"Amino Acids of the 21st Century" (7) –The Science of Amino Acid Supplements–

Amino acids are currently used around the world in a wide range of applications, including medicines, foods, and supplements. Under a theme entitled "Amino Acids for the 21st Century," Professor Otani of the Graduate School of Frontier Sciences, The University of Tokyo, will discuss several specific examples of the latest research on the use of amino acids.

Introduction

Amino acid infusions containing all 20 amino acids are used in a wide range of contexts, including digestive surgery departments, for preoperative nutritional management and to hasten recovery from surgical procedures. However, despite the wide use and current availability of amino acid supplements, few studies have assessed the effectiveness and significance of these substances as dietary supplements. This paper reports on studies venturing such assessments.

Efficacy of amino acids vs. protein

Amino acid supplements generally consist of 20 crystalline amino acids, set at compounding ratios ranging from 0 to 100. This latitude permits the preparation of supplements containing just the nine essential amino acids. In contrast, the ratio of essential amino acids occurring in dietary protein is constant (around 30% to 35%) and cannot be readily changed.

The most significant differences between protein and amino acids include physiological absorption time and utilization ratio. Since amino acids are protein building blocks, relative to protein it takes less time for them to be completely absorbed by the body, causing the pharmacological actions of amino acids to appear earlier than those of proteins.

Amino acids are generally regarded as valuable supplements for applications in which the properties of amino acids, as shown in Table 1 (early absorption, high utilization ratio, and potential pharmacological actions), are important.

Pharmacological actions of amino acids

Table 2 gives the various pharmacological actions of the major amino acids.

Much-discussed amino acids

The amino acids receiving attention as amino acid supplements are generally the three essential amino acids - valine, leucine, and isoleucine - that have similar chemical structures (collectively referred to as branched-chain amino acids: BCAA) and two nonessential amino acids - arginine and glutamine - that play key physiological roles. Some examples of the physiological actions of the amino acids are listed below.

(1) Physiological actions of BCAA
- Inhibits breakdown of body protein
- Promotes synthesis of body protein
- Reduces central fatigue

(2) Physiological actions of arginine
- Promotes endocrine system function
- Reduces serum ammonia
- Regulates the physiological functions of the circulatory system (NO production)

(3) Physiological actions of glutamine
- Inhibits breakdown of body protein
- Promotes immune function
- Regulates glucose and glycogen production

Studies of amino acid mixtures

While reports exist of studies involving the ingestion of just BCAAs, arginine, or glutamine, few studies have examined the value or efficacy of supplements containing amino acid mixtures. In part, this is because of the near-infinite permutations possible with 20 amino acids and the enormous effort required to assess the actions exerted by different amounts of the various amino acids.

The authors prepared a supplement of a mixture of 12 types of amino acids (Amino Vital Pro, AVP) containing as main ingredients BCAA, arginine, and glutamine, then undertook studies across several domains, including athletics, lifestyle diseases, and cosmetics. Below is a partial report on such studies.

1. Research on effects among athletes

It is well-established that the prompt ingestion of carbohydrates immediately after exercise accelerates glycogen recovery, while protein ingestion promotes the synthesis of body protein. However, most of us are averse to consuming a 400-g steak immediately after crossing the finish line of a full marathon to offset the 2,000 kcal burned. Even if one could somehow manage to consume the steak, the body is poorly prepared to digest the meal at such times, resulting in stress upon the digestive system. At such times, the ingestion of amino acids and glucose that can be absorbed promptly would help promote protein synthesis and glycogen recovery.

With an emphasis on the current problems of athletes, reports on studies of the significance of AVP consumption are described below.

1)Recovery of muscle strength and muscle damage after upper arm training

Those with any experience of heavy training are familiar with the sensations of muscle weakness or delayed onset muscle soreness (DOMS), conditions that slow athletic progress.

In a double-blind crossover study, Sugita et al. divided 22 healthy male university students into two groups, having them undergo training involving eccentric training of elbow joints on the first day only [2]. The subjects then ingested an amino acid mixture (AVP, 11.2 g/day, 10 days) or a placebo after each breakfast and dinner. Recovery of muscle strength was assessed from immediately after training to 10 days after training. The same experiment was repeated two months later, but with subjects who ingested the placebo in the previous trial administered the amino acid mixture instead, and subjects previously administered the amino acid mixture given the placebo.

Following the eccentric training session, muscle strength generally fell to about 60% of maximum muscle strength, due to muscle fatigue. The amino acid group began to show signs of recovering isometric elbow extension group muscle strength two days after training. In

Table 1. Comparison of amino acids and protein

	Amino acids	Protein
Application	Drugs, cosmetics, food	Food
Allergen	No	Yes
Essential amino acid ratio (%)	Selectable from 0-100	Fixed within the range of 30-40
Absorption time	30-40 minutes	3-4 hours
Utilization ratio (%)	About 100	37-100 Note:
Pharmacological action	Yes	None
Nutritional value	Yes	Yes

Note: The utilization ratio of protein is based on Reference (1).

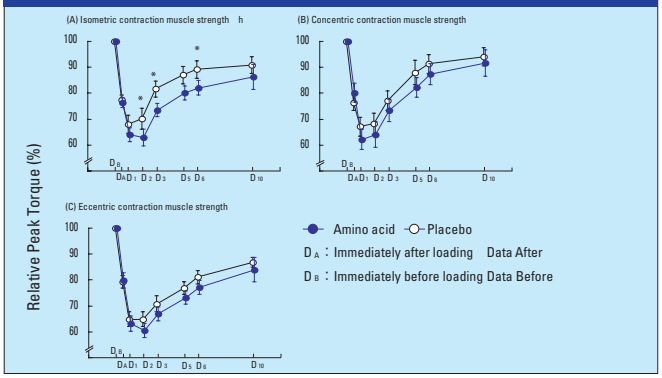
Table 2. Pharmacological actions of amino acids

Name of amino acid	Pharmacological action
Alanine	Promotes alcohol metabolism
Arginine	Improves immune system functions and circulation; helps prevent arteriosclerosis; activates the urea cycle; promotes ammonia breakdown; promotes secretion of insulin and glucagon
Glutamic acid	Promotes ammonia breakdown
Glutamine	Promotes gastric mucosa formation
Leucine	Promotes protein anabolism
Isoleucine	Promotes protein anabolism
Methionine	Protects against fatty liver syndrome
Tryptophan	Serves as a serotonin precursor
Lysine	Promotes calcium absorption
Histidine	Regulates parasympathetic nerve function
Proline	Normalizes collagen metabolism
Cystine	Normalizes skin metabolism

<Cited from Reference (1)>

contrast, at two days after training, the placebo group showed a highly pronounced reduction in muscle strength (Figure 1-A).

Figure 1. Recovery process for elbow extension muscle group after eccentric training <Cited from Reference (2)>



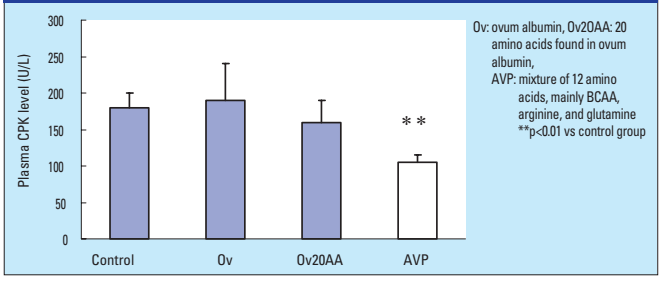
Recovery of muscle strength tended to be delayed in the placebo group, suggesting that consuming amino acids aids in the recovery of isometric muscle strength. Subjectively, many subjects in the amino acid group also reported reduced muscle soreness and faster recovery from muscle strain.

In a similar manner, Nosaka et al. divided 24 healthy male students into two groups, having them undergo an upper arm endurance regime in a crossover test [3], followed by assessments of differences in DOMS in the upper arm muscles following ingestion of an amino acid mixture (AVP, 7.2g/day, 5 days) or placebo. These differences were measured by blood CPK levels (Note 1), myoglobin (Mb) levels, and subjective tenderness, as reported upon palpation. Subjects consuming the amino acid mixture exhibited less pronounced increases in blood CPK levels ($p<0.01$) and Mb levels ($p<0.05$), as well as less pronounced muscle damage. Additionally, subjects consuming the amino acid mixture reported significantly reduced muscle soreness ($p<0.05$) [3].

Ohta et al. examined changes in levels of muscle damage in animals (mice) following sessions of forced exercise following ingestion of protein (ovum albumin, Ov), ovum albumin containing all 20 amino acids (Ov20AA), or an amino acid mixture (AVP) containing 12 amino acids [4].

Ingesting protein (ovum albumin) did not inhibit increases in plasma CPK levels. Only the AVP amino acid mixture significantly ($p<0.01$) inhibited increases in CPK levels (Figure 2).

Figure 2: Changes in CPK levels following ingestion of amino acids or protein <Cited from Reference (4)>



These results indicate that the amino acid mixture (AVP) containing 12 amino acids inhibited muscle damage, while the 20 amino acids found in the ovum albumin (Ov20AA) and ovum albumin protein had no discernible effects. In addition, the latest studies have shown that not all amino acids are effective, and that the ratio of amino acids in a mixture has significant effects with respect to protection against muscle damage.

2)Changes in hematological parameters following ingestion of amino acids over extended periods

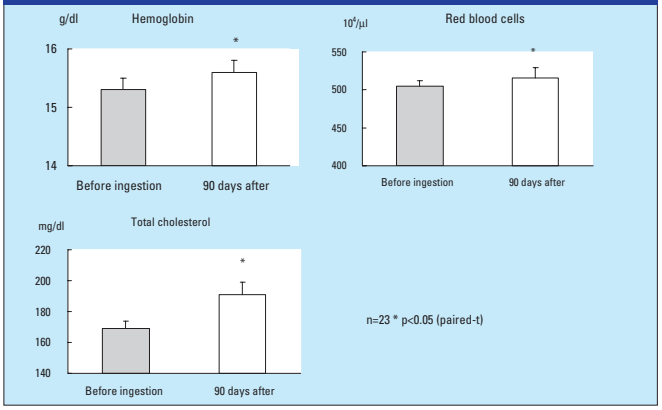
In a subsequent study, we examined the effects of long-term ingestion of the amino acid mixture (AVP) on hematological parameters and physical condition. The group of study subjects consisted of 23 members belonging to a company rugby team (Japan's number one team for the 7th consecutive year).[5] Twice a day for 90 days, the subjects were examined for changes in hematological parameters following ingestion of the amino acid mixture (AVP, 3.6 g). Since a parallel placebo test was not feasible (the subjects were professional athletes contending for their 7th consecutive tournament championships), we compared hematological parameters before and after ingestion of the amino acid mixture and hematological parameters obtained at the same time the following year, when the subjects were no longer administered the amino acid mixture.

This group exhibited or reported certain physiological deficiencies or problems, in particular low levels of total cholesterol (TC) (169 +/- 5 mg/dl) and frequent fatigue. Rapid recovery from muscle soreness and lower back pain was particularly desirable for this group. Comparisons of hematological parameters before and after ingestion of the amino acid mixture (AVP) (Figure 3) showed that TC levels increased to 191 mg/dl. Increases in hemoglobin and red blood cells ($p<0.05$) indicated hematopoiesis. We also observed a decrease in alkaline phosphatase (ALP). The ingestion of the amino acid mixture, a nitrogen source, at 7.2 g/day for a period of approximately 90 days, caused no changes in levels of nitrogen metabolites such as BUN or creatine. Most study subjects reported subjective improvements in physical condition. Roughly a third of the subjects reported reduced muscle soreness and lower back pain.

The test conducted at the same time the following year without administration of the amino acid mixture showed decreased levels of total cholesterol, red blood cells, and hemoglobin ($p<0.05$).

The preceding report describes some of the characteristic effects of a mixture of 12 amino acids (AVP) in the domain of athletic endeavor. We expect further studies of the results of amino acid consumption, followed by reports of results.

Figure 3. Changes in hematological parameters before and 90 days after ingestion of amino acid mixture (AVP)



The subsequent issue will discuss research on applications for amino acids in the areas of lifestyle and cosmetology.

References

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(2) Sugita M, Ohtani M, Ishii N et al : Effect of a selected amino acid mixture on the recovery from muscle fatigue during and after eccentric contraction exercise training. Biosci. Biotechnol. Biochem : 67, 372-375, 2003

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Profile of Professor Masaru Otani

Received a degree in amino acid sports nutrition at the Graduate School of Arts and Sciences, The University of Tokyo.
Visiting professor of the Sports Science for Health and Activity Course, Graduate School of Frontier Sciences, The University of Tokyo
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Based on experience with amino acid conditioning for top athletes, Professor Masaru Otani is currently involved in developing exercise, nutrition, and diet programs for middle-aged and elderly individuals.
Research interests include the application of amino acid mixtures to lifestyle diseases and disease prevention programs, as well as the effects of long-term consumption of amino acids on nutritional status and exercise results.