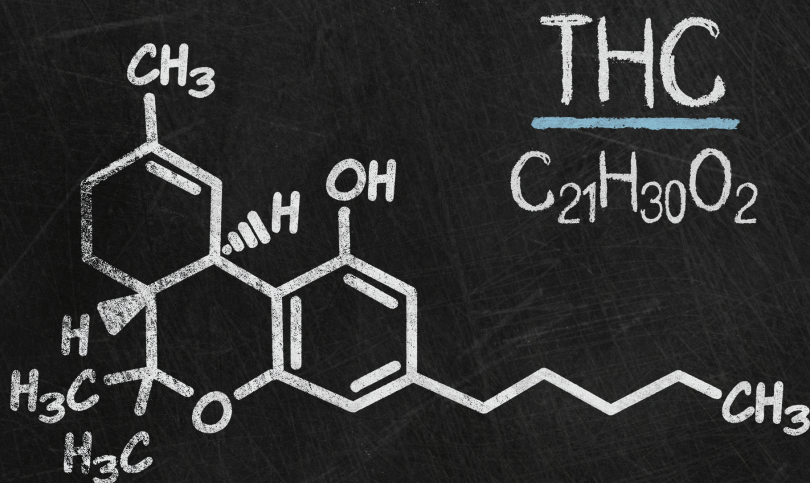


GLOSSARY OF CANNABINOID TERMS



ABBREVIATIONS:

LGL=Legal Term; MKT=Marketing Term; SCI=Scientific Term

CANNABIS-RELATED TERMS

Bioaccumulation (SCI)¹

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

Cannabis (LGL)²⁻⁴

“Cannabis” is the generic term for the plant, *Cannabis sativa* L. Cannabis is a plant that is widely cultivated for fiber, food, oil, and medicine.

Under U.S. federal law, cannabis is subdivided into two categories: hemp and marijuana. Hemp (LGL) is defined as the cannabis plant and/or its constituents containing less than 0.3% Δ -9 tetrahydrocannabinol (THC) by dry weight volume. Marijuana (LGL) is defined as all cannabis plants and/or constituents containing greater than 0.3% THC by dry weight basis. Hemp and products derived from it are descheduled, whereas, marijuana and products derived from it are Schedule 1.

Cannabis Halo Effect⁵⁻⁷

A term to describe the misconception that cannabis and cannabis-based products are harmless and free of side effects because cannabis is a “natural plant”. Many drug molecules come from plants and have been shown to be both beneficial and harmful (eg, digitalis from foxglove plant, nicotine from tobacco plant). FDA has recognized (or acknowledged) this phenomena.

Cannabis sativa L. (SCI)⁸

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

CANNABIS-RELATED TERMS (CONTINUED)

Entourage Effect* (MKT)^{9,10}

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. More data are needed to support or refute this theory in specific disease states.

Phytoremediation (SCI)^{11,12}

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. Cannabis is a known phytoremediator.

Terpenes/Terpenoids (SCI)¹³⁻¹⁵

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

Trichomes (SCI)^{16,17}

Fine hair-like structures or other outgrowth from the epidermis of cannabis plants that secrete cannabinoids and terpenoid compounds.

They function to absorb harmful UV-B rays, protect from cold and heat stress, and likely act as deterrents to herbivores.



*For this term 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.

CANNABINOIDS AND RELATED TERMS

Cannabinoids (SCI)¹⁸⁻²⁰

Term used to refer to molecules found in the cannabis plant and/or that interact with cannabinoid receptors that fall into three classes: phytocannabinoids, endocannabinoids, or synthetic cannabinoids.

Endocannabinoids (SCI)²¹

Endocannabinoids are molecules that help regulate a number of physiological processes needed to maintain a healthy body. They most commonly bind to the cannabinoid receptor 1 (CB1) and cannabinoid receptor 2 (CB2). Endocannabinoids were identified after discovering the mechanism of THC on CB1 and CB2 receptors.

FDA-Approved Formulations of Cannabinoids (SCI)²²

A purified cannabinoid preparation that, through the FDA approval pathway, meets the standard for quality, consistency, stability, safety, and efficacy. It can be plant-derived or synthetic.

Endocannabinoid System & Receptors (SCI)^{23,24}

Internal communication system expressed in all of the body's organs and systems involved in maintaining homeostasis. It is composed of receptors activated by cannabinoids, endocannabinoids, and the enzymes responsible for synthesis and degradation of endocannabinoids.

Cannabinoid Receptors^{23,24}: The receptors known as CB1 and CB2 are two different G-protein coupled receptors (GPCRs) where endocannabinoids and some phytocannabinoids bind and initiate their physiological effects.



CANNABINOIDS AND RELATED TERMS (CONTINUED)

Phytocannabinoids (SCI)^{9,21,25-27}

Phytocannabinoids are molecules found in the *cannabis sativa* L. plant. The cannabis plant contains over 100 known phytocannabinoids with THC and cannabidiol (CBD) being the most well-characterized.

- **CBD:** Cannabidiol, the by-product of heating CBDA, is one of the major cannabinoids derived from cannabis or synthesized. CBD has very low affinity for cannabinoid receptor CB1, thus lacks the euphoric side effects commonly associated with THC. There is one plant-derived cannabidiol that is FDA-approved.
- **THC:** Δ -9-Tetrahydrocannabinol is the by-product of heating THCA. It is a major cannabinoid that may be derived from cannabis or synthesized. THC has a high affinity for the CB1 receptor thus, when ingested, can cause the dose-related euphoric effects. There are FDA-approved synthetic and analogue THC products on the market.
- **CBDV:** Cannabidivarin, a lesser-known cannabinoid, is produced from cannabidivarinic acid (CBDVA). It has been investigated in rodent models of epilepsy and autism spectrum disorder.
- **THCV:** Tetrahydrocannabivarin, a lesser-known cannabinoid, is produced from tetrahydrocannabivarin acid (THCVA). It has been investigated in rodent models of both Parkinson's disease and insulin sensitivity (a model of diabetes).
- **THCA:** Δ -1-Tetrahydrocannabinolic acid is how THC naturally occurs in the cannabis plant and is the most abundant cannabinoid in cannabis bred for recreational use. As a non-psychoactive precursor of THC, THCA converts to THC when heated or smoked. It has been investigated in a limited number of studies.
- **CBDA:** Cannabidiolic acid is how CBD naturally occurs in the plant. CBDA has been shown to prevent vomiting and suppress nausea and anxiety in rodent and rodent-like models through action at the serotonin receptor (specifically 5HT1A). CBDA converts to CBD through heat, similar to THC.

Synthetic Cannabinoids (SCI)²¹

Synthetic cannabinoids are compounds made in the laboratory to structurally or functionally mimic the phytocannabinoids and endocannabinoids. There are 3 FDA-approved synthetic cannabinoids. 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.

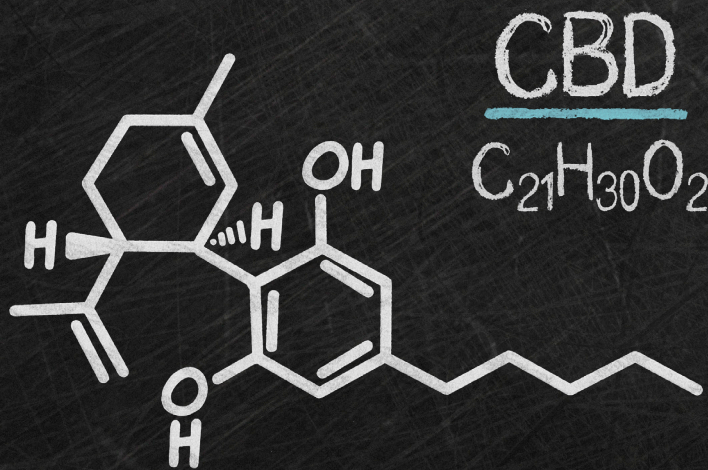
MARIJUANA, HEMP, AND RELATED TERMS

Broad Spectrum* (MKT)²⁸

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.

CBD Oil*/Hemp CBD Oil* (MKT)²⁴

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.



Full Spectrum* (MKT)²⁸

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.

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MARIJUANA, HEMP, AND RELATED TERMS (CONTINUED)

Hemp (LGL)²⁹⁻³²

Hemp is a strain of *Cannabis sativa* L. that after the passage of the 2014 Agriculture Improvement Act (Farm Bill), was legally defined as containing no more than 0.3% THC on a dry weight basis. The 2018 Farm Bill expanded the definition of hemp to include extracts, derivatives, and cannabinoids with less than 0.3% of THC by dry weight. Hemp and the products made from it are now descheduled, whereas marijuana (plant containing more than 0.3% THC by dry weight) remains in Schedule 1. Historically, hemp was grown for the fibrous materials found in stalks and oils in seeds. The flowering portions of the hemp plant may be used to extract phytocannabinoids, like CBD.

Hemp Oil*/Hempseed Oil (MKT)²⁹

A marketing term that describes the byproduct of cold pressing cannabis seeds to obtain oil. 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* (MKT)²⁸

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. The cut-off of purity to be deemed an isolate is arbitrary.

Marijuana (LGL)²⁵

Legal term defined by federal law for the dry, shredded, green/brown mix of flowers, stems, seeds and leaves from the cannabis plant containing more than 0.3% THC, by dry weight.



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MARIJUANA, HEMP, AND RELATED TERMS (CONTINUED)

Medical Cannabis* (MKT)³²⁻³⁴

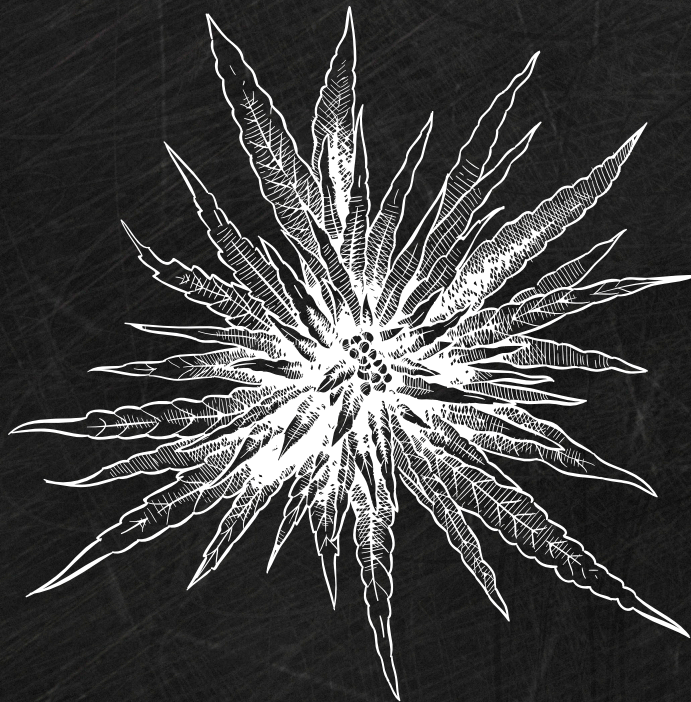
The term medical cannabis can include medical marijuana, CBD, and hemp products. There are no requirements for THC/CBD ratios to be deemed medical cannabis. Often, medical cannabis only differs from recreational marijuana by intent of use, not composition or formulation.

Medical cannabis is sold to consumers who have been certified by a healthcare provider to have a qualified condition deemed appropriate by state law.

Unlike medications approved through the formal data-driven process of the FDA, medical cannabis dosage, safety, and efficacy is not specified.

Recreational Marijuana* (MKT)³⁵

Use of cannabis or cannabis products used to induce pleasure, euphoria or relaxation, and to enhance sociability. Generally used to produce intoxication.



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NUTRACEUTICALS AND DIETARY SUPPLEMENTS

Bioaccessibility (SCI)³⁶

The concept of bioaccessibility can be defined as the quantity or fraction which is released from the food matrix in the GI tract and becomes available for absorption. The same drug in different formulations, solvents, and oils can lead to varied absorption and subsequent plasma levels.

Dietary Supplement (LGL)³⁷⁻³⁹

A product (other than tobacco) intended for ingestion to add further nutritional value to supplement the diet that contains one or more of the following dietary ingredients (or a constituent/extract of these ingredients)

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

Dietary supplements are FDA regulated as foods. The FDA has stated that CBD may **not** be marketed as a dietary supplement.

Nutraceutical* (MKT)^{40,41}

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. Individual nutraceuticals do not undergo testing for medical or health benefits, nor safety.



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REGULATORY GUIDELINES*

Agricultural Improvement Act of 2018 (LGL)^{42,43}

Known as the “Farm Bill”, this bill descheduled industrial hemp and hemp-derived products that have a THC concentration of less than 0.3% by dry weight, thus removing it from Schedule I of the Controlled Substances Act. States and Indian tribes may regulate the production of hemp by submitting a plan to the Department of Agriculture (USDA). The bill also makes hemp producers eligible for the federal crop insurance program and certain USDA research grants. The FDA states, “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.

Botanical Drug Product (SCI)^{44,45}

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. A medication that contains a mixture of constituents from the cannabis plant or mixture of plant derived cannabinoids would be considered to be a botanical drug product.

Drug Enforcement Administration (DEA) Drug Scheduling (LGL)⁴⁶

Drugs, substances, and certain chemicals used to make drugs are classified into five distinct categories (or Schedules) at the federal level by the DEA; these depend upon the drug’s acceptable medical use in treatment in the US, their relative abuse potential, and the likelihood of causing dependence when abused.

FDA-Approved Medication (LGL)⁴⁷

A designation granted by the Center for Drug Evaluation and Research after rigorous placebo-controlled studies to guide correct dosing, safety, and efficacy of new compounds for medical use. Demonstration of product consistency is also required for FDA approval.

*In this document, federal laws and acts are cited because, although an individual state may enact its own laws regarding cannabis, the federal laws (in theory) supersede any state laws in place.

EVIDENCE PYRAMID FOR CANNABINOIDS

Evidence Pyramid (MKT)⁴⁸⁻⁵⁰

A descriptive metaphor that shows how scientific opinion builds onto scientific testing, leading to hypothesis-driven research. This then feeds into randomized, placebo-controlled trials to show the strongest evidence of drug efficacy and safety. 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).



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