Jan;51:585-8. doi: 10.1016/j.psyneuen.2014.11.002. Epub 2014 Nov 8. PMID: 25467221 Clinical Trial.

North Carolina Laws and Regulations

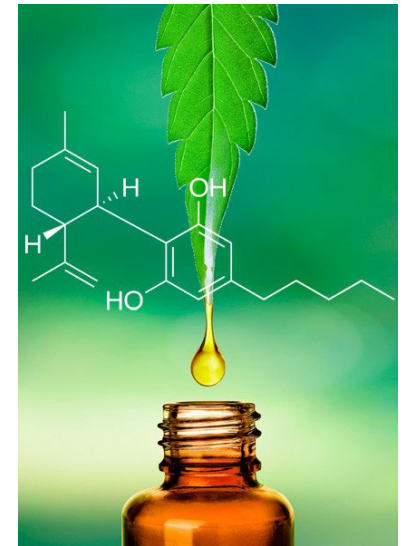
Hemp-derived CBD with less than 0.3% THC became legal at the federal level in 2018 and it is legal in North Carolina.

A proposal that would [legalize medical marijuana](#) for conditions like cancer, HIV/AIDS and severe PTSD in North Carolina will be back up for debate in 2022.

The Compassionate Care Act has gotten bipartisan support in the North Carolina Senate, but has not yet gone to the full Senate for a vote. Expected to begin discussions in spring 2022.

The sponsors say this act would give North Carolina the strictest medical marijuana law in the country.

https://docs.google.com/presentation/d/1NybSnuOLo8-olzf4tO2ZQSjGs3Vy2RrxpZ0qunC6ZSo/edit#slide=id.g10db5046efa_0_95



What you would like to know from your patients?



If using CBD, inquire about the product or ask them to give you the name so you can research. Extraction method is important as well as potency and product quality. CBD manufacturers are expected to release their testing data on request.

Why are you using it?

What do you notice?

How much are you using?

How long have you been using this product

Common beneficial dose usually starts around 50 mg/day

Where Do I Go to Learn More?

Society of Cannabis Clinicians <https://www.cannabisclinicians.org/>

The Cannabis Medical Institute <https://themedicalcannabisinstitute.org/>

Radicle Health <https://www.radiclehealthcare.com/>

American Cannabis Nurse Association <https://www.cannabisnurses.org/>

Cannabis Nurses Network <https://www.cannabisnursesnetwork.com/>

CannaKeys 360 cannabis database subscription <https://cannakeys.com/>

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