

Pain Management Specialist in San Diego & La Jolla

Palmitoylethanolamide "PEA" – Review of Anti-inflammatory, Analgesic, Neuroprotective Mechanisms

07/27/2014 — Nancy Sajben MD

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A review of palmitoylethanolamide, or PEA, has been published this June by Mireille Alhouayek and Guilio G. Muccioli from the Bioanalysis and Pharmacology of Bioactive Lipids Research Group, Louvain Drug Research Institute, Bruxelles, Belgium.

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The authors review the impact of PEA on inflammatory and neurodegenerative diseases, and show that inhibiting the breakdown of PEA (the hydrolysis) may increase levels of PEA. This could lead to treatment of inflammatory and neurodegenerative diseases.

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To address the loss of PEA that occurs in various diseases we must either

1. replace the decreased levels of endogenous PEA that is made by the brain by taking a capsule such as PeaPure, a food supplement that contains 100% palmitoylethanolamide, to reconstitute the needed levels

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2. inhibit the breakdown (hydrolysis) of PEA.

.I directly quote [palmitoylethanolamide4pain](#) that has outlined key quotes from that scientific review:

They start outlining the focus of the paper:

Our focus here is on PEA, which is a known anti-inflammatory compound with analgesic, neuroprotective and antiallergic properties.

Important for understanding the therapeutic relevance of PEA is the next remark:

Evidence suggests that PEA metabolism is disturbed during inflammation, and that a decrease in PEA levels contributes to the inflammatory response.

This explains why it is so useful to administer exogenous PEA as a supplement during states of chronic inflammation. Decreased PEA levels induce more inflammation and a vicious circle has started. Administering PEA (for instance as PeaPure capsules of 400 mg, a food supplement) can stop this circle and help the organism to restore the PEA levels and decrease inflammation.

PEA's mechanism of action

The next quote is related to PEA's main mechanism of action:

Although it is now clear that PEA is a ligand for PPAR- α , some of its effects occur through as yet unidentified receptors.

Although there are many ways PEA acts in the cell, the PPAR- α receptor indeed seems the most important one; through that receptor PEA can downregulate overactive inflammatory responses.

PEA levels also decreased following sciatic nerve constriction injury or ligation of the sciatic nerve in spinal cord and brain areas involved in nociception

PEA levels are not only decreased during chronic inflammation, also during chronic pain states, such as in sciatic pain.

The fact that an anti-inflammatory treatment restores PEA levels reinforces the role of PEA as an anti-inflammatory mediator.

PEA levels can be restored also by treatment with classical anti-inflammatory compounds such as NSAIDs, this however triggers many side effects and that can be avoided by treating with PEA itself!

PEA as a protective molecule

In the brain, PEA levels seem to be increased following injurious stimuli, and this has been proposed as a homeostatic mechanism aimed at counteracting inflammation and blunting the inflammatory response.

PEA has self-reparative properties and indeed can be defined as the molecule of self-reparation and self-protection.

This 'pro-homeostatic' increase, although probably slowing disease progression, seems insufficient to exert anti-inflammatory effects in itself, and should be further amplified...

One of the classical ways to amplify PEA is to administer it as food supplement:

start dose is 1200 mg/daily and in cases of insufficient response we suggest to double the dose.

Although the first identification of PEA as an anti-inflammatory compound occurred more than 50 years ago, general interest in its anti-inflammatory and analgesic properties was not sparked again until the mid-1990s.

It was due to the work of the Nobel laureate professor Rita Levi-Montalcini that the scientific community understood the importance of PEA in the 90s. However, as patents on this natural compound were not possible, no great interest emerged, as pharmaceutical companies were uninterested. It was due to the work of small companies, such as Epitech Srl and JP Russell Science that PEA was brought to the attention of the general public.

Mechanism of action in addition to the PPAR receptor

The authors nicely summarized the effects of PEA:

PEA inhibits phosphorylation of kinases involved in activation of pro-inflammatory pathways, such as mitogen-activated protein kinase (MAPK), c- Jun N-terminal kinase (JNK) and extracellular signal-regulated kinases (ERK), and the nuclear translocation of the transcription factors nuclear factor (NF)-kB and activator protein 1 (AP-1) and prevents degradation of the inhibitory IkB-a, which when associated to NF-kB prevents its nuclear translocation.

Besides reducing inflammatory cells activation and recruitment, PEA modulates the expression of enzymes involved in pro-inflammatory processes, such as COX-2 and inducible nitric oxide synthase (iNOS) and reduces nitric oxide and pro-inflammatory cytokines production in vitro and in vivo.

Relevance for Alzheimer, Parkinson's and MS

The neuroprotective effects of PEA are in part the result of its effects on downregulating the inflammatory cascade. Indeed, many neurodegenerative diseases are associated with a strong inflammatory component, such as Alzheimer's disease (AD), Parkinson's disease (PD) or MS

The follow stating:

This neuroinflammation is no longer simply considered as a consequence of neurodegeneration, but might be a primary factor in some cases; therefore, anti-inflammatory treatments might represent interesting therapeutic strategies in these diseases

After discussing modern pharmaceutical ways to block the hydrolysis of PEA with pharmaceutical new compounds, they end their overview with an important

statement:

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The potential of using PEA as a beneficial endogenous bioactive lipid in the setting of inflammation is well established

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My thanks to [palmitoylethanolamide4pain](#) for the outline of key points in this review of PEA.

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