Thanks to their efficacy and popularity, THC and CBD have become well-known acronyms among medical professionals and patients alike. Research into their medicinal effects has revealed their usefulness for an ever-expanding list of health issues.

But pure THC and CBD extracts may not offer the best possible therapeutic results. A growing number of researchers believe these substances produce superior results when administered in a more natural form, either together or in combination with other chemical compounds found in cannabis plants like the minor cannabinoids, terpenes, and flavonoids. Such compounds are often referred to as whole-plant or full-spectrum products.

They claim this is the result of a theoretical principle known as the entourage effect. While some still have doubts, experimental and anecdotal evidence has convinced many cannabis consumers and industry professionals that the entourage effect is real.

**What is the Entourage Effect?**

When multiple cannabis compounds are integrated, their medicinal effects may be altered or enhanced. The flavors and psychoactive capacities may also be affected, creating distinct products with varying characteristics.

According to its advocates, the group dynamics of the entourage effect can create emergent properties that would otherwise not be present in pure THC or CBD. Many who work closely with cannabis believe the entourage effect can dramatically increase the medicinal utility of THC and CBD, either by magnifying their known effects or by expanding their menu of therapeutic applications.

The therapeutic effects of cannabis compounds arise from their capacity to bind with naturally occurring endocannabinoid receptors in the brain and throughout the central nervous system. The human endocannabinoid system is designed to link with endogenous cannabinoids produced by the body, but compounds found in cannabis plants can bind with these receptors just as efficiently.

Health benefits abound when high-quality medicinal cannabis is consumed by humans. The entourage effect may be one of the reasons why marijuana is such an effective medicine.

**Cannabinoids, Terpenes, and Flavonoids: Natural Healing Partnerships**

The entourage effect is believed to emerge from the interactions between cannabinoids and between terpenes and cannabinoids. Terpenes are essential oils with distinctive aromas and flavors, and the characteristics of individual cannabis products are often determined by their relative concentrations of specific terpenes.

Currently, most of the research into the entourage effect has focused on the interactions between THC and CBD, and more specifically, on how the latter might affect the former.
“The biggest influence [on THC] is CBD,” states Ethan Russo, a neurologist who serves as Director of Research and Development at the International Cannabis and Cannabinoids Institute in Prague. Perhaps no one in the industry has gone to greater lengths to prove the existence of the entourage effect than Russo, who has been scouring the scientific literature in search of its footprints for decades.

As evidence of CBD’s impact on THC expression, Russo mentions a 2010 clinical trial involving the pain reliever Sativex, which is prescribed for patients with multiple sclerosis. The drug includes a relatively balanced mixture of THC and CBD.

In a controlled study, Sativex was given to individuals suffering from great pain associated with cancer. Some participants enrolled in the study received a preparation of pure THC extract, while others were given a placebo. Sativex was found to offer a significant pain-killing effect in 40 percent of the patients who took it, which made it twice as potent as the THC extract. This difference was observed even though the THC content of each preparation was identical, which could only mean that the CBD was somehow increasing the pain-killing potency of the THC.

Additional research indicates that Sativex does not produce the psychotic side effects that are experienced on some occasions by those who consume pure THC regularly.

Another study, carried out in 2016, compared the experiences of cannabis users who smoked pure THC to those who smoked cannabis products that included both THC and CBD. While those who consumed pure THC experienced memory problems and other cognitive difficulties (typical results associated with that compound), those who smoked THC and CBD together experienced no such troubles.

In analyzing the results of these studies, researchers credit the capacity of CBD to either moderate or intensify the binding activity of THC with cannabinoid receptors in the brain.

At present, research into the effects of specific cannabinoid-terpene combinations is scant. One 2018 meta-analysis did reveal that pure CBD extracts were far less effective in reducing the occurrence of seizures in epilepsy patients than extracts that included a mixture of cannabis cannabinoids, including terpenes. While 71 percent of those who took the mixed preparation had fewer seizures, only 46 percent of those treated with pure CBD experienced the same result.

Laboratory studies may one day establish the existence of the entourage effect beyond a reasonable doubt. That day has not yet arrived, but the research that strongly suggests the effect is real is starting to accumulate, along with ample anecdotal evidence from users whose experiences with medicinal cannabis vary based on the chemical composition of the products they’ve been consuming.

**Anecdotal Evidence is Still Evidence**

Researchers who remain skeptical of the entourage effect point to the lack of controlled, double-blind laboratory studies to verify its reality. By its very nature, the entourage effect is a complicated process to trace and identify.
Advocates for the entourage effect acknowledge the limitations in the current research.

“We can’t do very basic studies about what’s really true,” laments Mowgli Holmes, a geneticist who founded Phylos Bioscience, a hemp and cannabis genetics company located in Portland, Oregon. “But you have thousands and thousands of people reporting the same thing. It gets hard to ignore.”

The federal government’s stubborn misclassification of recreational cannabis as a Schedule I substance has poisoned the well for legitimate research. In the meantime, some scientists who study the healing properties of cannabis are reluctant to accept anecdotal evidence as authoritative, which is what the entourage effect largely relies on to demonstrate its validity.

But the anecdotal evidence is extensive and precise.

“We’ve done a lot of focus groups and data collection and analysis, and 80 or 85 percent of people fall right into the effect we say they will get,” declares chemist Chris Emerson, the cofounder of Level Blends, a company that leverages the entourage effect to create a diverse range of distinct products. “We don’t understand how all these things are working in concert. But I put everything on the line for this [the entourage effect] because I know [believe in] this so strongly.”

As one of the foremost experts on the science of the entourage effect, Ethan Russo admits that more work is needed to clarify the exact mechanisms involved.

“Do we need better studies to prove the concept?” he asks rhetorically. “The answer is yes. I believe in this because I’ve known for 40 years the differences between different [types of] cannabis. They smell different. They taste different. They have different effects.”

The testimony of cannabis consumers is consistent with the thesis that small differences in cannabinoid and terpene mixtures create different user experiences. This would seem to indicate that new and unique properties may emerge from the interaction of various cannabis chemical compounds and that even minuscule alterations in the formula may be enough to produce medically significant differences.

While the anecdotal evidence supporting the reality of the entourage effect may not be conclusive, it should be convincing enough to motivate researchers to continue their quest for the truth.

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