Hydrolysed Collagen Peptides Clinical Data

Skin barrier function

The skin is the largest organ of the human body, serving as a vital protective barrier between the internal organs and the external environment. It consists of multiple layers, including the epidermis, dermis, and subcutaneous tissue, each with distinct functions. The skin plays a vital role in regulating body temperature and pH, regulating sebum, housing a community of balanced microbes, protecting against pathogens and harmful substances, and sensing touch, pressure, and pain. Additionally, it is responsible for synthesising vitamin D when exposed to UVB sunlight and is crucial for regulating water balance (1).

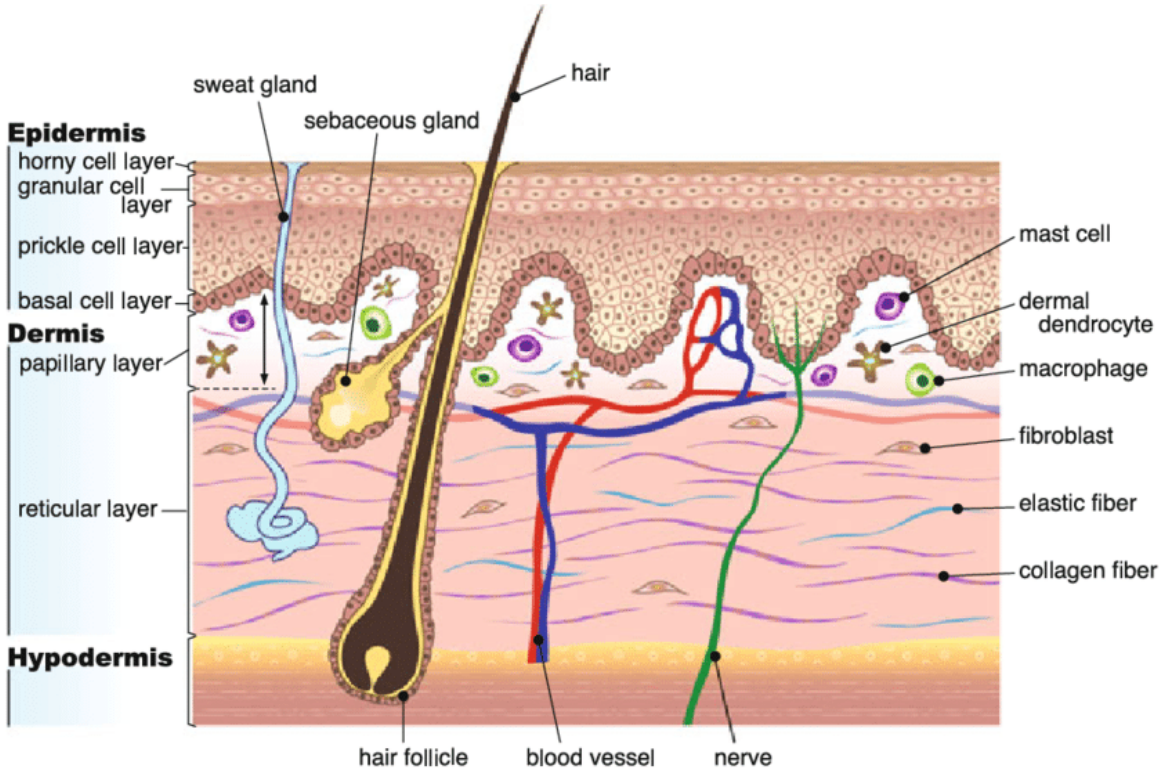


Figure 1: Skin anatomy (2)

Barrier overview

The skin barrier is comprised of a complex outer layer called the epidermis. The outermost protective horny layer is called the Stratum corneum: This is the outermost layer of the epidermis and serves as the primary barrier against external factors such as pathogens, pollutants, and solar radiation. The stratum corneum consists of structural proteins and lipids:

I. Stratum corneum Lipids: Lipids, including ceramides, cholesterol, and fatty acids, form a protective lipid barrier within the stratum corneum, helping to prevent water loss and maintain hydration levels.

II. Stratum Corneum Proteins:

(a) Keratin providing strength and integrity to the skin barrier

(b) Filaggrin, playing a role in organising keratin and contributing to the NMF (natural moisture factor) Natural moisturizing factors (NMFs): NMFs, such as amino acids and urea, help to retain water within the skin and contribute to its overall hydration.

(c) Involucrin which contributes to forming the strong outer wall of the corneocytes.

(d) Corneodesmosomes, no single simple proteins themselves but specialised cell structures composed of multiple proteins that connect the keratinocytes in the stratum corneum. They are a type of desmosome that has been modified to function in the outermost layer of the skin. They are protective but also degrade to allow for natural shedding of dead skin cells.

Below the stratum corneum, the epidermis consists of three main layers:

I. Stratum granulosum: This layer is characterized by the presence of granules filled with keratin, a protein that provides strength and structure to the skin. Keratinocytes in this layer also produce lipids that help form the skin's protective barrier.

II. Stratum spinosum: This layer contains keratinocytes that are connected by desmosomes, which give the cells a spiny appearance. This layer also houses Langerhans cells, which are immune cells that help protect the skin from infection.

III. Stratum basale: This is the deepest layer of the epidermis. It contains keratinocytes, melanocytes (which produce melanin, the pigment that gives skin its colour), and Merkel cells (which are touch receptors). This layer is responsible for cell renewal and the production of new keratinocytes.

Below the epidermis, is the dermal layer and the Extracellular Matrix (ECM):

The extracellular matrix, which includes proteins like collagen and elastin as well as hyaluronic acid to provide structural support to the skin and helps maintain its elasticity, firmness and hydration (10).

By protecting the skin from environmental stressors like pollution, UV radiation, and irritants, the skin barrier helps prevent damage, sensitivity, and inflammation. Additionally, the barrier's ability to retain water is essential for keeping the skin hydrated, plump, and youthful in appearance. The skin barrier also facilitates the transport of essential nutrients to nourish the skin. When the barrier is compromised, it can lead to a range of issues, including dryness, flakiness, and accelerated signs of ageing and has been identified in conditions like acne, psoriasis, and atopic dermatitis. Maintaining the integrity of the skin barrier is, therefore, paramount for preserving the skin's overall health, function, and resilience against external challenges (10).

Maintaining optimal skin structure, barrier integrity and hydration is crucial for promoting skin health and appearance. The skin is susceptible to various forms of damage, including inflammatory conditions like acne, eczema, atopic dermatitis, rosacea and hyperpigmentation. Solar radiation, pollutants, microbiome imbalance, harmful chemicals and oxidative damage all contribute to inflammation and negative skin conditions.

Studies indicate that specific nutrients can assist in enhancing cellular regeneration in skin by strengthening connective tissue and increasing hydration, thereby enhancing the integrity of healthy skin. VERISOL® collagen peptides have been proven effective in clinical trials in supporting collagen synthesis, preserving the skin's structural integrity and elasticity (3), reducing fine lines and wrinkles (4) and reducing cellulite (5).

Collagen explained

Collagen is the most abundant protein in the human body, making up 25-35% of the whole-body protein content. It is the main structural protein providing strength and structure and is found in the extracellular matrix of various connective tissues, such as skin, bones, tendons, ligaments, and cartilage.

Collagen consists of amino acid building blocks bound together to form a triple helix structure known as a collagen helix. Collagen has great tensile strength and can be put under significant tension without breaking.

Compared to other proteins, collagen has a unique amino acid composition rich in the modified amino acid **hydroxyproline** (12%), **glycine** (22%) and **proline** (13%). There are 28 different types of collagen, but the most common ones are types I, II, and III:

- **Type I collagen:** This is the most plentiful type, making up about 90% of the collagen in your body. It's found in skin, bones, tendons, and organs.
- **Type II collagen:** This type is found in cartilage, which cushions your joints.
- **Type III collagen:** This type supports the structure of your skin, muscles, organs, and blood vessels (6)

Collagen plays a pivotal role in maintaining supple skin, lustrous hair, and resilient fingernails, flexible joints, stable bones, healthy muscles, and resilient ligaments and tendons. As one of the main structural proteins in connective tissues, it is also plentiful in blood vessel walls, intervertebral discs, the blood-brain barrier, the cornea, tooth dentin, and the intestinal wall. Its presence is indispensable for the overall health and integrity of the entire body (6).

VERISOL® collagen peptides

Collagen is an essential component of healthy, youthful skin, comprising of 80 % of the dry weight, providing structure by supporting skin elasticity and firmness (4). Collagen Peptides are functional short chains of amino acids produced by the simple hydrolysis of collagen protein and are characterised by their molecular weight distribution profile and high bioavailability to cross the intestinal wall. These are pure sources of collagen protein amino acids and peptides that are rapidly digested and fully utilised by the body (7).

VERISOL® is a bovine source of type I and III collagen containing Bioactive Collagen Peptides® (BCP) and uses an enzymatic hydrolysis process to produce BCPs from the parent collagen protein. The BCPs include a range of specific polypeptides of optimal molecular weight, containing circa 20-50 amino acid residues, which corresponds to a bioavailable 2kDa (KiloDaltons) in size.

When ingested orally, VERISOL® offers extremely high bioavailability, and is absorbed and distributed through the blood stream where it reaches the target cells, including fibroblasts in the dermal layer of the skin. The collagen peptides stimulate the fibroblast cells via receptor interaction to produce more extra cellular matrix substances, including collagen. Research demonstrates that the VERISOL® collagen peptides boost the production of collagen, elastin, and hyaluronic acid glycosaminoglycans within the dermal layer, leading to decreased wrinkles and enhanced skin elasticity and hydration (6).

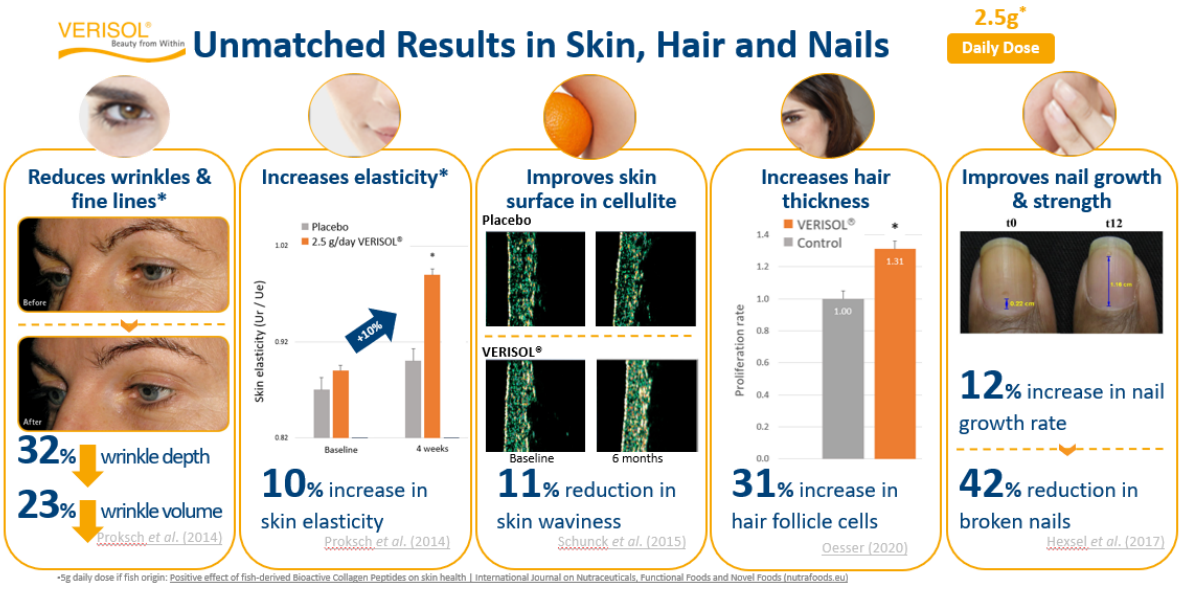
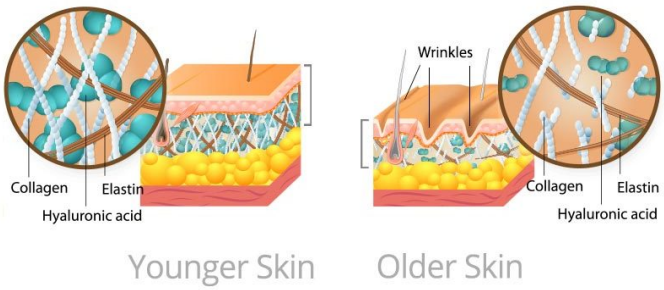


Figure 2: VERISOL® clinical improvement in skin, hair and nails (6).

Collagen peptides and skin ageing

Skin ageing is a complex process that involves both intrinsic and extrinsic factors. As one ages chronologically (intrinsic ageing), the body's natural ability to replenish collagen diminishes at a rate of approximately 1.5% per year from the age of 30 years. This decline results in a reduction of type I collagen, the primary and most abundant collagen in skin, and a decrease in the density of collagen and elastin within the dermis. Consequently, the skin becomes thinner and loses firmness and elasticity. Additionally, normal ageing involves a reduction in hyaluronic acid levels, leading to decreased moisture, volume and suppleness. All these factors contribute to visible skin ageing and the formation of fine lines and wrinkles (8).

Extrinsic ageing describes the accelerated deterioration of the skin caused by external, environmental factors such as sun exposure, smoking, pollution, and lifestyle choices. Extrinsically aged skin is characterised by wrinkles, fine lines, age spots, uneven pigmentation, loss of elasticity, hydration, dryness and loss of optimal texture. Sun exposure and environmental stressors lead to oxidative damage in the skin which can trigger the production of matrix metalloproteinases (MMPs). These MMP's break down collagen and elastin within the dermal layer leading to premature ageing. Approximately, 80% of the observable signs of skin ageing may stem from exposure to solar radiation (9).



In vivo studies: wrinkle reduction and skin elasticity

1. Placebo-controlled human study. 114 women aged between 45 and 65 years evaluated the effects of oral intake of specific VERISOL® Bioactive Collagen Peptides (BCP) on skin wrinkles and synthesis of dermal matrix proteins.

   Results:

- Oral administration of VERISOL® (2.5 g/day) led to a statistically significant reduction in eye wrinkle volume by 20% compared to the placebo group, after both 4 and 8 weeks of supplementation.
- The positive effect on wrinkle reduction persisted for 4 weeks after the last intake, indicating a long-lasting benefit.
- After 8 weeks of BCP supplementation, there was a statistically significant increase in the content of procollagen type I (65%) and elastin (18%) in the skin, compared to the placebo group.
- For fibrillin, a 6% increase was observed in the BCP group, but this effect did not reach statistical significance (4).

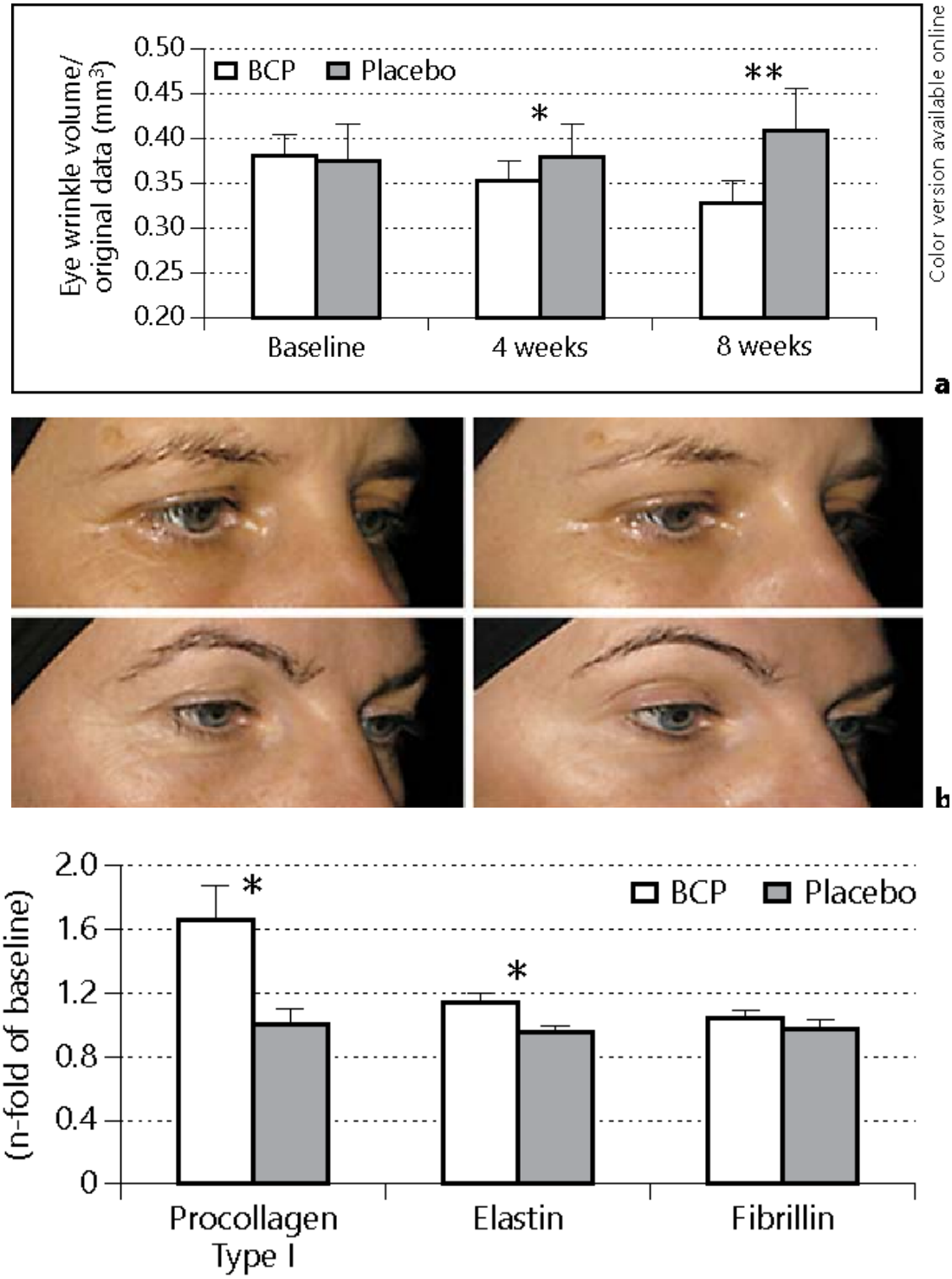


Figure 3: Oral Intake of Specific Bioactive Collagen Peptides Reduces Skin Wrinkles and Increases Dermal Matrix Synthesis (4).

2. Double-blind, placebo controlled human study evaluating the effectiveness of VERISOL® collagen peptides on skin biophysical parameters related to visible cutaneous ageing (wrinkles, sagging skin, age spots, and decreased elasticity). 69 women aged 35-55 years were randomised to receive 2.5 g or 5.0 g of VERISOL® or placebo once daily for 8 weeks.

Results:

VERISOL® lead to significantly higher skin elasticity compared to placebo. In some women, a maximum increase of skin elasticity up to +30% was observed after 8 weeks.

Subgroup analysis revealed increased skin hydration by +11% to 14% in women > 50 years old (3).

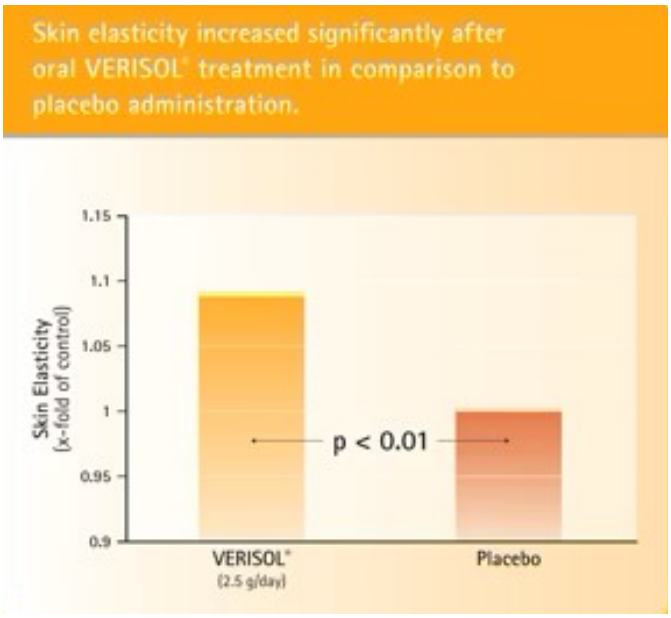


Figure 4: VERISOL® dosage of 2.5g/day leads to significantly higher skin elasticity (3).

3. Summary and meta-analysis study to summarise the evidence on the effects of hydrolysed collagen on human skin. Systematic review and analysis of clinical trials focusing on collagen peptide supplementation and its impact on the process of skin ageing.

   Meta-analysis:

   19 randomised, double-blind controlled studies were selected. Total of 1,125 participants aged between 20 and 70 years (95% women).

   Results of a grouped analysis of studies:

   Favourable results of hydrolysed collagen supplementation compared with placebo in terms of skin hydration, elasticity, and wrinkles. The findings of improved hydration and elasticity were also confirmed in the subgroup meta-analysis.

   Based on these results, ingestion of hydrolysed collagen peptides for 90 days is effective in reducing skin aging, via reducing wrinkles, improves skin elasticity and increasing hydration (13).

In-vivo studies: Collagen peptides and hydration, barrier integrity, density and elasticity.

1. A systematic review and meta-analysis of 26 randomised controlled trials to assess the effects of oral hydrolysed collagen supplementation on skin hydration and elasticity.

With a total of 1,721 patients trialled, the meta-analysis found that oral hydrolysed collagen supplementation significantly improved skin hydration ($p < 0.00001$) and elasticity ($p < 0.00001$) compared to the placebo group.

These findings revealed that supplementation with hydrolysed collagen improves skin elasticity, which are consistent with previous clinical findings. In addition, they concluded that long-term use of hydrolysed collagen yields more favourable effects on skin hydration and elasticity than the short-term use of collagen peptides (11).

2. A randomised, placebo-controlled, double-blind study on 72 females evaluated the effects of a 2.5 g of collagen peptides, vitamin C (acerola fruit extract), zinc, biotin, and a native vitamin E complex on skin hydration, elasticity, roughness, and density.

   Results showed that mean skin hydration was significantly increased by 28.0% ± 11.5% (44.5 ± 4.4 AU vs. 36.6 ± 5.7 AU, $p < 0.0001$). The final measurements at 16 weeks showed that the positive effects persisted for some time.

   After four weeks without further supplementation of the collagen peptide test product, skin hydration, elasticity, roughness, and density all showed a significant improvement in comparison to the initial baseline reading. (8).

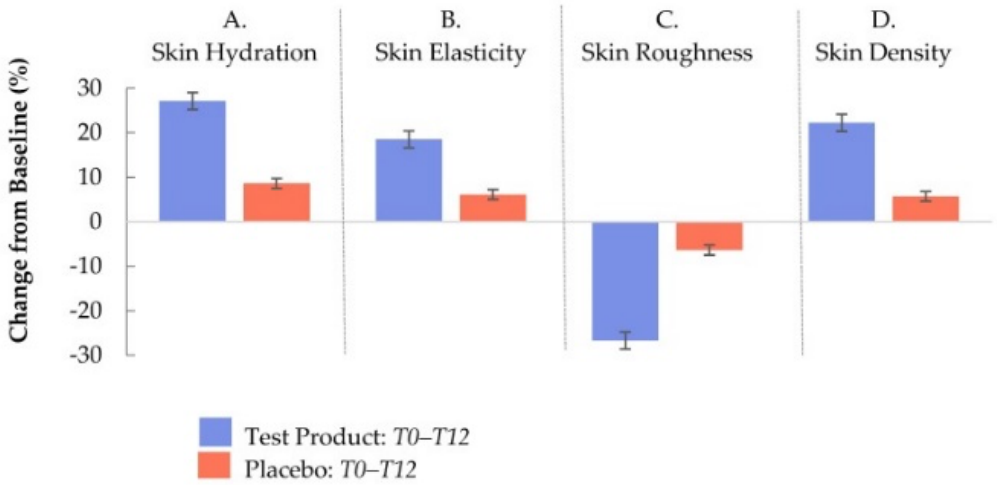


Figure 5: Percentage change of skin parameters between the baseline and the end of the twelve-week interventional period (8).

Collagen peptides and cellulite reduction

Cellulite, which affects a significant portion of post-pubertal females, is characterised by a less dense connective tissue framework, allowing adipose tissue to protrude into the dermis creating a dimpling effect. This results in reduced skin elasticity and thinning of the dermal layer, and weakened connective tissue plays a significant role in the development of cellulite.

Occurring in 80% to 90% of females, mostly on the thighs, buttocks, and hips, it is associated with profound negative psychosocial and quality of life issues. Collagen peptides work by stimulating the production of new collagen fibres, thereby improving the structural integrity of the dermis and subcutaneous tissues. This increased density and strength of the connective tissue help to smooth out the skin's surface, reducing the visibility of celluite (12).

In-Vivo clinical trial:

A randomised controlled trial (RCT) investigated the effects of 2.5 g/day of VERISOL® collagen peptides for six months in a group of 97 females with cellulite.

In women with a normal body mass index (BMI <25), cellulite scores decreased by 9% compared to placebo. In overweight women (BMI >25) cellulite scored reduced by 4%.16

Skin Waviness (a measure of skin surface profile) reduced by 11.1% in those with a BMI <25 and 3.6% in BMI >25.

Collagen peptides and fingernail growth

Many experience issues with the growth and appearance of fingernails such as cracked or chipped nails, as well as peeling and roughness. Bioactive Collagen Peptides in VERISOL® can help enhance the growth and health of fingernails.

Human in-vivo trial: An open-label, single-centre trial evaluated the effects of daily oral supplementation with 2.5g of specific bioactive collagen peptides (VERISOL®) for 24 weeks in 25 participants with brittle nails.

Results:

1. A significant decrease of cracked and/or chipped nails, reaching a decrease of 42% after 6 months.
2. The speed of nail growth significantly increased by 10% after 6 months of VERISOL® supplementation.
3. Nail peeling was notably reduced.
4. Nail edge irregularity was clearly reduced.
5. 80% of participants were satisfied with the performance of the VERISOL® regimen.
6. 75% of participants perceived their nails as stronger.
7. 71% felt that their nails were growing faster and longer (15).

Collagen peptides and hair growth

Collagen peptides may promote hair growth by providing essential amino acids that support the production of keratin, the main protein that makes up hair.

Human in-vivo trial:

A randomised, placebo-controlled study investigated the effects of VERISOL® on hair thickness. The study was conducted in 44 women aged between 39 and 75 years, who supplemented with 2.5 g VERISOL® daily or placebo for 16 weeks.

Results:

VERISOL® collagen peptides led to a statistically significant increase in hair thickness, with a slight decrease observed in the placebo group. The study confirming the benefits of VERISOL® for improved hair structure (16).

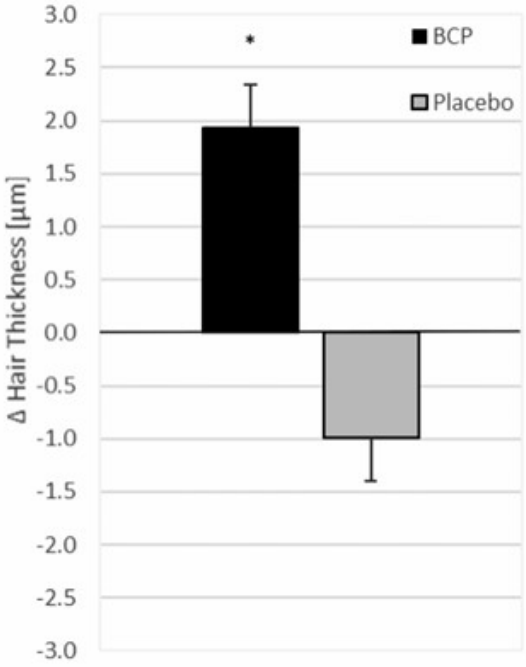


Figure 6: Changes in hair thickness after BCP treatment compared with placebo. Data represent the mean + SE for n = 22. *p<0.01 (16).

Collagen peptides and gut support

Increased intestinal permeability is a condition where the tight junctions between intestinal cells open, allowing substances leaking into the bloodstream which can result in elevated blood endotoxin levels. In a healthy gut, these cells allow low molecular weight substances in but prevents harmful substances from passing through. This can trigger inflammation and lead to digestive issues such as bloating, diarrhea, constipation, increased gas, nausea, and abdominal pain. It can also impact the hormonal, immune, nervous, respiratory and reproductive systems. Interestingly, intense exercise can also negatively impact the gut.

In-vivo study:

A randomised, controlled trial evaluated the impact of collagen peptide supplementation on gastrointestinal (GI) stress caused by exercise.

Results:

The study concluded that those in the collagen peptide group experienced a significant reduction in GI symptoms, such as bloating and cramping, and showed lower levels of biomarkers associated with GI damage and inflammation compared to the placebo group. These results suggest that collagen peptides can effectively mitigate exercise-induced GI stress (17).

In-vivo human trial:

Evaluation of the impact of daily collagen peptide supplementation on digestive symptoms.

Results:

The results showed that daily supplementation with collagen peptides significantly improved digestive symptoms, with participants also reporting enhanced digestive comfort and reduced bloating (18).

Collagen peptides improve sleep and cognition

In-vivo 2023 human trial:

A randomised controlled trial aimed to assess the effects of collagen peptide supplementation on sleep quality and cognitive function in physically active males experiencing sleep issues.

Results:

Supplementation with collagen peptides led to reduced sleep fragmentation and improved cognitive function (19).

Overview

Collagen, a primary structural protein found abundantly in the skin and other connective tissues, is vital for maintaining skin health and integrity.

VERISOL® collagen peptides used in SynTernals ProCollagen-C are highlighted for their ability to enhance collagen synthesis, reduce fine lines, wrinkles, and cellulite, and improve skin hydration and elasticity. Additionally, studies demonstrate collagen peptides' potential to support nail and hair growth. Beyond skin health, collagen peptides are suggested to alleviate gastrointestinal symptoms and improve sleep quality and cognitive function in physically active individuals with sleep issues.

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