HIGH COLLAGEN Vegan Boost®

Stimulates the body's own collagen production

Scientific report on VeCollal®

Abstract

VeCollal® is the first science-based vegan alternative to animal collagen.
The underlying principles and science are described in this summary

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Collagen Type I: basic science

Collagen type I is the most abundant collagen present in skin, tendons, vasculature, as well as the organic portion of the calcified tissue of bone and teeth.

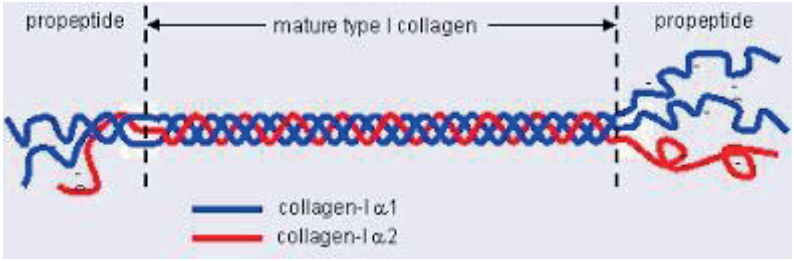
Type I collagen molecules consist of two α1 chains and one α2 chain, which are encoded by two different genes located on different chromosomes (chromosomes 17 and 7 in humans, respectively). These chains are synthesized in a 2:1 ratio, and they undergo extensive post- traductional modifications before assembling in a characteristic triple helix. Despite the fact that type I collagen is present in most organs, it is synthesized only by a small number of discrete cell types, including fibroblasts, osteoblasts, and odontoblasts [3].

The abundance of collagen in animal systems, and particularly the fibrillar collagen type I, owes primarily to the unique mechanical and physiological characteristics, including thermal and chemical stability, mechanical strength, and physiological interactions. These parameters are derived from the complexity of the molecular and fibrillar structure at secondary, tertiary, and quaternary levels of protein organization. At both the secondary and tertiary level, intermolecular and intramolecular forces also promote stability. Left-handed α-chains are stabilized by interstrand hydrogen bonding, whereas the tertiary triple helix is stabilized by intra-strand $n \rightarrow \pi^*$ interactions. In an $n \rightarrow \pi^*$ interaction, a nucleophile donates lone pair electron density to the empty πorbital of a nearby carbonyl group. These tertiary fibril-forming collagens are initially synthesized as procollagen polymers, which undergo post-translational modification in the lumen of the endoplasmic reticulum. Propyl-4- hydroxylase and lysyl-hydroxylase hydroxylate procollagen proline and lysine residues, further contributing to molecular stability by preventing enzymatic degradation. Once post-translationally modified procollagen is secreted from the cell, extracellular terminal N- and C-propeptides are cleaved from the ends of the procollagen molecules by metalloproteinases. The newly-formed tropocollagen spontaneously aligns in longitudinally- staggered parallel strands, forming collagen fibrils [4, 5].

Collagen undergoes many types of post-translational modifications (PTMs), including intracellular modifications and extracellular modifications. A peculiarity of collagen is the presence of post-translational modified amino acids, including 4-hydroxyproline (Hyp), 5-hydroxylysine (Hyl) and glycosylated Hyl at Y position and 3- hydroxyproline (3-Hyp) at X position. While the high proportion of Hyp enhances the stability of collagen triple helices, Hyl is indispensable for collagen glycosylation and cross-linking required for fibril formation. Among all the PTMs of collagen, glycosylation, which involves covalent attachment of sugar moieties to Hyl, is the most structurally complicated [6].

The amino acid compositions of collagen types vary considerably between species, and these variations affect chemical and physical properties, thermal stability, solution viscosity, and crosslinking density [4].

The **takeaway** from this is that collagen Type 1 consists of 3 chains of amino acids in a particular triple-helix structure and that the amino acid profile is species-specific.



Absorption Mechanism

Although collagen has been used in therapeutic applications for a long time, the absorption mechanism is not well understood. Prior to absorption, peptides generally undergo proteolytic digestion in the gastrointestinal tract. However, it has been reported that orally administered collagen hydrolysate can be absorbed from the intestine in a high molecular weight form and be preferentially accumulated in the cartilage tissue in mice [9]. Watanabe- Kamiyama et. al. suggest that collagen was partly absorbed into the blood in the peptide form and accumulated in the kidneys of rats [10].

So it seems that ingested collagen is broken down in individual amino acids but that some chains of amino acids also make it into the tissue.

Collagen Synthesis Induction

Recent evidence suggests that the consumption of essential amino acids (AA) and/or those abundantly present in collagen may have the capacity to influence the synthesis of new collagen in ligaments and tendons. Recent research has shown that the consumption of 15 g of dietary collagen; 1 h prior to intermittent exercise led to an increase in procollagen I N- terminal propeptide (P1NP), compared to a placebo control [11].

De Paz-Lugo et al. have shown that increased concentrations of glycine, proline and lysine in the basal medium enhance type II collagen synthesis in particular chondrocytes culture [12]. Murakami et al. have reported that single amino acids and Branched-chain amino acids (BCAA) did not increase the synthesis rate of skin tropocollagen.

However, combinations of specific amino acids, especially BCAA + Gln or BCAA + Pro are vital in stimulating the synthesis of skin tropocollagen in mice [13]. Also, it has been demonstrated that ingesting L-Hydroxyproline (Hyp) by rats increased both the soluble collagen content of the skin and the serum collagen peptide content, suggesting that Hyp had the ability to up-regulate collagen biosynthesis and degradation [14].

Takeaway: single amino acids do not seem to be efficient at stimulating or increasing collagen production, combinations do.

Ascorbic acid (Vitamin C) shifts the level of protein synthesis devoted to collagen from 5 to 10% to 20 to 30% and greatly increases the hydroxylation of proline residues in collagen [15]. The effect is unrelated to intracellular degradation of newly synthesized procollagen. It is proposed that intracellularly accumulated procollagen in ascorbate deficiency may lead to a translational repression of procollagen synthesis. Ascorbic acid may relieve this block by promoting hydroxyproline formation and, consequently, secretion of procollagen from the cell. The increased level of procollagen mRNA under the influence of ascorbic acid may be secondary to increased synthesis of procollagen polypeptides [16].

Some research has shown that **ginseng** promotes collagen production in human dermal fibroblast cells. Ginseng was found to induce the phosphorylation of Smad2, an important transcription factor in the production of Type I procollagen [17

Asiaticoside can induce type I collagen synthesis via the activation of the TβRI kinase- independent Smad pathway [18].

VECOLLAL®'s principles

Several different methods to stimulate collagen synthesis have been patented. Proteins [19], plants, seed extracts [20], and amino acid compositions [21] systems have been patented.

Due to the complexity of type I collagen, it is not possible to create a synthetic protein just by mimicking their quantity of amino acids.

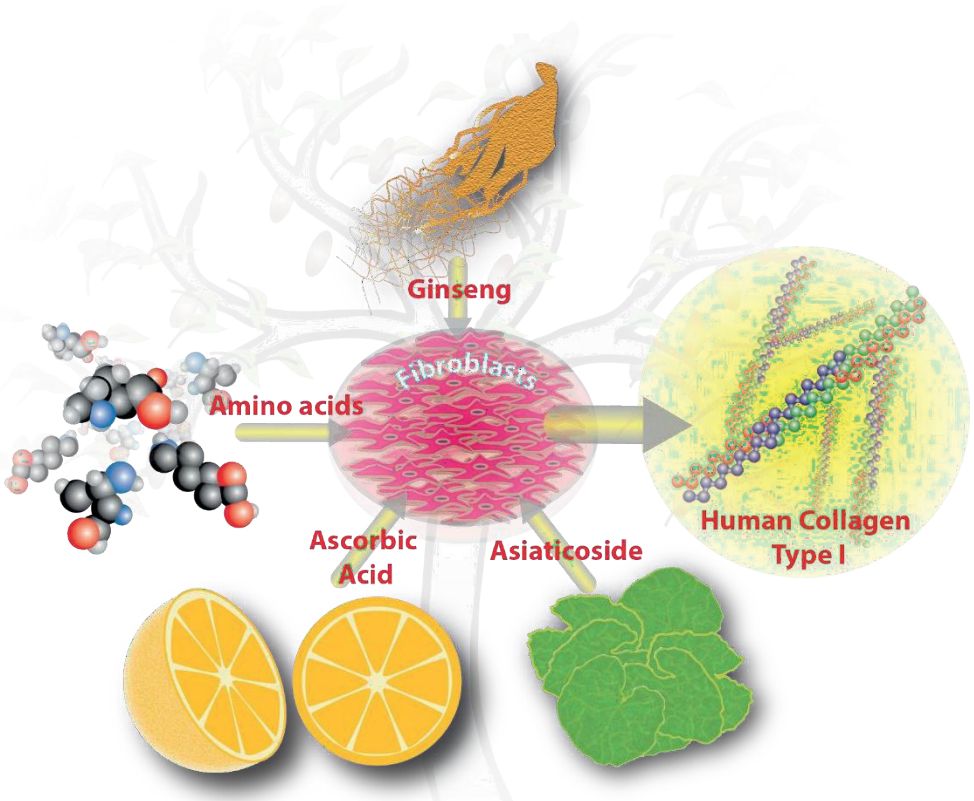
Nevertheless, the reviewed theory indicates that it is possible to create a formulation with vegan sources that can induce and boost the collagen synthesis in the body.

Chotphruethipong et al. have reported that hydrolyzed collagen induces collagen production in fibroblasts [22]. As well, it has been shown that some specifics AAs can induce collagen production in cultured fibroblasts [23, 24].

It can be supposed that when an amino acid source is ingested orally, it is degraded, and the unitary AAs go to the blood where they will arrive at all the body cells. As mentioned before, animal collagen differs from human collagen in AA composition. Also, the lack of a single amino acid can stop protein production.

That is why it is necessary to focus on the human type I collagen sequence, and not on the bovine / marine profile. This can ensure that all the amino acids in the product can be efficiently transformed into collagen.

VeCollal®'s underlying mechanism is that the collagen-producing cells have all molecular building blocks to synthesize the perfect collagen and make post-traditional modifications to obtain the Hyp and Hyl in the sequence. These just need the precisely correct quantity of raw material, and the correct stimulus that "indicate" them to start to produce collagen (Figure 1). The amino acids and the inductors (ascorbic acid, ginseng, and asiaticoside) are derived from vegan sources.



GENERAL PRINCIPLE:

VeCollal® provides the body the perfect building blocks for the production of collagen Type I by mimicking the exact amino acid profile from human Type I Collagen. It can be considered as a biomimetic of Human Type 1 Collagen.

VeCollal® aims to emulate the natural synthesis process for type 1 collagen using vegan analogues

To ensure these building blocks are used to their best, carefully selected inductors signal the body to use the available amino acids for the production of collagen.

Supporting studies used in the formulation

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