Collagen Perfect Bible

Digest version

- Collagen in your body
- Differences among collagen, gelatin, and collagen peptide
- How collagen is absorbed into the body
- Staying youthful with collagen peptide
- How collagen works on your “skin”
- How collagen works on your “hair and nails”
- How collagen works on “bones”
- How collagen works on “joints”
- Start diffusing “collagen peptides throughout your whole body”
- Potential medical applications for collagen
- How to take collagen peptides effectively
- How to select good collagen peptide

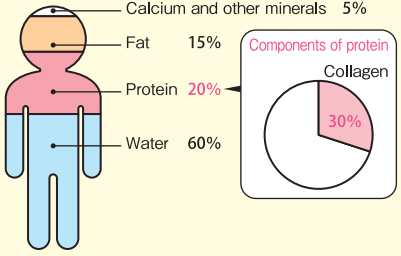
Created by “Take Collagen from Food♪” Promotion Committee

Collagen in your body

✸What is collagen?

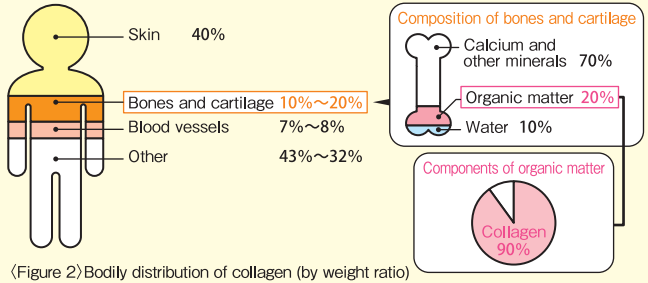
Collagen is a protein. It is one of the major constituent elements in the makeup of the human body.

By weight ratio, the human body is roughly made up of 60% water, 20% proteins, and 15% fats, with the remainder being various minerals. Of the protein content, collagen accounts for about 30%.



〈Figure 1〉Composition of human body (by weight ratio)

So, where in the body is collagen mostly found? About 40% of collagen is present in the skin, about 10–20% in bones and cartilage, and the remainder distributed in blood vessels and internal organs. In a nutshell: it plays a foundational role in our body.

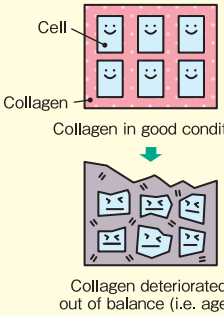


〈Figure 2〉Bodily distribution of collagen (by weight ratio)

✸Roles of collagen

Collagen plays important roles in connecting cells, supporting them, and creating external extremities.

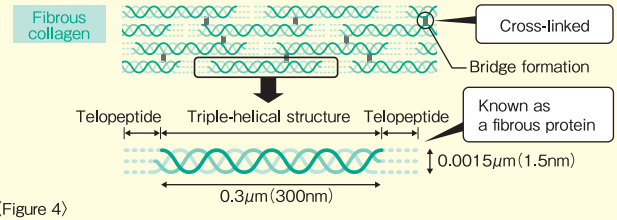
The extracellular matrix is found between cells with collagen as the primary constituent. This matrix protects cells from the extracellular environment. It is found throughout supporting tissues, which act to support and interconnect other tissues within the body. In other words, we can thank collagen for the structural framework of our bodies.



〈Figure 3〉Collagen and cells

✸Structure of collagen

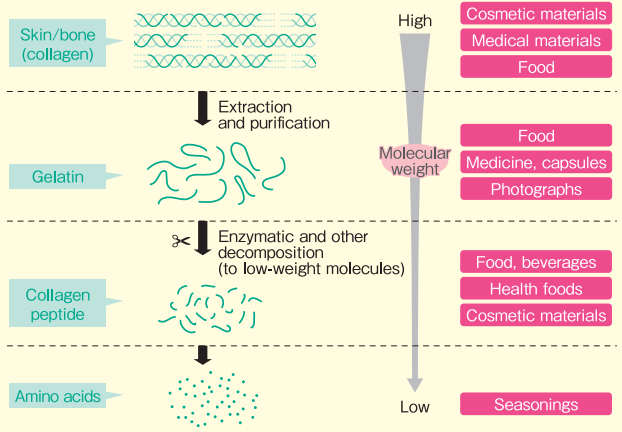
Collagen takes the form of a triple-helical structure, in which three chains are wound like coils. Each of these coils is made up of a string of thousands of amino acids connected together, in a form unique to collagen which is characterized by numerous repetitions of a "glycine-X-Y" pattern (where both X and Y represent various amino acids; each pattern consists of glycine combined with two other amino acids). To further strengthen itself, collagen contains various compounds which link molecules together; this is called cross-linking.



〈Figure 4〉
Triple-helical structure of collagen

Differences among collagen, gelatin, and collagen peptide

Collagen can be obtained in the form of the jellied broth which is produced by cooking and cooling bony parts of a fish or chicken wings in a stock.
While collagen is plentiful in the bones and skin of animals and fish, it can be challenging to consume such a broth on an everyday basis and, anyway, such collagen is not digested or absorbed very well.
To help improve its digestibility and absorbability, collagen is heated, extracted, and purified to obtain gelatin. Gelatin is not highly soluble in cold water, but it is in hot water; and, when it is cooled, it becomes "wobbly" and jelly-like, as you would see in a gelatin dessert.
Then, if you enzyme-degrade gelatin very finely to make it even easier to digest and absorb, you arrive at collagen peptide. With a very low molecular weight, collagen peptide is highly soluble in water, and can be readily absorbed into the body. Generally, products labeled as "collagen" are more likely to be "collagen peptides."



〈Figure 5〉Different forms of collagen

✸Amino acid composition

Because they are all proteins, amino acid composition is identical in collagen, gelatin and collagen peptide, only the molecular sizes vary.
One-third of the whole is glycine, followed by proline, alanine, and hydroxyproline, which is unique to collagen. Because it does not contain amino acids in optimal proportions, it is not exactly a "good" protein from a nutritional perspective. In particular, the lack of tryptophan means that it rates zero on the amino acid score.

Collagen peptide from pig skin

1000残基あたりのアミノ酸数量

Amino acid	Three-letter acronym	One-letter acronym	Residues (number of amino acids)
Glycine	Gly	G	337.0
Proline	Pro	P	134.9
Alanine	Ala	A	113.4
Hydroxyproline	Hyp	O	88.6
Glutamic acid	Glu	E	67.2
Arginine	Arg	R	47.4
Asparagine acid	Asp	D	44.1
Serine	Ser	S	32.0
Lysine	Lys	K	28.5
Valine	Val	V	24.1
Leucine	Leu	L	24.0
Threonine	Thr	T	15.5
Phenylalanine	Phe	F	15.1
Isoleucine	Ile	I	9.9
Methionine	Met	M	6.5
Histidine	His	H	4.9
Tyrosine	Tyr	Y	3.6
Hydroxylysine	Hyl	-	3.3
Cystine	Cys	C	0.0
Tryptophan	Trp	W	0.0
Total			1000.0

*Residues : Number of amino acids in the case of a protein (Source: Nitta Gelatin Inc.)

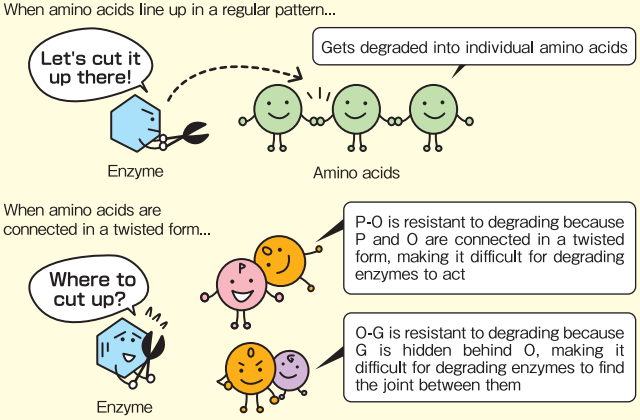
〈Figure 6〉Amino acid composition of porcine collagen

How collagen is absorbed into the body

Formerly, it was believed that all proteins are degraded into separate amino acids in the body. However, unlike other proteins, collagen has been found to have a sizable proportion absorbed in the form of peptides, where several amino acids remain connected and exist in the blood for an extended period. It has also been discovered that two peptides, namely proline-hydroxyproline (P-O) and hydroxyproline-glycine (O-G), have particularly high absorption rates.

✸Key to absorption : “O”

Unique to collagen, O (hydroxyproline) is an amino acid found in all collagen peptides. Peptides containing O are connected in a particular way that causes them to work against the actions of proteolytic enzymes, enabling them to still be absorbed in the form of peptides.



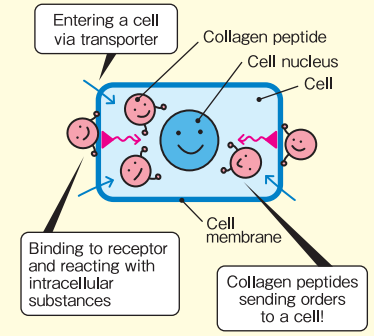
〈Figure 7〉Peptide bonds specific to amino acids

✸Where peptides go

In a study to investigate where collagen peptides would be delivered in the body, P-O, among other collagen peptides, was labeled and then fed to rats. The results confirmed that the peptide was delivered to bones, joints, and the skin. When the researchers examined how far the peptide had penetrated, they found that it had reached to the “cellular level.”
The findings suggest that in humans, similarly, peptides dissolved in blood are also delivered to cells in various parts of the body, traveling through the bloodstream.

✸Collagen peptide issues commands

It used to be assumed that collagen peptides, having been transferred to cells around the body, “become materials for making collagenous body tissues.” However, today's mainstream concept is that collagen peptides send out certain “signals” (commands) to cells and energize them.
While it is not yet clear what those signals actually are or specifically how they work, it is thought that collagen peptides send commands in order to create a better environment for active production of collagens by fibrocytes and chondrocytes, promote growth of hyaluronic acid, which creates resilient tissues, and stimulate cell division.
It is postulated that there are openings in the cell membrane, the outermost section of a cell, to enable these commands to enter. As illustrated in the figure, it is thought that these commands are received when the peptides have been transferred to the nucleus through a path that lets them in (transporter) and a receiver that enables peptides to react with intracellular substances (receptor).



〈Figure 8〉Collagen peptides acting on a cell

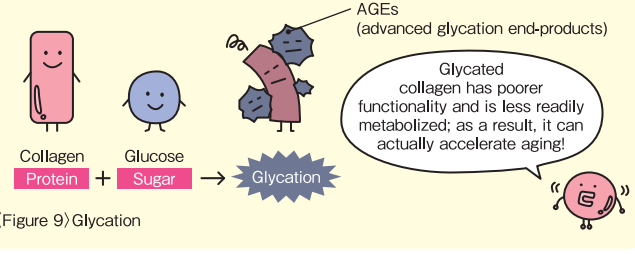
Staying youthful with collagen peptide

✸Collagen arrives at a crossroads when you turn 20

Collagen increases as we are growing up and our bone structure and muscles are developing. It peaks at around age 20. As the cycle of collagen metabolism lengthens due to aging, collagen's "power to support the body from within" dwindles; by the time some problem surfaces in the form of pain, etc., collagen decay has reached a serious level.

✸Glycation of collagen

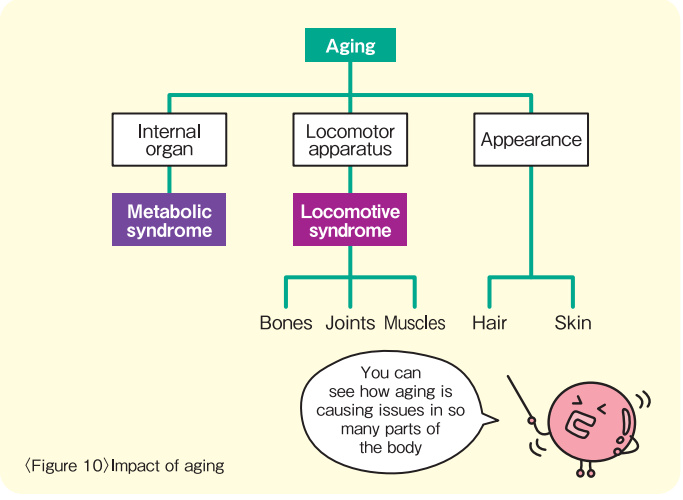
Among the known contributors to aging are oxidation and glycation; the latter has recently been attracting greater attention.
Oxidation is caused by active oxygen, which remains unused in the body after oxygen is taken in through breathing. This forms a sort of "rust," causing damage in lipids, proteins, enzymes, and DNA in cells.
Glycation was discovered through research on diabetes, as a phenomenon in which part of the sugar ingested through our everyday diets reacts with amino acids in protein within the body, causing an increase in aging substances called AGEs, or advanced glycation end-products. Proteins with these AGEs attached are robbed of their original functions and are difficult to metabolize. As a kind of protein, collagen becomes old and hard as a result of glycation, and its functions deteriorate.



〈Figure 9〉Glycation

✸Fighting aging with collagen peptide

Oxidation and glycation have much to do with aging of the entire body. On the outside, we see such symptoms as skin and hair problems, while symptoms of internal organs include hyperglycemia and hyperlipidemia —so-called metabolic syndrome, and bone and joint problems are among the motor organ issues. These functional declines in the locomotor apparatus, namely locomotive syndrome—or as they are often called in Japanese, "lokomo"—are becoming an increasingly larger issue.



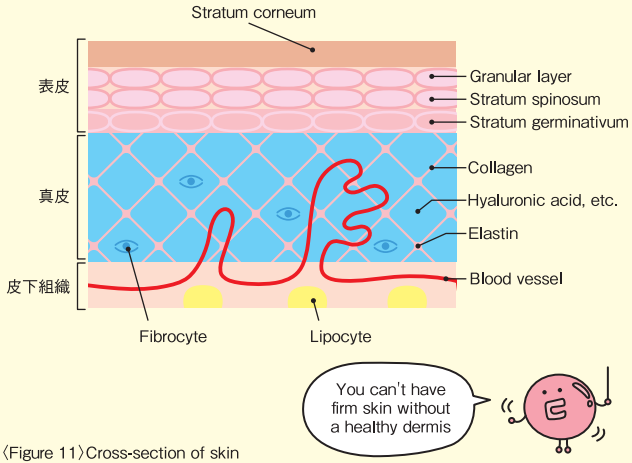
〈Figure 10〉Impact of aging

If you want to slow the onset of aging effects, one very important step you can take is to reconsider your lifestyle. Oxidation can result from stress, smoking, and nutritional imbalance, while glycation may be associated with an excessive intake of sugar. You may also find it necessary to obtain outside sources of collagen peptides in the form of health foods; collagen peptide is believed to send signals to the cells of bones, joints, skin, and to activate these cells, thereby enhancing metabolism.

How collagen works on your “skin”

✸Skin tissues and collagen

Collagen makes up about 70% of the dermis, which lies inside the epidermis. The dermis has a network of resilient fibers such as collagen and elastin stretching around, with hyaluronic acid contained between them. The combination of these strong fibers and freshly secreted hyaluronic acid is what makes your skin firm.



〈Figure 11〉Cross-section of skin

✸Results of research

A recent study has found that continuous intake of collagen peptides at 5 g a day for a period of 4 weeks or longer increases the amount of moisture in the skin and improves its resilience. This suggests that collagen peptides can help keep your skin moist and firm.

✸Mechanism

Collagen peptides are carried via the bloodstream to fibrocytes in the dermis, and they send out commands to “make tissues maintain resilience.” In response, resilient fibers such as collagen and elastin are created in great numbers in the dermis; this is believed to help make skin more elastic. It has also been found that commands sent by P-O may promote synthesis of hyaluronic acid. Newly synthesized hyaluronic acid is what gives your skin that “springy” feel.

Meanwhile, other studies have shown that “hidden blemishes” arising from ultraviolet ray damage can be mitigated through intake of collagen peptides. This also indicates that collagen peptide works on the skin at a cellular level, and helps to repair skin damage.

How collagen works on your “hair and nails”

✸Effects on your hair

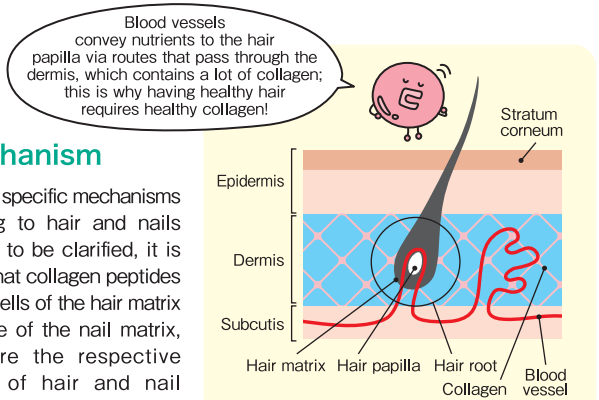
According to a recent study, taking 5 g of collagen peptides a day for 8 weeks helps the hair become thicker. We frequently hear people talking about how their “hair has become bouncy.” This would be because their hair has become thicker.
A questionnaire survey on hair conditions conducted with participants in this study found that many of them had felt improvements in all measurable aspects, including “manageability,” “glow,” “smoothness,” “moisture,” and “ease of finger combing.”

✸Effects on nails

It was reported as far back as the 1950s that intake of gelatin, consisting of collagen peptides, helped improve brittle nails, while other studies conducted in Japan reported that intake of collagen peptide improved nail condition.

✸Mechanism

While the specific mechanisms pertaining to hair and nails have still to be clarified, it is thought that collagen peptides work on cells of the hair matrix and those of the nail matrix, which are the respective sources of hair and nail production, thereby promoting the metabolism.

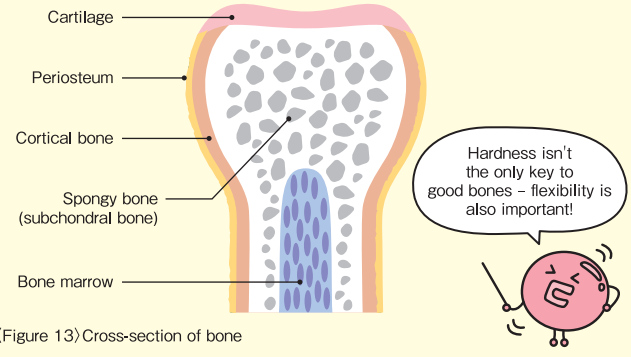


〈Figure 12〉Relationship between hair and collagen

How collagen works on “bones”

✸Structure of bones and collagen

About 70% of bone is made up of minerals such as calcium and phosphorus, which are contained in particular parts such as cortical bone and spongy bone. Collagen is also found primarily in cortical and spongy bone, making up some 20% of bone, which contributes to the stretching out of a network of resilient tissues.
This structure is often likened to that of a reinforced concrete building, whereby collagen serves as the “reinforcement” to the “concrete,” comprising minerals such as calcium and phosphorus. Not only does collagen act as the skeleton of the structure, it also creates resilient tissues to make bones flexible.

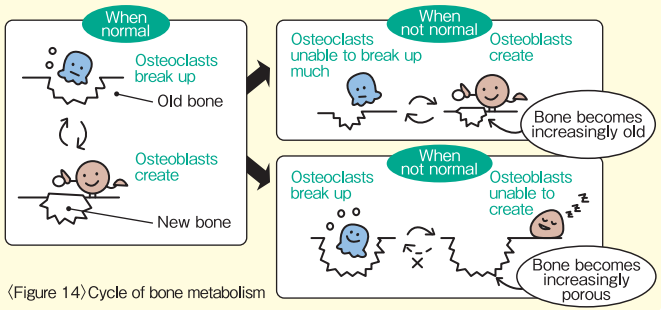


〈Figure 13〉Cross-section of bone

When considering osteoporosis, we tend to think of reduced “bone density” as the cause. But, recently, it has become clear that bone quality also has much to do with onset of this condition, and this is where collagen matters. Just as the strength of reinforcement of a building becomes an issue over time, collagen in bones deteriorates as we age, making them prone to fracturing.

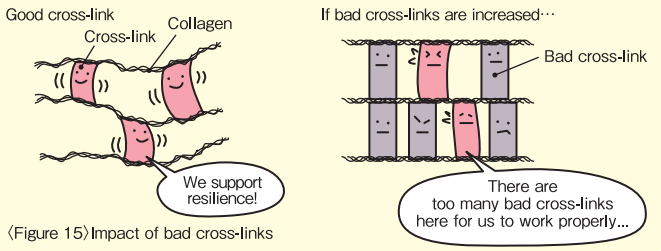
✸Bone metabolism

Metabolism of bones involves two kinds of cells: osteoclasts and osteoblasts. While osteoclasts break up old bones, osteoblasts produce proteins, including collagen, as the foundation for new bones that are currently being created.



〈Figure 14〉Cycle of bone metabolism

However, as we age, bones come to have bad cross-links that are hard to break up, thereby hindering efficient metabolism. This causes collagen to lose its unique characteristic of resilience, which in turn worsens "bone quality," thereby compromising bone strength. It is important to reduce the number of bad cross-links and prevent deterioration of collagen before it's too late.



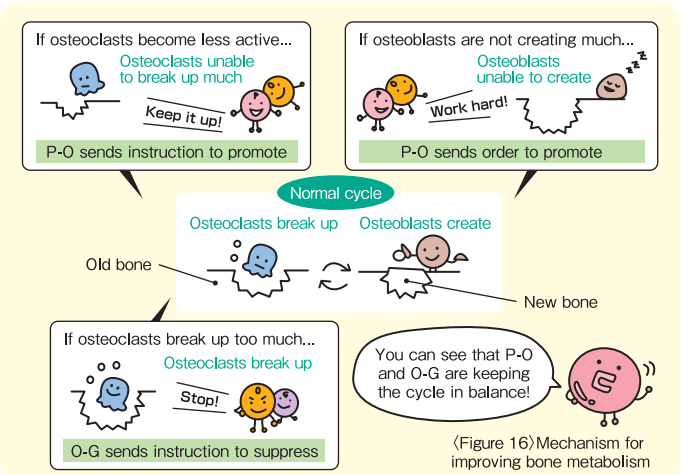
〈Figure 15〉Impact of bad cross-links

✸Study results

A study in mice demonstrated that giving them collagen peptides for 3 weeks helped inhibit decline in bone density. This suggests that collagen peptides may contribute to maintenance and improvement of bone density through bone metabolism.
Recent studies also suggest that collagen peptides play an important part in improvement of bone quality, as well as bone density.

✸Mechanism

Recent studies have demonstrated that P-O serves as an accelerator for osteoclasts that break up old bone by instructing them to "start working" and, when enough work has been done, O-G then serves as a suppressor by ordering them to "stop working." It has also been found that P-O promotes the activities of osteoblasts, which create new bone. This work cycle helps to make bone metabolism run efficiently, and thus improve bone condition.

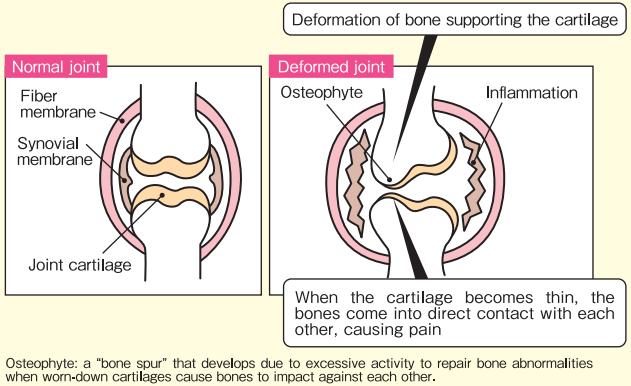


〈Figure 16〉Mechanism for improving bone metabolism

How collagen works on “joints”

✸Structure of a joint

A joint has a structure whereby a type of tissue, referred as the “articular capsule,” creates a cushion between bones. The surfaces of the bones at a joint are covered with highly moist cartilage, and this plays a cushioning role. Joint pain is caused as a result of a deterioration of the cushioning function of the cartilage. Aging causes the cartilage to be degenerated into a hard state, namely calcification; this makes the cartilage wear down, causing deformation of the bones as its foundation, and pain as a result.



Osteophyte: a “bone spur” that develops due to excessive activity to repair bone abnormalities when worn-down cartilages cause bones to impact against each other.

〈Figure 17〉Structure of joint

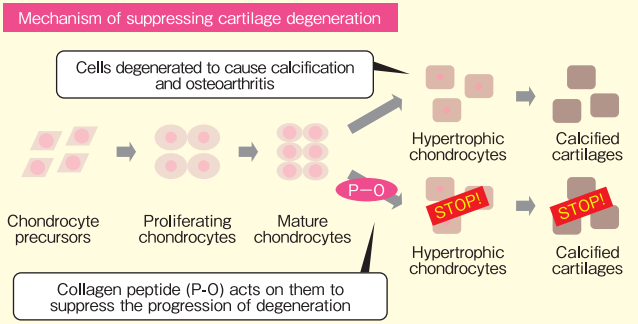
✸Study results

A 3-week animal study was conducted in which mice on high phosphorus diets (which decrease bone density) were compared with mice on high-phosphorus diets combined with collagen peptides. The results showed that mice in the latter group had thicker cartilage layers and more cartilage cells than those in the non-collagen group. In the latter group, bones, as the foundation of cartilage, were also found to be less likely to become uneven in structure and better preserved. These results suggest that collagen peptides help to slow the aging of articular cartilages by delaying their degeneration.

Meanwhile, another study examined patients with knee osteoarthritis taking collagen peptides at a daily dose of 10 g over a period of 91 days. The results demonstrated improvements on the comprehensive evaluation index as well as on the pain relief index for the knee joint. Some patients showed knee joint improvements not only on an index but also on images. Further studies are awaited.

✸Mechanism

Intake of collagen peptides promotes synthesis of hyaluronic acids as P-O acts on cells that produce hyaluronic acids, while inhibiting the progression of cartilage cell degeneration, such as calcification and hypertrophy. This is how collagen peptides are thought to facilitate smooth joint movement.

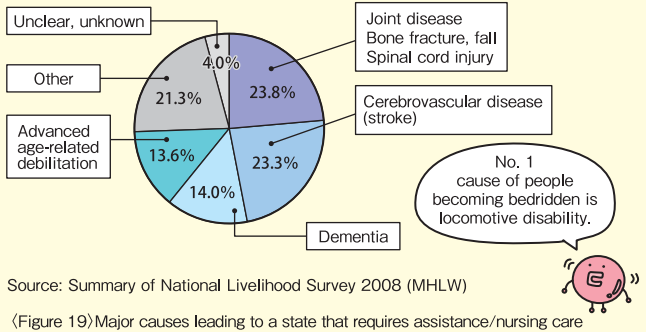


〈Figure 18〉Collagen peptide action on a joint

Start diffusing “collagen peptides throughout your whole body”

✷New lifestyle-related disease: LS (locomotive syndrome)

LS was proposed in 2007 by the Japanese Orthopaedic Association as a form of metabolic syndrome, which has since gained attention in the medical field. It refers to declines in the motor functions of muscles, joints and bones which can put affected individuals at high risk of eventually becoming bedridden. This is a matter of serious concern in Japan, given its super-graying society; one of the major factors in patients needing nursing care or assistance is “locomotive disability,” including bone fractures and joint diseases. Because LS can progress slowly and steadily inside our body without displaying much in the way of subjective symptoms, it is often the case that a victim breaks a bone in a minor fall and ends up bedridden.

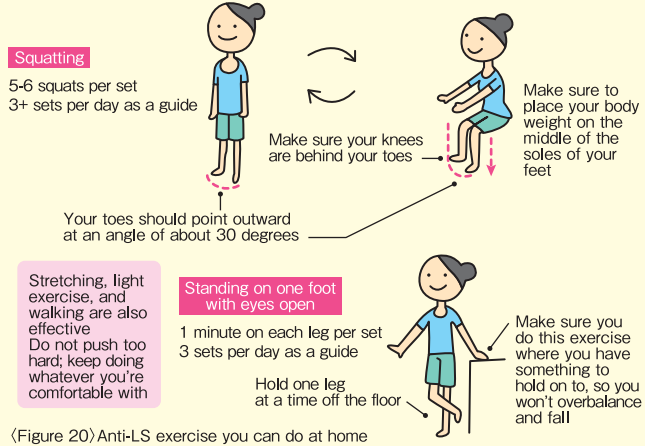


Source: Summary of National Livelihood Survey 2008 (MHLW)

〈Figure 19〉Major causes leading to a state that requires assistance/nursing care

✷Fight LS with exercise and collagen peptides

LS prevention comes down to two things: building muscle strength and strengthening the bones and joints. Muscles can be built up through training, regardless of age. Rather than hard exercise, doing squats and balancing on one foot at a time, which you can do in your own home, are recommended.



〈Figure 20〉Anti-LS exercise you can do at home

While a well-balanced diet is obviously essential, collagen peptides also hold promise. It has been shown in studies to promote development of the foundation for robust bones, suppress wearing-down of the cartilage, and inhibit deterioration of subchondral bone. With their contributions to controlling muscle reduction and maintaining current condition, collagen peptides have the potential to produce synergic effects in combination with exercise to build strong bodies, as has been demonstrated in studies conducted on athletes. Another report suggests that collagen fibers become thicker in the Achilles tendon. It is thought that taking collagen peptides frequently in adequate amounts will help you “prepare” yourself to enjoy an active lifestyle over coming years.

Potential medical applications for collagen

✸Bedsore mitigation

One of the issues people face in a super-graying society, such as Japan today, is decubitus ulcers, or "bedsores." This condition occurs when oxygen and other nutrients cannot be delivered to skin cells because a person is bedridden, among other reasons. A clinical study found that subjects who took collagen peptides at a daily dose of 10 g for 16 weeks showed significant improvements in scores measuring size and progression of ulcers, with the trauma areas becoming smaller, compared to those of subjects who did not take collagen peptides.
This is thought to be due to collagen peptide's functions of increasing the number of enzymes involved in skin regeneration and activating fibrocytes that produce hyaluronic acid and collagen, hence promoting skin regeneration.

✸Also potential for treatment of periodontal disease

In a study where mice were given collagen peptide for 3 weeks, it was shown to have a protective effect on the jaw bone, including the alveolar bone which provides the foundation for the teeth. This means that the same mechanism of bone metabolism applies to the jaw bone. This study shows that collagen peptide not only helps strengthen the gums but also tones the foundation for teeth, which is believed to have the potential to facilitate advanced treatments such as dental implantation.

✸Improvement of metabolic syndrome (hypertension, hyperglycemia)

As collagen is one of the major components of blood vessels, it is thought that taking collagen peptides could enhance the abilities of cells to produce collagen, which may in turn help to restore the elasticity of blood vessels.
The mechanism of hypertension development, in principle, is that blood is forced to travel through hardened vessels, thereby increasing pressure. It may be possible to address this issue at a fundamental level.
Meanwhile, it has been shown that various peptides, such as sesame and soy peptides, are effective in inhibiting the action of enzymes that are involved in the elevation of blood pressure; collagen peptide has been observed to have similar effects.
Regarding hyperglycemia, a study in mice found that giving them collagen peptides suppressed elevation of blood sugar levels. Overseas clinical studies have showed that intake of collagen peptides results in a marked decline in both blood sugar levels and diastolic blood pressure in patients with type II diabetes. The precise mechanism remains unexplained, but research is underway both in Japan and abroad.

✸Bridging dreams of mankind with "regenerative medicine"

Regenerative medicine is a branch of medicine aimed at regenerating tissues or organs that have been lost due to disease or injury, and recovering their functions. Since collagen is found naturally in the human body, there is little concern about rejection responses, which is bringing it considerable attention as a promising material for use in regenerative medicine (biomaterial)
It is widely expected that collagen, gelatin, and collagen peptides will be used in regenerative medicine, not only in the area of artificial skin and bones, but also for various other tissues such as blood vessels and the cornea, and relevant technical development is being undertaken. Research is also underway on applications to the artificial extracellular matrix and drug delivery system. They are now critical parts of the development of modern medical care.

How to take collagen peptides effectively

✸Adequate daily intake

Studies to date have shown positive effects from taking collagen peptides at a daily dose of 10 g (10,000 mg) for bones and joints, and 5 g (5,000 mg) for skin.
However, everyday foodstuffs contain very little collagen peptide. When we consume food, any collagen it contains will be degraded by the digestive enzymes in the body. And, while some may be absorbed as collagen peptide, it can be challenging to obtain as much as 5–10 g of collagen peptides per day from normal meals alone.

✸Use of supplements

For nutrients such as collagen peptide that are difficult to ingest in the required amounts based solely on normal diet, it is recommended that you make use of supplements containing such nutrients, which are available in extract/concentrate forms for daily intake convenience. Supplements are not "drugs." They belong to the family of everyday foodstuffs. From powders through tablets and drinks, there are many different forms of supplements available for purchase, so you can choose what best suits your preference and fits your lifestyle.

✸Daily intake is the key

As explained above, it has been found that after you ingest collagen peptides, they travel throughout your body via the bloodstream, issuing commands to the bones, joints and skin along the way. However, these commands are thought to dissipate in a matter of a day or two. To ensure efficient metabolism, it is necessary for commands to vitalize cells of the body to be issued continuously.
To this end, it is important to develop a regimen of taking collagen peptides every day.

How to select good collagen peptide

✸What makes good collagen peptide?

With regard to collagen peptide supplements, the most important requirement is that peptides that act on the body get properly absorbed and reach the target cells. In ensuring this, what matters is not the raw materials and their molecular weights but the manufacturing methodology, such as how enzymatic degradation occurs.

✸Points to check

That said, differences in manufacturing methods are not exactly simple for consumers to understand. Hence, it is very important to ascertain if the manufacturer of a particular supplement is reliable, as difficult as identification of reliable manufacturers may be.

One way to research reliability is to search manufacturers' websites and check if:

- ○Company profile and product information are meticulously presented
- ○Traceability is good
- ○The manufacturer has an integrated system, from raw materials procurement through research and development to production
- ○The company does not run advertising with exaggerated claims that their products "cure diseases," even though they are not drugs

This may help you determine whether or not they are reliable.

✸Era of "intellectual eating"

Our body is made up of nutrients contained in the foods we eat every day. Many of these foods may have functions that are unknown to us; there is ample potential for the existence of such hidden health-enhancing powers. Meanwhile, some are claimed to be beneficial to your health, based on flimsy evidence. It may not be difficult for you to sate your hunger, but when you seek to use diet to promote good health, you may frequently come across biased or erroneous information. The time has come when it is essential for each of us to choose what is good for us based on appropriate information - namely, "intellectual eating" - in order to build and protect good health.

What is the “Take Collagen from Food♪” Promotion Committee?

We want you to take collagen for the health of you and your family. To make that happen, it is important that collagen peptides can be found on your table as a staple, like your essential seasonings. With the aim of helping you to realize a “life with collagen as an everyday item,” we endeavor to consistently provide accurate information on how to use collagen in everyday living through websites and books. Our constant focus is on ensuring that it is widely appreciated that taking collagen helps keep your body healthy, and that collagen is not only helpful for aesthetic purposes, particularly for women, but is also beneficial with respect to bone and joint health in both men and women.

* This booklet is a reprint of modified contents of *Collagen Perfect Bible* (by Hiroshi Mano, Gentosha Media Consulting).

Author : Hiroshi Mano, Ph.D. (agricultural chemistry)
Professor
Department of Clinical Dietetics and Human Nutrition,
Faculty of Pharmaceutical Sciences, Josai University