EFFECTS OF GROUND CINNAMON ON POSTPRANDIAL BLOOD GLUCOSE LEVELS BETWEEN OBESE AND NORMAL WEIGHT INDIVIDUALS

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ABSTRACT

THESIS: Effects of Ground Cinnamon on Postprandial Blood Glucose Levels between Obese and Normal Weight Individuals

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The purpose of this project was to determine the effects of 6 g of ground cinnamon added to farina (Cream of Wheat) cereal on blood glucose levels between obese and normal weight individuals. Thirty students, aged 19-30 years, were recruited to participate in this study. During study visits, participants were given one of two test meals (74 g of farina with and without 6 g of cinnamon) followed by seven blood glucose measurements over a two-hour period. A significant difference was seen in glycemic response between the two dietary conditions, but not between the two BMI groups (normal and obese). The two BMI groups were combined for analysis of dietary conditions. Ingestion of the cinnamon cereal resulted in significantly lower blood glucose responses at minutes 15, 30, 45 and 60 compared to the plain cereal. The results of this study confirm the positive glucose-lowering effects of cinnamon.
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Chapter 1 - Introduction

Obesity is rapidly becoming a major public health concern across the United States, with rising economical and medical costs paid by Medicare and Medicaid (O’Neil & Nicklas, 2007). Those individuals who are obese are predisposed to developing a number of chronic nutrition-related conditions, including hypertension, high cholesterol, heart disease, arthritis, cancer and, most importantly, type 2 diabetes (Dominiczak & Baynes, 2005). The body’s ability to metabolize glucose is largely influenced by body mass index (BMI), which suggests that individuals who have a higher BMI may have a lower efficiency of glucose metabolism. For this reason, dietary changes to achieve weight loss and improve lifestyle habits should be a primary focus when considering treatment and/or management strategies for obesity (Dominiczak & Baynes, 2005; Greenstone, 2007; O’Neil & Nicklas, 2007).

Cinnamon has been used for years as a spice or food additive in cooking, but just recently has become increasingly popular for its benefits in glucose metabolism (Preuss, Echard, Polansky, Anderson, 2006). It has been documented that the bioactive compound polyphenol type-A polymer is responsible, at least in part, for these benefits attributed to cinnamon (Anderson, 2008; Cao, Polansky, & Anderson, 2007). Research in both healthy individuals and those with type 2 diabetes has shown that cinnamon
enhances glucose transport and utilization in the body, ultimately leading to improved glucose metabolism (Anderson, 2008; Cao et al., 2007; Khan, Safdar, Khan, Khattar, & Anderson, 2003; Mang et al., 2006; Qin et al., 2004; Solomon & Blannin, 2007). Because it has been suggested that obese individuals with a higher BMI may have a lower efficiency to metabolize glucose, they may also experience greater improvements in blood glucose response after eating carbohydrates with cinnamon compared to individuals with a normal BMI.

**Problem Statement**

Recognition of obesity as an epidemic and a universal health threat to society has never been more apparent. Because obesity is a well known risk factor for many nutrition-related chronic diseases, dietary intervention strategies should be in the forefront of nutrition research. More importantly, with the close link of obesity and the development of type 2 diabetes, research looking at ways to improve glycemic control is essential.

**Rationale**

To date, there is no known research that has examined the effects of cinnamon on blood glucose levels between obese individuals (BMI ≥ 30) and those with a normal weight (BMI 18.5 – 24.9). Therefore, the purpose of this study was to determine the effects of 6 g of ground cinnamon added to farina (Cream of Wheat) cereal on blood glucose levels in both obese and normal weight individuals.
**Research Questions**

1) What is the difference in area under the curve (AUC) for glucose between the two dietary conditions (farina cereal with and without 6g of ground cinnamon)?

2) What is the difference in blood glucose levels at each measured time interval (e.g. 0, 15, 30, 45, 60, 90 and 120 min) between the two dietary conditions (farina cereal with and without 6g of ground cinnamon)?

3) What is the difference in overall blood glucose response between participants with normal and obese BMIs?

4) What is the difference in blood glucose levels at 0, 15, 30, 45, 60, 90 and 120 minutes between participants with normal and obese BMIs?

5) Is there an interaction between the two dietary conditions (farina cereal with and without 6g of ground cinnamon) and BMI groups (normal BMI and obese BMI)?

**Limitations**

The study had one main major limitation. Because the sample was a relatively homogeneous group of young, healthy adults, the results cannot be generalized to a larger, more diverse population.

**Assumptions**

This study had two key assumptions. First, it was assumed that study participants had fasted for at least eight hours prior to the testing period; there was no objective confirmation of the fasted state. In addition, it was also assumed that the study participants answered all survey questions truthfully.
Definitions

For the purpose of this study, the following definitions will be used:

1) Obesity – According to the American Diabetes Association (2010), obesity is “a condition in which a greater than normal amount of fat is in the body; more severe than overweight; having a body mass index of 30 or more”

2) Postprandial blood glucose levels – According to the American Diabetes Association (2010), postprandial blood glucose levels refer to “blood glucose levels 1-2 hours after a meal”

3) Fasting blood glucose levels – According to the American Diabetes Association (2010), fasting blood glucose levels refer to “blood glucose levels after the person has not eaten for 8 to 12 hours (usually overnight)”

4) Hyperglycemia – According to the American Diabetes Association (2010), hyperglycemia refers to “excessive blood glucose. Fasting hyperglycemia is blood glucose above a desirable level after a person has fasted for at least 8 hours. Postprandial hyperglycemia is blood glucose above a desirable level 1 to 2 hours after a person has eaten”

5) Hypoglycemia – According to the American Diabetes Association (2010), hypoglycemia refers to “a condition that occurs when one's blood glucose is lower than normal, usually less than 70 mg/dL”

6) Beta cells – According to the American Diabetes Association (2010), beta cells are “cells that makes insulin. Beta cells are located in the islets of the pancreas”
7) Body mass index (BMI) – According to the American Diabetes Association (2010), body mass index (BMI) is “a measure used to evaluate body weight relative to a person's height. BMI is used to find out if a person is underweight, normal weight, overweight or obese”

8) Insulin resistance – According to the American Diabetes Association (2010), insulin resistance refers to “the body's inability to respond to and use the insulin it produces”

9) Glycogen Synthase (GS) – glycogen synthase (GS) refers to the reregulatory enzyme in glycogen synthesis (Dominiczak & Baynes, 2005)

10) GLUT-4 transport proteins – insulin-dependent glucose transporter proteins which allow glucose to enter into the cell (Dominiczak & Baynes, 2005)

**Summary**

As the obesity epidemic continues to rise, new treatment and management strategies are essential to help lower complications and medical costs. In the forefront of those new strategies should include improvements in dietary and lifestyle habits to achieve a normal and/or desirable weight. Because obesity has been linked with insulin resistance and type 2 diabetes, strategies to help maintain or achieve normal blood glucose levels should be researched. For this reason cinnamon has recently been explored as a possible alternative dietary therapy, because of its proposed glucose-lowering and insulin-enhancing effects.
Chapter 2 - Literature Review

Obesity

Obesity is rapidly becoming a major public health concern across the United States. Although obesity was considered a potential public health problem as early as 1948, it was not until 1997 that greater consideration was given to the escalating health and economical burden of the disease (James, 2008). The economical costs of obesity have now risen to over 117 billion dollars, with a majority of those costs paid by Medicare and Medicaid (O’Neil & Nicklas, 2007). Governmental agencies, including The World Health Organization (WHO), now recognize obesity as a major critical health concern, with detrimental health, social, and economic consequences which must be addressed through global health policies (James, 2008).

**Prevalence and trends.** Over the past three decades, prevalence rates for obesity have dramatically increased; over 65 percent of the U.S. adult population is considered to be overweight and/or obese. It is estimated that another 1 percent of Americans will be diagnosed as overweight and/or obese each year (Flegal, Carroll, Ogden, & Curtin, 2010; Greenstone, 2007; Kushner, 2003a; O’Neil & Nicklas, 2007; Virgil Brown, Fujioka, Peter, Wilson, & Kristina, 2009). Obesity accounts for about 31.3 percent of men and 32.2 percent of women in America as defined by a body mass index (BMI) of \( \geq 30 \).
In adults, body mass index (BMI) is used to diagnose the obese state of an individual, and can be classified into 3 categories - class 1/mild obesity (BMI 30.0-34.9), class 2/moderate obesity (BMI 35.0-39.9) and class 3/severe obesity (BMI ≥40) (Kushner, 2003b).

**Risk factors and complications.** Those individuals who are obese, especially those with severe obesity, are predisposed to developing a number of chronic nutrition-related conditions including hypertension, high cholesterol, heart disease, arthritis, cancer and, most importantly, type 2 diabetes (Dominiczak & Baynes, 2005; Greenstone, 2007; O’Neil & Nicklas, 2007). Large population studies have confirmed that there is a positive relationship between excess weight from obesity and insulin resistance, suggesting that individuals who have a higher BMI have a lower efficiency of glucose metabolism due to increased body fat (Dominiczak & Baynes, 2005; Ferroni, Basili, Falco, & Davi, 2004; Virgil Brown et al., 2009). In fact, about 80 percent of the newly diagnosed cases of type 2 diabetes are associated with obesity, because the body’s ability to metabolize glucose is largely influenced by body fat (Dominiczak & Baynes, 2005).

Another major concern associated with obesity is the increased risk of premature death. Obesity is identified as one of the leading causes of preventable premature deaths in the U.S., accounting for approximately 300,000 deaths per year (Flegal et al., 2010; Kushner, 2003a; Tyler, Johnston, & Foreyt, 2007). Due to this and the many other contributing factors, the epidemic of obesity is one of the fastest growing public health threats in need of prevention and management strategies.

**Prevention, treatment and management strategies.** Large-scale prevention efforts have been implemented to help manage and treat obesity, but it is clear that more
strategies are needed to address the health risks and resulting medical costs to those who currently suffer from the disease (Tyler et al., 2007; Virgil Brown et al., 2009). Treatment and management strategies should include modest weight loss through calorie restrictions, increased physical activity, behavioral health counseling, and pharmacologic treatments (Virgil Brown et al., 2009). Weight loss seems to be a significant factor in helping reduce the severity and morbid complications associated with this disease. Even a 5-10 percent weight loss is associated with improved lipid profiles, blood pressure, glycemic response and insulin sensitivity (O’Neil & Nicklas, 2007). Because over 65 percent of the adult population is considered overweight or obese, and over 80 percent of the newly diagnosed cases of type 2 diabetes are associated with obesity, dietary changes to achieve weight loss and improve glycemic control should be a primary focus when considering treatment and/or management strategies (James, 2008; Greenstone, 2007).

**Glycemic Response**

**Glycemic response and carbohydrate intake.** The term glycemic response describes an individual’s blood glucose response to the amount and type of carbohydrate consumed. The glycemic response is measured by the glycemic index (GI) (OSU: Glycemic Index and Glycemic Load, 2009). Carbohydrates are almost always metabolized directly into glucose, and supply the largest amount of glucose (energy) to the body at any given time (Champe, Harvey, & Ferrier, 2005). Because carbohydrates metabolize into glucose, they raise the blood glucose levels more quickly than either protein or fat. Therefore, control over the rate at which blood glucose levels rise and/or fall between meals is largely dependent upon the consistent and controlled amount of carbohydrate consumed at those meals/snacks.
Glycemic index and area under the curve (AUC). In order to determine glycemic index, 50 g of carbohydrate from the food being tested is compared with the effect of 50 g of carbohydrate from white bread (control food) (Monro, 2002). Blood glucose levels are taken before (pre-prandial) the 50g dose, usually after an 8 hour fast, and then at timed intervals (e.g. 0, 15, 30, 45, 60, 90 and 120 min) over a two-hour period (postprandial blood glucose). The changes in blood glucose levels over that two-hour period are plotted as a curve, also known as the area under the curve (AUC). The glycemic index is then calculated by dividing area under the glucose curve after the test food is eaten by the area after the control food is eaten (OSU: Glycemic index and glycemic load, 2009).

Classification of food items. Food items are classified as either high-glycemic index (high GI) foods or low-glycemic index (low GI) foods based on how quickly the blood glucose rises in response to consumption of that food. High GI foods are generally refined and processed carbohydrates/sugars (e.g. white bread, white rice, baked potato, candy, orange juice) that are quickly digested, and raise blood glucose levels rapidly. In comparison, low GI foods, typically complex carbohydrates, (i.e. nuts, legumes, oatmeal, bran, apple, barley, wheat) contain more fiber, are digested more slowly, and increase blood glucose levels at a steadier rate (OSU: Glycemic index and glycemic load, 2009). Furthermore, these complex carbohydrates are generally recommended as a dietary strategy to help lower postprandial blood glucose levels and enhance blood glucose regulation (Nilsson, Ostman, Granfeldt, & Björck, 2008).
Normal Glucose Metabolism

**Hormones.** Blood glucose levels in the body are controlled mainly by the endocrine hormones insulin and glucagon that are released from the pancreas. When blood glucose levels drop too low, the pancreas releases glucagon, which then stimulates glycogen, stored glucose in the liver, to be broken down. Glycogen breakdown releases glucose into the blood stream to raise blood glucose levels (Dominiczak & Baynes, 2005). Conversely, when blood glucose levels are high, insulin is secreted. The main function of insulin is to lower blood glucose levels, but it can also influence protein and fat metabolism.

**Insulin production.** Insulin is a hormone that decreases blood glucose through a variety of mechanisms which are often tissue specific. After a meal is consumed, the increase in plasma glucose stimulates the secretion of the anabolic hormone insulin, which is produced from the beta cells of the pancreas that are located on the islets of Langerhans (Champe et al., 2005). Insulin decreases plasma glucose levels by increasing glucose uptake for energy metabolism in the liver, muscle, and adipose tissues; increasing glycogen synthesis in the liver and muscle; increasing fatty acid and triglyceride production in the liver and storage of triglycerides in adipose tissue (Dominiczak & Baynes, 2005).

**Glucose entry into the cell.** Glucose from the meal is absorbed through the gut and transported to the cells of the liver, muscle and adipose tissues. Glucose entry into the cells is mediated by insulin-independent or insulin-dependent glucose transport proteins, also known as GLUTs (Champe et al., 2005; Dominiczak & Baynes, 2005). The glucose transport protein GLUT-2, located in the liver tissue, is insulin-independent and
does not require insulin to transport glucose into the cell. The glucose transport protein, GLUT-4, located in the skeletal muscle and adipocytes of the adipose tissue require insulin to transport glucose into the cell (Champe et al., 2005; Dominiczak & Baynes, 2005). After insulin is secreted, it binds and activates the insulin receptor located on the outer surface of the cell. The activated insulin receptor promotes recruitment of insulin-sensitive glucose transport proteins from the intracellular vesicle pool to the cell membrane in order to bring glucose into the cell (Champe et al., 2005; Dominiczak & Baynes, 2005). As insulin levels decrease and blood glucose levels are reduced, the glucose transport proteins move from the cell membrane to an intracellular storage organelle, called an endosome, to be reused (Champe et al., 2005; Dominiczak & Baynes, 2005).

**Abnormal Glucose Metabolism, Insulin Resistance and Obesity**

**Abnormal glucose metabolism and obesity.** In abnormal glucose metabolism, insulin is either not secreted properly by the pancreas (hyposecretion of insulin) or not used properly by the body’s insulin-dependent muscle or adipose tissues (insulin resistance). It has been well documented that insulin resistance is one of the major contributing factors in the development of abnormal glucose metabolism in obese individuals and one of the major risk factors in the development of type 2 diabetes (Dominiczak & Baynes, 2005; Garvey, Huecksteadt, Matthael, & Olefsky, 1988; Kahn & Flier, 2000; Surampudi, John-Kalarickal, & Fonseca, 2009). Evidence of insulin resistance in obesity is seen in both the skeletal muscle and adipose tissue, but the majority of the insulin resistance manifests in the adipose tissue.
**Mechanism of action.** Mechanisms involved in the development of insulin resistance in obesity include: decreased number of insulin receptors (IR), decreased number of insulin-dependent GLUT-4 glucose transport proteins to facilitate the entry of glucose into the tissues, impairment of insulin signaling of the target tissues, and dephosphorylation (deactivation) of insulin signaling pathways (Dominiczak & Baynes, 2005; Huether & McCance, 2000; Kahn, Hull, & Utzschneider, 2006; Roussel, Hininger, Benaraba, Ziegenfuss, & Anderson, 2009).

Another proposed reason influencing the development of insulin resistance in obesity is the increased level of oxidative stress and damaging free radicals resulting from adiposity (Roussel et al., 2009; Shoelson, Herrerro, & Naaz, 2007). This increased level of oxidative stress causes impairment in distribution of insulin receptors and a reduced level of insulin-dependent GLUT-4 transport proteins and, ultimately, further insulin resistance (Roussel et al., 2009).

**Insulin resistance and the development of type 2 diabetes.** An increased level of insulin resistance decreases the ability of the cells in the insulin-regulated tissues to efficiently take up glucose, resulting in a buildup of glucose in the blood. In order to compensate for the build-up of glucose, the pancreas produces more insulin to try and lower blood glucose levels. However, the pancreas has a limited amount of insulin that can be produced at one time, and at some point reaches its maximal production level. Over time, this lack of additional insulin production, combined with increased insulin resistance, prevents glucose from entering into the insulin-dependent tissues; in some cases this subsequently leads to impaired glucose tolerance (IGT) and, further, type 2 diabetes (Dominiczak & Baynes, 2005).
Introduction to Cinnamon

Cinnamon is commonly thought of as a spice or food additive used for added taste and flavoring in cooking, but more recently recognized for its pharmalogical benefits in glucose metabolism (Preuss, Echard, Polansky, & Anderson, R.A. 2006). Cinnamon is sourced from dried bark of the _Cinnamomum_ species of the wild evergreen tree. Generally cinnamon comes from China, Indonesia and/or Sri Lanka (Barceloux, 2009). There are two varieties of cinnamon - _Cinnamomum Zeylanicum_ (Ceylon cinnamon) from Sri Lanka and _Cinnamomum cassia_ (Cassia “Chinese” Cinnamon) from either China or Indonesia (Barceloux, 2009; Encyclopedia of spices, 2003). For medicinal and culinary purposes, cinnamon can be found in “quill” tube form, ground form or aqueous form. Previous studies have used both ground and aqueous forms of cinnamon to demonstrate its health benefits. It appears that no matter which form is consumed, similar glucose-lowering and insulin-potentiating properties are seen (Hlebowicz, Darwiche, Bjorgell, & Almer, 2007; Hlebowicz et al., 2009; Mang et al., 2006, Solomon & Blannin, 2007; Solomon & Blannin, 2009).

**Enhancing glucose metabolism.** Cinnamon has been associated with glucose-lowering and insulin-potentiating properties and may help prevent progression of insulin resistance often seen in obesity (Hlebowicz et al., 2007; Kahn, Hull, & Utzschneider, 2006; Shoelson, Herrlro, & Naaz, 2007). The biologically active compound, water-soluble polyphenol type-A polymer, has been isolated from cinnamon and shown to potentiate insulin’s action in vitro (Anderson et al., 2004; Hlebowicz et al., 2007). This polyphenol is the proposed bioactive compound in cinnamon which positively affects glucose and insulin function (Anderson et al., 2004).
Cinnamon polyphenols (CP) influence glucose metabolism within the cell through a variety of mechanisms (Figure 1). These include: 1) increased autophosphorylation of the beta protein of the insulin receptor, 2) decreased phosphatase activity 3) decreased glycogen synthase kinase -3 beta activities, and 4) increased number of GLUT-4 transport proteins. Autophosphorylation of the beta protein increases activation of intracellular pathways that result in insulin’s biological effects (Cao, Polansky, & Anderson, 2007). This includes movement of GLUT-4 proteins to the outer surface of the cell, ultimately producing an increase in glucose uptake (Cao et al., 2007). In general, phosphatase takes an active protein and de-activates or de-phosphorylates it. In glucose metabolism, the decrease of phosphatase activity increases activation of the insulin receptor beta protein; this also increases glucose uptake by the cell (Cao et al., 2007). Glycogen synthase kinase-3 beta (GSK3B) is responsible for inactivating glycogen synthase (GS), the regulatory enzyme in glycogen synthesis. CP decreases GSK3B activity; this increases activity of GS and promotes glycogen accumulation (Anderson, 2008; Cao et al., 2007). The overall effects of these actions are increased glucose uptake and increased glycogen synthesis, which leads to improved glucose transport and utilization in the body (Anderson, 2008; Cao et al., 2007).
Figure 1

A Model of Actions of Cinnamon Polyphenol (Anderson, 2008; Cao et al., 2007)

A model of actions of cinnamon polyphenols (CP) in the insulin signal transduction pathway leading to beneficial effects in subjects with glucose intolerance or type 2 diabetes: (1) CP activate insulin receptors (IR) by increasing their tyrosine phosphorylation activity and by decreasing phosphatase activity that inactivates the receptor; (2) CP increase the amount of insulin receptor-β and GLUT4 proteins; (3) CP increase glycogen synthase activity and glycogen accumulation; (4) CP decrease glycogen synthetase (GS) kinase-3 β (GSK3β) activity; (5) CP increase the amount of tristetraprolin (TTP) protein; (6) CP may increase the activity of TTP by decreasing its phosphorylation through inhibition of GSK3β activity; IRS, insulin receptor substrate; PI3K, 1-phosphatidylinositol 3-kinase; PIP2, phosphatidylinositol 4,5-bisphosphate; PIP3, phosphatidylinositol 3,4,5-trisphosphate; PTP-1, protein tyrosine phosphatase-1; PDK1, phosphatidylinositol-dependent protein kinase 1; FAT, fat; G-6-P, glucose 6-phosphate; PKB, protein kinase B; UDPG, uridine diphosphoglucose; GM-CSF, granulocyte–macrophage colony-stimulating factor; Cox2, cyclooxygenase-2; VEGF, vascular endothelial growth factor; −, negative effect; +, positive effect. (From Cao et al.(43))
**Antioxidant benefits.** In addition to improving cellular glucose metabolism, cinnamon may provide additional benefits through its antioxidant qualities and ability to reduce oxidative stress (Anderson et al., 2004). Cinnamon is rich in polyphenols, flavonoids and phytochemicals; all are naturally occurring antioxidants which help to combat free radicals in the body (Anderson et al., 2004). Research has shown that inclusion of this spice into the diet may have the ability to reduce oxidative stress in those individuals who are obese and showing signs of insulin resistance (Roussel et al., 2009). This may help to further explain cinnamons insulin potentiating qualities, and possibly its ability to reduce insulin resistance and increase glucose metabolism.

**Research in healthy individuals.** Previous short term studies in healthy subjects have proven that inclusion of cinnamon into the diet, either as ground or as its aqueous equivalent, demonstrates the ability to improve glycemic response and insulin sensitivity. A majority of these studies have looked at immediate benefits of cinnamon; however, one study was completed with the intent to look at both immediate and lasting effects 12 hours after consumption (Solomon & Blannin, 2007). In this study, participants were supplemented with 5 g placebo capsules or 5 g cinnamon capsules just prior to a two-hour oral glucose tolerance test (OGTT), or 5 g of cinnamon capsules 12 hours before a the 2 hour OGTT. Results from this study showed that cinnamon ingestion significantly reduced total plasma glucose responses (AUC) as well as significantly improved insulin sensitivity. These effects appeared to be sustained for 12 hours after ingestion of the cinnamon supplement. The researchers concluded that cinnamon spice supplementation would be a useful tool in improving glycemic response and insulin sensitivity.
Solomon & Blannin (2009) then completed a longer term study to assess whether these benefits seen in the previous study would be sustained for a longer period of time. In this study, subjects were asked to undergo two 14 day interventions of either cinnamon or placebo supplementation (3 g per day) with a two week washout period. Oral glucose tolerance tests (OGTT) were conducted on days 0, 1, 14, 16, 18, and 20. The researchers found that cinnamon ingestion reduced glucose response, insulin response and improved insulin sensitivity on day 14. However, the positive effects of cinnamon were lost once the cinnamon ingestion subsided. The researchers concluded that cinnamon may improve glucose response and insulin sensitivity in the short term, but effects were quickly reversed.

Another short term study conducted by Hlebowicz et al. (2007), observed cinnamon’s effects on healthy subjects after ingestion of rice pudding either with or without 6 g cinnamon. Results showed that ingestion of 48 g of carbohydrate in the form of rice pudding with 6 g of cinnamon resulted in a significantly lower blood glucose at individual postprandial time points and in area under the curve (AUCs) (0-30, 0-45, 0-60, 0-90, and 0-120 minutes) in the rice pudding with cinnamon compared to the reference meal. These differences in blood glucose between the rice pudding with and without cinnamon ranged from 45 percent (14 versus 31 mmol/L, respectively) to 54 percent (75 versus 139 mmol/L, respectively). This study concluded that inclusion of 6 g of cinnamon into the diet lowers postprandial glucose response.

A comparable study was conducted two years later, looking at the immediate effects of 1 and 3 g cinnamon in rice pudding. Hlebowicz et al. (2009) found that the addition of 1 and 3 g cinnamon in rice pudding had no significant effect on blood glucose
response, but the addition of 3 g significantly reduced postprandial serum insulin secretion. These results suggest that there is a relationship between the amount of cinnamon consumed and the amount of insulin secreted, and that a minimal dosage of 3 g cinnamon is needed to see significant results.

**Summary**

Overall, it appears that consumption of 3-6 g cinnamon significantly reduces postprandial blood glucose response and increases insulin sensitivity among a healthy population. However, to date, no known research has been done when comparing the effects of cinnamon in individuals with normal and obese BMIs. Because obesity is a well known risk factor and cause of type 2 diabetes, additional research is needed to assess cinnamons insulin potentiating qualities and abilities to improve glucose utilization and transport in an obese state where insulin resistance is present.
Chapter 3 – Methods

Study Design

This study used a randomized, controlled, repeated measures design.

Recruitment

Healthy young adults were recruited from college classes within the Family and Consumer Sciences Department at Ball State University. Information presented to the class during the recruitment session included inclusion criteria, incentive to participants, condensed information about participation and contact information for the researcher. Interested individuals were asked to contact the researcher within two weeks of the recruitment date if interested in participation. As an incentive, a small amount of extra credit (5-10 pts) was offered to study participants. Availability of extra credit was dependent upon the preference of the professor for each class. In those classes where extra credit was offered, students were given an alternative extra credit opportunity if they were not eligible or chose not to participate in the study. The alternative extra credit opportunity required students to come onto campus on a Saturday from 12-5 pm to watch nutrition-related videos and write a short paper related to the videos. As an additional incentive, all study participants were offered a dietary food frequency questionnaire (FFQ) and follow-up consultation with a dietitian.
Sample

Thirty college students (15 normal BMI and 15 obese BMI), aged 19-30 years, were recruited. In order to concentrate subjects in the categories of normal weight and obese, only students with BMIs of 18.5-24.9 (normal weight) and ≥30 (obese) were included. Any individuals with a known medical condition which would affect blood glucose levels (i.e. type 1 or type 2 diabetes, acromegaly, Cushing syndrome, impaired fasting glucose, hyperthyroidism, pancreatic cancer, pancreatitis, pheochromocytoma, hypopituitarism, hypothyroidism) or a known allergy to wheat or cinnamon were excluded. Individuals were also excluded if they had any problem with giving blood samples via finger prick analysis or if they were pregnant.

Protocol

This study took place in the Nutrition Assessment Lab on Ball State University’s campus in Muncie, IN. Interested individuals were asked to meet with the researcher for an initial 10-15 minute meeting to sign an informed consent document, complete a prescreening form, and to answer questions about the study (Appendix A, B, C). At the same initial meeting, study participants were asked to complete a survey about demographics, physical activity, family history of type 2 diabetes, personal history of hypertension, and any known allergy to wheat or cinnamon (Appendix, D). Results of this survey were used to calculate each individual’s risk level (low, increased, or high) for developing diabetes, as defined by the American Diabetes Association Diabetes Risk Test (American Diabetes Association, 2010; Diabetes Care, 2008). Because the minimum age of this risk test was 20 years, risk levels were not determined for those study participants under the age of 20. The individual’s height and weight was also obtained the initial
meeting for the purpose of determining BMI (body mass index) for eligibility. No shoes, socks or coats were worn when assessing height and weight. A Seca brand portable stadiometer (Seca Corporation, Hanover, MD) was used to measure height, and a Tanita Body Composition scale (Tanita Corp. of America, Arlington Heights, IL) was used to obtain weight. Subjects were excluded from the study after the initial meeting if they did not meet the inclusion criteria. Participation in the study included two visits, at least seven days apart. Subjects were assigned two testing dates at the initial meeting and given general instructions for the day of testing. Subjects were asked to fast for at least eight hours prior to both study visits, and maintain their typical diet, lifestyle habits and physical activity schedule throughout the study. Up to four study participants could be scheduled on each test day.

During each visit, participants were given one of two test meals in random order followed by seven blood glucose measurements, over a two-hour period. The dietary conditions were as follows: plain cereal (74 g of farina), and cinnamon cereal (74 g farina with 6 g of ground cinnamon). Both dietary conditions contained 50 g of carbohydrate from instant Cream of Wheat (farina). The test meals were pre-weighted and pre-packaged into plastic bags prior to the start of the study. The cereal was prepared each morning of the test day 45 minutes prior to participant consumption according to standard directions on the Cream of Wheat package. Participants were allowed to use up to one packet (1 g) of sucralose (Splenda) sweetener in their cereal and consume up to 2 cups (16 oz/480 ml) of water during the study period if desired. Participants were required to consume their cereal within 15 minutes. If the study participant did not finish the cereal within the 15 minute time period, he or she was excused and given the opportunity to
come back again for another testing session or to participate in the alternative extra credit activity. Trained research assistants were used to assist with data collection. For convenience purposes, finger prick capillary analysis was used to assess blood glucose levels. Blood samples were taken before each meal and then at 15, 30, 45, 60, 90 and 120 minutes. Participants remained seated and sedentary during the two-hour study period, with the exception of using the restroom. Participants were allowed to complete the food frequency questionnaire, work on homework, listen to music or watch a movie during the two-hour period, as long as they remained seated.

**Data Entry**

All data were maintained as confidential and no identifying information appeared in any presentation of the data. Once the informed consent documents were signed, prior to completion of the pre-screening form, each study participant was assigned a unique identifier. This unique identifier was used for all study related forms, including screening forms and data collection forms, to maintain anonymity. All data entered and collected were stored under the study participant’s unique identifier number, not name. The key/master list containing participants’ names and identifier numbers was stored in a locked file cabinet. The de-identified data collected from the study, were entered into an Excel spreadsheet and used for statistical analysis.

**Statistical Analysis**

A power analysis was performed to determine sample size. With a type 1 error (alpha) of 5 percent and a type 2 error (beta) of 20 percent, an initial sample size of 13-15 subjects, with an allowance for a 5-10 percent dropout rate, was determined sufficient to detect differences in glycemic response if present.
Diabetes risk test was used to assess the risk of each study participant (“American Diabetes Association,” 2010). Mann-Whitney-U test was used to determine significant differences in risk level between the two BMI groups. T-tests were used to assess continuous variables between the two BMI groups. The areas under the curve (AUC) for each subject were measured for blood glucose response using Wolever’s method (Wolever, Jenkins, Jenkins, & Josse, 1991). The AUC was calculated above zero. Three way ANOVA repeated measures analysis was used to evaluate glycemic response for both group effect and dietary condition effect. The values were reported as means ± standard deviations (SDs). Variations in distribution of glycemic response were evaluated using Mauchley’s test of sphericity, with adjustments made as needed using Greenhouse-Geisser correction. Paired T-tests were used to assess glycemic response to dietary conditions after combining BMI groups. All statistical calculations were performed with Statistical Package for the Social Sciences (SPSS) for Windows software (version 17.0; SPSS Institute, Chicago, IL). Statistical significance was set at P ≤ 0.05.

Institutional Review Board Consent

Prior to the start of the study, Ball State University Institutional Review Board (IRB) approval (expedited review) was obtained to ensure compliance of all ethical issues and regulations for protection of human subjects (Appendix E). The researcher completed the National Institute of Health (NIH) tutorial (Appendix F). The research assistants completed Collaborative Institutional Training Initiative (CITI) tutorial. Following data collection and analysis, the final IRB competition form was submitted and approved (Appendix G).
Chapter 4 - Results

Subjects

Thirty seven men and women, age 18-30 yrs, were recruited to participate in this study. A total of seven individuals did not complete the study (five with normal BMI and two with obese BMI); five individuals could not finish the cereal in the allotted time, one individual did not report for testing, and one individual left the study due to personal reasons. Table 1 describes characteristics of the 30 (6 men and 24 women) subjects who completed all study requirements; there were 15 individuals with a normal BMI (age: 21.00 ± 2.45, BMI: 21.13 ± 1.06) and 15 individuals with an obese BMI (age: 22.13 ± 2.39, BMI: 33.07 ± 4.59). The majority of the study population (n = 28, 93%) was Caucasian (n = 24, 80%). Diabetes risk levels were assessed for 23 participants aged 20 or older (normal BMI (n = 10) and obese BMI (n = 13)). Results determined that all individuals in the normal BMI group were at low risk (n = 10). Individuals in the obese BMI group were at either low (n = 7) or increased risk (n = 6). Results also showed that the obese BMI group had a significantly increased diabetes risk level compared to the normal BMI group (p = .015).
Table 1

*Characteristics of the Study Population*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal BMI (n = 15)</th>
<th>Obese BMI (n = 15)</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject Age (yrs)</td>
<td>21.0 ± 2.5</td>
<td>22.1 ± 2.4</td>
<td>-1.28</td>
<td>.210</td>
</tr>
<tr>
<td>Wt (kg)</td>
<td>60.3 ± 7.0</td>
<td>91.0 ± 13.3</td>
<td>-7.91</td>
<td>.000</td>
</tr>
<tr>
<td>Ht (cm)</td>
<td>168.1 ± 7.6</td>
<td>165.9 ± 6.2</td>
<td>.87</td>
<td>.392</td>
</tr>
<tr>
<td>BMI</td>
<td>21.1 ± 1.1</td>
<td>33.1 ± 4.6</td>
<td>-9.81</td>
<td>.000</td>
</tr>
</tbody>
</table>

Data are means ± standard deviation (SD)
Glycemic Response - Area under the Curve (AUC)

Results indicated that there was a significant difference in area under the curve (AUC) between the two dietary conditions (cinnamon cereal mean 171.44 ± 13.5 unit of measure, plain cereal mean 224.27 ± 13.5 unit of measure) (p =.008). However, no significant difference in AUC for glucose was found between the two BMI groups (p = .605). There was no interaction between dietary conditions and BMI group (p =.528).

Glycemic Response – Repeated Measures Analysis

Results of a repeated measures analysis also found a significant difference in glycemic response between the two dietary conditions (cinnamon cereal and plain cereal) (p =.002), but no significant differences in glycemic response between the two BMI groups (p =.586) (Figure 2). For this reason, BMI groups were combined for analysis of dietary conditions at individual time points.

Combined BMI Group Analysis of Dietary Conditions at Individual Time Points

Figure 3 and Table 2 describe glycemic response to the two dietary conditions among all study participants. There was a statistically significant interaction between dietary condition and time (p ≤ .001) on postprandial blood glucose response. Specifically, ingestion of the cinnamon cereal resulted in significantly lower blood glucose responses at 15 min (p = .001), 30 min (p = .000), 45 min (p = .000) and 60 min (p = .001) compared to the plain cereal. It should also be noted that blood glucose response in the two dietary conditions were similar at 90 minutes (p = .053), but at 120 minutes the blood glucose response in the plain cereal was significantly lower than in the cinnamon cereal (p = .000).
Figure 2

Glycemic Responses to the Dietary Conditions in Normal and Obese Subjects

Data are means ± SD
Figure 3

*Glycemic Responses to the Dietary Conditions in All Subjects*

![Graph showing glycemic responses to dietary conditions](image)

Data are means ± SD. * (p = .001) ** (p = .000)
Table 2

*Postprandial Blood Glucose Responses to the Dietary Conditions in All Subjects*

<table>
<thead>
<tr>
<th>Time</th>
<th>Plain Cereal</th>
<th>Cinnamon Cereal</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minute 0</td>
<td>4.79 ± .71</td>
<td>4.86 ± .69</td>
<td>.63</td>
<td>.535</td>
</tr>
<tr>
<td>Minute 15</td>
<td>6.07 ± .84</td>
<td>5.47 ± .73</td>
<td>-3.65</td>
<td>.001</td>
</tr>
<tr>
<td>Minute 30</td>
<td>7.85 ± .85</td>
<td>6.75 ± 1.07</td>
<td>-5.34</td>
<td>.000</td>
</tr>
<tr>
<td>Minute 45</td>
<td>8.24 ± 1.43</td>
<td>6.77 ± 1.07</td>
<td>-6.60</td>
<td>.000</td>
</tr>
<tr>
<td>Minute 60</td>
<td>7.69 ± 1.86</td>
<td>6.68 ± 1.24</td>
<td>-3.51</td>
<td>.001</td>
</tr>
<tr>
<td>Minute 90</td>
<td>6.03 ± 1.32</td>
<td>6.38 ± .97</td>
<td>2.02</td>
<td>.053</td>
</tr>
<tr>
<td>Minute 120</td>
<td>5.03 ± .94</td>
<td>6.03 ± 1.13</td>
<td>4.31</td>
<td>.000</td>
</tr>
</tbody>
</table>

Data are means ± SD
Summary

Results from the current study found that there were no significant differences in glycemic response (overall and at individual time points) between the two BMI groups. However, there was a significant difference seen in glycemic response (overall and at individual time points) for the dietary conditions. Specifically, ingestion of the cinnamon cereal resulted in significantly lower blood glucose responses at 15, 30, 45 and 60 minutes compared to the plain cereal. It should also be noted that blood glucose response in the two dietary conditions were similar at 90 minute, but at 120 minutes the blood glucose response in the plain cereal was significantly lower than in the cinnamon cereal.
Chapter 5 - Discussion

Insulin Resistance, Glucose Metabolism and Obesity

It has been documented that insulin resistance occurs in obesity and been suggested that this insulin resistance affects glycemic response (Shoelson et al., 2007; Kahn et al., 2006). The aim of the current study was to look at the effects of cinnamon on glycemic response between individuals with an obese BMI compared to individuals with a normal BMI. Coopack et al. (1996) discovered that when comparing glycemic response between obese and non-obese subjects, obese subjects had a greater level of hyperinsulinaemia in both the postabsorptive and postprandial states. This may explain why glucose uptake was shown to be similar between the obese and non-obese groups in both the postabsorptive and postprandial states (Garvey, Huecksteadt, Matthael, & Olefsky, 1988). On the other hand, Virtanen et al. (2002) uncovered that per kilogram of fat, glucose uptake in the adipose tissue of those who were obese was markedly reduced compared to normal weight individuals. However, they suggested that because of enlargement of fat mass, the total amount of glucose uptake in the adipose tissue was not reduced in obese individuals (Virtanen et al., 2002). Mitrou et al. (2009) had similar findings. These authors concluded that increased total fat mass provided a reservoir for the excess glucose and, ultimately, that obese individuals were able to compensate for
insulin resistance. In the current study, there were also no differences seen in glycemic response between subjects with an obese BMI when compared to those with a normal BMI. Based on the current and previous findings, evidence suggests that those individuals with an obese BMI may have higher baseline and postprandial insulin levels, as well as an increased fat mass, which help to compensate for the extra glucose in the blood independent of cinnamon ingestion.

**Application in Healthy Individuals**

There is a dose-dependent relationship between cinnamon ingestion and benefits seen. In fact, previous studies in healthy subjects found that using less than 3 g of cinnamon showed no improvements in glycemic response or insulin sensitivity, suggesting that a minimal dosage of 3 g of ground cinnamon or, its aqueous equivalent, is needed to see significant improvements in glucose response and/or insulin sensitivity (Hlebowicz et al., 2009). In studies using 3-6 g of cinnamon, there seems to be dose-dependent relationship in lowering blood glucose levels and increasing insulin sensitivity (Hlebowicz et al., 2007; Solomon & Blannin, 2007; Solomon & Blannin, 2009). Hlebowicz et al. (2007) found that ingestion of 6 g cinnamon with rice pudding significantly reduced postprandial blood glucose as well as delayed gastric emptying (GER) without affecting satiety. A later study conducted by Hlebowicz et al. (2009) confirmed these effects after finding that ingestion of 3 g of cinnamon reduced postprandial serum insulin concentrations without significantly affecting blood glucose or GER in healthy subjects. The results indicate that not only does cinnamon have a glucose lowering affect, but that it appears to lower insulin concentrations as well. The current
study did not seek to address insulin concentrations, but found similar significant reductions in glycemic response after ingestion of cereal with 6 g of cinnamon in it.

Most of the effects of cinnamon appear to be immediate, but Solomon and Blannin (2007) discovered that the effects appear to last 12 hours after consumption of cinnamon. More specifically, these researchers found that inclusion of 5 g cinnamon supplementation reduced in vivo glycemic response and improved insulin sensitivity in otherwise healthy humans immediately and 12 hours after consumption. Only one study has looked at the effects of long term cinnamon supplementation in healthy subjects. The results showed that after a 14 day intervention, glucose and insulin responses were reduced and insulin sensitivity was improved (Solomon & Blannin, 2009). However, these effects were quickly reversed after cinnamon ingestion subsided. Combined results from the current and previous studies suggest that inclusion of cinnamon into the diet helps to improve immediate glycemic and insulin response in healthy subjects.

**Application in Type 2 Diabetes**

Because individuals with impaired glucose tolerance and/or type 2 diabetes often have reoccurring hyperglycemic events, cinnamon has become more and more popular among this population. In fact, results from a study looking at the long term effects of cinnamon in those individuals with type 2 diabetes found that daily intake of 1, 3, or 6 g of cinnamon for 40 days reduced serum glucose, triglyceride, low-density lipoproteins (LDL) cholesterol, and total cholesterol in people with type 2 diabetes (Khan et al., 2003). Mang et al. (2006) also found significant reductions in fasting blood glucose (FBG) levels after consumption of 3 g cinnamon supplementation for 4 months, but did not detect a significant reduction in hemoglobin A1c (HbA1c), triglyceride or total
cholesterol levels. This suggests that cinnamon may have glucose-lowering effects, but
there is an inconsistency in previous findings regarding cinnamon’s ability to lower
HbA1c and lipid levels. Ziegufuss, Hofheins, Mendel, Landis and Anderson (2006),
detected that supplementation with water-soluble cinnamon extract (Cinnulin) 500
mg/day significantly reduced fasting blood glucose (FBG), lowered systolic blood
pressure (SBP), decreased body fat percentage and increased lean mass in those subjects
with pre-diabetes and metabolic syndrome. All these results suggest that the inclusion of
cinnamon into the diet of people with type 2 diabetes may reduce risk factors associated
with diabetes and cardiovascular diseases.

Currently the American Diabetes Association emphasizes the importance of
glycemic control and weight reduction in the control of type 2 diabetes (Bantle et al.,
2008; Wheeler & Pi-Sunyer, 2008). Studies have shown that use of low glycemic index
(GI) foods can help to lower postprandial glycemia in subjects with type 2 diabetes, and
may even help to moderately lower HbA1c levels compared to a high GI diet (Jenkins et
al., 2008; Nilsson, Ostman, Granfeldt, & Bjorck, 2008). The current study used a high GI
food (GI = 74) with a low fiber content in order to focus on cinnamon’s independent
effects on glycemic response (Brand-Miller, Stockman, Atkinson, Petocz, & Denyer,
2009; “Fifty50”, 2010). Results from the current study found that cinnamon not only
significantly lowered postprandial blood glucose levels, but also helped to control the
rapid spike and decline in blood glucose levels of the high GI food. These results suggest
that if consumed with a high-GI low-fiber food, cinnamon may be used as an added
benefit to help lower fasting and/or postprandial blood glucose levels as well as aid in
improved glycemic control in those individual with type 2 diabetes.
Chapter 6 – Conclusion

Summary

Cinnamon has been used for thousands of years for culinary purposes (Barceloux, 2009), but is just now becoming popular as an added benefit for glycemic control. Its pharma logical benefits in glucose metabolism for both healthy individuals and those with type 2 diabetes have been well documented. Results from the current study did not show any significant difference in glycemic response between normal and obese individuals. However, significant reductions in blood glucose levels were seen in both groups after consumption of 6 g cinnamon in a high glycemic index (GI) food.

Recommendations for Future Research

There is some evidence which links higher glycemic response, characterized by higher blood glucose and insulin levels, with the increased onset of early aging and chronic disease (Radmila et al., 2007). Thus lowering blood glucose and insulin levels may provide a wealth of benefits to a healthy and/or insulin resistant population and not just those with type 2 diabetes. With the shift towards prevention and overall wellness, cinnamon once thought of for its use in cooking, should be explored further as an alternative diet therapy for glycemic control. Specifically, future research should narrow in on adult obese (BMI ≥ 30) and insulin-resistant populations with some level abnormal
glucose levels who are most at risk for developing type 2 diabetes. In fact, the ideal population for future research would be those individuals who are greater than 30 yrs of age, obese and diagnosed with impaired glucose tolerance (pre-diabetes). Research has consistently shown that 3-6 g of cinnamon significantly reduces postprandial blood glucose levels. Future research should consider looking at different forms (ground versus aqueous) and timing of cinnamon. This would provide consumers with practical knowledge about the use of cinnamon as an added benefit for glycemic control in their diet.
References

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kinase by fractions from cinnamon: Implications for cinnamon regulation of insulin signaling. *Hormone Research, 50*, 177-182.


OSU (Oregon State University): Glycemic index and glycemic load

lpi.oregonstate.edu/infocenter/foods/grains/gigl.html 9/22/09.


Appendix A

Subjects Informed Consent Document with Extra Credit

Study Purpose and Rationale

Research in normal weight individuals has shown that cinnamon enhances glucose transport and utilization in the body, ultimately leading to improved glucose metabolism. The body’s ability to metabolize glucose is largely influenced by body mass index (BMI), the amount of body fat based on a person’s height and weight.

Individuals who have a higher BMI have a lower efficiency of glucose metabolism due to increased body fat. Thus, they may experience greater improvements in blood glucose after eating carbohydrates with cinnamon than individuals with normal BMI.

The purpose of this research is to determine the effects of 6g of ground cinnamon in farina (Cream of Wheat) cereal on blood glucose levels in individuals with normal and higher body mass indexes (BMI’s).

Inclusion/Exclusion Criteria

To be eligible to participate in this research, you must be between the ages of 19 and 30, be within the pre-determined BMI categories, have no known wheat and/or cinnamon allergies, not pregnant, have no problem with giving blood samples via finger poke, and have no known medical condition which would affect blood glucose levels (i.e. Type 1 or Type 2 Diabetes, Acromegaly, Cushing syndrome, Impaired fasting glucose (pre-diabetes), Hyperthyroidism, Pancreatic cancer, Pancreatitis, Pheochromocytoma, Hypopituitarism, Hypothyroidism) will be excluded. You may be excluded after the initial screening if you do not meet inclusion/eligibility criteria.

Participation Procedures and Duration

You will be asked to meet with the researcher for 10-15 minutes to sign an informed consent document, complete a prescreening form and to discuss and answer questions about the study. You may be excluded from the study after the initial screening if you do not meet the inclusion criteria. Once enrolled, you will be asked to visit the Nutrition Assessment Lab for 2 ½ hours on two different occasions, at least 7 days apart. You will be asked to maintain your typical diet, lifestyle habits, physical activity schedule throughout the study, and fast for at least 8 hours prior to both study visits. At the beginning of the first visit, you will complete a survey to collect information on demographics, physical activity, family history of type 2 diabetes, personal history of...
hypertension and/or any known allergy to wheat or cinnamon. During each visit, you will be given one of two test meals in random order followed by 7 blood glucose measurements over a 2 ½ hour period. The total participation time for the entire study will be 5 hours. The test meals will be as follows: test meal one (74 g of farina), test meal two (74 g farina with 6 g of ground cinnamon). All test meals will contain 50 g of carbohydrate. Test meals will be prepared according to standard directions. If included, cinnamon will be added once the cooked cereal has been portioned into bowls. You will be allowed to use up to 1 packet of sucralose (Splenda) sweetener in the test meal and consume up to 2 cups (16 oz/480 ml) of water during the study period if desired. You will be asked to consume the test meal within 15 minutes. Finger prick capillary analysis will be used to assess blood glucose levels.

You will be scheduled in groups of four; on test day you will come into the nutrition assessment lab and be asked to sit down in your assigned station. Once you are comfortably sitting down at your station, a fasting blood sample will be taken before the test meal is consumed. Once the fasted sample has been taken, you will be given the test meal and blood samples will be collected at minute 15, 30, 45, 60, 90 and 120 for a total of seven times during the 2 ½ hour duration of the visit. During the study you will have the option of either completing the diet analysis on the first visit followed by a consultation with a dietitian on the second visit, or using this time to work on homework, watch a movie, listen to music and/or use your computer. The only requirement is that you remain seated and sedentary during the 2 ½ hour visit, with the only exception being getting up to use the washroom.

**Data Confidentiality or Anonymity**

All data will be maintained as confidential and no identifying information such as names will appear in any publication or presentation of the data. Once the informed consent document has been signed, you will be assigned a unique identifier. This unique identifier or code number will be used for all study related forms, including screening forms and data collection forms. You will be assigned a study identification number for the study; all data will be collected and stored under your identification number, not your name.

**Storage of Data**

The key/master list containing your name and code number will be stored in the PI’s thesis advisor’s office in a file in a locked file drawer in a locked office. This master list will be destroyed after data collection has been concluded and extra credit has been awarded. All study forms, including completed screening and data collection forms, will be placed in a file folder and stored in the PI’s thesis advisor’s office in a locked file drawer for three years and will then be shredded. The de-identified data will be entered
into an Excel spreadsheet; this electronic data will be stored on the researcher’s password-protected desktop computer with a backup copy on ilocker. Data will be presented only in aggregate; no individual data will ever be released. Only members of the research team will have access to the data.

**Risks or Discomforts**

The research is of minimal risk to you. You may experience mild discomfort from the pricking of your finger to determine your blood glucose level. In the unlikely event of an allergic reaction, emergency medical treatment is available if you become injured or ill during your participation in this research project. You will be responsible for the costs of any medical care that is provided. If any injury or illness occurs in the course of your participation in this research project, please seek treatment as appropriate and notify the Principle Investigator as soon as possible. The PI will carry a charged cell phone on her at all time and immediately contact 911 for emergency care if needed.

There is a possibility that having your finger pricked to determine your blood glucose level may evoke some feelings of anxiety. If you experience anxiety during the study, report it to the investigator; you can choose to stop your participation at any time. In the extreme unlikely event that you should feel any anxiety or uncomfortable feelings resulting from the finger prick counseling services are available to you through the Counseling Center at Ball State University (765-285-1376), and will be referred by the PI. You will be responsible for the costs of any care that is provided [note: Ball State students may have some or all of these services provided to them at no cost].

It is understood that in the unlikely event that treatment is necessary as a result of your participation in this research project that Ball State University, its agents and employees will assume whatever responsibility is required by law.

**Benefits and Incentives**

By participating in this study, you may benefit by learning more about your blood glucose levels and glucose metabolism in general. You will be given a fact sheet about blood glucose and a chart showing your blood glucose response during the study period.

To thank you for your study participation, you will be offered a complete dietary analysis, valued at $125, for free. The analysis will include both a written report and consultation with a Registered Dietitian. If you should withdraw before the completion of the study, you will still be eligible to receive the free diet analysis and consultation.

In addition, as a study participant, you will receive a small amount of extra credit in one of the following classes: FCS 403, FCSFN 103, FCSFN 444, FCSFN 475, FCSFN 262,
FCSFN 340, FCSFN 275, FCSFN 101, FCSFN 648, FCSFN 390, FCSFN 447, FCSFN 642, FCSFN 363, FCSFN 371 or FCSFN 697. If you do not wish to participate in this study there will be an additional equivalent extra credit opportunity available. This additional extra credit opportunity will require you to come to campus on a Saturday for 5 hours to watch a nutrition related video and write an in class paper.

**Voluntary Participation**

Your participation in this study is completely voluntary, and you are free to withdraw your permission at anytime for any reason without penalty or prejudice from the investigator. Please feel free to ask any questions of the investigator before signing this form and at any time during the study.

**IRB Contact Information**

For your rights as a research subject, you may contact the following: Research Compliance, Sponsored Programs Office, Ball State University, Muncie, IN 47306, (765) 285-5070, irb@bsu.edu.

**Consent**

I, ____________________________________________, agree to participate in this research project entitled, “Effects of Ground Cinnamon on Postprandial Blood Glucose Levels between BMI Categories.” I have had the study explained to me, and my questions have been answered to my satisfaction. I have read the description of this project and give my consent to participate. I understand that I will receive a copy of this informed consent form to keep for future reference.

To the best of my knowledge, I meet the inclusion/exclusion criteria for participation (described on the previous page) in this study and do not have any known allergies to wheat and/or cinnamon.

_____________________________________________  ______________________
Participant’s Signature                      Date

**Researcher Contact Information**

Principal Investigator: Ashley Magistrelli, RD  Faculty Supervisor: Dr. Jo Carol Chezem, PhD, RD
Graduate Student: Associate Professor
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Telephone: (765) 285-5931
Email: 00jcchezem@bsu.edu
Appendix B

Subjects Informed Consent Document without Extra Credit

**Study Purpose and Rationale**

Research in normal weight individuals has shown that cinnamon enhances glucose transport and utilization in the body, ultimately leading to improved glucose metabolism. The body’s ability to metabolize glucose is largely influenced by body mass index (BMI), the amount of body fat based on a person’s height and weight.

Individuals who have a higher BMI have a lower efficiency of glucose metabolism due to increased body fat. Thus, they may experience greater improvements in blood glucose after eating carbohydrates with cinnamon than individuals with normal BMI.

The purpose of this research is to determine the effects of 6g of ground cinnamon in farina (Cream of Wheat) cereal on blood glucose levels in individuals with normal and higher body mass indexes (BMI’s).

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To be eligible to participate in this research, you must be between the ages of 19 and 30, be within the pre-determined BMI categories, have no known wheat and/or cinnamon allergies, not pregnant, have no problem with giving blood samples via finger poke, and have no known medical condition which would affect blood glucose levels (i.e. Type 1 or Type 2 Diabetes, Acromegaly, Cushing syndrome, Impaired fasting glucose (pre-diabetes), Hyperthyroidism, Pancreatic cancer, Pancreatitis, Pheochromocytoma, Hypopituitarism, Hypothyroidism) will be excluded. You may be excluded after the initial screening if you do not meet inclusion/eligibility criteria.

**Participation Procedures and Duration**

You will be asked to meet with the researcher for 10-15 minutes to sign an informed consent document, complete a prescreening form and to discuss and answer questions about the study. You may be excluded from the study after the initial screening if you do not meet the inclusion criteria. Once enrolled, you will be asked to visit the Nutrition Assessment Lab for 2 ½ hours on two different occasions, at least 7 days apart. You will be asked to maintain your typical diet, lifestyle habits, physical activity schedule throughout the study, and fast for at least 8 hours prior to both study visits. At the beginning of the first visit, you will complete a survey to collect information on demographics, physical activity, family history of type 2 diabetes, personal history of hypertension and/or any known allergy to wheat or cinnamon. During each visit, you will
be given one of two test meals in random order followed by 7 blood glucose measurements over a 2 ½ hour period. The total participation time for the entire study will be 5 hours. The test meals will be as follows: test meal one (74 g of farina), test meal two (74 g farina with 6 g of ground cinnamon). All test meals will contain 50 g of carbohydrate. Test meals will be prepared according to standard directions. If included, cinnamon will be added once the cooked cereal has been portioned into bowls. You will be allowed to use up to 1 packet of sucralose (Splenda) sweetener in the test meal and consume up to 2 cups (16 oz/480 ml) of water during the study period if desired. You will be asked to consume the test meal within 15 minutes. Finger prick capillary analysis will be used to assess blood glucose levels.

You will be scheduled in groups of four; on test day you will come into the nutrition assessment lab and be asked to sit down in your assigned station. Once you are comfortably sitting down at your station, a fasting blood sample will be taken before the test meal is consumed. Once the fasted sample has been taken, you will be given the test meal and blood samples will be collected at minute 15, 30, 45, 60, 90 and 120 for a total of seven times during the 2 ½ hour duration of the visit. During the study you will have the option of either completing the diet analysis on the first visit followed by a consultation with a dietitian on the second visit, or using this time to work on homework, watch a movie, listen to music and/or use your computer. The only requirement is that you remain seated and sedentary during the 2 ½ hour visit, with the only exception being getting up to use the washroom.

Data Confidentiality or Anonymity

All data will be maintained as confidential and no identifying information such as names will appear in any publication or presentation of the data. Once the informed consent document has been signed, you will be assigned a unique identifier. This unique identifier or code number will be used for all study related forms, including screening forms and data collection forms. You will be assigned a study identification number for the study; all data will be collected and stored under your identification number, not your name.

Storage of Data

The key/master list containing your name and code number will be stored in the PI’s thesis advisor’s office in a file in a locked file drawer in a locked office. This master list will be destroyed after data collection has been concluded and extra credit has been awarded. All study forms, including completed screening and data collection forms, will be placed in a file folder and stored in the PI’s thesis advisor’s office in a locked file drawer for three years and will then be shredded. The de-identified data will be entered into an Excel spreadsheet; this electronic data will be stored on the researcher’s
password-protected desktop computer with a backup copy on ilocker. Data will be presented only in aggregate; no individual data will ever be released. Only members of the research team will have access to the data.

**Risks or Discomforts**

The research is of minimal risk to you. You may experience mild discomfort from the pricking of your finger to determine your blood glucose level. In the unlikely event of an allergic reaction, emergency medical treatment is available if you become injured or ill during your participation in this research project. You will be responsible for the costs of any medical care that is provided. If any injury or illness occurs in the course of your participation in this research project, please seek treatment as appropriate and notify the Principle Investigator as soon as possible. The PI will carry a charged cell phone on her at all time and immediately contact 911 for emergency care if needed.

There is a possibility that having your finger pricked to determine your blood glucose level may evoke some feelings of anxiety. If you experience anxiety during the study, report it to the investigator; you can choose to stop your participation at any time. In the extreme unlikely event that you should feel any anxiety or uncomfortable feelings resulting from the finger prick counseling services are available to you through the Counseling Center at Ball State University (765-285-1376), and will be referred by the PI. You will be responsible for the costs of any care that is provided [note: Ball State students may have some or all of these services provided to them at no cost].

It is understood that in the unlikely event that treatment is necessary as a result of your participation in this research project that Ball State University, its agents and employees will assume whatever responsibility is required by law.

**Benefits and Incentives**

By participating in this study, you may benefit by learning more about your blood glucose levels and glucose metabolism in general. You will be given a fact sheet about blood glucose and a chart showing your blood glucose response during the study period.

To thank you for your study participation, you will be offered a complete dietary analysis, valued at $125, for free. The analysis will include both a written report and consultation with a Registered Dietitian. If you should withdraw before the completion of the study, you will still be eligible to receive the free diet analysis and consultation.

**Voluntary Participation**

Your participation in this study is completely voluntary, and you are free to withdraw your permission at anytime for any reason without penalty or prejudice from the
investigator. Please feel free to ask any questions of the investigator before signing this form and at any time during the study.

**IRB Contact Information**

For your rights as a research subject, you may contact the following: Research Compliance, Sponsored Programs Office, Ball State University, Muncie, IN 47306, (765) 285-5070, [irb@bsu.edu](mailto:irb@bsu.edu).

**Consent**

I, _______________________________, agree to participate in this research project entitled, “Effects of Ground Cinnamon on Postprandial Blood Glucose Levels Between BMI Categories.” I have had the study explained to me, and my questions have been answered to my satisfaction. I have read the description of this project and give my consent to participate. I understand that I will receive a copy of this informed consent form to keep for future reference.

To the best of my knowledge, I meet the inclusion/exclusion criteria for participation (described on the previous page) in this study and do not have any known allergies to wheat and/or cinnamon.

________________________________   ____________________________
Participant’s Signature   Date

**Researcher Contact Information**

Principal Investigator: Ashley Magistrelli, RD  
Graduate Student  
Family and Consumer Science  
Ball State University  
Muncie, IN  47306  
Telephone: (847) 989-6136  
Email: [ammagistrell@gmail.com](mailto:ammagistrell@gmail.com)

Faculty Supervisor: Dr. Jo Carol Chezem, PhD, RD  
Associate Professor  
Family and Consumer Science  
Ball State University  
Muncie, IN  47306  
Telephone: (765) 285-5931  
Email: [00jcchezem@bsu.edu](mailto:00jcchezem@bsu.edu)
Appendix C

Pre-Screening Form

Assigned # ______

Effects of Ground Cinnamon on Postprandial Blood Glucose Levels between BMI Categories

Age: ______

Sex: M / F

Height: ______

Weight: ______

BMI: ______

*Calculation for BMI (body mass index): \( \frac{Wt \ (lbs)}{Ht \ (in)^2} \times 705 \)

1. Are you currently pregnant?
   _____ No  _____ Yes

2. Do you have any known allergy to wheat or cinnamon?
   _____ No  _____ Yes

3. Do you currently have any known medical condition which would affect your blood glucose levels? (i.e. Type 1 or Type 2 Diabetes, Acromegaly, Cushing syndrome, Impaired fasting glucose (pre-diabetes), Hyperthyroidism, Pancreatic cancer, Pancreatitis, Pheochromocytoma, Hypopituitarism, Hypothyroidism) *
   _____ No  _____ Yes

4. Do you have any problems with giving blood samples by finger prick?
   _____ No  _____ Yes

* From NIH (National Institute of Health)
Appendix D

Demographic Survey

<table>
<thead>
<tr>
<th>Participant #: ________________________</th>
<th>Date___/<strong><strong>/</strong></strong>___</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ht: _____ Wt: _____ BMI: ______</td>
<td>Gender: ___ Male ___ Female</td>
</tr>
</tbody>
</table>

If female, have you ever developed diabetes in pregnancy?*

| ____ No | ____ Yes | ____ Doesn’t apply |

In a typical week, how often do you take part in physical activities. (Examples: walking, jogging, bike riding or anything that increases your heart rate).

| ____ None | ___ 3-4 days/week | ___ 1-2 days/week | ___ 5-7 days/week |

On days when you take part in physical activity, you usually spend __________ minutes in this activity.

Compared with most men or women your age, would you say that you are ____.*

| ____ More active | ____ Less active | ____ About the same |

Do you currently have any known allergy to wheat or cinnamon?

| ____ No | ____ Yes |

Have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure?*

| ____ No | ____ Yes |

To your knowledge, have your mother, father, brother(s) and/or sister(s) been diagnosed with type 2 diabetes? If yes please select all that apply:

| ____ Mother | ____ Sister(s) |
| ____Father | ____ Brother(s) |

What race or ethnicity best describes you?*

| ____ White/Caucasian | ____ Black/African American |
| ____ Hispanic | ____ Native American | ____ Asian | ____ Other |

Appendix E

Approval Letter from Ball State IRB

Institutional Review Board

DATE: March 25, 2010
TO: Ashley Magistrelli
FROM: Ball State University IRB
RE: IRB protocol # 139733-7
TITLE: Effects of Ground Cinnamon on Postprandial Blood Glucose Levels Between BMI Categories
SUBMISSION TYPE: Amendment/Modification
ACTION: APPROVED
DECISION DATE: March 24, 2010
EXPIRATION DATE: December 15, 2010
REVIEW TYPE: Expedited Review

The Institutional Review Board has approved your Amendment/Modification for the above protocol, effective March 24, 2010 through December 15, 2010. All research under this protocol must be conducted in accordance with the approved submission.

As a reminder, it is the responsibility of the P.I. and/or faculty sponsor to inform the IRB in a timely manner:

- when the project is completed,
- if the project is to be continued beyond the approved end date,
- if the project is to be modified,
- if the project encounters problems, or
- if the project is discontinued.

Any of the above notifications should be addressed in writing and submitted electronically to the IRB (http://www.bsu.edu/irb). Please reference the IRB protocol number given above in any communication to the IRB regarding this project. Be sure to allow sufficient time for review and approval of requests for modification or continuation. If you have questions, please contact Amy Boos at (765) 285-5034 or akboos@bsu.edu.
Appendix F

NIH Tutorial Certificate

Certificate of Completion
The National Institutes of Health (NIH) Office of Extramural Research certifies that Ashley Magistrelli successfully completed the NIH Web-based training course “Protecting Human Research Participants”.
Date of completion: 03/10/2009
Certification Number: 199821
Appendix G

Final Completion Form Ball State IRB

Final Report

IRBNet Protocol Number: 139733.7  
Today’s Date: 13-05-2010

Principal Investigator: Ashley Magistrelli

Protocol Title: Effects of Ground Cinnamon on Postprandial Blood Glucose Levels Between BMI Categories

Date Data Collection Completed: 14-04-2010

Number of Subjects that:
Completed the Study: 30
Were not eligible (excluded): 20

Report Findings (directly related to the purpose of the study – 300 word limit):

AUC was calculated

a. There was not a statistically significant difference in AUC found when looking at BMI groups (p = .605) or dietary conditions and BMI groups (p = .528). There was a statistically significant difference found between the two dietary conditions (cinnamon mean 171.44 ± 13.5) (plain mean 224.27 ± 13.5) (p = .008).

Repeated measures analysis was conducted to look at glycemic response.

b. There was a significant difference in glycemic response between the 2 dietary conditions (cinnamon and plain) (p = .002)

c. There was not a significant difference in glycemic response between the two BMI groups. (p = .586)

Because the glycemic response after ingestion of the two dietary conditions was similar between the two BMI groups, they were combined for analysis of dietary conditions at individual time points

a. There was a statistically significant effect of interaction between dietary condition and time (p ≤ .001) on postprandial blood glucose response (15, 30, 45, 60 and 120) (Figure 3).

b. Ingestion of cream of wheat cereal with cinnamon resulted in significantly lower blood glucose response in the postprandial phase (15 (p = .001), 30 (p = .001), 45 (p = .000) and 60 (p = .001)) than did the cream of wheat without the cinnamon (Figure 3 and Table 2).

c. It should also be noted that there was a trend toward lower blood glucose response in the plain condition at 90 minute (p = .053), which continues to drop at minute 120. However, at minute 120 the cream of wheat with the cinnamon was significantly higher (p = .000) than plain cream of wheat.
Did any subjects withdraw from your study?

YES ☐       NO ☐

If yes, please explain:

7 subjects withdrew from the study; 5 of those individuals could not finish the cream of wheat cereal in the allotted time of 15 minutes, 1 individual withdrew due to personal reasons and 1 individual did not report for testing.

Did you encounter any unanticipated problems or adverse events while conducting your study? (For definitions and further information see: http://www.hhs.gov/ohrp/policy/AdvEvntGuid.htm)

YES ☐       NO ☐

If yes, please describe the complaint and what action, if any, was taken along with the date an adverse event/unanticipated problem report was filed with the IRB (this form can be found within IRBNet):


Did you receive any complaints from your subjects?

YES ☐       NO ☐

If yes, please describe the complaint and what action, if any, was taken:


Were any changes made to this study’s protocol?

YES ☐       NO ☐

If yes, please list the dates in which these modifications were approved by the IRB:

03/24/2010        12/02/2009
03/04/2010        11/11/2009
02/17/2010
02/03/2010
12/16/2009
Final Report Form, cont.

Have you complied with the data handling procedures as described in your study’s narrative (Section 5.1)?
   YES ☐   NO ☐

If no, please explain:

The new package created for submission of this Final Report must be electronically signed within IRBNet by the Principal Investigator (and Faculty Sponsor, when applicable). Your electronic signature indicates your certification that the information provided in this document is accurate and current.