Relief Elevator Pitch:

+PlusCBD-- Relief address minor aches and pains and low-grade chronic inflammation that drives all health issues.

Relief contains three of the most effective, non-habit-forming anti-inflammatories, CBDA/CBD and PEA offering a safe alternative to risky non-steroidal anti-inflammatories and dangerous opioid pain killers.

Relief is the first and only, triple action CBDA/CBD and PEA combination available.

Relief is an easy to swallow, soft gel capsule that targets all three pathways of pain and inflammation offering enhanced and synergistic effects for maximum comfort, and systemic relief.

+PlusCBD award winning products are the highest quality CBD products available and are backed by more science, than any other CBD available without prescription.

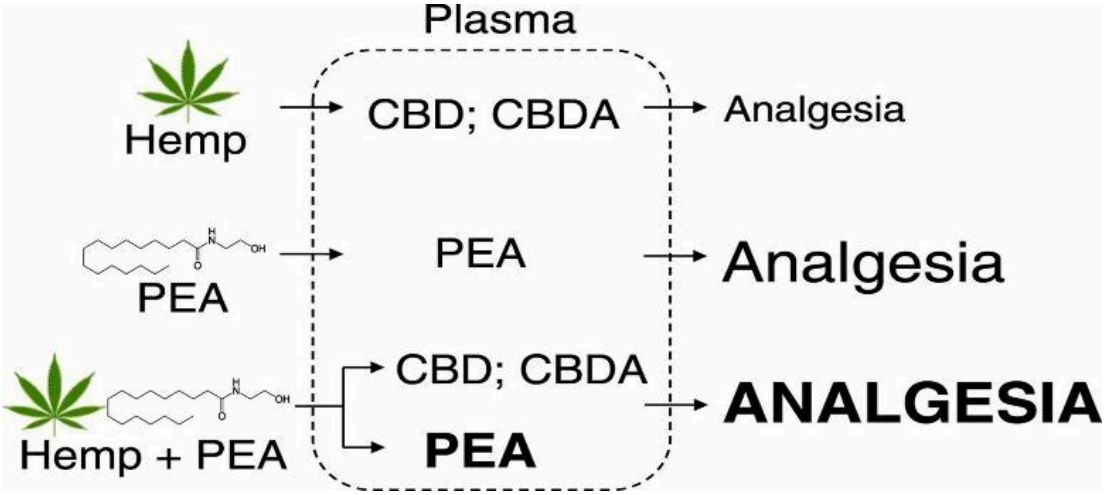
Experience the comfort and relief, you deserve.



How does Relief work? What makes it unique?

- Cannabis is extremely biologically active, and we have just begun unlocking the remarkable anti-inflammatory and immune supporting powers, of the plant. Relief works by restoring normal levels of your body's anti-inflammatory and analgesic agents and is more effective than using CBD, CBDA, or PEA alone. *

*. *Palmitoylethanolamide and hemp oil extract exert synergistic anti-nociceptive effects in mouse models of acute and chronic pain. Pharmacological Research* (2021)





3 pathways of pain summary

CBD-ECS is a key endogenous system regulating pain sensation with modulatory actions at all stages of pain processing. CBD also regulates innate immunity and inflammatory responses through the inhibition of pro-inflammatory cytokines and upregulation of anti-inflammatory cytokines.

CBDA- Selective COX-2 inhibitor modulate the first key steps in the synthesis of prostaglandins that convert AA into the hormone like compounds, that increase sensitivity to pain and thicken blood.

PEA- N-acylethanolamine acid amidase (NAAA) previously unrecognized control node in the transition from acute to chronic pain, which can be targeted by PEA.

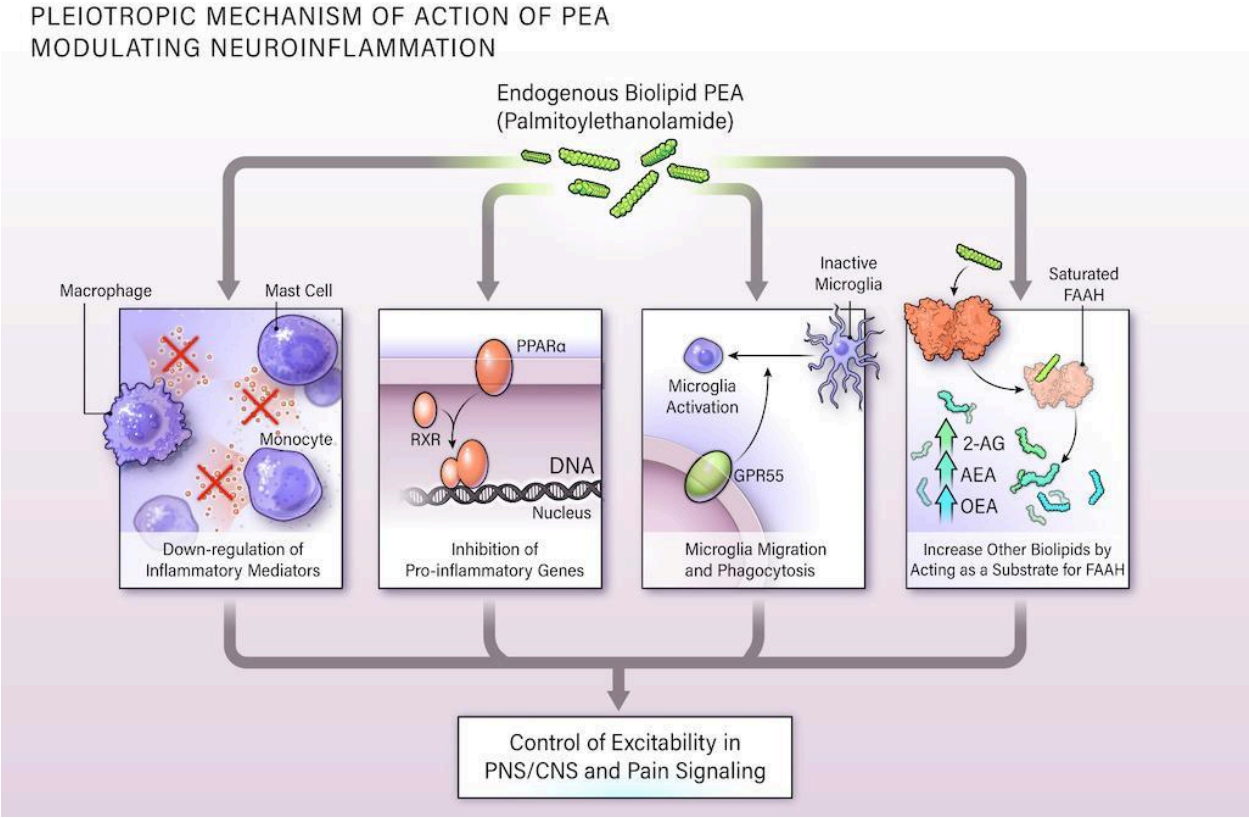
What is PEA

Palmitoylethanolamide (PEA), is a non-habit forming endogenous bioactive lipid known to modulate neuroinflammation and pain signaling, representing a promising

potential mechanism to treat multiple conditions of chronic pain 1-2-3.

2,500 patients have been treated with PEA for various pain conditions in more than 30 clinical studies 6-13. Fifteen of these studies were randomized, controlled trials (RCTs) in a total of approximately 1,500 patients, where PEA consistently demonstrated statistically significant reductions in pain with favorable safety and tolerability. We believe it has the potential to address the shortfalls of current supplements across a range of chronic pain conditions.

PEA is a broad modulator of inflammatory processes which also affect pain sensation and neuroprotection. Its mode of action has multiple effects (i.e., pleiotropic), as it involves many pathways and targets in both the peripheral and central nervous systems.



- Addresses large markets with growth opportunities in opioid-sparing indications (pain, post-surgical pain, morphine tolerance, etc.), endometriosis, osteoarthritis, fibromyalgia, etc.
- An endogenous compound, and a key regulator of endocannabinoid system in inflammation
- PEA increased expression of CB2 receptors
- PEA increases 2-AG and AEA, which directly activate CB1, CB2, and TRPV1 receptors
- PEA inhibits the activation of mast cells (peripheral)
- PEA reduces the activation of microglia and astrocytes (CNS)
- Clinical data available that suggests that FSD-PEA is superior to Ibuprofen and the opiates in the treatment of pain
- A well-researched compound in preclinical and clinical studies
- A “Pharmaceutically Green” API, a growing trend in inflammatory and related therapeutics

NNT is specific to an outcome, which in this case is "≥50% Pain relief in lumbosciatic algias".

- So, 1.7 people would need to take 600 mg of micronized PEA daily for 1 person to experience ≥50% pain relief from low back pain due to compression of the sciatic nerve.

In these conditions, it has been demonstrated that the increase of endogenous Palmitoylethanolamide—either by decreasing its degradation or exogenous administration—is able to keep neuroinflammation within its physiological limits. In this review the large number of studies on the benefits derived from oral administration of micronized and highly bioavailable forms of Palmitoylethanolamide is discussed, with special reference to neuroinflammatory disorders.

"The analysis yielded a Number Needed to Treat (NNT) value of 1.7 for PEA-m 600 mg daily, which is considerably better than that of first-line drugs, with tricyclic antidepressants yielding a score of 3.5, serotonin-norepinephrine reuptake inhibitors of 6.4, gabapentin of 7.2, and pregabalin of 7.7 [168]."

Conclusion: Palmitoylethanolamide was extremely effective on pain and function in a large cohort of patients with low back pain – sciatica. Although the multiple mechanisms of action of PEA are ideal for mixed pain conditions such as low back pain – sciatica, the correlation between pain relief and the likelihood of neuropathic pain suggests that this drug exerts a predominant action on the neuropathic pain component.