

## 1. What is in Metagenics full-spectrum hemp extract?

Metagenics full-spectrum hemp extract is responsibly sourced from hemp stalk, stems, seeds, and flower that contain a wide range of beneficial phytocannabinoids, terpenes, and other plant compounds. When the various elements of full-spectrum hemp extract are combined, their benefit is greater than what each individual component provides.<sup>1</sup>

## 2. Where is Metagenics hemp grown?

Our source of hemp is grown in Europe, using Certified European Industrial Hemp that is both European Certified Organic and USDA Organic. We take pride in the fact that Metagenics full-spectrum hemp extract is farmed with eco-farming practices, Kosher Certified, allergen free, and non-GMO.

## 3. How can I be sure that what's on the label is what's in the bottle?

We document our quality through TruQuality, an innovative transparency program that provides full access to the data from third-party analytical tests performed on each lot. From heavy metal and glyphosate testing to active ingredient potency, we have laid it all on the table so that you know exactly what is inside each of our bottles.

## 4. Why is it important that Metagenics hemp formulas are certified Glyphosate Residue Free from the Detox Project?

Glyphosate is the most commonly used herbicide in the world and has the highest public profile of any chemical used in food production. The revelation from WHO's International Agency for Research on Cancer (IARC) in 2015 that glyphosate is a "probable carcinogen" has led to consumers across the globe asking for transparency regarding the levels of glyphosate in their food.

## 5. Why doesn't Metagenics label the amount of individual phytocannabinoids featured in its full-spectrum hemp extract?

Certain phytocannabinoids labeled individually are currently excluded from the dietary supplement definition under section 201(ff)(3)(B) of the FD&C Act [21 U.S.C. § 321(ff)(3)(B)]. Labeling individual constituents of certain phytocannabinoids would be inaccurate (as a full-spectrum hemp) and would also cause this product to be considered misbranded.

## 6. Are hemp products legal in the US?

On a federal level, products made from industrial hemp are legal. Industrial hemp has a separate definition from "marijuana" and is no longer classified under the DEA's Controlled Substances Act. Metagenics sources compliant high-quality, non-GMO industrial hemp extract from aerial plant parts (hemp stalk, stems, seeds, and flower) with a tetrahydrocannabinol (THC) content of less than 0.3%.

## 7. Does Metagenics hemp extract contain marijuana?

Metagenics hemp products do not contain marijuana. Federal law defines "hemp" as *Cannabis sativa* plants that contain no more than 0.3% THC. *Cannabis sativa* plants above 0.3% THC are classified as "marijuana."

## 8. What are phytocannabinoids?

Phytocannabinoids are naturally occurring plant-based bioactive compounds that can support and influence the body's endocannabinoid system (ECS). Through direct and indirect actions, phytocannabinoids modulate a variety of physiological systems influenced by the ECS. More than 80 different phytocannabinoids have been identified in different Cannabis species (hemp and marijuana subspecies), including cannabidiol (CBD), cannabigerol (CBG), cannabidiolic acid (CBDA), and many others. In nature, phytocannabinoids work together with other constituents in plants producing synergistic effect on the ECS.<sup>2\*</sup>

## 9. What are terpenes?

Terpenes are a group of compounds naturally present in all plants and spices including pepper, cloves, and cinnamon and contribute to their flavor and scent. These molecules are also known to carry a wide array of therapeutic properties.<sup>2</sup> Terpenes work together with phytocannabinoids to enhance the overall benefit of hemp extract.<sup>1,2</sup>

## 10. What is the endocannabinoid system?

The endocannabinoid system (ECS) is the most complex regulatory system involved in many aspects of physiology, including a healthy stress response, the immune response, food intake and appetite regulation, and neurological health. In fact, the ECS is the body's primary regulatory system.<sup>3</sup> This system consists of receptors, endogenous cannabinoids (known as endocannabinoids), and metabolic enzymes.<sup>3</sup> The two major endocannabinoids, anandamide (AEA) and 2-arachidonolglycerol (2-AG), bind to cannabinoid receptors type 1 (CB1) and type 2 (CB2) located throughout the body, and their biological function is terminated by hydrolyzing enzymes, FAAH and MAGL, respectively. Endocannabinoids are "messengers," produced and released on demand from the brain and peripheral tissues and activate their targets only when and where needed.<sup>4\*</sup>

## 11. What factors impact the ECS?

Just like for other systems in the body, factors such as genetics, nutrition, lifestyle, and overall health status can impact endocannabinoid tone and the ability of the ECS to function optimally. Certain foods and activities can help to boost the ECS functions. A healthy diet with balanced essential fatty acids along with medium- to high-intensity aerobic activity have been shown to enhance the activity of the ECS.<sup>7\*</sup>

## 12. How do phytocannabinoids interact with and benefit the ECS?

Most of the biological properties related to phytocannabinoids rely on their interactions with the ECS in the body. Phytocannabinoids have been identified to act uniquely on cannabinoid receptors separately and simultaneously and/or to inhibit or activate receptor function.<sup>5</sup> In addition, phytocannabinoids can affect the tissue levels of endocannabinoids. Therefore, phytocannabinoids display unique therapeutic effects by supporting a healthy stress response, neurological health, digestive health, and promoting immune function, among others.<sup>6\*</sup>

## 13. What is the difference between full-spectrum hemp extract and hemp seed oil?

Full-spectrum hemp extract is sourced from aerial plant parts (stalk, stems, seed, and flower) of the hemp plant and contains beneficial phytocannabinoids and terpenes. As stated before, it has been suggested that phytocannabinoids and terpenes work together to influence each other and have a synergistic effect on the ECS. Hemp seed oil is extracted only from the seeds of hemp and is mainly used as a source of dietary oil. The levels of phytocannabinoids in hemp seed oil are very low and, therefore, do not promote the same kind of benefits as full-spectrum hemp extract.\*

## 14. What is the difference between full-spectrum hemp extract and single phytocannabinoid isolate?

Single phytocannabinoid isolate products are made with a pure isolated concentration of a single phytocannabinoid and do not contain other phytocannabinoids and terpenes. Alternatively, full-spectrum hemp extract contains a range of the beneficial phytocannabinoids and terpenes. It has been suggested that phytocannabinoids and terpenes work together to influence each other and have synergistic effects on the ECS.\*

## 15. What is supercritical CO<sub>2</sub> extraction?

Supercritical CO<sub>2</sub> extraction uses pressurized carbon dioxide to extract the desired phytocannabinoids, terpenes, and other beneficial phytochemicals from a plant. Unlike other extraction methods, the supercritical CO<sub>2</sub> extraction process is free of any harsh chemical solvents. CO<sub>2</sub> extraction is an environmentally friendly method to deliver potent concentrates that are free of toxins and safe for consumption.<sup>8</sup> This approach is also known as "green extraction."

## 16. What are the various delivery formats for hemp extract?

Hemp extract can be delivered in a variety of different ways. Hemp extract products can be administered as a liquid, ingested as edibles or tinctures, and gel caps. One of the most common methods to deliver hemp extract is in capsules or gel caps. While it provides the most direct and precise method of dosing, oral bioavailability of phytocannabinoids can be low due to first-pass metabolism in the liver, which breaks them down before reaching the circulation.<sup>9</sup>

## 17. How long does it take for hemp extract to take effect?

The uptake of hemp extract depends on several factors such as current health, metabolism, amount (mg) of phytocannabinoid in hemp extract, and delivery format.

## 18. How much hemp extract should be taken?

Unfortunately, there are no dosage studies yet on hemp extract, and potencies can vary based on extraction methods and phytocannabinoid content. Despite lack of formal recommendations, anecdotal evidence suggests ranges from 5–100 mg of phytocannabinoids per serving, depending on the desired support, body weight, age, and the individual's metabolism. Depending on the support needs, the practitioner may recommend specific dosage, starting off low and titrating as desired.\*

## 19. Is hemp extract legal for professional athletes?

The World Anti-Doping Agency (WADA) no longer prohibits hemp products, but that does not mean hemp is legal and approved for all athletes. Other naturally present cannabinoids in hemp extracts remain prohibited by WADA.<sup>13</sup>

## 20. What is PEA?

Palmitoylethanolamide (PEA) is an endogenous bioactive lipid that is structurally related to the well-known endocannabinoids, such as anandamide (AEA). However, unlike AEA, PEA does not bind to the classical CB1 and CB2 receptor; therefore, it is known as an endocannabinoid-like lipid. PEA could also be found in nature in lipid extracts of plants and vegetables such as egg yolks, soybean lecithin, and many more.<sup>14,15</sup>

## 21. How does PEA work?

PEA is produced “on demand” from membrane phospholipids as a response to external stimuli and exerts a variety of biological effects via multiple mechanisms.<sup>14</sup> PEA not only directly activates nonclassical cannabinoid receptors, but also indirectly potentiates endocannabinoid actions by an entourage effect.<sup>14\*</sup>

## 22. Why did Metagenics combine PEA and hemp together?

PEA and active compounds within full-spectrum hemp extract share series of pharmacological similarities and are believed to have the potential to work synergistically to support endocannabinoid signaling. They also share a number of effects in regulating healthy stress and immune responses, energy balance, digestion, and more. Recently, researchers at University of California, Irvine, found in a mechanistic study that adding full-spectrum hemp extract to PEA prolonged PEA in the circulation, and therefore amplified the effects of PEA.<sup>17\*</sup>

## 23. What technology is used for increased bioavailability of PEA in PEA Relief™?

PEA Relief utilizes Levagen®+, which is a cold water dispersible technology specially designed to enhance absorption of PEA.

Levagen+ is a trademark of Gencor

\*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

## References:

1. Russo E. *Br J Pharmacol*. 2011;163:1344–1364.
2. Andre CM et al. *Front Plant Sci*. 2016;7:19.
3. Aizpurua-Olaizola O et al. *Drug Discov Today*. 2017;22(1):105–110.
4. Di Marzo V et al. *Nat Rev Drug Discov*. 2004;3(9):771–784.
5. Maroon J et al. *Surg Neurol Int*. 2018;9:91.
6. Andre CM et al. *Front Plant Sci*. 2016;7:19.
7. McPartland JM et al. *PLoS ONE*. 2016;9(3):e89566.
8. Stahl E et al. *J Agri and Food Chem*. 1980;28(6):1153–1157.
9. Ujvary I et al. *Cannabis Cannabinoid Res*. 2016;1(1):90–101.
10. Mannila J et al. *J Pharm Sci*. 2007;96(2):312–319.
11. Nahtigal I et al. *J Pain Manage*. 2016;9(4):481–491.
12. MacCallum C. A. et al. *Euro J Int Med*. 2018;49, 12–19.
13. <https://www.wada-ama.org/en/content/what-is-prohibited/prohibited-in-competition/cannabinoids>
14. Paladini A et al. *Pain Physician*. 2016;19(2):11–24.
15. Gabrielsson L et al. *Br J Clin Pharmacol*. 2016;82(4):932–942.
16. Davis et al. *Am J Hosp Palliat Care*. 2019;36(12):1134–1154.
17. Tagne AM et al. *Pharmacol Res*. 2021:105545.

