

## Research Article

# A Clinical Study of the Immediate and Delayed Effects of New Dietary Supplements on Exercise-Related Fatigue and the Inhibition of Delayed-Onset Muscle Soreness

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- Complex supplements
- Fatigue
- Exercise
- DOMS

**Abstract**

**Objective:** In these studies, we examined the immediate and delayed effects of the health food called "Inner Power®" in healthy adults during and after physical exercise. Complex supplements contain branched chain amino acids (BCAAs), citric acid, L-carnitine, coenzyme Q10, zinc and various vitamins.

**Methods:** Study I: The subjects were randomly divided into two groups, and subjected to cross-over study of oral administration to alternately in two phases, using complex supplements or a control food in each group. The oral ingestion of the test beverage 30 minutes before the load by quantitative bicycle ergometer, during and after exercise, and the blood concentration level of lactate, heart rate, fatigue were measured after exercise. Study II: we did a cross-over test in the same manner as study. Oral ingestion of the test beverage occurred 30 minutes before exercise, and was then followed by muscle endurance exercise. The measurement was carried out for muscle pain after exercise and muscle fatigue before and after exercise.

**Results:** Study I: As the test substance effect, the fatigue and lactate levels were significantly different during and after the exercise.

**Study II:** As the test substance effect, DOMS was significantly different at all days.

**Conclusions:** We found that the consumption of complex supplements before exercise had an immediate recuperative effect on exercise-related fatigue and a lasting inhibitory effect on DOMS.

**ABBREVIATIONS**

BCAA: Branched Chain Amino Acids; NST: Nutrition Support Team; DOMS: Delayed-Onset Muscle Soreness; VAS: Visual Analogue Scale.

**INTRODUCTION**

The term rehabilitation is currently used extensively in the fields of healthcare and welfare, and its necessity and importance

are generally well recognized. Nutritional support is also essential for the recovery of physical function through rehabilitation, and it is self-evident that an improvement in nutritional status is crucial for successful rehabilitation. Therefore, the importance of nutritional management and the operation of a nutrition support team (NST) in the field of rehabilitation has recently come to be widely acknowledged [1-3]. Japan boasts one of the world's longest life expectancies and is becoming an aging society.

However, support for living environments and social welfare has fallen behind, and the considerable number of elderly individuals who are unable to continue an independent lifestyle from the age of 70 years, thus approaching death after a period of physical frailty, is a growing social problem [4].

Multidisciplinary NST have been in operation in our hospital since July 2000, and for over 10 years, they have continuously been conducting nutritional screenings for all inpatients and rehabilitation for patients in need [5,6]. Nonetheless, we frequently encounter patients whose rehabilitation regimen must be interrupted because of severe fatigue and delayed-onset muscle soreness (DOMS). The reasons for these problems include the fact that many patients are frail elderly individuals with comorbidities and muscle strength that is already in decline before initiation of rehabilitation [7]. In order to conduct rehabilitation properly and achieve a favorable outcome, it is necessary to alleviate fatigue and DOMS in such patients throughout the course of rehabilitation.

Some of the ingredients of various nutritional supplements and food products that are commercially available have been reported to be effective against fatigue and DOMS. One such component is branched-chain amino acids (BCAA), which inhibit the breakdown of protein in skeletal muscle under invasive conditions and promote protein synthesis [8,9]. Furthermore, consuming 4 g of BCAA before exercise is reported to promote recovery from muscle pain and fatigue after exercise [10]. Another component is citric acid, which plays a central role in energy metabolism as an intermediate in the tri carboxylic acid (TCA) cycle of carbohydrate metabolism [11,12]. Citric acid easily binds to calcium lactate that accumulates during fatigue and improves blood flow to fatigued sites by converting calcium lactate to lactic acid, thereby promoting recovery from fatigue [13]. However, reports on this topic focus on a single component, and very few studies have examined the effects of coenzyme Q10 (CoQ10) administration on recovery of physical function. CoQ10 is a key coenzyme that contributes to metabolic activity at the mitochondrial level. In addition, we found no studies examining the effects of complex nutrient administration on the activity and recovery of various physical functions. Therefore, in the present study, we examined these effects (both immediate and delayed) on healthy adults.

## MATERIALS AND METHODS

We used "Inner Power®" as complex supplements and Glucose jelly as a control food. Inner Power®: Purchased from Otsuka Pharmaceutical Co., Ltd. Glucose jelly: Prepared at our hospital by the nutritional management unit as a placebo containing only carbohydrates with a calorie content equivalent to that of Inner Power® (Table 1).

The subjects were blinded to treatment in this study. To ensure that they remained unaware of whether they were receiving complex supplements or a control food, we minimized the differences in appearance of the beverages by offering them to the subjects in paper cups.

### Study I: Immediate effect during exercise

**Subjects and research methods:** A total of 20 healthy adults

**Table 1:** Composition of Inner Power and glucose jelly.

Ingredients	Content (per sachet)	
	Inner Power	Glucose jelly
calories (kcal)	139	140
carbohydrates (g)	33	35
CoQ10 (mg)	30	–
BCAA (mg)	2,500	–
L-carnitine (mg)	50	–
vitamin E (mg)	10	–
B group vitamins (mg)	5	–
zinc (mg)	3	–
copper (mg)	0.3	–
citric acid (mg)	1,000	–
overall (g)	125	125

(15 men, 5 women; mean age, 24.8 ± 6 years; age range, 20–39 years) who consented to participate in this study were included. None of the subjects reported any medical history that could affect the results of this study.

**Study design and grouping:** The subjects were randomly allocated to 2 groups, and were orally administered either complex supplements or a control food in a crossover study as follows. The first and second periods of the crossover study were termed Period 1 and Period 2, respectively. Ingestion of complex supplements was designated as IP, whereas ingestion of a control food was designated as GJ.

**Test schedule:** The subjects orally ingested two sachets (250 g) of the test beverage 30 min before exercise. Measurements were obtained immediately before exercise, 3 and 6 min after the initiation of exercise, and 5 and 10 min after the completion of exercise. Period 2 was initiated one week after Period 1, and the beverage was switched accordingly; the same exercise sessions and measurements were repeated (Figure 1).

**Description of the exercise:** The exercise sessions involved quantitative loading on a bicycle ergometer (6 min at 100 W after 3 min of warm-up).

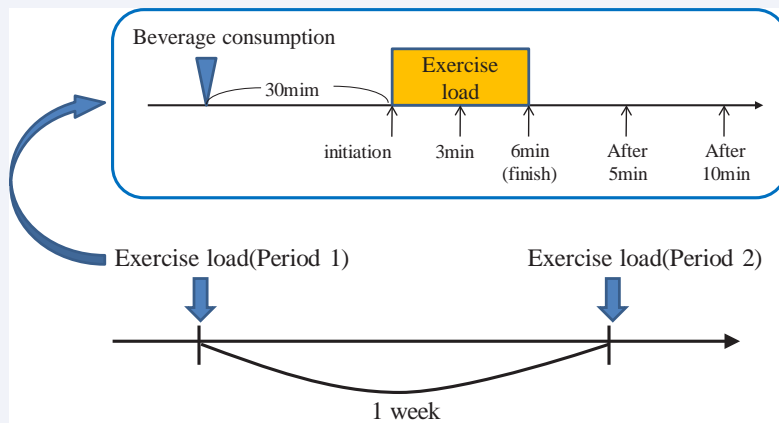
**Variables measured:** We measured blood lactate levels, heart rate, and fatigue (Visual Analogue Scale: VAS).

### Study II: DOMS

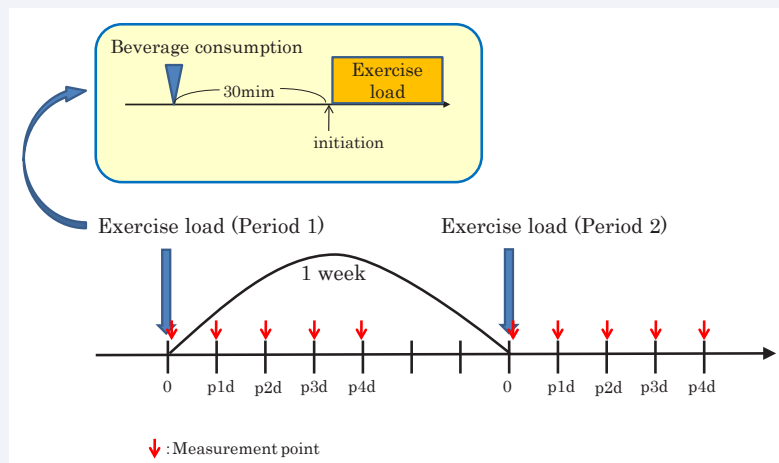
**Subjects and research methods:** A total of 12 healthy adults (8 men, 4 women; 30.9 ± 8.83 years; range, 21–48 years) who consented to participate in this study. None of the subjects reported any medical history that could affect the results of the study. Study design and grouping was done in the same manner as study.

**Test schedule:** The subjects orally ingested two sachets (250 g) of complex supplements or a control food 30 min before exercise. Measurements were obtained immediately before exercise and post day 1,2,3,4 of exercise. Period 2 was initiated one week after Period 1, and the beverage was switched accordingly; the same exercise sessions and measurements were repeated (Figure 2).

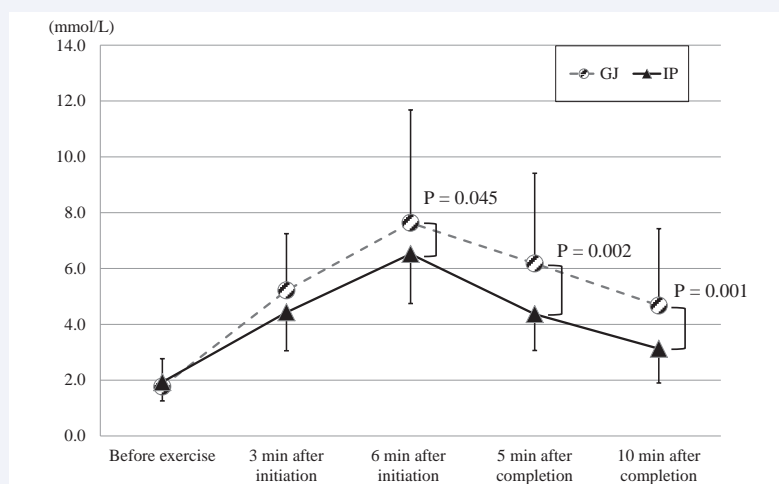
**Description of the exercise:** Exercise involved repeated elbow flexion in a seated position. The elbow of the non-dominant



**Figure 1 Study I design.** The subjects orally ingested the test beverage 30 min before physical exercise. Measurements were obtained immediately before and after exercise (Period 1). The beverage was switched after 6 days of rest (1 week from the last day of exercise), and the same exercise sessions and measurements were repeated (Period 2).



**Figure 2 Study II design.** The subjects orally ingested two sachets (250 g) of the test beverage 30 min before exercise. Measurements were obtained immediately before exercise, 3 and 6 min after the initiation of exercise, and 5 and 10 min after the completion of exercise (Period 1). The beverage was switched after 6 days of rest (1 week from the last day of exercise), and the same exercise sessions and measurements were repeated (Period 2).



**Figure 3 Effects on blood lactate levels (study II)** 6 min after initiation  $P=0.045$  between IP and GJ, 5 min after completion  $P=0.002$  between IP and GJ, 10 min after completion  $P=0.001$  between IP and GJ.

arm was placed against the inside of the thigh on the same side while the subject was in a seated position, and a plumb bob of a weight equivalent to 30% of the subject's maximum strength (one repetition maximum: 1RM) was fastened to the wrist. Maximum strength of the subject was then measured using a handheld dynamometer (Isoforce, OG Giken Co., Ltd.), following which 30% of this weight was calculated and set as the measurement load. A flexion angle of 90° during elbow flexion exercises was confirmed with a goniometer, and repetitions were implemented. The number of repetitions until elbow flexion of >90° became impossible was calculated. The subjects were allowed to set their own timing because pressure to the blood vessels in the muscles during sustained muscle contraction could affect the measured variables.

**Variables measured:** We measured DOMS (VAS).

## Statistical analysis

All statistical analyses were performed using SAS (version 9.1.3, Service Pack4). The results have been expressed as means  $\pm$  standard deviation. Statistical significance of the effects of the beverage was evaluated using ANOVA.

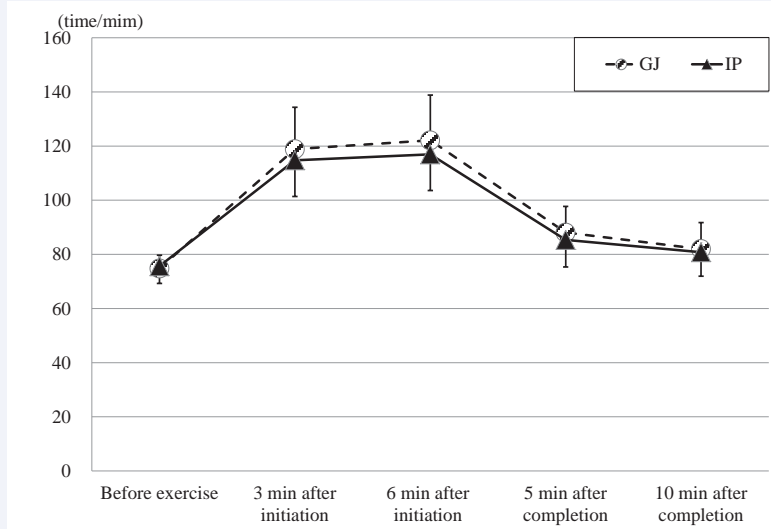
## RESULTS

### Blood lactate levels (Figure 3)

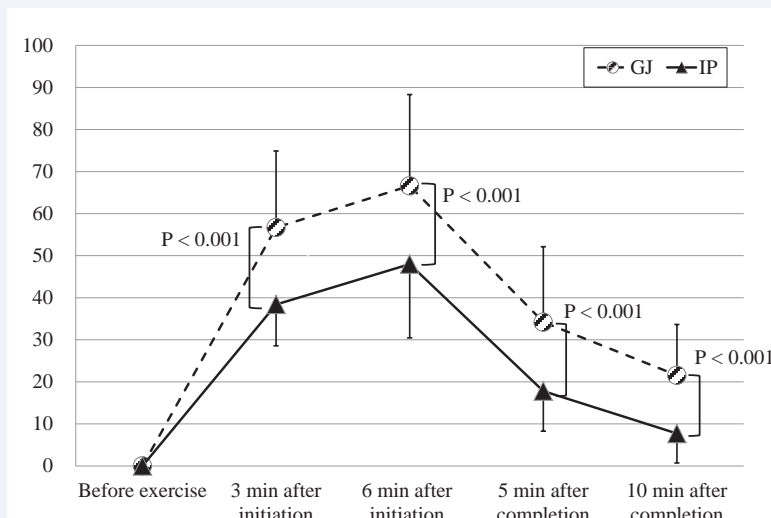
Blood lactate levels were significantly lower in IP than in GJ 6 min after the initiation of exercise ( $P=0.045$ ) and 5 ( $P=0.002$ ) and 10 ( $P=0.001$ ) min after the completion of exercise.

### Heart rate (Figure 4)

Heart rate was not different between IP and GJ.

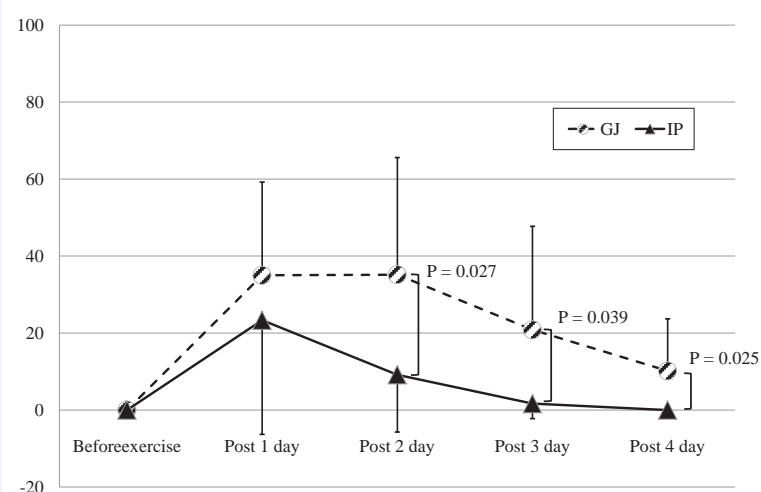


**Figure 4** Effects on heart rate (Study II).



**Figure 5** Effect on fatigue (VAS; Study II).

3 min after initiation  $P<0.001$  between IP and GJ, 6 min after initiation  $P<0.001$  between IP and GJ, 5 min after completion  $P<0.001$  between IP and GJ, 10 min after completion  $P<0.001$  between IP and GJ.



**Figure 6 Effects on DOMS (VAS; Study II).**

Post 2 day  $P = 0.027$  between IP and GJ, Post 3 day  $P = 0.039$  between IP and GJ, Post 4 day  $P = 0.025$  between IP and GJ.

## Fatigue (Figure 5)

Compared with GJ, IP showed a significantly different level of fatigue at all times (all  $P < 0.001$ ).

## DOMS (Figure 6)

We confirmed that the value for muscle pain in Periods 1 and 2 in Group A and Periods 1 and 2 in Group B was 0 before the initiation of exercise. Significant differences in muscle pain were observed between two groups at all times: post day 1 ( $P=0.0021$ ), 2 ( $P=0.0224$ ), 3 ( $P=0.029$ ), and 4 ( $P=0.04$ ).

## DISCUSSION

We conducted the two crossover studies in healthy adults. Compared with ingestion of control food, the ingestion of complex supplements was suggested to alleviate fatigue immediately and DOMS after exercise. Fatigue and DOMS are known to occur as a result of obstacles in the relevant metabolic pathways. Adenosine triphosphate (ATP) is required as an energy source to maintain the contractility of muscle cells during exercise. It is produced by the metabolic pathways of the glycolytic system, the TCA cycle, and the electron transport chain. When carbohydrate stores are depleted, ATP acts as a metabolic pathway to produce energy via degradation of muscle protein [14], a process thought to promote muscle atrophy. Furthermore, when muscle contraction occurs on application of a strong load, muscle fibers and the surrounding connective tissue undergo some damage, which is followed by the onset of DOMS as an inflammatory sign indicating that reparative processes are taking place. However, these obstacles are not confined to a single metabolic reaction; therefore, even if a single component is used as reported in studies till date, there is a good chance of another hurdle obstructing other cellular processes. The likely result of this phenomenon is the lack of metabolic improvement or only a marginal improvement after nutritional supplementation with a single ingredient. This result suggests that complex supplements both offer the benefits of these nutrients as well as facilitate metabolic function via relevant metabolic pathways, having more remarkable improvement than a single component.

We think they can be applied to not only healthy individuals but also fragile elderly individuals. If fatigue and DOMS, which currently impede the rehabilitation of patients, can be alleviated by ingesting complex supplements, rehabilitation can improve greatly. This will aid in maintaining and improving the activities of daily living and quality of life of patients. We think it would be best to review the rehabilitation program with the cooperation of a large patient sample. On the other hand, there is considerable variation in the general well-being of patients, which makes it difficult to find many patients with similar conditions for a rigorous study. We expect that the interpretation of the results of this type of nutritional intervention will be challenging. Therefore, we intend to initially study the effects of complex supplements in healthy adults, as in this study, and plan to conduct a volunteer study in a format closer to that of a clinical trial in the future.

## CONCLUSION

We found that the ingestion of complex supplements before exercise had an immediate recuperative effect on exercise-related fatigue and a lasting inhibitory effect on DOMS. These results suggest that in healthy adults, ingesting complex supplements alleviate fatigue and DOMS, which are major obstacles to efficient rehabilitation. Therefore, this supplement should also be tested in frail elderly individuals, in whom favorable outcomes are expected.

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