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# Beta 1,3/1,6 glucan decreases upper respiratory tract infection symptoms and improves psychological well-being in moderate to highly-stressed subjects

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**ABSTRACT:** A randomized, placebo-controlled, double blind design study was conducted to evaluate the effect of  $\beta$ -1,3/1,6 glucan derived from bakers yeast, a commercially available dietary supplement, on symptoms associated with upper-respiratory tract infections and psychological well-being. Moderate to highly stressed subjects (45 men, 105 women) ranging in age from 18–65 (mean age:  $39 \pm 11$  years) were administered placebo, 250 mg, or 500 mg  $\beta$ -1,3/1,6 glucan during a 4 week treatment period. Subjects in both treatment groups (250 mg and 500 mg  $\beta$ -1,3/1,6 glucan per day) reported fewer upper respiratory tract infection symptoms, better overall health and increased vigour, and decreased tension, fatigue, and confusion based on the profile of mood states assessment.

**KEYWORDS:** yeast  $\beta$ -glucan,  $\beta$ -glucan,  $\beta$ -1,3/1,6 glucan, dietary supplements, respiratory tract infections, stress.

## INTRODUCTION

The relationship between stress and decreased immune function is well established (1-3), but the mechanisms are unclear. Psychological stress also increases susceptibility to the common cold and increases upper respiratory tract infection (URTI) episodes (3-5). Psychological stress reduces immune cell populations, lowers antibody production and alters cytokine responses (6, 7). Subjects reporting higher levels of psychological stress have a higher incidence and greater severity of illness (2-4). Chronic stress can cause deleterious effects on the immune system by reducing the responsiveness of the innate and humoral systems and increasing inflammatory mediators. A variety of dietary supplements have been studied for the prevention and treatment of both experimentally induced and naturally occurring colds, including Echinacea (8), vitamin C (9, 10), ginseng (11) vitamin E (12, 13) and zinc (14). None of these supplements has clearly demonstrated a clinically-relevant reduction in URTI symptoms. In previous clinical trials,  $\beta$ -glucan has been shown to reduce the severity and duration of URTI symptoms in physically stressed subjects (15) and non-stressed subjects (16).  $\beta$ -glucan has enhanced the microbicidal activity of innate immune cells *in vitro* (17-19) and increased survival in animals challenged with a variety of pathogens *in vivo* (20, 21). Therefore,  $\beta$ -glucan may be effective in reducing the incidence or severity of URTI in humans whose immune systems have been affected by chronic self-reported stress. In the current study, we report the effects of  $\beta$ -1,3/1,6

glucan derived from bakers yeast ( $\beta$ -glucan), on the physical and psychological well-being of subjects who self-reported moderate to high levels of perceived stress.

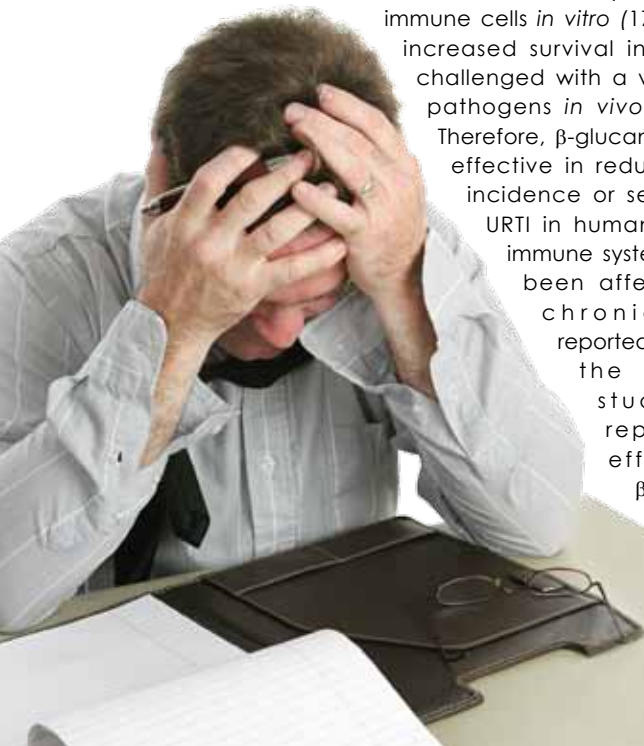
## MATERIALS AND METHODS

### Study design

This study followed the Helsinki Declaration as revised in 1983 for clinical research involving humans. Subjects received study details and signed an informed consent document. The study used a randomized placebo-controlled, double-blind design. Each subject was evaluated for inclusion and exclusion criteria and included in the study if meeting appropriate criteria, mentioned below. Subjects were randomly assigned, through a random number generator, to one of three groups of 50 subject each: placebo, 250 mg / day  $\beta$ -1,3/1,6 glucan or 500 mg /day  $\beta$ -1,3/1,6 glucan (commercial name Wellmune WGP®). Placebo capsules contained 250 mg of rice flour. Subjects self-administered the allotted dose once daily in the morning at least 30 minutes before breakfast for 4 weeks. Participants completed a baseline POMS and health log questionnaire on the first day of the study. Subjects completed a daily health log, filled out a POMS assessment, and a physical health questionnaire after both 2- and 4-week treatment periods.

### Subjects

Subjects were screened for "moderate" to "high" levels of perceived stress using a screening survey. We used a screening survey that has been used in past studies of stress/POMS to identify individuals with high levels of perceived stress. Although this screening survey is not clinically validated in a large population, we have successfully used it in 2 studies of exercise training and 4 studies of weight loss to stratify subjects with respect to levels of perceived stress (22, 23). The stress survey (15 questions) strongly correlates (22, 23) with other measures such as the Profile of Mood States (POMS) (24, 25) and served as a reliable screening tool for identifying subjects undergoing "moderate" to "high" levels of perceived stress. Subjects scoring 6 or greater on this screening survey were eligible for enrolment. A score of 6-10 indicates moderate stress; a score of >10 indicates high stress. Inclusion criteria included healthy, asymptomatic adults, screened as moderate to high stress level,



providing a completed informed consent form. Exclusion criteria included those with current URTI symptoms, injury, and inability to complete all questionnaires, low stress level and current use of antibiotic or other "immune" support product. The final subject pool (150 subjects, 50 per group) was composed of healthy men (n = 45) and women (n = 105) ranging in age from 18–65 (mean age: 39 ± 11 years).

#### Profile of mood states

We employed the Profile Of Mood States questionnaire (POMS) (24, 25) to measure 6 primary psychological factors (tension, depression, anger, fatigue, vigour or confusion). The POMS methodology has been used in more than 2,900 studies (24); and its validity is well established. The POMS profile uses 65 adjective-based intensity scales scored on a 0-4 scale (0 = not at all, 4 = extremely). The 65 adjective responses are categorized into the six mood factors, tabulated, scored and analyzed. The output of the POMS questionnaire is an assessment of the positive and negative moods of each subject at baseline, 2- and 4-week intervals of the study.

#### Health log

The daily health log contained questions related to overall health status and specific URTI symptoms. The URTI-related symptoms included nasal congestion, runny nose, sore throat, sneezing, cough, fatigue, headache, body aches, and general malaise. There were 11 URTI symptoms evaluated using a check box format with frequency assessment (ranging from no symptoms to multiple symptoms per day). In the current study, total URTI symptoms were summed by subject and symptoms were not evaluated for severity (symptom score). The URTI symptoms reported by subjects are typical of cold and flu symptoms and analogous to symptoms reported in other studies (26, 27). In addition to the symptom form, subjects were asked to record various health codes into 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). Subjects were also asked to score their daily health during the supplementation using a typical hedonic scale (1 = worse, 10 = better). Additionally, subjects completed an overall health questionnaire at baseline, and at 2- and 4-week intervals. Subjects were asked to rate how their health was affected by the supplement (β-glucan or placebo) and asked to compare their current health status to their typical health history.

#### Data management and 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 using standard parametric paired t-tests and significance was assessed with a two-tailed alpha level set at 0.05.

## RESULTS

#### URTI Symptoms

One-hundred-fifty subjects (45 male, 105 female; mean age 39 years, range 18-65 years) completed and returned all questionnaires, any incomplete or non-returned forms were excluded from the dataset. Compliance was nearly equal in all three subject groups; therefore, bias is not considered likely in the data analysis. Healthy, stressed subjects in both treatment groups had statistically significant ( $p < 0.05$ )

improvements in measurements of physical health including fewer reported URTI symptoms and better overall health status compared to the placebo group (Table 1). There was a significant ( $p < 0.05$ ) decrease in reported URTI symptoms in both β-glucan treatment groups. After 2 weeks, 32 percent of subjects in the placebo group reported symptoms associated with URTI, but only 10 percent in the 250 mg group and 8 percent in the 500 mg β-glucan group reported URTI symptoms. The most common URTI symptoms reported by subjects were sore throat, stuffy or runny nose, and cough. Other symptoms were reported infrequently or not reported at all. In general, subjects completed the URTI symptom check box form, but there was poor compliance to completing the daily health log. Thus, data was analyzed for overall URTI symptoms, but not for individual symptom severity scores.

#### Health perception

Subjects also completed a health perception log. Subjects rated how their health was affected by the supplement (β-glucan or placebo) compared to their current health status and their typical health history. Both treatment groups reported significantly higher scores in the health perception survey (Table 1). Study subjects scored their overall health compared to their historical health status at the end of each 2-week period (2 and 4 weeks, respectively). Both treatment groups rated their health significantly higher as compared to placebo (Table 1).

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**Boosting the immune system with bakers yeast β-glucan has been shown to have a noticeable effect on maintaining health and a positive mental attitude in psychologically stressed individuals in this study**

		Placebo	250 mg WGP/day	500 mg WGP/day
Q1 - During the course of the supplement regimen my health has been... (1 = worse, 10 = better)	End of 2-week period	4.3±1.0	6.2*±1.2	7.0*±1.3
	End of 4-week period	4.6±1.0	6.5*±1.1	7.2*±1.2
Q2 - At the END of this 2-week period how would rate your overall health... (1 = worse, 10 = better)	End of 2-week period	5.0±1.2	6.9*±1.6	7.4*±1.6
	End of 4-week period	5.3±1.4	7.1*±1.7	7.9*±1.9
Reported symptoms (headache, thirst, tiredness, weakness, fatigue, runny nose, nasal congestion, itchy nose, sneezing, coughing, sore throat, general aches)	End of 2-week period	16 subjects	5* subjects	4* subjects
	End of 4-week period	14 subjects	4* subjects	4* subjects

\*p<0.05 vs. placebo

Table 1. Effect of WGP treatment or placebo on physical health of subjects reporting moderate to high lifestyle stress over a four-week monitoring period.

### POMS Assessment

The POMS assessment for psychological health strongly supported and mirrored the physical health assessment. The data analysis included an assessment of mood state at baseline (day 0), and 2- and 4-weeks after subjects began treatment (placebo, 250 mg or 500 mg  $\beta$ -glucan). Significant ( $p < 0.05$ ) differences in mood state responses between the placebo and the 500 mg  $\beta$ -glucan treatment group was observed after 2 weeks (Figure 1) for tension (reduced) and confusion (reduced). After four weeks both the 250 mg and 500 mg treatment groups were significantly different ( $P < 0.05$ ) from the placebo for confusion (reduced 15 percent at 250 mg and 17 percent at 500 mg), fatigue (reduced 35 percent at 250mg and 42 percent at 500 mg), vigour (increased 16 percent at 250 mg and 21 percent at 500 mg), and tension (reduced 19 percent at 250 mg and 30 percent at 500 mg) (Figure 1). Mood state factors not related to physical health (depression and anger) were not statistically different between placebo and either treatment group (data not shown).

### DISCUSSION

Previous reports have suggested a link between chronic stress and increased susceptibility to the common cold and URTIs (3-5). In the current study, moderate to highly stressed participants in both  $\beta$ -glucan treatment groups reported fewer URTI symptoms and better overall health (Table 1), as well as a more positive psychological assessment (Figure 1) than did subjects receiving placebo during a 4-week treatment period. The reduction in URTI symptoms reported here is similar those reported in other trials evaluating the effect of bakers yeast derived  $\beta$ -1,3/1,6 glucan on URTI symptoms of healthy and physically stressed individuals (16, 15). This strongly suggests that bakers yeast  $\beta$ -glucan is able to counteract the negative effects of stress on the immune system which can increase susceptibility to URTI. Bakers yeast  $\beta$ -glucan has been shown to bind to specific receptors on innate immune cells (CR3), priming them to be more effective in killing opsonized foreign challenges (28). This binding site preferentially recognizes bakers yeast derived  $\beta$ -1,3/1,6-glucan over other forms of  $\beta$ -glucans resulting in a significantly higher level of immune system activation as compared to other immune modulators in an *in vivo* murine mouse model system (29). The specificity of the activation mechanism and preferential binding of bakers yeast  $\beta$ -glucan on the CR3 receptor site on innate immune cells also explains the lack of effect on URTI symptoms reported with cereal derived  $\beta$ -glucan supplementation (30).

The results of the POMS survey (Figure 1) suggest that the reduction in URTI symptoms reported in Table 1 for the  $\beta$ -glucan groups (250 mg and 500 mg per day) resulted in an improvement of the 4 psychological factors measured by POMS that could be directly related to an individual's state of physical well being (fatigue, vigour, tension and confusion). It is logical to speculate that the subjects in the placebo groups who experienced increased prevalence of URTI symptoms "felt" worse physically and this was then reflected in their psychological assessment. Conversely subjects taking  $\beta$ -glucan reported lower levels of URTI symptoms and "felt" better which was then reflected in the psychological assessment techniques. The lack of any impact on the anger and depression scores is not surprising since yeast  $\beta$ -glucan should not have a psycho-active affect and the increase in vigour along with decreases in tension, fatigue and confusion can be explained as a logical result of improvement in physical well being. It is

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possible that  $\beta$ -glucan is directly active at reducing stress levels in subjects, but this is considered a less likely mechanism of action given the well understood biological mechanism of action of the  $\beta$ -glucan on the immune system. Further, the  $\beta$ -glucan used in this study was a highly purified form (>75 percent). Although it is possible that non-glucan elements in the product tested are responsible for the observed effect it is considered unlikely because other studies using  $\beta$ -glucan have had similar findings (15, 16) and the only standardized component is the  $\beta$ -glucan.

Boosting the immune system with baker's yeast  $\beta$ -glucan has been shown to have a noticeable effect on maintaining health and a positive mental attitude in psychologically stressed individuals in this study. Daily supplementation with  $\beta$ -glucan reduced the incidence of symptoms associated with URTIs and improved psychological well-being. Additional research is needed to explore the relationship between various doses of  $\beta$ -glucan and maintenance of a healthy immune system.

**AUTHOR DISCLOSURE STATEMENT**

Biothera, Inc. funded this study. GLH Nutrition conducted the study as an independent contract research organization; S. Talbot and J. Talbot are employees of GLH Nutrition.

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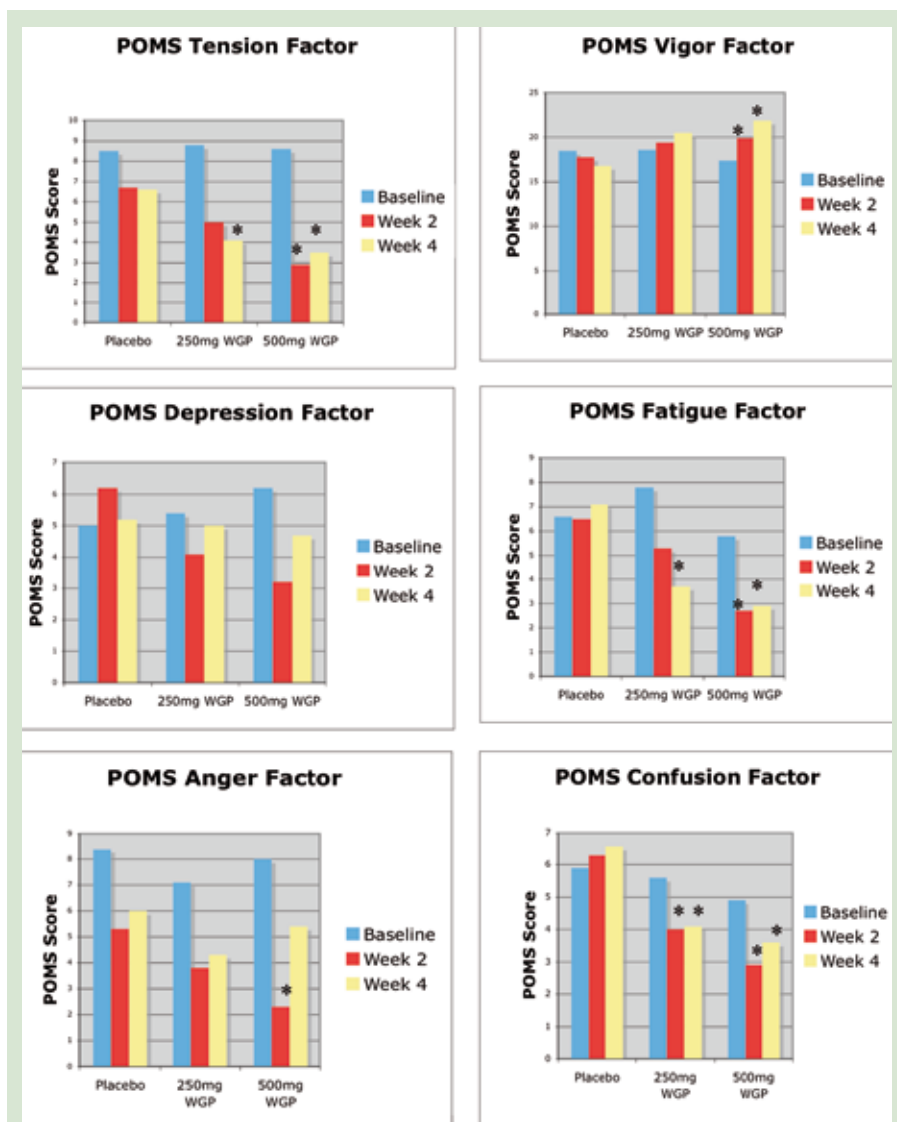


Figure 1. Analyzed data for specific POMS factors calculated from POMS Score Sheet. Data analysis was by paired t-test. A value of p<0.05 was considered significant. Each factor was determined using answers to specific adjective based scales as described in Profile of Mood States manual (25). \*p<0.05

The results ... suggest that the reduction in URTI symptoms ... for the  $\beta$ -glucan groups (250 mg and 500 mg per day) resulted in an improvement of the 4 psychological factors measured by POMS

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