

# CANNABINOIDS

# A *to* Z

A GLOSSARY OF COMMONLY-USED TERMS

# WELCOME

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As the landscape surrounding cannabis and derived products continues to evolve, staying informed is crucial. This glossary aims to provide you with clear, concise, and up-to-date information on a wide range of terms used by marketing, legal, regulatory and scientists. Our goal is to support you by offering a reliable science-based reference that enhances your understanding of cannabis and cannabinoids.

Whether you are new to the field or looking to deepen your knowledge, this glossary and numerous other resources on [CannabinoidClinical.com](https://www.cannabinoidclinical.com) can support your continued learning. We encourage you to explore the entries, utilize the information in your practice or health care journey, and stay abreast of the latest developments in cannabinoid research.

## NOTE

The following abbreviations and footnote apply throughout this document. All other abbreviations are defined when used.

CBD, cannabidiol; FDA, US Food and Drug Administration; THC, tetrahydrocannabinol

For terms with an asterisk (\*) there is no scientifically or legally accepted definition. There is no regulatory definition, and it does not fall within a recognized regulatory category of the FDA

# Agricultural Improvement Act of 2018

Known as the 2018 Farm Bill, this bill descheduled industrial hemp and hemp-derived products with a  $\Delta^9$ -THC concentration of less than 0.3% by dry weight, thus removing them from Schedule I of the Controlled Substances Act.<sup>1</sup>

States and American Indian tribes may regulate the production of hemp by submitting a plan to the Department of Agriculture (USDA).<sup>1</sup> The bill also makes hemp producers eligible for the federal crop insurance program and certain USDA research grants. The FDA states,<sup>2</sup> “however, Congress explicitly preserved the agency’s current authority to regulate products containing cannabis or cannabis-derived compounds under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and section 351 of the Public Health Service Act.”

## Bioaccessibility

The concept of bioaccessibility can be defined as the quantity or fraction of a compound that remains available for absorption in the gastrointestinal tract.<sup>3</sup> The same drug in different formulations, solvents, and oils can lead to varied absorption and subsequent plasma levels.<sup>4</sup>

## Bioaccumulation

Bioaccumulation is defined as the net accumulation of a contaminant in or on an organism from all sources including water, air, soil, and diet.<sup>5</sup> Contaminants have been shown to bioaccumulate in cannabis plants.<sup>6</sup>

## Botanical Drug Product

A multi-component standardized medicine extracted from plant sources that is intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in humans.<sup>7,8</sup> A medication that contains a mixture of constituents from the cannabis plant or mixture of plant derived cannabinoids would be a botanical drug product.<sup>7</sup>

## Broad Spectrum\*

A marketing term for a cannabis-based formulation that is meant to imply that the product contains many plant constituents, cannabinoids, and terpenes, but is claimed to contain no THC content.<sup>9</sup>

## Cannabinoid

Term used to refer to molecules that can be found in a cannabis plant, made in our bodies, or synthesized in a laboratory and that may interact with cannabinoid receptors.<sup>10,11</sup> They fall into 3 classes: phytocannabinoids, endocannabinoids, or synthetic cannabinoids.<sup>11</sup>

*Please see those terms for further information*

## Cannabinoid Receptors

The receptors known as cannabinoid receptor 1 (CB1) and CB2 are G-protein coupled receptors (GPCRs) where endocannabinoids and some phytocannabinoids or synthetic cannabinoids bind to initiate their physiological effects.<sup>12</sup>

## Cannabis

The common term for the plant *Cannabis sativa* L, which is widely cultivated for fiber, food, oil, and medicine.<sup>13,14</sup>

Under US federal law, cannabis is subdivided into 2 categories: hemp and marijuana.<sup>1</sup> Hemp is defined as the cannabis plant and/or its constituents containing less than 0.3%  $\Delta^9$ -THC by dry weight volume. Marijuana is defined as all cannabis plants and/or constituents containing greater than 0.3%  $\Delta^9$ -THC by dry weight basis. Hemp and products derived from it are descheduled, whereas marijuana and derives are currently Schedule 1.

## Cannabis Halo Effect

A term to describe the misconception that cannabis and derivatives are harmless and free of side effects because cannabis is a “natural plant”.<sup>15</sup> Many drug molecules come from plants and can be both beneficial and harmful (eg, digitalis from foxglove, nicotine from tobacco).<sup>15,16</sup> The FDA has acknowledged this phenomenon.<sup>17</sup>





## ***Cannabis sativa* L.**

The most well-known varieties of cannabis—sativa and indica— were historically considered subspecies.<sup>18</sup> However, current botanical thinking refers only to a single species *Cannabis sativa* L., as most cannabis plants grown today are hybrids of these varieties.<sup>7,18</sup> The hybrid nature of current cannabis plants mean their cannabinoid content cannot be determined by their variety description or appearance.<sup>18</sup> Therefore, composition analysis is necessary for all plants to determine cannabinoid content.

## **CBD Oil / Hemp CBD Oil\***

A marketing term for a cannabis-based product that is meant to imply it is an extract obtained from the flowering portions and leaves of the hemp plant, then dissolved in another oil (coconut, sesame, etc.) but is claimed to have “minimal” THC content.<sup>11</sup>

## **Dietary Supplement**

A regulatory term referring to a product (other than tobacco) intended for ingestion to add further nutritional value to supplement the diet that contains 1 or more of the following dietary ingredients:<sup>19</sup>

- Vitamin
- Concentrate
- Metabolite
- Herb or other botanical
- Mineral
- Amino acid
- Substance to increase total dietary intake

Dietary supplements are FDA-regulated as foods.<sup>19</sup> The FDA has stated that CBD and THC products may not be marketed as a dietary supplement.<sup>20</sup>

## **DEA Drug Scheduling**

Drugs, substances, and some chemicals are classified into 5 distinct categories (or Schedules) at the federal level by the Drug Enforcement Administration (DEA).<sup>21</sup> Schedules are based on the drug’s acceptable medical use in treatment in the US, relative abuse potential, and likelihood of causing dependence when abused.

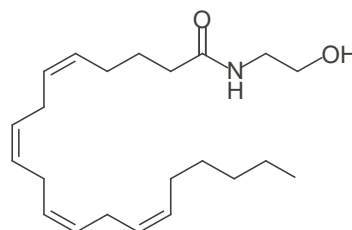
## **Endocannabinoid System**

Internal communication system expressed in all organs and systems and involved in maintaining homeostasis.<sup>11</sup> It is composed of the receptors activated by cannabinoids, endocannabinoids, and the enzymes responsible for synthesis and degradation of endocannabinoids.<sup>12</sup>

## **Endocannabinoids**

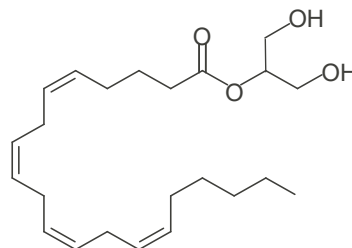
A term for cannabinoids created in the body, these molecules help regulate several physiological processes needed to maintain health.<sup>11</sup> Endocannabinoids most commonly bind to CB1 and CB2 where they play a role in dampening action potential signals in the central nervous system, a process called retrograde signaling.<sup>11,22</sup> Endocannabinoids were identified after discovering the activity of THC on CB1 and CB2 and were thus named after cannabinoids.<sup>10</sup>

*Below are well-known examples.*



### **AEA**

Anandamide, also known as N-arachidonylethanolamine, is a fatty acid neurotransmitter.<sup>10,14</sup> It was the first endocannabinoid to be discovered in 1992.<sup>10</sup> The name 'anandamide' is taken from the Sanskrit word *ananda*, which means "joy, bliss, delight", plus amide. It has lower potency than THC at the CB1 receptor and is a partial agonist at CB2.<sup>23,24</sup>



### **2-AG**

2-arachidonoylglycerol is the second endocannabinoid found and was isolated in 1994.<sup>25,26</sup> It is considered the endogenous agonist for CB1 and CB2.<sup>27</sup>

## Entourage Effect\*

This commonly used term originates in endocannabinoid science to suggest that combining multiple constituents of the whole cannabis plant may result in enhanced therapeutic effects, compared to each constituent individually.<sup>28,29</sup> More data are needed to support or refute this theory in specific disease states.

## FDA-Approved Cannabinoid Medicine

A purified cannabinoid preparation that, through the FDA approval pathway, meets the standard for quality, consistency, stability, safety, and efficacy.<sup>20</sup> It can be plant-derived or synthetic. The Center for Drug Evaluation and Research after rigorous placebo-controlled studies guide correct dosing, safety, and efficacy of new compounds for medical use.<sup>30</sup> Demonstration of product consistency is also required for FDA approval.

## Full Spectrum\*

A marketing term for a cannabis-based formulation that is meant to imply that the product contains many plant constituents, cannabinoids, and terpenes, which could include a significant amount of unlabeled THC.<sup>9</sup>

## Hemp

A legal term for strains of *Cannabis sativa* L. that after the 2014 Farm Bill are defined as containing less than 0.3%  $\Delta^9$ -THC by dry weight and are descheduled.<sup>1,31</sup>

The 2018 Farm Bill expanded the definition of hemp to include its extracts, derivatives, and cannabinoids with less than 0.3% of  $\Delta^9$ -THC by dry weight.<sup>1</sup>

Historically, hemp was grown for its fibrous material in stalks and oils in seeds.<sup>32</sup> The flowering portions of the hemp plant may be used to extract phytocannabinoids, like CBD.

## Hemp Oil / Hempseed Oil

A marketing term that describes the byproduct of cold pressing cannabis seeds to obtain oil.<sup>32</sup> It contains only trace amounts of cannabinoids and terpenes and is high in unsaturated fatty acids. Hemp oil is generally used in paints, varnishes, in manufacturing soap, and a wide variety of food products.

## Isolate\*

A marketing term for a cannabis-based formulation that is meant to imply that the product contains a single cannabinoid that has been isolated from the rest of the botanical mixture.<sup>9</sup> The cut-off of purity to be deemed an isolate is arbitrary.

## Marijuana

Term defined by federal law for the dry, shredded, mix of flowers, stems, seeds and leaves from the cannabis plant containing more than 0.3%  $\Delta^9$ -THC by dry weight.<sup>1,33</sup>

## Medical Cannabis\*

The term medical cannabis can include medical marijuana, CBD, and hemp products.<sup>34</sup> There are no requirements for THC/CBD ratios to be deemed medical cannabis. Often, medical cannabis only differs from recreational marijuana by intent of use, not composition or formulation.<sup>35,36</sup>

Medical cannabis is sold to consumers who have been certified by a health care professional to have a qualified condition deemed appropriate by state law.<sup>37</sup> Unlike medications approved through the formal data-driven process of the FDA, medical cannabis dosage, safety, and efficacy is not specified.<sup>34,38</sup>

## Nutraceutical\*

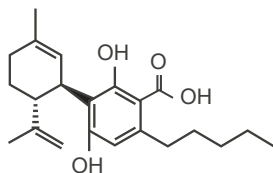
A term derived from combining “nutrition” and “pharmaceutical;” there is no regulatory definition, and it does not fall within a recognized regulatory category of the FDA.<sup>39</sup> Individual nutraceuticals do not undergo testing for medical or health benefits, nor safety.



# Phytocannabinoids

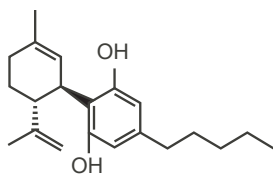
Phytocannabinoids are molecules found in the *Cannabis sativa* L. plant.<sup>40</sup> The cannabis plant contains over 100 known phytocannabinoids with THC and CBD being the most extensively researched.<sup>28</sup>

*Below are well-known examples of phytocannabinoids and some research. These provide a sense for the range of conditions affected by phytocannabinoids but are not comprehensive.*



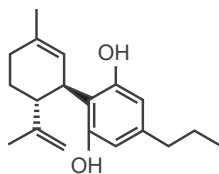
## CBDA

Cannabidiolic acid is how CBD naturally occurs in the plant.<sup>41</sup> CBDA has been shown to prevent vomiting and suppress nausea and anxiety in rodent models through action at the serotonin receptor 5HT1A.<sup>42,43</sup> CBDA converts to CBD through heat, similar to THC.<sup>41</sup>



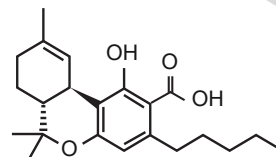
## CBD

Cannabidiol, the by-product of heating CBDA, is one of the major cannabinoids derived from cannabis or synthesized.<sup>11,44</sup> CBD has very low affinity for the CB1 receptor and thus lacks the euphoric side effects commonly associated with THC.<sup>28,45</sup> A single formulation of plant-derived cannabidiol is FDA-approved for rare drug-resistant epilepsies.<sup>46</sup>



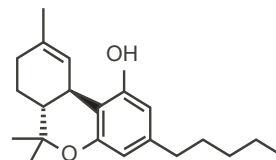
## CBDV

Cannabidivarin, a lesser-known cannabinoid, is produced from cannabidivarinic acid (CBDVA).<sup>28,41</sup> It has been investigated in rodent models of epilepsy and autism spectrum disorder.<sup>44,45</sup>



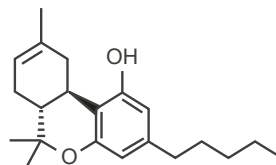
## THCA

Tetrahydrocannabinolic acid is how THC naturally occurs in the plant and is one of the most abundant cannabinoids in cannabis bred for recreational use.<sup>41</sup> While not itself psychoactive, THCA converts to THC when heated or smoked.<sup>41,47</sup> It has been investigated in limited studies.



## $\Delta^9$ -THC

$\Delta^9$ -tetrahydrocannabinol, the molecule commonly called THC, is the by-product of heating THCA.<sup>41</sup> It is a major cannabinoid that may be derived from cannabis or synthesized.<sup>11</sup> THC has a high affinity for the CB1 receptor and can cause dose-related euphoric effects.<sup>28</sup>



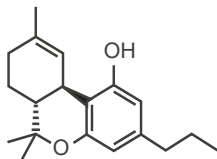
## $\Delta^8$ -THC

$\Delta^8$ -tetrahydrocannabinol is a THC isomer in which the double bond moves to the eighth carbon.<sup>48</sup> It is typically synthesized from CBD extracted from hemp, as the quantities found in cannabis are low. It has a similar pharmacological profile to THC but slightly less potent.<sup>48,49</sup>



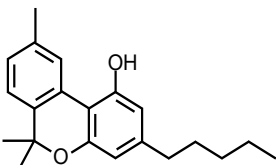
## THCV

Tetrahydrocannabivarin, a lesser-known cannabinoid, is produced from tetrahydrocannabivarin acid (THCVA).<sup>44</sup> It has been investigated in rodent models of both Parkinson disease and insulin sensitivity (diabetes model).



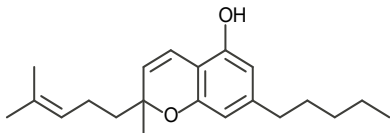
## CBN

Cannabinol is an oxidation product of THC and is a weak psychoactive substance with a higher affinity for CB<sub>2</sub> receptors over CB<sub>1</sub>.<sup>14,40,41</sup> CBN influences disease progression but not survival in the mouse model of amyotrophic lateral sclerosis (ALS).<sup>50</sup>



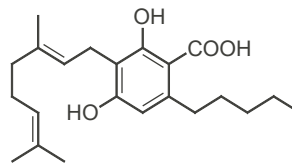
## CBC

Cannabichromene in its acid form, cannabichromenic acid (CBCA), is the most abundant phytocannabinoid in cannabis.<sup>40</sup> It has a low affinity for CB<sub>1</sub> and CB<sub>2</sub> receptors but affects the endocannabinoid system by inhibiting AEA uptake. CBC has antinociceptive and anti-inflammatory effects in vitro and in vivo.<sup>51</sup>



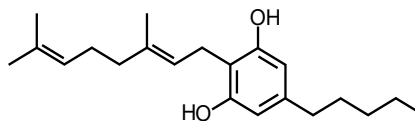
## CBGA

Cannabigerolic acid is the acidic form of CBG. It is the precursor for most phytocannabinoids.<sup>40</sup> CBGA has been shown to have anticonvulsant effects in a mouse model of Dravet syndrome and was investigated as an antiviral for COVID-19.<sup>52,53</sup>



## CBG

Cannabigerol, a non-psychoactive phytocannabinoid, has a low affinity for CB<sub>1</sub> and CB<sub>2</sub> receptors, but inhibits AEA uptake, affecting the endocannabinoid system.<sup>40</sup> CBG was shown to exert antiproliferative, antibacterial, and anti-glaucoma actions and to antagonize the anti-nausea effect of CBD.<sup>54</sup> It was further found to have protective and curative effects in the model of murine colitis.



## Real-World Data

Real-World Data (RWD) is the routinely collected data relating to patient health status and/or the delivery of health care from a variety of sources (ie, electronic health records, claims and billing, product/disease registries, patient-generated data, and other health status sources).<sup>63</sup> RWD does not account for controlled variability in clinical trials and therefore does not replace data from RCTs.

## Real-World Evidence

Real-World Evidence (RWE) is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of real-world data.<sup>63</sup> RWE can be generated by different study designs or analyses, including but not limited to, randomized trials, large simple trials, and observational studies. The FDA states that RWE alone does not replace clinical trials, nor can it lead to drug approvals.

## Recreational Marijuana\*

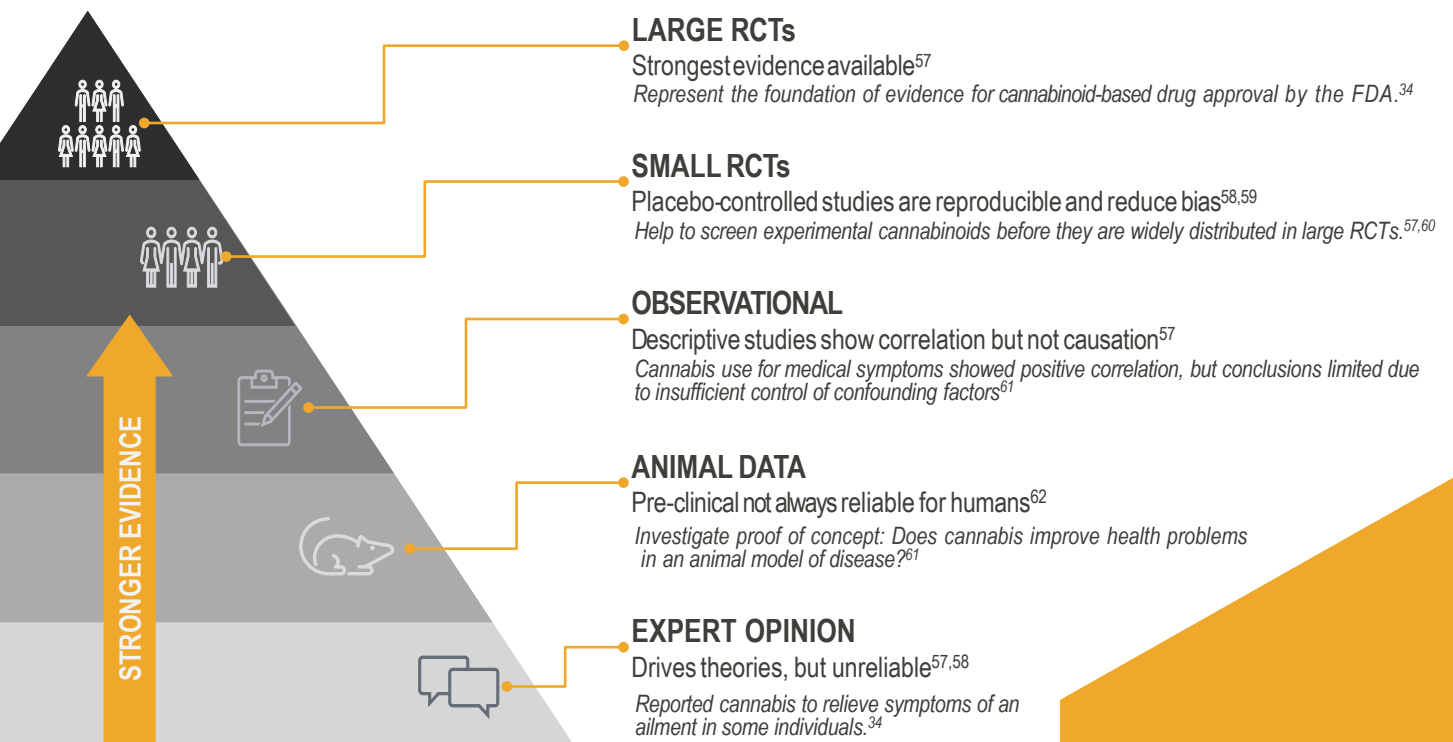
Term for the use of cannabis or cannabis products to induce pleasure, euphoria or relaxation, and to enhance sociability.<sup>64</sup> Generally, the goal is to produce intoxication.

## Phytoremediation

Phytoremediation refers to the use of plants and associated soil microbes to reduce the concentrations of toxic contaminants in soils, surface waters, and groundwater through absorption.<sup>55</sup> Cannabis is a known and effective phytoremediator.<sup>6</sup>

## Pyramid of Evidence

A descriptive metaphor that shows how scientific opinion builds onto scientific testing, leading to hypothesis-driven research.<sup>56</sup> This then feeds into randomized, placebo-controlled trials to show the strongest evidence of drug efficacy and safety.<sup>57</sup> The bottom of the pyramid starts with the lowest level of evidence, expert opinion, and spans all the way up to the highest level, evidence-based medicine, randomized-controlled trials (RCT).<sup>56</sup>

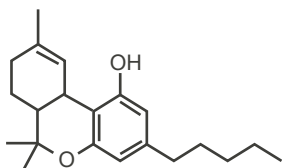




## Synthetic Cannabinoids

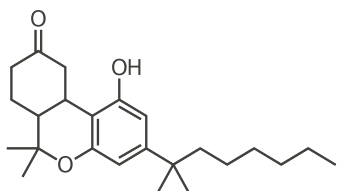
Synthetic cannabinoids are compounds made in the laboratory to structurally or functionally mimic the phytocannabinoids and endocannabinoids.<sup>11,65</sup> There are 3 FDA-approved synthetic cannabinoids.<sup>34</sup> In contrast, there are many illegal synthetic cannabinoid products, sometimes called spice or K2, sold online, in stores, or found in CBD products, some of which have caused illnesses and deaths.<sup>66</sup>

*Below are examples of synthetic cannabinoid drugs.*



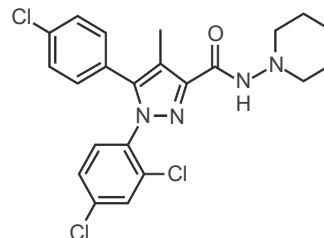
### Dronabinol

Dronabinol is the generic name used pharmacologically for the enantiomer form, (-)-trans- $\Delta^9$ -tetrahydrocannabinol.<sup>67</sup> It is a synthetic form of THC. There are 2 FDA-approved drugs which have indications as an appetite stimulant and antiemetic.<sup>34</sup>



### Nabilone

Nabilone is a synthetic THC homologue and is also a partial agonist of the CB1 and CB2 receptors.<sup>67</sup> Nabilone is FDA-approved to treat nausea and vomiting in people under chemotherapy.<sup>34</sup>



### Rimonabant

Rimonabant (also known as SR141716) is an anorectic anti-obesity drug approved in Europe in 2006 but was withdrawn worldwide in 2008 due to serious psychiatric side effects; it was never approved in the US. Rimonabant is an inverse agonist for CB1.<sup>68</sup>

## Terpenes / Terpenoids

The primary aromatic constituents found in the glandular trichomes of the cannabis plant, providing its scent and flavor.<sup>69</sup> Ongoing preliminary research is investigating therapeutic potential of terpenes.

## Trichomes

Fine hair-like structures or other outgrowth from the epidermis of cannabis plants that secrete cannabinoids and terpenoid compounds.<sup>69,70</sup> They function to absorb harmful ultraviolet B (UVB) rays, protect from cold and heat stress, and likely act as deterrents to herbivores.<sup>69</sup>



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