Steep Hill®

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An Introduction to Terpenes **Science & Cultivation**

Terpenoids *(terpenes)* are the compounds responsible for a plant's fragrance, found in plant resin glands, or trichomes. Terpenes are recognized by the FDA as food-safe additives. Their interaction with cannabinoids—a phenomenon called the *'entourage effect'*—helps define a cannabis strain's distinctive effect. At present, there are over 50,000 unique terpenoids that have been discovered in plants globally, with over 250 non-cannabinoid terpenoids and 145-150 cannabinoid terpenoids naturally occurring in cannabis. The most common terpenes occurring in cannabis include pinene, limonene, myrcene, ocimene, terpinolene, linalool, and beta-caryophyllene. The smoke or vapor of heated cannabis contains up to 50% terpenes, with cannabinoids normally accounting for 10-20%, and the other (less potent) terpenes accounting for another 10-30%.

Humankind has long been fascinated with terpenes—our interaction with terpenes dates back thousands of years. Outside of their unique relationship to cannabis, we enjoy the characteristic aromas and flavors of products containing terpenes daily, in beer, candy, perfumes, fruits, incense, and more. In addition to the smells and tastes of terpenes, we have also continuously benefited from the diversity of medicinal and nutritional aspects of terpenes. Globally speaking, terpenes/terpenoids likely comprise the single largest family of chemical compounds available for use in compounding remedies and medicine, though for many years these benefits have had limited use outside of traditional herbalism, ethnobotany, and pharmacognosy.

For Citations: ↗ http://steephill.com/pdf/Leading-the-Science-Cannabis.pdf

Terpene	Boiling Point °F	Boiling Point °C	Potential Therapeutic Effects
Humulene	222.8	106	*Analgesic, Antibacterial, Anti-Inflammatory, Anti-Proliferative, Anoretic*
Caryophyllene	226	130	*Anti-Inflammatory, Antimalarial, Cytoprotective (gastric mucosa)*
Pinene	311	155	*Anti-Inflammatory, Bronchodilator, Stimulant, Antibiotic, AChE inhibitor*
Myrcene	332.6	167	*Analgesic, Anti-Inflammatory, Antibiotic, Antimutagenic*
D-Limonene	348.8	176	*Immune potentiator, Antidepressant, Antimutagenic*
Linalool	388.4	198	*Sedative, Antidepressant, Anxiolytic, Immune potentiator*
Terpineol	426.2	219	*Sedative, Antibiotic, AChE inhibitor, Antioxidant, Antimalarial*
α-Pinene	311	155	*Antibacterial, Anti-fungal, Anti-Inflammatory, Bronchodilator*
Borneol	415.4	213	*Analgesic, Anti-Insomnia, Anti-Septic, Bronchodilator*
Cineole (Eucalyptol)	349-351	176-177	*Anti-Bacterial, Anti-Depressant, Anti-Inflammatory, Anti-ischemic, Bronchodilator*
Citronellol	437	225	*Anti-Cancer, Anti-Inflammatory, Anti-Insomnia, Anti-spasmodic*
Nerolidol	251.6	122	*Anti-Fungal, Anti-Insomnia*
Phytol	399.2	204	*Anti-Insomnia*
Terpinolene	366.8	186	*Anti-bacterial, Anti-fungal, Anti-insomnia, Anti-septic*

Most of the commonly occurring terpenoids can be found existing in a remarkable variety of diverse plants. As an example, ß-Caryophyllene can be found in plants as varied as black pepper, cloves, some cannabis sativa strains, rosemary, and hops.

Terpenes have many functions in plants—certain fragrant terpenes attract bees and other animals that carry the plant's pollen to other plants. This is not the case for cannabis, since the cannabis plant depends on the wind, not other carriers, for pollination. In many plants, terpenes are used as a biological defense mechanism, either as a deterrent to drive away herbivores that would otherwise eat the plant, or to attract predators of the herbivore to deter the plant's consumption. With hundreds of millions of years of evolutionary refinement to plant terpenes, it makes sense that humans are strongly attracted to some terpenes and repelled by others.

Documented Therapeutic Properties of Terpenoids

In addition to the use of terpenes in the perfume and food industries, there is a wide array of medicinal properties to terpenes. The fact that each terpene has many different medical benefits gives rise to the overlapping synergies between them; this is something every ethnobotanist knows. The strategy of deliberately overlapping terpene benefits greatly increases the chances of effective results in treatment.

ß-Myrcene is the most commonly found terpene in cannabis, often in high concentrations. Its medicinal properties are well-known, most significantly for use in treating pain and inflammation. Because of its calming effect both mentally and physically, Myrcene is also used to treat psychosis and muscle spasms. Its properties are also used synergistically with other terpenes and cannabinoids: THC for pain, THC-A for inflammation, CBD and Linalool as an antipsychotic, and with all three—THC, THC-A and CBD—in the treatment of muscle spasms.

The Limonene family of terpenes are also abundant in cannabis, second only to Myrcene. Limonenes have antidepressant, anxiety-relief, immuno-stimulant (like garlic), anti-tumor, and anti-fungal/bacterial properties, also aiding in treatment of gastric reflux, including esophageal ulcers. Limonenes can be used topically as an antiseptic agent and are often used to repel insects: the leaves of the lemon or grapefruit tree are used for this purpose. Limonenes have synergies with THC-A, CBD-A, CBC-A, CBC, CBC, CBG, Caryophyllene Oxide, and Linalool.

The Science and Cultivation of Terpenoids

Isoprene is a five-carbon long molecule that is the foundation of all terpenoids. Think of each five-carbon isoprene as a single chain link: terpenes are constructed of these chain links, with most terpenes being comprised of chains of 5, 10, 15—up to 40 carbons long. Limonene and Linalool are both 10 carbons long—or contain 2 isoprene chain links—whereas Phytol, being a larger, oilier molecule, contains 20 carbons or 4 isoprene links, similar to cannabinoids. In most cases, the larger the terpene molecule, the more viscous and less vaporous it is. Limonene evaporates very quickly, with a pungent fragrance, like acetone. Cannabinoids, on the other hand, are much larger molecules, are nearly solid at room temperature and have only a faint odor, like pine pitch. The size and structure of the terpenoid also determines factors such as how soluble it is in water, ethyl alcohol, oil, or other solvents; as well as how easily it decomposes from heat, light, and air.

Research has demonstrated that there are several factors that potentially affect terpenoid production in cannabis cultivation. Among the most critical are plant genetics, pest presence, cultivation conditions, the ecological history of resources, and overall plant health. While soil nutrient and microbiological diversity and fertilization have an impact on plant chemistry, research on the impact on terpene production is limited and variable. To our knowledge, terpene enhancers do not boost production or quality of terpenes. These products may have the potential to increase terpenes, although not directly—these products improve overall plant health, which in turn encourages terpene expression.

As some terpenes are produced by the plants for defense, the presence of these compounds will be affected by pest pressure or drought, depending on the terpene. In cases of defensive terpenes, environmental factors such as pest pressure or drought may increase terpene production, as part of the plant's built-in survival tactic. Biotic and abiotic conditions affect terpene production. Mechanisms by which light, temperature, or physical damage modify terpene concentrations have been well-studied. Light and plant competition are critical environmental factors affecting defensive terpenoid development at the cultivation stage, especially regarding fertilization, which changes the biotic/abiotic dynamics of plant nutrients. Nutrient availability, such as nitrogen, promotes terpene development as these components are crucial for photosynthesis and generation of ATP, but at present, there is no conclusive evidence pointing to nitrogen alone as a chemical assisting terpene modulation.

However, nutrient interactions with plant development are affected by other factors and direct correlations have not yet been conclusively drawn to these factors and terpene emissions. Additionally, different terpenes react to different soil types—pH levels, nutrient availability, and soil texture are causal influences. Diversity in the soil microbiome and the presence of beneficial, well-balanced microbes enhances rooting ability, resulting in a healthier plant. In general, healthy microbes enhance plant rooting ability, efficiency, and resistance to stressors. Certain microbes create specific compounds, which, when absorbed by the plant, may selectively increase terpene production. Growth-promoting plant bacteria and fungi boost crop growth and yield by balancing nutrients, hormones, and mineral/water uptake. They also serve to alleviate stress; reducing plant susceptibility to diseases and pests, thereby promoting induced systemic resistance. These beneficial effects result in the accelerated production of secondary metabolites, which include terpenes *(Ormeño, et al.)*

While research indicates that some pesticides and fungicides have the capacity to act as plant growth regulators (PGRs), increasing terpene production, it's important to note that this does not necessarily contribute to a healthier plant overall. Lower concentrations of these compounds may increase terpene synthesis, and higher concentrations of specific fungicides may also result in decreased levels of terpene synthesis. Here, any substance which modulates the geranyl pyrophosphate pathway in plants has the potential to increase terpenes, but not enough is known about the long-term effects on cannabis cultivation, and as such, should be approached with caution.

Terpene Storage

Like any plant material, once harvested, cannabis is perishable. As volatile organic compounds, incorrectly stored, terpenes dissipate quickly from cured cannabis. Post-production, terpene retention depends on environmental conditions and time—for example, light boilers dissolve terpenes faster, and considerable terpene reduction has been observed during handling and storage.

To prevent the structural breakdown of terpenes, the cannabis trichomes where the terpenes are concentrated must be kept intact and unbruised. Optimally, cannabis should be stored in airtight, rigid containers, away from sunlight, at ideal temperatures of 50°F, with long-term and short-term storage solutions varying slightly. Storage in blue, UV-resistant glass is ideal; with NSF polypropylene, polycarbonate, and polyethylene suitable storage alternatives. Light terpenes will dissolve in soft plastics, like plastic bags. Storage in soft containers or plastics is not recommended, as crushed trichome heads promote oxidation of both terpenoids and cannabinoids, promoting rapid deterioration of cannabis and reducing overall potency.

When suspended in lipid oils, shelf-stability of terpenes changes. Terpenoids reduce the speed at which lipids go rancid; however, the mixture's concentration would affect stability—with a higher concentration of terpenes resulting in more stable product, dependent on lipid type and storage conditions. Dilute essential oils, terpenes stabilized in lipids, can be drawn for comparison when discussing degradation of terpenes in cannabis products. When you break a seal on a bottle of lipid oil, the degradation clock starts ticking due to oxygen-exposure—unless repacked with nitrogen or argon gas, which is highly unlikely in most cannabis production operations. Water vapor expedites the degradation process. Color, texture, and clarity of lipid-suspended cannabis products will change over time. Rancidity occurs when the fats decompose into other compounds, causing the development of an unpleasant smell and/or taste.

The Future of Terpenes

Though our historic interaction with terpenes goes back centuries—millennia, even—there's still much to learn about their benefits, and new terpenoids are constantly being discovered. Researchers and scientists—like the experts at Steep Hill and Eybna—continue to map new territory, identifying and extracting new terpenes for clinical research and testing. We envision a future cannabis industry where terpenoids lead the way for innovation and discovery, unlocking door after door of potential for patients and consumers. We look forward to new applications of terpenoids, making it possible to access strain-specific cannabis oils, or made-to-order cannabis extracts tailored to the specifications of the user to create a specific effect, experience, or medicinal quality. Through research and development, we see a future where the science of terpenes gradually becomes an art form, improving our knowledge of the cannabis plant terpenoid by terpenoid. As the stigma around cannabis fades into the past, we can look towards a future full of discovery, innovation, and therapeutic benefits—all from the "small but mighty" terpene.

Beta (ß)-Caryophyllene

A common terpene found in cannabis, as well as hops, black pepper, aged mango, bay leaves, and lemongrass, with an odor commonly described as an herbal, balsamic, rooty, or spicy.

Cannabinoid

a class of diverse chemical compounds, meroditerpenoids, that act on cannabinoid and other receptors, in cells that alter neurotransmitter release in the brain.

Entourage Effect

A concept/proposed mechanism theorizing that compounds present in cannabis which are largely non-psychoactive by themselves modulate overall psychoactive effects of the plant.

Ethnobotany

The scientific study of the indigenous or traditional knowledge of plants, including medical, cultural, and religious applications of plants, exploring the intersections of knowledge across cultures. Pharmacognosy is a subset of ethnobotany which focuses specifically on the medicinal extraction and applications of various plants.

Isoprene

A five-carbon long molecule that is the basis of all terpenoids.

Limonene

A terpene found in the peel of citrus and other fruits, and also in many flowers, with a sweet, fresh, citrusy, and fruity aroma.

Linalool

A terpene found in cannabis and many essential oils, including orange, lavender, rose, rosewood, and coriander.

Myrcene

A terpene found several plants, including cannabis, bay, cannabis, ylang-ylang, wild thyme, parsley, and cardamom.

Pharmacognosy

A branch of knowledge and subset of ethnobotany concerned with the extraction of medicinal drugs obtained from plants or other natural sources.

Plant Growth Regulator (PGR)

Chemical envoys for intercellular communication. There are currently five recognized groups of plant hormones: auxins, gibberellins, cytokinins, abscisic acid (ABA) and ethylene, which work together to coordinate the growth and development of cells.

Terpene (terpenoid)

A large group of volatile, unsaturated hydrocarbons commonly found in the essential oils of plants, especially cannabis, conifers, and citrus trees.

Trichome

A small hair or other outgrowth from the epidermis of a plant, typically unicellular and glandular. In cannabis cultivation, this is where the greatest concentrations of terpenes are found.

RESOURCES

1. "Terpenes." https://www.steephill.com/science/terpenes. Steep Hill. Accessed February 21, 2018.

2. "Cannabis, Terpenes, and the Entourage Effect." https://www.steephill.com/blogs/32/Cannabis,-Terpenes-and-the-Entourage-Effect. Steep Hill. Accessed February 21, 2018.

3. "Resources." http://steephilllab.com/resource. Steep Hill. Accessed February 21, 2018.

4. Backes, Michael. *Cannabis Pharmacy: The Practical Guide to Medical Marijuana*. Black Dog & Leventhal; September 9, 2014.

5. Bottini, Rubén & Piccoli, Patricia. (2013). "Terpene Production by Bacteria and its Involvement in Plant Growth Promotion, Stress Alleviation, and Yield Increase." *Molecular Microbial Ecology of the Rhizosphere*. 1. 335-343. 10.1002/9781118297674.ch31. https://www.researchgate.net/publication/275153003_Terpene_Production_by_Bacteria_and_its_Involvement_in_Plant_Growth_Promotion_Stress_Alleviation_and_Yield_Increase Accessed February 27, 2018.

6. Matarese F., A. Cuzzola, G. Scalabrelli, C. D'Onofrio. "Expression of Terpene Synthase Genes Associated with the Formation of Volatiles in Different Organs of *Vitis vinifera."* *Phytochemistry.* September 2014, Volume 105, pp 12-24. Accessed February 21, 2018.

7. Muzika R. M., K. S. Pregitzer, J. W. Hanover. "Changes in Terpene Production Following Nitrogen Fertilization of Grand Fir *(Abies grandis* (Dougl.) Lindl.) Seedlings." *Oecologia*. September 1989, Volume 80, Issue 4, pp 485–489. Accessed February 21, 2018.

8. Ormeño, E. and Fernandez, C. "Effect of Soil Nutrient on Production and Diversity of Volatile Terpenoids from Plants." *Current Bioactive Compounds/Bentham Science Publishers*. 2012 Jan. (8)1: 71-79. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3474957/ Accessed February 27, 2018.

9. Ormeño, Elena & Baldy, Virginie & Ballini, Christine & Fernandez, Catherine. (2008). "Production and Diversity of Volatile Terpenes from Plants on Calcareous and Siliceous Soils: Effect of Soil Nutrients." *Journal of Chemical Ecology.* 34. 1219-29. 10.1007/s10886-008-9515-2. https://www.researchgate.net/publication/23141130_Production_and_Diversity_of_Volatile_Terpenes_from_Plants_on_Calcareous_and_Siliceous_Soils_Effect_of_Soil_Nutrients Accessed February 27, 2018.