

# TRUE LEAF PET™ WHITE PAPER

## True Hemp™ Meta-Analysis



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### Summary and Purpose

The content of this paper will explore the safety and benefits of hempseed products as nutraceuticals. Additionally, this paper will examine published sources from both human and veterinary literature to substantiate the other ingredients used in True Leaf's unique product line.

### Introduction to Hemp

*Cannabis sativa* L., most recognizable as the source of marijuana, has been an important and sustainable resource for thousands of years.<sup>1, 2, 3, 4, 5</sup> For legal reasons, research and product development of both narcotic and non-narcotic varieties have been suppressed for most of the 20th century.<sup>5</sup>

Different varieties and parts of the *Cannabis* plant have been used for a multitude of purposes. These include fiber from the main stalk, narcotic drugs from the flowering parts, and oilseed. Oilseed has numerous uses which include human food, livestock feed, nutritional supplements, industrial oils, and occasionally biofuel.<sup>5</sup>

Appropriate nomenclature is commonly misused when referring to Cannabis. For clarification purposes, *Cannabis sativa* is typically labelled as "hemp" when used as a source of fiber, "hempseed" when used as a source of seed oil or seed meal, and "marijuana" when used for narcotic, recreational, or therapeutic drugs.<sup>5</sup> "Industrial hemp" refers to non-narcotic varieties of the crop grown for fiber or oil. These by definition contain less than 0.3% THC on a dry-matter basis. THC or delta-9-tetrahydrocannabinol, is the well-known psychoactive cannabinoid (CB) found in *Cannabis* plant.<sup>6</sup> Marijuana contains high amounts of THC, or more than 0.3% THC on a dry-matter basis. THC is a CB of concern because it is known to cause toxicosis with considerable morbidity in dogs.<sup>7</sup> However, the THC lethal dose in rats, mice and dogs, is approximately 1000 times higher than the lowest dose known to reproduce toxicity symptoms in these animals.<sup>8, 9</sup>

Hempseed products, such as hempseed oil and hempseed meal, are derived from the achenes or fruit of the *Cannabis* plant. Hempseed meal powder is currently a major human food product in Canada, and it is derived from sieved hempseed meal.<sup>10</sup> The new True Leaf product line provides an easy to administer source of hempseed for dogs. It is important to note, that the majority of information here on the nutritional components of hemp products has been derived from studies on hempseed oil.

### Hemp as a Nutraceutical

"The word "nutraceutical" is a combination of terms describing nutrition or the use of nutrients and "cuticles"(from "pharmaceutical"), simply meaning nutrients that have a therapeutic effect on the body.<sup>11</sup>

Hempseed meal has been used as a source of dietary protein by a variety of species.<sup>12, 13</sup> Albumin and edestin are the two main proteins in hempseed, and both are rich in amino acids essential to human and animal health.<sup>14</sup> An examination of hempseed, egg white and soy bean amino acid profiles concludes that hempseed protein is comparable to these high quality proteins.<sup>14</sup> Arginine and glutamic acid are also found in especially high levels in hempseed.<sup>14</sup>

Hempseed oil has a unique fatty acid profile, which can contain over 80% polyunsaturated fatty acids (PUFA).<sup>10</sup> The essential fatty acids (EFAs) are abundant in hempseed oil; desaturation products of the EFAs, such as stearidonic acid (SDA) and gamma-linolenic acid (GLA), are found in hempseed oil as well.<sup>15</sup> These fatty acids are not commonly found in most of the oils used in the human diet. Studies in humans have reported health benefits associated with consumption of these fatty acids in cardiovascular diseases, rheumatoid arthritis, and some types of dermatitis.<sup>16, 17, 18</sup> Additionally, SDA has been found to have anti-tumorigenic effects in human cancers,<sup>19, 20</sup> and may have chemosensitizing effects on canine lymphoid tumor cells.<sup>21</sup>

As a plant based oil, it is important to mention that hempseed oil does not contain eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA), two beneficial PUFAs found in fish oils. Dietary alpha-linolenic acid (ALA) alone in humans, dogs, and cats is not an efficient source for conversion into EPA and DHA.<sup>22, 23, 24</sup> SDA, provided in hempseed oil, has a superior ability to convert to EPA over ALA.<sup>25</sup>

Additionally, it is important to consider the metabolic competition of the EFAs, and therefore the ratio of omega-6 to omega-3 (n6/n3). An n6/n3 balance between 2:1 and 3:1 is suggested, and thus, the typical ratio found in hempseed oils is optimal at 2.5:1.<sup>15, 26, 27</sup> This makes hempseed oil a beneficial additive to an n6/n3 balanced diet, as it will not disrupt of the optimal n6/n3 ratio.

Cannabidiol (CBD) is a cannabinoid that has several desirable properties that are seen without psychoactive effects.<sup>28</sup> It has been found to be present in hempseed oil at low levels of 10 mg/kg.<sup>29</sup> CBD is not explicitly produced within the achenes, however traces of contamination in hempseed products have been reported<sup>30</sup>. Although the level of CBD within hempseed products is typically small, it may still be a beneficial dose<sup>29</sup>. Just some of the many actions of CBD include anti-inflammatory, analgesic, anxiolytic, anti-cancer, and neuroprotection from antioxidant effects.<sup>31, 32, 33, 34, 35, 36, 37, 38, 39, 40</sup> With current research, the knowledge of CBD action and efficacy is constantly expanding.

Other components found within hempseed products like terpenoid compounds, may also add to hempseed health benefits.<sup>29</sup> Similar to CBD, the presence of terpenes is most likely the result of contamination from processing, however even at their low concentrations, they may be significant. Terpenes have been cited as having anti-inflammatory, anti-allergenic, and cytoprotective pharmacological properties.<sup>41</sup>

Current information regarding dosing hempseed products for beneficial effects in dogs is unavailable. Multiple studies, however, have been conducted on the use of hempseed products for animal feed in poultry, bovine, caprine and aquatic species. These have demonstrated the safety and efficacy of hempseed products in animal nutrition. For example, studies in laying hens did not see adverse effects on laying performance and egg sensory characteristics.<sup>13, 42, 43</sup> A study in fistulated cows and lambs concluded hemp meal was a good source of rumen undegraded protein, with high post-ruminal availability.<sup>12</sup> A study in steers found diets containing 14% hempseed had no negative effects on gain, gain to feed ratio and carcass traits.<sup>44</sup> In a comparative study with soybean-meal and barley, hempseed cake as a protein feed resulted in similar production and improved rumen function.<sup>45</sup> In a ten week feeding study on juvenile sunshine bass, the use of hempseed meal in the diet had no negative effects on performance.<sup>46</sup>

In conclusion, hempseed is a good source of protein and fatty acids with additional components including cannabidiol and terpenoids. It has been found to be a safe and efficacious additive in animal feed for a variety of species. For these reasons, hempseed is the focus of True Leaf's nutraceutical product line for dogs. 🌿

# White Paper

## REFERENCES



1. Zias J, Stark H, Sellgman J, et al. Early medical use of cannabis. *Nature*. 1993;363:215.
2. Xiaozhai L, Clarke R. The cultivation and use of hemp (*Cannabis sativa* L.) in ancient China. *J Int Hemp Assoc*. 1995;1(2):26–33.
3. de Padua L, Bunyaprafatsara N, RHMJ L. Plant Resources of South-East Asia: *Medicinal and Poisonous Plants. Vol 12*: Leiden, Backhuys Publishers; 1999.
4. Pringle H. Ice age community may be earliest known net hunters. *Science*. 1997;277:1203-1204.
5. Small E. Evolution and Classification of *Cannabis sativa* (Marijuana, Hemp) in Relation to Human Utilization. *Botanical Review*. 2015;81:189-294.
6. Clark RaWD. Cannabis and Natural Cannabis Medicines. In: ElSohly MA, ed. *Marijuana and the Cannabinoids*: Humana Press; 2007.
7. Meola S, Tearney C, Haas S, Hackett T, Mazzaferro E. Evaluation of trends in marijuana toxicosis in dogs living in a state with legalized medical marijuana: 125 dogs (2005–2010). *J of Vet Emergency and Critical Care*. 2012;6(22):690-696.
8. Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clinical Pharmacokinetics*. 2003;42:327- 360.
9. EFSA. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP). Scientific Opinion on the safety of hemp (*Cannabis* genus) for use as animal feed. *EFSA Journal*. 2011;3(9):1-41.
10. Callaway JaPD. "Hempseed oil". In: Kamal-Eldin RAMaA, ed. *Gourmet and Health-Promoting Specialty Oil: American Oil Chemists Society Press*; 2009.
11. Goldstein R. A Modern Approach to Therapeutic Nutraceuticals. In: Blackwell RSGaW, ed. *Integrating Complementary Medicine into Veterinary Practice*; 2008.
12. Mustafa A, McKinnon J, Christensen DT, vohmfrCJAS. The nutritive value of hemp meal for ruminants. *Can. J. An. Sci*. 1999;1(79):91-95.
13. Silversides F, Budgell K, Lefrançois M. Effect of feeding hempseed meal to laying hens. *British Poultry Science*. 2005;2(46):231-235.
14. Callaway J. Hempseed as a nutritional resource: an overview. *Euphytica*. 2004;140:65-72.
15. Callaway J, Tennilä T, Pate D. Occurrence of "omega-3" stearidonic acid (cis-6,9,12,15-octadecatetraenoic acid) in hemp (*Cannabis sativa* L.) seed. *J. Internat. Hemp Assoc*. 1997;3:61-63.
16. Callaway J, Schwab U, Harvima I, et al. Efficacy of dietary hempseed oil in patients with atopic dermatitis. *Journal of Dermatological Treatment*. 2005;2(16):87-94.
17. Chow C. *Fatty acid in foods and their health implications (3rd edition)*. 3 ed: New York: CRC Press; 2008.
18. Oomah D, Busson M, Godfrey D, Drover J. Characteristics of hemp (*Cannabis sativa* L.) seed oil. *Food Chemistry*. 2002;76:33-43.
19. Trebelhorn C, Dennis J, Pondugula S, et al. Plant-based omega-3 stearidonic acid enhances antitumor activity of doxorubicin in human prostate cancer cell lines. *J Cancer Res Ther*. 2014;2:132.
20. Kelavkar U, Hutzley J, McHugh K, Allen K, Parwani A. Prostate tumor growth can be modulated by dietarily targeting the 15-lipoxygenase-1 and cyclooxygenase-2 enzymes. *Neoplasia*. 2009;11(692-699).
21. Pondugula S, Ferniany G, Ashraf F, et al. Stearidonic acid, a plant-based dietary fatty acid, enhances the chemosensitivity of canine lymphoid tumor cells. *Biochem and Biophysical Research Comm*. 2015;460:1002-1007.
22. Brenna J, Salem N, Sinclair A, Cunnane S. α-Linolenic acid supplementation and conversion to n-3 long-chain polyunsaturated fatty acids in humans. *Prostaglandins, Leukotrienes and Essential Fatty Acids*. 2009;2-3(80):85-91.
23. Bauer J, Dunbar B, Bigley K. Dietary Flaxseed in Dogs Results in Differential Transport and Metabolism of (n-3) Polyunsaturated Fatty Acids. *J Nutr*. 1998;128:2641S-2644S.
24. Pawlosky R, Denkina Y, Ward G, Salem N. Retinal and brain accretion of long-chain polyunsaturated fatty acids in developing felines: the effects of corn oil-based maternal diets. *Am J Clin Nutr*. 1997;2(65):465-472.
25. Walker C, Jebb S, Calder P. Stearidonic acid as a supplemental source of ω3 Polyunsaturated fatty acids to enhance status for improved human health. *Nutrition*. 2013;2:363-369.
26. Simopoulos A, Leaf A, Salem N. Workshop statement on the essentiality of and recommended dietary intakes from omega-6 and omega-3 fatty acids. *Prostaglandins Leukot. Essent. Fatty Acids*. 2000;3(63):119.121.
27. Kriese U, Schumann E, Weber W, Beyer M, Bruhl L, Matthaus B. Oil content, tocopherol composition and fatty acid patterns of the seeds of 51 *Cannabis sativa* L. genotypes. *Euphytica*. 2004;137:339-351.
28. Karler B, Turkais S. The cannabinoids as potential antiepileptics. *J. Clin Pharmacol*. 1981;21:437-448.
29. Leizer C, Ribnicky D, Poulev A, Dushenkov S, Raskin I. The composition of hemp seed oil and its potential as an important source of nutrition. *Journal of Nutraceuticals, Functional & Medical Foods*. 2000;4(2):35-54.
30. Grotenhermen F, Karus M, Lohmeyer D. THC limits for food: A scientific study. *Journal of the International Hemp Association*. 1998;2(5):101-105.
31. Mecha M, Felui A, Inigo P, Mestre L, Carrillo-Salinas F, Guaza C. Cannabidiol provides long lasting protection against the deleterious effects of inflammation in a viral model of multiple sclerosis: a role for A2A receptors. *Neurobiol Dis*. 2013;59:141-150.
32. Russo E. Cannabinoids in the management of difficult to treat pain. *Ther Clin Risk Management*. 2008;4:245-259.
33. Piomelli D, Giuffrida A, Callignano A, De Fonseca F. The endocannabinoid system as a target for therapeutic drugs. *Trends Pharmacol Sci*. 2000;21:218-224.
34. Grotenhermen F. Cannabinoids in cancer pain. *Cannabinoids*. 2010;5:1-3,22.
35. Zuardi A. Cannabidiol: from an inactive cannabinoid to a drug with wide spectrum of action. *Rev Bras Psiquiatr*. 2008;30:271-280.
36. Schier A, Ribeiro N, Silva A, et al. Cannabidiol, a *Cannabis sativa* constituent, as an anxiolytic drug. *Rev Bras Psiquiatr*. 2012;34:104-110.
37. Fernandez-Ruiz J, Pazos M, Garcia-Arencibia M, Sagredo O, Ramos J. Role of CB2 receptors in neuroprotective effects of cannabinoids. *Mol Cell Endocrinology*. 2008;286:91-96.
38. Shohami E, Cohen-Yeshurun A, Magin L, Algali M, Mechoulam R. Endocannabinoids and traumatic brain injury. *Br J Pharmacology*. 2011;163:1402-1410.