

# Keeping the metabolism balanced is a matter of health, lifestyle is crucial, and natural ingredients may help much

## Why a balanced metabolism is so important?

Metabolism is the set of life-sustaining chemical reactions in organisms. These processes are crucial for the maintenance of life, allowing cells to grow, reproduce, maintain their structures, and respond to their environments. One essential aspect of metabolism is the metabolism of fats, which involves the breakdown, storage, and synthesis of fats within the body.

Maintaining a balanced fat metabolism is critical for overall health. Fats, or lipids, serve several essential functions: they are a major energy source, help in the absorption of vitamins, and play a key role in cellular structure and function. However, an imbalance in fat metabolism can lead to various health issues, including obesity, cardiovascular diseases, diabetes, and metabolic syndrome.

Talking about obesity, which is a major risk factor for cardiovascular diseases, the World Health Organization (WHO) last data show that about 16% of adults aged 18 years and older worldwide were obese in 2022, and the worldwide prevalence of obesity more than doubled between 1990 and 2022. This epidemic is not limited to adults; childhood obesity is also on the rise: while just 2% of children and adolescents aged 5–19 were obese in 1990 (31 million young people), by 2022, 8% of children and adolescents were living with obesity (160 million young people). (<https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>)

Talking about obesity, which is a major risk factor for cardiovascular diseases, the World Health Organization (WHO) last data show that about 16% of adults aged 18 years and older worldwide were obese in 2022, and the worldwide prevalence of obesity more than doubled between 1990 and 2022. This epidemic is not limited to adults; childhood obesity is also on the rise (<https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>)

[www.who.int/news-room/fact-sheets/detail/obesity-and-overweight](https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight)) According to this, a good management of metabolic health is one of the key goals to reach for overall wellbeing and healthy ageing.

## How to maintain a metabolic balance?

To address the global issue of metabolic imbalance, the World Health Organization (WHO), The American Heart Association (AHA), the European Society of Cardiology (ESC), and other authoritative health organizations provide several recommendations, like

- healthy diet, rich in fruits, vegetables, whole grains, and lean proteins, limiting the intake of saturated fats, trans fats, cholesterol, and high-sugar foods, and also paying attention to portion sizes, to avoid overeating;
- physical activity through regular exercise, at least 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous-intensity activity each week;
- lifestyle changes, like reduce sedentary behavior or quit smoking;
- regularly monitor weight, blood pressure, and cholesterol levels to detect and address potential metabolic issues early.

In a few words, individuals can take proactive steps to maintain their metabolic health and reduce the risk of serious health conditions.

## The role of natural ingredients: Berberine and Bergamot, in Indena's formulation for a high efficacy

Nature is able to produce treasures for human wellbeing. As for the balance of metabolism, one of the most effective natural ingredients is **berberine**, a plant alkaloid with a long history of traditional use in both Ayurvedic and Chinese medicine thanks to its wide medicinal properties. The main natural source of berberine is the genus

Berberis belonging to the Berberidaceae family and comprising around 450–500 species.

Among the various species of Berberis genus, *Berberis aristata* DC is one of the most important species. It has been used in traditional medicine for its antimicrobial, antiprotozoal, antidiarrheal and antitrichoma activity<sup>1</sup>. Berberine is a quaternary ammonium salt derived from isoquinoline alkaloid and it is supported by reliable scientific literature proving its health benefits in multifactorial conditions, including the support in controlling healthy blood levels<sup>2</sup>. The berberine alkaloid can be found in the roots, rhizomes, and stem bark of the plants.

Specifically, berberine's proven effectiveness in the management of multifactorial conditions is related to its so-called "Cloud Effect": its pleiotropic effect simultaneously targets both root causes (e.g. low-grade chronic inflammation and oxidative stress,) and marks (e.g. insulin levels) through the modulation of several cellular targets (e.g. AMPK, mitochondria, insulin-receptor, key metabolic and pro-inflammatory enzymes, etc.). This helps optimize peripheral blood metabolic profiles by modulating plasma sugar, insulin and lipids levels, thus resulting as a precious resource for the metabolic wellbeing<sup>3</sup>.

Unfortunately, berberine has a poor bioavailability, like many natural compounds. For this reason, high dosages are traditionally recommended for berberine, that means low tolerability and gastrointestinal side effects. To face such issue, Indena developed since years Indena Phytosome™, a multi-talented technology platform to improve the effectiveness and target ability of a wide range of natural compounds, creating lecithin-based solid dispersions that allows enhanced ingredient's distribution in gastrointestinal fluids and bioaccessibility profile. Indena Phytosome™ combines food-grade sunflower lecithin with botanical and natural substances maintaining the original

components' profile and benefits. Numerous scientific studies have proven that Indena Phytosome™ technology offers optimized human pharmacokinetic profiles and effectiveness compared to non-formulated equivalent natural ingredients.

Working on berberine, Indena developed BERBEVIS®, a new and innovative Indena Phytosome™, which includes both pea proteins, as a natural vegetable protein carrier, and a powerful, natural antioxidant such as grape seed extract to optimize berberine tolerability profile<sup>4</sup>.

Remarkably, a human pharmacokinetic study has confirmed that BERBEVIS® has optimized berberine bioabsorption with observed dose linearity, fostering the compound's biological performances<sup>5</sup>.

In vitro studies have been also showed that Indena Phytosome™ formulation enhances berberine solubility in gastrointestinal fluids; has a better bioaccessibility than unformulated Berberis extract, improving the amount of berberine released into the gastrointestinal tract and available for absorption; has a higher safety profile than unformulated Berberis extract with the absence of negative impact on intestinal membranes. BERBEVIS® appears then to be suitable for a long-term administration.

Several clinical evidences show that BERBEVIS® is proven to efficaciously improve metabolic health in men and women, enhance blood sugar control, modulate critical markers in the blood lipid profile, rebalance body composition to a healthier standard, ameliorate natural female hormonal balance, promote a healthy inflammatory response and improve skin health.

A first study (6) showed that BERBEVIS®:

- significantly rebalanced blood glycemia (fasting plasma glucose): -12 % vs baseline after 60 days, -9% vs placebo after 60 days, effective already after 30 days;

- normalized glycaemia values taking subjects out of impaired fasting glucose (prediabetes) classification;
- offset insulin resistance significantly acting on insulin and HOMA index
- positively modulates lipid parameters;

Other scientific results<sup>7</sup> confirm the efficacy of BERBEVIS® in managing blood lipid profile. Both in a borderline, occasional high lipidemic, non-permanent condition, and in a borderline but stable hyperlipidemic condition, Indena's Berberine Phytosome™ showed to positively modulates lipid parameters and to help maintain a healthy body composition.

Thanks to optimized bioaccessibility, bioabsorption and tolerability, BERBEVIS® exploits all health benefits of natural berberine.

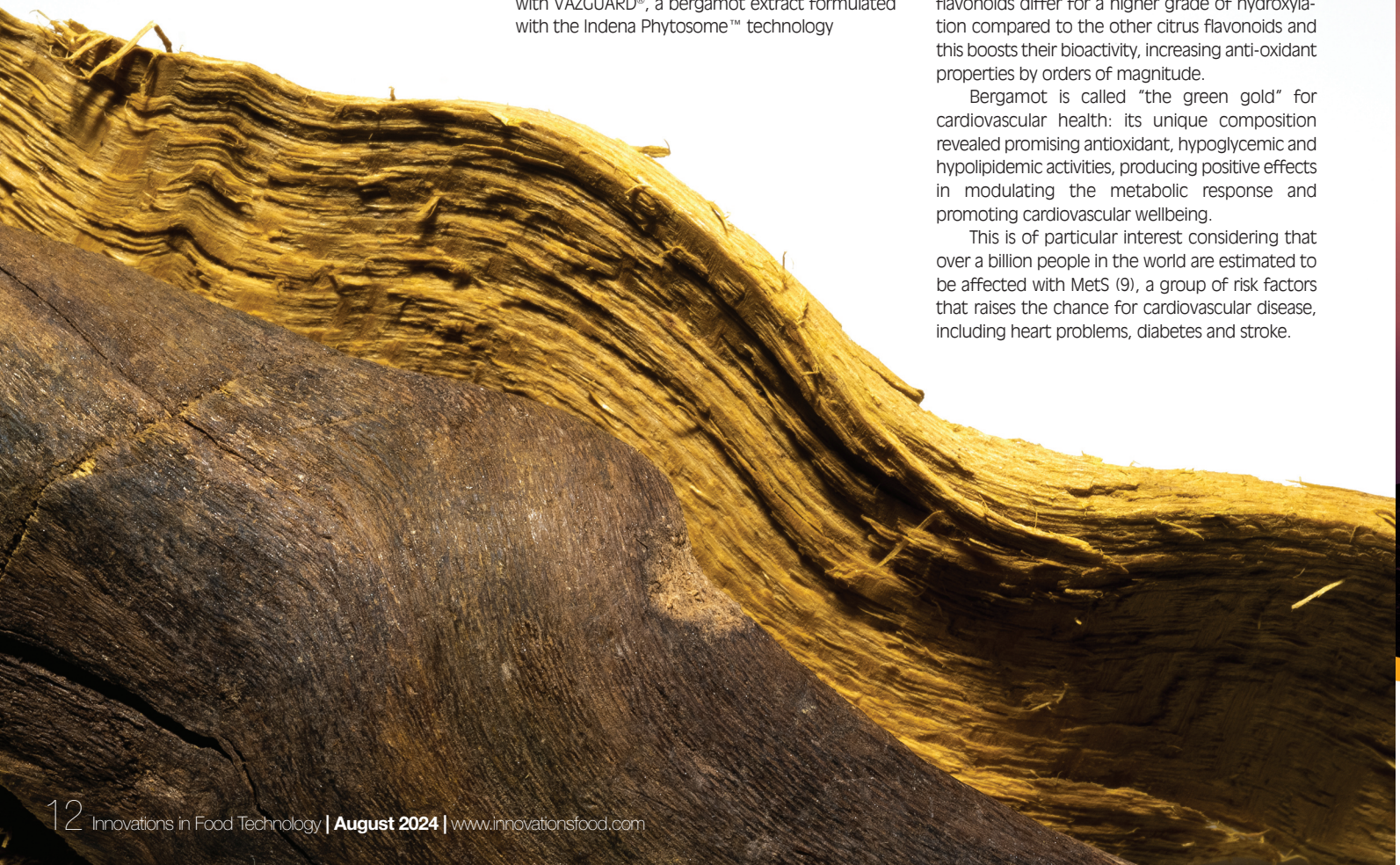
**Bergamot** is another natural ingredient that may help in keeping the metabolism balanced. And Indena was able to make this extract very effective with VAZGUARD®, a bergamot extract formulated with the Indena Phytosome™ technology

*Citrus bergamia* Risso et Poiteau, the scientific name of bergamot, is a fruit whose production is almost exclusively limited to the Calabria region in Southern Italy. From bergamot Indena produces VAZGUARD®, a standardized extract formulated with the Indena Phytosome™ to optimize the usually poor biological absorption of polyphenols, in the production of VAZGUARD®, only bergamot from a very small and specific part of the southern Italian region Calabria is used and its phytochemical composition is extensively characterized to make VAZGUARD® retain the same, unique phytochemical profile of the natural bergamot juice, foodstuff acknowledged for its health benefits.

The scientific community has been evidencing the marked antioxidant activity and the interesting well-being potential of bergamot fruit, due to its characteristic pattern almost unique in nature of polyphenols<sup>8</sup>; In fact bergamot natural flavonoids differ for a higher grade of hydroxylation compared to the other citrus flavonoids and this boosts their bioactivity, increasing anti-oxidant properties by orders of magnitude.

Bergamot is called "the green gold" for cardiovascular health: its unique composition revealed promising antioxidant, hypoglycemic and hypolipidemic activities, producing positive effects in modulating the metabolic response and promoting cardiovascular wellbeing.

This is of particular interest considering that over a billion people in the world are estimated to be affected with MetS (9), a group of risk factors that raises the chance for cardiovascular disease, including heart problems, diabetes and stroke.



One of the five risk factors of Metabolic Syndrome (MetS) is Visceral Adipose Tissue (VAT). Human body has different type of fats, which are Brown Adipose Tissue (BAT), the "good" fat; Subcutaneous Adipose Tissue (SAT), the "ugly" one; Visceral Adipose Tissue (VAT), the "bad" one: this is localized intra- abdominally, adjacent to internal organs, is highly metabolically active, constantly releasing substances and contributes to metabolic syndrome.

According to this, as far as metabolism is concerned, fat distribution can be even more important than fat quantity: while having same BMI and, consequently, same characterization of obesity, two persons might be metabolically different. The one with more VAT is more prone to health issues including insulin resistance, dysglycaemia, dyslipidemia, systemic inflammation and liver dysfunction.

Clinical evidences<sup>10</sup> show that VAZGUARD® provides remarkable beneficial effects such as rebalance of VAT physiological levels and modulation of metabolic response after just 30 days of supplementation. These effects remain stable afterwards, thus resulting in a very promising agent for protection of cardiovascular health.

Going deeper on the study results, the main outcomes show that VAZGUARD®:

- has a significant effect on visceral adipose tissue (VAT) level already after 30 days (- 12.4 % vs t0), and it is active on visceral fat independently from body weight loss;

- is effective in positively modulating parameters of insulin- resistance: controlling VAT means indeed to control insulin levels thus tackling insulin-resistance, which is a key parameter for the diagnosis of metabolic syndrome and primes the organism for type II diabetes and cardiovascular diseases;
- is effective in remodeling the ratio between bad and good cholesterol;
- induces a fine modulation of apolipoproteins. The ratio ApoB/ApoA (i.e. LDL & larger particles vs HDL particles) has a stronger correlation with myocardial infarction event rates: the lower is the ratio, the lower is the cardiovascular risk. VAZGUARD® successfully maintains ApoB/ApoA in a favourable ratio (-4.8%) after 30 days (vs + 3.5% of placebo);
- is effective in favourably levelling biomarkers of liver function. Liver is a major target for substances released by visceral fat in the portal circulation, including inflammatory cytokines (adipokines) and free fatty acids (FFA). That's why optimizing VAT means to improve liver function.

While a right lifestyle is the main way to maintain metabolism balanced, botanical extracts may be an effective, natural help. The quality and the scientifically proven efficacy of Indena's berberine and bergamot extracts formulated with Indena Phytosome™, make BERBEVIS® and VAZGUARD® very powerful, innovative, safe products to support one of the most important current challenges for human health.

#### References:

- 1 Chander, Vikas, et al., The Journal of Phytopharmacology 6.1 (2017): 53-58.
- 2 Feng, Xiaojun, et al., Theranostics 9.7 (2019): 1923.
- 3 Kong, Wei-Jia, et al., Pharmacology & therapeutics 209 (2020): 107496.
- 4 Ma, Bing-Liang, et al., Scientific reports 6.1 (2016): 1-11.
- 5 Petrangolini et al., Evidence-Based Complementary and Alternative Medicine (2021): 2021: ID 7563889.
- 6 Rondanelli, M., et al. "Berberine phospholipid exerts a positive effect on the glycemic profile of overweight subjects with impaired fasting blood glucose (IFG): a randomized double-blind placebo-controlled clinical trial." *European Review for Medical and Pharmacological Sciences* 27 (2023): 6718-6727.
- 7 Cesarone, Maria R., et al. "Borderline hyperlipidemia preventive management with Berberine PL in asymptomatic prevention of early atherosclerosis." *Minerva Gastroenterology* (2023).
- 8 Rapisarda A, Germanò MP, "Citrus bergamia risso and poiteau botanical classification, morphology and anatomy", in: G. Dugo, I. Bonaccorsi (Eds.), *Citrus Bergamia: Bergamot and Its Derivatives*, CRCPress, BocaRaton, FL, 2013, pp. 592.
- 9 Saklayen, Mohammad G. "The global epidemic of the metabolic syndrome." *Current hypertension reports* 20.2 (2018): 12. [https:// www.metabolicsyndrome-canada.ca/about- metabolic-syndrome - accessed on April 2021](https://www.metabolicsyndrome-canada.ca/about- metabolic-syndrome - accessed on April 2021).
- 10 Rondanelli, Mariangela, et al. "Bergamot phytosome improved visceral fat and plasma lipid profiles in overweight and obese class I subject with mild hypercholesterolemia: A randomized placebo controlled trial." *Phytotherapy Research* (2020).



SCIENCE IS OUR NATURE. SINCE 1921

[www.indena.com](http://www.indena.com)