1. Palmitoylethanolamide (PEA) & Related Compounds
This category includes documents primarily focused on Palmitoylethanolamide (PEA), its mechanisms, efficacy in various conditions, and new formulations.

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Excerpts from "12917_2017_Article_1151.pdf"1...: This study explored a combination of Palmitoylethanolamide (PEA) and Quercetin (PEA-Q) for osteoarthritis (OA) pain in rodents. It found that PEA-Q reduces inflammation and pain by influencing specific body pathways1. Researchers measured various inflammatory and pain markers in blood, such as TNF-α and IL-1β, to assess the effects2. The study's detailed methods for statistical analysis are also described3. The findings suggest PEA-Q is a promising treatment, and its use in pets with OA is currently being investigated1.

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Excerpts from "2022_Studio_normast_pharmaceuticals.pdf"45: This document presents baseline symptom data for study participants, noting that neurological symptoms like loss of smell (anosmia), taste (ageusia), muscle aches, and headaches were the most common4. It also provides the composition of ultramicronized Palmitoylethanolamide (um-PEA) and micronized PEA (m-PEA) formulations5. The document details the statistical methods used for data analysis5.

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Excerpts from "2017;20;353-362.pdf" / "https://www.painphysicianjournal.com/current/pdf?article=NDUwMg%3D%3D&journal=106"67: This section of the source describes a meta-analysis that aimed to evaluate the effectiveness of PEA for managing chronic pain. The study collected data on various aspects, including patient conditions, trial design, PEA dosage, and treatment duration, using a visual analog scale (VAS) to measure subjective pain6. It explored whether PEA is effective, if higher doses or longer treatment durations increase its efficacy, and if study characteristics (like blinding) influence the results7.

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Excerpts from "3192465.pdf"89: This document explains that PEA is a natural fatty acid in the body that helps control tissue reactivity, inflammation, and pain8. Its anti-inflammatory and pain-relieving effects are attributed to activating specific receptors (like CB2-like and PPAR) and reducing the activity of mast cells, which are immune cells involved in inflammation8. The document also highlights that

Acetyl-L-carnitine (ALC) is effective and safe for various chronic pain types, including neuropathic pain8.

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Excerpts from "Cannabimimetic Eicosanoids in Cancer and Inflammation: an Update | SpringerLink"10: This source indicates that PEA is orally effective at reducing swelling (edema) and pain from inflammation by calming down mast cell activation10. It also briefly mentions the role of nerve growth factor (NGF) in gut inflammation and the body's natural cannabinoid system in persistent pain10.

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Excerpts from "Cannabinoids_2020.pdf"11...: This review included a study that found ultramicronized Palmitoylethanolamide (PEA/Normast) did *not* significantly improve chronic neuropathic pain after spinal cord injury, a finding supported by high-quality evidence (level 1b)13. The most common side effects reported for PEA in this context included dry mouth, constipation, fatigue, and drowsiness12.

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Excerpts from "Dialnet-SystematicReviewOfNeuroprotectiveActionsOfTheECPIn-10142941.pdf"14...: This systematic review investigated PEA's neuroprotective and anti-inflammatory effects, particularly in brain cells exposed to oxygen deprivation and reoxygenation1416. It highlights that PEA is a natural fatty acid known for reducing inflammation and pain14. The review suggests that PEA, potentially with antioxidant supplements, could help alleviate chronic pain and protect against nerve damage in patients with neurodegenerative diseases like Alzheimer's and Parkinson's14.... It emphasizes a growing interest in PEA's potential to prevent cognitive neurological damage and improve memory17.

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Excerpts from "Efficacy of a fixed combination of palmitoylethanolamide and acetyl-l-carnitine (PEA+ALC FC) in the treatment of neuropathies secondary to rheumatic diseases - Minerva Medica 2021 August;112(4):492-9 - Minerva Medica - Journals"18: This document highlights the effectiveness of a fixed combination of PEA and Acetyl-L-Carnitine (ALC) in treating nerve pain (neuropathies) that develop as a result of rheumatic diseases18.

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Excerpts from "Fip+D'Antongiovanni+et+al+2021.pdf"19...: This study found that PEA can counteract the build-up of proteins linked to neurodegenerative disorders (like Aβ, t-tau, and α-syn) in the colon, and it helps restore a specific enzyme activity there20. Furthermore, PEA was shown to reduce inflammation in

the intestines and a process called "enteric gliosis" (related to gut supporting cells), both of which are connected to cognitive decline21. This suggests PEA's potential benefits for brain health via gut mechanisms.

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Excerpts from "Guida_Palmitoylethanolamide_2015.pdf" / "https://iris.uniroma1.it/bitstream/11573/870282/1/Guida_Palmitoylethanolamide_2015.pdf"22: This document describes the laboratory methods for measuring natural fatty acid compounds like PEA and OEA from tissues using advanced techniques like liquid chromatography-mass spectrometry22.

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Excerpts from "International Journal of Inflammation - 2013 - Keppel Hesselink - Palmitoylethanolamide A Natural Body‐Own.pdf"23: This extensive review summarizes over 50 years of research on PEA, describing it as a natural body substance with a broad range of biological targets23. Clinical trials involving nearly 4,000 patients demonstrated PEA's effectiveness and safety for treating influenza and the common cold23. Animal studies have shown PEA's benefits in various conditions, including central and peripheral neuropathic pain, osteoarthritis pain, traumatic brain injury, multiple sclerosis, Alzheimer's disease, and irritable bowel disease23. Its effective dose range in animals is typically 10-30mg PEA/kg bodyweight23. Recent English literature supports its use in sciatic and related neuropathic pain disorders23.

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Excerpts from "JBR.38.20240053.pdf"2425: This review highlights PEA as a naturally occurring, cannabis-like compound that has been extensively studied for its anti-inflammatory, anti-microbial, immune-boosting, brain-protective, and pain-reducing effects24. It is considered highly tolerable and safe24. Due to its multiple targets, PEA has shown benefits across various medical conditions, including neurological, psychiatric, ophthalmic, and rheumatological disorders24. Specifically, PEA treatment has been associated with reduced skin-related side effects and lower levels of inflammatory markers in patients with multiple sclerosis25.

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Excerpts from "JPR-32143-therapeutic-utility-of-palmitoylethanolamide-in-the-treatmen_102512.pdf"2627: This source details PEA's therapeutic effects, including its role in a virus model of multiple sclerosis and its impact on mast cell chemicals and nerve-nourishing factors after spinal cord injury26. PEA has been shown to

reduce pain from inflammation by controlling mast cell activity27. It also suggests that PEA acts as a "glia modulator," affecting specialized brain support cells that are a new target for treating neuropathic pain27.

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Excerpts from "Latini_Alpha-lipoic-acid_2023.pdf"28...: This study investigated treatments for acute low back pain (LBP) from disc herniation. Patients received standard medication, or medication plus nutritional supplements (including alpha lipoic acid, palmitoylethanolamide (PEA), and myrrh), or oxygen-ozone therapy, or a combination2829. While the average days of opioid use were similar across groups, the percentage of patients needing additional opioid therapy varied significantly between the different treatment approaches30.

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Excerpts from "Palmitoylethanolamide (PEA) - PEA Recommendations-for-Use-of-Supplements-in-the-COVID-19-Pandemic-12-12-20-1.pdf"31: This document suggests prioritizing safe, inexpensive interventions with a clear scientific basis for trials during a pandemic, noting that PEA is among those substances with potential pain benefits31.

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Excerpts from "R10Y2021N04A0492.pdf"3233: This study evaluated the addition of a fixed combination of PEA (600 mg) and Acetyl-L-Carnitine (ALC) (Kalanit®) to standard therapy for patients with peripheral neuropathy secondary to rheumatic diseases32. The group receiving PEA+ALC showed a significant improvement in pain levels (VAS) for conditions like sciatic pain, carpal tunnel syndrome, and lower limbs neuropathy compared to those on standard therapy alone32. The study suggests a synergistic effect of PEA and ALC, contributing to anti-inflammatory benefits and potentially improving treatment adherence32.

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Excerpts from "Role of palmitoylethanolamide (PEA) in depression: Translational evidence Special Section on “Translational and Neuroscience Studies in Affective Disorders”. Section Editor, Maria Nobile MD, PhD. This Section of JAD focuses on the relevance of translational and neuroscience studies in providing a better understanding of the neural basis of affective disorders. The main aim is to briefly summaries relevant research findings in clinical neuroscience with particular regards to specific innovative topics in mood and anxiety disorders"34: This source briefly mentions PEA in the context of depression, dietary supplements, endocannabinoids, and its interaction with the PPAR-alpha receptor, suggesting its potential relevance in mood and anxiety disorders34.

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Excerpts from "Santonocito+et+al+Pharmaceutics+2023.pdf"3536: This document reviews the potential of PEA for managing orofacial pain (pain in the mouth and face), which can be acute or chronic, such as temporomandibular joint (TMJ) disorders or burning mouth syndrome35. PEA is described as a natural lipid mediator produced by the body in response to tissue damage, possessing anti-inflammatory, analgesic, and neuroprotective properties3536. While more clinical data are needed, PEA is suggested to play a role in managing conditions like periodontal disease and may reduce pain after dental treatments36.

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Excerpts from "Short-Term Efficacy of Ultramicronized Palmitoylethanolamide in Peripheral Neuropathic Pain 301960936.txt"37...: This study assessed the short-term effectiveness of ultramicronized PEA (PEA-um) in patients with peripheral neuropathic pain, including those with diabetic neuropathy and traumatic nerve pain3739. Pain was measured using a visual analog scale (VAS) and the Neuropathic Pain Symptom Inventory (NPSI), which evaluates different types of pain sensations like burning and tingling3738.

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Excerpts from "Treating+chronic+stress+and+chronic+pain+by+manipulating+gut+microbiota+with+diet+can+we+kill+two+birds+with+one+stone.pdf"40: This document highlights PEA and similar fatty acid compounds as natural lipid mediators that modulate pain and inflammation in both the body and brain, sharing effects with the endocannabinoid system40. It states that PEA has shown therapeutic benefits in neuropathic pain, inflammatory pain, musculoskeletal pain, and palliative care40.

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Excerpts from "biomolecules-12-01161.pdf" / "https://sfera.unife.it/retrieve/05420918-c211-4b3f-9f6a-fe9fd6ccc11e/biomolecules-12-01161.pdf"4142: This document highlights the role of brain inflammation (neuroinflammation) in neurodegenerative diseases and identifies PEA and a new combination called co-ultraPEALut (PEA with luteolin) as potential treatments41. These compounds are thought to have beneficial effects on brain degeneration and inflammation by affecting brain cell communication4142.

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Excerpts from "fnut-1-1560654.pdf"43...: This document describes a clinical study protocol for a combination of hydrodispersible PEA and melatonin (PEATONIDE®) as a treatment for migraine headaches43. The study aimed to reduce migraine frequency, intensity, duration, and disability44. No adverse effects were reported by participants45.

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Excerpts from "fpsyt-13-1038122.pdf"46...: This systematic review and meta-analysis explores PEA's therapeutic effects on cognitive decline46. It suggests PEA could protect against brain degeneration and support repair47. Human studies showed PEA improved memory and cognitive function and reduced behavioral disturbances in patients with a type of dementia called Frontotemporal Dementia (FTD) and after traumatic brain injury (TBI)4849. Animal studies consistently demonstrated PEA's ability to reduce brain inflammation, protect nerve cells, improve memory, and counteract damage in models of Alzheimer's and vascular dementia50.... The review concludes that the evidence strongly supports PEA's benefits for core cognitive symptoms58.

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Excerpts from "https://www.amedeolucente.it/pdf/neuroprtoectvie-effect-PEA.pdf" / "neuroprtoectvie-effect-PEA.pdf"59...: This research found that PEA protects brain cells by reducing the overgrowth of support cells (astroglia) and preventing the death of nerve cells in brain cell cultures exposed to amyloid-beta (Aβ), a protein linked to Alzheimer's disease5961. PEA also showed promise in reducing brain cell activation and rescuing nerve damage in rat brain sections exposed to Aβ6062.

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Excerpts from "jpr-8-729.pdf" / "jpr-8-729_2.pdf"63...: This document reviews PEA, an endogenous lipid, noting its evaluation as an anti-inflammatory and analgesic drug in over 30 clinical trials since the 1970s6366. It specifically highlights PEA's efficacy and safety in nerve compression syndromes like sciatic pain and carpal tunnel syndrome6366. A key double-blind study involving 636 patients compared different daily doses of PEA (300mg and 600mg) to placebo, showing promising results64....

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Excerpts from "medical_management_of_endometriosis___pmc___https___pmc_ncbi_nlm_nih_gov__variablz.txt"69...: This review on endometriosis management included

searching for studies on PEA, along with cannabis and melatonin, as potential medical options for painful symptoms69....

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Excerpts from "nutrients-16-01653.pdf"7374: This systematic review on chronic pain found that extended supplementation with micron-sized oral PEA leads to additional pain relief74. A 60-day treatment showed a significant reduction in pain intensity (over 35% reduction in both the first and second month)7374. This benefit is explained by PEA's ability to reduce neuroinflammation by calming down specific non-nerve cells like microglia and mast cells74.

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Excerpts from "palmitoylethanolam____pmc___ncbi___https___www_ncbi_nlm_nih_gov__variablz.txt"7576: Recent search results highlight research on the therapeutic potential of PEA in gastrointestinal disorders75 and how PEA can cause dose-dependent changes in brain function and fat molecules in the brain76.

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Excerpts from "palmitoylethanolamine___pmc___ncbi___https___www_ncbi_nlm_nih_gov__variablz.txt"77: Recent search results show a study on PEA as a supplement and the importance of dose-dependent effects for improving nervous tissue health in laboratory models77.

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Excerpts from "phd_unimib_714069.pdf"78...: This PhD thesis explores PEA's therapeutic potential for neuropathic pain related to osteoarthritis (OA), diabetic neuropathy, and chemotherapy-induced pain78.... PEA, a natural substance, has anti-inflammatory and pain-relieving effects, partly by reducing mast cell activity79. In animal models, PEA significantly reduced knee swelling and pain in OA, protected cartilage, and improved mobility7983. For diabetic neuropathy, PEA relieved pain, helped nerve growth, improved insulin levels, and protected insulin-producing cells79.... The findings suggest PEA works through multiple targets, including activating PPAR-α, and could be a valid alternative treatment8283.

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Excerpts from "s40122-024-00685-4.pdf"84...: This review summarizes publications on PEA in neuropathic pain management, discussing its pharmacodynamics (how it works) and pharmacokinetics (how it moves through the body)84. It highlights PEA's anti-inflammatory, antioxidant, and analgesic

properties84. Key mechanisms include PEA's interactions with cannabinoid receptors and its neuroprotective effects on mast and glial cells, relevant for both pain relief and neurodegenerative diseases85. The review also notes new PEA formulations, like Equisetum-PEA, designed to improve its absorption and targeted delivery, enhancing its therapeutic effectiveness84.