2009

Effects of a yeast β-glucan supplement on symptoms of upper respiratory tract infection in free-living college-aged males

Casey E. Gorham
The University of Montana

EFFECTS OF A YEAST ß-GLUCAN SUPPLEMENT ON SYMPTOMS
OF UPPER RESPIRATORY TRACT INFECTIONS

By

CASEY E. GORHAM

B.S.P.E., Pacific Lutheran University, Tacoma, WA, 2007
B.A., Pacific Lutheran University, Tacoma, WA, 2007

Thesis

presented in partial fulfillment of the requirements
for the degree of

Master of Science
in Health and Human Performance, Exercise Science

The University of Montana
Missoula, MT

August 2010

Approved by:

Perry Brown, Associate Provost for Graduate Education
Graduate School

Brent Ruby
Department of Health and Human Performance

Charles Dumke
Department of Health and Human Performance

Jack Nunberg
Division of Biological Sciences

Gorham, Casey, M.S., Summer 2010   Exercise Science

Effects of a yeast ß-glucan supplement on symptoms of upper respiratory tract infections

Chairperson: Brent Ruby, Ph.D.

   The focus of previous research has demonstrated that both oat and yeast ß-glucan
benefits immunosuppressed populations. However, previous research has not, to our
knowledge, investigated the effects of a yeast ß-glucan on the ummune functioning of
healthy, free-living human populations. **PURPOSE:** The goal of this research was to
evaluate the effects of a yeast ß-glucan on symptoms of upper respiratory tract infection
in healthy, free-living, college-aged males. **METHODOLOGY:** The WURSS-44, a
reliable, validated survey used for determining symptoms of upper respiratory tract
infection was filled out online daily by 79 male subjects between the ages of 18 and 40.
Subjects were given a bottle of 250 mg capsules of either yeast ß-glucan or placebo to
take daily. **RESULTS:** Yeast ß-glucan demonstrated no statistically significant effect
on the experimental subject population for any of the variables associated with symptoms
of upper respiratory tract infection. **CONCLUSION:** Yeast ß-glucan does not
significantly improve immune functioning in healthy, free-living college aged males.

Keywords: ß-glucan, immune, susceptibility, resistance

Table of Contents

Chapter One: Introduction

Introduction

The immune system is a complex composition of cells and biological processes that acts to protect the body from foreign pathogens and emergent tumor cells. The human body is an ideal host for bacteria, fungi, and viruses, and there is a constant battle between the evolving pathogens and the adaptation of the organism's immune system to protect the body. There are a number of pathogens that frequently escape the immune system's first defenses, which can affect other systems. Perhaps the most common area affected by the incidence of immune system failure to detect and eliminate a threat is the upper tract of the respiratory system. The result is often what we call an upper respiratory tract infection (URTI), or the "common cold". Research done in 2002 revealed that the average cold resulted in approximately 8.7 hours of work lost (Bramley et al., 2002). Adults average 2-3 colds per year, which result in more than 45 million days of work lost in the United States alone (Barrett et al., 2007; Bramley et al. 2002). Lost productivity due to the common cold is estimated at over $25 billion per year (Bramley et al. 2002). Research has been hard-pressed for decades to develop a clear understanding of the common cold, let alone a cure or successful treatment.

There are a number of behaviors that have negative effects on the immune system including the lack of exercise (Pederson and Hoffman-Goetz, 2000), excessive amounts of exercise (Davis et al., 1997; Ceddia and Woods, 1999; Pederson and Hoffman-Goetz,

2000; Nieman, 2000; Nieman, 2003), poor nutrition habits (Beisel, 1996), lack of sleep (Dinges et al., 1995), and psychological stress (Wonnacott and Bonneau, 2002; Kiecolt-Glaser, 1999). College-aged students generally suffer any combination of these behaviors, which may cause them to suffer physiologically and academically as a result of getting an URTI (Tsai and Li, 2004).

Since it is necessary to find methods of preventing URTI in humans, research has been directed to examine the effects of different supplements on immune function. Over the past two decades, researchers have assessed the different affects of the carbohydrate ß-glucan on the immune system. ß-glucan is a complex carbohydrate polymer found in the cell walls of plants. It has been shown to lower cholesterol in humans (Jenkins et al., 2002), promote antitumor activity in both humans and mice (Vetvicka et al., 1996), and improve immune function in immunosuppressed populations of humans and mice (Yun et al., 2003; Brown and Gordon, 2003; Brown and Gordon, 2005). The mode of ingestion for mice and humans is generally oral; however, some human research uses muscular injection. There is some debate among current research as to whether or not ß-glucan can assist the immune system in preventing URTI (Nieman et al., 2008). These debates generally arise because ß-glucan may have the most benefit in subjects who are clinically diagnosed as immunosuppressed (Vetvicka et al., 1996; Yun et al., 2003; Brown and Gordon, 2003; Brown and Gordon, 2005); however research is extremely limited in improvements in immune function in healthy, free-living, human populations. Because the immune system can improve with moderate exercise (Nieman, 2003;) but may see deterioration with excessive and/or vigorous exercise (Davis et al., 1997; Ceddia and Woods, 1999; Pederson and Hoffman-Goetz, 2000; Nieman, 2000; Nieman, 2003), it is

4

difficult to determine the effects of ß-glucan in improving immune function in free-living humans (Nieman et al., 2008); especially young, active humans. It is also possible that this phenomenon is problematic with lack of or excessive sleep and/or psychological stress. ß-glucan comes in many different forms such as oat, barley, rye, wheat, and yeast. Oat ß-glucan has been studied far more than any of the other forms and has been shown repeatedly to aid human physiological function in many ways (Jenkins et al., 2002; Vetvicka et al., 1996; Yun et al., 2003; Brown and Gordon, 2003; Brown and Gordon, 2005). The study of yeast ß-glucan is on the rise, but has struggled to demonstrate significant benefits at the level of oat ß-glucan.

Because college-aged students generally have high amounts of perceived stress, vary in their amount of sleep and physical activity, and are more often exposed to viral and fungal infections due to group living situations, they may be an ideal population to examine symptoms of URTI and the potential benefits of ß-glucan supplementation.

Problem One

The first purpose of this study is to examine the effects of a yeast β-glucan supplement on symptoms of upper respiratory tract infection in college-aged males.

Problem Two

The second purpose of this study is to examine how time spent in sleep, psychological stress, time spent in physical activity, and exposure relate to duration and severity of an upper respiratory tract infection.

Research Hypotheses

Evaluation of Upper Respiratory Tract Infections and β-glucan

The present study used a reliable and valid survey to evaluate symptoms of URTI. Determination of an URTI was defined by the use of the survey as well as additional questions asked of the subjects. Subjects were asked what they believed was the cause of their illness or symptoms in addition to the questions on the survey about symptoms of URTI. If subjects believed the cause was an URTI, then the day was defined as a symptom day. If, however the subject only met the criteria of the survey, the day was defined as a sick day. The survey defined an URTI as two or more symptoms observed on any given day. Episodes were defined as symptoms persisting for more than seven days. We hypothesized that the individuals receiving the β-glucan supplement would not have a:

1.   Reduced total number of symptom days of upper respiratory tract infection.

2.   Reduced symptom day severity score of upper respiratory tract infection.

3.   Reduced symptom day maximum severity score of upper respiratory tract infection.

4.   Reduced symptom day quality of life score of upper respiratory tract infection.

5.   Reduced symptom day maximum quality of life score of upper respiratory tract infection.

6.   Increased number of days before the first symptom day past 3 days of supplementation

7.   Reduced total number of sick days of upper respiratory tract infection.

8.   Reduced sick day severity score of upper respiratory tract infection.

9.   Reduced sick day maximum severity score of upper respiratory tract infection.

10.   Reduced sick day quality of life score of upper respiratory tract infection.

11.   Reduced sick day maximum quality of life score of upper respiratory tract infection.

12.   Increased number of days before the first sick day past the first three days of supplementation.

13.   Reduced total number of symptom episodes of upper respiratory tract infection.

14. Reduced symptom episode severity score of upper respiratory tract infection.

15. Reduced symptom episode quality of life score of upper respiratory tract infection.

16. Reduced symptom episode duration of upper respiratory tract infection.

17. Reduced symptom episode maximum duration of upper respiratory tract infection.

18. Increased number of days before the first symptom episode past the first 3 days of supplementation.

19. Reduced total number of sick episodes of upper respiratory tract infection.

20. Reduced sick episode severity score of upper respiratory tract infection.

21. Reduced sick episode quality of life score of upper respiratory tract infection.

22. Reduced sick episode duration of upper respiratory tract infection.

23. Reduced sick episode maximum duration of upper respiratory tract infection.

24. Increased number of days before the first sick episode past the first 3 days of supplementation.

1. We hypothesized that individuals who sleep less will not have higher severity scores and effect on quality of life scores throughout the duration of an episode than those who sleep more.

2. We hypothesized that individuals who have higher stress scores will have higher severity scores and effect on quality of life scores throughout the duration of an episode than those who have lower stress scores.

Rationale for Hypothesis Two

Previous research has demonstrated that psychological stress increases blood cortisol levels (Tortora and Derrickson, 2006). Cohen et al., 1991 presented that increased blood cortisol levels and psychological stress are associated with an increased risk of acute infections of the upper respiratory tract.

3. We hypothesized that individuals who get moderate amounts of exercise prior to and during an episode will have lower severity scores and quality of life scores through the duration of an episode than those who are generally sedentary and those who get vigorous amounts of exercise.

Previous research has shown that physical activity has varying effects on the immune system. Generally, regular, moderate exercise improves immune function while extended vigorous exercise as well as no exercise has adverse effects on immune function (Nieman, 2003; Woods, 2005; Nieman, 2007).

4. We hypothesized that individuals who have higher exposure scores prior to an episode will not have higher severity scores and quality of life throughout the duration of an episode.

Significance of the Study

Previous research has concluded that excessive amounts of time and money are wasted every year attempting to prevent and remedy symptoms of upper respiratory tract infection. ß-glucan has been demonstrated to improve immune function in many populations. Studies show that lab measurements to indicate upper respiratory tract infections are not as accurate when compared to the individual's perceived symptoms of upper respiratory tract infection (Jackson et al., 1957; Barrett et al., 2002; Barrett et al., 2005; Barrett et al., 2007). Barrett et al. (2007) found that treatments of the common cold

such as antihistimine, decongestants, steroids, zinc, vitamin C, and Echinacea did not decrease illness duration and ultimately cold remedies offer only limited benefits. Most research agrees that oat ß-glucan can help prevent infection of the upper respiratory tract in clinically diagnosed immunosuppressed individuals, however, to our knowledge no research has succeeded in showing that a yeast ß-glucan supplement can improve symptoms of upper respiratory tract infection in relatively healthy populations.

Rationale for the Study

Collecting survey data daily may allow for a more accurate picture of URTI in male college students throughout a semester. Examining whether or not ß-glucan can prevent these symptoms may have implications for maintaining immune function in healthy, free-living populations. Also, this research may provide a better understanding of how much each of the risk factors for URTI plays a role in preventing and fighting URTI.

Limitations

i/Non-randomized sample. Subjects were not from a randomized sample. Subjects were recruited from The University of Montana campus. Most were from classes in the Department of Health and Human Performance.

ii/Participants. Although we aimed for socioeconomic diversity, our participants were volunteers and may not have been representative of cold-sufferers.

iii/Age and Sex. The data collected only applies to college-aged males.

iv/Survey. Qualitative, self-reported survey data, may have been biased.

iv/Free-living individuals. We did not control for lifestyle habits or dietary habits.

Delimitations

i/Type of subjects. Due to the large number of potential participants in the study

population, the population involved in the current study focused only on students at The

University of Montana.

ii/Age of subjects. Due to problems with getting consent for persons under the age of 18,

our age range began at 18 years. Due to the differences in pulmonary function seen in

older populations, our age range ended at 41 years.

iii/Survey. Survey instruments used only scale items and did not include many open-

ended response items.

Definition of Terms

Immune System: the integrated body system of organs, tissues, cells, and cell products such as antibodies that differentiates self from non-self and neutralizes potentially pathogenic organisms or substances.

Immunosuppression: the inhibition of the normal immune response because of disease, the administration of drugs, or surgery.

Resistance: the ability to ward off damage or disease through immune defenses.

Dietary Supplement: a product taken orally that contains one or more ingredients that are intended to supplement one's diet.

Susceptibility: vulnerability or lack of resistance to illness.

Upper respiratory tract infections: are the illnesses caused by an acute infection which involves the upper respiratory tract: nose, sinuses, pharynx or larynx.

Chapter Two: Review of Literature

β-glucan

Fiber is a necessary part of the human diet. ß-glucan is a type of fiber that is soluble, viscous, and fermentable. There are six forms of ß-glucan found in the cell walls of green plants and some fungi. Glucans are glucose polysaccharides containing one kind of simple sugar, or monosaccharide, glucose. ß-glucans are made up of ß-bonds, which are more difficult to digest for some mammalian digestive tracts.

The structure of ß-glucan is slightly different from source to source. Generally, ß-glucans are composed of linear (β-1 $\rightarrow$ 3) backbone chains with different side chains (β-1 $\rightarrow$ 4 or β-1 $\rightarrow$ 6) (Castro et al., 2007). Cellulose is a source of (β-1 $\rightarrow$ 4)-ß-glucan, which is a long and linear polymer that is difficult for humans to digest. Both oat and barley have mixed-linkage (β-1 $\rightarrow$ 3, β-1 $\rightarrow$ 4)-ß-glucans and are easily fermented in the intestine. Other grains, such as wheat, rye, and rice, contain small amounts of ß-glucan. Microbial (β-1 $\rightarrow$ 3)-ß-glucan is another component of cell walls or can be secreted by microorganisms growing on or in plants, such as yeast. Mushrooms also contain (β-1 $\rightarrow$ 3)-ß-glucans, with (β-1 $\rightarrow$ 6) side chains.

The percentage and distribution of ß-glucan in the source may also determine its structure. Mushrooms typically contain 0.3% ß-glucan, whereas the distribution of the carbohydrate in grains range between 17% and 46%. Generally, soluble ß-glucan content

15

is much higher in cereals than insoluble ß-glucan; in mushrooms and microorganisms this ratio varies (Manzi and Pizzoferrato, 2000).

ß-glucan chemical structure is made up of mostly beta-bonds. Human digestive enzymes can generally only break down α-bonds easily. The human body can only break down these beta-bonds in mastication and in the lower gastrointestinal tract by bacterial enzymes (Whitney and Rolfes, 2002). Soluble ß-glucans are theorized to translocate from the gastrointestinal tract into systemic circulation by uptake of Peyer's patches, clusters of lymphoid tissue in the lower gastrointestinal tract (Rice et al., 2005).

All forms of ß-glucan have demonstrated both null effect and improvements in all populations; rarely has it been shown to induce damage. One study did find that using an altered form of oat ß-glucan, rather than leaving the ß-glucan in its most natural state, induced statistically significant damages to pulmonary function in immunosuppressed mice (Young et al., 2003). Even toxicity level studies have failed to show significant results for toxic levels of consumed or injected ß-glucan. Research in many areas of illness and chronic disease have recently been investigating potential benefits of different derivatives of ß-glucan supplementation.

Oat and Yeast ß-glucan

Cholesterol

Oat ß-glucan has been studied in clinical trials, and has been identified as the component responsible for the significant cholesterol-lowering properties in oats; the

most attention is given to oat ß-glucan in its effectiveness to decrease low-density lipoprotein (LDL) cholesterol in human populations. After 5 weeks of orally ingesting 2.5 g of oat-derived ß-glucan twice daily, men and women were both seen to have lower LDL cholesterol than the control group (Naumann et al., 2006). Similarly, Jenkins et al. (2002) found that hyperlipidemic patients who consumed more soluble fiber containing oat ß-glucan or psyllium (8 g per day or more) in their diet over a one month period decreased their LDL cholesterol significantly more than those who did not consume a high amount of soluble fiber in their diet.

Yeast, has also been shown to lower LDL cholesterol in hyperlipidemic human populations. Obese male patients were given 7.5 g of yeast-derived ß-glucan twice daily for a two-week period and lipid panels were measured. Results showed a significant decrease in LDL cholesterol (Nicolosi et al., 1999).

These complimentary results suggest that oat and yeast ß-glucan may follow similar pathways or may have similar mechanisms for decreasing LDL cholesterol in humans. This parallel may indicate that the two may be comparable in affecting different aspects of human physiology.

Cancer

Oat ß-glucan may also help in cancer therapy by enhancing lung macrophage activity. Murphy et al. (2004) discovered that oat ß-glucan can decrease the spread of melanoma cells and that these effects may be mediated by macrophage activity. Mice

received 0.6 mg oat ß-glucan dissolved per 1 ml of drinking water daily for 10 days before tumor administration. Results of this research show that the mice that were given an oat ß-glucan saw a significantly lower metastatic spread rate of the tumors.

Yeast ß-glucan was shown to combine with and enhance an antibody, which fights a vascular endothelial cancer found in the human cervix (Salvador et al., 2008). The protocol consisted of screening and removing active tumor cells from living human females and implanted in immunodeficient mice. Mice that received supplementation of 1.2 mg of yeast-derived ß-glucan twice a week via intravenous injection, showed significantly reduced tumor size when compared with those that did not receive the supplementation. The authors of this research suggest that, if the mechanism is similar in humans, cancer growth might be delayed by intravenous injection of yeast ß-glucan. Hong et al. (2004) also found that certain types of cancer cells were completely eliminated when yeast ß-glucan was orally administered to a similar murine population. These mice were given 400 µg of the yeast ß-glucan daily for three weeks.

Supplementing with a yeast ß-glucan was also shown to stimulate proliferation and activation of peripheral blood monocytes in patients with advanced breast cancer (Demir et al., 2007). The patients in the research were newly diagnosed or relapsed with metastatic breast cancer. Each subject orally ingested 10 mg of yeast-derived ß-glucan for two weeks. Peripheral blood was drawn at day 0 and day 15. Although the majority of cancer fighting immune cells did not improve in any way, blood monocytes were shown to increase in number and amount of activity. This study suggests that short-term treatment with yeast ß-glucan may improve blood monocyte number and function, which, in turn, indicates an improvement in immune function. Both mice and human

populations suffering from various cancers have been shown to benefit from a yeast ß-glucan supplement.

Supplementation with an oat or yeast ß-glucan have both been successfully used in murine populations to slow tumor development. The addition of human research demonstrating an improvement in blood monocyte number and function with yeast ß-glucan implies that if the mechanisms and/or pathway of ß-glucan is similar in humans and mice, tumor activity may be semi-controlled with the aid of an oat or yeast ß-glucan supplementation. Also, because this research supports that ß-glucan is translocated from the gut in humans into the blood stream, research in other areas of immune function are being conducted.

Bacterial and Viral Infections

Oat ß-glucan has also been found to fight certain infections in murine populations (Yun et al., 2003).   In this study mice were administered either intragastrically or intraperitoneally 3 mg of oat ß-glucan every other day for 10 days. At 10 days, mice were exposed to either *Staphylococcus aureus* or *Eimeria vermiformis.* These bacteria are known to cause similar, common infections in both mice and humans. The experimental group was shown to have a lower mortality rate than the control group as well as an increased resistance to developing any infection. This suggests that short-term treatment with an oat ß-glucan, prior to exposure, can enhance immune function against common infections in mice.

Similarly, Murphy et al. (2008) administered mice with 0.8 mg oat ß-glucan dissolved per 1 ml of drinking water for 10 days before inoculation with a virus. In both studies, mice that orally ingested the oat ß-glucan demonstrated benefits in their immune function.

Promising research results investigating benefits of supplementation with oat ß-glucan to aid in fighting infections has been shown. Recently research has started to evaluate benefits of a yeast ß-glucan supplement in fighting infections, mainly URTI. Because similar results are seen between oat and yeast ß-glucan supplementation in cancer and cholesterol research in both mice and humans it is suggested that the two follow similar pathways in the murine and human bodies, have similar mechanisms in the two organisms, or both. With the addition of successful research in showing that oat ß-glucan supplementation is beneficial to the murine population in aiding the immune system in fighting infections, it is necessary to explore the murine and human population and effects of both oat and yeast ß-glucan supplementation in specific infections.

Upper Respiratory Tract Infections

URTI and their symptoms are common and generally do not result in hospitalization or fatality. However, because they are so common, money and time are spent excessively every year to prevent and treat symptoms of URTI (Bramley et al., 2002). The common cold, as URTI are generally known, can cause measurable, significant declines in quality of life (Linder and Singer, 2003).

There are many suggestions as to why immune function is suppressed enough to allow an URTI to thrive. Nieman (2007) concludes that excessive physical activity is enough of a physiological stress that the body experiences many changes in immune function: drop in natural killer cells and T cells, decrease in T cell function, decrease in nasal neutrophil phagocytosis and mucociliary clearance, etc. Because of these changes, the body is much more susceptible to upper respiratory tract infections. Carbohydrate feeding may help the immune system in some ways to protect it from the damages caused by prolonged, vigorous exercise, but may not aid in preventing upper respiratory tract infections (Nieman, 2007).

ß-glucan and Upper Respiratory Tract Infections

Murine Subjects

Mice are a useful model for studying effects on the immune system and URTI. They appear to be susceptible to similar stimuli for immunosuppression to humans. For example, both psychological and physical stressors are shown to increase risk of upper respiratory tract infections in mice (Hunzeker et al., 2004). Previous research has shown that mice participating in a single bout of prolonged, vigorous exercise are at a higher risk for upper respiratory tract infections than those who either underwent a short-term exercise or no exercise (Davis et al., 1997). The results of this particular study demonstrated that lung alveolar macrophage activity was reduced in the mice that

exercised for long durations. This research suggests that mice could serve as a model for risk of URTI in humans.

ß-glucan and its effects on immune function and URTI research began with mice models. Oat ß-glucan has been shown to enhance immunity in mice and prevent infection of the upper respiratory tract. ß-glucan may play a key role in offsetting the risk for infection following exercise stress in mice (Murphy et al., 2008). This research examined lung macrophage activity and proliferation in mice that were supplemented with oat ß-glucan. The mice were given 0.8 mg of oat ß-glucan 10 days prior to trial days. One group of mice was exercised to volitional fatigue three consecutive days after supplementation days. Depletion of lung macrophages negated the positive effects of the oat ß-glucan post exercise. Results of this study demonstrated that lung macrophage activity is partially responsible for mediating supplemental effects of oat ß-glucan on susceptibility to URTI. Because macrophages and lymphocytes are important for immune function, these studies imply ß-glucan may improve the number or function of these immune cells, which may help fight or prevent the prevalence of URTI.

Davis et al. (2003) reported that only moderate exercise and not supplemental oat ß-glucan significantly improved immune function. Similar to other ß-glucan research done in mice, the subjects were given 0.6 mg of oat ß-glucan dissolved into every 1 ml of drinking water daily for 10 days prior to inoculation with a herpes virus. Mice were exercised on a treadmill for 1 hour per day for 6 days after the 10-day supplementation period with oat ß-glucan. Results showed no significant improvement with the oat ß-glucan alone, but with exercise there were significant improvements in immune function.

With the same research group, Murphy et al. (2007) demonstrated slightly

different results. Male mice were given 0.6 mg of oat ß-glucan dissolved into every 1 ml of drinking water daily for 10 days prior to exercise trials. Mice were divided into six groups (control, oat ß-glucan with no exercise, moderate exercise, oat ß-glucan with moderate exercise, fatiguing exercise, and oat ß-glucan with fatiguing exercise). Results of this study showed that moderate exercise and oat ß-glucan supplementation increased neutrophil burst activity. The control group and fatiguing exercise groups did not see an increase in immune cell function. There was no additive benefit of the moderate exercise and the oat ß-glucan supplementation.

These combined results suggest that supplementing with an oat ß-glucan is beneficial in mice immunocompromised by infection or tumor as well as healthy moderately exercised mice.

Willment et al. (2001) found that the human receptor of ß-glucan is both structurally and functionally similar to the mouse receptor. The mouse ß-glucan receptor, Dectin-1, is a type II transmembrane protein, as is the corresponding receptor in humans. These receptors are capable of recognizing a variety of (β-1 $\rightarrow$ 3, β-1 $\rightarrow$ 6) ß-glucans and can also recognize intact yeast. As we have found that both the mouse and human receptors recognize ß-glucans. The human and mouse ß-glucan receptors differ in that the transcript encoding the human receptor is alternatively spliced, which does not seem to have an effect on the ability of the receptor to recognize ß-glucan or intact yeast (Willment et al. 2001). Other research found specific receptors of fungal ß-glucan (Dectin-1) were also functionally similar to the molecule found in mice (Herre et al., 2004). The receptors were shown to be similar on the surface of both mouse and human leukocytes and that they both recognize β-glucan. The receptor recognizes and binds

cells of the immune system (T-lymphocytes and leukocytes). This evidence, along with the beneficial effects of oat ß-glucan in mice, suggests that the effects of ß-glucan as aids in proliferation of immune cells in mice should have similar effects in humans.

Human Subjects

Human research has found that oat ß-glucan offset increased upper respiratory tract infection risk associated with exercise stress (Ceddia and Woods, 1999; Davis et al., 2004). Because exercise can both improve and degenerate immune function, it is difficult to demonstrate the effects of a ß-glucan supplement in healthy, free-living populations.

Similar research has been conducted in humans as well with conflicting results (Nieman et al., 2008). Trained male cyclists were randomized to an experimental or control group. The experimental group received 5.6 g per day of an orally administered oat ß-glucan supplement 2 weeks before, during, and1 day after 3 day trial. Trial consisted of cycling for 3 hours per day at approximately 57% maximal watts. URTI symptoms were monitored during supplementation and for 2 weeks after trial. Blood samples were collected before and after 2 week of supplementation, immediately after the 3-h exercise bout on day 3, and 14 hours after exercise. Immune cellular activity associated with fighting UTRI was assessed and no significant differences were found between the two groups.

The similarities seen between oat and yeast ß-glucan in both murine and human

populations suggest that similar effects may be seen in other areas of physiology, such as immune function. Research on the effects of yeast ß-glucan on symptoms of URTI are currently lacking in beneficial results. URTI pose a complicated threat to the immune system in that symptoms are difficult to diagnose as well as the cause could be viral or bacterial infection. Also, because free-living humans are exposed to much more diverse threats to their immune systems that lab living mice, it is likely more difficult to see effects of a ß-glucan supplement in human populations. It is necessary to understand the human immune system and factors that may compromise its function in order to investigate whether a yeast ß-glucan could potentially benefit healthy, free-living humans.

Immune System Function

The immune system is the primary defense system of the body to ward of harmful agents and is vital in maintaining homeostasis. This system is comprised of two developmental components: innate immunity and specific immunity. Innate immunity is present at birth and provides immediate, but general protection against invasion by a number of different pathogens. Specific immunity develops more slowly and becomes a response mechanism activated by a specific invader. The skin and mucous membranes of the human body provide the first line of defense and protection against these invaders. Gastric fluids, at a high acidity, allow digestion of food and kill many different types of bacteria found in the food ingested. Antimicrobial proteins, phagocytes (neutrophils and

macrophages), natural killer cells, inflammation, and fever comprise the second line of defense against pathogens (Tortora and Derrickson, 2006). The lymphatic system, working together with other systems of the body, makes up the immune system of the human body (Tortora and Derrickson, 2006).

If the first line of defense fails to identify and ward off foreign invaders, the second line of defense will take over. While inflammation and fever work to eliminate a threat, antimicrobial proteins are produced in a number of ways by lymphocytes, macrophages, and fibroblasts and allow cells to prevent further replication of viruses (Medzhitov and Janeway, 1997). Other proteins activated can cause cytolysis, or bursting, of microbes, promote phagocytosis, and contribute to inflammation. Some proteins inhibit growth of bacteria by limiting the amount of iron available. Natural killer cells attack any cells that display abnormal proteins. These cells release a wide range of cell destruction enzymes and proteins in order to eliminate a threat. Phagocytes target and ingest microbes or other cellular debris. These cells can wander to sites of infection or remain stationary in different specific tissues. Alveolar macrophages reside in lung tissue to prevent damage by foreign particles and protect against other unwanted pathogens (Medzhitov and Janeway, 1997; Tortora and Derrickson, 2006).

Factors that Affect Immune Function

A disease or illness can be a result of a failure of the immune system to protect the body from pathogens or cancer cells. Even though the immune system is complex

and highly developed, there are many pathogens that manage to surpass the body's defenses, often resulting in disease or illness. There are many behaviors which can result in a decline in immune function.

Nutrition Behaviors

Malnutrition and other poor nutritional habits can impact generalized host defense mechanisms (Beisel, 1996). Children and the elderly are more susceptible to malnutrition than adults; however, immune function can be altered through all stages of life with poor nutrition habits, which include excessive nutrient intakes (Beisel, 1996). Beisel (1996) concluded that lack of protein and vitamin A were whereas excess in caloric intake consisting of high fat content were both associated with immune compromise.

Sleep Behaviors

Sleep is a basic biological need in humans. It is well known that sleep deprivation can have adverse effects on brain and motor function (Tortora and Derrickson, 2006). There is some debate in research as to whether partial or total sleep deprivation can be conceptualized as only being immunosuppressive (Dinges et al., 1995). Experiments generally find significant changes in blood levels of immunity cells; however, not all changes in these levels can be considered negative for the immune system (Dinges et al.,

1995). Although there is a lack of conclusive evidence that sleep deprivation alone has adverse affects on the immune system, it may indirectly influence immune dysfunction with the combination of increased adrenal catecholamine release in the blood.

Psychological Stress

Cortisol is a hormone that has been associated with mental stress. Cortisol has different effects on the human body including changes in the body such as inhibition of immune system activity (Tortora and Derrickson, 2006). Psychological stress is also associated with an increased risk of acute infections of the upper respiratory tract (Cohen et al., 1991). Sleep deprivation has been shown to cause cortisol blood level increases (Lac and Chamoux, 2003). This combined evidence suggests that sleep deprivation can lead to an increase in psychological stress and cortisol, leading to a decline in immune function (Glaser and Kiecolt-Glaser, 2005; Fukuda and Morimoto, 2001; Kiecolt-Glaser, 1999).

Physical Stress

Adrenal catecholamines are other stress hormones similar to cortisol in that they are all released from the adrenal cortex. Physical and psychological stressors alter plasma catecholamine levels in different ways (Landmann et al., 1984). Kohut et al.

(1998) found evidence that an increased release of adrenal catecholamines may cause a decrease in macrophage antiviral function following exercise. Physical activity has sundry effects on the human body, which are dependent on intensity, frequency, and duration of sessions (Woods, 2005). Generally, regular, moderate exercise improves immune function (Tortora and Derrickson, 2006; Gleeson, 2007) and is recommended as a strategy for managing stress (Nguyen-Michel et al., 2006), while extended, vigorous exercise and no exercise may have adverse affects on the immune system (Nieman, 2003; Woods, 2005; Nieman, 2007). Immune function declines in similar ways between elite endurance athletes and a sedentary population (Nieman et al., 1995), which suggests that sedentary and extremely active populations may have similar immune function declines overall.

Because of the wide range of changes seen in immune function due to sleep deprivation, psychological stress, physical activity, and poor nutrition habits, it is difficult to discern what the true mechanisms behind these changes are. The evidence is conclusive, however, that both positive and negative changes in immune function are experienced due to any combination of these stressors. It is beneficial to understand the variations between the different stressors and their effects on immunity. Kiecolt-Glaser et al. (2002) discussed that that immune dysregulation may be one of the core mechanisms for a spectrum of conditions associated with cardiovascular disease, osteoporosis, arthritis, Type II diabetes, certain cancers, and other older-age-related functional declines.

College Students and Immune Function

Stress is a part of every person's life. As previously discussed, too much stress can have adverse affects on immune function. College students experience a considerable amount of stress due to educational workload, financial difficulties, peer pressure, development of future plans, etc. Generally, colleges require that a student live in a campus dorm for at least the first two years of school. These close living conditions expose students to many different viral and bacterial infections, many of which affect the upper respiratory tract. Research done in the 1990s suggested that college students' amount of stress is negatively associated with self-concept, self-esteem (Goldman and Wong, 1997), and perceptions of performance in school (Garden, 1991). Most research supports the conclusion that regular physical activity is a viable means of reducing stress in college students; however it is believed that extreme levels of stress discourages physical activity due to lack of time or energy in many college students, thus increasing perceived stress levels (Nguyen-Michel et al., 2006).

College students also have variable sleep patterns compared to other populations. Trockel et al. (2000) observed that college students with the most variable sleep patterns, particularly time of rising, accounted for the largest amount of variance in grade point average in college students living in residence halls. Previous research has found that college students with poor sleep quality had greater schedule variability in the timing of social rhythms and activities with active social environment (Carney et al., 2006). The authors of the previous study suggested also that quality of sleep is highly correlated with stress levels and thus, indirectly risk of URTI.

Sleep, stress, physical activity, nutritional behaviors, and level of immune function are all factors that, when compromised, become a risk factor for developing an URTI. Because of the variability of all of these factors, with the exception of immune function, college students are at a high risk for developing URTI.   Because college students are at high risk for UTRI and have healthy functioning immune systems, they represent a good sample population of healthy, free-living individuals.

Chapter Three: Methodology

Setting

All data collection was conducted through the Montana Center for Work Physiology and Exercise Metabolism on the campus of The University of Montana, Missoula, MT. Survey data was collected using a secured online survey program (surveymonkey.com).

Subjects

Approximately 175 males were initially recruited as the subjects in this investigation. Of these recruits, 81 served as the subjects in the study. These subjects were recruited through dorm communications, class recruitment presentations, and sign-up in the University Center at The University of Montana. Prior to participation, all subjects completed an Institutional Review Board (IRB) approved informed consent form.

Descriptive Data

Descriptive Data was collected using four different methods. (1) A background survey was completed by each subject which included age, gender, marital status, living conditions, injuries which limit physical activity, dieting, caffeine intake, tobacco use,

and estimated consumption of foods with high amounts of ß-glucan; (2) a daily survey completed by each subject during the twelve week study included twenty-four hour sleep record in hours, twenty-four hour physical activity time in minutes, and twenty-four hour stress level; and (3) an optional post study survey completed by the majority of subjects included current height, current weight, estimated weight prior to study, how often and/or easily subject accrues illness, and whether subject believed they were taking 250mg of ß-glucan or placebo (rice flour).

Exclusion Criteria

Subjects were excluded from the study results if (1) they were not within the 18-41 year age requirement throughout the study; (2) they did not complete the background survey; or (3) they did not complete at least 75% (63) of the daily surveys.

Instrumentation

WURSS

The Wisconsin Upper Respiratory Symptoms Survey (WURSS) was developed as an evaluative illness specific quality-of-life instrument (Barrett et al., 2008). The construct validity of the WURSS-44, a forty-four question version of the survey, is supported by measures of reliability and responsiveness of subjects (Barrett et al., 2005).

This survey looks at thirty-two symptoms of upper respiratory tract infection, ten functional quality-of-life items, one global illness severity item (How sick do you feel today?), and one item assessing global change (Compared to yesterday how do you feel?) (Barrett et al., 2005; Barrett et al., 2002). The survey allows subjects to score their symptoms using a seven-point scale (0 = none, 1 = very mild, 3 = mile, 5 = moderate, 7 = severe).

Data Collection

Each subject signed an Institutional Review Board (IRB) approved informed consent form prior to participation in the study. Subjects were asked to take either a β-glucan 250mg supplement or a placebo (rice flour) daily. Distribution of supplement and placebo was done in a double-blind fashion. Along with taking the daily supplement or placebo, each subject filled out an online survey (surveymonkey.com) which includes questions about sleep, stress, physical activity, exposure to illness, includes the WURSS, and asks a final question about the subject's belief of the cause of any symptoms (flu, cold, allergies, etc.).

Operational Definitions

An upper respiratory tract infection **symptom day** was defined as any day that a subject (1) scored above a zero on the global illness severity question, (2) scored above a zero on at least two of the thirty-two symptoms of upper respiratory tract infection, and (3) believed that their symptoms were due to a cold.

Symptom day severity of an upper respiratory tract infection symptom day was defined as the total sum of all thirty-two symptom scores from the WURSS for each *symptom day* of a subject.

Symptom day severity max of an upper respiratory tract infection symptom day was defined as the highest *symptom day severity* score for each individual subject.

Symptom day quality of life severity of an upper respiratory tract infection symptom day was defined as the total sum of all ten effect on quality of life scores from the WURSS for each *symptom day* of a subject.

Symptom day quality of life severity max of an upper respiratory tract infection symptom day was defined as the highest *symptom day quality of life severity* score for each individual subject.

Number of days until first symptom day was defined as the total number of days prior to the first symptom day past the first seven days for each individual subject.

An upper respiratory tract infection **sick day** was defined as any day that a subject (1) scored above a zero on the global illness severity question, (2) scored above a zero on at least two of the thirty-two symptoms of upper respiratory tract infection, and (3) believed that their symptoms were due to allergies, flu, cold, or other (specified).

Sick day severity of an upper respiratory tract infection symptom day was defined as the total sum of all thirty-two symptom scores from the WURSS for each *sick day* of a subject.

Sick day severity max of an upper respiratory tract infection symptom day was defined as the highest *sick day severity* score for each individual subject.

Sick day quality of life severity of an upper respiratory tract infection symptom day was defined as the total sum of all ten effect on quality of life scores from the WURSS for each *sick day* of a subject.

Sick day quality of life severity max of an upper respiratory tract infection symptom day was defined as the highest *sick day quality of life severity* score for each individual subject.

Number of days until first sick day was defined as the total number of days prior to the first sick day past the first seven days for each individual subject.

An upper respiratory tract infection *symptom episode* was defined as a subject (1) scored above a zero on the global illness severity question for seven or more consecutive days, (2) scored above a zero on at least two of the thirty-two symptoms of upper respiratory tract infection, and (3) believed that their symptoms were due to a cold. The end of a symptom episode was defined as two or more consecutive days where the

36

subject scored a zero on the global illness severity question. If there was only one day when the subject scored a zero on the global illness severity question followed by one or more days of a score above zero with two or more symptoms, the episode was considered to be continuing. If there were less than two symptoms in this case, the episode was classified as ended on the most recent symptom day when the subject scored above a zero on the global illness severity question with two or more symptom scored above zero.

Symptom Episode symptom severity of an upper respiratory tract infection episode was defined as the average *symptom day severity* scores for each *symptom episode* of a subject.

Symptom Episode quality of life severity of an upper respiratory tract infection episode was defined as the average *symptom day quality of life severity* scores for each *symptom episode* of a subject.

Symptom Episode duration of an upper respiratory tract infection episode was defined as the total number of *symptom days* in a *symptom episode*. This definition also included non-symptom days that are still considered part of a *symptom episode*.

Symptom Episode duration max of an upper respiratory tract infection episode was defined as the highest *symptom episode* duration experienced by each subject.

Number of days until first symptom episode was defined as the total number of days prior to the first symptom episode past the first seven days for each individual subject.

An upper respiratory tract infection ***sick episode*** was defined as a subject (1) scored above a zero on the global illness severity question for seven or more consecutive days, (2) scored above a zero on at least two of the thirty-two symptoms of upper respiratory tract infection, and (3) believed that their symptoms were due to allergies, flu, cold, or other (specified). The end of a sick episode was defined as two or more consecutive days where the subject scored a zero on the global illness severity question. If there was only one day when the subject scored a zero on the global illness severity question followed by one or more days of a score above zero with two or more symptoms, the episode was considered to be continuing. If there were less than two symptoms in this case, the episode was classified as ended on the most recent sick day when the subject scored above a zero on the global illness severity question with two or more symptom scored above zero.

Sick Episode symptom severity of an upper respiratory tract infection episode was defined as the average *symptom day severity* scores for each *sick episode* of a subject.

Sick Episode quality of life severity of an upper respiratory tract infection episode was defined as the average *symptom day quality of life severity* scores for each *sick episode* of a subject.

Sick Episode duration of an upper respiratory tract infection episode was defined as the total number of *symptom days* in a *sick episode*. This definition also included non-symptom days that are still considered part of a *sick episode*.

Sick Episode duration max of an upper respiratory tract infection episode was defined as the highest *sick episode* duration experienced by each subject.

Number of days until first sick episode was defined as the total number of days prior to the first sick episode past the first seven days for each individual subject.

Data from the WURSS was collected daily to determine, as defined above, the (1) total number of symptom days for each subject, (2) average symptom day severity for each subject, (3) symptom day severity max for each subject, (4) average symptom day quality of life severity for each subject, (5) symptom day quality of life severity max for each subject, (6) total number of days prior to first symptom day for each subject (7) total number of sick days for each subject, (8) average sick day severity for each subject, (9) sick day severity max for each subject, (10) average sick day quality of life severity for each subject, (11) sick day quality of life severity max for each subject, (12) total number of days prior to first sick day for each subject (13) total number of symptom episodes for each subject, (14) average symptom episode severity for each subject, (15) average

symptom episode quality of life severity for each subject, (16) average symptom episode duration for each subject, (17) symptom episode duration max for each subject, (18) total number of days prior to first symptom episode for each subject (19) total number of sick episodes for each subject, (20) average sick episode severity for each subject, (21) average sick episode quality of life severity for each subject, (22) average sick episode duration for each subject, (23) sick episode duration max for each subject, (24) total number of days prior to first sick episode for each subject

Compliance of subjects

The study coordinator monitored subject compliance by telephoning or emailing subjects who missed three or more consecutive surveys. Technological problems were resolved or subject was excluded at their own discretion. Surveys were resent twice to non-responded subjects within two weeks of the originally sent daily survey date.

Statistical Procedures

Background descriptive data were analyzed using an independent t-test for age, height (inches), pre-study weight (kg), post-study weight (kg), weight change (kg), physical activity time (minutes spent daily participating in aerobic, resistance, and organized sport activities, number of high school sports, caffeine intake (mg per week

from coffee, tea, or cola beverages), average sleep time (hours per night), average stress level (0-10; not stressed-extremely stressed), number of allergies, average estimated β-glucan intake (servings per week total and servings per week of oatmeal, cereal with oats, other items with oats, barley, cereal with barley, other items with barley, mushrooms, whole wheat bread, whole wheat pasta, other whole wheat foods, rye bread, other rye foods) and will be expressed as Mean ± SD. For measures of daily sleep (hours per night), stress (0-10; not stressed-extremely stressed), and physical activity (aerobic exercise, resistance training, and organized sport; total physical activity minutes per day), and average score was calculated for each variable for each subject. These measures were analyzed using an independent t-test. Statistical significance was established at the $p < 0.05$ level. These analyses were used to compare differences between the experimental group (supplement) and the control group (placebo).

WURSS

Total number of symptom days

Each subject had a total number of **symptom days** from the 12-week investigation (i.e. 0, 1, 2, etc.). These data (indicating a total number of symptom days per participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average severity of symptom days

Each subject had an average ***symptom day severity score*** from the 12-week investigation. These data (indicating an average severity score per participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average symptom day severity max

Each subject had a ***maximum symptom day severity score*** from the 12-week investigation. These data (indicating a maximum severity score per participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average quality of life severity of symptom days

Each subject had an average ***symptom day quality of life severity score*** from the 12-week investigation. These data (indicating an average effect severity of symptom days on quality of life of each participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average symptom day quality of life severity max

Each subject had a ***maximum symptom day quality of life severity score*** from the 12-week investigation. These data (indicating a maximum effect of symptom day severity on quality of life of each participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Total number of sick days

Each subject had a total number of ***sick days*** from the 12-week investigation (i.e. 0, 1, 2, etc.). These data (indicating a total number of sick days per participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average severity of sick days

Each subject had an average ***sick day severity score*** from the 12-week investigation. These data (indicating an average severity score per participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average symptom day severity max

Each subject had a ***maximum sick day severity score*** from the 12-week investigation. These data (indicating a maximum severity score per participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average quality of life severity of sick days

Each subject had an average ***sick day quality of life severity score*** from the 12-week investigation. These data (indicating an average effect severity of sick days on quality of life of each participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average sick day quality of life severity max

Each subject had a ***maximum sick day quality of life severity score*** from the 12-week investigation. These data (indicating a maximum effect of sick day severity on quality of life of each participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Total number of symptom episodes

Each subject had a total ***number of symptom episodes*** from the 12-week investigation (i.e. 0, 1, 2, etc.). These data (indicating an average number of symptom episodes per participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average symptom episode severity

Each subject had an average ***symptom episode severity score*** (average severity scores for symptom days in each episode) from the 12-week investigation. These data (indicating an average severity score per symptom episode of each participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average symptom episode quality of life severity

Each subject had an average ***symptom episode quality of life severity score*** average quality of life severity scores for symptom days in each episode) from the 12-week investigation. These data (indicating an average quality of life severity score per symptom episode of each participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Duration of symptom episodes

Each subject had an average ***symptom episode duration*** (average of total days for each symptom episode per participant) from the 12-week investigation. These data (indicating an average number of days in each symptom episode per participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Maximum duration of symptom episodes

Each subject had a ***maximum symptom episode duration*** (symptom episode with highest number of days for each participant) from the 12-week investigation. These data (indicating a maximum duration of symptom episodes) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Total number of sick episodes

Each subject had a total ***number of sick episodes*** from the 12-week investigation (i.e. 0, 1, 2, etc.). These data (indicating an average number of sick episodes per participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average sick episode severity

Each subject had an average ***sick episode severity score*** (average severity scores for sick days in each episode) from the 12-week investigation. These data (indicating an average severity score per sick episode of each participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Average sick episode quality of life severity

Each subject had an average ***sick episode quality of life severity score*** average quality of life severity scores for sick days in each episode) from the 12-week investigation. These data (indicating an average quality of life severity score per sick episode of each participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Duration of sick episodes

Each subject had an average ***sick episode duration*** (average of total days for each sick episode per participant) from the 12-week investigation. These data (indicating an average number of days in each sick episode per participant) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Maximum duration of sick episodes

Each subject had a ***maximum sick episode duration*** (sick episode with highest number of days for each participant) from the 12-week investigation. These data (indicating a maximum duration of sick episodes) were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Symptom Episodes Severity Comparison

Average severity scores for corresponding symptom episode days starting at Day 1 of each symptom episode were calculated for all symptom episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Symptom Episodes Quality of Life Comparison

Average quality of life scores for corresponding symptom episode days starting at Day 1 of each symptom episode were calculated for all symptom episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Symptom Episode Exposure Comparison

Average exposure scores for corresponding symptom episode days starting at five days prior to Day 1 of each symptom episode were calculated for all symptom episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Symptom Episode Sleep Comparison

Average sleep scores for corresponding symptom episode days starting at five days prior to Day 1 of each symptom episode were calculated for all symptom episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Symptom Episode Stress Comparison

Average stress scores for corresponding symptom episode days starting at five days prior to Day 1 of each symptom episode were calculated for all symptom episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test ($p < 0.05$).

Symptom Episode Physical Activity Comparison

Average physical activity scores for corresponding symptom episode days starting at five days prior to Day 1 of each symptom episode were calculated for all symptom episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test (p<0.05).

Sick Episodes Severity Comparison

Average severity scores for corresponding sick episode days starting at five days prior to Day 1 of each sick episode were calculated for all sick episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test (p<0.05).

Sick Episodes Quality of Life Comparison

Average quality of life scores for corresponding sick episode days starting at five days prior to Day 1 of each sick episode were calculated for all sick episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test (p<0.05).

Sick Episode Exposure Comparison

Severity scores for corresponding sick episode days starting at five days prior to Day 1 of each sick episode were calculated for all sick episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test (p<0.05).

Sick Episode Sleep Comparison

Average sleep scores for corresponding sick episode days starting at five days prior to Day 1 of each sick episode were calculated for all sick episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test (p<0.05).

Sick Episode Stress Comparison

Average stress scores for corresponding sick episode days starting at five days prior to Day 1 of each sick episode were calculated for all sick episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test (p<0.05).

Sick Episode Physical Activity Comparison

Average physical activity scores for corresponding sick episode days starting at five days prior to Day 1 of each sick episode were calculated for all sick episode days for the two groups. These data were analyzed using a 2-tailed, independent t-test ($p<0.05$).

SPSS

Symptom Episode Correlation

A bivariate correlation matrix was calculated for Symptom Episode average severity scores, quality of life scores, sleep time, stress scores, physical activity time during the first five days of symptom episodes using SPSS ($p<0.05$).

Sick Episode Correlation

A bivariate correlation matrix was calculated for Sick Episode average severity scores, quality of life scores, sleep time, stress scores, physical activity time during the first five days of sick episodes using SPSS ($p<0.05$).

Chapter Four: Results

Descriptive Data

Comparative baseline descriptive data are summarized in **Table 1**. There were no

significant differences between baseline descriptive data between groups. For measures

of pre-study and post-study weights there were no significant losses or gains for any

subjects, thus weight is reported as an average weight of the group calculated from the

average of each subject's weight (kg) over the twelve weeks. Comparative subject intake

habits are summarized in **Table 2**. There were no significant differences between groups

with the exception of other food items consumed with oats ($p = 0.02$). Comparative

percent subject lifestyle characteristics are summarized in **Table 3**. There were no

significant differences between groups, with the exception of percentage of those who are

single ($p = 0.01$) and those who are partnered (p = .05).

Table 1. Subject Descriptive Characteristics

Variable	Beta-Glucan (N=40) Mean ± SD	Placebo (N=39) Mean ± SD	*p*
Age (yr)	22.40 ± 3.82	23.44 ± 4.30	0.25
Height (cm)	180.00 ± 7.59	181.83 ± 5.77	0.44
Weight (kg)	81.70 ± 11.32	83.37 ± 14.33	0.60

Table 2. Subject Intake Habits

Variable	Beta-Glucan (N=40) Mean	±	SD	Placebo (N=39) Mean	±	SD	p
Caffeine Intake (mg/day)	112.50	±	203.05	106.92	±	126.43	0.88
Coffee (cups/day)	0.75	±	1.68	0.74	±	1.16	0.98
Tea (cups/day)	0.45	±	0.88	0.36	±	0.71	0.61
Cola (12 oz drinks/day)	0.50	±	0.85	0.49	±	0.70	0.94
Intake of Foods Containing							
Beta-Glucan (times/week)	16.05	±	11.03	15.54	±	9.16	0.82
Oatmeal	0.92	±	1.53	1.69	±	2.27	0.08
Cereal with oats	1.48	±	1.75	1.49	±	1.99	0.98
Other items with oats	2.16	±	2.39	1.03	±	1.79	0.02
Barley	0.84	±	2.34	0.53	±	0.89	0.44
Cereal with barley	0.66	±	1.46	0.45	±	1.01	0.47
Other items with barley	0.92	±	1.88	0.84	±	1.52	0.84
Mushrooms	1.41	±	1.58	1.05	±	1.28	0.27
Whole wheat bread	4.72	±	3.36	4.64	±	3.67	0.92
Whole wheat pasta	1.13	±	1.04	1.55	±	1.75	0.21
Other whole wheat foods	1.92	±	2.03	2.10	±	2.55	0.73
Rye bread	0.29	±	1.18	0.18	±	0.61	0.63
Other rye foods	0.13	±	0.41	0.11	±	0.51	0.81

Table 3. Percent Subject Lifestyle Characteristics

Variable	Beta-Glucan (N=40) Mean	±	SD	Placebo (N=39) Mean	±	SD	p
Marital Status							
Single	0.88	±	0.33	0.64	±	0.49	0.01
Married	0.05	±	0.22	0.10	±	0.31	0.38
Partnered	0.08	±	0.27	0.23	±	0.43	0.05
Separated	0.00	±	0.00	0.03	±	0.16	0.31
Living Conditions							
House/Apt. with Roomates	0.50	±	0.51	0.64	±	0.49	0.21
House/Apartment Alone	0.08	±	0.27	0.05	±	0.22	0.67
With Family	0.13	±	0.33	0.15	±	0.37	0.72
Dormatory	0.25	±	0.44	0.13	±	0.34	0.17
Fraternity	0.05	±	0.22	0.03	±	0.16	0.58
Injury Limiting Physical Activity	0.03	±	0.16	0.08	±	0.27	0.30
Currently Dieting	0.10	±	0.30	0.10	±	0.31	0.97
Tobacco Use	0.15	±	0.36	0.13	±	0.34	0.78
Smoke	0.05	±	0.22	0.05	±	0.22	0.98
Chew/Dip	0.10	±	0.30	0.08	±	0.27	0.72
Flu Shot within 1 year prior	0.15	±	0.36	0.18	±	0.39	0.73

WURSS

Comparative data from the Wisconsin Upper Respiratory Symptom Survey are summarized in **Table 4**. Yeast ß-glucan demonstrated no statistically significant effect on the subjects for any of the variables (number of symptom days, symptom day severity score, symptom day quality of life score, symptom day maximum severity score, symptom day maximum quality of life score, number of sick days, sick day severity score, sick day quality of life score, sick day maximum severity score, sick day maximum quality of life score, number of symptom episodes, number of sick episodes, average duration of symptom episodes, maximum duration of symptom episodes, average duration of sick episodes, maximum duration of sick episodes, symptom episode severity score, symptom episode quality of life score, sick episode severity score, and sick episodes quality of life score).

Table 4. Wisconsin Upper Respiratory Symptom Survey Data

Variable	N	ß-glucan (N=40) Mean ± SD	N	Placebo (N=39) Mean ± SD	*p*
Symptom Days	664	18.44 ± 13.14	507	14.91 ± 11.66	0.24
Symptom Day Severity Score	---	23.82 ± 22.28	---	22.36 ± 20.44	0.78
Symptom Day QOL Score	---	7.35 ± 7.28	---	8.35 ± 7.72	0.60
Symptom Day Max Severity Score	---	54.36 ± 41.72	---	45.26 ± 41.84	0.37
Symptom Day Max QOL Score	---	14.76 ± 13.79	---	15.85 ± 15.35	0.77
Number of Days until First Symptom Day	---	45.93 ± 31.76	---	37.88 ± 31.35	0.48
Sick Days	821	21.61 ± 13.98	702	20.06 ± 17.64	0.68
Sick Day Severity Score	---	23.13 ± 20.97	---	24.01 ± 18.77	0.85
Sick Day QOL Score	---	7.80 ± 7.05	---	10.57 ± 8.51	0.15
Sick Day Max Severity Score	---	59.79 ± 47.03	---	59.91 ± 45.43	0.99
Sick Day Max QOL Score	---	19.35 ± 17.17	---	22.73 ± 16.82	0.42
Number of Days until First Sick Day	---	42.60 ± 33.43	---	38.43 ± 32.03	0.76
Number of Symptom Episodes	39	1.39 ± 0.57	27	1.23 ± 0.61	0.33
Number of Sick Episodes	44	1.42 ± 0.56	33	1.38 ± 0.71	0.80
Number of Days until First Symptom Episode	---	54.54 ± 30.50	---	57.47 ± 29.87	0.71
Number of Days until First Sick Episode	---	49.00 ± 30.85	---	58.88 ± 28.43	0.24
Average Duration of Symptom Episodes	---	13.95 ± 6.39	---	13.86 ± 4.30	0.95
Max Duration of Symptom Episodes	---	15.29 ± 8.23	---	14.73 ± 5.57	0.79
Average Duration of Sick Episodes	---	15.38 ± 7.93	---	17.24 ± 14.79	0.55
Max Duration of Sick Episodes	---	17.03 ± 9.71	---	18.79 ± 15.28	0.61
Symptom Episode Severity Score	---	23.57 ± 25.90	---	24.67 ± 23.15	0.88
Symptom Episode QOL Score	---	6.71 ± 7.07	---	8.31 ± 8.98	0.50
Sick Episode Severity Score	---	23.62 ± 19.71	---	26.66 ± 20.43	0.58
Sick Episode QOL Score	---	7.14 ± 6.18	---	10.07 ± 8.82	0.16

QOL = Quality of Life

SPSS

Symptom Episodes

The severity score and quality of life score are highly correlated with each other for symptom episodes. Stress was the only independent variable that was correlated with both severity score and quality of life score during the first five days of the symptom episode.

Symptom Episode Correlation

Correlations

		Severity	QOL	Sleep	Stress	PA
Severity	Pearson Correlation	1	.924**	-.017	.441**	-.045
	Sig. (2-tailed)		.000	.893	.000	.721
	N	66	66	66	66	66
QOL	Pearson Correlation	.924**	1	.039	.411**	-.017
	Sig. (2-tailed)	.000		.756	.001	.891
	N	66	66	66	66	66
Sleep	Pearson Correlation	-.017	.039	1	-.015	.335**
	Sig. (2-tailed)	.893	.756		.902	.006
	N	66	66	66	66	66
Stress	Pearson Correlation	.441**	.411**	-.015	1	-.100
	Sig. (2-tailed)	.000	.001	.902		.422
	N	66	66	66	66	66
PA	Pearson Correlation	-.045	-.017	.335**	-.100	1
	Sig. (2-tailed)	.721	.891	.006	.422	
	N	66	66	66	66	66

**. Correlation is significant at the 0.01 level (2-tailed).

Sick Episodes

The severity score and quality of life score are highly correlated with each other for sick episodes. Stress was the only independent variable that was correlated with both severity score and quality of life score during the first five days of the sick episode.

Sick Episode Correlation

Correlations

		Severity	QOL	Sleep	Stress	PA
Severity	Pearson Correlation	1	.904**	-.046	.276*	.034
	Sig. (2-tailed)		.000	.712	.025	.786
	N	66	66	66	66	66
QOL	Pearson Correlation	.904**	1	-.025	.286*	.015
	Sig. (2-tailed)	.000		.842	.020	.907
	N	66	66	66	66	66
Sleep	Pearson Correlation	-.046	-.025	1	.025	.299*
	Sig. (2-tailed)	.712	.842		.840	.015
	N	66	66	66	66	66
Stress	Pearson Correlation	.276*	.286*	.025	1	-.119
	Sig. (2-tailed)	.025	.020	.840		.340
	N	66	66	66	66	66
PA	Pearson Correlation	.034	.015	.299*	-.119	1
	Sig. (2-tailed)	.786	.907	.015	.340	
	N	66	66	66	66	66

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

References

Babineau, T.J., A. Hackford, A Kenler, B. Bistrian, R.A. Forse, P.G. Fairchild, S. Heard, M. Keroack, P. Caushaj, and P. Benotti (1994). "A phase II multicenter, double-bline, randomized, placebo-controlled study of three dosages of an immunomodulator (PGG-glucan) in high-risk surgical patients." Archives of Surrgery **129**: 1204-1210.

Barrett, B., K. Locken, R. Maberry, J. Schwamman, R. Brown, J. Bobula, and E.A. Stauffacher (2002). "The Wisconsin upper respiratory symptom survey (WURSS)." Journal of Family Practice **51**: 249-257.

Barrett, B., R. Brown, and M. Mundt (2008). "Comparison of anchor-based and distributional approaches in estimating important difference in common cold." Quality of Life Research **17**:75-85.

Barrett, B., R. Brown, M. Mundt, N. Safdar, L. Dye, R. Maberry, J. Alt (2005). "The Wisconsin upper respiratory symptom survey is responsive, reliable, and valid." Journal of clinical Epidemiology **58**: 609-617.

Barrett, B., S. Enrizzi, P. Andreoli, S. Barlow, Z. Zhang (2007). "Clinical Significance of Common Cold Treatment: Professionals' Opinions." Wisconsin Medical Journal **106**(8): 473-480.

Biesel, W.R. (1996). Nutrition and immune function: overview. Journal of Nutrition **126**: 2611S-2615S.

Bramley, T.J., D. Lerner, M. Sarnes (2002). "Productivity Losses Related to the common cold." Journal of Environmental Medicine **44**: 822-829.

Brown, G.D. and S. Gordon (2003). "Fungal β-glucans and mammalian immunity." Immunity **19**: 311-315.

Brown, G.D. and S. Gordon (2005). "Immune recognition of fungal β-glucans." <u>Cellular Microbiology</u> **7**(4): 471-479.

Carney, C.E., J.D. Edinger, B. Meyer, L. Lindman, T. Istre (2006). Daily activities and sleep qualities in college students. <u>Chronobiology Internationl</u> **23**(3): 623-637.

Castro, G.R., B. Panilaitis, E. Bora, and D.L. Kaplan (2007). "Controlled release biopolymers for enhancing immune response." <u>Molecular Pharmaceutics</u> **4**(1): 33-46.

Ceddia, M.A. and J.A. Woods (1999). "Exercise suppresses macrophage antigen presentation." <u>Journal of applied Physiology</u> **87**: 2253-2258.

Cohen, S., D.A.J. Tyrrell, and A.P. Smith (1991). "Psychological stress and susceptibility to the common cold." <u>New England Journal of Medicine</u> **325**: 606-612.

Davis, J.M., E.A. Murphy, A.S. Brown, M.D. Charmichael, A. Ghaffar, and E.P. Mayer (2003). "Effects of moderate exercise and oat β-glucan on innate immune function and susceptibility to respiratory infection." <u>American Journal of Physiology – Regulatory, Integrative, and Comparative Physiology</u> **286**: R366-R372.

Davis, J.M., E.A. Murphy, A.S. Brown, M.D. Charmichael, A. Ghaffar, and E.P. Mayer (2004). "Effects of oat β-glucan on innate immunity and infection after exercise stress." <u>Medicine and Science in Sports and Exercise</u> **36**(8): 1321-1327.

Davis, J.M., M.L/ Kohut, L.H. Colbert, D.A. Jackson, A. Ghaffar, and E.P. Mayer (1997). "Exercise, alveolar macrophage function, and susceptibility to respiratory infection." <u>Journal of Applied Physiology</u> **83**(5): 1461-1466.

Demir, G., H.O. Klein, N. Mandel-Molinas, N. Tuzuner (2007). "Beta glucan induces proliferation and activation of monocytes in peripheral blood of patients with advanced breast cancer." <u>International Immunology</u> **7**: 113-116.

Dinges, D.F., S.T. Douglas, S. Hamarman, L. Zaugg, and S. Kapoor (1995). Sleep deprivation and human immune function. <u>Advances in Neuroimmunology</u> **5**: 97-110.

Fukuda, S., K. Morimoto (2001). Lifestyle, stress, and cortisol response: review II. Environmental Health and Preventative Medicine **6**: 15-21.

Garden, A. (1991). "Relationship between burnout and performance." Psychological Reports **68**: 963-977.

Glaser, R. and J.K. Kiecolt-Glaser (2005). Stress-induced immune dysfunction: implications for health. Nature Reviews: Immunology **5**: 243-251.

Gleeson, M. (2007). "Immune function in sport and exercise." Journal of Applied Physiology **103**: 693-699.

Goldman, C.S. and E.H. Wong (1997). Stress and the college student. Education **117**(4): 604-610.

Herre, J., S. Gordon, and G.D. Brown (2004). "Dectin-1 and its role in the recognition of β-glucans by macrophages." Molecular Immunology **40**: 869-876.

Hong, F., J. Yan, et al. (2004). "Mechanism by which orally administered β-1,3-glucans enhance the tumoricidal activity of antitumor monoclonal antibodies in murine tumor models." Journal of Immunology **173**: 797-806.

Hunzeker, J., D.A. Padgett, P.A. Sheridan, F.S. Dhabhar, and J.F. Sheridan (2004). "Modulation of natural killer cell activity by restraint stress during an influenza A/PR8 infection in mice." Brain, Behavior, and Immunity **18**:526-535.

Jackson, G.G., H.F. Dowling, I.G. Spiesman, and A.V. Boand (1957). "Transmission of the common cold to volunteers under controlled conditions." American Medical Association Archives of Internal Medicine **101**: 267-278.

Jenkins, D.J.A., et al. (2002). Soluble fiber intake at a dose approved by the US Food and Drug Administration for cardiovascular disease assessed in a randomized controlled crossover trial. American Journal of Clinical Nutrition **75**: 834-839.

Kiecolt-Glaser, J.K. (1999). Stress, personal relationships, and immune function: health implications. Brain, Behavior, and Immunity **13**: 61-72.

Kiecolt-Glaser, J.K., L. McGuire, T.F. Robles, and R. Glaser (2002). Psychoneuroimmunology: psychological influences on immune function and health. <u>Journal of Consulting and Clinical Psychology</u> **70**(3): 537-547.

Kohut, M.L., J.M. Davis, et al. (1998). "The role of stress hormones in exercise-induced suppression of alveolar macrophage antiviral function." <u>Journal of Neuroimmunology</u> **81**: 193-200.

Lac, G. and A. Chamoux (2003). Elevated salivary cortisol levels as a result of sleep deprivation in a shift worker. <u>Occupational Medicine</u> **53**: 143-145.

Landmann, R.M.A., F.B. Muller, C. Perini, M. Wesp, P. Erne, and F.R. Buhler (1984). Changes of immunoregulatory cells induced by psychological and physical stress: relationship to plasma catecholamines. <u>Clinical Experiments in Immunology</u> **58**: 127-135.

Linder, J.A. and D.E. Singer (2003). "Health-related quality of life of adults with upper respiratory tract infections." <u>Journal of General Internal Medicine</u> **18**: 802-807.

Manzi, P. and L. Pizzoferrato (2000). "Beta glucans in edible mushrooms." <u>Food Chemistry</u> **68**: 315-318.

Medzhitov, R. and C.A. Janeway, Jr. (1997). "Innate immunity: impact on the adaptive immune response." <u>Current Opinion in Immunology</u> **9**:4-9.

Murphy, E.A., J.M. Davis, A.S. Brown, M.D. Carmichael, N. Van Rooijen, E. Ghaffar, and E.P. Mayer (2004). "Role of lung macrophages on susceptibility to respiratory infection following short-term moderate exercise training." <u>American Journal of Physiology – Regulatory, Integrative, and Comparative Physiology</u> **287**: R1354-R1358.

Murphy, E.A., J.M. Davis, A.S. Brown, M.D. Charmichael, A. Ghaffar, and E.P. Mayer (2007). "Oat β-glucan effects on neutrophil respiratory burst activity following exercise." <u>Medicine and Science in Sports and Exercise</u> **39**(4): 639-644.

Murphy, E.A., J.M. Davis, et al. (2008). "Benefits of oat β-glucan on respiratory infection following exercise stress: role of lung macrophages." <u>American Journal of Physiology – Regulatory, Integrative, and Comparative Physiology</u> **294**: R1593-R1599.

Murphy, E.A., J.M. Davis, M.D. Carmichael, E.P. Mayer, and E. Ghaffar (2004). "Effects of moderate exercise and oat β-glucan on lung tumor metastases and macrophage antitumor cytotoxicity." <u>Journal of Applied Physiology</u> **97**: 955-959.

Naumann, E., A.B. Van Rees, G. Onning, R. Oste, M. Wydra, and R.P. Mensink (2006). β-glucan incorporated into a fruit drink effectively lowers serum LDL-cholesterol concentrations. <u>American Journal of Clinical Nutrtion</u> **83**: 601-605.

Nazare, J.A., M. Laville, et al. (2007). "Ingredients from grains, fruits and vegetables for weight control: β-glucans." <u>Novel food ingredients for weight control</u> (II Pt 6): 131-152.

Nguyen-Michel, S.T., J.B. Unger, J. Hamilton, and D. Spruijt-Metz (2006). Associations between physical activity and perceived stress/hassles in college students. <u>Stress and Health</u> **22**: 179-188.

Nicolosi, R., S.J. Bell, B.R. Bistrian, I. Greenberg, R.A. Forse, and G.L. Blackburn (1999). Plasma lipid changes after supplementation with ß-glucan fiber from yeast. <u>American Journal of Clinical Nutrition</u> **70**: 208-212.

Nieman, D.C. (2000). Is infection risk linked to exercise workload? <u>Medicine and Science in Sports and Exercise</u>. **32**(7): S406-S411.

Nieman, D.C. (2003). "Current Perspective on Exercise Immunology." <u>Current Sports Medicine Reports</u> **23**: 239-242.

Nieman, D.C. (2007). "Marathon training and immune function." <u>Sports Medicine</u> **37**(4-5): 412-415.

Nieman, D.C., D.A. Henson, et al. (2008). "β-glucan, immune function, and upper respiratory tract infections in athletes." <u>Medicine and Science in Sports and Exercise</u> **40**(8): 1463-1471.

Nieman, D.C., J.M. Davis, et al. (2003). "Carbohydrate ingestion influences skeletal muscle cytokine mRNA and plasma cytokine levels after a 3-h run." <u>Journal of Applied Physiology</u> **94**: 1917-1925.

Nieman, D.C., K.S. Buckley, D.A. Henson, B.J. Warren, J. Suttles, J.C. Ahle, S. Simandle, O.R. Fagoaga, and S.L. Nehlsen-Cannarella (1995). "Immune function in marathon runners verus sedentary controls." <u>Medicine and Science in Sports and Exercise</u> **27**(7): 986-992.

Pederson, B.K., and L. Hoffman-Goetz (2000). "Exercise and the immune system: regulation, integration, and adaptation." <u>Physiological Reviews</u> **80**(3): 1055-1081.

Peters, E.M., J.M. Goetzsche, B. Grobbelaar, T.D. Noakes (1993). "Vitamin C supplementation reduces the incidence of postrace symptoms of upper-respiratory-tract infection in ultramarathon runners." <u>American Journal of Clinical Nutrition</u> **57**: 170

Rice, P.J., E.L. Adams, et al. (2005). "Oral delivery and gastrointestinal absorption of soluble glucans stimulate increased resistance to infectious challenge." <u>Journal of Pharmacology and Experimental Therapeutics</u> **314**: 1079-1086.

Ross, G.D., V. Vetvicka, J. Yan, Y. Xia, and J. Vetvivkova (1998). "Therapeutic intervention with complement and β-glucan in cancer." <u>Immunopharmacology</u> **42**:61-74.

Salvador, C., B. Li, R. Hansen, Cramer D.E., M. Kong, J. Yan (2008). "Yeast-derived ß-glucan augments the therapeutic efficacy mediated by anti-vascular endothelial growth factor monoclonal antibody in human carcinoma xenograft models." Clinical Cancer Research 14(4):1239-1247.

Singh, A., M.L. Failla, and P.A. Deuster (1994). "Exercise-induced changes in immune function: effects of zinc supplementation." Journal of Applied Physiology **76**(6): 2298-2303.

Tortora, G.J. and B. Derrickson (2006). The lymphatic system and immunity. In Principles of Anatomy and Physiology (pp. 804-837). Hoboken, NJ: John Wiley & Sons, Inc.

Trockel, M.T., M.D. Barnes, D. L. Egget (2000). Health-related variable and academic performance among first-year college student: implications for sleep and other behaviors. Journal of American College Health **49**: 125-131.

Tsai, L., S. Li (2004). Sleep patterns in college students: gender and grade differences. Journal of Psychosomatic Research **56**: 231-237.

Vetvicka, V., B.P. Thornton, and G.D. Ross (1996). "Soluble β-glucan polysaccharide binding to the lectin site of neutrophil or natural killer cell complement receptor type 3 (CD11b/CD18) generates a primed state of the receptor capable of mediating cytotoxicity of iC3b-opsonized target cells." Journal of Clinical Investigation **98**(1): 50-61.

Weidner, T.G., T Cranston, T. Schurr, and L.A. Kaminsky (1998). The effect of exercise training on the severity and duration of a viral upper respiratory illness. Medicine and Science in Sports and Exercise **30**(11): 1578-1583.

Whitney, E.N. and S.R. Rolfes (2002). The carbohydrates: sugars, starches, fibers. In Understanding Nutrition (pp. 92-128). Belmont, CA: Thompson Learning, Inc.

Willment, J.A., S. Gordon, and G.D. Brown (2001). "Characterization of the Human β-glucan receptor and its alternatively spliced isoforms." Journal of Biological Chemistry **276**(47): 43818-4382.

Wonnacott, K.M. and R.H. Bonneau (2002). "The effects of stress on memory cytotoxic T-lymphocyte-mediated protection against herpes simplex virus infection at mucosal sites." Brain, Behavior, and Immunity **16**: 104-117.

Woods, J.A. (2005). Physical activity, exercise, and immune function. Brain, Behavior, and Immunity **19**: 369-370.

Young, S., V. Robinson, M. Barger, M. Whitmer, D. Porter, D. Frazer, and V. Castranova (2003). "Exposure to particulate 1-3-β-glucans induces greater pulmonary toxicity that soluble 1-3-β-glucans in rats." Journal of Toxicology and Environmental Health **66**: 25-38.

Yun, C.H., A. Estrada, A. Van Kessel, B. Park, B. Laarveld (2003). "β-glucan, extracted from oat, enhances disease resistance against bacterial and parasitic infections." FEMS Immunology and Medical Microbiology **35**: 67-75.

Chapter Five: Manuscript

Effects of a yeast β-glucan supplement on symptoms of upper respiratory tract infection in free-living college-aged males

Casey Gorham, Brent Ruby, Charles Dumke

Montana Center for Work Physiology and Exercise Metabolism

The University of Montana, Missoula, MT

Addresses for correspondence:

Brent. C. Ruby, Ph.D

Director of Montana Center for Work Physiology and Exercise Metabolism

The University of Montana

Tel: (406) 243-2117

Fax: (406) 243-6252

Email: brent.ruby@umontana.edu

ABSTRACT

Purpose: The goal of this research was to evaluate the effects of a yeast ß-glucan on symptoms of upper respiratory tract infection in healthy, free-living, college-aged males. **Methods:** The WURSS-44, a reliable, validated survey used for determining symptoms of upper respiratory tract infection was filled out online daily by 79 male subjects between the ages of 18 and 40. Subjects orally ingested 250 mg capsules of either yeast ß-glucan or placebo daily. **Results:** Yeast ß-glucan demonstrated no statistically significant effect on the experimental subject population for any of the variables associated with symptoms of upper respiratory tract infection. **Conclusion:** Yeast ß-glucan does not significantly improve immune functioning in healthy, free-living college aged males.

INTRODUCTION

ß-glucan is a complex carbohydrate polymer found in the cell walls of plants that has been shown to lower cholesterol in humans (Jenkins et al., 2002), promote antitumor activity in both humans and mice (Vetvicka et al., 1996), and improve immune function in immunosuppressed populations of humans and mice (Yun et al., 2003; Brown and Gordon, 2003; Brown and Gordon, 2005). Oat ß-glucan has been studied far more than any other forms and has been shown repeatedly to aid human physiological functioning (Jenkins et al., 2002; Vetvicka et al., 1996; Yun et al., 2003; Brown and Gordon, 2003; Brown and Gordon, 2005).

Yun et al. (2003) argues that oat ß-glucan can alleviate certain infections in murine populations. These mice were administered oat ß-glucan for 10 days and then

exposed to bacteria known to cause common upper respiratory tract infections in both mice and humans. Similarly, Murphy et al. (2008) administered mice with oat ß-glucan dissolved per 1 ml of drinking water for 10 days before inoculation with a virus. In both studies, mice that orally ingested the oat ß-glucan demonstrated benefits in their immune function. The results suggest that short-term treatment with an oat ß-glucan, prior to exposure, can enhance immune function against common infections in mice.

Supplementing with a yeast ß-glucan has been shown to stimulate proliferation and activation of peripheral blood monocytes in patients with advanced breast cancer (Demir et al., 2007). Both mice and human populations suffering from various cancers have been shown to benefit from a yeast ß-glucan supplement. Both oat and yeast ß-glucan have been shown to decrease low-density lipoprotein (LDL) cholesterol in humans (Naumann et al., 2006; Nicolosi et al., 1999). This parallel may indicate that oat and yeast ß-glucan may be comparable in affecting different aspects of human physiology.

Both psychological and physical stressors are shown to increase risk of upper respiratory tract infections in mice and humans similarly (Davis et al., 1997; Nieman et al., 2008; Hunzeker et al., 2004). Previous research has shown that mice participating in a single bout of prolonged, vigorous exercise are at a higher risk for upper respiratory tract infections than those who either underwent a short-term exercise or no exercise (Davis et al., 1997). Oat ß-glucan has been shown to enhance immunity in mice and prevent infection of the upper respiratory tract. Willment et al. (2001) found that the human receptor of ß-glucan is both structurally and functionally similar to the mouse receptor.

69

Human research has found that oat ß-glucan offset increased upper respiratory tract infection risk associated with exercise stress (Ceddia and Woods, 1999; Davis et al., 2004). The similarities seen between oat and yeast ß-glucan in both murine and human populations suggest that similar effects may be seen in other areas of physiology, such as immune function. College-aged students generally suffer any combination of different health affecting behaviors, which may cause a weakened immune system and increased susceptibility to developing an URTI (Tsai and Li, 2004). To our knowledge no research has succeeded in showing that a yeast ß-glucan supplement can improve symptoms of upper respiratory tract infection in relatively healthy populations. Examining whether or not ß-glucan can prevent these symptoms may have implications for maintaining immune function in healthy, free-living populations. This research may also provide a better understanding of how much each of the risk factors for URTI plays a role in preventing and fighting URTI. The purpose of this study is to examine the effects of a yeast β-glucan supplement on symptoms of upper respiratory tract infection in healthy, free-living, college-aged males.

We hypothesized that the yeast β-glucan supplement would have no effect on symptoms of upper respiratory tract infection in free-living, college-aged males.

METHODS

Subjects

There were 81 male, college-aged subjects in the study. Prior to participation, all subjects completed an Institutional Review Board (IRB) approved informed consent form (**Tables 1-3**).

Table 1. Subject Descriptive Characteristics

Variable	Beta-Glucan (N=40) Mean ± SD			Placebo (N=39) Mean ± SD			p
Age (yr)	22.40	±	3.82	23.44	±	4.30	0.25
Height (cm)	180.00	±	7.59	181.83	±	5.77	0.44
Weight (kg)	81.70	±	11.32	83.37	±	14.33	0.60

Descriptive Data

Descriptive Data was collected using four different methods. (1) A background survey was completed by each subject which included age, gender, marital status, living conditions, injuries which limit physical activity, dieting, caffeine intake, tobacco use, and estimated consumption of foods with high amounts of ß-glucan; (2) a daily survey completed by each subject during the twelve week study included twenty-four hour sleep record in hours, twenty-four hour physical activity time in minutes, and twenty-four hour stress level; and (3) an optional post study survey completed by the majority of subjects included current height, current weight, estimated weight prior to study, how often and/or easily subject accrues illness. Subjects were excluded from the study results if (1) they were not within the 18-41 year age requirement throughout the study; (2) they did not complete the background survey; or (3) they did not complete at least 75% (63) of the daily surveys.

Table 2. Subject Intake Habits

Variable	Beta-Glucan (N=40) Mean	±	SD	Placebo (N=39) Mean	±	SD	p
Caffeine Intake (mg/day)	112.50	±	203.05	106.92	±	126.43	0.88
Coffee (cups/day)	0.75	±	1.68	0.74	±	1.16	0.98
Tea (cups/day)	0.45	±	0.88	0.36	±	0.71	0.61
Cola (12 oz drinks/day)	0.50	±	0.85	0.49	±	0.70	0.94
Intake of Foods Containing							
Beta-Glucan (times/week)	16.05	±	11.03	15.54	±	9.16	0.82
Oatmeal	0.92	±	1.53	1.69	±	2.27	0.08
Cereal with oats	1.48	±	1.75	1.49	±	1.99	0.98
Other items with oats	2.16	±	2.39	1.03	±	1.79	0.02
Barley	0.84	±	2.34	0.53	±	0.89	0.44
Cereal with barley	0.66	±	1.46	0.45	±	1.01	0.47
Other items with barley	0.92	±	1.88	0.84	±	1.52	0.84
Mushrooms	1.41	±	1.58	1.05	±	1.28	0.27
Whole wheat bread	4.72	±	3.36	4.64	±	3.67	0.92
Whole wheat pasta	1.13	±	1.04	1.55	±	1.75	0.21
Other whole wheat foods	1.92	±	2.03	2.10	±	2.55	0.73
Rye bread	0.29	±	1.18	0.18	±	0.61	0.63
Other rye foods	0.13	±	0.41	0.11	±	0.51	0.81

Table 3. Percent Subject Lifestyle Characteristics

Variable	Beta-Glucan (N=40) Mean	±	SD	Placebo (N=39) Mean	±	SD	p
Marital Status							
Single	0.88	±	0.33	0.64	±	0.49	0.01
Married	0.05	±	0.22	0.10	±	0.31	0.38
Partnered	0.08	±	0.27	0.23	±	0.43	0.05
Separated	0.00	±	0.00	0.03	±	0.16	0.31
Living Conditions							
House/Apt. with Roomates	0.50	±	0.51	0.64	±	0.49	0.21
House/Apartment Alone	0.08	±	0.27	0.05	±	0.22	0.67
With Family	0.13	±	0.33	0.15	±	0.37	0.72
Dormatory	0.25	±	0.44	0.13	±	0.34	0.17
Fraternity	0.05	±	0.22	0.03	±	0.16	0.58
Injury Limiting Physical Activity	0.03	±	0.16	0.08	±	0.27	0.30
Currently Dieting	0.10	±	0.30	0.10	±	0.31	0.97
Tobacco Use	0.15	±	0.36	0.13	±	0.34	0.78
Smoke	0.05	±	0.22	0.05	±	0.22	0.98
Chew/Dip	0.10	±	0.30	0.08	±	0.27	0.72
Flu Shot within 1 year prior	0.15	±	0.36	0.18	±	0.39	0.73

Survey

Studies show that lab measurements to indicate upper respiratory tract infections are not as accurate when compared to the individual's perceived symptoms of upper respiratory tract infection (Jackson et al., 1957; Barrett et al., 2002; Barrett et al., 2005; Barrett et al., 2007). The Wisconsin Upper Respiratory Symptoms Survey (WURSS) was developed as an evaluative illness specific quality-of-life instrument (Barrett et al., 2008). The construct validity of the WURSS-44, a forty-four question version of the survey, is supported by measures of reliability and responsiveness of subjects (Barrett et al., 2005). This survey looks at thirty-two symptoms of upper respiratory tract infection, ten functional quality-of-life items, one global illness severity item (How sick do you feel today?), and one item assessing global change (Compared to yesterday how do you feel?) (Barrett et al., 2005; Barrett et al., 2002). The survey allows subjects to score their symptoms using a seven-point scale (0 = none, 1 = very mild, 3 = mile, 5 = moderate, 7 = severe).

Data Collection

Each subject signed an Institutional Review Board (IRB) approved informed consent form prior to participation in the study. Subjects were asked to take either a β-glucan 250mg supplement or a placebo (rice flour) daily. Distribution of supplement and placebo was done in a double-blind fashion. Along with taking the daily supplement or placebo, each subject filled out an online survey (surveymonkey.com) which includes questions about sleep, stress, physical activity, exposure to illness, includes the WURSS,

and asks a final question about the subject's belief of the cause of any symptoms (flu, cold, allergies, etc.).

Statistical Procedures

Background descriptive data were analyzed using an independent t-test for age, height (inches), pre-study weight (kg), post-study weight (kg), weight change (kg), physical activity time (minutes spent daily participating in aerobic, resistance, and organized sport activities, number of high school sports, caffeine intake (mg per week from coffee, tea, or cola beverages), average sleep time (hours per night), average stress level (0-10; not stressed-extremely stressed), number of allergies, average estimated β-glucan intake (servings per week total and servings per week of oatmeal, cereal with oats, other items with oats, barley, cereal with barley, other items with barley, mushrooms, whole wheat bread, whole wheat pasta, other whole wheat foods, rye bread, other rye foods) and will be expressed as Mean ± SD. For measures of daily sleep (hours per night), stress (0-10; not stressed-extremely stressed), and physical activity (aerobic exercise, resistance training, and organized sport; total physical activity minutes per day), and average score was calculated for each variable for each subject. These measures were analyzed using an independent t-test. Statistical significance was established at the $p < 0.05$ level. These analyses were used to compare differences between the experimental group (supplement) and the control group (placebo).

RESULTS

Comparative baseline descriptive data are summarized in **Table 1**. There were no significant differences between baseline descriptive data between groups. For measures of pre-study and post-study weights there were no significant losses or gains for any subjects, thus weight is reported as an average weight of the group calculated from the average of each subject's weight (kg) over the twelve weeks. Comparative subject intake habits are summarized in **Table 2**. There were no significant differences between groups with the exception of other food items consumed with oats ($p = 0.02$). Comparative percent subject lifestyle characteristics are summarized in **Table 3**. There were no significant differences between groups, with the exception of percentage of those who are single ($p = 0.01$) and those who are partnered (p = .05).

Comparative data from the Wisconsin Upper Respiratory Symptom Survey are summarized in **Table 4**. Yeast ß-glucan demonstrated no statistically significant effect on the subjects for any of the variables (total number of days with symptoms, number of URTI episodes, total number of days until the occurence of an URTI episode, the average or maximum duration of an URTI episode, and the severity of URTI episodes).

Table 4. Wisconsin Upper Respiratory Symptom Survey Data

Variable	N	ß-glucan (N=40) Mean ± SD	N	Placebo (N=39) Mean ± SD	p
Number of Days with Symptoms	664	18.44 ± 13.14	507	14.91 ± 11.66	0.24
Number of Episodes	39	1.39 ± 0.57	27	1.23 ± 0.61	0.33
Number of Days until First Episode	---	54.54 ± 30.50	---	57.47 ± 29.87	0.71
Average Duration Episodes	---	13.95 ± 6.39	---	13.86 ± 4.30	0.95
Max Duration of Episodes	---	15.29 ± 8.23	---	14.73 ± 5.57	0.79
Episode Severity Score	---	23.57 ± 25.90	---	24.67 ± 23.15	0.88

DISCUSSION

The purpose of this study was to examine the effects of a yeast β-glucan supplement on symptoms of upper respiratory tract infection in healthy, free-living, college-aged males.

The combination of prior research in mice and immunnosuppressed humans suggests that β-glucan may have a beneficial effect on the immune system (Murphy et al., 2008; Murphy et al., 2007; Davis et al., 2003). However, research also implies that sleep, stress, nutritional behaviors, and physical activity has such diverse and profound effects on the immune system that any benefits from a beta-glucan supplement seen in free-living, healthy persons, are likely to be insignificant (Beisel, 1996; Dinges et al., 1995; Cohen et al., 1991; Lac and Chamoux, 2003; Woods, 2005; Gleeson, 2007; Nieman, 2003; Nieman 2007). Previous research suggests that humans and mice have similar immune systems and should see similar effects with a β-glucan supplement (Dinges et al., 1995; Gleeson, 2007; Nieman, 2003; Nieman 2007). Along with this assertion is the theory of an immune ceiling from beneficial effects from proper amounts of sleep, stress, healthy nutritional behaviors, and healthy amounts of physical activity (Dinges et al., 1995; Nieman, 2003; Nieman 2007). The non-significant findings of the present study between the experimental and placebo groups agree with these theories.

Limitations

Although we aimed for socioeconomic diversity, our participants were volunteers and may not have been representative of cold-sufferers. The data collected only applies to healthy, free-living, college-aged males. Qualitative, self-reported survey data, may

76

have been biased. The present research did not control for lifestyle habits, dietary habits, or for any exposure to disease or infection.

CONCLUSION

The present research presents that a yeast β-glucan does not significantly decrease occurrence of symptoms of URTI in humans. However, the population of healthy, free-living, college-aged males tested in the present research may have an immune system with a maximum level of prevention of URTI. Thus, any effects that a supplement may have on the immune system may be masked by these levels. The limitations of the study may prevent any effect that yeast β-glucan has on the immune functioning of the subjects. It is recommended that future research on healthy, free-living subjects directs attention toward statistically controlling for dietary, sleep, exposure, stress, and physical activity habits.

REFERENCES

Barrett, B., K. Locken, R. Maberry, J. Schwamman, R. Brown, J. Bobula, and E.A. Stauffacher (2002). "The Wisconsin upper respiratory symptom survey (WURSS)." Journal of Family Practice **51**: 249-257.

Barrett, B., R. Brown, and M. Mundt (2008). "Comparison of anchor-based and distributional approaches in estimating important difference in common cold." Quality of Life Research **17**:75-85.

Barrett, B., R. Brown, M. Mundt, N. Safdar, L. Dye, R. Maberry, J. Alt (2005). "The Wisconsin upper respiratory symptom survey is responsive, reliable, and valid." Journal of clinical Epidemiology **58**: 609-617.

Barrett, B., S. Enrizzi, P. Andreoli, S. Barlow, Z. Zhang (2007). "Clinical Significance of Common Cold Treatment: Professionals' Opinions." <u>Wisconsin Medical Journal</u> **106**(8): 473-480.

Biesel, W.R. (1996). Nutrition and immune function: overview. <u>Journal of Nutrition</u> **126**: 2611S-2615S.

Brown, G.D. and S. Gordon (2003). "Fungal β-glucans and mammalian immunity." <u>Immunity</u> **19**: 311-315.

Brown, G.D. and S. Gordon (2005). "Immune recognition of fungal β-glucans." <u>Cellular Microbiology</u> **7**(4): 471-479.

Ceddia, M.A. and J.A. Woods (1999). "Exercise suppresses macrophage antigen presentation." <u>Journal of applied Physiology</u> **87**: 2253-2258.

Cohen, S., D.A.J. Tyrrell, and A.P. Smith (1991). "Psychological stress and susceptibility to the common cold." <u>New England Journal of Medicine</u> **325**: 606-612.

Davis, J.M., E.A. Murphy, A.S. Brown, M.D. Charmichael, A. Ghaffar, and E.P. Mayer (2003). "Effects of moderate exercise and oat β-glucan on innate immune function and susceptibility to respiratory infection." <u>American Journal of Physiology – Regulatory, Integrative, and Comparative Physiology</u> **286**: R366-R372.

Davis, J.M., E.A. Murphy, A.S. Brown, M.D. Charmichael, A. Ghaffar, and E.P. Mayer (2004). "Effects of oat β-glucan on innate immunity and infection after exercise stress." <u>Medicine and Science in Sports and Exercise</u> **36**(8): 1321-1327.

Davis, J.M., M.L/ Kohut, L.H. Colbert, D.A. Jackson, A. Ghaffar, and E.P. Mayer (1997). "Exercise, alveolar macrophage function, and susceptibility to respiratory infection." <u>Journal of Applied Physiology</u> **83**(5): 1461-1466.

Demir, G., H.O. Klein, N. Mandel-Molinas, N. Tuzuner (2007). "Beta glucan induces proliferation and activation of monocytes in peripheral blood of patients with advanced breast cancer." <u>International Immunology</u> **7**: 113-116.

Dinges, D.F., S.T. Douglas, S. Hamarman, L. Zaugg, and S. Kapoor (1995). Sleep deprivation and human immune function. <u>Advances in Neuroimmunology</u> **5**: 97-110.

Gleeson, M. (2007). "Immune function in sport and exercise." <u>Journal of Applied Physiology</u> **103**: 693-699.

Hunzeker, J., D.A. Padgett, P.A. Sheridan, F.S. Dhabhar, and J.F. Sheridan (2004). "Modulation of natural killer cell activity by restraint stress during an influenza A/PR8 infection in mice." <u>Brain, Behavior, and Immunity</u> **18**:526-535.

Jackson, G.G., H.F. Dowling, I.G. Spiesman, and A.V. Boand (1957). "Transmission of the common cold to volunteers under controlled conditions." <u>American Medical Association Archives of Internal Medicine</u> **101**: 267-278.

Jenkins, D.J.A., et al. (2002). Soluble fiber intake at a dose approved by the US Food and Drug Administration for cardiovascular disease assessed in a randomized controlled crossover trial. <u>American Journal of Clinical Nutrition</u> **75**: 834-839.

Lac, G. and A. Chamoux (2003). Elevated salivary cortisol levels as a result of sleep deprivation in a shift worker. <u>Occupational Medicine</u> **53**: 143-145.

Murphy, E.A., J.M. Davis, A.S. Brown, M.D. Charmichael, A. Ghaffar, and E.P. Mayer (2007). "Oat β-glucan effects on neutrophil respiratory burst activity following exercise." <u>Medicine and Science in Sports and Exercise</u> **39**(4): 639-644.

Murphy, E.A., J.M. Davis, et al. (2008). "Benefits of oat β-glucan on respiratory infection following exercise stress: role of lung macrophages." <u>American Journal of Physiology – Regulatory, Integrative, and Comparative Physiology</u> **294**: R1593-R1599.

Naumann, E., A.B. Van Rees, G. Onning, R. Oste, M. Wydra, and R.P. Mensink (2006). β-glucan incorporated into a fruit drink effectively lowers serum LDL-cholesterol concentrations. <u>American Journal of Clinical Nutrtion</u> **83**: 601-605.

Nicolosi, R., S.J. Bell, B.R. Bistrian, I. Greenberg, R.A. Forse, and G.L. Blackburn (1999). Plasma lipid changes after supplementation with ß-glucan fiber from yeast. <u>American Journal of Clinical Nutrition</u> **70**: 208-212.

Nieman, D.C. (2003). "Current Perspective on Exercise Immunology." <u>Current Sports Medicine Reports</u> **23**: 239-242.

Nieman, D.C. (2007). "Marathon training and immune function." <u>Sports Medicine</u> **37**(4-5): 412-415.

Nieman, D.C., D.A. Henson, et al. (2008). "β-glucan, immune function, and upper respiratory tract infections in athletes." <u>Medicine and Science in Sports and Exercise</u> **40**(8): 1463-1471.

Tsai, L., S. Li (2004). Sleep patterns in college students: gender and grade differences. <u>Journal of Psychosomatic Research</u> **56**: 231-237.

Vetvicka, V., B.P. Thornton, and G.D. Ross (1996). "Soluble β-glucan polysaccharide binding to the lectin site of neutrophil or natural killer cell complement receptor type 3 (CD11b/CD18) generates a primed state of the receptor capable of mediating cytotoxicity of iC3b-opsonized target cells." <u>Journal of Clinical Investigation</u> **98**(1): 50-61.

Willment, J.A., S. Gordon, and G.D. Brown (2001). "Characterization of the Human β-glucan receptor and its alternatively spliced isoforms." <u>Journal of Biological Chemistry</u> **276**(47): 43818-4382.

Woods, J.A. (2005). Physical activity, exercise, and immune function. <u>Brain, Behavior, and Immunity</u> **19**: 369-370.

Yun, C.H., A. Estrada, A. Van Kessel, B. Park, B. Laarveld (2003). "β-glucan, extracted from oat, enhances disease resistance against bacterial and parasitic infections." <u>FEMS Immunology and Medical Microbiology</u> **35**: 67-75.

Appendix I

PROJECT IN BRIEF: Twelve weeks of a daily beta-glucan supplement or placebo to determine the impact on cold and/or flu symptoms.

RESEARCHERS: Brent Ruby (Principal Investigator) x2117
John Cuddy x6108
Casey Gorham

The University of Montana
Montana Center for Work Physiology and Exercise Metabolism
32 Campus Drive
Missoula, MT 59812

Please read the following information carefully and feel free to ask questions. Sign the final page only when you are satisfied that all procedures and risks have been sufficiently explained to you.

A. REQUIREMENTS
This study requires that you meet the following criteria:

✴ You must be between the ages of 18-40 years of age
✴ You must attend a meeting for an explanation of the project and to receive the supplement

B. PURPOSE OF THE STUDY
This study is designed to determine the effects of a B-glucan supplement on immune function in college aged persons. β-glucan is a fiber-type complex (polysaccharide, a complex carbohydrate) that is found in various foods that contain baker's yeast, oat or barley fiber, or mushrooms. β-glucan can be added to other foods because the Food and Drug Administration considers it a component of normal foods.

C. TEST PROCEDURES

If you choose to participate in the study, you will be required to attend an informational meeting prior to the start of the project. The research team will discuss the study protocol, distribute supplement or placebo pills, and answer your questions. At the meeting, you will be assigned a subject identification number so that your confidentiality will be maintained. Also, you will be provided with supplement capsules for daily consumption. You have a 50/50 chance of receiving the β-glucan supplement or placebo capsule. You will be administered the supplement in a double blind fashion, meaning that the research team and you will not know whether you have the β-glucan or placebo capsule. If you receive the β-glucan supplement, you will be consuming 250 mg per day.

Data will be collected using online surveys via the website http://www.surveymonkey.com/. The surveys have secure sockets layer (SSL) so that your data is collected in a totally encrypted environment, providing for security and data integrity for communications over the internet. This is the highest form of secure data transmission currently available on the internet. The first time you log onto the computer

you will create a user account with your subject identification number and complete a questionnaire to collect lifestyle information: age, sex, marital status, physical activity patterns, high school sport participation, injuries, dieting, caffeine intake, tobacco use, multivitamin intake, current medication use, sleeping habits, stress levels, and nutritional habits. This questionnaire should not take more than 15 minutes. Additionally, you will complete an online survey every day that will take approximately 1 minute of your time. You will receive an email each day with a link to the survey, follow the link, and then complete the survey. This survey will ask you information about the previous 24 hours: pill consumption, hours of sleep, physical activity patterns, stress levels, and health status. If you have a problem completing this questionnaire you will be asked to call the principal investigator or study coordinator listed on the front page of this informed consent. A copy of these surveys are attached.

A. LOCATION
The study will take place at The University of Montana Center for Work Physiology and Exercise Metabolism in McGill Hall in Missoula, Montana.

B. BENEFITS OF PARTICIPATING IN THE STUDY
Once you sign this informed consent there is a 50/50 chance, just like the flip of a coin, that you will receive either the experimental or control pill (i.e., the one with or without β-glucan). The pill without β-glucan should offer no benefit. If you receive the β-glucan, studies have shown that you may have a reduction in cholesterol levels and an immune system benefit. However, there is no guarantee of this. If you complete the study, you will be awarded with a $25 gift certificate.

C. HEALTH RISKS
The risk associated with this study is minimal. The yeast derived multi-vitamin is Generally Recognized as Safe (GRAS) under the provisions of the US Food and Drug Administration 21CFR170.35. The probability of harm or discomfort anticipated in this research is no greater than those ordinarily encountered in daily life during your semester as a college student. You will be told about any new information that might change your decision to be in this study.

D. CONFIDENTIALITY
1. Your records will be kept private and will not be released without your consent except as required by law.
2. Only the researcher and his research assistants will have access to the files.
3. Your identity will be kept confidential.
4. If the results of this study are written in a scientific journal or presented at a scientific meeting, your name will not be used.
5. All data, identified only by an anonymous ID #, will be stored in our laboratory.
6. The signed consent form and information sheet will be stored in a locked office. Once the manuscript is completed, all hard copy data files will be destroyed.

E. COMPENSATION FOR INJURY
Although we believe that the risk of taking part in this study is minimal, the following liability statement is required in all University of Montana consent forms.

"In the event that you are injured as a result of this research you should individually seek appropriate medical treatment. If the injury is caused by negligence of the University or any of its employees, you may be entitled to reimbursement pursuant to the Comprehensive State Insurance Plan established by the Department of Administration under the authority of M.C.A., Title 2, Chapter 9. In the event of a claim for such injury, further information may be obtained from the University's Claim representative or University Legal Counsel,"

F. VOLUNTARY PARTICIPATION/WITHDRAWAL
You have the right to request that a test be stopped at any time.

1. Your decision to take part in this research study is entirely voluntary.
2. You may refuse to take part in or you may withdraw from the study at any time without penalty or loss of benefits to which you are normally entitled.
3. You may leave the study for any reason.

You may be asked to leave the study for any of the following reasons:
1. Failure to follow the study investigator's instructions.
2. A serious adverse reaction, which may require evaluation.
3. The study director/investigator thinks it is in the best interest of your health and welfare.
4. The study is terminated.

A. QUESTIONS
• You may wish to discuss this with others before you agree to take part in this study.
• If you have any questions about the research now or during the study contact: Brent Ruby (406) 243-2117.
• If you have any questions regarding your rights as a research subject, you may contact the Chairperson of the IRB, Judy Fredenberg, through the Research Office at The University of Montana at (406) 243-6670.

B. SUBJECT'S STATEMENT OF CONSENT
I have read the above description of this research study. I have been informed of the risks and benefits involved, and all my questions have been answered to my satisfaction. Furthermore, I have been assured that a member of the research team will also answer any future questions I may have. I voluntarily agree to take part. I understand I will receive a copy of this consent form.

_____
    Printed (Typed) Name of Subject

_____   _____
    Subject's Signature   Date

L. SUBJECT'S STATEMENT OF CONSENT TO BE PHOTOGRAPHED DURING DATA COLLECTION

I provide my consent to be photographed during periods of the data collection. I realize that these digital images may be used during presentation of the data at regional and national meetings.

_____   _____
    Subject's Signature   Date

Appendix II

Background Information

1. Background Survey

THIS SURVEY CONTAINS SELF-REPORTED ANSWERS THAT MUST ALL BE FILLED IN EVERYDAY. IF A QUESTION IS NOT FILLED OUT, A REMINDER TO FILL OUT THE ANSWER WILL APPEAR PRIOR TO SUBMITTING THE SURVEY. IF YOU HAVE NOT SELECTED AN ANSWER BECAUSE YOU FIND THE QUESTION OBJECTIONABLE, TOO PERSONAL, OR INAPPROPRIATE, PLEASE CLICK "EXIT THIS SURVEY" IN THE TOP RIGHT HAND CORNER AND CONTACT THE RESEARCH ADMINISTRATOR: john.cuddy@mso.umt.edu or 243-6108. IF YOU SIMPLY FORGOT TO FILL IN AN ANSWER PLEASE FILL IT OUT AND CLICK "DONE" AT THE BOTTOM OF SURVEY TO SUBMIT IT.

1. Enter your subject number.

2. Sex

○ Male

○ Female

3. Age

4. Marital Status

○ Single   ○ Partnered   ○ Married   ○ Separated   ○ Divorced   ○ Widowed

5. What are your living conditions?

○ Dorm

○ Sorority

○ Fraternity

○ House/apartment with roommates

○ House/apartment alone

○ With your family

Other (please specify)

6. How would you describe your physical activity level?

○ Predominantly Sedentary -- Not participating in physical activity on a regular basis (less than once a week)

○ Occasionally Active -- Participating in physical activity on an intermittent basis (once or twice a week)

○ Moderately Active -- Accumulating 30 minutes of moderate-intensity physical activity (equivalent to brisk walking, recreational swimming, or bicycling on some hills) on most if not all days of the week

○ Vigorously Active -- Participating in vigorous physical activity (running, swimming laps, bicycling up steep terrain) 3 to 5 days a week

Background Information

7. What high school sports did you participate in?

- [ ] None
- [ ] Football
- [ ] Cross Country
- [ ] Volleyball
- [ ] Soccer
- [ ] Wrestling
- [ ] Basketball

- [ ] Swimming
- [ ] Golf
- [ ] Baseball
- [ ] Softball
- [ ] Outdoor Track and Field
- [ ] Indoor Track and Field
- [ ] Ice Hockey

- [ ] Field Hockey
- [ ] Tennis
- [ ] Lacrosse
- [ ] Gymnastics
- [ ] Cheerleading
- [ ] Dance Team

Other (please specify)

_____

8. Do you have any current injuries that prevent you from participating in physical activity?

- ( ) Yes
- ( ) No

9. If so, what? If none, put N/A.

_____

10. Are you currently dieting?

- ( ) Yes
- ( ) No

11. Describe your caffeine intake

	Coffee (cups/day)	Tea (cups/day)	Cola (12 oz drinks/per day)
Sources	[▼][▼]	[▼][▼]	[▼][▼]

12. Do you currenty use tobacco?

- ( ) Yes
- ( ) No

13. If you are a tobacco user, do you smoke or chew?

- ( ) Smoke
- ( ) Chew/Dip
- ( ) Does not apply to me

14. What multivitamins do you currently take? If you don't take any, put N/A.

_____

Background Information

15. What medications do you currently take? If you don't take any, put N/A.

16. On average, how many hours of sleep do you get per night?

17. On a scale of 0-10, what is the overall level of stress in your life? (0 = NO STRESS, 10 = EXTREMELY STRESSED)

○ 0   ○ 1   ○ 2   ○ 3   ○ 4   ○ 5   ○ 6   ○ 7   ○ 8   ○ 9   ○ 10

18. Did you have a flu shot this season (last fall or this winter)?

○ Yes   ○ No

19. What allergies do you have?

☐ None   ☐ Dogs   ☐ Egg
☐ Pollen   ☐ Rabbits   ☐ Tree nut (walnuts, cashews, etc.)
☐ Mold   ☐ Feathers   ☐ Fish
☐ House dust   ☐ Bee stings   ☐ Shellfish
☐ Mites   ☐ Peanuts   ☐ Soy
☐ Cats   ☐ Milk   ☐ Wheat

Other (please specify)

20. Do you currently take allergy medications or receive allergy shots?

○ Yes   ○ No

21. If you do take allergy medications or receive shots, what medications do you use and how frequently do you use them? If this question does not apply to you, please type N/A.

Background Information

22. How often do you consume the following foods?

	Times/week
Oatmeal	[ ]
Cereal with oats	[ ]
Other food items with oats	[ ]
Barley	[ ]
Cereal with barley	[ ]
Other food items with barley	[ ]
Mushrooms	[ ]
Whole wheat bread	[ ]
Whole wheat pasta	[ ]
Other whole wheat foods	[ ]
Rye bread	[ ]
Other rye foods	[ ]

1. Daily Survey

THIS SURVEY CONTAINS SELF-REPORTED ANSWERS THAT MUST ALL BE FILLED IN EVERYDAY. IF A QUESTION IS NOT FILLED OUT, A REMINDER TO FILL OUT THE ANSWER WILL APPEAR PRIOR TO SUBMITTING THE SURVEY. IF YOU HAVE NOT SELECTED AN ANSWER BECAUSE YOU FIND THE QUESTION OBJECTIONABLE, TOO PERSONAL, OR INAPPROPRIATE, PLEASE CLICK "EXIT THIS SURVEY" IN THE TOP RIGHT HAND CORNER AND CONTACT THE RESEARCH ADMINISTRATOR: john.cuddy@mso.umt.edu or 243-6108. IF YOU SIMPLY FORGOT TO FILL IN AN ANSWER PLEASE FILL IT OUT AND CLICK "DONE" AT THE BOTTOM OF SURVEY TO SUBMIT IT.

1. Enter your subject number.

2. Did you take your supplement pill today?

- ○ Yes
- ○ No

3. How many hours of sleep did you get last night?

4. In the last 24 hours, how much time (mins) did you spend participating in aerobic exercise (walking, hiking, jogging, running, cycling, elliptical, rowing, etc.)?

5. In the last 24 hours, how much time did you spend participating in resistance (strength) training, ie lifting weights at the gym?

6. In the last 24 hours, how much time did you spend participating in organized sport activities (softball, football, volleyball, dodgeball, etc.)?

7. On a scale of 0-10, how stressed have you felt in the last 24 hours (0 = NO STRESS, 10 = EXTREMELY STRESSED)?

- ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

8. Have you been in contact with someone who currently has a cold?

- ○ No, I have not been in contact with anyone who has a cold
- ○ Yes, I live with that person
- ○ Yes, I hung out with that person
- ○ Yes, I had physical contact with that person
- ○ Yes, I was in close proximity to someone with a cold (such as sitting next to, work with, etc.)
- ○ Yes, other . . .

9. Please check the box for each of the following items.

	Not Sick	Very Mildly	-	Mildly	-	Moderately	-	Severely
	0	1	2	3	4	5	6	7
How sick do you feel today?	○	○	○	○	○	○	○	○

10. Please rate the average severity of your cold symptoms over the last 24 hours.

	Not Sick	Very Mildly	-	Mildly	-	Moderately	-	Severely
	0	1	2	3	4	5	6	7
Cough	○	○	○	○	○	○	○	○
Coughing stuff up	○	○	○	○	○	○	○	○
Cough interfering with sleep	○	○	○	○	○	○	○	○
Sore throat	○	○	○	○	○	○	○	○
Scratchy throat	○	○	○	○	○	○	○	○
Hoarseness	○	○	○	○	○	○	○	○
Runny nose	○	○	○	○	○	○	○	○
Plugged nose	○	○	○	○	○	○	○	○
Sneezing	○	○	○	○	○	○	○	○
Headache	○	○	○	○	○	○	○	○
Body aches	○	○	○	○	○	○	○	○
Feeling "run down"	○	○	○	○	○	○	○	○
Sweats	○	○	○	○	○	○	○	○
Chills	○	○	○	○	○	○	○	○
Feeling feverish	○	○	○	○	○	○	○	○
Feeling dizzy	○	○	○	○	○	○	○	○
Feeling tired	○	○	○	○	○	○	○	○
Irritability	○	○	○	○	○	○	○	○

11. Please rate the average severity of your cold symptoms over the last 24 hours.

	Not Sick	Very Mildly	-	Mildly	-	Moderately	-	Severely
	0	1	2	3	4	5	6	7
Sinus pain	○	○	○	○	○	○	○	○
Sinus pressure	○	○	○	○	○	○	○	○
Sinus drainage	○	○	○	○	○	○	○	○
Swollen glands	○	○	○	○	○	○	○	○
Plugged ears	○	○	○	○	○	○	○	○
Ear discomfort	○	○	○	○	○	○	○	○
Watery eyes	○	○	○	○	○	○	○	○
Eye discomfort	○	○	○	○	○	○	○	○
Head congestion	○	○	○	○	○	○	○	○
Chest congestion	○	○	○	○	○	○	○	○
Chest tightness	○	○	○	○	○	○	○	○
Heaviness in chest	○	○	○	○	○	○	○	○
Lack of energy	○	○	○	○	○	○	○	○
Loss of appetite	○	○	○	○	○	○	○	○

12. Over the last 24 hours, how much has your cold interfered with your ability to:

	Not Sick	Very Mildly	-	Mildly	-	Moderately	-	Severely
	0	1	2	3	4	5	6	7
Think clearly	○	○	○	○	○	○	○	○
Speak clearly	○	○	○	○	○	○	○	○
Sleep well	○	○	○	○	○	○	○	○
Breathe easily	○	○	○	○	○	○	○	○
Walk, climb stairs, exercise	○	○	○	○	○	○	○	○
Accomplish daily activities	○	○	○	○	○	○	○	○
Work outside the home	○	○	○	○	○	○	○	○
Work inside the home	○	○	○	○	○	○	○	○
Interact with others	○	○	○	○	○	○	○	○
Live your personal life	○	○	○	○	○	○	○	○

13. Compared to yesterday, I feel that my cold is . . .

	Very much better	Somewhat better	A little better	The same	A little worse	Somewhat worse	Very much worse
Select	○	○	○	○	○	○	○

14. Do you think your symptoms are a result of:

○ Allergies

○ Cold

○ Flu

○ I have no symptoms of illness

Other (please specify)