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# The Supplementation of Oligonol, the New Lychee Fruit-derived Polyphenol Converting into a Low-molecular Form, Has a Positive Effect on Fatigue during Regular Track-and-field Training in Young Athletes

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## Abstract

OHNO, H., SAKURAI, T., HISAJIMA, T., ABE, S., KIZAKI, T., OGASAWARA, J., ISHIBASHI, Y., IMAIZUMI, K., TAKEMASA, T., HAGA, S., KITADATE, K., NISHIOKA, H. and FUJII, H., The Supplementation of Oligonol, the New Lychee Fruit-derived Polyphenol Converting into a Low-molecular Form, Has a Positive Effect on Fatigue during Regular Track-and-field Training in Young Athletes. Adv. Exerc. Sports Physiol., Vol.13, No.4 pp.93-99, 2008. Oligonol is a new lychee fruit-derived polyphenol converted into a low-molecular-form, which has improved absorption and strong antioxidative activity. The aim of the current study was to investigate the effects of Oligonol supplementation on perceived subjective mood states in addition to oxidative stress in 47 undergraduate athletes during 52 days of track-and-field training. This was a prospective single blind crossover study. The ratings of perceived exertion (RPE) responses were significantly ($P < 0.05$) lower following Oligonol supplementation, suggesting that Oligonol intake caused the subjects to feel less fatigued during regular training. The results of our own questionnaire on fatigue and pain were as follows: Oligonol supplementation significantly ($P < 0.05$) improved all the fatigue scores and tended to attenuate the feeling of three kinds of pains (muscular/anticular pain, lumbago, and menstrual pain), followed by a change fot the worse after the discontinuance of Oligonol intake. Unexpectedly, however, there were no definite changes in the Profile of Moods States (POMS) scores or oxidative stress markers (8-hydroxy-2'-deoxyguanosine and hexanoyl lysine) in urine after Oligonol supplementation. The results obtained suggest that Oligonol supplementation in young athletes shows significant subjective positive effects particularly on the feeling of fatigue during regular track-and-field training, possibly contributing to the maintenance of good conditioning.

**Keywords:** Oligonol, track-and-field training, oxidative stress, RPE, fatigue

## Introduction

Alvarez et al. (1) have claimed that nowdays, consumption of natural products is a matter of major importance as regards health. Indeed, consumption of fruit and vegetable was already associated with a reduced risk of chronic diseases and age-related functional decline several years ago (9). For example, polyphenol intake has been associated with low cancer and coronary heart disease mortality rates. Antioxidant and anti-inflammatory properties and improvements in endothelial dysfunction and the lipid profile have been reported for dietary polyphenols (29). Nevertheless, less attention has been focused on the importance of phytochemicals from tropical fruits, especially the more exotic species, in maintaining health (10).

Lychee (*Litchi Chinensis,* Sapindaceae) is a tree that originates from China and is cultivated for its sweet fruits all over the world in warm climates. Lychee fruit pericarp contains significant amounts of polyphenolic compounds,

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of which principal characteristic is their ortho-diphenolic structure, which gives them high oxidability (26). Lychee pericarp tissues account for approximately 15% of the total weight of fresh fruit (30), which exhibits powerful antioxidative activity against fat oxidation *in vitro* (23, 31) and inhibits proliferation of breast cancer cells *in vitro* and *in vivo* (29, 30) as well as fat oxidation *in vivo* (23). As far as we know, however, there is no report about the effect of lychee supplementation in humans.

On the other hand, Morgan et al. (14) have noted that positive mental health is associated with high performance levels, whereas mood disturbances are predicted to result in performance decrements. In other words, the relationship between training distance and mood has been found to follow a dose-dependent pattern; mood progressively worsens as the training load is increased, while mood improves when training is reduced (19). Thus, some information is now available on the relationship between physical activity and mood state (4, 11, 13, 15, 21, 24, 27, 28).

It has long been known that, with some exceptions, antioxidant supplement offers protection against exercise-induced oxidative stress (7, 25). Also, compared with a placebo, a replacement drink with polyphenolic antioxidants proved capable of reducing the degree of protein oxidation caused by physical activity (16). Exercise intensity measures by ratings of perceived exertion (RPE), however, were similar across vitamin C supplementation (6). In addition, there was no evidence that six months of antioxidant selenium supplementation benefited mood or quality of life in elderly volunteers (20).

Quite recently, we succeeded in converting lychee-derived polyphenol into a low-molecular form (Oligonol). The aim of this prospective single blind crossover study, thus, was to investigate the effects of Oligonol during regular track-and-field training in undergraduate athletes. The hypothesis was that the Oligonol supplementation would lead to positive subjective effects and reduced oxidative stress.

## Materials and Methods

Oligonol was obtained by oligomerization of polyphenol polymers in lychee fruit-derived polyphenols, because of the limited absorption of polyphenol polymers due to their high molecular-weight. We have developed a proprietary process that shortens polyphenol polymers from lychee fruit into monomers and oligomers including dimers and trimers. The process involves to mix proanthocyanidins with tea extract but not L-cysteine, and to purify the mixture using a column. Oligonol contains 33.1% oligomeric polyphenols (monomers, dimmers, and trimers) with improved absorption. Patent technology as previously described with some modifications was used for oligomerization of polyphenols (5). Moreover, Oligonol was approved as a new dietary ingredient (NDI) by The Food and Drug Administration of the United States (FDA) on May 23rd, 2007, and is commercially available at present (Amino Up Chemical Co., Ltd., Sapporo).

Twenty-five male and twenty-two female undergraduate athletes, aged 18-22 years (19.7±0.2 years), volunteered for the current study after being informed of the purpose, methods, and possible complications of the experimental procedures. This work was approved by the Ethical Committee of Kyorin University, School of Medicine, Mitaka. Their mean height, mass, and body mass index were 170±1 cm (males: 175±1 cm; females: 164±1 cm), 61.1±1.4 kg (males: 66.4±1.7 kg; females: 55.2±1.5 kg), and 21.2±0.3 kg/m$^2$ (males: 21.8±0.5 kg/m$^2$; females: 20.6±0.4 kg/m$^2$), respectively.

The training protocol consisted of approximately 3-h regular track-and-field training occasionally on a competitive level, 5 times/week. Forty-seven subjects were randomly assigned into two groups (group A: 13 males and 11 females; group B: 12 males and 11 females). The study was designed in a subject-blinded manner and according to a crossover strategy; that is, the subjects were blinded to which treatment they received. A schematic picture of the study is shown in Fig. 1; that is, group A received placebo with the same appearance as Oligonol everyday during the first test period (26 days), and then received 200 mg Oligonol everyday during the second period (26 days) following a washout period (9 days), whereas group B received Oligonol or placebo everyday in the reverse order. All the subjects were requested not to take either antioxidant or other special supplements as much as practicable throughout the experimental period.

Three test sessions were performed in the morning immediately before the regular training before the start of the experiment and in the end of each testing period. The sessions included three questionnaires and urine samplings. The subjects were asked to complete the Profile of Moods States (POMS) psychological inventory, RPE, and questionnaires of our own making.

The POMS is a highly reliable and valid adjective scale that measures six distinct affective states as follows: five negative moods (tension-anxiety, depression-dejection, anger-hostility, fatigue-inertia, and confusion-bewilderment) and one positive mood (vigor-activity) (12).

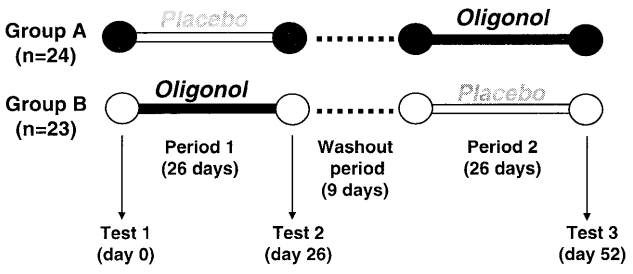


Fig. 1 Schematic picture of the study on Oligonol supplementation.

These factors are calculated according to the subject's level of agreement with each of 65 test items, determined by weighed intensity modifiers ranging from "not at all" to "extremely".

The RPE was obtained using the 15-category Borg RPE scale (22). Subjects had to give RPE corresponding to their sensations during the last training.

Next, the subjects filled out our own questionnaire with the following seven items: fatigue in daily living, recovery from fatigue in daily living, fatigue by exercise training, recovery from fatigue by exercise training, muscular/articular pain, lumbago, and menstrual pain. The subjects used a 5-point scale (1-"extremely" to 5-"not at all" for the five items other than "recovery from fatigue in daily living" and "recovery from fatigue by exercise training"; 1-"very slow" to 5-"very quick" for "recovery from fatigue in daily living" and "recovery from fatigue by exercise training") to respond to each item according to the question: "How have you been feeling for the past week including today ?". Each control value (which was obtained at the start of the experiment (Test 1)) was set up as "3".

Urine samples collected from 45 subjects (being two subjects short of all the subjects, because of the breakage of sample cases) were kept at -20℃ until assays of parameters of oxidative stress. 8-Hydroxy-2'-deoxyguanosine (8-OHdG) concentration was determined by an ELISA kit for 8-hydroxy-2'-deoxyguanosine (Japan Institute for the Control of Aging (JaICA), Nikken SEIL Corporation, Fukuroi), and Nε-(hexanoyl)lysine (HEL) concentration was measured using a Hexanoyl-Lys adduct: HEL ELISA kit (JaICA). In addition, creatinine level was assayed by a Creatinine Assay Kit (Cayman Chemical Company, Ann Arbor, MI). The levels of both parameters in urine were corrected by that of creatinine.

Data are expressed as means ± S.E.M. The Mann-Whitney test was applied to the data and a 0.05 level of significance was used.

## Results

As shown in Fig. 2, in both groups the RPE responses during regular training were significantly ($P<0.05$) lower following Oligonol supplementation, thereby suggesting that Oligonol intake caused the subjects to feel less fatigued during regular training.

Figs. 3 and 4 show the results of our original questionnaire on fatigue and pain, respectively. As to four items on fatigue, Oligonol supplementation significantly ($P<0.05$) improved all the fatigue scores in both Groups A and B, followed by a change for the worse after the discontinuance of Oligonol intake (Group B) (Fig. 3). Meanwhile, muscular/articular pain score in Group B, but not in Group A, was significamtly ($P<0.05$) increased (less pain) after Oligonol supplementation (Fig. 4A). Oligonol intake considerably attenuated lumbago in both groups (Fig. 4B). Also, discontinuous use of Oligonol in Group B significantly ($P<0.05$) decreased both muscular/articular pain and lumbago scores (Fig. 4A and B), meaning more pain. Moreover, menstrual pain only in Group A (only females) was significantly ($P<0.05$) abated by Oligonol supplementation (Fig. 4C).

Unexpectedly, however, no significant changes in any of POMS scores were found in either group throughout the experimental period, although Oligonol supplementation in both groups slightly, albeit insignificantly, decreased global mood state scales except for vigor-activity (data not shown).

Likewise, no significant differences were observed for 8-OHdG or HEL level in urine in any comparison; however, Oligonol intake did not increase either level (Table 1).

In the current study, no significant differences in any parameter measured were observed between the sexes (data not shown), except for physical characteristics.

## Discussion

As already stated, lychee fruit pericarp contains significant amounts of polyphenolic compounds, involving condensed tannins (polymeric proanthocyanidins), epicatechin, procyanidin A2, and flavonoids (26), strongly suggesting antioxidant activity. Actually, phenolics extracted from lychee fruit pericarp strongly inhibited linoleic acid oxidation and exhibited a dose-dependent free-radical scavenging activity against α,α-diphenyl-β-picrylhydrazyl (DPPH) and hydroxyl radicals and superoxide

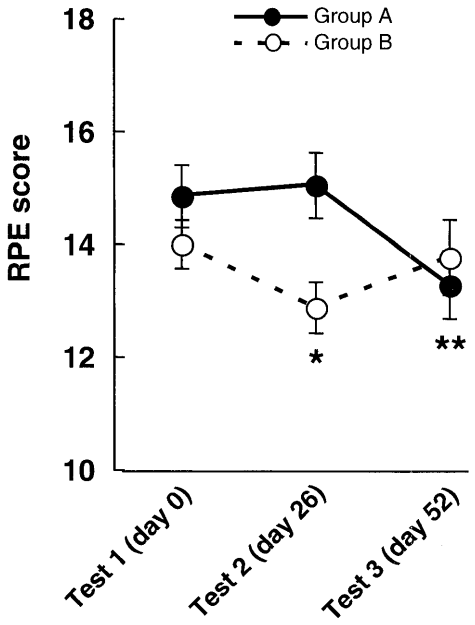


Fig. 2 Effects of Oligonol supplementation on the ratings of perceived exertion (RPE) responses during exercise training. Group A, n = 24; Group B, n = 23. *$P<0.05$ vs. on day 0; **$P<0.05$ vs. on day 26.

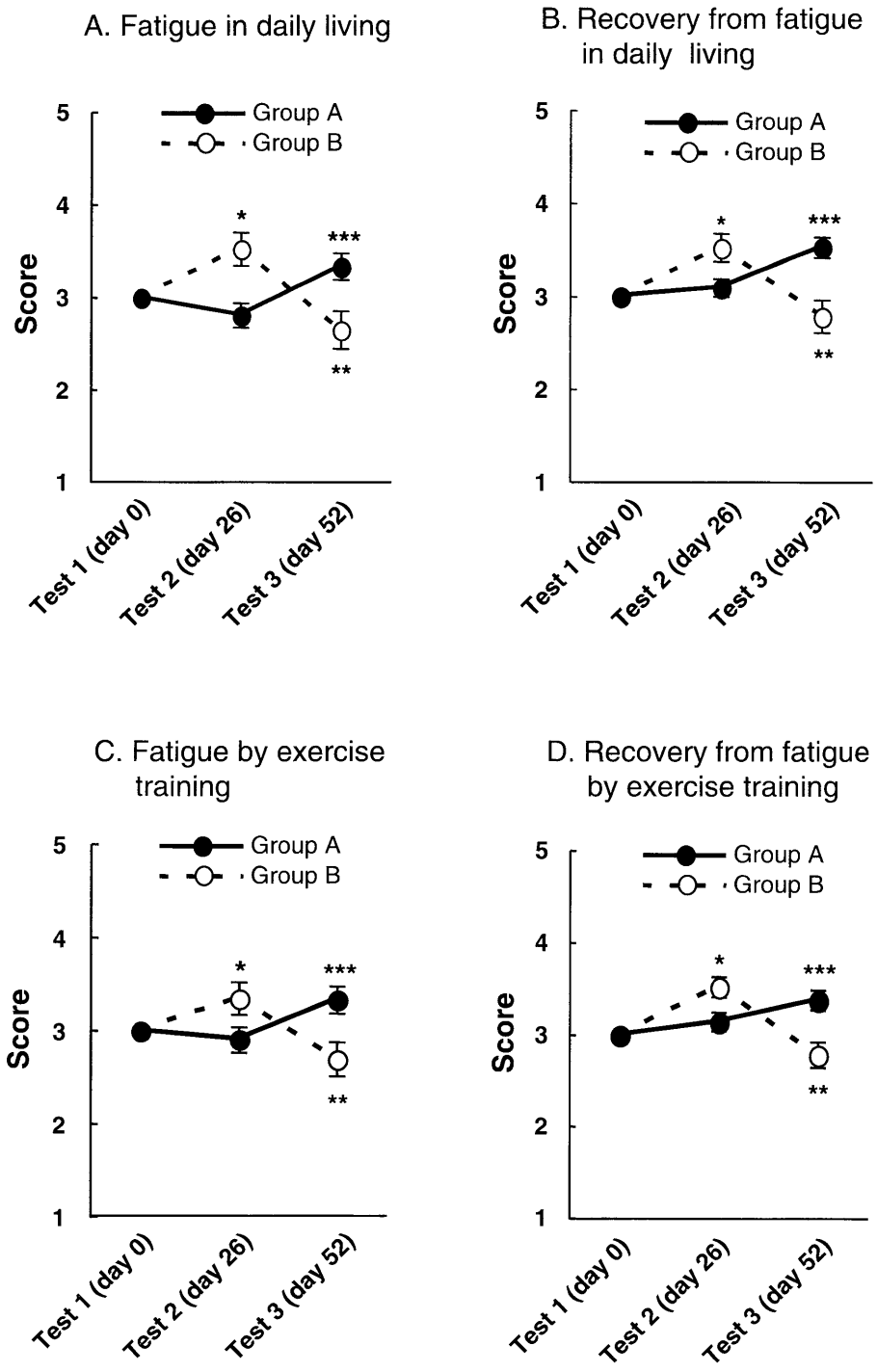


Fig. 3 Effects of Oligonol supplementation on the fatigue scores by our original questionnaire during exercise training. Group A, n = 24; Group B, n = 23. *P < 0.05 vs. on day 0; **P < 0.05 vs. on day 26 (Group B); ***P < 0.05 vs. on day 26 (Group A).

anions (2). The degradation of deoxyribose by hydroxyl radicals was inhibited by the phenolics acting mainly as iron ion chelators, rather than by directly scavenging the radicals.

The current study was the first to investigate the *in vivo* effect of lychee fruit-derived polyphenol in humans. Despite the use of Oligonol with improved absorption, however, the new phenolics failed to offer protection against oxidative stress during regular track-and-field training. 8-OHdG (32) and HEL (8) in urine were used as oxidative stress markers for DNA and lipid, respectively. It has been well known that responses of various oxidative stress markers to physical exercise are different and conflicting (17). Moreover, Sen and Goldfarb (25) have claimed that

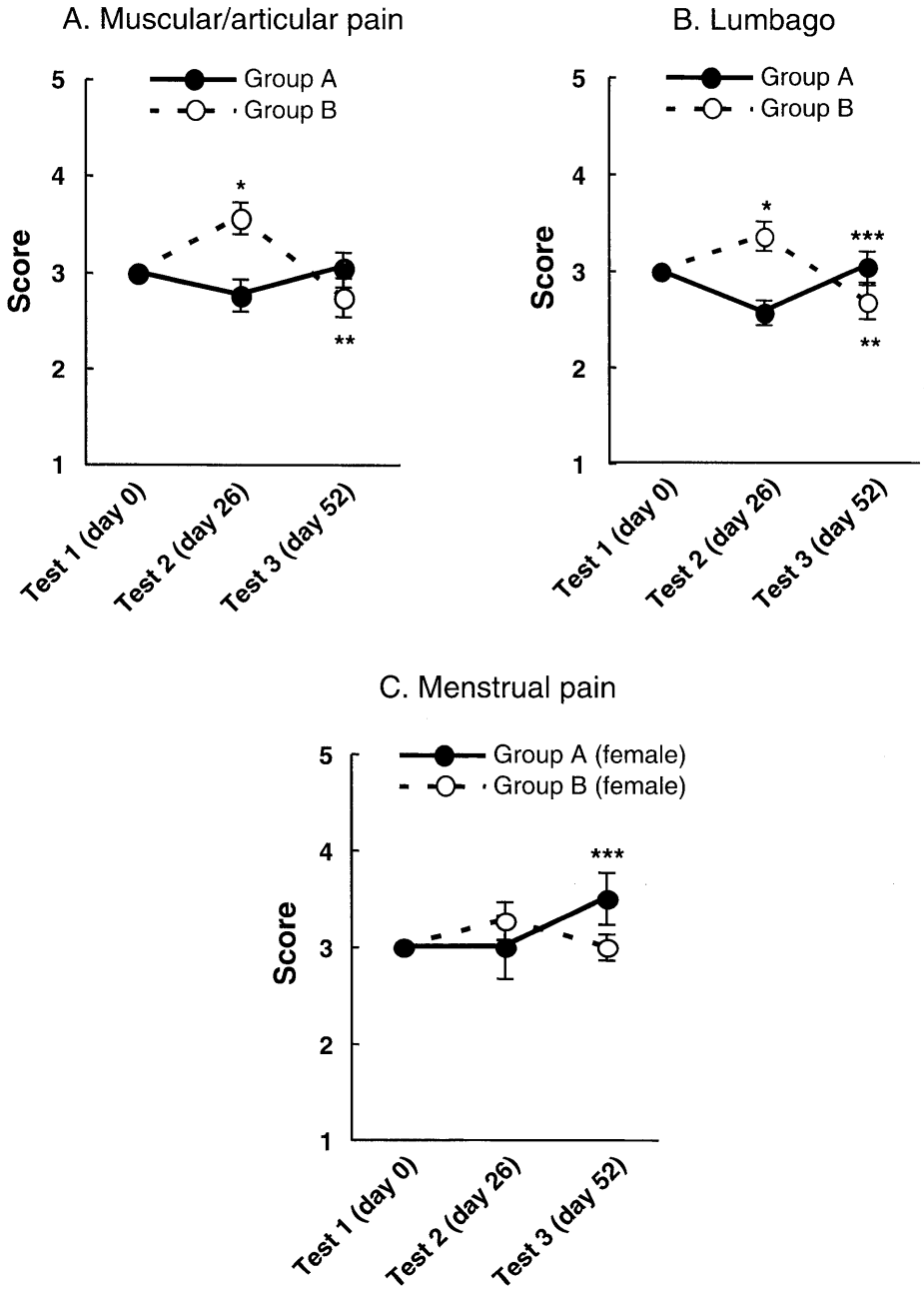


Fig. 4 Effects of Oligonol supplementation on the pain scores by our original questionnaire during exercise training. Group A, n = 24; Group B, n = 23. *P < 0.05 vs. on day 0; **P < 0.05 vs. on day 26 (Group B); ***P < 0.05 vs. on day 26 (Group A).

results from antioxidant supplementation studies considerably vary depending on the study design and measures of outcome, and that physical performance is regulated by multifactorial processes and may not serve as a good indicator to test the effect of antioxidant supplementation. At all events, further studies are needed not only to estimate the efficacy of Oligonol supplementation for varying periods but also to examine other oxidative stress markers such as protein carbonyl group. Additionally, it would not presumably be denied that Oligonol has unknown effects and/or components, and that the subjects had already acquired sufficient antioxidant capacity, due to regular physical training (18), prior to the start of the current study.

Nevertheless, the RPE responses as well as most of seven items of our own questionnaire on fatigue and pain were significamtly improved by Oligonol intake (Figs. 2-4). As also indicated by Sen and Goldfarb (25), it might be that Oligonol supplementation protected against exercise training-induced tissue damage, although the general trend of results showed no effect of antioxidant supplementation on physical performance. Actually, the three pain scores of our own questionnaire tended to be improved by Oligonol

Table 1 Effects of Oligonol supplementation on the levels of 8-OHdG and HEL in plasma

8-OHdG (ng)/CREA (mg)

| | Test 1 (day 0) | Test 2 (day 26) | Test 3 (day 52) |
|---|---|---|---|
| Group A (n = 23) | 6.1 ± 0.4 | 6.8 ± 0.7 | 6.4 ± 0.4 |
| Group B (n = 22) | 6.8 ± 0.7 | 6.0 ± 0.4 | 6.7 ± 0.5 |

HEL (pmol)/CREA (mg)

| | Test 1 (day 0) | Test 2 (day 26) | Test 3 (day 52) |
|---|---|---|---|
| Group A (n = 23) | 58.9 ± 5.0 | 68.2 ± 6.6 | 68.1 ± 6.6 |
| Group B (n = 22) | 83.7 ± 17.9 | 78.4 ± 8.1 | 63.6 ± 7.2 |

Means ± S.E.M. 8-OHdG = 8-hydroxy-2′-deoxyguanosine; HEL = N ε -(hexanoyl) lysine; CREA = creatinine

supplementation (Fig. 4).

The lowered scales of RPE observed following Oligonol supplementation were considered to be not due to training, but mostly due to Oligonol itself , because placebo had no definite effects during training. Oligonol is a water-soluble antioxidant like vitamin C (23), located for example in the cytosol, mitochondrial matrix or extracellular fluids, which may not have access to reactive oxygen species generated in membranes. Goldfarb et al. (6) have demonstrated that vitamin C supplementation can attenuate exercise-induced protein oxidation in a dose-dependent manner with no effect on RPE responses, thus suggesting that Oligonol and vitamin C have diverse effects on physical performance. One of the most sensitive parameters for detecting overreaching is RPE, suggesting that central fatigue precedes peripheral fatigue (21). Additionally, RPE is a valid measure of exercise monitoring and prescription owing to the observed association between RPE and more objective physiological markers of intensity, such as heart rate or oxygen consumption (13).

As to our original questionnaire, all the items on fatigue were also improved (Fig. 3). Since the RPE scores gave a quantitative identification of the feeling of fatigue (14), the results of RPE obtained in the current study appeared to reflect those of the questionnaire. These did not conflict with the findings on pain by the questionnaire. Collectively, Oligonol supplementation leads to positive subjective effects during regular track-and-field training, although its mechanism remains to be elucidated.

On the other hand, there were no significant changes in any of POMS scores after Oligonol supplementation. Rietjens et al. (21) have indicated that POMS is not a strong early instrument for overreaching, whereas there is a moderate correlation between the fatigue subset of the POMS and fatigue components, such as maximal oxygen uptake and running economy (28). As already stated, however, subjective positive effects especially on fatigue were observed in our original questionnaire. Fahlstrom et al. (3) also demonstrated that there were perceived subjective positive effects in badminton players, accompanied by no changes in the POMS scores, following sports drink supplementation, and explained the discrepancy also seen in the current study as follows: this is not surprising, since the POMS tests were performed only every 2 weeks, and a previous study has shown that emotions may fluctuate on a daily, even hourly basis. The question whether such an explanation can be extrapolated to the current study, however, cannot be answered at present.

In conclusion, the results obtained suggest that Oligonol supplementation in young athletes shows significant subjective positive effects particularly on fatigue during regular track-and-field training, and thus may contribute to the maintenance of good conditioning.

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