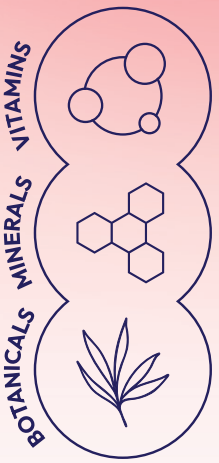
Evera®
NUTRITION

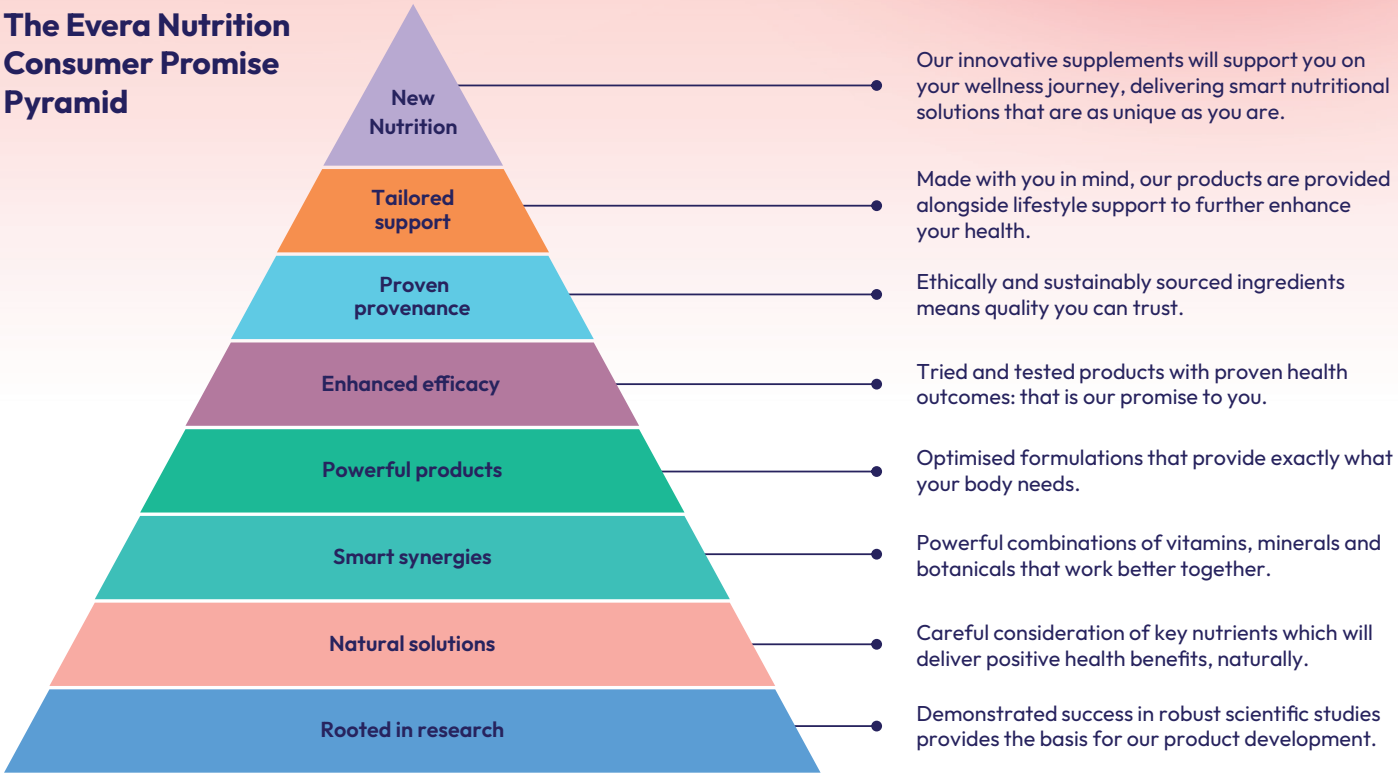
Your Health Redefined

INNER BEAUTY



As the population is becoming an ageing society and the living standards are improving, there is now a growing interest in the topic of ageing among modern societies as they seek to understand and counter the adverse effects of ageing.

The Evera Nutrition Consumer Promise Pyramid



Delivering innovation in supplementation

Evera® NUTRITION

One of the most prominent features of ageing is skin ageing, which is of particular concern to women. The main characteristics of skin ageing are skin sagging and wrinkles, which are related to skin cell ageing and decreased collagen synthesis or increased degradation (1). The causes of skin ageing can be divided into endogenous and exogenous factors. Endogenous factors mainly involve the accumulation of time and the influence of related physiological traits, while exogenous factors mainly include ultraviolet radiation, smoking, wind exposure, and exposure to harmful chemicals (2).

Mechanisms of Skin Ageing Processes

At present, classic theories on the mechanism of skin ageing include four theories: free radicals and oxidative stress, inflammatory ageing, skin photoageing, and nonenzymatic glycosyl chemistry (3).

Free Radicals and Oxidative Stress Theory

Free radicals are one of the main causes of decreased body function and skin ageing (4). Reactive Oxygen Species (ROS) are a type of unstable molecule that contain oxygen and that easily react with other molecules in a cell and cause oxidative stress. When there is too much ROS in cells, the mitochondria will be damaged, the production of mitochondrial ATP (the source of energy for the cell) is reduced, and a chain reaction is generated that accelerates ageing (5).

A significant increase in these ROS levels not only accelerates skin replication ageing but also promotes a decrease in the collagen levels in skin tissue, leading to skin relaxation and wrinkles (6). The molecular mechanism is related to the increase in compounds known as Matrix Metallopeptidases (MMPs). MMPs can specifically degrade the extracellular matrix, including collagen, and can cause damage which ultimately leads to skin ageing (7). Consequently, removing excess ROS from the skin cells has become one of the most common ways to combat skin ageing.

Inflammation Theory

Inflammation is one of the major causes of cellular senescence (8). Senescent cells are cells that have permanently stopped dividing but haven't died. They are sometimes referred to as "zombie cells" due to their ability to persist in the body without dividing or dying (8). "Inflammatory ageing" is characterised by increased levels in the proinflammatory factors in the body. These changes will lead to the ageing of body cells, including the skin, and induce many ageing diseases (9).

At the skin level, fibroblasts (cells which contribute to connective tissue and secrete collagen proteins) and keratinocytes (cells that form the outer layer of the skin) can become senescent and stop doing their jobs (10). They secrete a large number of "senescence associated secretory phenotypes (SASP)", including proinflammatory cytokines and MMPs (11). These pro-inflammatory cytokines stimulate skin cell senescence by promoting the production of ROS and activating various signalling pathways (12). Although senescence is primarily activated to protect the skin from insults, senescent cells in the skin accumulate with ageing, promoting tissue dysfunction through SASP, which in turn induces further senescence in neighbouring cells. It is an ongoing process.

Interestingly, evidence shows that skin ageing mirrors and predicts the age-related dysfunction of other organs, suggesting that senescent skin contributes to accelerating ageing of other tissues (13). Inhibiting skin cell inflammation is, therefore, one of the most important strategies to control skin cell ageing.

Photoageing Theory

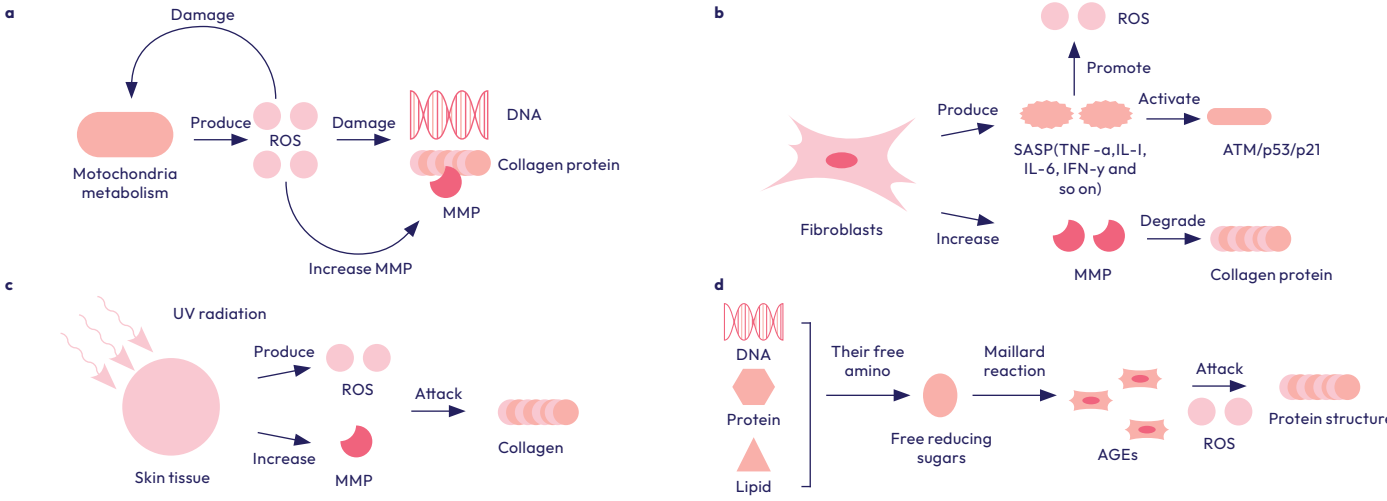
Ultraviolet (UV) light such as that emitted by the sun leads to the production of ROS and the secretion of MMPs. Long term exposure to solar UV radiation will cause photoageing, which will affect skin pigmentation, immunity, and the vascular system (14). Adult dermal collagen content decreases every year, and this decrease in collagen is mainly caused by the increase in MMPs and the decrease in collagen synthesis (15). With an increase in age, the level of MMPs increases, while procollagen mRNA decreases significantly, which leads to a decrease in dermal collagen content (16). This decrease can lead to visible changes to the skin structure including wrinkles and a loss of elasticity.

Significant evidence has proved that MMPs play a major role in the onset of photoageing (17). Exposure to UV radiation stimulates keratinocytes and fibroblasts to secrete MMPs, which in turn degrade important skin components such as collagen. Limiting exposure to UV radiation is another important strategy to prevent skin cell ageing.

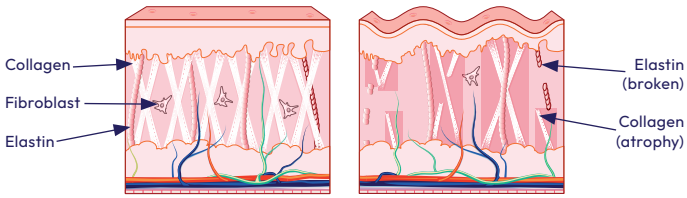
Nonenzymatic Glycosyl Chemistry Theory

Nonenzymatic glycosylation (known as a "Maillard" reaction) also plays a very important role in skin cell ageing (18). According to this theory, the damage to proteins caused by glycosylation is the main reason for ageing. Glycosylation is a nonenzymatic reaction between free reducing sugars and free amino groups of proteins, DNA, and lipids, which produces compounds called Advanced Glycation End-products (AGEs). The accumulation of AGEs affects cellular stability and causes protein structure changes, leading to skin darkening and skin ageing (19). The accumulation of AGEs also leads to ROS production and inflammation, thus accelerating skin ageing (20). Moreover, skin cells age more rapidly when there are higher levels of glycation. The formation of AGEs is irreversible, hence inhibiting skin glycosylation is also one of the important ways to control skin ageing (21).

How the Mechanisms of Skin Ageing Exert Their Effects



Mechanisms of skin aging processes. (a) Free radicals and oxidative stress theory. Mitochondria produce ROS through oxidative metabolism. Excessive ROS can damage the mitochondrial and DNA structures, leading to a decrease in collagen levels and an increase in MMP levels in skin tissue. (b) Inflammation theory. Senescent fibroblasts and keratinocytes secrete a large number of senescence-associated secretory phenotypes, including TNF-a, IL-1, IL-6, IFN-y and MMPs. These proinflammatory cytokines induce skin cell senescence by promoting ROS production and activating the ATM/ p53/p21-signaling pathway. (c) Photoaging theory. Ultraviolet irradiation induces the production of ROS and the secretion of MMPs, which degrades skin extracellular matrix components such as collagen. (d) Nonenzymatic glycosyl chemistry theory. Non-enzymatic glycosylation is a reaction between free reducing sugars and free amino groups of proteins, DNA and lipids to produce AGEs and ROS. The accumulation of AGEs, together with ROS, can lead to changes in the cell homeostasis and protein structure.



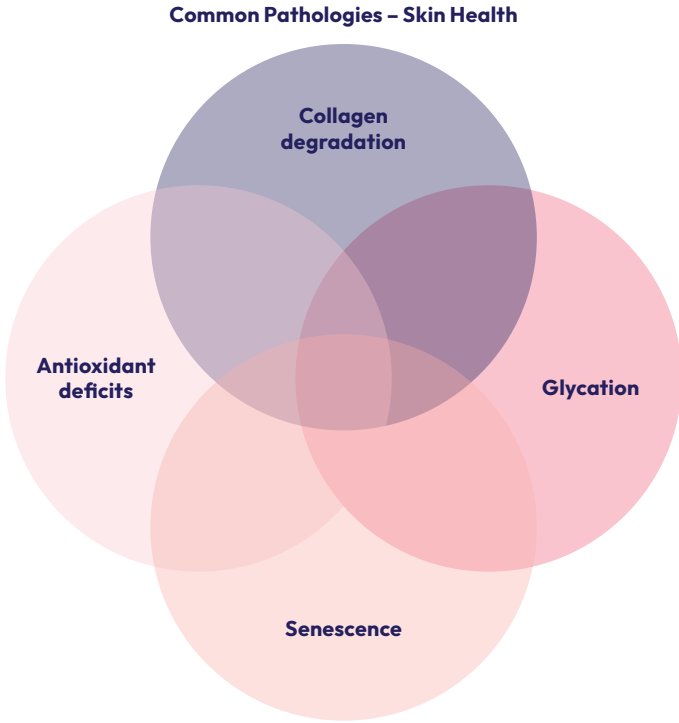
How Evera Inner Beauty Delivers More Youthful-Looking Skin

At Evera Nutrition we realise that the issues which might impact upon ageing skin are complex and vary from individual to individual. Our team of scientists has reviewed the scientific literature to identify the most common causes and created a formulation that uses specific ingredients that work together synergistically to address the most likely causes and deliver efficacy in the most natural way.

The Evera Inner Beauty Formulation

Ingredient	Amount per 13g serving	% NRV*
Vitamin A	800mcg RE	100
Vitamin D	10mcg	100
Vitamin E	12mg αTE	200
Vitamin K2	75mcg	100
Vitamin C	80mg	100
Vitamin B1 (Thiamine)	1.1mg	100
Vitamin B2 (Riboflavin)	1.4mg	100
Vitamin B3 (Nicotinamide)	16mg NE	100
Vitamin B5 (Calcium Pantothenate)	6mg	100
Vitamin B6 (Pyridoxal-5 Phosphate)	1.4mg	100
Folic Acid (5-methyltetrahydrofolate)	200mcg	100
Vitamin B12 (methylcobalamin)	2.5mcg	100
Biotin	50mcg	100
Zinc	10mg	100
Selenium	55mcg	100
Copper	1mg	100
Manganese	2mg	100
Iodine	150mcg	100
CoQ10	10mg	**
Resveratrol	25mg	**
Astaxanthin	2mg	**
Carnitine Tartrate	100mg	**
Collagen Peptides	10,000mg	**
Hyaluronic Acid	75mg	**
Evera AGEs Control Botanical Fusion™: Consisting of standardised extracts of Curcumin; Maritime Pine Bark; Green Tea; Grapeseed; Milk Thistle; Ecklonia Cava Seaweed; Grapefruit; Chamomile	Equivalent to 5315mg of natural botanicals	**

Inner Beauty Addresses the Most Frequent Common Issues of Ageing Skin



Collagen Support: Vitamins A, C, and E, Co Q 10, Carnitine, Collagen, and Hyaluronic acid (22-28). Collagen is the most abundant protein in the body and forms the basis of hair, skin and nails, as well as bones, tendons and cartilage.

Antiglycation Actives: B Vitamins, Vitamin C, selenium, manganese, Co Enzyme Q10, astaxanthin, carnitine, resveratrol, and specific extracts of Maritime Pine Bark, Milk Thistle, Ecklonia kava, Grapeseed, Green Tea, Curcumin, Chamomile and Grapefruit all have potent anti-AGEs activity (29-44). In addition, there is clinical evidence to demonstrate that they also deliver specific benefits to improve parameters of skin function such as hydration, elasticity and trans epidermal water loss which all contribute to healthier and younger-looking skin (45).

Senolytics: B Vitamins, Vitamin C, Vitamin K, selenium, manganese, Co Enzyme Q10, astaxanthin, carnitine, resveratrol, Curcumin, and Green Tea (46-56). Senolytics help eliminate senescent cells.

Antioxidant Nutrients: Vitamins and minerals, Green Tea, Co Enzyme Q10, astaxanthin, resveratrol, Chamomile, and Grapeseed extract (57-63). Antioxidants protect the body from free radicals.

Although all of the ingredients in Inner Beauty have been investigated in numerous high-quality clinical studies, the robustness of efficacy is further demonstrated by the outcomes of the systematic reviews and meta-analyses right:

Ingredient	Studies	Participants	Outcomes
Collagen	26	1721	Significantly improved skin hydration and suggests positive effects on skin health (64).
Collagen	19	1125	Favourable results for skin hydration, elasticity, and wrinkles (65)
Collagen	10	609	Remarkable effects on skin hydration (66)
Hyaluronic acid (HA)	7	196	Remarkable effects on skin hydration (66)
Procyanidins/ Green tea polyphenols	6	308	Procyanidins significantly improves-tratum corneum water content. Green tea polyphenols gave a positive effect on decreasing TEWL (66)
Astaxanthin	6	159	Significant effect on improving skin hydration (66)
Astaxanthin	9	185	Significantly restored moisture content and improved elasticity (67)
Collagen	5	309	Numerous clinical trials show they can mitigate some signs of skin aging (68)
Hyaluronic acid	5	272	
Co Enzyme Q 10	34	2012	Statistically significant support for attenuating oxidative stress status in adults (69)
Green Tea catechins	6	100	Highly effective for low-intensity ultraviolet radiation-induced erythema response (70)
Natural fruit extracts	7	341	Significantly enhance skin hydration and reduce TEWL(71)
Resveratrol	Umbrella meta analysis	15 meta analyses	The umbrella meta-analysis supports the alleviating effects of resveratrol on inflammatory markers (72)

Why Recommend Inner Beauty?

Inner Beauty can help to combat signs of aging from within by:

Addressing skin aging issues: The accumulation of AGEs and senescent cells which accelerate skin aging are combatted with ingredients proven to address these issues (73).

Reaching Deeper Skin Layers: Oral supplements can reach deeper layers than topical products, improving skin structure, elasticity, and hydration from within (74).

Targeting Specific Concerns: Collagen peptides, hyaluronic acid, and antioxidants target wrinkles, loss of elasticity, and uneven skin tone (75).

Boosting Antioxidant Defence: Oral antioxidant supplements help combat free radicals and protect against skin damage (76).

Enhancing Collagen Production: Oral collagen peptides, hyaluronic acid and other nutrients support collagen synthesis, improving skin firmness and reducing the appearance of wrinkles (77).

Improving Skin Hydration: Supplements can help retain moisture in the skin, contributing to a plumper, more hydrated appearance (78).

Supporting Overall Skin Health: Certain vitamins, minerals and botanicals work together to support barrier function, reduce inflammation, and promote cell regeneration (79). (References available upon request)

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