RESEARCH TO REALITY: EVIDENCE OF THE PEA SOLUTION

Gencor™

Lifestage Solutions

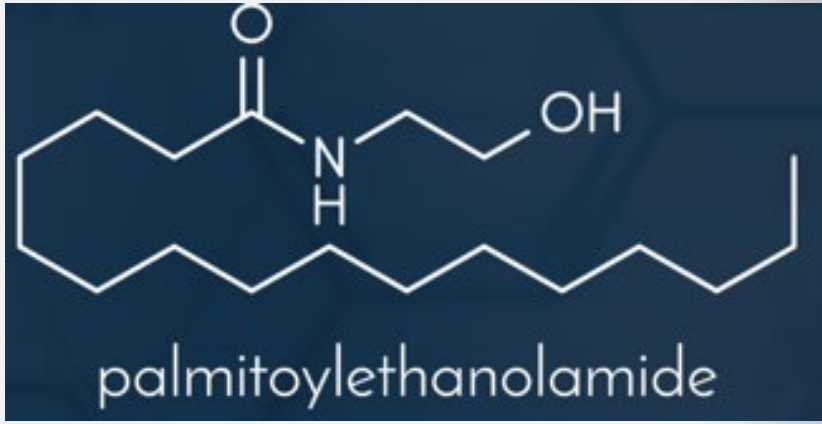
PRESENTED BY DR CHRIS BAILEY

An Introduction to Gencor

- Established in 1999, Gencor Pacific Ltd. first began as a pharmaceutical ingredient distributor based in Hong Kong
- In 2002, a new entity, Gencor Pacific Inc. was formed in Austin, TX to specifically serve the nutraceutical industry
- With a presence in over 55 countries, Gencor has an expertise in bringing proprietary, clinically-backed ingredients to the market to support the robust substantiation needs of finished product brands around the world
- In addition to Gencor's in-house ingredient portfolio, the company has partnered with other international partners to broaden the customer base Gencor can support

Palmitoylethanolamide

- A fatty acid amide that is endogenous to the human body.[1]
- Readily found in foods such as eggs, soy, peanuts, and corn[2]
- Released by cells in the body in response to harmful stimuli.[3]
- The most well - studied benefits of PEA administration stem include its ability to support a balanced inflammatory response[4] and relief from occasional discomfort[5]
- The primary mechanism for both these benefits appears to be the activation of peroxisome proliferator-activated receptor-α (PPARα)[6,7]



1. Pain: Current Understanding, Emerging Therapies, and Novel Approaches to Drug Discovery. (2003). United States: CRC Press.
2. Peritore, A. F., Siracusa, R., Crupi, R., & Cuzzocrea, S. (2019). Therapeutic efficacy of palmitoylethanolamide and its new formulations in synergy with different antioxidant molecules present in diets. *Nutrients*, *11*(9), 2175.
3. Briskey, D., Mallard, A. R., & Rao, A. (2020). Increased absorption of palmitoylethanolamide using a novel dispersion technology system (LipiSperse®). *Nutraceuticals Food Sci*, *5*, 3.
4. Costa, B., Conti, S., Giagnoni, G., & Colleoni, M. (2002). Therapeutic effect of the endogenous fatty acid amide, palmitoylethanolamide, in rat acute inflammation: inhibition of nitric oxide and cyclo-oxygenase systems. *British journal of pharmacology*, *137*(4), 413-420.
5. Calignano, A., Rana, G. L., Giuffrida, A., & Piomelli, D. (1998). Control of pain initiation by endogenous cannabinoids. *Nature*, *394*(6690), 277-281.
6. Verme, J. L., Fu, J., Astarita, G., La Rana, G., Russo, R., Calignano, A., & Piomelli, D. (2005). The nuclear receptor peroxisome proliferator-activated receptor-α mediates the anti-inflammatory actions of palmitoylethanolamide. *Molecular pharmacology*, *67*(1), 15-19.
7. Di Cesare Mannelli, L., D'Agostino, G., Pacini, A., Russo, R., Zanardelli, M., Ghelardini, C., & Calignano, A. (2013). Palmitoylethanolamide is a disease-modifying agent in peripheral neuropathy: pain relief and neuroprotection share a PPAR-alpha-mediated mechanism. *Mediators of Inflammation*, *2013*.

Importance of Solubility and Lipophilicity

- As with curcuminoids, PEA is a lipophilic substance and has been reported to have poor solubility in aqueous (water-based) solutions.[1]

- The material's lipophilic properties may explain how, with oral ingestion, PEA only produces limited levels of systemic exposure in the body that lasts for short periods of time.[1]

1. Vacondio, F., Bassi, M., Silva, C., Castelli, R., Carmi, C., Scalvini, L., ... & Rivara, S. (2015). Amino acid derivatives as palmitoylethanolamide prodrugs: synthesis, in vitro metabolism and in vivo plasma profile in rats. *PLoS One*, *10*(6), e0128699.

Levagen® and Levagen®+ History

2015

Levagen® Palmitoylethanolamide launched by Gencor

2017

Levagen®+ Launched with Pharmako Biotechnologies' LipiSperse® platform

2019

First Levagen® Joint Health Study

2020

Levagen®+ Pharmacokinetics Study and Exercise Recovery Study

2021

Levagen®+ Joint Health Study and Sleep Health Study

2022

Levagen®+ Balanced Inflammatory Response Study, Nerve Health Study, and Occasional Head Discomfort Study

2023

Levagen®+ Immue Health Study and Seasonal Immune Health Study

2024

Levagen®+ Occasional Head Discomfort Study (extension of first study)

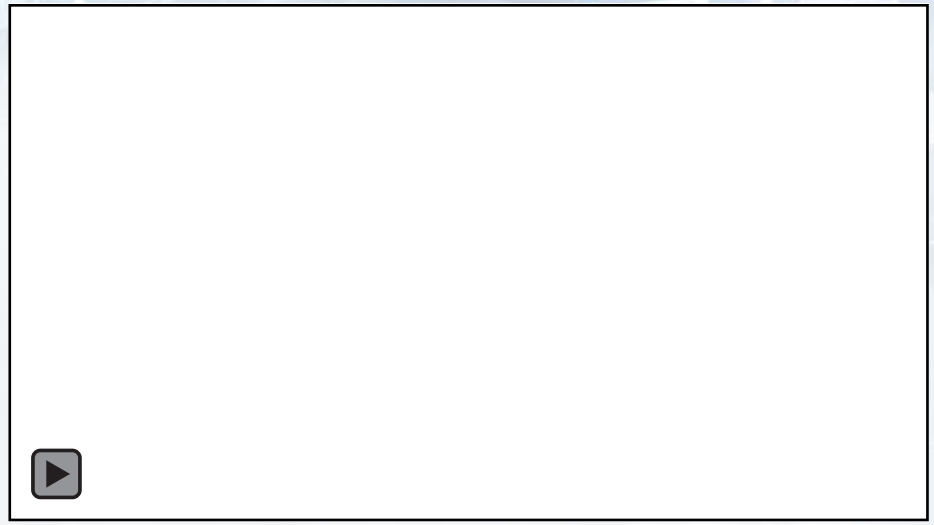
1. Vacondio, F., Bassi, M., Silva, C., Castelli, R., Carmi, C., Scalvini, L., ... & Rivara, S. (2015). Amino acid derivatives as palmitoylethanolamide prodrugs: synthesis, in vitro metabolism and in vivo plasma profile in rats. *PLoS One*, *10*(6), e0128699.

Levagen®+ Advantage

- Combination of Levagen® palmitoylethanolamide (PEA) with Pharmako Biotechnologies' LipiSperse® technology
  - Palmitoylethanolamide by Gencor has Self-Affirmed GRAS.

- Clinically demonstrated to have improved bioavailability[1] over unformulated PEA and improved the material's functionality (cold water dispersibility).

- LipiSperse® technology allows for diverse applications previously unavailable to unformulated palmitoylethanolamide.



Unformulated palmitoylethanolamide mixed in water (left) compared to Levagen®+ mixed in water (right)

LipiSperse is a registered trademark of Pharmako Biotechnologies.

1. Briskey, D., Mallard, A. R., & Rao, A. (2020). Increased absorption of palmitoylethanolamide using a novel dispersion technology system (LipiSperse®). *Nutraceuticals Food Sci*, *5*(2), 3.

Levagen®+ Delivery Systems

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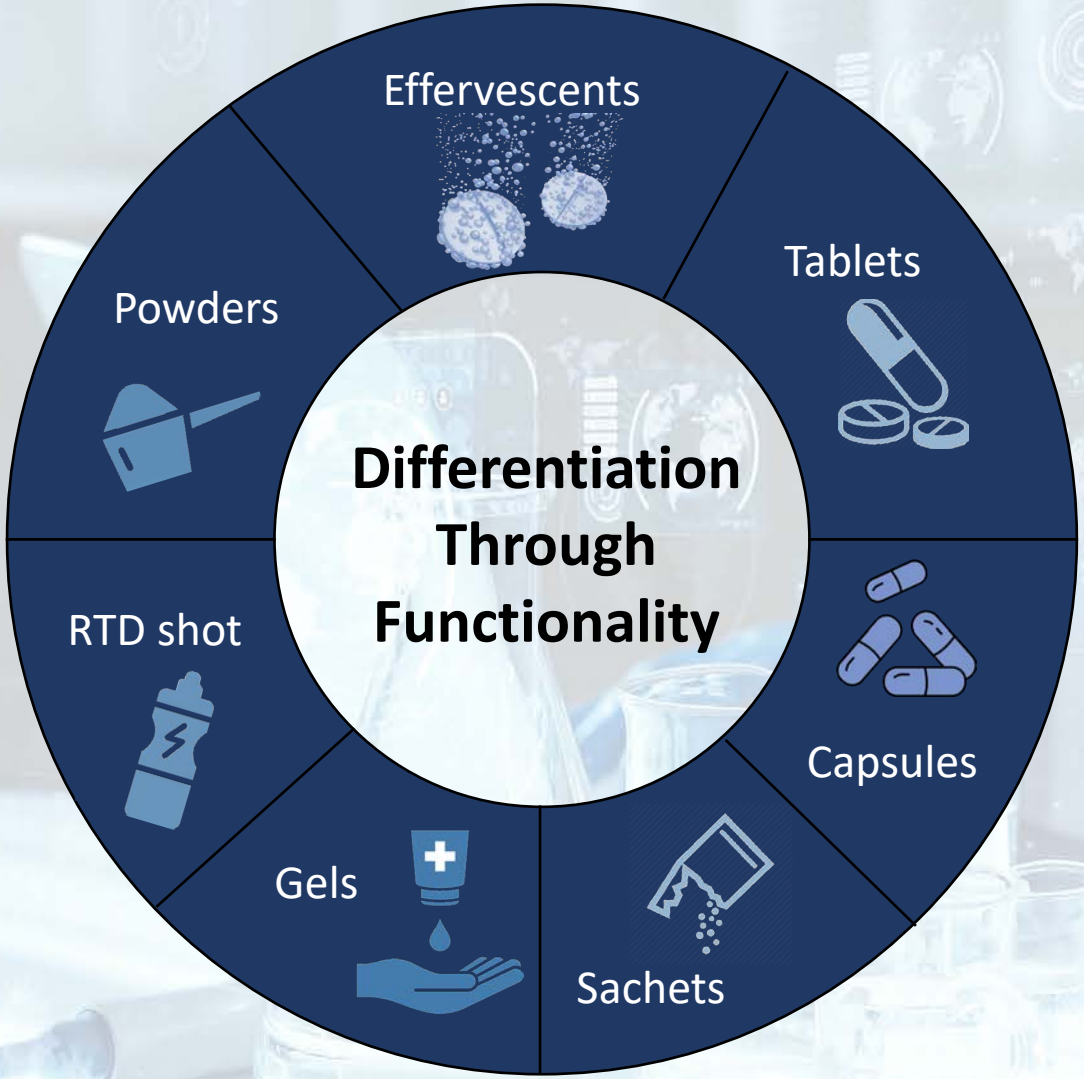
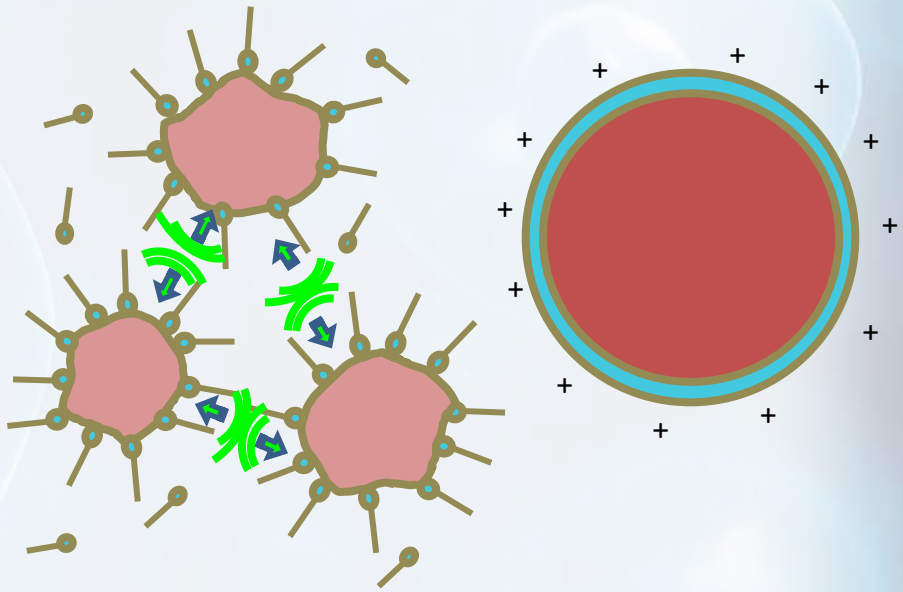


Levagen®+

LipiSperse®

- Cold-water dispersion technology designed to enhance the bioavailability and functionality of lipophilic ingredients,
- Minimal excipient usage while maximizing the load of active ingredients
- By coating the lipophilic actives with LipiSperse®:
  - Repulsive forces are created between the particles to prevent aggregation
  - Surface tension is also reduced, enabling liquid to adhere to the particles



LipiSperse®

LipiSperse®

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- Bioavailability enhancement substantiated by published human clinical trials for:
  - Curcuminoids-(As HydroCurc®)[1]
  - Resveratrol (as VeriSperse®)[2]
  - Palmitoylethanolamide (PEA) (as Levagen®+)[3]

HydroCurc®

Veri•Sperse®

Levagen®+

LipiSperse®

1. Briskey, D., Sax, A., Mallard, A. R., & Rao, A. (2019). Increased bioavailability of curcumin using a novel dispersion technology system (LipiSperse®). *European journal of nutrition*, *58*, 2087-2097.
2. Briskey, D., & Rao, A. (2020). Trans-resveratrol oral bioavailability in humans using LipiSperse™ dispersion technology. *Pharmaceutics*, *12*(12), 1190.
3. Briskey, D., Mallard, A. R., & Rao, A. (2020). Increased absorption of palmitoylethanolamide using a novel dispersion technology system (LipiSperse®). *Nutraceuticals Food Sci*, *5*, 3.

Levagen®+: Joint Health

74 Men and Women

350 mg/Day

2 Weeks

Joint Health Substantiation

- **Study Design**
  - Double-blind, randomized, placebo-controlled trial[1]
  - 74 men and women with joint discomfort that does not originate from an acute injury or a chronic disorder
  - Administered one of the following for 2 weeks
    - 175 Levagen®+ (NLT 150 mg PEA) twice daily
      - 350 mg/day Levagen®+ (NLT 300 mg/day PEA)
    - Matching placebo
- **Key Results**
  - Significantly ($p < 0.05$) lower joint discomfort on both morning and evening visual analogue scale (VAS) score in comparison to the placebo on day 14

1. Briskey, D., Roche, G., & Rao, A. (2021). The Effect of a Dispersible Palmitoylethanolamide (Levagen+) Compared to a Placebo for Reducing Joint Pain in an Adult Population–A Randomised, Double-Blind Study. *Int. J. Nutr. Food Sci*, *10*(9).

Levagen®+: Sleep

103 Men and Women

350 mg/Day

8 Weeks

Sleep Substantiation

- **Study Design**
  - Double-blind, randomized, placebo-controlled trial[1]
  - 103 men and women with a disturbed sleeping pattern
  - Administered one of the following for 8 weeks
    - 350 mg Levagen®+ (NLT 300 mg PEA) once daily an hour before bedtime
    - Matching placebo
- **Key Results**
  - Significantly ($p < 0.05$) lower sleep latency at week 8 in comparison to the placebo in those with a sleep latency >10 minutes at baseline
  - Significantly lower time to feel awake and higher cognition upon waking at week 8 in comparison to the placebo

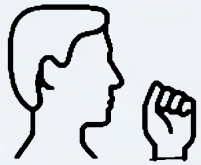
1. Rao, A., Ebelt, P., Mallard, A., & Briskey, D. (2021). Palmitoylethanolamide for sleep disturbance. A double-blind, randomised, placebo-controlled interventional study. *Sleep Science and Practice*, *5*(1), 1-8.

Levagen®+: Immune Support

398 Men and Women

700 mg/day

3 Months



Year-round Immune Support Substantiation

- **Study Design**
  - Double-blind, randomized, placebo-controlled trial[1]
  - 398 men and women
  - Administered one of the following:
    - 350 mg Levagen®+ (NLT 300 mg PEA) twice daily
      - 750 mg/day Levagen®+ (NLT 600 mg/day PEA)
    - Matching placebo
- **Key Results**
  - Significantly ($p < 0.05$) lower number of subjects reporting an upper respiratory tract infection (URTI) in comparison to the placebo
  - Significantly ($p < 0.05$) lower number of episodes of URTI in comparison to the placebo
  - Significantly ($p < 0.05$) lower % of URTI episodes in relation to the number of subjects in comparison to the placebo
  - Significantly ($p < 0.05$) lower severity of scratchy throat and cough in those who reported a symptom in comparison to the placebo

1. Rao, A., Skinner, R., & Briskey, D. (2023). The Efficacy of Palmitoylethanolamide (Levagen+) on the Incidence and Symptoms of Upper Respiratory Tract Infection—A Double-Blind, Randomised, Placebo-Controlled Trial. *Nutrients*, *15*(20), 4453.

New Research: Cognitive Health

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Join us for our live presentation at Natural Products Expo West 2024 on:

The Impact of Levagen®+, a branded Palmitoylethanolamide, on Cognition.

with speaker **Dr. Mohammed Gulrez Zariwala**,
Director of the Center of Nutraceuticals,
University of Westminster

Friday, March 15, 2024 at 9:00 AM PST at
The Marriot, Platinum Ballroom 3-4

Anaheim Convention Center

Levagen®+: Topical Application

Sunkiss Health

XBD Cream

LYMA

Skincare

Cream / Serum

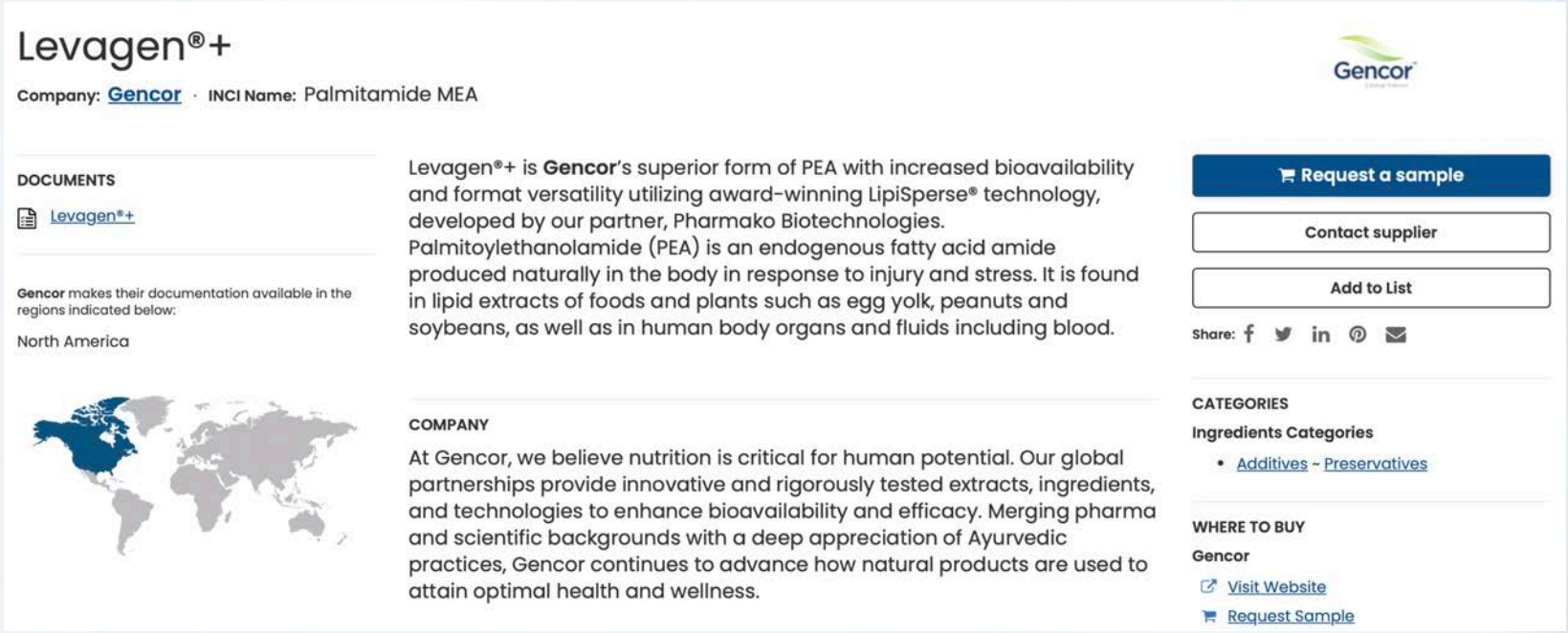
Sample Formula

Serum/Cleanser/ Cream

Advantages of Levagen®/Levagen®+

With so many great options for PEA on UL Prospector, Levagen®+ enhanced with LipiSperse technology offers **distinctive advantages** for formulation with:

- enhanced bioavailability
- wide format versatility
- easily water dispersible
- non-GMO, gluten-free, allergen-free
- Gencor self-affirmed GRAS
- clinically studied and proven
- Informed-Ingredient Certified by LGC
- multi-award-winning



Learn more about Levagen®+ and our entire ingredient portfolio on UL Prospector!

Contact An Ingredient Specialist

Molly Joo
Director of Sales U.S.A.
molly@gencorpacific.com

Mariko Hill
Global Innovation Manager
Europe & Asia
mariko@gencorpacific.com

Ramasamy V Venkatesh
Founder and Managing Director
Europe & Asia
Venkat@gencorpacific.com

info@gencorpacific.com


Thank You!
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