AIS SPORTS SUPPLEMENT FRAMEWORK
COLLAGEN

What is it?

> Collagen is the most abundant protein within the body, residing in the extracellular matrix (ECM) of several tissues including skin, bone, ligaments and tendons.[1] It is unique in that it forms as a triple helical structure, resulting in a rigid and durable tissue, which provides structure and support to the body, as well as playing a role in locomotion.[2] To date, there are 28 different types of collagen known which are composed of polypeptide chains.[3]

> Within bone, muscle and connective tissue, Type 1 collagen predominates, consisting of non-essential amino acids (NEAAs) including glycine, proline, hydroxyproline and hydroxylysine.[4] The specific role of each of these AAs and/or peptides after the consumption of collagen is still being explored.

What does it do?

> Plasma levels of glycine decline post exercise, potentially due to increased utilisation. This suggests an increased need for glycine while collagen synthesis is elevated post exercise.[5] It has been hypothesized that under circumstances of high demand such as a heavy training stimulus, dietary collagen may be of potential benefit.

> The addition of ascorbic acid and proline to cell culture growth media), results in an increased collagen content and improvement to mechanical properties[6]. This suggests both are important nutrients for the synthesis of collagen in connective tissue. However, whether intake beyond dietary sufficiency is required *in vivo* is yet to be determined.

- Although AAs derived from the consumption of diary protein (casein), including proline are incorporated into intramuscular connective tissue after a bout of resistance training, this does not result in a further increase of intramuscular connective tissue protein synthesis rates, compared to when a placebo is consumed. This may be due to the low glycine content of casein compared to collagen proteins.[5]
- Inflammation results in the disorganisation of collagen fibrils in the ECM, and has been proposed to lead to conditions such as tendinopathy.[6] Glycine has been shown to inhibit inflammatory cell activation[7], and therefore may be able to exert a beneficial effect in inflammatory conditions. The administration of glycine results in an improvement in the biochemical and biomechanical properties of an inflamed rat tendon[8], and restores the anabolic response of muscle tissue to leucine under acute inflammatory conditions.[9]
- Plasma di and tri peptide amino acids of hydroxyproline available post the ingestion of collagen proteins appear to trigger a range of signalling responses in the human body. How this translates into functional outcomes of enhanced collagen synthesis or improved connective tissue health in vivo is still unclear.[10]

Does the type of collagen impact its ability to be absorbed?

> Hydrolysed collagen is a form of collagen that has undergone enzymatic hydrolysis to reduce its' gelling properties to enable it to be easily mixed with water, and ingested.[11] Meanwhile, specific collagen peptide formulations have been developed to optimise the amount of di and tri AA peptides of hydroxyproline with different molecular weights. Such formulations are claimed to have increased bioavailability,and exert additional biological functions specific to the target tissues.[12-15] However, it should be noted that there does not appear to be significant differences in the bioavailability of key AAs after the consumption of different forms of collagen.[16]

> The consumption of collagen results in a transient increase of circulating NEAA within the blood, peaking between 40-60 minutes after consumption.[16, 17] However, there appears to be some individual variability with the availability of AAs after the consumption of collagen protein. Variability in amino acid appearance between subjects and interventions likely influenced by body weight, and possible polymorphisms of transporters and enzymes, which is potentially linked to habitual dietary intake of collagen sources.[18] Further research is required to determine these individual factors.

Collagen ingestion and exercise

> Although bone collagen is responsive to feeding in the absence of exercise[19], collagen in musculoskeletal tissue is non-responsive to feeding in the absence of exercise.[20] Exercise is necessary to "switch-on" synthetic machinery in muscle and connective tissue[21], and may also increase the delivery of specific AAs when their availability is increased (i.e. after the consumption of protein sources), particularly in dense connective tissues which are otherwise poorly vascularised.[22] Further, as it has been shown that proline is integrated into muscle collagen when dairy protein is ingested post exercise[5], it is possible that protein to support muscle recovery/repair may be better consumed post exercise.

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- A recent study has shown that serum obtained from individuals after the consumption of dietary collagen (gelatin) resulted in an increased collagen content, and improved tissue mechanics of an engineered ligament. Meanwhile, an in vitro arm of the same study illustrated an increased availability of collagen specific AAs within the blood, and an increase in a blood marker of collagen synthesis (Procollagen type I Intact N-Terminal) after collagen was consumed 1h prior to a 6-minute skipping exercise.[17] This suggests that the increased availability of collagen specific AAs and/or peptides in combination with exercise may result in an increased collagen synthesis within connective tissue.
- Although gelatin (a partially hydrolysed form of collagen utilised predominantly in food manufacturing) has been utilised in formative research exploring the impact of collagen intake on the synthesis of collagen, it is not considered to be palatable in its raw form to consume mixed in water due to collagens gelling properties, and therefore alternative formulations may be better tolerated. Incorporation of gelatin into food sources or forms should not influence its AA availability.

Current evidence for use withing Sport

- Although *in vivo* research remains limited, it has been suggested that collagen supplementation may assist in the prevention and/or treatment of muscle, cartilage, connective and bone tissue injury and/or degenerative disorders.[23] A recent case study has shown that the combination of a rehabilitation protocol, including exercise and supplemental collagen protein may help hastened return to play.[24] Meanwhile, collagen specific peptides in conjunction with calf-strengthening exercises has been shown to increase functionality and reduce pain during tendinopathy.[14] Other investigations have shown a reduction in subjective joint pain[25], plus decreased inflammation and muscle damage after strenuous exercise.[26]
- Collectively, collagen supplementation, and/or the increased availability of AA which predominate in collagen may be beneficial for both the prevention and treatment of injury and degenerative bone and connective tissue disorders. However, the research remains within its' infancy and more long-term studies are required to determine optimal doses, formulations and contra-indications for use. Thus, the use of collagen as part of an injury-prevention or management protocol should be considered carefully and should be used as an adjunct, not a replacement for traditional well-established processes.

What does it look like?

- Hydrolysed collagen and collagen peptide formulas are available in the form of pills or powder, and can be derived from porcine, bovine or marine animals. The differences in the AA content of various animal and human collagen sources are presented in Table 1. Recent research has shown there is no significant difference in plasma availability of key AAs after the consumption of various collagen protein sources.[16] Therefore, the source of collagen is unlikely to influence its' effectiveness.
- Collagen in the form of gelatin is considered as a food product, and therefore, does not require batch-testing for use in athletes., Where access and/or budget is a consideration, gelatin may be a preferential option, especially if made into more palatable jellies or jubes.
- Some collagen formulations include ascorbic acid, due to its role as a cofactor in collagen synthesis.[17] However, whether there is benefit beyond dietary sufficiency of ascorbic acid for collagen synthesis remains to be determined.
- Unfortunately, Australian food databases do not contain information on the collagen content of foodstuffs (measured as hydroxyproline), and therefore, it is not possible to determine collagen intake through food sources. Further, research has indicated that the AA content of collagen in bone broth, is too variable to use as a therapeutic source of collagen.[27]

Table 1: Amino acid composition of the 5 major mammalian collagens and gelatin

Amino Acid	Animal Gelatin						Human Collagen	
	Ox-hide	Commercial bone	Pig skin	Ox-bone	Shark-skin	Lung-fish skin	Bone	Tendon
Glycine	27.5	27.2	26.4	25.3	26.5	24	25.8	25.4
Leucine	3.3	3.5	3.3	3.9	3.5	2.8	3.6	3.6
Proline	16.4	15.5	16.2	14.7	13.9	15.8	15.3	15.2
Hydroxyproline	14.1	13.3	13.5	14.1	10.9	10.8	14.1	12.6
Hydroxylysine	1	0.7	1.0	1.1	0.8	1.1	0.6	1.5

Amounts given in grams per 100 grams of dry ash-free Protein. Adapted from.[28]

How and when do I use it?

- Although recent research utilised 15 grams of gelatin, this was due to the requirement to blind participants from the intervention. Other studies have shown an increased availability of AAs after the intake of up to 20-25 grams of collagen, Consequentially a minimum of 20 grams is likely optimal for increased AA availability around exercise in a timely manner[16, 29]. It is possible that similar to other types of protein, a dose response relationship exists, however, this requires further research.

> Although more research is required to confirm the use of hydrolysed collagen and/or specific collagen peptide formulas for a range of scenarios and/or target tissues, it may be beneficial in the following situations as part of an overall injury management and/or prevention plan (in conjunction to well established methods):

> As mentioned, Vitamin C (ascorbic acid) is important as a cofactor in collagen synthesis, so the diet must be sufficient in Vit C.

> **Consumed daily:**

- In conjunction with specific exercise to help pain management for inflammatory conditions such as tendinitis
- To help reduce activity-related joint pain
- For the treatment/prevention of degenerative diseases, such as osteoarthritis.
- To assist in bone strength in order to reduce fracture risk.

> **Consumed 40-60 minutes prior to exercise to:**

- Help to support collagen turnover in connective tissue by providing an increased availability of AAs during periods of increased turnover, particularly when the body is unable to keep up with demand and/or when total protein intake is suboptimal, such as during a high training stimulus.
- Help support tissue integrity for those with previous connective tissue injury.
- Support the repair of various tissues, including bone, skin and ligaments/tendons during rehabilitation.

> **Consumed immediately post exercise in order to:**

- Support the repair/recovery of muscle tissue, and potentially reduce delayed onset muscle soreness.

Are there any concerns or considerations?

There is insufficient evidence to support the use of vegetarian/vegan alternatives

Collagen protein is animal-derived and therefore may not be appropriate for vegetarian/vegan athletes. Although there are vegan/vegetarian products available that are claimed to mimic animal sources of collagen, if peptides specific to animal proteins are proved to have specific biological activity, then vegetarian/vegan options may be viewed as less effective. More work is required to determine the AA availability and effectiveness of vegan collagen alternatives.

Potential individual variability of availability of AAs that may support collagen synthesis

As per any supplement, an individual approach should be considered. The individual availability of AAs proposed to increase collagen synthesis may be impacted by the following: habitual intake of protein, particularly collagenous proteins which may lead to differences in baseline AAs availability and/or reduced capacity to digest specific AA; training load in which the requirement of AAs such as glycine are conditionally increased; an individual's body mass, leading to increased utilisation; the use of AAs in other processes such as bone remodelling.

Addition of ascorbic acid and its' impact on interference with physiological adaptation

Chronic Vitamin C supplementation may impair physiological adaptation (see Vitamin C). Adequacy of dietary derived Vitamin C should be confirmed.

Religions requiring Halaal products

Halal certified collagen protein supplements are commercially available

Where can I find more information?

Gatorade Sports Science Institute

www.gssiweb.org

Supplement safety information

www.sportintegrity.gov.au/what-we-do/anti-doping/supplements-sport

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The Australian Institute of Sport (AIS) Supplement Framework is an initiative of the Australian High Performance Sport System. The AIS acknowledges the support of members of the National Institute Network (NIN) and National Sporting Organisations (NSO) and their staff in delivering content expertise. This information is intended to help athletes, coaches and scientists make evidence-based decisions about the use of supplements and sports foods. Before engaging in supplement use, we recommend that each individual refer to the specific supplement policies of their sporting organisation, sports institute or parent body, and seek appropriate professional advice from an accredited sports dietitian (**www.sportsdietitians.com.au**).

Athletes should be aware that the use of supplements may have doping implications. Athletes are reminded that they are responsible for all substances that enter their body under the 'strict liability' rules of the World Anti-Doping Code. Some supplements are riskier than others. The Sport Integrity Australia (SIA) app is a useful resource to help mitigate the risk of inadvertent doping by helping to identify supplements that have been batch-tested. The SIA App provides a list of more than 11,000 batch-tested products. We recommend that all athletes consult the educational resources of SIA regarding the risks associated with supplements and sports foods.. While batch-tested products have the lowest risk of a product containing prohibited substances, they cannot offer you a guarantee that they are not contaminated (**www.sportintegrity.gov.au/what-we-do/supplements-sport**).

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