Whole Plant Therapy

Harnessing the Therapeutic Potential of Cannabis

Introduction

Cannabis has been used medicinally for thousands of years, but only in recent decades have scientists begun to uncover the complex chemistry underlying its therapeutic effects. Over 500 compounds have been identified in the cannabis plant, including cannabinoids, terpenes, and flavonoids, each contributing unique therapeutic properties.

The concept of ***Whole Plant Therapy*** embraces the synergistic interplay of these compounds, rather than isolating or stripping them away through over-processing. Whole plant formulations provide the full symphony of cannabis' healing potential.

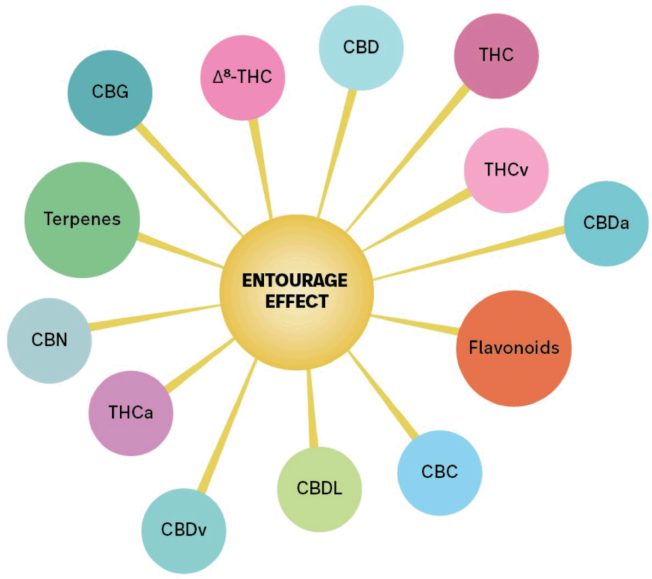
This white paper explores the phytochemical diversity of cannabis, mechanisms of synergy, and evidence for whole plant therapy. Key topics include:

- The '*Entourage Effect*' and cannabis synergy
- Major and minor cannabinoids
- Terpenes and their therapeutic properties
- Flavonoids, fatty acids, and other key compounds
- Differences between Cannabis Sativa and Cannabis Indica
- Whole plant extraction methods
- The benefits of minimally processed cannabis oil (RSO)
- Halo Infusion's whole plant cannabis products

By understanding cannabis' intricate phytochemistry and applying whole plant extraction methods, product developers can deliver more comprehensive, efficient cannabis therapies to patients.

The Entourage Effect: Unlocking the Power of Cannabis Synergy

The Entourage Effect refers to the synergistic interaction between the multitude of compounds found in cannabis, particularly tetrahydrocannabinol (THC) and cannabidiol (CBD). Rather than relying on isolated components, the Entourage Effect posits that full spectrum cannabis formulations provide enhanced therapeutic effects and reduced side effects compared to single compounds.



This synergistic activity arises from the complex biological network engaged by the variety of phytochemicals present in cannabis. The two most abundant cannabinoids, THC and CBD, interact extensively with the mammalian endocannabinoid system to modulate pain, appetite, mood, inflammation, and other critical processes.

THC mimics the effects of the endocannabinoid anandamide, binding CB1 receptors highly concentrated in the brain and central nervous system. This produces the well-known psychoactive effects of cannabis. CBD also binds CB1 but has higher affinity for CB2 receptors located predominantly in the periphery of immune cells, contributing to its anti-inflammatory action.

Beyond cannabinoids, terpenes constitute another major class of cannabis phytochemicals with therapeutic activity. The terpene myrcene, for example, produces muscle relaxation and sedative effects by increasing permeability of the blood-brain barrier to compounds like THC. Limonene binds TRPV1 receptors also engaged by cannabinoids, contributing complementary analgesic and anti-inflammatory properties.

Pinene exhibits acetylcholinesterase inhibition leading to alertness and memory enhancement. These activities synergistically interact with cannabinoids to provide more comprehensive, nuanced effects.

Additional compounds like flavonoids and phytosterols contribute anti-inflammatory, antioxidant, and anti-cancer effects through both direct and indirect biochemical mechanisms. Even compounds present in minute concentrations can profoundly influence overall pharmacological impact. This chemical plurality allows cannabis to affect diverse biological systems simultaneously, creating emergent activity greater than isolated constituents.

While individual cannabis compounds have value, nature's evolutionary wisdom shines through the intricacies of botanical synergy. Just as people once consumed whole willow bark instead of purified aspirin, whole plant cannabis formulations maximize therapeutic potential compared to isolates through the Entourage Effect. This concept has critical relevance for product formulation as well as future cannabis research and medicine.

Research reveals how specific cannabis component combinations enhance effects beyond their individual contributions:

- **THC + CBD:** CBD modulates the intoxicating effects of THC while enhancing its pain-relieving properties.
- **THC + Terpenes:** Terpenes like linalool and limonene modulate the psychoactivity of THC and boost its anti-inflammatory effects.
- **CBD + Terpenes:** Terpenes increase CBD bioavailability and maximize its anxiety and pain relief potential.
- **Flavonoids + Cannabinoids:** Flavonoids potentiate the anti-inflammatory effects of cannabinoids.

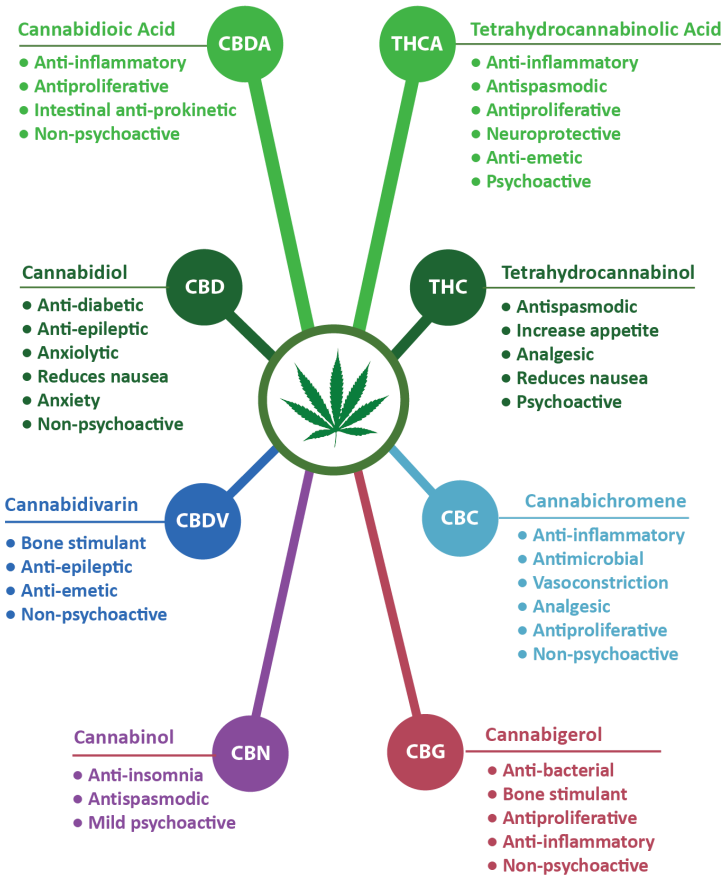
These and many other synergies make the case for whole plant therapy.

Major and Minor Cannabinoids

Over 120 cannabinoids have been identified in cannabis. While THC and CBD dominate scientific study, minor cannabinoids contribute significantly to whole plant synergy. Here are some of the most prominent cannabinoids:

- **THC:** The main psychoactive compound in cannabis responsible for the characteristic mental effects. THC relieves pain, nausea, appetite loss and has potential in managing autoimmune disorders.
- **CBD:** A non-intoxicating compound with anti-inflammatory, analgesic, anxiolytic and antipsychotic properties. CBD modulates THC effects and shows efficacy against seizures, anxiety disorders and neuropathic pain.

- **THCV:** An analogue of THC with appetite suppressing effects and potential against diabetes and metabolic disorders. Lower doses can amplify THC activity.
- **CBG:** The precursor of THC and CBD. Potent anti-inflammatory and neuroprotective effects. Boosts anandamide levels contributing to antidepressant activity.
- **CBC:** Anti-inflammatory, antidepressant and analgesic effects. Synergizes with THC, amplifying its pain relieving properties.
- **CBDV:** Anticonvulsant effects comparable to CBD. Reduces nausea and inhibits cancer cell growth. Enhances REM sleep.



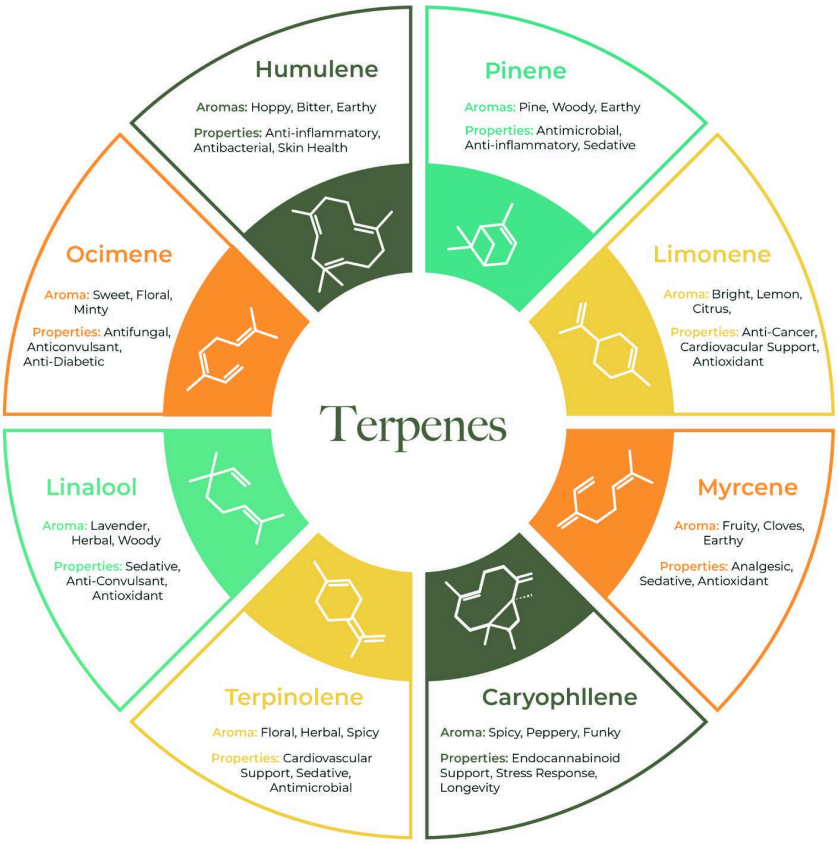
These minor players exhibit diverse pharmacology and therapeutic applications. Though minute in concentration, their presence contributes to cannabis' multifaceted benefits.

Terpenes: Aromatic Therapeutic Compounds

Terpenes give cannabis its characteristic aroma and flavor. But beyond aesthetics, terpenes interact with cannabinoids to enhance therapeutic effects. Here are some key cannabis terpenes:

- **Limonene:** Citrus scent. Elevates mood and relieves stress/anxiety. Anti-cancer and heartburn relieving effects. Enhances CBD and THC absorption.
- **Linalool:** Lavender scent. Sedative and stress-relieving. Antidepressant and analgesic properties. Linalool modulates effects of THC, slightly reducing the euphoric effects.
- **Myrcene:** Earthy, clove-like aroma. Muscle relaxant. Contributes anti-inflammatory and analgesic activity. Myrcene increases THC potency.
- **Caryophyllene:** Pepper/spice scent. Gastroprotective. Anti-inflammatory and neuroprotective. Compounds relief from alcohol dependency.
- **Pinene: Pine scent.** Mental focus-enhancing. Bronchodilatory benefits in asthma. Pinene is known to synergize with CBD as an anti-inflammatory therapy.

Just as cannabinoids work together, unique terpene combinations provide synergistic therapeutic benefits. This diversity makes whole plant extracts more efficacious and consistent compared to isolated preparations.



Other Key Phytochemicals

Additional compounds round out cannabis' therapeutic riches:

- **Flavonoids:** Cannflavins A and B are unique cannabis flavonoids. Potent anti-inflammatory activity and neuroprotective antioxidants. They have shown the ability to enhance cannabinoid effects.
- **Fatty Acids:** Essential fatty acids in cannabis enhance endocannabinoid system tone and aid THC/CBD absorption. They have demonstrated anti-inflammatory effects.
- **Phytosterols:** Beta-sitosterol and others reduce intestinal inflammation. Phytosterols have cholesterol lowering effects, and studies have shown anti-cancer and neuroprotective activity.

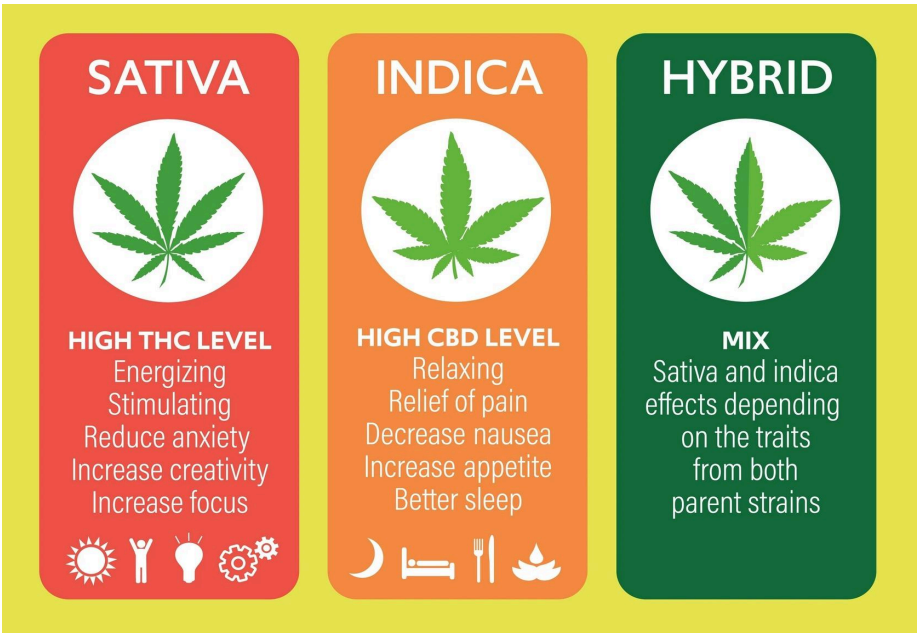
While minute in concentration, these lesser-known components contribute significantly to cannabis' holistic therapeutic impact through both synergies and independent effects, underscoring the importance of whole plant preparations.

Cannabis Sativa vs. Indica

The two main species of cannabis, Cannabis sativa and Cannabis indica, have distinct phytochemical profiles influencing their effects. Hemp is considered a subspecies and is also rich in compounds.

Cannabis Sativa: Typically higher in energizing terpenes like limonene and THC. Effects tend toward euphoric, creative, and uplifting. Used to relieve depression, nausea, headaches. Higher CBD varieties provide alert relaxation.

Cannabis Indica: Often contains more sedating terpenes such as myrcene and higher THC levels. Provides full body relaxation effects. Helpful for sleep, muscle spasms, pain. CBD-rich indicas provide relaxation without sedation.



While these trends hold, substantial crossover exists. Advanced breeding produces strains not readily categorized. Additionally, cultivation techniques alter chemical phenotypes through environmental impacts on gene expression. Effects ultimately depend on the unique phytochemical profile regardless of sativa/indica classification.

Maintaining Cannabis' Chemical Integrity

Many standard cannabis extraction methods selectively isolate key compounds like THC and CBD. However, whole plant philosophy avoids over-processing to retain the full suite of beneficial phytochemicals. Two techniques optimize whole plant integrity:

Cold Extraction

Cold Extraction is the gentle, low-heat plant extraction that preserves fragile terpenes and flavonoids lost via combustive smoking or chemical processing using solvents at high pressure and/or temperature. Maintaining modest temperatures below 190°F retains volatile compounds and protects thermolabile molecules from structural alteration. Cold Extraction can be performed using solvents ranging from water to hydrocarbons like Ethanol and Butane, to CO2.

Minimal Refinement

The problem with most extraction methodologies is that post-extraction refinement often strips away terpenes, flavonoids and other compounds to isolate cannabinoids like CBD and THC.

Using Ethanol as a solvent and minimizing post processing provides the best and most consistent approach to preserving non-cannabinoid compounds. Whole plant preparations using this approach, undergo only minimal refinement to preserve native compounds. Both major and minor cannabinoids are preserved, together with their co-resident terpenes, flavonoids, and other phytonutrients.

The Potency of Minimally Processed Cannabis Oil

Rick Simpson Oil (RSO) is a full spectrum cannabis extract containing all native cannabis compounds in their natural ratios. Made using food-grade ethanol, RSO retains chlorophyll, flavonoids, terpenes, phytosterols and other components alongside major and minor cannabinoids.

Named after Canadian engineer Rick Simpson, RSO was developed in 2003 to treat Simpson's own skin cancer. RSO's potent anti-cancer effects have since extended to other diseases responsive to cannabis but resistant to purified extracts.

Research identifies several key advantages of RSO compared to isolated preparations:

- RSO contains higher fractions of THC than CBD isolates. THC shows synergistic anti-cancer activity with other cannabis components.
- Phytosterols in RSO like beta-sitosterol have direct apoptotic effects on cancer cells.
- Terpenes present in RSO but lost in isolates enhance bioavailability and maximize cannabinoid effects.
- The combination of cannabinoids, terpenes and other compounds creates optimal therapeutic impact through synergy.

For diseases benefiting from whole plant cannabis therapy, RSO represents an easily produced, minimally refined extract for harnessing cannabis' full therapeutic potential.

Using Cannabis Flower in Topical Production

While most methods of consuming cannabis provide whole body effects, topical products allow for targeted, localized benefits. Traditional cannabis topicals utilize purified oils containing isolated cannabinoids like CBD and THC. However, a novel approach involves incorporating unprocessed, fresh cannabis flower into topical formulations.

Through an optimized intermediate decarboxylation process, a broad spectrum of cannabinoids are expressed in their active forms as well as their native acidic precursors, including THC, THCa, CBD, CBDa, and rare compounds like CBGa. This "dirty" oil harnesses the full phytochemical profile of cannabis flower into the final product.

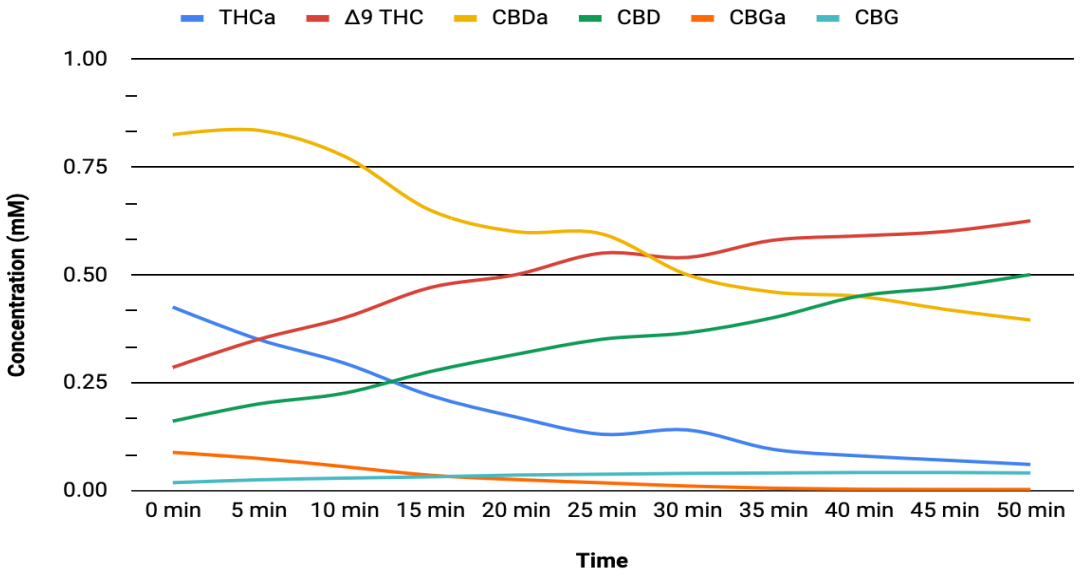
The result is magnified anti-inflammatory, analgesic, and anti-microbial activity ideal for joint/muscle pain, arthritis, and skin conditions. Unlike topicals relying on CBD isolates, whole flower formulations provide the multidimensional benefits of minor cannabinoids, terpenes, flavonoids and other cannabis flower components.

Intermediate Decarboxylation

Intermediate Decarboxylation is a novel method for extracting cannabinoids and terpenes from cannabis and hemp plant matter. It involves partially decarboxylating the plant material while directly infusing it into base oils, allowing better preservation of both cannabinoid precursors and activated cannabinoids as well as terpenes.

Initially, cannabis contains cannabinoid acids such as THCa, CBDa, and CBGa. The application of energy in the form of heat causes the hydroxyl group to separate, converting these acidic precursors into the better-known activated forms THC, CBD, and CBG that provide euphoric and therapeutic effects. However, excessive heat degrades terpenes and converts all cannabinoid acids, leaving none of the beneficial precursors.

Halo Infusion's proprietary Intermediate Decarboxylation Process (IDP[TN]) uses finely controlled, modest heating to induce only partial decarboxylation. Around 65% of the cannabinoid acids are retained, while about 35% get converted into their activated forms (see figure below). This strikes an optimal balance between getting some conversion to THC, CBD, etc. for therapeutic benefit while preserving levels of THCa, CBDa, CBGa, and other acids that exhibit their own therapeutic effects.



Source: *Decarboxylation Study of Acidic Cannabinoids: A Novel Approach Using Ultra-High- Performance Supercritical Fluid Chromatography/Photodiode Array-Mass Spectrometry, Wang, et al, 2016*

The moderate heat also helps retain terpenes and other plant compounds that are volatile and easily damaged. Maximizing terpene content is crucial for harnessing the Entourage Effect, and the synergy between cannabinoids and terpenes that enhances therapeutic impact.

Overall, the IDP provides customized, partial decarboxylation that preserves valuable cannabinoid acids and terpenes for whole-plant extracts with maximum cannabinoid diversity and rich terpene profiles. The method eschews excessive processing and heat exposure to create products mirroring the phytochemical wealth of the raw cannabis plant.

Halo Infusions' Test Results Show Diverse Cannabinoids

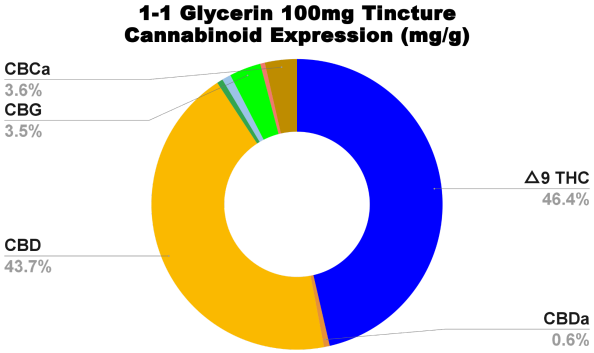
In contrast to products containing only THC and CBD isolates, Halo Infusions' whole plant preparations express a wide array of cannabinoids.

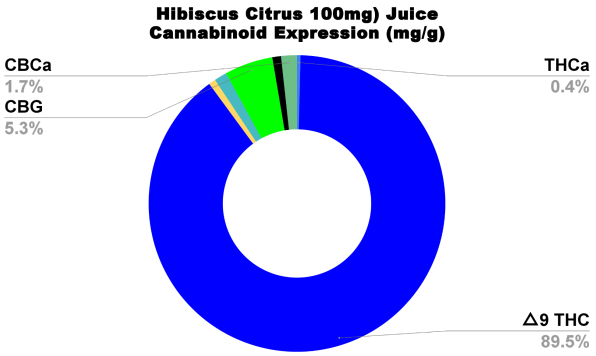
Independent lab testing reveals our products consistently contain THC, CBD, CBN, CBG, THCV, and CBC. The diversity of cannabinoids mirrors the chemical variety of the raw cannabis flower.

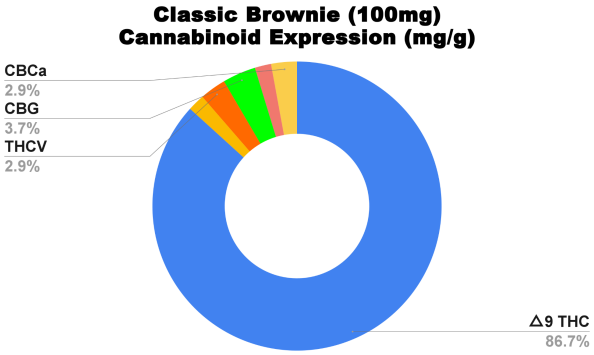
For example, testing of our Chronic Health lotion showed the presence of THC, CBD, CBN, CBG, CBC, and THCV. Rather than simply delivering CBD to localized receptors, the multitude of cannabinoids provides comprehensive therapeutic activity.

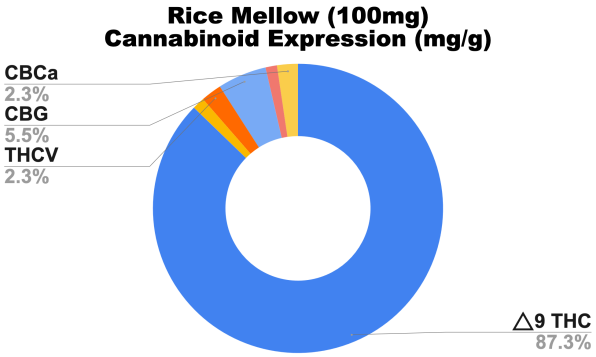
This demonstrates how whole plant techniques like intermediate decarboxylation of raw flower enable finished products to mirror the phytochemical breadth of the cannabis plant.

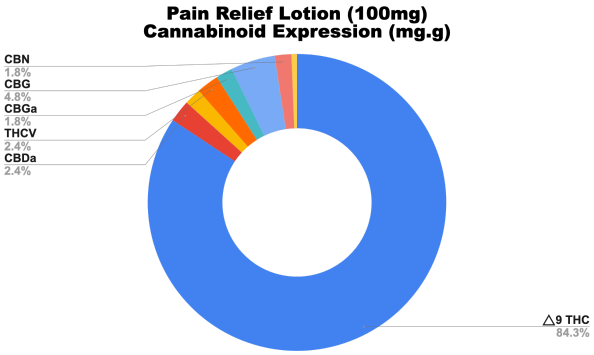
The figures below illustrate the cannabinoid expression for a number of Halo Infusions-branded finished products. As shown, both major and minor cannabinoids are present.











Conclusion

Evidence suggests whole plant cannabis formulations provide enhanced therapeutic activity compared to isolated constituents, a phenomenon described as the Entourage Effect. While individual compounds have merits, Full Spectrum extracts better represent the intricate biochemical complexity of the Cannabis sativa plant.

As analytical techniques continue elucidating this intricate phytochemistry, refinement protocols preserving native diversity will likely provide improved clinical outcomes. Gently preserving delicate terpenes alongside customized, partial cannabinoid decarboxylation retains acidic and activated cannabinoids integral to emerging models of synergy. Delicate balances struck during extraction and refinement seem to mirror nature's ratios.

Processes like Intermediate Decarboxylation provide key examples of biomimicry through nuanced thermal and mechanical energy inputs. The resultant whole-plant concentrates and distillates contain over a hundred phytocannabinoids, terpenes, flavonoids, and lesser studied compounds.

While concentrations fluctuate between chemovars, whole plant products provide concentrations on par with artisanal medical cannabis.

As hypotheses of ensemble effects evolve, gentle processing and holistic refinement seem poised to deliver efficient therapies congruent with nature's intricate ratios. Companies integrating biochemistry with ethical extraction stand at research's cutting edge. Still in its early stages, this reintegration of traditional herbalism with modern analysis offers much promise.

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