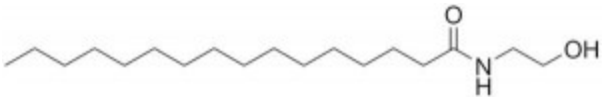
Palmitoylethanolamide (PEA) – A Medical Food for Fibromyalgia (and ME/CFS?)

by **Cort Johnson** | Sep 19, 2014 | **Alternative Health**, **Fibromyalgia**, **Homepage**, **Supplements**, **Treatment** | **61 comments**

Pain Reliever, Anti-inflammatory, Microglial and Mast Cell Inhibitor?

> "However, a great body of evidence exists for PEA, comprising at least 40 clinical trials in around 6,000 subjects. This body of evidence shows a positive risk/benefit ratio for PEA, warranting much wider use of this compound by the medical community" Hesselink



First isolated from soybean lecithin, egg yolk and peanut meal in 1954, palmitoylethanolamide or PEA is a naturally occurring substance produced in our body, apparently in response to inflammation. A fatty acide amide and nuclear factor, PEA binds to receptors in the nucleus, affecting processes involved in inflammation and chronic pain. PEA is not well known in the U.S., but it's well-studied with over 350 references in PubMed dating back more than fifty years.

PEA appears to be produced on demand in areas of local inflammation. It's purpose appears to be to tamp down inflammation/microglial activation where it occurs. For instance, PEA synthesis triggered by glutamate excitotoxicity appears to be an attempt to heal over-stimulated neurons and return them to normal status.

Jan Hesselink, of the Dept. of Pharmacology at the University of Witten/Herdecke in Germany, has produced several review papers on PEA. He has proposed that PEA represents a case study of how the research community ignores effective treatments it does not understand. He asserts that studies from 1957-1992 demonstrated PEA's effectiveness in the clinic, but it was not until Nobel Laureate Levi-Montalcini's paper in 1993 demonstrating PEA's effects in mast cells that PEA began to be taken seriously.

Animal model studies

PEA demonstrates a variety of properties in animal model studies that suggest it might be helpful in fibromyalgia and/or chronic fatigue syndrome (ME/CFS). Animal and laboratory studies suggest PEA has neuroprotective properties, can reduce glial (microglia and astrocyte) activation, inhibit astrocyte death (astrogliosis), and reduce inflammation by inhibiting histamine and TNF-a release in mast cells and by blocking **cyclooxygenase-2** (COX-2) and **inducible nitric oxide synthase** (iNOS) synthesis.

Human Studies

Hesselink reports PEA may be helpful in autoimmune conditions (influenza pap). Recently PEA was shown to shown to reduce the levels of reperfusion injury occurring during ischemia (low blood flows to the tissues).

Chronic Pain

A Wikipedia article suggests PEA may be most effective in chronic pain disorders such as peripheral neuropathy, chronic regional pain syndrome (CRPS), sciatica, and nerve entrapment. A recent study suggests it could be helpful in fibromyalgia.

Hesselink reports that clinical trials involving over 6,000 people have established PEA's effectiveness in treating chronic pain and inflammation. Animal models suggest PEA is able to prevent or inhibit two key processes in production of chronic nerve pain: nerve sprouting and dorsal root ganglia activation. **cyclooxygenase-2** (COX-2) and **inducible nitric oxide synthase** (iNOS).

Many chronic pain studies have taken place in Europe

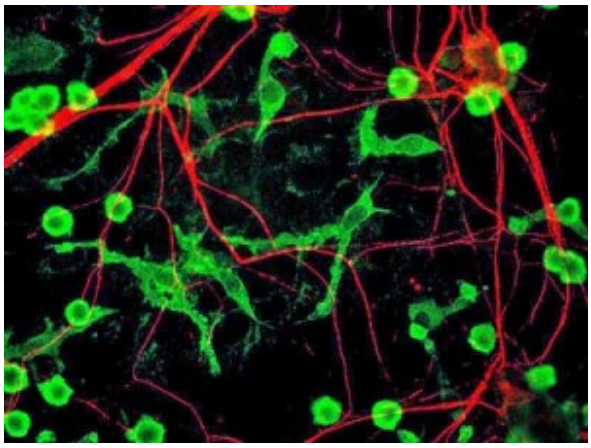
Why is PEA not better known in the West? PEA appears to have been used in Italy and Spain for quite some time. Interest picked up in the Netherlands and Germany when a Netherlands distributor came on the scene. It's hardly known in the U.S., although **Palmitoylethanolamide For Pain** reports that "many people" on the West coast of the U.S. as well as Australia and Canada are using it.

My first glimpse of PEA was in Dr. Younger's list of possible microglial inhibitors. Hesselink reports that forty PEA clinical trials for chronic pain, alone, have been done, but most have been published in Spanish and Italian medical journals. Most studies published in English journals continue to involve animals or are lab studies, but some studies suggest PEA may be effective in **endometriosis** and **chronic pelvic pain**. The

few clinical trials currently underway include trials on neuropathic pain, IBS, and post-operative pain.

Microglial Inhibitor

Jarred Younger included PEA in his list of potential microglial inhibitors that might be of use in ME/CFS and FM. Microglial cells surround the neurons and are responsible for the elimination of pathogens that attack them.



Several German researchers believe PEA may be up to upregulate microglia killing ability without causing inflammation

Not all microglial cells may be the same. Some microglial cells may specialize in phagocytosing invaders while others kill invaders using nitric oxide causing inflammation and potentially killing neurons. Most treatments that appear to turn off inflammation also appear to reduce microglial cells' ability to clear central nervous system pathogens. Finding a way to support microglial cells that kill invaders without causing inflammation would be very helpful.

Mast Cell Inhibitor

PEA appears to play a similar role with activated mast cells to what it does with over-activated neurons.

Because mast cells are often found near sensory nerve endings, chronic mast cell degranulation – which produces a variety of pro-inflammatory and pain-enhancing substances – could play a role in many pain disorders including pelvic pain, sciatic pain, headache, postsurgical pain, CRPS, fibromyalgia, and ME/CFS. Nerve growth factor – one of the many substances mast cells synthesize, store, and release – produces inflammation and sensitizes sensory neurons.

Studies suggest PEA can reduce mast cell migration and degranulation and can shift them from their activated to their resting states. Hesselink reports that over twenty studies have elucidated PEA's mast-cell inhibiting effects.

Fibromyalgia

A retrospective study found that **PEA may be helpfu**l as an add-on treatment in FM.

COVID-19 and Long COVID

PEA produced a "significant reduction in inflammation" and may help reduce coagulation in **COVID-19 patients**. A **long COVID trial** of uncertain rigor found that PEA plus olfactory

training help improve the ability to smell in long COVID more than olfactory training alone – suggesting that PEA have have reduced neuroinflammation.

Chronic Regional Pain Syndrome (CRPS)

Hesselink reported a case study of a 13-year CRPS patient who had not responded to numerous prior treatments. Her CRPS had progressed in typical fashion. Following a minor injury (bruised ankle), she experienced pain, swelling, changes in skin color, and severe burning pain that increased over time and then spread to her opposite foot. She subsequently developed allodynia and had trouble walking and sleeping. A second injury to her knee caused CRPS to flare up in her knee, and she became largely wheelchair-bound.

She was given ketamine 10% cream to be applied locally three times daily and PEA, as PeaPure® 400 mg capsules (JP Russell Sciences Ltd, Nicosia, Cyprus) which were taken orally three times daily. For the first ten days, she poured the capsules under her tongue and then took them orally.

After ten days she entered the doctor's office walking with a cane with the swelling and discoloration in her legs and pain reduced by more than 50%. She continued to improve and soon was able to discard her cane.

Small Fiber Neuropathy

One woman with small fiber neuropathy reported **on a pain group site** that she was in complete despair until she was able to get off prescription pain drugs by using PEA and alpha lipoic acid. She was still in pain but life was bearable.

MD recommends PEA

Jan Keppel Hesselink MD reports side effects are rare, and he's found it effective enough to use as a first-line treatment for neuropathic pain. He states he's used it in 200+ patients.

Side Effects – The only side effects he's seen are a feeling of heaviness in the story and rarely gastrointestinal upset and diarrhea with the sublingual preparation, probably due to the sorbitol in it. He has not seen any side effects with PeaPure.

Interactions – Hesselink reports no adverse reactions with other commonly used pain relievers such as tramadol, pregabalin, gabapentin, amitriptyline, and duloxetine.

Getting PEA

In 2008 and 2012, PEA became available in Italy and Cyprus under the brand names Normast® (Epitech Group Srl, Milan, Italy) and PeaPure® (JP Russell Science Ltd,

Nicosia, Cyprus). Normast is available through **www.ergomax.nl**. PeaPure is available in the Netherlands **via this website.**

Medical Food – Normast is classified as "a food for medical purposes". Because of that designation and a statement that it should be used under a doctor's care, some people in the U.S. have reported some difficulty in getting it through the mail (i.e., a doctor's note may be required). Other PEA products produced as nutraceuticals or supplements such as PeaPure apparently don't encounter this problem.

Neutraceutical – **Palmitoylethanolamide For Pain** reports that PEA is available as a nutraceutical under these brand names: Pelvilen (consists of 49% of PEA), Pelvilen Forte (60% PEA), Normast sachets (60% PEA), Normast tablets (68% PEA), Visimast (68% PEA), Achilles (12% PEA), and PeaPure (100% PEA).

Nancy Sajben MD reports that a compounding pharmacy in San Diego called PJ's Prescription Shoppe carries PeaPure shipped over from the Netherlands.

There's no information available suggesting that one product is better than the other; however, an author of a review article suggests using PeaPure because it is 100% PEA.

Some of the more popular formulations are below.

- Normast compressed tablets contain 600 mg micronized PEA in a magnesium stearate matrix.
- Normast sachets for sublingual use contain 600 mg micronized PEA that is sweetened with 300 mg sorbitol.
- PeaPure is produced in vegetable capsules containing 400 mg micronized PEA only or as a cream **via this website**.
- **Palmitoylethanolamide For Pain** states PeaPure contains the most PEA per serving and that a recent review article recommends it. It costs about a dollar a pill (without shipping) or about .80/pill if you buy in larger quantities.

Using PEA

In a discussion **on a pain group site, Hesselink** suggested using ultra-micronized Normast (sachets) under the tongue for the first ten days to fill up the cells with the compound. After that continue for 6 weeks with 600 mg tablets twice daily.

If pain decreases of more than 30% are not seen, he adds "a period of 10 days with the powder under the tongue" and do not lower the dose for another 6 weeks. Once 50% reductions in pain are seen, he reduces the dose to 300 mg twice daily. He cautioned to

“Always use this food for medical purposes in the context of a treatment cycle supervised by your own physician.”

Palmitoylethanolamide For Pain reported that pain relief is sometimes seen within a week but may take up to six to eight weeks.

Resources

Palmitoylethanolamide For Pain is a non-commercial site devoted to spreading the news about PEA and other non-pharmacological products that can help with the pain.