



Medicinal Potential of the Certified Organic Hemp-Derived Cannabinoid CBDa For Chronic Pain

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Executive Summary

Chronic pain affects more than 50 million adults in the United States and remains one of the leading causes of long-term disability and healthcare utilization. Despite a wide range of available treatments, many individuals experience only partial relief that is often accompanied by significant side effects or long-term risks. These limitations have contributed to growing interest in alternative approaches that target underlying mechanisms of pain, including inflammation and nervous system dysregulation.

While countless people feel hopelessly trapped in this cycle, CBDa (cannabidiolic acid), the acidic precursor to CBD, has recently gained attention as a potential therapeutic compound. Emerging evidence suggests that CBDa may influence underlying inflammatory and neurological processes associated with chronic pain, rather than acting solely as a symptomatic analgesic.¹

This review article reveals the therapeutic potential of Nesa's Hemp oil, a Certified Organic Hemp-Derived CBDa product. Unlike decarboxylated cannabinoids, CBDa retains a distinct pharmacological profile when appropriately extracted. Our unique cold-extraction method keeps CBDa intact — not decarboxylated, not degraded, not weakened. The result is a living, medicinal extract that delivers rapid, targeted relief free of the harsher side effects that may occur with conventional medications.

CBDa has shown promise in managing inflammation, neuropathic discomfort, muscle and joint pain, and stress-related tension without intoxication or dependency.¹

Introduction to Chronic Pain and CBDa

Chronic pain is among the top health complaints worldwide. It is an important signal because it is the body's way of telling us that something is out of balance. Despite decades of advancements in modern medicine, most conventional treatments do little more than mask the discomfort. Patients are often left dependent on painkillers that can cause cognitive impairment that affects a person's daily performance of general tasks and decision-making. Internally, these drugs may harm the liver, disrupt digestion, or lead to addiction.



The endocannabinoid system (ECS) is increasingly recognized as a key regulator of pain, inflammation, and immune function. Yet most healthcare professionals receive little or no training about it in medical school. Without a clear understanding of the ECS, many treatment plans fall short, especially for those battling long-term pain conditions.

Certified Organic Hemp Extract by Nesa's Hemp represents a shift in how we think about natural pain relief. This is not a typical CBD product. It contains cannabidiolic acid (CBDa), the raw, unheated form of CBD, carefully preserved through a solventless cold extraction process. This method preserves the plant's complete therapeutic integrity, yielding a bioavailable, full-spectrum extract that works in harmony with the body.

¹ Formato M, Crescente G, Scognamiglio M, et al. (–)-Cannabidiolic Acid, a Still Overlooked Bioactive Compound: An Introductory Review and Preliminary Research. *Molecules*. 2020;25(11):2638. doi:<https://doi.org/10.3390/molecules25112638>

The Endocannabinoid System and Chronic Pain Modulation

The ECS is a vital regulator of balance in the body, influencing pain, inflammation, immune response, mood, and other physiological processes. It includes endogenous cannabinoids such as anandamide and 2-AG, CB1 and CB2 receptors, and enzymes that synthesize and degrade these compounds.² When the ECS becomes imbalanced, a condition known as clinical endocannabinoid deficiency (CECD) may play an important role, contributing to a wide range of issues, including chronic pain, autoimmune disorders, and neuroinflammatory diseases.³

This theory, first introduced by Dr. Ethan Russo, suggests that insufficient levels or impaired function of endocannabinoids can lead to widespread physiological imbalances. Studies have linked this deficiency to conditions such as fibromyalgia, migraine, and irritable bowel syndrome, all of which involve chronic pain, heightened sensitivity, and inflammatory components.³

Emerging evidence suggests that enhancing endocannabinoid tone through strategies that increase endocannabinoid levels or mimic their activity may help restore physiological balance in patients with complex or treatment-resistant chronic pain. Cannabinoids such as CBD and its raw, acidic precursor CBDA have shown promise in modulating the ECS to support this balance.³

CBDA demonstrates promising ECS-modulating effects by interacting with serotonin receptors.⁴ It also supports anti-inflammatory activity through COX-2 inhibition and may influence pain-related TRP channels.^{5,6}

Preclinical Evidence and Emerging Research

Emerging research suggests CBDA may offer enhanced benefits compared to CBD in several key areas, including;

Anti-Inflammatory and Analgesic Properties

CBDA exhibits strong anti-inflammatory effects by selectively inhibiting COX-2, a mechanism similar to that of non-steroidal anti-inflammatory drugs (NSAIDs).⁵ In preclinical animal models, CBDA was found to reduce inflammation and pain sensitivity more effectively than CBD.⁷ However, these findings

² Lu HC, Mackie K. Review of the Endocannabinoid System. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. 2020;6(6). doi:<https://doi.org/10.1016/j.bpsc.2020.07.016>

³ Russo EB. Clinical Endocannabinoid Deficiency Reconsidered: Current Research Supports the Theory in Migraine, Fibromyalgia, Irritable Bowel, and Other Treatment-Resistant Syndromes. *Cannabis Cannabinoid Res*. 2016;1(1):154-165. Published 2016 Jul 1. doi:10.1089/can.2016.0009

⁴ Rock EM, Parker LA. The Role of 5-HT_{1A} Receptor, and Nausea and Vomiting Relief by Cannabidiol (CBD), Cannabidiolic Acid (CBDA), and Cannabigerol (CBG). In: *Handbook of Cannabis and Related Pathologies Biology, Pharmacology, Diagnosis, and Treatment*. Elsevier Science; 2017:703-712. <https://doi.org/10.1016/B978-0-12-800756-3.00083-1>

⁵ Takeda S, Misawa K, Yamamoto I, Watanabe K. Cannabidiolic acid as a selective cyclooxygenase-2 inhibitory component in cannabis. *Drug Metabolism and Disposition: The Biological Fate of Chemicals*. 2008;36(9):1917-1921. doi:<https://doi.org/10.1124/dmd.108.020909>

⁶ De Petrocellis L, Ligresti A, Moriello AS, et al. Effects of cannabinoids and cannabinoid-enriched Cannabis extracts on TRP channels and endocannabinoid metabolic enzymes. *British Journal of Pharmacology*. 2011;163(7):1479-1494. doi:<https://doi.org/10.1111/j.1476-5381.2010.01166.x>

⁷ Rock EM, Limebeer CL, Parker LA. Effect of cannabidiolic acid and Δ⁹-tetrahydrocannabinol on carrageenan-induced

have not yet been consistently validated in human clinical studies.

Neuroprotective and Stress-Relief Benefits

A preclinical animal study reported that a high dose of CBD/CBDA-rich hemp extract improved cognitive impairment caused by chronic restraint stress (CRS) in animal models. The extract was found to reverse HPA axis hyperactivity, lowering corticosterone levels and adrenal gland weight. It also protected hippocampal neurons from CRS-induced damage. Further analysis showed that the extract reduced markers of microglial activation and astrocyte activation, indicating reduced neuroinflammation. These results suggest that CBD/CBDA-rich hemp extract may offer neuroprotective benefits by modulating stress responses and reducing brain inflammation.⁸

Mechanism of Action: How CBDa Works on Pain Receptors and Channels?

CBDa exerts its therapeutic effects through multiple biological targets implicated in pain perception, inflammation, and neurological regulation. Its multi-faceted mechanism of action suggests potential relevance for its use in chronic pain management, especially for patients with complex or treatment-resistant conditions.¹

5-HT1A Receptor Agonism

CBDa is a potent activator of the 5-HT1A serotonin receptor, which plays a critical role in mood regulation, anxiety control, and emesis suppression.⁴ Activation of this receptor has been shown to produce anxiolytic and antidepressant-like effects, both of which are highly relevant in chronic pain patients who frequently suffer from comorbid mood disorders.^{9,10,11} Additionally, 5-HT1A agonism is associated with anti-nociceptive properties, which may reduce pain perception through central mechanisms.¹²

TRP Channels

Transient receptor potential (TRP) channels are ion channels that play a crucial role in transmitting thermal and chemical pain signals. TRPV1, often referred to as the capsaicin receptor, is activated in conditions involving inflammation and hyperalgesia. CBDa may modulate various TRP channels, such as the TRPV1 and TRPA1, potentially leading to desensitization and reduced pain signaling.⁶

hyperalgesia and edema in a rodent model of inflammatory pain. *Psychopharmacology*. 2018;235(11):3259-3271. doi:<https://doi.org/10.1007/s00213-018-5034-1>

⁸ Kamsrijai U, Charoensup R, Jaidee W, Hawiset T, Thaweethee-Sukjai B, Praman S. Cannabidiol/cannabidiolic acid-rich hemp (*Cannabis sativa* L.) extract attenuates cognitive impairments and glial activations in rats exposed to chronic stress. *Journal of Ethnopharmacology*. 2025;338:119113. doi:<https://doi.org/10.1016/j.jep.2024.119113>

⁹ Garcia-Garcia AL, Newman-Tancredi A, Leonardo ED. 5-HT1A receptors in mood and anxiety: recent insights into autoreceptor versus heteroreceptor function. *Psychopharmacology* 2013;231(4):623-636. doi:<https://doi.org/10.1007/s00213-013-3389-x>

¹⁰ Celada P, Puig M, Amargós-Bosch M, Adell A, Artigas F. The therapeutic role of 5-HT1A and 5-HT2A receptors in depression. *J Psychiatry Neurosci*. 2004;29(4):252-265.

¹¹ Aaron RV, Ravyts SG, Carnahan ND, et al. Prevalence of Depression and Anxiety Among Adults With Chronic Pain. *JAMA Network Open*. 2025;8(3):e250268. doi:<https://doi.org/10.1001/jamanetworkopen.2025.0268>

¹² Megumu Y, Hidemasa F. Mechanisms for the Anti-nociceptive Actions of the Descending Noradrenergic and Serotonergic Systems in the Spinal Cord. *Journal of Pharmacological Sciences*. 2006;101(2):107-117. doi:<https://doi.org/10.1254/jphs.CRJ06008X>

Selective COX-2 Inhibition

CBDa has been shown in cell lines to selectively inhibit cyclooxygenase-2 (COX-2), an enzyme upregulated in inflamed and damaged tissues. COX-2 catalyzes the conversion of arachidonic acid to pro-inflammatory prostaglandins, contributing to both inflammation and pain. Traditional NSAIDs also target this enzyme but are associated with gastrointestinal and cardiovascular risks, especially with long-term use. CBDa's selective COX-2 inhibition offers a potentially safer, plant-derived anti-inflammatory option, making it a compelling alternative for patients requiring chronic inflammation control.⁵

PPAR Activation

Peroxisome proliferator-activated receptors (PPARs), particularly PPAR α and PPAR γ , play an important role in modulating pain.¹³ The activation of these receptors by cannabinoids like CBDa may contribute to reductions in pain sensations, however more clinical research is needed.^{14, 15, 16}

Patient-Reported Outcomes and Testimonials

While clinical trials are the gold standard in evaluating therapeutic efficacy, patient experiences can often provide valuable insights into the real-world impact of emerging therapies. Nesa's Hemp has collected a growing number of testimonials from individuals who have used its Certified Organic Hemp-Derived CBDa to manage chronic pain and related conditions. These accounts reflect not only symptom relief but also improvements in quality of life and function, as well as reduced reliance on conventional pharmaceuticals.

Case Highlights:

- **Leah H.:** Diagnosed with osteoarthritis, Leah reported “way less stiffness” and that “most of the pain is gone” after regular use of Nesa's Hemp CBDa.
- **Rodney P.:** Experienced chronic gout and arthritis. After using Nesa's CBDa for over two years, he discontinued multiple medications, stating the results were “life-changing.”
- **Jennifer S.:** Living with rheumatoid arthritis, she noted significant reductions in joint pain and morning stiffness, even while on pharmaceutical treatment.
- **Tom W.:** With degenerative disc disease, he noticed a “significant increase in joint mobility” and less lower back pain after a few weeks of consistent use.
- **Vaidas D.:** A professional athlete, Vaidas experienced faster recovery times and reduced pain from sports-related injuries.

¹³ Okine BN, Gaspar JC, Finn DP. PPARs and pain. *Br J Pharmacol*. 2019;176(10):1421-1442. doi:10.1111/bph.14339

¹⁴ O'Sullivan SE. An update on PPAR activation by cannabinoids. *Br J Pharmacol*. 2016;173(12):1899-1910. doi:10.1111/bph.13497

¹⁵ Hirao-Suzuki M, Takayuki K, Takiguchi M, Peters JM, Takeda S. Cannabidiolic acid activates the expression of the PPAR β/δ target genes in MDA-MB-231 cells. *Archives of Biochemistry and Biophysics*. 2022;731:109428. doi:https://doi.org/10.1016/j.abb.2022.109428

¹⁶ D'Aniello E, Fellous T, Iannotti FA, et al. Identification and characterization of phytocannabinoids as novel dual PPAR α/γ agonists by a computational and in vitro experimental approach. *Biochimica Et Biophysica Acta General Subjects*. 2019;1863(3):586-597. doi:https://doi.org/10.1016/j.bbagen.2019.01.002

- **Kelly N.:** A chronic migraine sufferer for over 25 years, Kelly reported reduced neuro-inflammation and fewer symptoms.

Product Overview

Certified Organic Hemp Extract by Nesa's Hemp is a full-spectrum, organic, certified hemp extract. It is crafted with precision to ensure the highest levels of purity, potency, and safety. Made from carefully selected organic hemp seeds, hemp, and sunflower seeds, the product is free from pesticides, herbicides, and contaminants. The entire process, from soil selection to bottling, is executed with meticulous attention to quality, starting with nutrient-rich soil and organic cow manure for fertilization to ensure healthy, thriving plants.

Nesa's Hemp uses a cold-extraction method that retains the full range of cannabinoids, terpenes, flavonoids, and other natural therapeutic compounds, eliminating the need for heat, solvents, chemicals, or preservatives. This process maintains the plant's natural integrity, resulting in a powerful and bioavailable extract. Rigorous third-party lab testing is performed at every stage, including testing soil, water, seeds, fertilizers, and the final product, to ensure the extract is free of impurities and contaminants.

The product holds multiple certifications, including Certified Organic, Non-GMO, Kosher, and Vegan-friendly, reinforcing its commitment to organic integrity.

What's in our product?

1. Full-Spectrum Hemp-Derived Compounds

Nesa's Hemp Extract offers a full spectrum of cannabinoids, terpenes, and flavonoids preserved in their raw, natural state through cold extraction. This includes both primary cannabinoids like CBD and rare, delicate acidic forms such as CBDA and CBGA, which are often destroyed in traditional processing. These compounds work together to support mood, reduce inflammation, maintain immune balance, and promote overall wellness. A full Certificate of Analysis (COA) is available for detailed lab results.

Each milliliter of Certified Organic Hemp Extract by Nesa's Hemp contains approximately 16.7 mg of CBDA, along with 11.91 mg CBD, and notable levels of CBCA, CBGA, THC-A, CBC, and CBG. It also includes therapeutic terpenes such as beta-Caryophyllene, beta-Myrcene, Pinene, and Linalool.

2. Organic Sunflower Seed

Nesa's Hemp uses raw sunflower seeds, not those processed into oil with chemical additives. Through our low-temperature extraction process, we produce our own organic carrier oil from raw organic sunflower seeds without harmful chemicals. The oil is rich in vitamin E and omega fatty acids, promoting absorption while offering its own anti-inflammatory and skin-supportive benefits.¹⁷ It's clean, hypoallergenic, and supports our commitment to purity and quality.

Our product Form

The delivery method is just as crucial as the extraction method. Nesa's Hemp Extract is offered as a

¹⁷ Guo S, Ge Y, Na Jom K. A review of phytochemistry, metabolite changes, and medicinal uses of the common sunflower seed and sprouts (*Helianthus annuus* L.). *Chemistry Central Journal*. 2017;11(1). doi:<https://doi.org/10.1186/s13065-017-0328-7>

sublingual tincture. We selected this particular product type to enhance the bioavailability of CBDa. When taken sublingually, the raw extract bypasses the liver, enabling cannabinoids to enter the bloodstream more quickly and efficiently. This rapid systemic delivery is essential for those seeking immediate symptom relief.

Dosing precision is also essential in clinical settings. We included a calibrated dropper with each bottle, allowing healthcare providers to measure the exact, customized dose a patient needs accurately.

Regulatory and Legal Considerations

Federal Legal Status

Certified Organic Hemp Extract by Nesa's Hemp is made from hemp plants that comply with the legal standards set by the 2018 Farm Bill. According to this law, hemp and its derivatives are federally legal in the United States as long as the Delta-9 THC level stays below 0.3 percent by dry weight. This distinction allows hemp-derived cannabinoids, such as CBDa, to be grown, processed, and sold under a federally regulated system.

FDA Position

The U.S. Food and Drug Administration (FDA) has not approved non-prescription CBD or CBDa products for treating or preventing any disease. Although Epidiolex, a CBD-based medication, has received FDA approval for certain seizure disorders, the agency continues to assess the safety and effectiveness of hemp-derived compounds in other situations. Clinicians should know that hemp products cannot be marketed with therapeutic claims unless they go through formal regulatory approval.

Medical and Manufacturing Standards

Nesa's Hemp follows the highest standards of quality, safety, and regulatory compliance. Its Certified Organic Hemp Extract is made using a solventless cold extraction process, which retains the full spectrum of the plant's therapeutic compounds, including delicate cannabinoids, terpenes, and flavonoids.

All products are:

- USDA Certified Organic
- Manufactured in GMP-certified facilities
- Free from solvents, pesticides, heavy metals, and microbiological contaminants
- Independently tested by ISO-accredited laboratories

Every batch is accompanied by a detailed Certificate of Analysis (COA) that verifies cannabinoid content, purity, and safety. The Delta-9 THC level remains consistently below the federal legal limit of 0.3%, ensuring full compliance with the 2018 Farm Bill and safe use within clinical settings.

Safety Profile and Contraindications

Known Side Effects

CBDa is generally well-tolerated, particularly in its raw, unheated form, as found in Certified Organic Hemp Extract by Nesa's Hemp. Unlike decarboxylated cannabinoids such as CBD and THC, CBDa has a gentler interaction with the body's systems. Reported side effects are mild and may include

drowsiness, dry mouth, or gastrointestinal discomfort in individuals who are sensitive to these effects. These effects are usually dose-dependent and reversible upon discontinuation.

Drug Interactions

Cannabinoids, including CBDa, can influence the cytochrome P450 enzyme system, which metabolizes many common medications. Caution is advised when used concurrently with anticoagulants (e.g., warfarin), antiepileptics, or immunosuppressants, as cannabinoid intake may alter the serum levels of these medications. Clinicians should monitor patients for signs of altered therapeutic response or toxicity when introducing hemp-derived extracts alongside these medications.

Special Populations

1. Pediatric

The safety data of CBDa in pediatric populations remain limited. Although CBD has been studied in children with treatment-resistant epilepsy, the raw acidic form is less researched and should be used with caution and under medical supervision.

2. Geriatric

In geriatric patients, the potential for polypharmacy underscores the importance of monitoring drug interactions. However, CBDa may offer an alternative to opioids and NSAIDs in this group, particularly for managing chronic pain and inflammation.

3. Pregnant and nursing population

Use during pregnancy or lactation is not recommended due to the absence of safety data and potential effects on fetal development. Until further studies clarify the safety profile, clinicians should advise against use in pregnant or breastfeeding individuals.

Recommendations for Use in Pain Management

Certified Organic Hemp Extract by Nesa's Hemp may serve as a valuable adjunct in managing complex pain presentations, particularly when conventional therapies offer limited relief or cause unwanted side effects. Clinical scenarios where CBDa may be especially beneficial include:

- Neuropathic pain (e.g., fibromyalgia, diabetic neuropathy, postherpetic neuralgia)
- Chronic inflammatory pain (e.g., rheumatoid arthritis, osteoarthritis)
- Cancer-associated pain, especially in palliative care settings
- Post-surgical pain where patients are sensitive to opioids or at risk for dependence
- Central sensitization syndromes and other treatment-resistant pain disorders

Its anti-inflammatory, analgesic, and serotonergic properties make CBDa well-suited for patients who have not responded adequately to NSAIDs or wish to avoid opioids.

Dosage Guidelines

Start with 0.25-0.5 mL once or twice daily under the tongue. Each milliliter provides about 32 mg of CBDA, along with a variety of supportive cannabinoids, terpenes, and flavonoids. Adjust the dose every 3 to 7 days based on individual response and tolerability.

Patients with severe or chronic pain may need slightly higher doses, always starting conservatively and increasing as necessary.

Clinical Integration

Nesa's Organic Hemp Extract can be used alongside clinical care as a supplementary option for managing chronic pain and inflammation. With its high CBDA levels and solventless extraction method, it offers a safe, natural alternative to traditional treatments.

Clinicians can begin by identifying patients who do not respond to NSAIDs, suffer from opioid side effects, or are looking for plant-based pain relief. For example:

- In primary care, patients with chronic back pain or joint stiffness may benefit from 0.25 mL of extract taken sublingually once or twice daily, with dosage adjusted as needed.
- In geriatrics, those with arthritis can use the extract to reduce inflammation without the risks associated with NSAIDs.
- In oncology, it may help alleviate chemotherapy-induced pain, nausea, and discomfort.
- In mental health, it may support patients dealing with pain compounded by anxiety or sleep disturbances.

Integration should include patient education, careful documentation, and regular follow-up. Always verify product quality through third-party testing and ensure compliance with state and institutional regulations.

Conclusion

Chronic pain continues to challenge clinicians and patients alike, often requiring safer, more effective alternatives to traditional therapies. Nesa's Hemp Certified Organic Hemp Extract, rich in the raw cannabinoid CBDA, offers a promising option. Its unique bioavailability and targeted mechanisms make it a valuable tool in managing inflammation and pain at the source.

Preliminary evidence and patient experiences support its use in conditions ranging from arthritis to neuropathic pain. As interest in cannabinoid-based therapies grows, further clinical research is needed to establish standardized protocols and expand the evidence base.

Clinicians are encouraged to initiate trials with Nesa's Hemp in appropriate cases and to educate patients on its benefits and use. With its GMP-certified, solventless extraction process and verified cannabinoid profile, Nesa's Hemp provides a high-quality, compliant solution for integrative pain management.

CBDa vs. CBD: A Comparative Overview		
Feature	CBDa (Cannabidiolic Acid)	CBD (Cannabidiol)
Source	Found in raw, unheated hemp and cannabis plants	Derived from CBDa through heat (decarboxylation)
Molecular Structure	Acidic form with a carboxyl group	Neutral form after the CO ₂ group is removed via heat
Extraction Method	Requires cold or raw extraction to preserve the acid form	Typically extracted with heat-based methods
Bioavailability	Up to 11x more bioavailable than CBD in certain forms	Lower bioavailability; often requires larger doses
Receptor Interaction	Strong affinity for 5-HT1A (serotonin) receptors	Indirect interaction with CB1, CB2, and serotonin receptors
Anti-Inflammatory Effects	Strong COX-2 inhibitor, mimicking NSAIDs	Anti-inflammatory, but less selective for COX-2
Anti-Nausea & Vomiting	More potent than CBD in preclinical anti-nausea studies	Offers relief, but is less effective than CBDa in this area
Anxiety & Depression	Promising results through serotonin modulation	Widely used for anxiety; mechanisms include GABA and serotonin activity
Neuroprotection	Shows potential in stress resilience and cognitive support	Established neuroprotective effects; used in epilepsy (e.g., Epidiolex)
Anti-Cancer Research	Inhibits the migration of certain aggressive cancer cells (e.g., breast cancer)	Investigated for anti-tumor, pro-apoptotic effects
Legal Status	Same as CBD in most countries; it depends on the source and THC content	Widely legal in most jurisdictions when derived from hemp

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