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Effects of Supplements on Cartilage Regeneration



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ABSTRACT

Currently, extending the healthy life expectancy of the elderly is an important issue in Japan. Therefore, the national government is actively promoting the prevention and early detection, and treatment of sarcopenia. One of the keys to achieving this goal is through supplements available in the market. These are not classified as medicines but as health foods. Daily intake of supplements is thought to compensate for the lack of nutrients in food. In recent years, ingredients having special health functions have been attracting attention, and although the effects are not as strong as that of pharmaceuticals, some products have mild and unique effects. This study focused on cartilage regeneration. With the increase in the aging population in Japan, the occurrence of sarcopenia is considered to be inevitable, and therefore, many supplements are available for its prevention. However, it is difficult to say whether these are effective. There are a few products that seem to have little effect. Therefore, we outlined the mechanism of cartilage regeneration to clarify whether supplements are effective for the treatment and prevention of sarcopenia.

INTRODUCTION

Currently, extending the healthy life expectancy of the elderly is an important issue in Japan. Accordingly, the national government is actively promoting the prevention, and early detection and treatment of sarcopenia (reduction in muscle mass due to aging, along with the reduction in muscle strength and physical function), frailty syndrome (age-related decline in muscle strength, and mental and physical vitality), and locomotive syndrome (a state in which muscle strength weakens with age, and the function of the locomotive organs deteriorates owing to the development of joint and spine diseases, and mobility functions such as standing and walking deteriorate). One way to tackle these issues is by supplements that are currently available in the market in large numbers. These are classified as health foods and were originally considered to supplement the nutrients that may not be consumed in sufficient quantities from regular foods. In recent years, ingredients that have health functions have attracted much attention, and many products, whose effects are not as strong as pharmaceutical products but have mild and unique effects, are available in the market^{1),2)}. Unlike pharmaceutical products that are consumed after the onset of illness, these are not intended to be used for temporary therapeutic purposes. Supplements are also not very effective but can be easily used from an early stage for prevention. Moreover, there are fewer restrictions on usage and dosage, with almost no toxicity. Currently, many types of supplements can be purchased from stores and online shops. In addition, sales competition is fierce, and new products are actively advertised in different media, including television and newspapers. Hence, information on these supplements, including the kind of product, its price, and its benefits, is easy to obtain.

This study focused on cartilage regeneration. Cartilage degeneration is a serious problem associated with aging³⁾. When the cartilage is worn down, the knees become painful, making walking difficult. Alternatively, when pain occurs, the consequent changes in gait cause an increased load on the other joints, leading to further health issues. As a result, exercise habits are reduced and muscle strength is weakened. This further results in a reduction in exercise capacity, leading to an increased risk of sarcopenia in the affected person. Currently, many supplements are available in the market to improve this condition, but unfortunately, they are not guaranteed to be effective. However, some products seem to have some effect. Therefore, we outlined the mechanism of cartilage regeneration to clarify whether the ingredients present in the supplements are effective for the treatment and prevention of sarcopenia.

Mechanism of cartilage regeneration

First, we describe the importance of cartilage. Some of the changes that occur in the body due to excessive exercise and aging can significantly reduce the quality of life. One such change is the development of joint pain⁴⁾. The joints are covered by elastic cartilage which acts as a cushion, enabling the joints to move freely. If the cartilage wears out owing to injury, illness or aging, the bones rub against each other directly, causing pain and inflammation. This can eventually lead to arthritis. Osteoarthritis is a condition that affects many people globally^{3),5)}.

At present, two procedures have been established to treat osteoarthritis. i) a procedure in which the surgeon replaces the damaged cartilage or joint, as asymptomatic treatment (arthroplasty), and ii) a procedure in which hyaluronic acid, a component of cartilage, is injected into the joints (intra-articular injection)⁵⁻⁷⁾. Since these are medical treatments, they are performed at medical institutions, such as hospitals, and are accompanied by high costs and hospitalization.

Recently, American researchers have reported that humans can regenerate cartilage⁸⁾. It is well-known that salamanders possess regenerative capabilities, but humans also have such capabilities. The director of a Japanese manipulative hospital has reported that patients are forced to undergo repeated symptomatic treatments owing to excess load on the knee joint that hinders cartilage self-renewal⁹⁾ and that the human body is constantly trying to regenerate the worn cartilage. By draining water from the knee using the symptomatic treatment described above, the pain greatly improves temporarily, but the natural resilience is suppressed. Skeletal changes such as pelvic distortion and bow-legs cause pain owing to the additional burden on the knees. Therefore, the distortion of the pelvis and spine should be corrected to allow the cartilage to regenerate⁹⁾. The general rationale is only to relieve pain and this relies on the subjectivity of the patient. However, we believe that there is some evidence for the rapid regeneration of cartilage.

Types and effects of supplements

Cartilage is composed of collagen, the major structural protein; hyaluronic acid, that binds the collagen; and sugar chains such as chondroitin sulfate, that retains water (Table 1)¹⁰⁾. The components that form the basis of the sugar chains are synthesized in the body using glucose as the raw material. Though there are established symptomatic treatment methods, alternative therapies are also being considered in Japan in recent years, such as supplementing cartilage

components using supplements. Currently, commercially available supplements include glucosamine, proteoglycans, collagen, chondroitin sulfate, hyaluronic acid, shark cartilage, and vitamin E and B groups. Some of these are components of cartilage while some others promote various metabolic processes in the human body. In addition, owing to manufacturing processes (e.g., heating), certain components, such as collagen, may become denatured²⁾, and therefore, it cannot be said that these components are the same as the components of the human body.

According to a report by Japanese researchers, glucosamine is effective for osteoarthritis⁴⁾. Osteoarthritis is a disease that causes localized joint pain and chronically enhanced motor dysfunction owing to cartilage destruction and is particularly common in the knee. In recent years, in addition to conventional conservative treatment, newer treatment methods with structure-modifying effect or cartilage-protecting effect, that improve cartilage metabolism and suppress the progression of osteoarthritis, are also expected. Several food ingredients such as glucosamine and chondroitin sulfate are attracting attention as promising candidates³⁾. In a study that evaluated the effect of glucosamine-containing foods on knee osteoarthritis using a joint diagnostic marker, it was reported that glucosamine exhibits an anti-inflammatory effect. The author also reported that it acts as a cartilage protector by promoting synthesis while simultaneously suppressing the decomposition of cartilage components (glycosaminoglycan, type II collagen)⁴⁾. However, this effect disappears when the intake of the supplement is ceased. Since the mechanism of this action is unclear, further studies are required in the future. Moreover, since the action is mild, these foods cannot be expected to be as effective as pharmaceuticals at this point in time¹¹⁾.

In addition, if taken with the belief that it is effective, even a placebo that does not contain any active ingredient may show an effect¹⁰⁾. Therefore, in drug development, a double-blind study is conducted, in which both patients and doctors who judge the effect are not informed of what a participant is receiving, and the investigational drug and placebo are randomly administered to compare the effects^{3),12)}. However, such tests are not mandated for healthy foods such as supplements. In recent years, many studies have denied the effectiveness of glucosamine in large-scale trials¹²⁾. Although some patients feel that the pain has resolved after taking the supplements, actual evidence for regeneration of cartilage and consequent extension of healthy life expectancy is insufficient. In other words, even though many

supplements are commercially available, it is thought that the presumed effects are largely due to assumptions, as seen in the placebo effect.

Effect of supplements

The health effects of substances taken orally, such as supplements, not limited to cartilage treatment, have long been regarded as an issue. First, the components are metabolized by digestive juices and decomposed into smaller substances before being absorbed into the body. These substances may be reconstituted into the original substances after being absorbed by the body, though the proportion is considered to be very small. In addition, absorbed substances may be utilized in various parts of the human body. Therefore, even if these are effective, the proportion that reaches the cartilage is probably very small and so, no effect can be expected. Moreover, while considering human metabolism, it is unreasonable to assume that glucosamine will reach the cartilage of joints in sufficient amounts¹⁰⁾. In addition, even if the effect has been verified by experiments, it may be because by using only cultured cells, the rate of absorption in the tissue, its metabolism, and the actual dose at the time of oral administration are ignored. However, if it is a drug, various measures are followed to ensure that it reaches the target organ. By applying the transport mechanism of biological components in the body, technologies that allow a substance to reach a certain tissue at a high rate or show activity only after it reaches the tissue, have been developed. However, one peculiar feature of cartilage is that it does not contain blood vessels. Therefore, it is considered that the components are rarely distributed in the cartilage by blood flow¹³⁾. From these observations, it can be concluded that even if the cartilage component is taken orally as a supplement, the probability that it is directly involved in cartilage regeneration is very small. Just as protein intake does not always build muscle, it needs to be verified whether the absorption of cartilage components into the body leads to cartilage regeneration. The American researchers mentioned in the previous section also state that substance transport also occurs outside of the bloodstream⁸⁾. Therefore, it may not be impossible to supply components to cartilage using the substance transport mechanism of the body, at least if the components are synthesized *in vivo*¹⁴⁾. However, if the synthesized amount is very small, it may not be useful for therapeutic purposes. Furthermore, if the rate of synthesis is very slow, the requirements cannot be met.

CONCLUSION

Herein, we described cartilage regeneration mainly from the viewpoint of the effect of supplements. At present, it seems that there is no evidence to show that cartilage has been regenerated owing to the effect of the supplement, leading to improved gait. Furthermore, many studies have reported that the placebo effect improves pain, but this has not been properly verified. Hence, to confirm the effect of supplements, it is necessary to conduct clinical trials similar to those for pharmaceuticals and obtain objective data on their effects. As a component of many supplements, glucosamine is a substance related to the cartilage that has been known for a long time, and to date, there are many reports on various pros and cons regarding its effect^(3),4),10-12),15). From these previous reports, it can be said that glucosamine per se is not a cartilage component, so it is difficult to say that it has a direct effect, and considering the available literature, cartilage regeneration cannot be confirmed in a short period of time^{3),10),12)}. Maybe it is because of these reasons that glucosamine is not used much as the main component of supplements currently sold in Japan²⁾. Other ingredients, mainly proteoglycans, have also not been investigated or verified yet, and their effects are also skeptical. Even if these do turn out to be effective, there may only be a slight effect. Moreover, many of these substances are present in various food products, hence careful consideration is required to decide whether it is necessary to be taken in the form of supplements.

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Table No. 1: Breakdown of typical cartilage components

Components	Content (%)	Efficacy, etc.
Water	60–80	
Type II collagen	15–20	Maintaining elasticity and strength.
Proteoglycans Hyaluronic acid Chondroitin sulfate	3–5 1	It has high water binding capacity and facilitates smooth movement of joints. High water retention. Retains water in the joints for smoother movement.
Others		

Glucosamine is the raw material required for the production of hyaluronic acid and chondroitin sulfate in the body.

Proteoglycans contain multiple components such as hyaluronic acid and chondroitin sulfate.

Others include minerals and chondrocytes.

Red letters represent the ingredients of commercially available supplements.

In addition, vitamin E that promotes calcium colonization, vitamin B group that promotes metabolism, and the cartilage itself, such as from fish, may be used as a supplement component.

Table No. 2: Typical cartilage regeneration supplements

Type	Principal component	Sub-components	Approximate price for one month (US \$)	Level of satisfaction (%)
A	Non-denatured proteoglycan	Non-denatured type II collagen	55	91
B	Proteoglycans	Type II collagen	70	85
C	Proteoglycans	Type II collagen	40	92
D	Proteoglycans	Creatine	100	-
E	Imidazole peptide	Vitamin D	55	-

Non-denatured proteoglycans are undenatured proteoglycans. It is considered that these are more effective than the denatured proteoglycans.

Imidazole is high in antioxidants. Antioxidants are expected to provide relief from physical fatigue and improve endurance and athletic ability.

Previously, glucosamine and chondroitin were well-known cartilage components; however, proteoglycans and type II collagen are now attracting more attention.

Satisfaction was calculated from the answers to the questionnaire given to the users via the Internet.

Based on the data in references 1) and 2).