Nutramedic 800 Smetics

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SupplySide SupplySide Global 2025 Preview Global

Beyond Milligrams: Bioavailability and Efficacy
/ Cellular Energy Boosting Ingredients
/ Interactions between Glucagon-Like Peptide-I and
the Gut Microbiota / Challenges and Difficulties
of Small-Scale Cosmetic Producers

Editor's Word



Welcome to the No.19 November/December edition of B2B Nutramedic&Cosmetics.

As the year draws to a close, we turn our focus to innovation, partnerships, and forward-looking trends shaping 2026. This issue spotlights **SupplySide Global 2025**, where expanded expo halls and future-focused education will once again bring the nutraceutical, functional food, and cosmet-

ics industries together under one global stage of innovation.

We are also excited to showcase **Valeovita, Fraktal, Fine Foods**, and **Sabinsa's Cirpusins™** - each setting new benchmarks in formulation excellence, functional performance, and the science behind better health and beauty solutions.

From Lallemand Health Solutions' latest biotic innovations to Kemin's upgraded portfolio and ProBiotix Health's ground-breaking probiotic menopause solutions, we continue to highlight companies driving evidence-based progress. Industry leaders including Prinova and GC Rieber VivoMega share their latest milestones, while our science feature explores the interactions between GLP-1 and gut microbiota in metabolic disorders.

This edition also covers the **challenges faced by small-scale cosmetic producers**, and **Symrise's new Neo Heliopan® Fusion** - a ready-to-use UV filter blend enabling efficient SPF 50+ formulations.

As we move into 2026, B2B Nutramedic&Cosmetics remains committed to connecting science, sustainability, and innovation across global nutraceutical and cosmetic industries.

Thank you for your continued trust and partnership. Best regards,

Daria Šurić, EDITOR-IN-CHIEF

Bimonthly digital magazine for industry professionals in health, nutrition and cosmetics sector

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Beyond Milligrams: Why Bioavailability Defines Efficacy in Cardiovascular, Cognitive, and Inflammatory Health

The mixed outcomes seen in trials of omega-3 fatty acids, curcumin, polyphenols, and vitamin D underscore the limitations of milligram-based dosing alone. In contrast, progress in advanced delivery systems, formulation science, and personalized medicine demonstrates that improving bioavailability is key to consistent therapeutic results.

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Introduction

Traditionally, the pharmaceutical and nutraceutical industries have equated efficacy with dosage, operating under the assumption that higher milligram amounts produce stronger clinical effects.

While this straightforward model has facilitated product development and prescribing practices, it fails to account for a key pharmacological principle: bioavailability is often a more decisive factor in therapeutic effectiveness than the sheer quantity administered. The benefits of a compound - whether aimed at improving cardiovascular health, supporting cognitive function, or reducing inflammation - depend on how much of the active ingredient is absorbed, survives metabolic processes, enters systemic circulation, and reaches the intended site of action in a biologically active form.

As scientific understanding of pharmacokinetics deepens, the conversation around efficacy is shifting. Increasingly, researchers and healthcare profes-

sionals are focusing on absorption efficiency, metabolic transformation, and targeted delivery rather than relying solely on dose-based metrics. This evolving perspective highlights the importance of formulating interventions that prioritize bioavailability as a core determinant of clinical impact.

In pharmacology, therapeutic efficacy is not determined solely by the amount of a compound consumed, but by its ADME profile - absorption, distribution, metabolism, and excretion. If a compound is poorly absorbed, rapidly metabolized, or inefficiently distributed, it is unlikely to reach therapeutic concentrations at the target site, regardless of the dose administered. This challenge is well illustrated by compounds such as curcumin, omega-3 fatty acids, and various nootropic agents. Despite encouraging preclinical findings, numerous clinical trials have failed to demonstrate efficacy due to formulations that did not adequately address bioavailability. Such outcomes underscore the inseparability of pharmacokinetics and therapeutic performance.



Bioavailability in cardiovascular health

Omega-3 fatty acids, most notably eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are widely recognized for their cardioprotective roles. They help lower triglyceride concentrations, stabilize cardiac cell membranes, reduce platelet aggregation, and give rise to specialized pro-resolving mediators (SPMs) such as resolvins and protectins that actively modulate vascular inflammation. However, the true clinical benefit of omega-3 supplementation cannot be gauged by milligram dosage alone. Bioavailability is the decisive factor in determining efficacy.

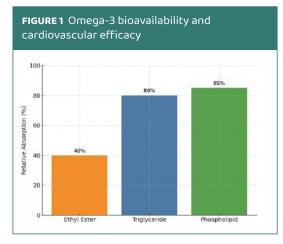
- Formulation: Ethyl ester omega-3s demonstrate lower absorption compared to re-esterified triglyceride or phospholipid-bound forms. As a result, two products both labelled "1000 mg fish oil" may lead to very different plasma EPA/DHA concentrations.
- Absorption context: Because omega-3s are fatsoluble, their uptake is significantly enhanced when taken with dietary fats. In contrast, consumption on an empty stomach reduces absorption, limiting their therapeutic value despite equivalent doses.
- Metabolic transformation: The cardiovascular benefits of omega-3s rely heavily on their enzymatic conversion into SPMs. Without adequate systemic availability, these downstream anti-inflammatory and lipid-regulating effects remain muted.

In cardiovascular care, efficacy is therefore not defined by capsule size or label claims, but by the proportion of EPA and DHA that successfully enter circulation in an active form and reach vascular targets. For clinicians, this underscores the importance of selecting formulations and strategies that optimize absorption and metabolic utilization, rather than focusing solely on nominal dosage.

The concept of bioavailability in cognitive health Omega-3 fatty acids - most notably docosahexaenoic acid (DHA) - are indispensable for preserving cognitive performance. DHA serves as a fundamental structural element of neuronal membranes, where it enhances membrane fluidity, supports synaptic plasticity, and regulates neurotransmitter function. It also contributes to neurogenesis and helps mitigate oxidative stress within the brain. Eicosapentaenoic acid (EPA), although less concentrated in neural tissue, provides complementary benefits through its anti-inflammatory effects and influence on mood regulation.

Despite these well-established roles, the cognitive impact of omega-3 supplementation cannot be assessed solely by the number of milligrams consumed. Bioavailability ultimately determines whether these fatty acids reach the brain in physiologically meaningful amounts.

- Gastrointestinal absorption Compounds must withstand digestive processes and be effectively absorbed through the intestinal lining into the bloodstream.
- Metabolic transformation Following absorption, many substances undergo first-pass metabolism in the liver, which can either enhance their biological activity or diminish it.



- * This image was generated with AI
- Systemic distribution and transport Once in circulation, compounds must remain stable, exhibit adequate solubility, and be efficiently transported to target tissues.
- Passage across the blood-brain barrier (BBB) –
 Only molecules with specific properties such as
 lipid solubility, low molecular weight, or compatibility with active transport mechanisms can cross
 the BBB and access brain tissue.
- Cellular uptake and functional integration Within the brain, compounds must be taken up by neurons, glial cells, or endothelial cells to influence neurotransmitter activity, oxidative balance, or the structural integrity of neural networks.

Examples

- Curcumin: Despite gram-level doses, plasma concentrations remain low, and CNS penetration is minimal. Bioavailability-enhanced formulations (liposomal curcumin, curcumin + piperine) demonstrate improved effects on cognition.
- Flavonoids (blueberry, green tea): Their cognitive benefits rely on metabolites that cross the BBB and modulate neuronal signalling and cerebral blood flow.
- Omega-3 DHA: Critical for neuronal membrane fluidity, yet bioavailability depends on dietary context and enzymatic conversion.

Bioavailability in inflammatory health

Inflammation is a central driver of cardiovascular disease, neurodegeneration, autoimmune disorders, and metabolic dysfunction.

Many bioactive compounds with proven anti-inflammatory potential - such as polyphenols, omega-3 fatty acids, vitamin D, and curcumin - have shown inconsistent results in clinical trials. A key reason is that dosage expressed only in milligrams overlooks the critical role of absorption and systemic availability.

Examples

Nutramedic &Cosmetics



TABLE 1 Beyond miligrams: why bioavilability defines efficacy	
Cardiovascular health	Omega-3 forms, statins, PCSK9 inhibitors Efficacy depends on systemic delivery
Cognitive health	DHA & EPA must cross the Blood-Brain Barrier Formulation impacts neuronal uptake
Inflammatory health	Curcumin, Vitamin D, Omega-3 Require enhanced absorption for cytokine modulation
Core message	Miligrams ≠ Efficacy Bioavailability = Clinical Impact

significant reductions in biomarkers such as CRP and IL-6.

- Vitamin D: As a fat-soluble vitamin, its immunomodulatory efficacy relies on efficient lipid transport and enzymatic conversion to active forms.
- Omega-3 fatty acids: Their anti-inflammatory effects, mediated through specialized pro-resolving mediators like resolvins and protectins, are determined not by sheer intake but by the extent to which these metabolites are bioavailable.

Omega-3 fatty acids, especially EPA and DHA, are key modulators of inflammatory pathways. They act as precursors to specialized pro-resolving mediators (SPMs) - including resolvins, protectins, and maresins - that actively resolve inflammation and facilitate tissue healing. Through the suppression of pro-inflammatory cytokines such as IL-6 and TNF- α , and by influencing immune cell activity, omega-3s help mitigate the chronic, low-grade inflammation that drives cardiovascular disease, neurodegeneration, autoimmune conditions, and metabolic disorders

Professional perspective: clinical and formulation considerations

For experts in the pharmaceutical and medical fields, moving from a milligram-focused approach to a bioavailability-centred framework carries significant implications:

- Clinical trial design: Many unsuccessful trials are not failures of the compound itself, but of inadequate formulation. Greater emphasis on pharmacokinetic assessment and the integration of advanced delivery technologies is essential to improve outcomes.
- Personalized medicine: Variability in absorption driven by factors such as gut microbiota composition, liver enzyme activity, and genetic differences underscores the need for patient-specific dosing
 strategies rather than a one-size-fits-all model.
- Formulation innovation: The use of nanocarriers, micelles, and lipid-based systems should be viewed as scientifically valid methods to enhance delivery and bioavailability, not as mere marketing tools.
- Regulatory landscape: Regulatory bodies are placing increasing weight on pharmacokinetic evidence to substantiate therapeutic claims. Demonstrating systemic exposure and biological activity,

rather than listing nominal doses, is becoming the standard for both pharmaceuticals and premium nutraceuticals.

Conclusion

The effectiveness of nutrients and bioactive compounds in cardiovascular, cognitive, and inflammatory health extends far beyond the milligram values listed on labels. True clinical benefit depends on bioavailability - the extent to which these compounds are absorbed, metabolized, and delivered to target tissues in concentrations sufficient to exert biological effects.

The mixed outcomes seen in trials of omega-3 fatty acids, curcumin, polyphenols, and vitamin D underscore the limitations of milligram-based dosing alone. In contrast, progress in advanced delivery systems, formulation science, and personalized medicine demonstrates that improving bioavailability is key to consistent therapeutic results.

For healthcare and pharmaceutical professionals, this requires shifting the focus from dosage to functional delivery and tissue-level activity. Future research and clinical practice must emphasize optimized formulations, validated biomarkers, and individualized strategies. Only by moving beyond milligrams can we fully realize the potential of these compounds in protecting the heart, enhancing cognition, and regulating inflammation.



MVS Pharma GmbH – advancing supplement science through purity, innovation, and transparency.

As a German innovator in pharmaceuticals and advanced nutritional science, the company combines medical expertise with uncompromising quality to deliver supplements that are clean, effective, and truly reliable.

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YOUR NATURAL AND SAFE PATHWAY TO WEIGHT LOSS

Natural, Time-Tested, Proven by Science

As a standardized extract of the Cyperus rotundus rhizomes, Cirpusins® leans on nature to enhance the body's fat burning mechanisms. Its potency has been observed throughout time and across the world.

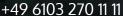
Recent studies carried out by Sabinsa have proven the safety of Cirpusins® while highlighting its ability to induce a significant decrease in body weight, BMI, waist circumference and lipid profiles. This opens up a host of opportunities in weight management applications.

With Cirpusins®, answer consumer demand for proven, natural and safe products tackling obesity, boosting fat burning for athletes, or helping the weight-conscious to stay trim.











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Natural,

Time-Tested & Safe



Obesity is now recognized as a global epidemic, and a quick look at the rates of overweight and obesity makes it very clear. Indeed, the worldwide prevalence of obesity nearly tripled between 1975 and 2016, and it is estimated that by 2030 over 1 billion people globally will be living with obesity (1). Being overweight poses intrinsic, serious risks and health impairments (2), driving many to fight for a healthy weight or to avoid putting on fat.

Consequently, consumers are turning to products to assist them in their weight management journey (3).

These products can prove to be very powerful allies, actively enabling weight loss while making diet and lifestyle changes easier to adopt. But then, while conceiving such products, two criteria should be absolutely paramount: their potency, and maybe even more importantly, their safety and ability to improve overall health without any compromises.

From Ancient Wisdom to Reliable Science

This is what sets Cirpusins® apart. Because it consists of a standardized extract of the roots *Cyperus rotundus* rhizomes, it actually utilizes a knowledge known for millennia, whose safety and potency have been observed and tested across ages and civilizations all over the world. It was employed, for example, in traditional Chinese medicine as well as in the Indian ayurvedic system, but also by the ancient Greek and Arabs of the Levant, as far back as 100 CE.

Drawing from these insights, the main components responsible for the powerful health benefits of this plant have been identified. This is how thousands of years of literature and consumption of *Cyperus rotundus* have been

condensed in one very potent and safe product for weight management: Cirpusins®, which encompasses the benefits of the three pharmacologically active molecules and is scientifically evaluated for its anti-obesity potentials in vitro and in vivo (4).

As an herbal extract, Cirpusins® is not only rooted in nature but also supported by multiple clinical and safety studies. This enables Cirpusins® to benefit from a strong documentation for its antiadipogenic potential, helping product formulators to appeal to consumers looking for proven, safe natural products.

Proven Benefits for Breaking Down Fat and Biochemistry Regulation

Cirpusins® is a standardized extract containing 6-8 % stilbenes, in the form of Scirpusin A, Scirpusin B and Piceatannol (5). These molecules originally have antimicrobial properties for the plant, protecting it from fungal infection and toxins. However, they have much broader biological applications, and naturally occurring stilbenes such as those concentrated in Cirpusins® delivers multi-functional effects.

This enables Cirpusins® to not only target one specific aspect of weight gain and adipocytic biochemistry but to encompass multiple processes, allowing for a more holistic, complete and fruitful approach:

 Boosting adipocyte browning. Contrary to white adipose tissues which are responsible for energy storage, brown adipose tissues are more prone to

- lipolysis (breaking down) and therefore contribute to fat loss (6).
- 2. **Lipid profile normalization.** Under a high-fat diet, Cirpusins® has been proven to bring the levels of total cholesterol, lipoproteins, and triglycerides back to values very close to those of a normal diet.
- 3. **Biochemistry normalization. Similarly,** Cirpusins® normalizes liver enzymes, blood glucose levels and uric acid levels without any adverse effects.

Overall, taking two 525 mg capsules per day of Cirpusins® shows in clinical studies a significant decrease in body weight, BMI, waist circumference and lipid profiles, with no serious adverse effects or safety concerns.

Rewiring Fat Gain: The Preventive Game Changer

Furthermore, this multifunctional effect serves another purpose: going beyond weight loss and making putting on fat more difficult. This is why Cirpusin® also appeals not only to overweight and obese people, but also to sportspeople as well as individuals conscious of their weight looking for weight management products. Because of it has been shown to inhibit adipogenesis in vitro, it has a preventive

and protective effect, making achieving long-term weight goals more doable.

You can learn more about Cirpusins® by visiting its website: https://cirpusins.com/. You can also download the white paper "Cirpusins® – A Potent Herbal Formulation for Weight Management" here: https://cirpusins.com/newsroom/whitepapers/cirpusins-a-potent-herbal-formulation-for-weight-management/.

About Sabinsa

Sabinsa Corporation, founded in 1988 by Dr. Muhammed Majeed, is a manufacturer and supplier of herbal extracts, cosmeceuticals, minerals and specialty fine chemicals. Sabinsa's mission is to provide evidence-based natural products for human functional nutrition and well-being.

- (1) World Obesity Atlas 2022 World Obesity Federation, 2022 (https://s3-eu-west-1.amazonaws.com/woffiles/World_Obesity_Atlas_2022.pdf), accessed July 25, 2023.
- (2) Obesity and overweight fact sheet World Health Organization, last updated June 9, 2021 (https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight), accessed July 25, 2023.
- (3) Dietary Supplements for Weight Loss fact sheet US Office of Dietary Supplements, National Institutes of Health, last updated May 18, 2022 (https://ods.od.nih.gov/factsheets/WeightLoss-Health Professional/), accessed July 25, 2023.

- (4) Majeed M, Nagabhushanam K, Bhat B, Ansari M, Pandey A, Bani S, Mundkur L. 2022. The anti-obesity potential of Cyperus rotundus extract containing Piceatannol, Scirpusin A and Scirpusin B from rhizomes: Preclinical and clinical evaluations. Diabetes Metab Syndr Obes. Targets Ther. 15: 369. doi: 10.2147/DMSO.S348412.
- (5) Chou Y, Ho C, Pan M. 2018. Stilbenes: Chemistry and molecular mechanisms of anti-obesity. Curr Pharmacol Rep. 4: 202–209. doi:10.1007/s40495-018-0134-5.
- (6) Anna Park, Won Kon Kim, and Kwang-Hee Bae 2014: Distinction of white, beige and brown adipocytes derived from mesenchymal stem cells. World J Stem Cells; 6(1): 33-42. doi: 10.4252/wjsc.v6.i1.33

fraktal



Fraktal Beauty receives MTick certification

We are pleased to announce that Fraktal Beauty products were awarded prestigious MTick certification issued by GenM organization from UK, a trailblazer in the field of menopause friendly products and services certification.

The MTick is the trusted symbol and certification for menopause-friendly shopping, meeting the overwhelming demand of 15.5 million menopausal women in the UK and 1 billion globally for better shopping experiences.

The MTick symbol is empowering women to search, source and shop with confidence, to find products to ease or relieve the signs of menopause, helping them have a better lived experience.

By joining The GenM Collective we are joining a growing group of internationally recognized menopause friendly brands, retailers and manufacturers, focused on providing products and services for perimenopausal and menopausal women.

Based on 48 menopausal symptoms, specified by GenM certification process, we are pleased that following Fraktal Beauty products have met these criteria in the category products backed by authorized medicinal, cosmetic and/or health claims:



We, at **Fraktal Beauty**, are looking forward to working with **GenM Collective** in developing further products that are focused on the needs of women in their best years!

Fraktal Beauty





Tea Višek, owner and CEO

Cos Chem d.o.o.









Valeovita – One Door to Open for Your Private Label Food Supplements

In today's nutraceutical market, speed, flexibility, and trust are more important than ever. Brands and retailers seeking to expand their product portfolio are often faced with a complex journey: finding reliable raw material suppliers, researching formulations, navigating regulatory frameworks, managing production, and ensuring full compliance with quality documentation. For many, this can feel like opening a dozen different doors at once. Valeovita offers a different approach: one door to open.

From idea to finished product

Valeovita d.o.o., headquartered in Slovenia, has built its reputation as a trusted partner in the distribution and development of high-quality nutraceutical and functional food ingredients across Europe. But the company has gone far beyond sourcing raw materials. Today, Valeovita acts as a complete private label partner - taking customers from the first spark of an idea to the launch of a finished, fully compliant food supplement.

It all starts with listening. What problem does the new product aim to solve? Which target group is it designed for - athletes, seniors, children, busy professionals, or pet owners? Once the concept is clear, Valeovita's team helps customers evaluate the latest scientific findings and consumer trends, and then supports them in shaping the formulation. Whether it's a classic vitamin blend, a targeted mineral supplement, or an innovative functional formula with botanicals, amino acids, or specialty actives, Valeovita ensures that the product starts from a sound scientific and regulatory basis.

High-quality ingredient supply

With more than 1,000 natural and synthetic raw materials available, Valeovita connects clients with some of the most established global ingredient producers. Magnesium, CoQ10, collagen, plant extracts, probiotics, omega-3s - whatever the formula requires, Valeovita can supply it. Exclusive distribution agreements with leading international partners give customers access to clinically supported, innovative ingredients not easily found elsewhere.

The advantage for brands is clear: rather than sourcing each material separately, they can rely on Valeovita as a single, transparent supplier who ensures consistent quality, secure supply, and competitive pricing.

Production and packaging solutions

Private label food supplement production requires more than just good ingredients. Valeovita manages the transition from formulation to manufacturing, ensuring that each product is produced under strict GMP and HACCP standards. Whether the





end product is capsules, tablets, powders, gummies, or ready-to-drink solutions, Valeovita can organize the appropriate production line.

Packaging is equally important for market success. Valeovita supports customers in selecting packaging formats that meet both regulatory and consumer expectations, combining practicality, safety, and shelf appeal.

Documentation and compliance - all covered

In nutraceuticals, a product is only as strong as its documentation. Labels, certificates of analysis, stability studies, safety data, regulatory references, and claims substantiation must all be in place before a supplement reaches the market. Valeovita takes care of this often overlooked but critical part of the process.



By preparing all the required technical and quality documentation, Valeovita helps brands launch confidently and compliantly in the European Union and beyond. This service is particularly valuable for small and mid-sized companies that lack in-house regulatory departments but still want to bring professional-grade products to market.

One partner, many benefits

The "one door to open" approach saves time, reduces costs, and minimizes risks. It also allows brands to focus on what they do best: building relationships with consumers and growing their business. By outsourcing the complexity of formulation, sourcing, production, and documentation to Valeovita, companies can shorten their time-to-market and ensure that each launch is backed by solid expertise.

With nearly two decades of experience in the nutraceutical and functional food sector, Valeovita combines the reliability of a seasoned distributor with the agility of an innovation partner. The company's team is passionate about helping clients succeed, whether they are introducing their very first food supplement or expanding an established product line.

Looking ahead

The demand for nutraceuticals and functional foods continues to grow, driven by consumers' focus on health, wellness, and prevention. At the same time, the market is becoming increasingly sophisticated, with higher expectations for transparency, scientific support, and quality.

Valeovita is ideally positioned to meet these demands. By offering an end-to-end solution, the company empowers brands to turn concepts into compliant, market-ready products - efficiently, reliably, and with confidence.

For any company considering a new product launch, the path forward can be simplified to just one step: **open the door to Valeovita.**



About Valeovita

Valeovita d.o.o. is a Slovenia-based company specializing in the distribution, development, and private label production of nutraceutical and functional food ingredients. With nearly 20 years of experience, Valeovita provides an all-inclusive service — from formulation and raw material sourcing to production, packaging, and full quality documentation. Partnering with world-leading ingredient suppliers, Valeovita supports brands and manufacturers across Europe in bringing innovative, compliant, and market-ready food supplements to life.

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ALEO VITA

www.valeovita.si



Connecting the Dots of Nutritional Innovation

Fine Foods at CPHI 2025: Innovation and New Synergies

Fine Foods & Pharmaceuticals N.T.M. S.p.A. will showcase its new brand identity and innovative holistic approach to well-being at CPHI 2025 in Frankfurt, highlighting synergies between the nutraceutical, pharmaceutical, and cosmetics sectors. Through strategic investments, expanded production capacity, and a strong focus on research and development, the company is positioning itself as a leading integrated Health & Beauty solutions provider.

he 2025 CPHI Frankfurt, taking place from 28–30 October, is just around the corner. Fine Foods & Pharmaceuticals N.T.M. S.p.A. (Euronext STAR Milan: FF) is setting up its latest innovations and refreshed corporate positioning to be presented to an international audience. For the Italian independent Contract Services Development & Manufacturing Organization (CSDMO), specialising in the contract development and manufacturing of

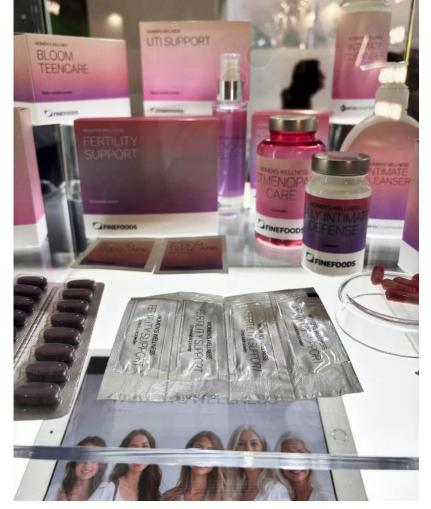
products for the nutraceutical, pharmaceutical, and cosmetics industries with a customer-centric, service-oriented philosophy, the event provides an ideal stage to demonstrate how nutraceutical and cosmetic solutions can integrate with the pharmaceutical world to deliver a holistic concept of well-being. Pharmaceutical brands are increasingly expanding their portfolios to include nutraceutical and cosmetic lines as strategic extensions. These sectors allow accelerating innovation, experimenting with new communication styles and responding to emerging market demands while using the authority of their parent brand.

Visitors to the Fine Foods stand will see the Group's new brand identity, first introduced in May with its new logo. This helps strengthen its unique position on the market. The updated brand features the "Health & Beauty CSDMO" payoff alongside the "Fine Foods" naming. The addition of the "S" for Services highlights the company's enduring commitment to providing high value-added, service-oriented solutions across its business sectors.



At CPHI, Fine Foods will showcase its expertise through products representing the three Group's core business units. A significant example is the women's area, that will be highlighted through cosmetic and nutraceutical ranges designed to help women at all stages of life, responding to their specific needs. From adolescence to post-menopause, the solutions combine supplements and cosmetics synergistically, promoting well-being from the inside out. A dedicated line of intimate cleansers, tailored to women's different needs, works alongside functional cosmetics and supplements, which are available in a variety of galenic preparations, including capsules and powders. These are formulated to support holistic well-being.

The focus extends to oral and topical formulations designed to ease symptoms and support overall well-being in synergy with traditional pharmaceuticals. Innovative supplements target specific needs such as headaches, joint pain, or gastrointestinal disorders, providing comprehensive health



support. Functional topical products complete the range. These are formulated to address issues such as heavy legs, sensitive gums, or fatigued joints, using different types of technology, including solid sticks, for targeted and complementary action.

Fine Foods will highlight other areas of nutraceutical innovation, including biotics (an emerging frontier in health) and solutions for metabolic syndrome, explored in its various subcategories.

The solutions stem from the Group's commitment to research and development, a cornerstone of its growth strategy. Fine Foods introduction of the CSDMO concept underscores its dedication to offering a complete range of premium services, including:

- Industry expertise: Decades of experience across the nutraceutical, pharmaceutical and cosmetics sectors.
- Strategic guidance and marketing support: Helping customers effectively define their market strategies.
- Cutting-edge innovation and formulation development: A proactive R&D team constantly anticipating new trends.
- Regulatory advice and certification support: Essential assistance in navigating complex regulatory environments.
- Quality analysis and control: Rigorous standards to ensure the highest quality of finished products.
- Structured project management: One contact provides the customer with the planning, coordination and monitoring of each project phase, for clear, efficient, and secure delivery.

The recent rebranding embodies Fine Foods' core values: reliability, modernity, dynamism, excellence, quality, ethics, integrity, sustainability, innovation and attention to detail. These principles form the foundation of the company's ability to respond comprehensively to customer needs and to build long-term partnerships.

Business unit growth and consolidation

Fine Foods commitment to strengthening its product range is reflected in its recent strategic investments. The completion of the new pharmaceutical plant in Brembate (Bergamo) marks a significant milestone. Following the recent inspection by AIFA, the company expects final authorisation for the start-up of the new production site by the end of the year. This expansion will enable Fine Foods to fulfil major multi-year agreements signed with international customers, and accelerate the development of the Pharma Business Unit, responding effectively to the growing demand within this rapidly expanding market.

Fine Foods is investing to increase its nutraceutical production capacity by purchasing new land needed for further facility extensions.

The Cosmetics Business Unit has reached a crucial stage in its evolution. Following the acquisition of Euro Cosmetic, now rebranded as Fine Cosmetics, the Group has undertaken substantial investments in upgrading production facilities and strengthening its management team with the addition of highly experienced professionals. The Group is investing in



R&D by creating a second cosmetics laboratory, the "Research & Innovation Hub", with a surface area nearly three times larger than the existing facility. This new centre will reinforce Fine Cosmetics' position as a strategic partner for leading brands in the global beauty and personal care industry.

Market trends point towards an increasing convergence between nutraceuticals and cosmetics, and the Group is working with several customers whose product portfolios span both sectors.

CPHI 2025 is the ideal platform to demonstrate how Fine Foods has evolved into a comprehensive solutions provider within the Health & Beauty sector. Fine Foods is actively shaping the future of the health and beauty landscape through a model built on innovation, synergy and outstanding customer service.



Cellular Energy Boosting Ingredients in Food Supplements and Functional Foods

Cellular energy-boosting ingredients such as CoQ10, creatine, B vitamins, alpha-lipoic acid, and NAD+ precursors play a vital role in optimizing mitochondrial function and ATP production. As the demand for functional foods and supplements rises, these bioactive compounds are increasingly recognized for enhancing metabolism, reducing fatigue, and supporting healthy aging.

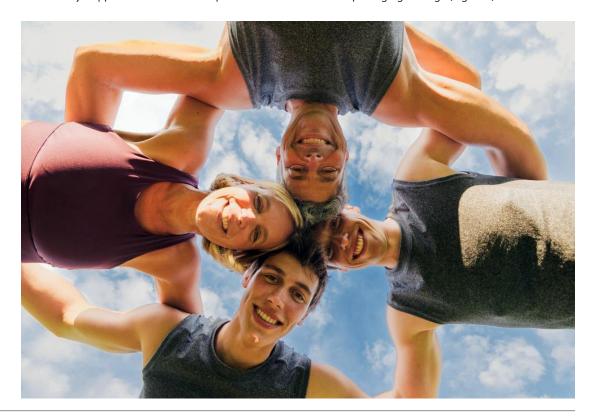
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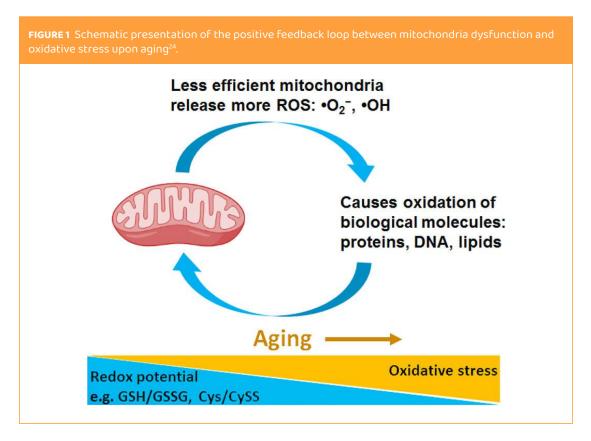
Background on cellular energy

Cellular energy, mainly in the form of adenosine triphosphate, is essential for almost all biological processes, from muscle contraction to neuronal signaling¹. This crucial molecule is produced through a complex network of metabolic pathways, including glycolysis, the Krebs cycle, and oxidative phosphorylation, all of which depend on a steady supply of specific micronutrients and cofactors². Functional foods and dietary supplements often incorporate bioac-

tive compounds to support these pathways, thereby improving cellular energy production and overall metabolic efficiency^{3,4}.

The wide range of ingredients found in these products includes vitamins, minerals, amino acids, botanicals, and other bioactive compounds, each with a unique role in regulating energy metabolism. Mitochondrial dysfunction upon aging results in increased ROS, thus causing enhanced oxidation of biomolecules (proteins, lipids) and opening a positive feedback loop of aging damage (Figure 1).





Food supplements containing cellular energy-boosting ingredients

Several essential ingredients in food supplements have shown significant potential to enhance cellular energy production and overall mitochondrial health. These ingredients often operate through various mechanisms, such as increasing substrate availability, optimizing enzyme activity, or strengthening antioxidant defenses to preserve mitochondrial integrity.

For example, compounds like coenzyme Q10 directly participate in the electron transport chain, while others like alpha-lipoic acid serve as powerful antioxidants and cofactors for mitochondrial enzymes. Additional notable supplements include L-carnitine, which helps transport fatty acids into mitochondria, and various NAD+ precursors that elevate cellular levels of this vital coenzyme. The reduction in NAD+ levels, commonly observed in myocardial cells, has been directly linked to insufficient ATP production and a higher risk of conditions such as heart failure, suggesting that NAD+ replenishment could improve energy deficiency in these cases. For instance, coenzyme Q10 plays a crucial role in mitochondrial energy generation and acts as a strong antioxidant, with its natural production decreasing with age, highlighting the need for supplementation to sustain cellular energy and counteract age-related decline.

Ingredients known to boost cellular energy

A diverse array of ingredients, ranging from vitamins and minerals to specialized botanical extracts, has been identified for their potential to enhance cellular energy production through various mechanisms. These ingredients often act as precursors, cofactors, or modulators within the intricate metabolic pathways that generate adenosine triphosphate, the primary energy currency of the cell. The careful regulation of these pathways is essential for maintaining cellular homeostasis and ensuring the optimal functioning of organs and tissues⁵. Specifically, various macro- and micronutrients are critical for efficient energy metabolism and mitochondrial function, either serving as substrates for catabolism or as vital components of enzymatic systems⁶.

The growing market for functional foods reflects a global trend toward health consciousness, with consumers increasingly seeking products that offer benefits beyond basic nutritional sustenance. This pursuit often leads to the exploration of dietary interventions and supplementation strategies aimed at optimizing energy metabolism and reducing fatigue, especially during periods of increased physiological demand⁷.

Coenzyme Q10 (CoQ10)

Coenzyme Q10, a ubiquinone, plays a key role in the mitochondrial electron transport chain as an essential cofactor for several enzymes involved in oxidative phosphorylation, thereby supporting ATP production. It functions as both an electron acceptor and donor, transferring electrons from complex I to complex II and then to complex III, a process crucial for creating the proton gradient that powers ATP synthase⁹.

Beyond its role in energy production, CoQ10 also acts as a powerful antioxidant, protecting mitochondrial membranes from oxidative damage, which is essential for maintaining metabolic efficiency¹⁰. Additionally, CoQ10 regulates cellular signaling and gene expression, affecting pathways related to meta-



bolism and transport by participating in various oxidation-reduction reactions that generate hydrogen peroxide, a secondary messenger that activates transcription factors such as NF- κ B.

Creatine

Creatine, an endogenous compound synthesized from amino acids, plays a vital role in rapid ATP regeneration, especially in tissues with high and variable energy demands, such as skeletal muscle and the brain. It functions as a key part of the phosphocreatine system, enabling quick phosphorylation of adenosine diphosphate back to ATP, thus providing an immediate energy reserve during high-intensity, short-duration activities11. Research shows that creatine supplementation not only boosts high-energy phosphate availability but also has antioxidative and neuroprotective effects, helping maintain mitochondrial health under stressful conditions¹². This makes it a highly desirable ingredient in dietary supplements designed to enhance athletic performance and support cognitive function. Furthermore, creatine supplementation has been studied for its potential to slow age-related decline in muscle function and overall physical ability by improving mitochondrial health^{13,14}. The ergogenic benefits of creatine monohydrate are well established, enhancing resistance training adaptations and improving performance in short, high-intensity activities¹⁵.

B vitamins

The B vitamins, including thiamine (B1), riboflavin (B2), niacin (B3), pantothenic acid (B5), pyridoxine (B6), biotin (B7), folate (B9), and cobalamin (B12), are essential water-soluble micronutrients that act as coenzymes in many metabolic pathways vital for cellular energy production. Although they do not directly provide energy, these vitamins are crucial for transforming macronutrients (carbohydrates, fats, and proteins) into ATP and for serving as important cofactors in enzymatic reactions central to glycolysis, the Krebs cycle, and oxidative phosphorylation. For example, thiamine (B1), riboflavin (B2), and niacin (B3) are especially vital, as they serve as coenzymes in key energy-producing metabolic reactions.

Alpha-lipoic acid (ALA)

Alpha-lipoic acid is a powerful antioxidant and an essential cofactor for mitochondrial enzymes involved in energy metabolism, especially pyruvate dehydrogenase and alpha-ketoglutarate dehydrogenase. This dithiol compound plays a key role in converting pyruvate into acetyl-CoA, a vital step connecting glycolysis to the Krebs cycle, and also takes part in the oxidative decarboxylation of alpha-ketoglutarate within the Krebs cycle. Its unique ability to switch between oxidized and reduced forms enables it to regenerate other antioxidants, such as vitamin C, vitamin E, and glutathione, thereby enhancing its protective effects against oxidative stress, which can damage mitochondrial function. Additionally, alpha-lipoic acid improves glucose uptake and utilization, increasing insulin sensitivity and potentially optimizing substrate availability for ATP production¹³.

Glutathione

Glutathione, a tripeptide composed of cysteine, glutamate, and glycine, is well known as the body's main antioxidant, playing a key role in cellular detoxification and redox balance, both of which are closely linked to mitochondrial health and energy production¹⁶. Its widespread presence across various cellular compartments enables it to neutralize reactive oxygen species and regenerate other natural antioxidants, helping protect mitochondria from oxidative damage that could otherwise reduce their ability to produce ATP. Besides its direct antioxidant role, glutathione also helps in important detoxification processes, linking with xenobiotics and natural metabolites to promote their removal, preventing their buildup and possible interference with mitochondrial function. Additionally, maintaining healthy glutathione levels is essential for supporting the activity of multiple enzymes involved in mitochondrial respiration and for preventing lipid peroxidation in mitochondrial membranes.

L-carnitine

L-carnitine is an essential quaternary ammonium compound vital for cellular energy metabolism, mainly aiding in the transport of long-chain fatty acids into the mitochondrial matrix for beta-oxidation. This transport process is crucial for producing acetyl-CoA, which then enters the tricarboxylic acid cycle, ultimately generating ATP. In addition to its primary role in fatty acid transport, L-carnitine also has antioxidant properties that help reduce oxidative stress within mitochondria.

NAD

Nicotinamide adenine dinucleotide (NAD+) is a vital coenzyme present in all living cells, essential for fundamental metabolic processes, especially those related to cellular energy production. NAD+ serves as a key electron acceptor in catabolic pathways, oxidizing nutrients like glucose, amino acids, and fatty acids to transfer electrons to NADH and FADH2, which then drive the electron transport chain for ATP production. Beyond its role in electron transfer, NAD+ is also an important substrate for enzymes such as sirtuins and poly-ADP-ribose polymerases, which are essential for DNA repair, gene regulation, and cellular aging, linking cellular energy status to critical regulatory functions. The balance between the oxidized form (NAD+) and the reduced form (NADH) is vital for maintaining metabolic homeostasis, mitochondrial function, and overall cell health¹⁷. The NAD+/NADH ratio specifically influences the activity of NAD-linked dehydrogenases, heavily affecting ATP synthesis efficiency.

Supplementing with NAD+ precursors like nicotinamide riboside or nicotinamide mononucleotide can raise cellular NAD+ levels, showing potential in improving mitochondrial performance and reducing age-related metabolic decline in various preclinical models. This strategy aims to enhance the cellular energy environment, potentially increasing resilience to stress and supporting overall health, especially with aging. Such approaches are increasingly being studied for their possible benefits in cardiovascular



health and neuroprotection, given NAD+'s fundamental role in energy metabolism and cell regulation. Since NAD+ is central to cellular bioenergetics, its levels and the NAD+/NADH ratio are crucial indicators of cell health and function.

SOD

Superoxide dismutase is a vital metalloenzyme that plays a key role in the cellular antioxidant defense system by catalyzing the dismutation of superoxide radicals into oxygen and hydrogen peroxide, thereby preventing oxidative damage to cellular components including mitochondria. This enzymatic process is essential because superoxide radicals, if left unchecked, can initiate lipid peroxidation and damage DNA and proteins, significantly impairing mitochondrial function and overall cellular energy production. Dysregulation of SOD activity, therefore, can directly lead to mitochondrial dysfunction and decreased ATP generation, emphasizing its importance in maintaining cellular energy balance. Additionally, specific isoforms of SOD, such as mitochondrial superoxide dismutase, are precisely localized to safeguard the primary site of reactive oxygen species production during oxidative phosphorylation, directly affecting the efficiency of ATP synthesis¹⁹. Furthermore, the complex regulation of SOD activity is crucial for balancing reactive oxygen species production and neutralization, which in turn influences mitochondrial health and cellular energy output.

Declining NAD+ levels with age impair tissue function, contributing to various age-related diseases, and highlight the potential for NAD+ replenishment strategies to counteract these degenerative conditions. As a result, approaches aimed at restoring NAD+ levels, such as supplementing with its precursors, are actively being studied to improve mitochondrial function and reduce age-related metabolic decline²⁰. The decrease in NAD+ bioavailability, a hallmark of metabolic decline with aging, is closely linked to failing mitochondrial function and signifi-

cantly contributes to the global burden of cardiovascular diseases.

Multi-ingredient supplements

While single-ingredient supplements target specific pathways, multi-ingredient formulations often provide a synergistic approach by combining various compounds to improve different aspects of cellular energy metabolism and mitochondrial function at the same time²¹. These formulations usually aim to address multiple bottlenecks in energy production, such as nutrient deficiencies, oxidative stress, and mitochondrial dysfunction, to deliver a more comprehensive therapeutic benefit¹³. For example, combining NAD+ precursors with antioxidants and mitochondrial support compounds can collectively strengthen cellular resilience against various stressors, thereby boosting energy output. Such all-encompassing supplements are designed to support the complex interaction of cellular processes, from substrate use to ATP synthesis, ensuring ongoing cellular vitality and adaptability.

Dosage and bioavailability considerations

The effectiveness of cellular energy-boosting ingredients in food supplements highly depends on their proper dosage and bioavailability, which determine the actual amount that reaches target cellular areas. Factors such as chemical form, absorption rates, and first-pass metabolism greatly affect how much of a supplement the cells can effectively use for energy production. Additionally, the timing and frequency of intake are crucial in maintaining steady intracellular levels of these compounds, further impacting their therapeutic effects.

Understanding these pharmacokinetic properties is key to maximizing the potential of these supplements in boosting cellular energy and mitochondrial health. This detailed understanding is essential for creating effective supplementation plans that truly



enhance cellular bioenergetics and help counteract age-related decline. Therefore, thorough scientific research into the best delivery methods and cellular uptake of these nutrients is vital for improving their use in supporting overall health and fighting chronic diseases.

Potential side effects and interactions

It is essential to consider the potential for adverse effects and interactions with other medications or supplements, particularly given the broad physiological roles of many cellular energy-boosting ingredients. This necessitates a thorough understanding of individual physiological responses and careful monitoring to ensure optimal therapeutic benefit without compromising patient safety. Therefore, comprehensive pharmacological and toxicological assessments are imperative for each ingredient to delineate safe dosage ranges and identify contraindications, ensuring a favorable risk-benefit profile for consumers. Furthermore, emerging research increasingly focuses on personalized nutrition approaches, leveraging genetic and metabolic profiles to tailor supplement regimens for enhanced efficacy and reduced adverse reactions.

This individualized strategy acknowledges the diverse biochemical landscapes of individuals, moving beyond a one-size-fits-all approach to supplementation²². This approach integrates an understanding of how specific nutrients and cofactors, such as NAD+ precursors, influence cellular bioenergetics at an individual level, optimizing interventions for improved mitochondrial function and overall cellular vitality.

Future trends

Future trends in cellular energy-boosting ingredients point towards personalized nutrition approaches, leveraging individual genetic and microbiome profiles to tailor supplement and functional food recommendations for maximal efficacy. This shift will likely involve advanced diagnostics, including metabolomics and genomics, to precisely identify specific energetic deficiencies and personalize interventions. Further research will focus on the intricate interplay between diet, gut microbiota, and host metabolism to unlock more sophisticated and

targeted nutritional strategies for optimizing cellular bioenergetics.

Moreover, ongoing investigations are exploring the long-term safety and optimal dosing of these compounds, particularly NAD+ precursors, where uncertainties remain regarding pharmacokinetics and pharmacodynamics. For instance, the global market for nicotinamide mononucleotide, a prominent NAD+ precursor, was valued at US\$252.7 million in 2020 and is projected to reach US\$385.7 million by 2027, underscoring the substantial commercial interest and investment in this sector²³. This substantial growth is primarily driven by an aging global population and increasing health consciousness, which fuels a rising demand for anti-aging and health-promoting products, including cellular energy boosters.

Conclusion

Improving cellular energy production is a key focus in modern nutritional science, as efficient mitochondrial function supports nearly every physiological process - from muscle movement and brain function to immune health and metabolism. The growing research on bioactive compounds such as CoQ10, creatine, alpha-lipoic acid, B vitamins, L-carnitine, glutathione, and NAD+ precursors emphasizes their combined potential to enhance mitochondrial efficiency, reduce oxidative stress, and slow down age-related decline.

However, despite promising evidence, differences in individual metabolic responses, bioavailability, and limited long-term safety data highlight the need for more tailored, personalized supplementation methods. Incorporating omics-based diagnostics - such as metabolomics and nutrigenomics - could enable precision nutrition strategies that maximize mitochondrial energy production tailored to each person's unique biochemical profile.

In parallel, advances in formulation science and delivery systems (e.g., liposomal encapsulation, sustained-release matrices) are expected to enhance the stability and cellular uptake of these ingredients, boosting their real-world effectiveness. Rigorous clinical studies are crucial to determine optimal dosages, verify synergistic effects among multi-ingredient formulations, and ensure long-term safety.

Given the growing consumer interest in functional foods and nutraceuticals for energy, vitality, and longevity, collaboration among researchers, manufacturers, and healthcare professionals will be essential to turn laboratory discoveries into safe, effective, and evidence-based products. Ongoing innovation and scientific validation will ultimately shape the next generation of cellular energy-boosting supplements, connecting nutrition, preventive medicine, and healthy aging.

References

- ¹ Rutkowska, J., & Pasqualone, A. (2025). Plant Extracts as Functional Food Ingredients. Foods, 14(3), 374. https://doi.org/10.3390/foods14030374
- ² Spriet, L. L. (2022). Diet and Nutraceuticals for Mental and Physical Performance in Athletes. Sports Medicine, 52, 1. https://doi.org/10.1007/s40279-022-01794-w
- ³ Vignesh, A., Amal, T. C., Sarvalingam, A., & Vasanth, K. (2024). A review on the influence of nutraceuticals and functional foods on

- health [Review of A review on the influence of nutraceuticals and functional foods on health]. Food Chemistry Advances, 5, 100749. Elsevier BV. https://doi.org/10.1016/j.focha.2024.100749
- ⁴ Boggia, R., Zunin, P., & Turrini, F. (2020). Functional Foods and Food Supplements. Applied Sciences, 10(23), 8538. https://doi.org/10.3390/app10238538
- Liu, H., Wang, S., Wang, J., Guo, X., Song, Y., Fu, K., Gao, Z., Liu, D., He, W., & Yang, L. (2025). Energy metabolism in health and diseases [Review of Energy metabolism in health and diseases]. Signal Transduction and Targeted Therapy, 10(1). Springer Nature. https://doi.org/10.1038/s41392-025-02141-x
- ⁶ Nieuwenhuizen, A. G., & Schothorst, E. M. van. (2021). Energy Metabolism and Diet. Nutrients, 13(6), 1907. https://doi.org/10.3390/nu13061907
- Lee, M., Hsu, Y.-J., Shen, S., Ho, C.-S., & Huang, C. (2023). A functional evaluation of anti-fatigue and exercise performance improvement following vitamin B complex supplementation in healthy humans, a randomized double-blind trial. International Journal of Medical Sciences, 20(10), 1272. https://doi.org/10.7150/ijms.86738
- Yasul, Y., Yılmaz, B., Şenel, Ö., Kurt, D., Akbulut, T., Çalıkuşu, A., Anadol, E., & Yılmaz, C. (2025). Evaluating the impact of coenzyme Q10 and high-intensity interval training on lactate threshold and Plasma blood gases in rats: a randomized controlled trial. European Journal of Applied Physiology. https://doi.org/10.1007/s00421-025-05756-8
- ⁹ Spinelli, J. B., & Haigis, M. C. (2018). The multifaceted contributions of mitochondria to cellular metabolism [Review of The multifaceted contributions of mitochondria to cellular metabolism]. Nature Cell Biology, 20(7), 745. Nature Portfolio. https://doi.org/10.1038/s41556-018-0124-1
- ¹⁰ Barnish, M., Sheikh, M., & Scholey, A. (2023). Nutrient Therapy for the Improvement of Fatigue Symptoms [Review of Nutrient Therapy for the Improvement of Fatigue Symptoms]. Nutrients, 15(9), 2154. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/nu15092154
- ¹¹ Alzharani, M. A., Alshuwaier, G. O., Aljaloud, K. S., Al-Tannak, N. F., & Watson, D. G. (2020). Metabolomics profiling of plasma, urine and saliva after short term training in young professional football players in Saudi Arabia. Scientific Reports, 10(1). https://doi.org/10.1038/s41598-020-75755-6
- Marshall, R. P., Droste, J.-N., Gießing, J., & Kreider, R. B. (2022). Role of Creatine Supplementation in Conditions Involving Mitochondrial Dysfunction: A Narrative Review [Review of Role of Creatine Supplementation in Conditions Involving Mitochondrial Dysfunction: A Narrative Review]. Nutrients, 14(3), 529. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/nu14030529
- ¹³ Broome, S. C., Whitfield, J., Karagounis, L. G., & Hawley, J. A. (2024). Mitochondria as Nutritional Targets to Maintain Muscle Health and Physical Function During Ageing [Review of Mitochondria as Nutritional Targets to Maintain Muscle Health and Physical Function During Ageing]. Sports Medicine, 54(9), 2291. Springer Science+Business Media. https://doi.org/10.1007/s40279-024-02072-7
- ¹⁴ Chang, H., & Leem, Y. (2023). The potential role of creatine supplementation in neurodegenerative diseases. Physical Activity and Nutrition, 27(4), 48. https://doi.org/10.20463/pan.2023.0037
- ¹⁵ Forbes, S. C., Candow, D. G., Neto, J. H. F., Kennedy, M. D., Forbes, J. L., Machado, M., Bustillo, E., Gomez-Lopez, J., Zapata, A., & António, J.

- (2023). Creatine supplementation and endurance performance: surges and sprints to win the race [Review of Creatine supplementation and endurance performance: surges and sprints to win the race]. Journal of the International Society of Sports Nutrition, 20(1). Springer Science+Business Media. https://doi.org/10.1080/15502783.2023.2204071
- ¹⁶ Mantle, D., & Hargreaves, I. P. (2022). Mitochondrial Dysfunction and Neurodegenerative Disorders: Role of Nutritional Supplementation [Review of Mitochondrial Dysfunction and Neurodegenerative Disorders: Role of Nutritional Supplementation]. International Journal of Molecular Sciences, 23(20), 12603. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/ijms232012603
- Yusri, K., Jose, S., Vermeulen, K., Tan, T. C., & Sorrentino, V. (2025). The role of NAD+ metabolism and its modulation of mitochondria in aging and disease [Review of The role of NAD+ metabolism and its modulation of mitochondria in aging and disease]. Npj Metabolic Health and Disease, 3(1). https://doi.org/10.1038/s44324-025-00067-0
- ¹⁸ Zeybel, M., Altay, Ö., Arif, M., Li, X., Yang, H., Fredolini, C., Akyıldız, M., Sağlam, B., Gönenli, M. G., Ural, D., Kim, W., Schwenk, J. M., Zhang, C., Shoaie, S., Nielsen, J., Uhlén, M., Borén, J., & Mardinoğlu, A. (2021). Combined Metabolic Activators Reduces Liver Fat in Nonalcoholic Fatty Liver Disease Patients. medRxiv (Cold Spring Harbor Laboratory). https://doi.org/10.1101/2021.05.20.21257480
- ¹⁹ Li, Y., Tian, X., Luo, J., Bao, T., Wang, S., & Wu, X. (2024). Molecular mechanisms of aging and anti-aging strategies [Review of Molecular mechanisms of aging and anti-aging strategies]. Cell Communication and Signaling, 22(1). BioMed Central. https://doi.org/10.1186/s12964-024-01663-1
- Marmolejo-Garza, A., Châtre, L., Croteau, D. L., Herron-Bedoya, A., Luu, M. D. A., Bernay, B., Pontin, J., Bohr, V. A., Boddeke, E., & Dolga, A. M. (2024). Nicotinamide riboside modulates the reactive species interactome, bioenergetic status and proteomic landscape in a brain-region-specific manner. Neurobiology of Disease, 200, 106645. https://doi.org/10.1016/i.nbd.2024.106645
- Neufeld, L. M., Ho, E., Obeid, R., Tzoulis, C., Green, M., Huber, L., Stout, M., & Griffiths, J. C. (2023). Advancing nutrition science to meet evolving global health needs. European Journal of Nutrition, 62, 1. https://doi.org/10.1007/s00394-023-03276-9
- ²² Tenchov, R., Sasso, J. M., Wang, X., & Zhou, Q. A. (2023). Aging Hallmarks and Progression and Age-Related Diseases: A Landscape View of Research Advancement [Review of Aging Hallmarks and Progression and Age-Related Diseases: A Landscape View of Research Advancement]. ACS Chemical Neuroscience, 15(1), 1. American Chemical Society. https://doi.org/10.1021/acschemneuro.3c00531
- ²³ Song, Q., Zhou, X., Xu, K., Liu, S., Zhu, X., & Yang, J. (2023). The Safety and Antiaging Effects of Nicotinamide Mononucleotide in Human Clinical Trials: an Update [Review of The Safety and Antiaging Effects of Nicotinamide Mononucleotide in Human Clinical Trials: an Update]. Advances in Nutrition, 14(6), 1416. Elsevier BV. https://doi.org/10.1016/j.advnut.2023.08.008
- ²⁴Tenchov, Rumiana, Janet M. Sasso, Xinmei Wang, and Qiongqiong Angela Zhou. "Aging Hallmarks and Progression and Age-Related Diseases: A Landscape View of Research Advancement." ACS Chemical Neuroscience 15, no. 1 (2024): 1–30. https://doi.org/10.1021/acschemneuro.3c00531



SupplySide Global 2025 Elevates Experience with Expo Hall Expansions and Future-Focused Education

New planning technology, high-impact education and the launch of Level 2 Expo Hall enhance personalized attendee experiences at industry's tentpole event.

SupplySide®

upplySide Global returns to Mandalay Bay (October 27-30) with new Al planning tools that streamline attendee preparation. The premier health and nutrition event now offers personalized resources for professionals from 80+countries to create tailored schedules and priority connections, reducing planning time while maximizing on-site impact.

SupplySide Global, organized by Informa Markets, is the premier business-to-business trade show where supplement, food, and beverage industry professionals make powerful connections. Consumer product decision-makers, suppliers and manufacturers develop partnerships that bring innovative products to life and to market. The supply chain connects at this global exhibition where ingredient and

technology companies debut the latest breakthroughs, nutrition scientists find solutions to formulation challenges, and consumer brands source ideas and ingredients that accelerate product development and business growth. A must-attend event, SupplySide Global is more than a trade show, it is the catalyst for nutrition innovation.

SupplySide Global, presented by Flagship Sponsor KSM-66 Ashwagandha, reigns as the world's definitive annual event where industry leaders converge to discover groundbreaking innovations in ingredients, formulation, research and development that are transforming the dietary supplement, food and beverage, pet health and personal care industries.

The wellness landscape is evolving as Gen Z and millennials represent just 36% of adults yet drive





over 41% of wellness spending in the US, with the global market projected to surge to \$9 trillion by 2028. This demographic is embracing wellness as an integrated lifestyle, revolutionizing key categories like functional nutrition, mental health and healthy aging. SupplySide Global is the essential gathering for industry leaders navigating the generational shift in consumer priorities and provides solutions for growing preferences for clean label formulations, sustainable ingredients and plant-based bioactives that support holistic wellness goals.

New tools including the AI Pass Picker ensure each participant selects the pass that best fits specific business roles, focuses and objectives. The experience continues with the AI-powered Show Planner, a personalized assistant that supports preparation before arrival by generating customized agendas and highlighting sessions, exhibitors and networking opportunities that align with stated objectives. These tools will deliver a more efficient, targeted and impactful experience, creating smarter pathways for discovery and maximizing the value of time on site.

"The attendee experience stands as the cornerstone of SupplySide's mission, with an unwavering commitment to transforming and elevating that experience to address the dynamic demands of a rapidly evolving industry," shares Danica Cullins, Executive Vice President of Health and Nutrition at Informa Markets. "By introducing tools that prioritize efficiency, personalization and connection, we are reducing barriers to planning and allowing participants to dedicate time on site to building relationships and gaining insights that drive long-term business success. These enhancements strengthen SupplySide Global's position as a catalyst for progress and leadership in the global health and nutrition industry."

In addition to planning tools, SupplySide Global offers extensive programming across the campus including education sessions, workshops and guided

tours. A professional development workshop provides practical skills and insights, while curated tours deliver targeted expertise, such as a natural food coloring tour and a data-driven supplement trend tour. Broader education spotlights the industry's most pressing topics, from GLP-1 medication and tariffs to AI, smart packaging and ingredient sourcing, ensuring participants confront the challenges shaping today's marketplace. These critical conversations will address crucial insights and strategies to turn complex issues into opportunities for business resilience, strategic growth and long-term adaptation.

This year's edition also introduces an expanded Expo Hall with the Level 2 Exhibition, providing additional space for networking and discovery, with more opportunities than ever before to discover breakthrough products. Targeted areas like the New Exhibitor Zone enable connections with emerging companies showcasing cutting-edge solutions.

Attendees may also enjoy interactive experiences such as the Bark Park, the Networking Pub and upgraded lounges, along with premium education and early access privileges. Complimentary meals and beverages enhance the environment, while the early opening hours provide a head start for focused conversations and exploration before the Level 1 Show Floor opens, maximizing opportunities for meaningful engagement.

SupplySide Global is at the forefront of the health and nutrition industry's transformation, revolutionizing businesses with cutting-edge education focused on game-changing topics shaping the future of health and nutrition complemented by the most extensive product display to date.

For the level 2 Expo Hall expansion information please visit **www.supplysideglobal.com**.

To join the SupplySide Global community register at **www.supplysideglobal.com**.

Take a glimpse at the exciting activities and showcases from some of the companies participating in the event.



Arjuna Natural



Arjuna Natural will launch a new ingredient, Shoden-R°, a root-only version of its unique ashwagandha extract. Shoden-R° is standardized to 35% withano-

lide glycosides, making it one of the most bioavailable, long-lasting forms of ashwagandha. It delivers clinically validated benefits at just 60mg per day. The company will sample chews and beverages featuring Shoden-R and will also highlight new scientific findings and functional claims for Shoden® as well as its 100% turmeric-derived extract, BCM-95®.

BCM-95° is supported by 45+ human clinical studies, and recently earned a new patent, giving brands an extract that combines robust science with patent protection.

Chase Johnston, VP of Operations, and Keely Johnson, VP of Sales and Marketing at Arjuna Natural, will be available for meetings.

To learn more, visit:

https://arjunanatural.com/



BioVivo Science



FIRST-TIME EXHIBITOR

BioVivo Science will showcase its U.S.made botanical solutions designed to withstand supply chain disruptions while ensuring high-quality and sustain-

able ingredients. Attendees can explore BioVivo Science's latest innovations, which include American ginseng, saw palmetto, broccoli seed, and sweetener blends made with stevia and monk fruit extracts.

Located in Indiana, BioVivo Science operates the largest extraction and toll processing facility of its kind in the United States. This facility strengthens global supply chains, fosters local innovation, and supports the growing U.S. industries in dietary supplements, food, beverages, personal care, and pet nutrition.

Additionally, BioVivo Science is hosting a Breakfast Brief to discuss supply chain resilience and functional ingredient innovation.

- Breakfast Brief (registration required): Strengthening supply chains with U.S.-made botanical innovation
- · Wednesday, Oct. 29, 9-10 a.m. PT
- South Pacific Ballroom A, Lower Level Elaine Yu, CCO, Jim Roza, VP of Technical Service,

Chris Smith, Director of Strategic Operations & Supply Chain and Doris Ip, Senior Marketing Manager will be available for meetings.

To learn more, visit:

https://biovivoscience.com/



Kemin Human Nutrition & Health



Visitors to the Kemin Human Nutrition & Health booth will find ingredient solutions that help brands elevate health and wellness products with science-

backed, upgraded nutritional solutions that have been clinically studied to support gut health, immune health, sleep, vision, cognition, and more. Highlights include:

FloraGLO® Lutein for cognitive and eye health benefits in teens and pre-teens. Visitors can also measure their macular pigment levels utilizing two different testing devices.

- Slendesta® Derived from upcycled potatoes, Slendesta is a natural satiety and weight management ingredient for fullness that feels right for today's weight loss journey.
- ButiShield™ The only clinically-studied calcium butyrate to help target the dietary fiber gap caused by low dietary fiber intake in Western diets.
- BetaVia® A beta-1,3 glucan derived from the proprietary Euglena gracilis algae, BetaVia® helps strengthen the body's natural defenses to build health resilience with immune and gut health support.

To learn more, visit:

https://www.kemin.com/na/en-us/markets/human-nutrition



Prinova



Prinova, a leading partner in contract manufacturing, harnesses its full range of capabilities to empower manufacturers in creating truly innovative products.

By blending flavors with functionality and leveraging branded ingredients, Prinova shows how products can be developed to meet - and even set - key consumer trends. Special focus will be placed on:

- Peach Mango Clear Whey RTM beverage This light and refreshing clear whey concept taps into the trend for clean-tasting, protein-packed options that deliver functionality without heaviness.
- Protein, a high-quality, premium sourced, micronized pea protein that delivers excellent solubility,

smooth mouthfeel and a clean plant-based profile.

- Cocoa Enhanced Brownie A rich indulgent brownie featuring Prinova's Cocoa Enhancer, which intensifies cocoa flavors while enabling up to a 30% reduction of cocoa in most applications.
- Paloma RTD Energy Drink A refreshing, mocktail-inspired energy beverage formulated with Prinova's cutting-edge Enhanced Energy Blend.

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ProBiotix Health



ProBiotix Health, a pioneer in advanced probiotic science, will showcase its flagship probiotic strain, LPLDL®, alongside its new menopause support solutions,

YourBiotixMH and YourBiotixPMH. SupplySide Global marks ProBiotix Health's entry into the U.S. women's health market, signaling a new approach to menopause care that goes beyond symptom relief.

YourBiotixMH and YourBiotixPMH were thoughtfully formulated to reshape the conversation around menopause. Visitors to the ProBiotix Health stand will have the opportunity to explore the benefits of these formulations and learn how they not only help manage day-to-day symptoms but also address long-term health considerations for women navigating the menopause transition.

To learn more, visit: https://probiotixhealth.com/

For product details, or to arrange a meeting with the team click <u>here</u>.



TriNutra™



FIRST-TIME EXHIBITOR

TriNutra is excited to launch its first high-potency ThymoQuin® powder, making this clinically validated, USP-grade,

premium brand of black seed oil available for tablets and hardshell applications. TriNutra will also unveil the latest research on ThymoQuin's effectiveness in managing both healthy cortisol levels and microbiome biodiversity, and the connection between the two.

Additionally, TriNutra invites SSG attendees to join Michael T. Murray, N.D., Chief Science Advisor at iHerb, for a presentation on these research findings.

- Unlocking Cortisol & Gut Microbiome Harmony with ThymoQuin®
- Wednesday, October 29 11:00 to 11:20 AM PT
- Product Development Theater, Booth #8076, Bayside B, Level 1

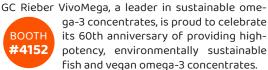
Morris Zelkha, CEO, Liki von Oppen-Bezalel, Ph.D., Business Development Director, and Elzaphan Hotam, Commercial Director of TriNutra, will be available for meetings.

To learn more, visit:

https://thymoquin.com/pages/bulk-ingredients



GC Rieber VivoMega



The company offers a wide range of sustainable EPA and DHA ratios, available in both ethyl ester (EE) and natural triglyceride (TG) forms, with total omega-3 content ranging from 70% to 90%.

At SupplySide Global, GC Rieber VivoMega will be celebrating this 60-year anniversary milestone, as well as the launch of its latest algal variation, 1060TG.

To set up a meeting, contact Ståle Søfting, Sales and Marketing Director, at Stale.Softing@gcrieber.com or visit **www.vivomega.com** to learn more.



LALLEMAND HEALTH SOLUTIONS

Lallemand Health Solutions



At SupplySide Global, Lallemand Health Solutions will present its latest science-backed innovations in probiotics and postbiotics. The spotlight will be on solutions for healthy aging, women's

health, immune support, and mental health $-\ \mbox{all}$ supported by robust clinical research:

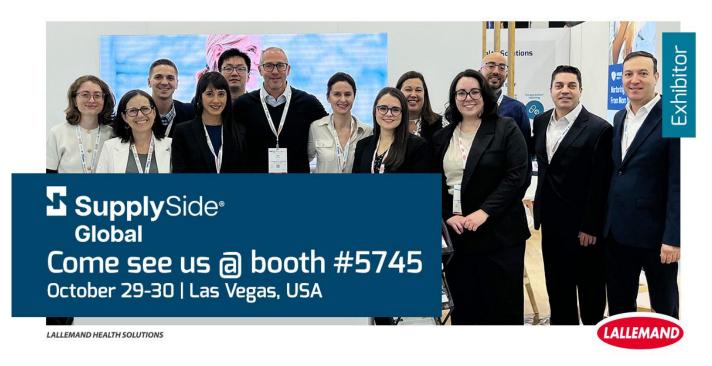
- Cerenity™ a powerful blend of three flagship probiotic strains designed to modulate the gut muscle axis and support mobility, strength, and overall vitality in aging or sedentary populations.
- Prenatis™ visitors will discover the results of two new clinical studies: one on probiotics and menstruation, and another focused on support during pregnancy.
- Award-Winning Postbiotic Immuse® one of the most documented postbiotics for immune support.
- Cerebiome® a flagship psychobiotic with benefits for overall well-being, including sleep quality and skin appearance.

To learn more, visit:

www.lallemand-health-solutions.com

Discover Lallemand Health Solutions' Latest Science-Backed Biotic Innovations

At Lallemand Health Solutions, we turn vision into action. Here is an overview of some of the innovations we have presented in the running year, illustrating how we have truly walked the talk, leading the way in probiotic innovation.





ith 90 years of know-how, we are a global leader in the probiotic industry, specializing in the development, production, and marketing of bacteria- and yeast-based probiotic supplements for human health, nutricosmetics and food applications.

Our production facilities meet the highest quality standards, including Good Manufacturing Practices, and we maintain a robust research program through the Rosell Institute for Microbiome and Probiotics. We offer our partners clinically documented probiotic strains for a wide range of health applications, including gut health, immune support, mental well-being, women's health, skin and oral health, sports, metabolic health, healthy aging, and infant health. Today, we offer more than 600 probiotic formulas across over 60 countries.

Our research, led by the Rosell Institute for Microbiome and Probiotics, supports a diverse portfolio of proprietary probiotic strains. Our team is at the forefront of innovation, with over 430 publications, more than 160 completed clinical trials, 100+ *in vitro*

and 80+ *in vivo* studies, and the management of 20+ ongoing clinical trials across four continents.

We maintain a strong focus on robust pre-clinical and clinical research programs, while forging strategic partnerships along the way. We do not just talk about innovation, we deliver it. And with a strong pipeline of innovations ahead, we remain committed to supporting our partners in achieving success in their markets.





2025 Innovation Highlights

Launch of Cerenity™ for healthy aging

Lallemand Health Solutions launched a complete offer for Healthy Aging, led by Cerenity™, a clinically documented formula to supports mobility, strength, and quality of life in healthy aging. Cerenity™ is a powerful blend of three flagship probiotic strains, designed to modulate the gut-muscle axis, for healthy aging from within. A 16-week clinical trial showed significant improvements in physical performance and muscle strength, reinforcing the role of gut health in aging well.



Women's health: new research results

Year after year, important R&D efforts are invested to bring forward innovative health solutions for women. Discover the results of a new clinical study exploring the benefits of probiotics on healthy women during the menstrual cycle. We also launched Prenatis® to maintain a healthy pregnancy and to contribute to the establishment of a healthy infant microbiome during the first months of life.



Cerebiome®: demonstrates benefits on overall wellbeing, including sleep

A pioneer in gut-brain axis research, Lallemand Health Solutions has new findings on Cerebiome®, its flagship psychobiotic. We have gathered compelling evidence showing Cerebiome®'s benefits on overall wellbeing, including sleep quality and skin appearance. A proof-of-concept study revealed improvements in perceived stress, circadian rhythm, and holistic beauty, reinforcing Cerebiome®'s potential beyond occasional stress.



Award-winning postbiotic Immuse[®] for immune health

Earlier this year, Lallemand Health Solutions and Kirin Holdings Company, Limited announced a strategic partnership to expand the visibility of Immuse®, a clinically researched lactic acid bacteria developed by Kirin Holdings Company, Limited. Immuse® is a heat-inactivated *Lactococcus lactis* strain Plasma, backed by 15 clinical trials demonstrating its efficacy in supporting immune health through a distinctive mode of action.



Kemin Highlights Latest Research and Portfolio of Upgraded Nutritional Solutions

Company's human nutrition and health business unit showcases science-backed solutions to support all ages and all stages of life.



emin Industries, a global ingredient manufacturer that strives to sustainably transform the quality of life every day for 80 percent of the world with its products and services, will exhibit at the 2025 SupplySide Global (SSG) trade show in Las Vegas on Wednesday, October 29, and Thursday, October 30. Attendees are invited to visit the Kemin Human Nutrition & Health business unit at booth #5231 to learn more about the latest health-forward functional ingredients that support a positive health journey.

"The Kemin team is excited to meet with this year's SupplySide Global attendees," said Filipa Quintela, Associate Director – Global Marketing, Kemin Human Nutrition & Health. "Our experts will be available to discuss the latest research and clinical findings behind our science-backed health ingredients that provide consumers with proven results to help create a positive health journey for all."

Visitors to the Kemin Human Nutrition & Health booth will find ingredient solutions that help brands elevate health and wellness products with science-backed, upgraded nutritional solutions that have been clinically studied to support gut health, immune health, sleep, vision, cognition, and more. Highlights include:

 Nutritional carotenoids – science-backed - not borrowed - for all ages and all stages of life, Kemin nutritional carotenoids lead the industry with over 100 clinical studies showing benefits for eye, brain, and skin health.

At SupplySide Global, Kemin experts will discuss the latest clinical research studying supplementa-

- tion with FloraGLO® Lutein for cognitive and eye health benefits in teens and pre-teens. Visitors can also measure their macular pigment levels utilizing two different testing devices.
- Slendesta® Derived from upcycled potatoes, Slendesta is a natural satiety and weight management ingredient for fullness that feels right for today's weight loss journey.
- ButiShield™ The only clinically-studied calcium butyrate to help target the dietary fiber gap caused by low dietary fiber intake in Western diets, ButiShield is an encapsulated low-odor source of butyric acid for sustained and controlled release where it matters most - the gut.
- BetaVia® A beta-1,3 glucan derived from the proprietary Euglena gracilis algae, BetaVia® helps strengthen the body's natural defenses to build health resilience with immune and gut health support. By combating digestive aging and stress and priming the immune system, BetaVia can help the body be ready to face daily stressors.

Visit Kemin Human Nutrition & Health at booth #5231 at SupplySide Global to see how the business unit strives to set the standards for sustainable health and wellness by delivering innovative, science-backed health ingredients that transform lives and shape a healthier, brighter future for everyone.

About Kemin Industries

Kemin Industries is a global ingredient manufacturer that strives to sustainably transform the quality of life every day for 80 percent of the world with its products and services. The company supplies over 500 specialty ingredients for human and animal health and nutrition, pet food, aquaculture, nutraceutical, food technologies, crop technologies, textile, biofuel, and animal vaccine industries.

For over half a century, Kemin has been dedicated to using applied science to address industry challenges and offer product solutions to customers in more than 120 countries. Kemin provides ingredients to feed a growing population with its commitment to the quality, safety, and efficacy of food, feed, and health-related products.

Established in 1961, Kemin is a privately held, familyowned-and-operated company with more than 3,000 global employees and operations in 90 countries.

For more information visit: www.kemin.com



Prinova Highlights Great-tasting, On-trend Functional Solutions

Prinova will showcase its functional nutrition capabilities in great-tasting concepts targeting consumer trends at SupplySide Global.

esearch by the premix, blends, and contract manufacturing specialist shows that 53% of consumers cite great taste as the primary influence on purchase¹. Backed by Prinova's turnkey contract manufacturing capabilities, the SupplySide Global concepts combine flavors with function and branded ingredients to demonstrate how manufacturers can develop innovative products that address key consumer trends. They include:

- Peach Mango Clear Whey RTM beverage With 85% of consumers saying they plan to increase protein intake from 2024², this light and refreshing clear whey concept taps into the trend for clean-tasting, protein-packed options that deliver functionality without heaviness.
- Chocolate Vegan Protein Blend RTM beverage –
 This concept includes Prinova's Microfuse™ Pea
 Protein, a high-quality, premium sourced, micronized pea protein that delivers excellent solubility,
 smooth mouthfeel and a clean plant-based profile. A great option for vegan or flexitarian consumers, as 58% of consumers who increased plant-based consumption did so to have a healthier diet³; seeking both performance and indulgent chocolate flavour in a ready-to-mix format.
- Cocoa Enhanced Brownie A rich indulgent brownie featuring Prinova's Cocoa Enhancer, which intensifies cocoa flavors while enabling up to a 30% reduction of cocoa in most applications. This delivers both cost savings and sustainability benefits without compromising on taste.
- Paloma RTD Energy Drink A refreshing, mock-tail-inspired energy beverage formulated with Prinova's cutting-edge Enhanced Energy Blend. Designed to fuel body and mind, the blend combines caffeine, Panax ginseng extract, L-carnitine, and guarana seed extract to support increased energy, mental focus, and endurance. Inspired by the growing sober-curious movement highlighted in Prinova's trends research, this alcohol-free innovation offers a sophisticated and functional alternative to traditional beverages.

Dan Force, Vice President of Innovative Products at Prinova. said:

"SupplySide Global is the perfect stage to demonstrate our ability to help our customers turn emerging trends into successful market-ready products. For example, in protein, consumer trends are driving innovation in new end-use market applications, and

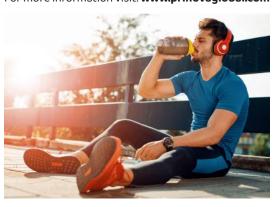
new protein ingredient technologies are often required. Prinova is partnering with protein ingredient manufacturers, 3rd party R&D facilities and contract manufacturers, to optimize new protein ingredients to meet the growing needs of the market. We're also opening this network to our customers to fast-track commercialization and help keep pace with the trend. SupplySide Global becomes the venue where all these elements of the supply chain can come together."

Prinova will exhibit at Supply Side Global at booth #5852.



Prinova is a leading global supplier of ingredients and premix manufacturing solutions for the food, beverage and nutrition industries. Prinova holds strategic stocks in numerous distribution centers around the world to ensure continuity of supply and has liquid and dry premix manufacturing facilities in the USA, China and the UK. In addition, its contract manufacturing facilities in Salt Lake City, Utah and Spring Hill, Tennessee are BRC Grade A, NSF- and GMP-certified, offering full-scale powder RTM and premix production, flavour development, and scaleup services to help brands bring concepts to market with confidence. Prinova's premix business is underpinned with over 45 years of experience in ingredient sourcing and distribution, servicing their customers with global inventories, market expertise and leading market positions in Vitamins, Amino Acids, Sweeteners, Preservatives, Proteins, Aroma Chemicals and more. Prinova joined the NAGASE Group

For more information visit: www.prinovaglobal.com





ProBiotix Health Focus on Groundbreaking Probiotic Menopause Solutions

ProBiotix Health, a pioneer in advanced probiotic science, will be exhibiting its flagship probiotic strain, LP_{LDL}®, along with its new menopause support solutions, YourBiotix_{MH} and YourBiotix_{PMH}. The event marks ProBiotix Health's entry into the U.S. women's health market, redefining women's health beyond symptom relief.



ourBiotix_{MH} and YourBiotix_{PMH} were formulated to reshape the conversation around menopause. Visitors to the ProBiotix Health stand at #7853 can explore the benefits of these formulations and discover how they not only address day-to-day symptom relief but long-term health risks for women in the menopause cohort.

Menopause – solving the heart of the problem

Says Steen Andersen, chief operating officer at ProBiotix Health. "Menopause is a natural stage of life for most women, yet its impact extends far beyond hot flushes or sleep disturbances. The decline in estrogen during menopause profoundly impacts women's health, increasing risks of high cholesterol, hypertension, arterial stiffness, and loss of bone density."

Cardiovascular disease remains the leading cause of death among American women, with post-meno-pausal women 5X more likely to suffer a heart attack, while 77% of women aged 45+ have raised cholesterol.

"Most supplements on the market today stop at short-term relief. Although the US menopause sup-

plement market is growing rapidly, it still lacks products that address these hidden long-term health risks such as cardiovascular health and loss of bone density. Our new formulations aim to close this critical gap," he says.

Unlike conventional supplements that focus mainly on vasomotor symptoms, YourBiotix $_{\text{MH}}$ and YourBiotix $_{\text{PMH}}$ harness the power of $\text{LP}_{\text{LDL}}^{\circ}$ (*Lactobacillus plantarum*), ProBiotix Health's clinically validated probiotic strain. Formulated in combination with selected nutrients, including isoflavones, thiamine, vitamin D, and vitamin B6, these two products support positive menopausal outcomes.

Says Andersen, "These are the first probioticbased solutions that offer a dual function: relieving and addressing the long-term cardiovascular, physiological, and bone health risks that accompany menopause, effectively enabling consumers to add life to years, not just years to life."

The power of YourBiotix $_{\rm MH}$ in transforming women's health is gaining acclaim throughout the nutraceutical industry. YourBiotix $_{\rm MH}$ was recently named as a finalist in the prestigious NutraIngredients Asia Women's Health Innovation Award and shortlisted for a WholeFoods Women's Health Award, further cementing its recognition as a breakthrough product.

Alongside YourBiotix $_{\rm MH}$ and $_{\rm PMH}$, ProBiotix will also showcase ${\rm LP_{LDL}}^{\circ}$ in finished formulations available for white label, highlighting its proven clinical benefits for cardiometabolic health.

LP_{LDL} represents the foundation of ProBiotix's innovation pipeline strategy to extend probiotics beyond the gut to focus on cardiometabolic health and healthy ageing.

"We believe menopause is more than just a phase, and declining estrogen is more than discomfort – it's a turning point in a woman's cardiovascular health," Andersen concluded. "With YourBiotix $_{\rm MH}$ and YourBiotix $_{\rm PMH}$, we offer more than just relief, but a way to protect women's health well into the future."

Visit the ProBiotix team at booth #7853 at Supply Side Global on October 29-30 to discover LP_{LDL}° and the YourBiotix product range.

For product details, or to arrange a meeting with the team visit: **probiotixhealth.com/contact-us/**

GC Rieber VivoMega: 60 Years of Omega-3 Excellence

GC Rieber VivoMega, a pioneer in sustainable omega-3 concentrates, celebrates its 60th anniversary of innovation and excellence at the SupplySide Global event in Las Vegas. The company continues to lead in sustainability with fully renewable operations, cuttingedge technology, and premium omega-3 products that exceed global quality standards.

C Rieber VivoMega, a leader in sustainable omega-3 concentrates, is proud to announce its 60th anniversary of providing high-potency, environmentally sustainable fish and vegan omega-3 concentrates. The company will also celebrate at the upcoming trade show, SupplySide Global booth #4152 in Las Vegas, October 29 and 30.

Originally founded in Kristiansund in 1965 as Alnes Marine Oils, the company began with a clear focus on producing and trading marine fish oils. GC Rieber later became the majority stakeholder in Alnes Marine Oils. The company now operates as GC Rieber VivoMega, drawing on the GC Rieber Group's long-standing expertise in the marine oils sector. Over the decades, the Kristiansund facility in Norway has honed its specialization in high-quality omega-3 production, earning a reputation as a benchmark in the global industry.

In 2010, GC Rieber completed the construction of a high-concentration production facility, branding its products as VivoMega™ and concentrating solely on the production of high- and ultra-grade omega-3 concentrates.

By 2020, GC Rieber VivoMega had expanded its infrastructure with the construction of a 38,000 metric ton tank park, enabling a steadier output of omega-3 concentrates to meet rising demand.

In 2023, GC Rieber VivoMega entered the vegan category with the launch of its non-GMO EPA+DHA Algae Oils to satisfy the growing demand for EPA + DHA alternatives.

In 2024, the company completed its sixth facility expansion, which included a key milestone: an electric steam boiler that enables its three facilities to operate on 100% renewable energy. The expansion also enhances heating capabilities to maintain the quality of the oils and facilitate easier extraction in winter. Moreover, the integration of additional nitrogen improves sensory profiles by removing oxygen, and the incorporation of a no-code AI platform enables real-time predictions for operational efficiency, quality, and sustainability. The \$75 million expansion has significantly increased the output of its high-end triglyceride forms of omega-3s, EPA and DHA, while also conserving resources and offering customization options.

"Over our long history, we have continually evolved to meet the growing demands of the global omega-3 market. We have achieved this by adhering to our three core values: creativity, diligence, and responsibility," said Snorre Glærum Strand, CEO at GC

Rieber VivoMega. "Our mission has always been to improve human health through sustainable and innovative omega-3 solutions. We are incredibly proud of this milestone and deeply thankful to our team, customers, and partners."

GC Rieber VivoMega offers a wide range of sustainable EPA and DHA ratios, available in both ethyl ester (EE) and natural triglyceride (TG) forms, with total omega-3 content ranging from 70% to 90%. The company employs state-of-the-art production equipment and rigorous testing protocols, allowing it to produce oils that consistently exceed international quality standards such as the GOED monograph and IFOS certification.

GC Rieber VivoMega will be celebrating this 60year anniversary milestone as well as the launch of its latest algal variation, 1060TG, at SupplySide Global, booth #4152.

To set up a meeting, contact Ståle Søfting, Sales and Marketing Director, at Stale.Softing@gcrieber.com, or visit Vivomeqa.com to learn more.

About GC Rieber VivoMega

GC Rieber VivoMega is a leading player in the omega-3 industry, dedicated to delivering safe, high-quality, and sustainably sourced omega-3 concentrates. With a strong commitment to responsible practices and ethical business, GC Rieber VivoMega strives to drive positive change within the industry toward a more sustainable future.

For more information visit: https://vivomega.com/





Interactions between Glucagon-Like Peptide-I and the Gut Microbiota in Metabolic Disorders

AUTHOR: **Sara Kralj**, MSc,

Master in Nutrition

he gut-endocrine system represents a key link between diet, metabolism, and the microbiota. Enteroendocrine L-cells of the gut respond to the presence of nutrients and microbial metabolites by secreting hormones that influence glucose homeostasis, appetite, and energy metabolism¹. Among these hormones, glucagon-like peptides (GLP-1 and GLP-2) play a central role in communication between the gut and other organ systems. These hormones act via specific G-protein-coupled receptors (GLP-1R and GLP-2R), which are differentially distributed across tissues, determining their physiological function².

GLP-1 - role in metabolic regulation

Glucagon-like peptide-1 (GLP-1) is a 30-amino-acid hormone secreted from enteroendocrine L-cells in response to nutrient intake, especially glucose. Two bioactive forms exist (GLP-1₇₋₃₇ and GLP-1₇₋₃₆ amide), and their secretion is stimulated by dietary components in the proximal gut as well as by microbial metabolites in distal gut regions, such as short-chain fatty acids (SCFAs), indoles, and bile acids^{3,4}. In this

way, the microbiota participates in the regulation and prolonged secretion of GLP-1 and peptide YY (PYY) after meals, maintaining postprandial homeostasis¹.

GLP-1 exerts multiple metabolic effects. It stimulates insulin synthesis and secretion in pancreatic β -cells while simultaneously inhibiting glucagon secretion, contributing to improved glucose homeostasis. By acting on the gastrointestinal tract, it slows gastric emptying and reduces gastric acid secretion, thereby lowering postprandial glycemia and enhancing satiety^{1,5}.

GLP-1 actions are mediated through specific GLP-1 receptors (GLP-1R) located in the pancreas, central nervous system (hypothalamus, brainstem, mesolimbic system), and peripheral tissues such as muscle and adipose tissue. Activation of GLP-1R in the brain reduces appetite, while in muscle and adipose tissue, GLP-1R agonists promote glucose uptake via AMP-activated protein kinase (AMPK) activation and GLUT-4 translocation, mimicking insulin effects. GLP-1R agonists (e.g., exenatide, liraglutide) also exert cytoprotective effects, promoting proliferation



and reducing apoptosis of pancreatic β -cells, thereby preserving their function and improving insulin sensitivity¹.

Endogenous GLP-1 is rapidly degraded by dipeptidyl peptidase-4 (DPP-4), but part of its effect is mediated via vagal afferent nerves. Vagus nerve activation (n. vagus) is critical for GLP-1's anorectic and incretin effects, as vagotomy abolishes GLP-1-induced appetite suppression. This connection, known as the neuroendocrine-incretin effect, links peripheral and central GLP-1 actions in regulating food intake and glucose metabolism^{1,6}.

In conclusion, GLP-1 represents a central regulator of glycemic control and appetite, with its actions arising from a complex interplay between the gut, microbiota, endocrine cells, and nervous system.

GLP-2 - role in maintaining gut integrity

GLP-2, secreted concurrently with GLP-1 in approximately equal ratios, acts primarily locally in the gut via GLP-2 receptors (GLP-2R). Its main functions include stimulating crypt cell proliferation, promoting intestinal mucosal growth, and epithelial regeneration^{7,8,9,10,11}. Through these effects, GLP-2 contributes to the maintenance of gut barrier integrity and reduced intestinal permeability, indirectly supporting systemic metabolic balance and immune homeostasis².

Impact of the gut microbiota on GLP-1

The gut microbiota significantly influences the secretion and activity of GLP-1. Microbial metabolites such as short-chain fatty acids (SCFAs), indoles, and secondary bile acids stimulate L-cells to secrete GLP-1 while simultaneously improving the sensitivity of target tissues to insulin and insulin signaling. Dysbiosis, defined as an imbalance in the microbiota composition, is associated with altered GLP-1 responses, reduced secretion, and the development of metabolic disorders such as insulin resistance, fatty liver, and obesity^{1,5}.

At the level of the gut barrier, GLP-1 reduces intestinal permeability and bacterial translocation, thereby contributing to gut integrity preservation and reduction of systemic inflammation associated with metabolic disorders. In energy metabolism, GLP-1 promotes lipolysis and energy expenditure, enhances glycogen storage in the liver, and reduces hepatic glucose output. Its effects on the central nervous system manifest as appetite suppression in the hypothalamus and increased satiety, contributing to decreased food intake and body weight regulation⁵.

Microbial metabolites in GLP-1 secretion control

The secretion of GLP-1 from enteroendocrine L-cells results from a complex network of interactions between dietary components, microbial metabolites, and endocrine signaling. The gut microbiota produces numerous bioactive molecules that directly or indirectly regulate L-cell function, thereby influencing glucose homeostasis, appetite, and body weight⁵.

Short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate, are key microbial metabo-

lites generated through the fermentation of indigestible dietary fibers in the colon. Since the human genome encodes fewer than 20 enzymes capable of digesting complex carbohydrates, a significant portion of polysaccharides reaches the colon undiqested, where the microbiota degrades them via carbohydrate-active enzymes¹². This process results in high SCFA concentrations precisely in gut regions abundant in L-cells, highlighting the physiological significance of this local interaction. Over 90% of SCFAs are absorbed by the intestinal epithelium or further metabolized by the microbiota, while the remainder acts locally on L-cells through free fatty acid receptors GPR43 (FFAR2) and GPR41 (FFAR3)5,13. Activation of these receptors increases intracellular calcium, promoting GLP-1 and peptide YY (PYY) secretion. Notably, reduced SCFA production or fermentation capacity is linked to metabolic diseases, including type 2 diabetes, further underscoring their role in metabolic regulation^{5,14,15}.

Secondary bile acids (BAs) also act as important signaling molecules in GLP-1 regulation. Primary bile acids, cholic acid (CA) and chenodeoxycholic acid (CDCA), synthesized in the liver, undergo microbial conversion into secondary forms - lithocholic acid (LCA) and deoxycholic acid (DCA). Since these transformations depend on bacterial activity, changes in gut microbiota composition can significantly affect the quantity and ratio of secondary BAs. Secondary BAs exhibit dual regulatory effects on GLP-1 secretion: they activate the Takeda G-protein-coupled receptor 5 (TGR5) on L-cell surfaces, stimulating GLP-1 release16,17, but can also exert inhibitory effects via farnesoid X receptor (FXR) activation, reducing hormone synthesis and secretion^{18,19}. This establishes a fine balance between stimulatory and inhibitory signals depending on bile acid type and concentration.

In addition to SCFAs and bile acids, other microbial metabolites modulate GLP-1 secretion. 2-Oleoyl glycerol (2-OG), derived from dietary fat digestion, activates GPR119 receptors on L-cells, while indoles, products of bacterial tryptophan metabolism, also stimulate GLP-1 secretion. Lipopolysaccharides (LPS), components of gram-negative bacterial cell walls, can further activate GLP-1 secretion via Toll-like receptor 4 (TLR4), linking microbial signaling to metabolic and inflammatory processes⁵.

Overall, these complex mechanisms demonstrate that GLP-1 secretion is closely associated with gut microbiota activity. Metabolites such as SCFAs and secondary bile acids serve as key signaling molecules in the microbiota-host communication, mediating interactions between nutrient intake, microbial fermentation, and endocrine responses. Maintaining a balanced gut microbiota and optimal metabolite production is therefore a fundamental factor in preventing and managing metabolic disorders associated with impaired GLP-1 signaling⁵.

Impact of prebiotics and probiotics on GLP-1 secretion

Prebiotics and probiotics play an important role in modulating the gut microbiota and stimulating the secretion of intestinal peptides, including glucagon-like peptide-1 (GLP-1) and peptide YY (PYY). Their effects are based on improving gut barrier integrity,

modulating immune responses, and influencing microbial metabolites such as short-chain fatty acids (SCFAs) and bile acids, which directly stimulate enteroendocrine cells⁵.

Prebiotics

Prebiotics, including oligofructose, fructans, resistant starch, and arabinoxylan-oligosaccharides, are fermented by the gut microbiota, increasing SCFA production (acetate, propionate, and butyrate). These metabolites activate GPR41 and GPR43 receptors on L-cells, promoting the secretion of GLP-1 and $PYY^{5,20}$.

Although the role of prebiotics in modulating intestinal peptide secretion is well documented in experimental models, clinical results in humans remain inconsistent⁵. Some studies reported that oligofructose supplementation increased PYY concentration but not GLP-121,22. Conversely, arabinoxylan-oligosaccharide supplementation reduced early postprandial GLP-1 secretion, accompanied by decreased gut microbiota alpha diversity and increased relative abundance of the genera Bifidobacterium, Akkermansia, and Lactobacillus²³. In hyperinsulinemic subjects, increased dietary fiber intake stimulated SCFA production, particularly acetate and butyrate, leading to elevated plasma GLP-1 levels and higher fasting and postprandial insulin concentrations, although without significant changes in body weight²⁴. Furthermore, a low-carbohydrate almond-based diet significantly increased the relative abundance of Roseburia and Ruminococcus, known SCFA producers, along with increased GLP-1 concentrations^{25,26}. Overall, clinical prebiotic interventions show heterogeneous effects on GLP-1 secretion, indicating the need for further standardized research to clarify their specific mechanisms and interindividual response variability.

Animal studies highlight significant variability in prebiotic effects on GLP-1 secretion. In animal models, prebiotics promoted the growth of butyrateproducing bacteria²⁷, increased GLP-1 secretion, and improved glucose homeostasis⁵. For example, Dendrobium polysaccharides increased the abundance of Akkermansia and Parabacteroides, as well as SCFA, tryptophan, and indole concentrations, stimulating GLP-1 secretion²⁸. Similarly, resveratrol and tetrahydrocurcumin enhanced GLP-1 release alongside changes in microbiota composition^{29,30}. Prebiotics such as oligofructose, fructo-oligosaccharides, fructans, and inulin increased GLP-1, PYY, and SCFA levels, although microbiota structural changes were not always consistent⁵. In type 2 diabetes models, fiber supplementation increased the abundance of Akkermansia muciniphila and Bacteroidetes, decreased Firmicutes and Proteobacteria, resulting in higher GLP-1 levels and improved metabolic parameters³¹. Additionally, flavonoids from Lycium barbarum and polysaccharides from adlay seeds modulated the microbiota and inflammatory processes while increasing GLP-1 and producing hypoglycemic effects^{32,33}. Overall, prebiotics can beneficially affect GLP-1 secretion via gut microbiota modulation and enhanced SCFA production.

Probiotics

Probiotics also show potential in modulating GLP-

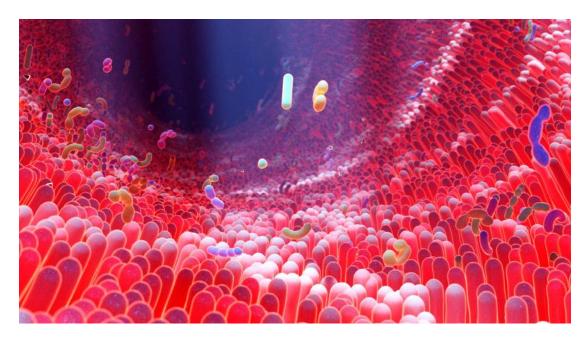
1 secretion through changes in gut microbiota composition and activity. Supplementation with *Anaerobutyricum soehngenii* increased secondary bile acids and postprandial GLP-1, improving glucose metabolism³⁴. Administration of *Lactobacillus reuteri* increased GLP-1 and insulin secretion in individuals with impaired glucose tolerance, while the probiotic mixture VSL#3 (containing eight strains including *Streptococcus thermophilus, Bifidobacterium [B. breve, B. infantis, B. longum], Lactobacillus acidophilus, L. plantarum, L. paracasei, and <i>L. delbrueckii* subsp. *bulgaricus*) elevated GLP-1 levels and reduced BMI in children with non-alcoholic fatty liver disease over four months^{35,36}.

A study in type 2 diabetic mice consuming Kombucha (a source of polyphenols and organic acids) showed improved inflammation and gut barrier integrity, with reduced LPS levels and increased expression of zonula occludens-1, claudin-1, occludin, and mucin. Simultaneously, SCFA-producing bacterial abundance increased, resulting in higher SCFA levels and elevated GLP-1 and PYY concentrations³⁷. Exopolysaccharides from *Bacillus amyloliquefaciens* also increased GLP-1 levels through gut tissue interaction³⁸. VSL#3 supplementation for eight weeks increased butyrate-producing bacteria, butyrate levels, and GLP-1, improving glucose tolerance in diabetic and obese mice³⁹.

A recombinant Lactobacillus paracasei NFBC 338 strain expressing a long-acting GLP-1 analog improved glucose and lipid metabolism in diet-induced obese rats without significant cecal microbiota changes⁴⁰. Similarly, composite probiotic supplementation enhanced GLP-1 and PYY secretion via microbiota modulation and increased SCFA production, improving glucose and lipid metabolism and pancreatic function in diabetic mice⁴¹. Oral administration of Lactobacillus casei increased the abundance of Bacteroidetes, Bifidobacterium, and Lactobacillus, resulting in enhanced butyrate production and GLP-1 stimulation⁴². Clostridium butyricum CGMCC0313.1 reduced the Firmicutes/Bacteroidetes ratio, increased SCFA-producing bacteria and FFAR2/FFAR3 receptor expression, and raised GLP-1 levels in serum and ileum, although this effect was absent in db/db mice with leptin receptor defects⁴³. Supplementation with L. fermentum MCC2759/MCC2760 reduced pathogenic bacteria, increased Lactobacillus spp., and promoted GLP-1 production^{44,45}. Furthermore, L. rhamnosus LGG increased beneficial bacterial abundance and GLP-1 levels, with elevated acetate and propionate concentrations⁴⁶. In piglets, L. plantarum supplementation decreased Bacteroides and Parabacteroides abundance and lithocholic acid (LCA) levels, resulting in improved glucose metabolism⁴⁷.

Impact of the gut microbiota on GLP-1 function

Incretin-based drugs have proven highly effective in treating type 2 diabetes. Numerous studies indicate that the incretin effect is impaired in individuals with obesity, impaired glucose tolerance (IGT), and type 2 diabetes. However, in some cases, reduced therapeutic efficacy of GLP-1 receptor agonists (GLP-1 RA) occurs, leading to treatment discon-



tinuation. This phenomenon, known as GLP-1 resistance, may be associated with gut microbiota dysbiosis 5 .

Clinical research shows that gut microbiota composition can influence the efficacy of GLP-1 receptor agonist therapy. In a study of patients receiving liraglutide or dulaglutide, only a subset exhibited reductions in HbA1c and BMI. Microbiota analysis revealed significant differences in beta diversity between these groups, including the presence of bacterial species such as *Bacteroides dorei* and *Roseburia inulinivorans*, suggesting that microbiota profiles may predict therapeutic response^{5,48}.

Experimental models further confirm the link between dysbiosis and GLP-1 resistance. A 2017 study developed two mouse models of type 2 diabetes diabetic obesity and diabetic leanness. Following an oral glucose tolerance test (OGTT), glucose levels were similar across groups, but lean diabetic mice had higher plasma GLP-1 concentrations and lower insulin levels, indicating the development of GLP-1 resistance. Transplantation of the ileal microbiota from these mice into germ-free animals resulted in impaired incretin response, confirming that GLP-1 function depends on gut microbiota balance. Dysbiosis can therefore directly weaken the GLP-1 response^{48,49}.

Impact of the gut microbiota on the circadian rhythm of GLP-1 secretion

Circadian rhythms are endogenous, approximately 24-hour cycles that regulate numerous physiological processes in the body, including metabolism and hormone secretion. In addition to the central nervous system, the biological clock is present in peripheral tissues such as the pancreas and gastrointestinal tract, where genes like CLOCK and BMAL1 coordinate metabolic functions 50,51. Dysfunction of these genes has been associated with the development of metabolic disorders, including diabetes mellitus 5.

GLP-1 secretion also follows a circadian pattern. Studies in humans and animal models have shown that GLP-1 secretion is higher in the morning, while

the lowest levels are observed in the evening or early morning hours⁵². These oscillations reflect the rhythmic activity of intestinal L cells, whose GLP-1 release depends on the expression of clock genes, particularly *BMAL1*, *PER1/2/3*, *DBP*, and *TEF*⁵.

The gut microbiota plays a key role in regulating the circadian rhythm of GLP-1 secretion. Studies in germ-free mice have shown that the absence of gut bacteria disrupts the rhythmic secretion of insulin and GLP-1, whereas their rhythm is restored after microbiota transplantation from healthy animals⁵³. Furthermore, the biological rhythms of L cells, especially the expression of clock genes such as *Bmal1*, *Per1/2/3*, *Dbp*, and *Tef*, regulate GLP-1 release. Reduced expression of *Bmal1* leads to disturbances in circadian GLP-1 secretion^{54,55}. Therefore, gut microbiota balance and proper L cell function jointly maintain the physiological rhythm of GLP-1 secretion.

Impact of GLP-1 on the gut microbiota

GLP-1 analogs and microbiota modulation

Recent research shows that drugs acting through the incretin system, particularly GLP-1 receptor agonists (GLP-1 RA), can influence the composition and functionality of the gut microbiota, extending beyond their primary pharmacological effects. Liraglutide is an example of a GLP-1 analog that, in experimental animal studies, increases the proportion of short-chain fatty acid (SCFA)-producing bacteria, including *Bacteroides* and members of the *Lachnospiraceae* family, as well as probiotic genera such as *Bifidobacterium*⁵⁶. Notably, an increase in *Akkermansia muciniphila*, a bacterium associated with intestinal homeostasis and metabolic health, has been observed 57,58,59.

In human studies, liraglutide administration increased microbiota diversity and richness, with a notable rise in the relative abundance of *Bacteroidetes, Proteobacteria*, and *Bacilli* ⁶⁰. However, results have not always been consistent. Combined therapy with metformin or sulfonylureas sometimes masked the effects of liraglutide on the microbiota, while in older populations with type 2 diabetes, no signifi-



cant changes in gut microbiota diversity were observed⁶¹. Additionally, liraglutide may act via activation of the gut sympathetic nervous system, representing an alternative mechanism for microbiota modulation⁶². Overall, GLP-1 analogs demonstrate the capacity to positively modulate the gut microbiota, although the extent of this effect depends on the therapeutic context and study population⁵.

DPP-4 inhibitors and microbiota

Dipeptidyl peptidase-4 (DPP-4) inhibitors improve oral glucose tolerance and elevate plasma GLP-1 concentrations, with concomitant changes in gut microbiota composition. Clinical studies using vildagliptin monotherapy in type 2 diabetes patients have shown a reduction in *Bacteroidetes* abundance⁸⁹, whereas in animal models, linagliptin and sitagliptin increased the proportion of *Bacteroidetes* and succinate concentration, an important metabolite for energy metabolism^{63,64}.

Vildagliptin additionally reduced *Oscillibacter* spp. and increased *Lactobacillus* spp. and propionate levels in animals fed a Western diet^{65,66}. Furthermore, DPP-4 inhibitors, such as PKF-275-055 and vildagliptin, decreased the *Firmicutes/Bacteroidetes* ratio and increased SCFA-producing bacteria, effects comparable to metformin^{67,68}. Overall, DPP-4 inhibitors moderately correct gut microbiota dysbiosis in obesity and type 2 diabetes.

Bidirectional communication between GLP-1 and the microbiota

Disruption of the gut microbiota can promote endotoxemia and the development of insulin resistance. In type 2 diabetes, there is an increased proportion of gram-negative *Enterobacteriaceae* and a reduced number of acetate-producing bacteria, such as *Bifidobacterium*, resulting in elevated LPS release and decreased acetate production⁶⁹. LPS binds to Toll-like receptor 4 (TLR4), disrupting the gut barrier⁶⁹ and increasing serum LPS levels, contributing to inflammation in prediabetes^{70,71}.

As compensation, enteroendocrine cells increase GLP-1 secretion in response to LPS exposure, and the cytokine IL-6 further stimulates its release^{5,72}. GLP-1 promotes insulin synthesis, enhances satiety, and reduces food intake through GLP-1 receptors⁷³, whose agonist, exendin-4, exhibits anti-inflammatory effects by inhibiting cytokine production and macrophage infiltration⁷⁴. Therapeutic interven-

tions that elevate GLP-1 levels have shown beneficial effects on the intestinal inflammatory response, confirming the immunomodulatory role of this hormone

Gut hormones as regulators of the microbiota

The gut microbiota operates in symbiosis with enteroendocrine cells (EECs), which are distributed among the epithelial cells of the intestinal mucosa and secrete various hormones. L cells, which produce GLP-1 and PYY, are predominantly located in the distal intestine and colon⁵. These peptides influence appetite, satiety, and food intake, while changes in the gut microbiota can reciprocally affect eating behavior^{75,76}. Intestinal peptides also regulate gut motility and permeability77 and may possess antimicrobial and protective properties⁷⁸. For example, peptide D3 increases the abundance of Akkermansia muciniphila and reduces appetite, whereas milk-derived peptides improve gut barrier integrity⁷⁹. Overall, intestinal peptides serve as key mediators of communication between the gut microbiota and the host.

Conclusion

The interaction between GLP-1 and the gut microbiota represents a complex bidirectional system that regulates host metabolism, appetite, and immune responses. The gut microbiota, through the production of metabolites such as short-chain fatty acids (SCFAs), indoles, and secondary bile acids, stimulates GLP-1 secretion, while GLP-1 modulates qut microbiota function and metabolic responses in the brain, intestines, and pancreas. Interventions such as prebiotics, probiotics, GLP-1 analogs, DPP-4 inhibitors, or bariatric surgery alter microbiota composition and activity, improving host metabolism and potentially enhancing therapeutic responses. Although study results remain heterogeneous, evidence suggests that modulation of the qut microbiota can indirectly enhance GLP-1 secretion and the production of key microbial metabolites, opening the way for personalized strategies in the prevention and treatment of metabolic disorders, including obesity and type 2 diabetes. Future application of multi-omic technologies may further clarify these relationships and support individualized therapeutic approaches based on GLP-1 and gut microbiota interactions.

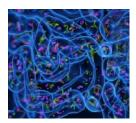
References:

- ¹ Longo S, Rizza S, Federici M. Microbiota-gut-brain axis: relationships among the vagus nerve, gut microbiota, obesity, and diabetes. Acta Diabetol. 2023 Aug;60(8):1007-1017.
- ² Abdalqadir N, Adeli K. GLP-1 and GLP-2 Orchestrate Intestine Integrity, Gut Microbiota, and Immune System Crosstalk. Microorganisms. 2022 Oct 19;10(10):2061.
- ³ Sam AH, Troke RC, Tan TM, Bewick GA. Uloga crijevno-mozdane osi u modulaciji unosa hrane. Neuropharmacology. 2012;63:4656.
- ⁴ Richards P, Thornberry NA, Pinto S. Os crijeva i mozga: Identificiranje novih terapijskih pristupa za dijabetes tipa 2, pretilost i srodne poremećaje. Mol Metab. 2021;46:101175.
- ⁵ Zeng Y, Wu Y, Zhang Q, Xiao X. Crosstalk between glucagon-like peptide 1 and gut microbiota in metabolic diseases. mBio. 2024 Jan 16;15(1):e0203223.
- ⁶ Krieger JP, Arnold M, Pettersen KG, Lossel P, Langhans W, Lee SJ. Smanjenje GLP-1 receptora u vagalnim aferentnim vlaknima utječe na normalan unos hrane i glikemiju. Dijabetes. 2016

- ⁷ Tsai CH, Hill M., Asa SL, Brubaker PL, Drucker DJ Svojstva glukagonu sličnog peptida-2 koja potiču rast crijeva u miševa. Am. J. Physiol. Endocrinol. Metab. 1997;273:E77–E84. doi:10.1152/ajpendo.1997.273.1.E77.
- Thulesen J., Hartmann B., Hare KJ, Kissow H., Ørskov C., Holst JJ, Poulsen SS Glukagonu sličan peptid 2 (GLP-2) ubrzava rast neoplazmi debelog crijeva u miševa. Gut. 2004;53:1145–1150
- ⁹ Estall JL, Drucker DJ Glukagonu sličan peptid-2. Annu. Rev. Nutr. 2006:26:391–411.
- ¹⁰ Brubaker PL Glukagonu sličan peptid-2 i regulacija rasta i funkcije crijeva. Compr. Physiol. 2011;8:1185–1210.
- ¹¹ Chen ME, Naeini SM, Srikrishnaraj A., Drucker DJ, Fesler Z., Brubaker PL Glukagonu sličan peptid-2 stimulira ulazak u S-fazu crijevnih Lgr5+ matičnih stanica. Cell. Mol. Gastroenterol. Hepatol. 2022;13:1829–1842.
- ¹² Cantarel BL, Lombard V, Henrissat B. 2012. Complex carbohydrate utilization by the healthy human microbiome. PLoS One 7:e28742.
- ¹³ Brown AJ, Goldsworthy SM, Barnes AA, Eilert MM, Tcheang L, Daniels D, Muir AI, Wigglesworth MJ, Kinghorn I, Fraser NJ, Pike NB, Strum JC, Steplewski KM, Murdock PR, Holder JC, Marshall FH, Szekeres PG, Wilson S, Ignar DM, Foord SM, Wise A, Dowell SJ. 2003. The orphan G protein-coupled receptors GPR41 and GPR43 are activated by propionate and other short chain carboxylic acids. J Biol Chem 278:11312–11319.
- ¹⁴ Qin J, Li R, Raes J, Arumugam M, Burgdorf KS, Manichanh C, Nielsen T, Pons N, Levenez F, Yamada T, et al. 2010. A human gut microbial gene catalogue established by metagenomic sequencing. Nature 464:59–65.
- ¹⁵ Le Chatelier E, Nielsen T, Qin J, Prifti E, Hildebrand F, Falony G, Almeida M, Arumugam M, Batto J-M, Kennedy S, et al. 2013. Richness of human gut microbiome correlates with metabolic markers. Nature 500:541–546.
- ¹⁶ Harach T, Pols TWH, Nomura M, Maida A, Watanabe M, Auwerx J, Schoonjans K. 2012. TGR5 potentiates GLP-1 secretion in response to anionic exchange resins. Sci Rep 2:430.
- ¹⁷ Thomas C, Gioiello A, Noriega L, Strehle A, Oury J, Rizzo G, Macchiarulo A, Yamamoto H, Mataki C, Pruzanski M, Pellicciari R, Auwerx J, Schoonjans K. 2009. TGR5-mediated bile acid sensing controls glucose homeostasis. Cell Metab 10:167–177.
- ¹⁸ Trabelsi MS, Daoudi M, Prawitt J, Ducastel S, Touche V, Sayin SI, Perino A, Brighton CA, Sebti Y, Kluza J, et al. 2015. Farnesoid X receptor inhibits glucagon-like peptide-1 production by enteroendocrine L cells. Nat Commun 6:7629.
- Ducastel S, Touche V, Trabelsi MS, Boulinguiez A, Butruille L, Nawrot M, Peschard S, Chávez-Talavera O, Dorchies E, Vallez E, Annicotte JS, Lancel S, Briand O, Bantubungi K, Caron S, Bindels LB, Delzenne NM, Tailleux A, Staels B, Lestavel S. 2020. The nuclear receptor FXR inhibits glucagon-like peptide-1 secretion in response to microbiota-derived short-chain fatty acids. Sci Rep 10:174.
- ²⁰Cani PD, Lecourt E, Dewulf EM, Sohet FM, Pachikian BD, Naslain D, De Backer F, Neyrinck AM, Delzenne NM. 2009. Gut microbiota fermentation of prebiotics increases satietogenic and incretin gut peptide production with consequences for appetite sensation and glucose response after a meal. Am J Clin Nutr 90:1236–1243.
- ²¹ Parnell JA, Reimer RA. 2009. Weight loss during oligofructose supplementation is associated with decreased ghrelin and increased peptide YY in overweight and obese adults. Am J Clin Nutr 89:1751–1759.
- ²² Daud NM, Ismail NA, Thomas EL, Fitzpatrick JA, Bell JD, Swann JR, Costabile A, Childs CE, Pedersen C, Goldstone AP, Frost GS. 2014. The impact of oligofructose on stimulation of gut hormones, appetite regulation and adiposity. Obesity 22:1430–1438.
- ²³ Müller M, Hermes GDA, Emanuel E C, Holst JJ, Zoetendal EG, Smidt H, Troost F, Schaap FG, Damink SO, Jocken JWE, Lenaerts K, Masclee AAM, Blaak EE. 2020. Effect of wheat bran derived prebiotic supplementation on gastrointestinal transit, gut microbiota, and metabolic health: a randomized controlled trial in healthy adults with a slow gut transit. Gut Microbes 12:1704141.
- ²⁴Freeland KR, Wilson C, Wolever TMS. 2010. Adaptation of colonic fermentation and glucagon-like peptide-1 secretion with increased wheat fibre intake for 1 year in hyperinsulinaemic human subjects. Br J Nutr 103:82–90.
- ²⁵ Holscher HD, Taylor AM, Swanson KS, Novotny JA, Baer DJ. 2018. Almond consumption and processing affects the composition of the gastrointestinal microbiota of healthy adult men and women: a randomized controlled trial. Nutrients 10:126.
- ²⁶ Ren M, Zhang H, Qi J, Hu A, Jiang Q, Hou Y, Feng Q, Ojo O, Wang X. 2020. An almond-based low carbohydrate diet improves depression and glycometabolism in patients with type 2 diabetes

- through modulating gut microbiota and GLP-1: a randomized controlled trial. Nutrients 12:3036.
- ²⁷ Shen L, Keenan MJ, Raggio A, Williams C, Martin RJ. 2011. Dietary-resistant starch improves maternal glycemic control in goto-kakizaki rat. Mol Nutr Food Res 55:1499–1508.
- ²⁸ Li M, Trapika IGSC, Tang SYS, Cho J-L, Qi Y, Li CG, Li Y, Yao M, Yang D, Liu B, Li R, Yang P, Ma G, Ren P, Huang X, Xie D, Chen S, Li M, Yang L, Leng P, Huang Y, Li GQ. 2021. Mechanisms and active compounds polysaccharides and bibenzyls of medicinal dendrobiums for diabetes management. Front Nutr 8:811870.
- ²⁹ Dao T-MA, Waget A, Klopp P, Serino M, Vachoux C, Pechere L, Drucker DJ, Champion S, Barthélemy S, Barra Y, Burcelin R, Sérée E. 2011. Resveratrol increases glucose induced GLP-1 secretion in mice: a mechanism which contributes to the glycemic control. PLoS One 6:e20700.
- ³⁰Yuan T, Yin Z, Yan Z, Hao Q, Zeng J, Li L, Zhao J. 2020. tetrahydrocurcumin ameliorates diabetes profiles of db/db mice by altering the composition of gut microbiota and up-regulating the expression of GLP-1 in the pancreas. Fitoterapia 146:104665.
- ³¹ Li X-X, Zhang X-X, Zhang R, Ni Z-J, Elam E, Thakur K, Cespedes-Acuña CL, Zhang J-G, Wei Z-J. 2021. Gut modulation based anti-diabetic effects of carboxymethylated wheat bran dietary fiber in high-fat diet/streptozotocin-induced diabetic mice and their potential mechanisms. Food Chem Toxicol 152:112235.
- ³² Yang T, Zhou W, Xu W, Ran L, Yan Y, Lu L, Mi J, Zeng X, Cao Y. 2022. Modulation of gut microbiota and hypoglycemic/hypolipidemic activity of Flavonoids from the fruits of Lycium barbarum on highfat diet/streptozotocin-induced type 2 diabetic mice. Food Funct 13:11169-11184.
- 33 Chen LC, Fan ZY, Wang HY, Wen DC, Zhang SY. 2019. Effect of poly-saccharides from adlay seed on anti-diabetic and gut microbiota. Food Funct 10:4372–4380.
- ³⁴ Koopen A, Witjes J, Wortelboer K, Majait S, Prodan A, Levin E, Herrema H, Winkelmeijer M, Aalvink S, Bergman J, et al. 2022. Duodenal Anaerobutyricum soehngenii infusion stimulates GLP-1 production, ameliorates glycaemic control and beneficially shapes the duodenal transcriptome in metabolic syndrome subjects: a randomised double-blind placebo-controlled cross-over study. Gut 71:1577–1587.
- 35 Simon M-C, Strassburger K, Nowotny B, Kolb H, Nowotny P, Burkart V, Zivehe F, Hwang J-H, Stehle P, Pacini G, Hartmann B, Holst JJ, MacKenzie C, Bindels LB, Martinez I, Walter J, Henrich B, Schloot NC, Roden M. 2015. Intake of Lactobacillus reuteri improves incretin and insulin secretion in glucose-tolerant humans: a proof of concept. Diab Care 38:1827–1834
- ³⁶ Alisi A, Bedogni G, Baviera G, Giorgio V, Porro E, Paris C, Giammaria P, Reali L, Anania F, Nobili V. 2014. Randomised clinical trial: the beneficial effects of VSL#3 in obese children with non-alcoholic steatohepatitis. Aliment Pharmacol Ther 39:1276–1285.
- ³⁷ Xu S, Wang Y, Wang J, Geng W. 2022. Kombucha reduces hyperglycemia in type 2 diabetes of mice by regulating gut microbiota and its metabolites. Foods 11:754.
- ³⁸Chen YC, Huang SD, Tu JH, Yu JS, Nurlatifah AO, Chiu WC, Su YH, Chang HL, Putri DA, Cheng HL. 2020. Exopolysaccharides of bacillus amyloliquefaciens modulate glycemic level in mice and promote glucose uptake of cells through the activation of AKT. Int J Biol Macromol 146:202–211.
- ³⁹ Yadav H, Lee JH, Lloyd J, Walter P, Rane SG. 2013. Beneficial metabolic effects of a probiotic via butyrate-induced GLP-1 hormone secretion. J Biol Chem 288:25088–25097.
- ⁴⁰ Ryan PM, Patterson E, Kent RM, Stack H, O'Connor PM, Murphy K, Peterson VL, Mandal R, Wishart DS, Dinan TG, Cryan JF, Seeley RJ, Stanton C, Ross RP. 2017. Recombinant incretin-secreting microbe improves metabolic dysfunction in high-fat diet fed rodents. Sci Rep 7:13523.
- ⁴¹ Wang Y, Dilidaxi D, Wu Y, Sailike J, Sun X, Nabi X-H. 2020. Composite probiotics alleviate type 2 diabetes by regulating intestinal microbiota and inducing GLP-1 secretion in db/db mice. Biomed Pharmacother 125:109914.
- ⁴² Li X, Wang E, Yin B, Fang D, Chen P, Wang G, Zhao J, Zhang H, Chen W. 2017. Effects of Lactobacillus casei CCFM419 on insulin resistance and gut microbiota in type 2 diabetic mice. Benef Microbes 8:421– 432.
- ⁴³ Jia L, Li D, Feng N, Shamoon M, Sun Z, Ding L, Zhang H, Chen W, Sun J, Chen YQ. 2017. Anti-diabetic effects of Clostridium butyricum CGMCC0313.1 through promoting the growth of gut butyrate-producing bacteria in type 2 diabetic mice. Sci Rep 7:7046.
- ⁴⁴Archer AC, Muthukumar SP, Halami PM. 2021. Lactobacillus fermentum MCC2759 and MCC2760 alleviate inflammation and

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- intestinal function in high-fat diet-fed and streptozotocin-induced diabetic rats. Probiotics Antimicrob Proteins 13:1068–1080.
- ⁴⁵Palani Kumar MK, Halami PM, Serva Peddha M. 2021. Effect of Lactobacillus fermentum MCC2760-based probiotic curd on hypercholesterolemic C57BI6 mice. ACS Omega 6:7701–7710.
- ⁴⁶Singh S, Sharma RK, Malhotra S, Pothuraju R, Shandilya UK. 2017. Lactobacillus Rhamnosus NCDC17 ameliorates type-2 diabetes by improving gut function, oxidative stress and inflammation in high-fat-diet fed and streptozotocintreated rats. Benef Microbes 8:243-255
- ⁴⁷Lin S, Yang X, Long Y, Zhong H, Wang P, Yuan P, Zhang X, Che L, Feng B, Li J, Zhuo Y, Lin Y, Xu S, Wu D, Fang Z. 2020. Dietary supplementation with Lactobacillus plantarum modified gut microbiota, bile acid profile and glucose homoeostasis in weaning piglets. Br J Nutr 124:797–808.
- ⁴⁸Grasset E, Puel A, Charpentier J, Collet X, Christensen JE, Tercé F, Burcelin R. 2017. A specific gut microbiota Dysbiosis of type 2 diabetic mice induces GLP-1 resistance through an Enteric NO-dependent and gut-brain axis mechanism. Cell Metab 26:278.
- ⁴⁹ Zhang X, Ren H, Zhao C, Shi Z, Qiu L, Yang F, Zhou X, Han X, Wu K, Zhong H, Li Y, Li J, Ji L. 2022. Metagenomic analysis reveals Crosstalk between gut microbiota and glucose-lowering drugs targeting the gastrointestinal tract in chinese patients with type 2 diabetes: a 6 month, two-arm randomised trial. Diabetologia 65:1613–1626.
- ⁵⁰Pulimeno P, Mannic T, Sage D, Giovannoni L, Salmon P, Lemeille S, Giry-Laterriere M, Unser M, Bosco D, Bauer C, Morf J, Halban P, Philippe J, Dibner C. 2013. Autonomous and self-sustained circadian oscillators displayed in human islet cells. Diabetologia 56:497–507.
- Marcheva B, Ramsey KM, Buhr ED, Kobayashi Y, Su H, Ko CH, Ivanova G, Omura C, Mo S, Vitaterna MH, Lopez JP, Philipson LH, Bradfield CA, Crosby SD, JeBailey L, Wang X, Takahashi JS, Bass J. 2010. Disruption of the clock components CLOCK and BMAL1 leads to hypoinsulinaemia and diabetes. Nature 466:627–631.
- ⁵² Lindgren O, Mari A, Deacon CF, Carr RD, Winzell MS, Vikman J, Ahrén B. 2009. Differential islet and incretin hormone responses in morning versus afternoon after standardized meal in healthy men. J Clin Endocrinol Metab 94:2887–2892.
- ⁵³ Martchenko SE, Martchenko A, Cox BJ, Naismith K, Waller A, Gurges P, Sweeney ME, Philpott DJ, Brubaker PL. 2020. Circadian GLP-1 secretion in mice is dependent on the intestinal microbiome for maintenance of diurnal metabolic homeostasis. Diabetes 69:2589–2602.
- Martchenko SE, Martchenko A, Biancolin AD, Waller A, Brubaker PL. 2021. L-cell arntl is required for rhythmic glucagon-like peptide-1 secretion and maintenance of intestinal homeostasis. Mol Metab 54:101340.
- ⁵⁵ Biancolin AD, Martchenko A, Mitova E, Gurges P, Michalchyshyn E, Chalmers JA, Doria A, Mychaleckyj JC, Adriaenssens AE, Reimann F, Gribble FM, Gil-Lozano M, Cox BJ, Brubaker PL. 2020. The core clock gene, Bmal1, and its downstream target, the SNARE regulatory protein secretagogin, are necessary for circadian secretion of glucagon-like peptide-1. Mol Metab 31:124–137.
- ⁵⁶Zhang Q, Xiao X, Zheng J, Li M, Yu M, Ping F, Wang T, Wang X. 2018. Featured article: structure moderation of gut microbiota in liraglutide-treated diabetic male rats. Exp Biol Med (Maywood) 243:34–44.
- ⁵⁷ Moreira GV, Azevedo FF, Ribeiro LM, Santos A, Guadagnini D, Gama P, Liberti EA, Saad M, Carvalho C. 2018. Liraglutide modulates gut microbiota and reduces NAFLD in obese mice. J Nutr Biochem 62:143–154.
- 58 Wang H, Wang L, Li Y, Luo S, Ye J, Lu Z, Li X, Lu H. 2021. The HIF-2α/PPARα pathway is essential for liraglutide-alleviated, lipid-induced hepatic steatosis. Biomed Pharmacother 140:111778.
- ⁵⁹Liu Q, Cai BY, Zhu LX, Xin X, Wang X, An ZM, Li S, Hu YY, Feng Q. 2020. Liraglutide modulates gut microbiome and attenuates nonalcoholic fatty liver in db/db mice. Life Sci 261:118457.
- ⁶⁰Ying X, Rongjiong Z, Kahaer M, Chunhui J, Wulasihan M. 2023. Therapeutic efficacy of liraglutide versus metformin in modulating the gut microbiota for treating type 2 diabetes mellitus complicated with nonalcoholic fatty liver disease. Front Microbiol 14:1088187.
- ⁶¹ Smits MM, Fluitman KS, Herrema H, Davids M, Kramer MHH, Groen AK, Belzer C, de Vos WM, Cahen DL, Nieuwdorp M, van Raalte DH. 2021. Liraglutide and sitagliptin have no effect on intestinal microbiota composition: a 12-week randomized placebo-controlled trial in adults with type 2 diabetes. Diabetes Metab 47:101223.
- ⁶²Rizza S, Pietrucci D, Longo S, Menghini R, Teofani A, Piciucchi G,

- Montagna M, Federici M. 2023. Impact of insulin Degludec/ Liraglutide fixed combination on the gut microbiomes of elderly patients with type 2 diabetes: results from A Subanalysis of A small non-randomised single arm study. Aging Dis 14:319–324.
- ⁶³ Silva-Veiga FM, Miranda CS, Vasques-Monteiro IML, Souza-Tavares H, Martins FF, Daleprane JB, Souza-Mello V. 2022. Peroxisome proliferator-activated receptor-alpha activation and dipeptidyl peptidase-4 inhibition target dysbiosis to treat fatty liver in obese mice. World J Gastroenterol 28:1814–1829.
- ⁶⁴Liao X, Song L, Zeng B, Liu B, Qiu Y, Qu H, Zheng Y, Long M, Zhou H, Wang Y, Du Y, Xu J, Shen R, Tong Q, Cai L, Li X, Guo S, Yang G, Zhu Z, Pu X, Wei H, Zheng H. 2019. Alteration of gut microbiota induced by DPP-4I treatment improves glucose homeostasis. EBioMedicine 44:665–674.
- ⁶⁵ Olivares M, Neyrinck AM, Pötgens SA, Beaumont M, Salazar N, Cani PD, Bindels LB, Delzenne NM. 2018. The DPP-4 inhibitor vildagliptin impacts the gut microbiota and prevents disruption of intestinal homeostasis induced by a Western diet in mice. Diabetologia 61:1838–1848.
- ⁶⁶Zhang M, Feng R, Yang M, Qian C, Wang Z, Liu W, Ma J. 2019. Effects of metformin, acarbose, and sitagliptin monotherapy on gut microbiota in zucker diabetic fatty rats. BMJ Open Diabetes Res Care 7:e000717.
- ⁶⁷ Ryan PM, Patterson E, Carafa I, Mandal R, Wishart DS, Dinan TG, Cryan JF, Tuohy KM, Stanton C, Ross RP. 2020. Metformin and dipeptidyl peptidase-4 inhibitor differentially modulate the intestinal microbiota and plasma metabolome of metabolically dysfunctional mice. Can J Diabetes 44:146–155.
- ⁶⁸ Zhang Q, Xiao X, Li M, Yu M, Ping F, Zheng J, Wang T, Wang X, Peterson JM. 2017. Vildagliptin increases butyrate-producing bacteria in the gut of diabetic rats. PLoS ONE 12:e0184735.
- ⁶⁹Guo S, Al-Sadi R, Said HM, Ma TY. 2013. Lipopolysaccharide causes an increase in intestinal tight junction permeability in vitro and in vivo by inducing enterocyte membrane expression and localization of TLR-4 and CD14. Am J Pathol 182:375–387.
- ⁷⁰ Zhou S-Y, Gillilland M III, Wu X, Leelasinjaroen P, Zhang G, Zhou H, Ye B, Lu Y, Owyang C. 2018. FODMAP diet modulates visceral nociception by lipopolysaccharide-mediated intestinal inflammation and barrier dysfunction. J Clin Invest 128:267–280.
- ⁷¹ Chen Q, Ma X, Li C, Shen Y, Zhu W, Zhang Y, Guo X, Zhou J, Liu C. 2020. Enteric phageome alterations in patients with type 2 diabetes. Front Cell Infect Microbiol 10:575084.
- Tellingsgaard H, Hauselmann I, Schuler B, Habib AM, Baggio LL, Meier DT, Eppler E, Bouzakri K, Wueest S, Muller YD, Hansen AMK, Reinecke M, Konrad D, Gassmann M, Reimann F, Halban PA, Gromada J, Drucker DJ, Gribble FM, Ehses JA, Donath MY. 2011. Interleukin-6 enhances insulin secretion by increasing glucagon-like peptide-1 secretion from L cells and alpha cells. Nat Med 17:1481–1489
- ⁷³ Costa A, Ai M, Nunn N, Culotta I, Hunter J, Boudjadja MB, Valencia-Torres L, Aviello G, Hodson DJ, Snider BM, Coskun T, Emmerson PJ, Luckman SM, D'Agostino G. 2022. Anorectic and aversive effects of GLP-1 receptor agonism are mediated by brainstem cholecystokinin neurons, and modulated by GIP receptor activation. Mol Metab 55:101407.
- Yusta B, Baggio LL, Koehler J, Holland D, Cao X, Pinnell LJ, Johnson-Henry KC, Yeung W, Surette MG, Bang KWA, Sherman PM, Drucker DJ. 2015. GLP-1R agonists modulate enteric immune responses through the intestinal intraepithelial lymphocyte GLP-1R. Diabetes 64:2537–2549.
- ⁷⁵ Sharon G, Cruz NJ, Kang DW, Gandal MJ, Wang B, Kim YM, Zink EM, Casey CP, Taylor BC, Lane CJ, Bramer LM, Isern NG, Hoyt DW, Noecker C, Sweredoski MJ, Moradian A, Borenstein E, Jansson JK, Knight R, Metz TO, Lois C, Geschwind DH, Krajmalnik-Brown R, Mazmanian SK. 2019. Human gut microbiota from autism spectrum disorder promote behavioral symptoms in mice. Cell 177:1600–1618.
- ⁷⁶ Breton J, Tirelle P, Hasanat S, Pernot A, L'Huillier C, do Rego J-C, Déchelotte P, Coëffier M, Bindels LB, Ribet D. 2021. Gut microbiota alteration in a mouse model of anorexia nervosa. Clin Nutr 40:181–189.
- ⁷⁷ Ren HX, Tang QC, Yan L, Xia H, Luo HS. 2018. Evodiamine inhibits gastrointestinal motility via CCK and CCK1 receptor in water-avoidence stress rat model. Life Sci 209:210–216.
- ⁷⁸ Marra A, Hanson MA, Kondo S, Erkosar B, Lemaitre B, Ja WW, McFall-Ngai MJ. 2021. Drosophila antimicrobial peptides and lysozymes regulate gut microbiota composition and abundance. mBio 12:e0082421.
- ⁷⁹ Li Z, Zhang B, Wang N, Zuo Z, Wei H, Zhao F. 2023. A novel peptide protects against diet-induced obesity by suppressing appetite and modulating the gut microbiota. Gut 72:686–698.

New Clinical Study Demonstrates Rapid Discomfort Relief from Topical PlexoZome® Levagen® in Post-Exercise Research

Gencor is thrilled to announce that its newly published randomized, double-blind, placebo-controlled clinical study has demonstrated that PlexoZome[®] Levagen[®], a topical liposomal formulation of palmitoylethanolamide (PEA), provides safe and effective relief of post-exercise knee joint discomfort.

his is the first published clinical trial to show that topical application of PEA can provide rapid and meaningful aches and discomfort relief," said Dr. Amanda Rao, lead investigator of the study. "The findings highlight Plexo-Zome" Levagen" as a promising natural analgesic alternative, particularly for individuals seeking fast-acting and well-tolerated solutions."

The peer-reviewed study, published in the Journal of Alternative, Complementary & Integrative Medicine, enrolled 86 healthy adults who experienced knee discomfort following exercise. Upon a knee pain rating of ≥3/10 on the VAS pain scale, participants applied three sprays of their investigational product (PlexoZome® Levagen® PEA or placebo). Participants recorded their pain on the VAS every 15 minutes for a maximum of 2 hours or until their pain subsided. If participants were still experiencing pain, they reapplied their investigational product at the 30-, 60-, and 90-minute marks - a total of 214 pain episodes qualified for analysis. The results showed that the PEA group significantly resolved more pain events within 60 minutes of onset compared with the placebo. At 60 minutes, the PEA group experienced a 71% reduction in pain from baseline, compared to a 43% reduction in the placebo group.

"The clinical research results support the growing demand for topical, non-NSAID solutions in the sports nutrition, active lifestyle, and joint health markets," said Ramasamy Venkatesh, Managing Director of Gencor Pacific. "With its liposomal delivery system, PlexoZome" Levagen" ensures enhanced absorption of PEA at the targeted site of discomfort, offering brands a clinically validated, innovative ingredient to differentiate their product portfolios."

PlexoZome® Levagen® is a patented liposomal formulation of palmitoylethanolamide (PEA), a naturally occurring fatty acid amide with well-documented analgesic and anti-inflammatory properties. Leveraging Pharmako Biotechnologies' advanced liposomal delivery system, PlexoZome®, the combination provides targeted, rapid relief for joint and muscle aches at a low dosage of 1.8 mg per spray.

To review the published clinical data and for more information on PlexoZome® Levagen®, visit pharmako.com.au or GencorPacific.com.



Challenges and Difficulties of Small-Scale Cosmetic Producers in Practice

Real-life experiences are always the most engaging stories: they educate, help identify shortcomings in one's own work, and encourage their elimination. In this way, business operations can be improved and optimized. The stories that follow may bring a smile to some readers, while prompting deeper reflection in others.



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Story 1: Misunderstanding the concept of a "product line"

Product line - what does it actually mean?

Misunderstanding of the term *product line* is a common occurrence in the cosmetics industry. Manufacturers are often misled by the marketing presentation of a "line" that includes different product categories connected only by fragrance - for example, a face cream, a hand cream, and a body lotion with a rose scent. However, from a regulatory perspective, this does not constitute a product line.

For a group of products to be considered a line, a basic condition must be met: they must be the same type of product within the same category, differing only in fragrance or colour. For instance, a body lotion with the scent of rose, vanilla, and lavender constitutes a product line because the formulation is identical, while the variation applies solely to the

fragrance, which may differ in a minimal percentage, without affecting safety or the core formulation.

This interpretation is confirmed by the *Guide to Using CPNP for Responsible Persons and Distributors* (p. 8.), which defines product shades as: "An individual colour variant of a cosmetic product. E.g. the different color names for the same lipstick, like 'Pure rouge', 'Ruby', 'Vermeil', etc." Cosmetics Europe guidelines likewise refer to "shades or fragrance variants" as acceptable variations within a product line.

Thus, all shades of the same product with the same function - whether based on colour or fragrance - may constitute a product line. On the other hand, changes involving active ingredients, substitution of extracts with vegetable oils, or changes in product category (e.g. face cream vs. body lotion) cannot be considered shades, and therefore do not form a product line.

In conclusion, a product line means the same formulation and the same intended use, with limi-



ted variations in colour or fragrance. All other changes constitute a new product, not a new shade within the line.

Story 2: The difference between a laboratory and a production facility

When is it a laboratory, and when is it a production facility?

In practice, the terms "laboratory" and "production facility" are often confused. A laboratory is primarily a place for research, development, and testing — where formulations are created, tested, and refined in small quantities under controlled conditions. A production facility, on the other hand, is intended for serial manufacturing — where those same formulations are reproduced in larger batches, while ensuring the hygiene and technical conditions prescribed by Good Manufacturing Practice (ISO 22716: 2007).

Among small producers, however, a "marketing substitution of terms" is often present: although they have in fact established a small production facility, they prefer to claim they have "founded a laboratory." The reason is simple – a laboratory sounds more scientific, professional, and credible, leaving a stronger impression on customers and business partners. Still, this is an incorrect use of the term, as a laboratory and a production facility serve different functions and purposes.

It is important to emphasize that any production site may also include a laboratory for internal self-control, i.e. for monitoring the quality and safety of raw materials and finished cosmetic products. However, this is not the reality for small producers, as it requires substantial investments in equipment and qualified personnel.

Moreover, there is a legal obligation that applies equally to all manufacturers: the health safety of cosmetic products must be tested in an accredited microbiological laboratory. This means that no producer – regardless of size, experience, internal equipment, or staff – is exempt from the obligation of external accredited testing.

In short: a laboratory is for development and control, a production facility is for manufacturing, and accredited microbiological testing is a legal requirement for everyone.

Story 3: Product labels in foreign languages

Is english enough for non-english markets?

Since I live and work in Croatia, and as a Croatian myself, the examples I will mention here refer to the Croatian market. Too often, I come across cases where the entire text of a product label is written exclusively in a foreign language – always, without exception, in English. The reasons given by manufacturers are usually the same: "it sounds better in English," "if it's in English, customers will think we're foreign and therefore better," "others are doing the same," "the safety assessment was done abroad, so they made the label for us"...

Without delving into the psychological background of such attitudes, the fact remains: regulations – not only in Croatia and the EU, but in every country worldwide – do not permit product labels to be written exclusively in a foreign language. The reason is simple: the national language is part of a country's identity, a tool of communication among its citizens, and the language that every consumer understands best. The information on a label must be comprehensible to all, allowing consumers to make informed purchasing decisions.

This is confirmed by Regulation (EC) No 1223/2009 on cosmetic products, Article 19(5), which states: "The language of the information mentioned in points (b), (c), (d) and (f) of paragraph 1 and in paragraphs (2), (3) and (4) shall be determined by the law of the Member States in which the product is made available to the end user."

And what does Croatian law say? The Act on General Use Articles (which includes cosmetics) is very clear in Article 7: "Articles of general use placed on the market in the Republic of Croatia must bear product information (product label) in the Croatian language, containing the data prescribed by regulations governing specific types of articles of general use."

The same requirement applies to goods arriving from other EU Member States as well as imports from third countries.

The conclusion is clear: no manufacturer is exempt from the obligation to provide product labels in the language of the country where the product is marketed. Each country, through its legislation, protects its own language and identity – and this is not a matter of impression, but a matter of legal obligation.

To take home

These three stories illustrate some of the most common misconceptions and challenges faced by small-scale cosmetic producers. Each of these examples highlights the same lesson – that good intentions, creativity, or marketing cannot replace requilitory compliance and professional accuracy.

Success in cosmetics, even for the smallest producers, is built on knowledge, responsibility, and respect for both the rules and the community. Only in this way can businesses not only survive but also grow, while consumers remain safe and well-informed.

To be continued...



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Symrise Unveils Neo Heliopan® Fusion: Ready-to-use 4-in-1 UV Filter Blend Enabling Fast, Flexible SPF 50+ in Cosmetics

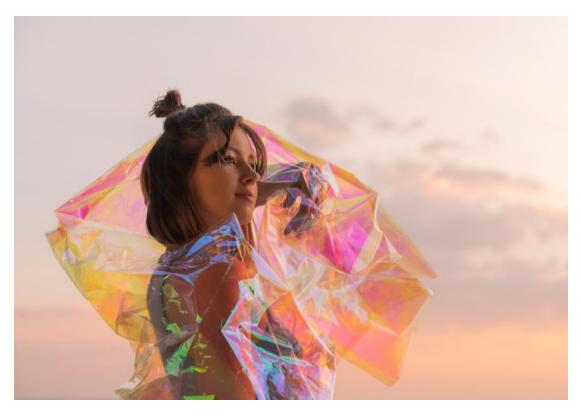
This is the innovation that simplifies sun care formulation, allowing for tailored broad-spectrum protection. The patent-pending viscous blend combines three crystalline UV filters solubilized in one liquid UV filter, providing exceptional stability and performance. With this launch Symrise further strengthens its position as a leading provider of efficient and globally relevant UV protection solutions.

ymrise presents Neo Heliopan® Fusion, a next-generation 4-in-1 UV filter blend devised to meet the growing demand for high-performance sun protection. This patent-pending innovation combines three modern crystalline UV filters seamlessly solubilized in a liquid UV filter. The resulting viscous liquid enables easy processing for formulators. As such, Neo Heliopan® Fusion facilitates tailor-made sunscreen solutions with customizable SPF levels – up to 50+ at 30% use level – de-

livering broad-spectrum, balanced UVA protection and a light skin feel. By consolidating multiple filters into one ingredient, it streamlines formulation, reduces complexity, and optimizes inventory and energy use.

Meeting evolving market needs

Neo Heliopan® Fusion empowers brands to create differentiated sun care products that resonate with today's consumer expectations for reliable protec-



tion, pleasant application, and transparent formulation. It supports efficient development cycles and helps manufacturers respond quickly to regulatory needs and market trends. Its cold-process capability and compatibility with hot, cold, or hybrid manufacturing setups make it inherently more sustainable and future-ready.

Composition and application versatility

With its unique 4-in-1 composition – three crystalline UV filters solubilized in one liquid UV filter – Neo Heliopan® Fusion forms a stable, homogeneous solution. It supports a wide range of applications: such as creams, lotions, sprays, sticks. It also works well for BB/CC creams, foundations, lipsticks as well as daily skincare, including anti-aging creams, moisturizers, and balms, with added SPF. The blend's oilsoluble, water-free format ensures easy processing.

Innovation to accelerate development

This liquid form, patent-pending UV filter blend simplifies and accelerates formulation, enabling precise SPF creation and broad-spectrum protection. It allows SPF levels up to 50+ at 30% use level, while ensuring balanced UVA coverage and a pleasant, light skin feel. Neo Heliopan® Fusion integrates seamlessly into the oil phase with a simple stir. It reduces the need for auxiliary ingredients such as solubilizers, streamlining inventory management – especially for small and mid-sized customers. Aligned with modern regulatory and consumer needs, it offers reliable protection, supporting consumer trust.

A first-of-its-kind solution

Unlike conventional products that include emollients or emulsifiers and limit customization, Neo Heliopan® Fusion consists of state-of-the-art crystalline UV filters in a convenient viscous format. This innovation gives formulators maximum flexibility and simplifies logistics, enabling the creation of differentiated products across diverse markets.

"We set out with a clear objective: to create a powerful UV filter blend that delivers simplicity, and aligns with today's standards - without compromise," says Julio Bombonati, Global Category Director Sun Protection at Symrise Cosmetic Ingredients.

With patents pending, Neo Heliopan® Fusion reinforces Symrise's commitment to innovation leadership in UV protection. The company will continue to expand its portfolio of formulator-friendly solutions that accelerate development, streamline supply chains, and help partners deliver effective, responsible sun care worldwide.



Symrise – always inspiring more... www.symrise.com

B2B Events Calendar 2025/2026

This is an overview of the B2B live events during 2025 and 2026

2025



28-30 October, Frankfurt

https://www.cphi.com/europe/en/home.html



12-13 November, London

https://nutrahealthspansummit.com/



19-20 November, Milano

https://www.making-cosmetics.it/



19-20 November, Malmömässan

https://www.nordicorganicexpo.com/en/



19-20 November, Milano

https://www.in-vitality.it/



30 November - 02 December, Paris

https://natexpo.com/



02-04 December, Paris

https://www.figlobal.com/europe/en/home.html

2026



22-24 February, Bologna

https://www.sana.it/en/home/1229.html



26-29 March, Bologna

https://www.cosmoprof.com/



04-16 April, Paris

https://www.in-cosmetics.com/global/en-gb.html



14-16 April, Warsaw

https://nutrafood.pl/en/





