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Research article

Effect of BETA 1, 3/1, 6 GLUCAN on upper respiratory tract infection symptoms and mood state in marathon athletes

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Abstract
This was a placebo-controlled, double-blind study designed to evaluate the effect of a commercially available dietary supplement on upper-respiratory tract symptoms (URTI) and mood state. Seventy-five marathon runners (35 men, 40 women) ranging in age from 18–53 years, mean age: 36 ± 9, self-administered placebo, 250 mg or 500 mg of BETA 1,3/1,6 GLUCAN (commercial name Wellmune WGP®) daily during the 4 week post-marathon trial period following the 2007 Carlsbad Marathon. Subjects filled out the profile of mood state (POMS) assessment and a questionnaire style health log measuring health status and URTI symptoms after 2- and 4-week treatment administrations. During the course of the 4-week study, subjects in the treatment groups (250 mg and 500 mg BETA-GLUCAN per day) reported significantly fewer URTI symptoms, better overall health and decreased confusion, fatigue, tension, and anger, and increased vigor based on the POMS survey compared to placebo. BETA-GLUCAN may prevent URTI symptoms, and improve overall health and mood following a competitive marathon.

Key words: Dietary supplements, exercise, beta-Glucans, respiratory tract infections.

Introduction

Heavy exercise or elite training may lead to increased susceptibility to upper respiratory tract infections (URTI) (Nieman et al., 1990; Peters and Bateman, 1983; Spence et al., 2007). Heavy exercise is a physical stressor that results in measurable immune challenges with reductions in key immune system components such as neutrophils, natural killer cells, T cells and B cells (Mackinnon and Hooper, 1994; Nieman et al., 1995; Ostrowski et al., 1998). Athletes are particularly susceptible in the 2 week recovery period after competitive marathons or ultra-marathons partially due to elevations in hormones that coordinate the stress response (Peters and Bateman, 1983). The net effect of an ongoing immune challenge is a weakened immune system, which often results in URTI.

Exercise stress is similar to other stressors, such as psychological stress, which can lead to a weakened immune system and increased susceptibility to URTI and other disease states (Mackinnon, 1997). Psychological stress can also result from prolonged training and competition at the elite level. Elite athletes have deterioration in mood state during intense training periods, and before and after a marathon race (Achten et al., 2004; Hassmen and Blomstrand, 1991). Lifestyle factors, such as coping with daily stress, may influence the immune response to exercise (Konig et al., 2000). Reductions in immune cell populations, lowered antibody production and altered cytokine response have been observed due to psychological stress (Cohen et al., 1999; Glaser et al., 1999).

A variety of intervention techniques can be used to ameliorate psychological and physical stress, such as administering selective dietary supplements containing immune modulating compounds (Akerstrom and Pedersen, 2007; Nieman and Bishop, 2006; Peters et al., 1993). In ultra-marathon runners, 600mg of vitamin C, taken 21 days before and 14 days after a 90 km race, reduced URTI symptoms (Peters et al., 1993). Biological response modifiers, for example BETA-GLUCAN, enhance the innate immune response (Luhm et al., 2006; Niederman et al., 2002). BETA-GLUCANS are glucose polymers derived from a variety of sources including yeast, grain, or fungus. *In vitro,* BETA-GLUCAN enhanced the microbicidal activity of neutrophils, macrophages and natural killer cells against a variety of pathogens (Bedirli et al., 2007; Ikewaki et al., 2007; Liang et al., 1998). *In vivo*, oat-derived BETA-GLUCAN, prevented increased risk of URTI after stressful exercise in mice (Davis et al., 2004;Murphy et al., 2008). In human clinical trials, BETA-GLUCAN reduced postoperative infection rates and shortens intensive care unit stay duration (Babineau et al., 1994a; 1994b; Dellinger et al., 1999).

In this study, we report the effect of using BETA-GLUCAN on the physical and psychological well-being of marathon runners who participated in the 2007 Carlsbad Marathon. The current study employed a series of subject self-assessment questionnaires that addressed overall health status and URTI symptoms. In addition to evaluation of subjects for physical health, a psychological assessment known as the Profile of Mood States (POMS) was conducted to assess mood state. A key objective of the study was to explore how BETA-GLUCAN affected various moods, URTI symptoms, and overall health status 4 weeks following a marathon competition.

Methods

Subjects

This study was done in accordance with the Helsinki Declaration, as revised in 1983, for clinical research involving humans. Subjects signed informed consent documents after the study details were explained. Seventy-five healthy men (n = 35) and women (n = 40) ranging in age from 18–53 years (mean age: 36 ± 9) participated in this study. Enrollment took place through a recruitment table in the runner registration area for the Carlsbad Marathon (Carlsbad, California, USA) on January 20, 2007. The marathon race took place on January 21, 2007. Inclusion

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criteria included healthy, asymptomatic adults who were marathon participants, and a completed informed consent form. Exclusion criteria included those with current URTI symptoms, injury, and inability to complete all questionnaires and current use of antibiotics or other "immune" support products.

Dietary supplement

A placebo-controlled, double-blind design was employed for this study. Each subject was evaluated for inclusion and exclusion criteria, and included in the study only if they met the appropriate criteria. Subjects began treatment the day following the marathon race. Subjects were randomly assigned, through a random number generator, to either BETA-GLUCAN (250 mg, 500 mg; BETA 1,3/1,6 GLUCAN; commercial name Wellmune WGP®) or a placebo group, immediately after enrolling in the study. Placebo capsules were 250 mg of rice flour; BETA-GLUCAN capsules were 250 mg of BETA 1,3/1,6 GLUCAN isolated from the yeast *Saccharomyces cerevisiae*. Participants completed a baseline POMS and health log questionnaire on the first day of the study. Dosing was placebo, 250 mg or 500 mg BETA-GLUCAN per day for 4 weeks. Subjects were instructed to self-administer the allotted dose once daily in the morning, at least 30 minutes prior to breakfast for a period of 4 weeks. Following the 2- and 4-week administration periods, subjects filled out the POMS test and a questionnaire style health log. Subjects were instructed to maintain their normal activity levels following the marathon.

Mood assessment

The Profile of Mood States is a validated psychometric test, a sensitive measurement of mood in normal healthy subjects, and has been employed in over 2,900 health studies (McNair et al., 1971; 2003). The POMS profile uses 65 adjective-based intensity scales that measures 6 mood factors: tension, depression, anger, fatigue, vigor and confusion (McNair et al., 1971). The adjective responses and scores were measured on a 0–4 scale (0 = not at all, 4 = extremely). Individual mood state factors were assessed using specific adjective scales. For example, the tension factor was assembled using responses to adjective scales 2, 10, 16, 20, 22, 26, 27, 34 and 41 in conjunction with the specified analysis. Other mood state factors used responses to other adjectives including depression (15 adjectives), anger (12 adjectives), vigor (8 adjectives), fatigue (7 adjectives) and confusion (7 adjectives). The output of the POMS questionnaire is an assessment of the positive and negative moods of each subject at the baseline assessment, 2- and 4-week intervals of the study. Combining the scores of all 6 mood state factors created a global mood state. Data is reported for each mood state and the global mood state.

Health log

Subjects completed a physical health questionnaire at baseline, 2- and 4-week assessment periods. The health log was a daily health perception log containing questions related to overall health status and specific URTI symptoms. The URTI-related symptoms measured included nasal congestion, runny nose, sore throat, sneezing, cough, fatigue, headache, general malaise and body aches. Subjects also responded to a supplement effectiveness question: "During the course of the supplement regimen, my health has been…:" Scores for the question were based on a scale of 0–10 with 0 being worse, 5 being same and 10 being better health. Subjects were also asked to record various health codes in a daily log using a numerical system ranging from no health problems to specific symptoms and rating for severity of the symptoms (A = mild, B = moderate and C = severe). In addition to the scaled questions, there were questions that evaluated the annual number of illness episodes; e.g., Compared to this time last year, do you feel that you generally have ____ episodes with the common cold or flu? Choices were fewer, about the same or a greater number.

Data analysis

All questionnaires were mailed to a central location and transcribed to a central database. Data was identified by subject number and examined for accuracy and completeness. Tabulated data was analyzed with StatView (SAS Institute) using standard parametric statistical tests (paired t-tests). Significance was set at $p < 0.05$.

Results

All descriptive data is expressed as mean ± SD. Seventy-five total subjects (35 male, 40 female; mean age 36 years, range 18–53 years) completed and returned all questionnaires. Marathon runners in both BETA-GLUCAN groups had statistically significant ($p < 0.05$) improvements in measurements of physical health, including reported URTI symptoms and overall health status.

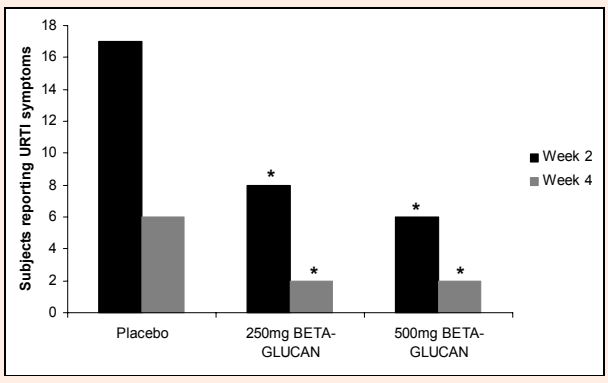

Figure 1. Total number of subjects reporting any of 11 preselected upper-respiratory tract infection symptoms. Subjects orally administered placebo, 250 mg or 500 mg BETA-GLUCAN. Data analysis was by paired t-tests. * $p \leq 0.05$

URTI symptoms

Figure 1 shows data for subjects reporting URTI symptoms at 2- and 4 weeks post-marathon. There was a significant ($p < 0.05$) decrease in URTI symptoms in both BETA-GLUCAN treatment groups after 2- and 4-weeks. After 2 weeks, 68% of subjects in the placebo group reported symptoms associated with URTI, while only 32% (250 mg) and 24% (500 mg) of the BETA-GLUCAN

groups reported similar URTI symptoms. Upper respiratory tract infections were reported by only 8% of subjects in both treatment groups at week 4 versus 24% of placebo subjects. The most common URTI symptoms reported by subjects were sore throat, stuffy or runny nose and cough. Compliance in completing the daily health log was not sufficient to allow analysis of individual symptom scores.

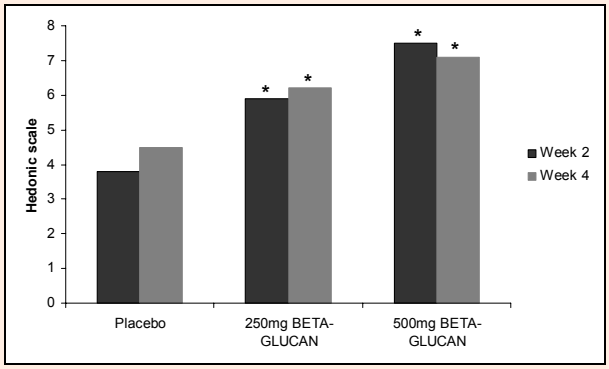

Figure 2. Health score during BETA-GLUCAN administration. Subjects responded to 2 and 4 week supplement effectiveness question: "During the course of the supplement regimen, my health has been…:" Scores for the question were based on a scale of 0–10 with 0 being worse, 5 being same and 10 being better health. Data analysis was by paired t-test. *$p \leq 0.05$.

Health perception

When asked how the supplement regimen was affecting their overall health, subjects taking 250 mg BETA-GLUCAN reported 38% higher scores and subjects administering 500 mg BETA-GLUCAN reported 58% higher health scores compared to placebo ($p < 0.05$) Figure 2. Subjects were asked to rate how their health was affected by the supplement (BETA-GLUCAN or placebo) and asked to compare their current health status to their typical health history, see Figure 3. Participants taking 250 mg BETA-GLUCAN rated their health 15% higher versus placebo; subjects taking 500 mg BETA-GLUCAN rated their health 44% higher as compared to placebo, $p < 0.05$. In addition to the scaled questions, there were questions that evaluated the annual number of illness episodes, but compliance to these questions was poor and the data obtained was not meaningful.

POMS assessment

The data analysis included an assessment of mood state at baseline (day 0), 2-, and 4 weeks after treatment. As described, the POMS survey consists of a number of adjective based scales. Significant mood state responses for confusion (reduced), fatigue (reduced), vigor (increased), and tension (reduced) were observed (Figure 4), $p < 0.05$. BETA-GLUCAN generated a statistically significant reduction in anger, $p < 0.05$, after 2 weeks on 500 mg. There were no changes in depression after treatment.

Observed improvements included a 48% reduction in fatigue for the 250 mg dose and 59% for the 500 mg doses of BETA-GLUCAN compared to placebo after 4 weeks of treatment. Vigor increased after 2 and 4 weeks of 500mg BETA GLUCAN, but no change in vigor occurred in the 250 mg dose group. Subjects reported a 38% and 47% reduction in tension (250 mg and 500 mg respectively) over the 4-week study period. Subjects also reported a 38% and 45% reduction in confusion (250 mg and 500 mg) respectively over the 4-week study period compared to placebo. After 4 weeks, both the 250 mg and 500 mg doses reduced tension ($p < 0.05$), but only the 500 mg dose reduced tension after week 2 ($p < 0.05$). Anger was only reduced after 2 weeks of treatment with the 500mg dose ($p < 0.05$).

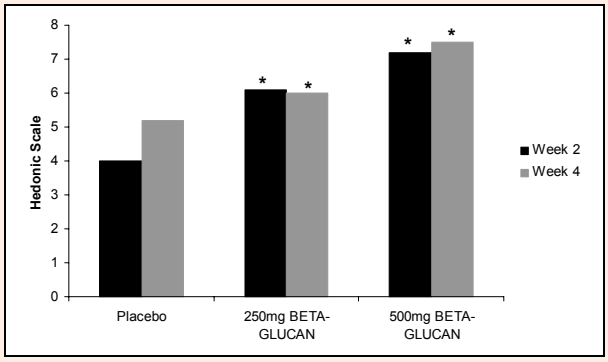

Figure 3. Overall health-score. Subjects responded to a 2- and 4-week health status question: "At the end of this 2-week period, how would you rate your overall health...?" Scores for the question were based on a scale of 0-10 with 0 being worse, 5 being same and 10 being better health. Data analysis was by paired t-test. *$p \leq 0.05$.

The global mood state, a combination of 6 main factors, improved after both the 250 mg dose at 4-weeks and both 2- and 4-weeks in the 500 mg treatment groups compared to placebo (Figure 5). The global mood state improved by 11% for subjects taking 250 mg and 13% for subjects taking 500 mg per day versus placebo, $p < 0.05$.

Discussion

During the course of the 4-week treatment period, subjects in both treatment groups, 250 mg and 500 mg BETA-GLUCAN, reported fewer URTI symptoms, better overall health and a more positive mood state compared to placebo 4 weeks after completing a marathon.

Marathon runners and other athletes, whose athletic activities cause significant physical stress, are more susceptible to URTI (Nieman et al., 1990; Peters and Bateman, 1983; Spence et al., 2007). Previous research reported that nutritional supplementation can modulate the health status of these high-performance athletes (Nieman and Bishop, 2006; Peters et al., 1993). In this study, BETA-GLUCAN, a commercially available dietary supplement, reduced the incidence of URTI symptoms and had a positive impact on mood state as measured by the POMS assessment. BETA-GLUCAN participants reported both fewer URTI symptoms and a better overall health status. The URTI symptoms reported by subjects are typical of cold and flu symptoms, and analogous to symptoms reported in other studies (Cohen et al., 1999; Konig et al., 2000). Total URTI symptoms were summed by subject, but individual symptoms could not be

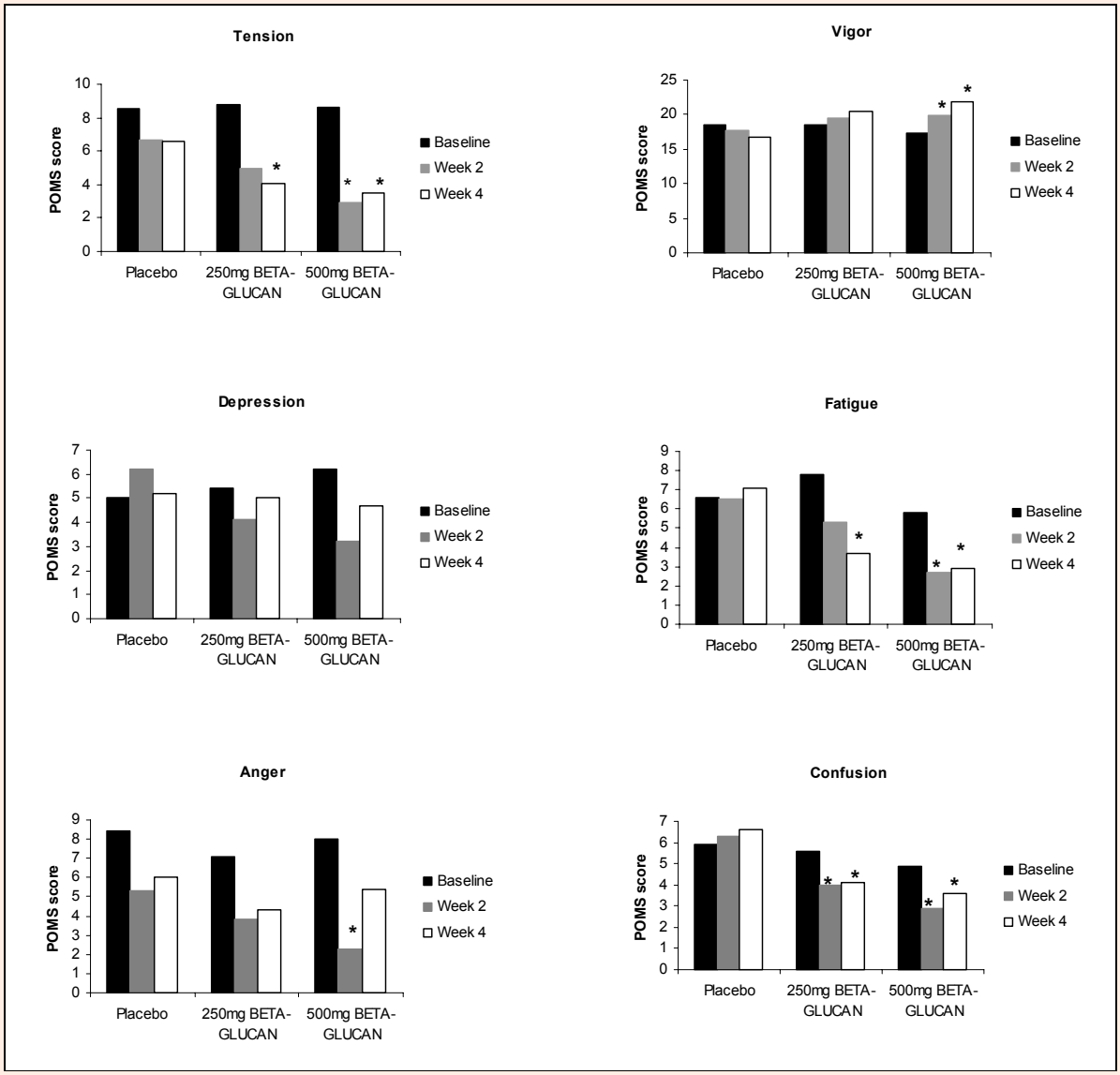

Figure 4. Data analysis for specific POMS factors calculated from POMS score sheet. Data analysis was by paired t-test. Each factor was determined using answers to specific adjective based scales as described in the Profile of Mood States manual by McNair et al., 1971.. A value of $p \leq 0.05$ was considered significant *$p \leq 0.05$.

analyzed due to a lack of data. Well-established and clinically valid techniques (POMS survey, URTI symptoms) were used during the course of this study, while exploring more subjective techniques such as the health status questions. Therefore, the results of the health status questions (Figures 2 and 3) are valid and will be employed in future studies.

Physical and psychological factors of subjects undergoing stressful situations are reported to increase URTI (Cohen et al., 1999; Konig et al., 2000). In all cases, the subjects on BETA-GLUCAN experienced better physical health and a significantly improved psychological status, including more positive feelings, than those in the placebo group. The results of the POMS survey suggest that subjects self-administering BETA-GLUCAN (250 mg and 500 mg per day) reported reduced fatigue and tension after 4 weeks and increased vigor for subjects on the 500 mg dose. The confusion factor was reduced for both treatment groups at 2- and 4-week intervals. In contrast, the anger and depression factors did not show statistical significance at the 4-week reporting period, although anger was reduced after 2 weeks in the 500 mg BETA-GLUCAN treatment group. Previous research reported that elite athletes training for a marathon experience a non-significant deterioration in global mood state and significantly decreased vigor and increased fatigue (Achten et al., 2004; Hassmen and Blomstrand, 1991). Although there is little evidence that mood changes occur *after* a strenuous exercise event, the global mood state score continued to be elevated 4 weeks post-marathon in the placebo group; while there were statistically significant improvements in both BETA-GLUCAN groups at the same time point. Our results suggest that BETA-GLUCAN may ameliorate mood changes occurring after heavy exercise exertion.

The POMS assessment for psychological health strongly supported and mirrored the physical health assessment. Illness and stress impact the immune system in

both physical and psychological ways (Konig et al., 2000; Strasner et al., 2001). The POMS methodology has been used in more that 2,900 studies (McNair et al., 1971); thus it has well-established validity. The survey instrument employs 65 adjective based scales that are scored by subjects without knowledge of how the scale scoring will be analyzed. The POMS survey instrument assesses the overall global mood state of subjects and provides feedback on specific moods and feelings such as tension, depression, fatigue, vigor, confusion and anger.

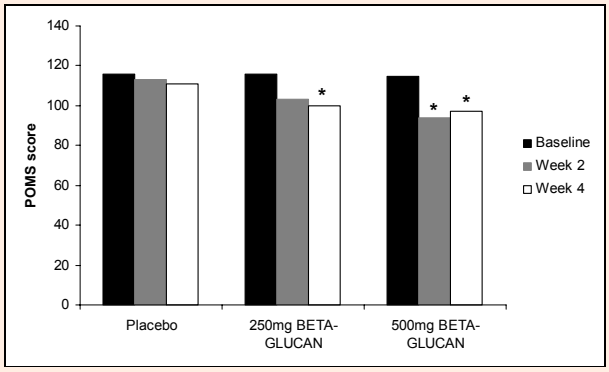

Figure 5. The global mood state was calculated based on scoring (0-4 with 0 = not at all, 2 = moderately and 4 = extremely) answers to 58 of the 65 adjectives. Data analysis was by paired t-test. *$p \leq 0.05$

BETA-GLUCAN improves immune function in a variety of animal models (Hetland et al., 1998; Hong et al., 2004;Kernodle et al., 1998; Vetvicka et al., 2002; 2008). Research by Vetvicka et al. (2002) demonstrated that BETA-GLUCAN helped prevent anthrax infection and mortality in mice. Additional studies support further antibacterial (Kernodle et al., 1998) and anti-tumor properties (Hong et al., 2004; Vetvicka et al., 2008). Other dietary supplements may reduce URTI symptoms (Cox et al., 2008; Kekkonen et al., 2007; Peters et al., 1993), i.e., zinc treatment reduced duration and severity of cold symptoms (Prasad et al., 2000). Probiotics (*Lactobacillus rhamnosus*) given 3 months prior to a marathon race had no effect on URTI symptoms or duration (Kekkonen et al., 2007). However a different probiotic (*Lactobacillus fermentum*) reduced the severity and duration of URTI in elite athletes (Cox et al., 2008). Vitamin C supplementation in ultramarathoners reduced the duration and severity of URTI when taken 21 days before an ultramarathon (90 km) (Peters et al., 1993).

A recent study reported no change in self-reported URTI symptoms in endurance athletes given a BETA-GLUCAN supplement for 18 days (Nieman et al., 2008). Beta-glucan was administered at 5.6 g·day^{-1} in a 600 ml beverage containing Gatorade® and Oatvantage®, a 54% oat BETA-GTLUCAN concentrate. Subjects ingested the supplements in two 300 ml doses each day before their first and last meals on an empty stomach. Nieman, et al., 2008 reported no changes in natural killer cell activity, polymorphonuclear respiratory burst activity, phytohemagglutinin-stimulated lymphocyte proliferation, plasma interleukin 6 (IL-6), IL-10, IL-1 receptor agonist (IL-1ra), and IL-8, and blood leukocyte IL-10, IL-8, and IL-1ra mRNA expression. This study is different from the present study in timing, chemical composition, and dosing making direct comparisons difficult. The current study administered the supplement after a marathon, whereas Nieman, et al., 2008 gave the supplement before strenuous exercise. Nieman, et al., 2008 gave a 600 ml beverage supplement, containing Gatorade® and Oatvantage® (soluble oat derived beta-glucan), whereas the current study administered 2 different doses (250 mg and 500mg) insoluble yeast-derived beta-glucan supplement (WGP®3-6). Soluble and insoluble BETA-GLUCANS may stimulate the immune system differently (Rice et al., 2005). The current study suggests that yeast derived BETA-GLUCAN may be effective in preventing URTI in athletes, while oat derived BETA-GLUCAN is not.

Conclusion

In this study, BETA-GLUCAN significantly decreased URTI incidence and improve mood state compared to placebo. Daily supplementation with BETA-GLUCAN reduced the incidence of symptoms associated with upper respiratory tract infections and improved the psychological well being of participants. Additional research is needed to investigate the ability of BETA-GLUCAN to reduce the incidence of URTI in high-performance athletes.

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Key points

- Beta-Glucan supplementation maintains immune function in endurance athletes.
- Beta-Glucan supplementation reduces post-exercise URTIs in marathon runners.
- Maintenance of post-exercise immune function is associated with improved mood state, including reduced fatigue and increased vigor in athletes.

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