Anti-hyperglycemic and Anti-hypercholesterolemic Effects of *Angelica keiskei* (Ashitaba)

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Abstract

Angelica keiskei koidzumi (Ashitaba) originated from the Island of Hachijo, Japan. Ashitaba has been claimed to be an anti-oxidant, anti- cancer, antibacterial, anti- inflammatory antihypertensive and anti-diabetic agent. This study aimed to evaluate and compare the beneficial effects of Ashitaba in people who have elevated blood glucose and blood cholesterol levels through an experiment. Results show that a seven-day consumption of Ashitaba has the ability to reduce blood glucose level but not to reduce cholesterol level.

Keywords: *Angelica keiskei, Sugar, Cholesterol, anti-hyperglycemic, anti-hypercholesterolemic*

INTRODUCTION

Angelica keiskei koidzumi (Ashitaba) belongs to the Apiaceae family, which grows naturally in Japan and, has been widely cultivated as a green vegetable juice ingredient. The main bioactive constituents of this plant are flavonoids, coumarins, and chalcones (Ji Ho Kim, 2013). The unique characteristic of Ashitaba is the yellow sap which cannot be found in other Apiaceae plants. The component of this yellow sap is Chalcones, a thick sticky pigment composition of yellow that are potent antioxidants which help to protect organs from free radical damage and slow the aging process on a cellular level. In many studies, it has been also reported that this plant has various physiological benefits including anti-bacterial, anti-tumor, anti-inflammatory, anti-cancer, anti-ulcer and artery relaxation actions (Nagata et al, 2007).

Hypercholesterolemia, or high blood cholesterol is a condition in which too much cholesterol circulates in the blood. It is a major risk for coronary heart disease and may cause of heart attacks. This condition usually have no signs and symptoms, thus many people don't know that their cholesterol levels are elevated (O'Donnell, 2012). Lifestyle is the most common contributor to increase the cholesterol in the body this include obesity, not exercising, and smoking (NorthPoint Domain, 2010).

Hyperglycemia, or high blood sugar, is a serious health problem for those with diabetes. Hyperglycemia is often manifested by experiencing an increase thirst, frequent urination, headaches, blurred vision, slow healing cuts and sores, fatigue and weight loss. In most cases, it is due to reduced insulin secretion by beta cells of pancreatic islets (Brent Wisse, et al, 2014).

Due to numerous occasionally fatal disease, there is a need to find the treatment methods and ways to reduce and prevent it. At the present time, synthetic drugs are often used which may cause some adverse effects to the patient. Some people have turned to herbal treatments as an alternative to taking these medications to avoid the potential risks. The use of complementary and alternative medicines (CAMs) is becoming more common worldwide. In the past few decades, studies from many countries, including Canada, the United States, the United Kingdom, and the United Arab Emirates, all demonstrated a significant increase in the use of CAMs amongst the general population (T. F. Sim et al, 2013).As a result, the use of herbal medicines has attracted the attention of researchers.

In the present study, the researchers compare and evaluate the efficacy of *Angelica keiskei* into two medical conditions, the hyperglycemia and hypercholesterolemia. For the evaluation of efficacy, blood chemistry analysis was conducted. The researchers focused on the physiological impacts of Ashitaba on the blood cholesterol and blood glucose level of 12 human subjects.

Review of Literature

It has been estimated by the World Health Organization (WHO) that the worldwide prevalence of diabetes was 9% among adults 18 and over while around 39% of adults aged 25 and older had raised cholesterol. Given the critical conditions associated with diabetes and the diseases linked to having high levels of cholesterol, it is important to discover a way to control glucose and cholesterol levels in order to avoid the consequences that may be faced with having high levels of these blood parameters.

In terms of decreasing blood glucose and cholesterol levels, there is a particular plant that has gained popularity due to its effectiveness, *Angelica keiskei* (Ashitaba). *Gynura procumbens* is another plant species that goes by the name Ashitaba and is also capable of producing effects similar to those of *Angelica keiskei*. Although, the main difference between them is that *A. keiskei* contains chalcones, the active ingredient of the plant that can be found in the stem. Many researchers have proven that these chalcones exhibit antidiabetic and insulin-like activities. A study by Enoki, et al. (2006) confirmed that the

extract of *Angelica keiskei* contained Xanthoangelol (XA) and 4-hydroxyderricin (4HD), which are major chalcone compounds specific to Ashitaba that showed strong insulin-like activities. Additionally, Murugan & Rao (2008) studied the influence of these chalcones on the affinity of erythrocyte insulin receptors of rats with type 2 diabetes mellitus. The rats were induced with a high fat diet and a small dose of streptozotocin. They were divided into four groups: a control group and high, medium, and low Ashitaba chalcone supplementation groups. The results of this experiment were that the hormone and receptor bind to each other tightly in high dosage group than those of the control group and that there was a significant decrease in the fasting plasma glucose. They concluded that Ashitaba chalcone could improve erythrocyte insulin receptor affinity in rats with type 2 diabetes and also improve insulin resistance. On the other hand, the study of Nagata et al (2007) showed no significant decrease in the lipid profiles of 28 day Ashitaba-fed rats

In a study by Choi, et al. (2012), the physiological activities of Ashitaba, Ashitaba juice, Ashitaba squeeze, and fermented juice in rats with high fat diets was investigated. The rats were given Ashitaba and its processed products for six weeks while on a high fat diet. This study focused on the effect of Ashitaba on the expression of antioxidant enzymes related to lipid profiles in a high fat diet. The results showed that the intake of Ashitaba and its products actively increased gene expression. Furthermore, results of the experiment did not demonstrate a synergistic effect in mixing the sample.

The current thesis examines the in vivo effects on the blood parameters of humans. This area has yet to be explored at a deeper level, as the majority of the literature on the anti-glucose and anti-cholesterol effects of Ashitaba have focused on the potency of these abilities in rats. To truly appreciate the effects of Ashitaba and apply its use in real world situations, we must examine, in detail, its effects in humans. Past researchers have aimed to examine the effects of chalcones, the main active component of Ashitaba, on the systems of laboratory rats under controlled environmental settings. However, such a narrow focus may not fully explain its potency once inside the human body because of the differences in the anatomy and physiology of rats and humans. Therefore, instead of testing and observing its effects in rats, researchers should now shift their focus on its effects in humans. In the aforementioned study, it was pointed out that the rats were fed a high fat diet in order to observe the effect of Ashitaba on the cholesterol levels of the rats.

In a study regarding the efficacy and safety of Ashitaba on patients with metabolic syndrome by Enoki, et al. (2012), the subjects were requested to keep their daily lifestyle habits, such as dietary habits, smoking, alcohol consumption, and exercise, as they were for the duration of the test period.

The same conditions hold true in the current study.

Most research involving *Angelica keiskei* seeks to identify the plants chemical components or the effects of these components in laboratory rats, and therefore, there is little information about its effects in humans and whether or not it is more potent at reducing the levels of a certain blood parameter over another. It may therefore be advantageous to study and observe the effects of this plant under realistic conditions, as this methodology would be relevant to its actual use in real life circumstances. However, few studies have used this methodology and little is known about the kind of results it would produce. Therefore, future investigation involving human subjects in natural settings would be helpful to better understand the effects of *Angelica keiskei* in a real life setting.

Objective of the Study

The study determined the ability of *Angelica keiskei* (Ashitaba) in reducing the blod glucose and blood cholesterol level in the human subject.

MATERIALS AND METHOD

Research Design

This study utilized an experimental research design. The experimental design specified an experimental group and a control group. The independent variable was administered to the experimental group and not to the control group, and both groups were measured on the same dependent variable (Mosby, Medical Dictionary).

Subjects of the Study

Eighteen selected respondents from Barangay Trapiche 3, Tanauan City, Batangas, particulary aged 30-70 years old, with a reported elevated blood sugar level or an elevated cholesterol level characterized the subjects of the study. The reference range for an elevated blood sugar level is 130mgldL to 169mg/dL, and the range for a borderline high cholesterol level is 200mg/dL to 239mg/dL. Included in the study were 12 persons who are not taking maintenance medicine or have no other illnesses to avoid any interference in the possible effects of Ashitaba. Six of the participants were tested for hyperglycemic conditions and the other six for hypercholesterolemic conditions. The control group consisted of four individuals: two for hyperglycemic and two for hypercholesterolemic groups. Blood analyses were conducted at San Sebastian Diagnostic Laboratory, Inc. located in Lipa,

Batangas. The instrument used for blood chemistry was the Biotecnica 1500, the controls are run every day and it is calibrated every month.

Plant Material

In early April, mature Ashitaba plants that were 11 months old each along with some immature plants that were 7 months old each were purchased. The plant was authenticated by the Philippine National Museum. The plants were grown from the ones that were initially purchased in a mixture of clay soil and rocks. This type of mixture was used in order to prevent the plant from receiving too much or too little water. The plants were watered whenever the topsoil had become dry and sprayed with water if they begin to wilt.

Ashitaba leaves and stems, where the chalcones are most prominent, were harvested from a mature plant early in the morning when it is not raining. The roots were separated from the parts that were used for the powder. The roots were discarded. The leaves and stems were then dried in open air under a shade net for approximately 2 to 3 hours not under direct sunlight because chalcones are photosensitive. The dried plant parts were cut up into smaller pieces with scissors before being shredded with a food processor. They were then re-dried under the same conditions. After the second drying the leaves and stems were again shredded to obtain a powder.

Procedure

Blood samples were extracted from the fasted subjects to determine the blood sugar and blood cholesterol levels prior to administration of the test material. The glucose oxidase method was used to determine the blood glucose level of the respondents. On the other hand, the Trinder method was used to measure the cholesterol levels of the individuals.

The respondents who were qualified to be a part of the experimental group were asked to consume the Ashitaba powder in the morning and in the evening for a period of seven (7) days. The subjects were requested not to alter their daily lifestyle habits such as dietary habits, exercise, alcohol consumption, and smoking. The subjects of the control group, those who did not consume the Ashitaba powder, were requested to do the same.

The subjects were asked to consume Ashitaba powder for one week. In regards to the post-test procedure, the researchers extracted blood from the respondents for the post-examination of their blood levels. The same methods, glucose oxidase and Trinder, were used to determine the blood sugar and

cholesterol levels, respectively.

The researchers monitored the blood sugar level, and the cholesterol level of the experimental group and the control group. Visitations were made every other day, for a total of three (3) visits in one week. During these visits, the subjects were asked about their consumption of the Ashitaba and if they felt any change or unusual symptoms.

Data Analysis

T-test for dependent samples was used to determine the effect of the Ashitaba in the glucose and cholesterol levels of the subjects.

RESULTS AND DISCUSSION

Table 1 shows the pre and post examination of blood cholesterol levels. Three out of six respondents or 50% of the experimental group got a higher cholesterol level in the post examination after taking the Ashitaba. This can serve as evidence that Ashitaba is not potent in lowering the blood cholesterol level within a short period of time since their blood analyses showed a significant increase. However, the three other individuals in the experimental group did not show a significant decrease in their blood cholesterol level.

Table 1. Pre and Post Examination of Blood Cholesterol level

PATIENT'S ID NUMBER	PRE-TEST: CHOLESTEROL	POST-TEST: CHOLESTEROL
001	212.8 mg/dL	234.0 mg/dL
002	226.6 mg/dL	217.7 mg/dL
003	216.6 mg/dL	214.9 mg/dL
004	209.6 mg/dL	239.5 mg/dL
005	266.6 mg/dL	275.5 mg/dL
006	234.9 mg/dL	219.9 mg/dL

The mean cholesterol level was found to be higher in the post analysis (233.58 mg/dL compared to the pre analysis (227.85 mg/dL). However, statistical analyses revealed that the difference is not significant (p= .459).

Table 2 shows that all subjects exhibited a decrease in the blood glucose level after the administration of Ashitaba. The blood glucose level prior to administration ranges from 134 mg/dL to as high as 357 mg/dL while

in the post administration the glucose level ranges from 95.5 mg/dl to as high as 270.8 mg/dL.

Table 2. Pre and Post Examination for Fasting Blood Sugar

PATIENT'S ID NUMBER	PRE-TEST: GLUCOSE	POST TEST: GLUCOSE
001	357.2 mg/dL	270.8 mg/dL
002	134.0 mg/dL	122.3 mg/dL
003	265.3 mg/dL	234.0 mg/dL
004	243.4 mg/dL	171.7 mg/dL
005	206.1 mg/dL	182.1 mg/dL
006	136.0 mg/dL	95.5 mg/dL

Statistical analysis revealed a significantly (p=.02) lower glucose level after the administration of Ashitaba (mean of 179.4 mg/dL) than before administration of Ashitaba (mean of 226 mg/dL). This implies that Ashitaba is potent in lowering blood sugar level.

Table 3 shows the summary of the experimental and the control group for the blood cholesterol level and the blood sugar level. Results show higher cholesterol level in the control group both in the pre and post administration of the Ashitaba. This however, contradicts the assumption that Ashitaba could be used to reduce the cholesterol level of the subjects.

The glucose level in the control group is lower in the pre administration but higher in the post administration of Ashitaba. This results strengthen the claim that Ashitaba can be used to reduce the blood sugar level in the subjects.

Table 3. Experimental and Control group

GROUP	MEAN	STANDARD DEVIATION	T-TEST VALUE	SIGNIFICANCE (2-TAILED)
Cholesterol Pre test				
Experimental	227.85	21.16	3.24	0.018
Control	283.90	21.35		
Cholesterol Post test				
Experimental	233.58	22.72	2.65	0.038
Control	281.30	18.53		
Glucose Pre test				
Experimental	226.67	90.63	0.53	0.615
Control	186.40	104.65		
Glucose Post test				
Experimental	179.40	65.88	0.24	0.821
Control	194.00	113.00		

Discussion

Pancreas is the primary organ involved in sensing the dietary and energetic states of an individual via glucose concentration in the blood and in response to elevated blood glucose. During a hyperglycemia state, insulin is secreted by the β cells of the pancreatic islets of Langerhans. Insulin causes the cells in the liver, muscle, and adipose tissue to take up glucose from blood and convert it to glycogen (Bishop, 2010). An insufficient release of insulin, that leads high blood glucose. In the study conducted by Enoki, et al., it is stated that Ashitaba contains two chalcones, xanthoangelol and 4-hydroxyderricin which produce insulin- like activities. Indeed, the administration of Ashitaba powder for seven (7) days remarkably reduced the blood glucose level of the qualified respondents.

Hypercholesterolemia are controlled by the liver. Cholesterol is an extremely important biological molecule that has roles in membrane structure as well as being a precursor for the synthesis of the steroid hormones, the bile acids, and vitamin D. Both dietary cholesterol, and that synthesized de novo, are transported through the circulation in lipoprotein particles. The synthesis and utilization of cholesterol must be tightly regulated in order to prevent over-accumulation and abnormal deposition within the body (King, 2015). The elevation of cholesterol is primarily associated with an increase in LDL cholesterol. LDL builds up due to some individuals who have insufficient

receptors to bind LDL and transfer cholesterol in the cells. The rate of internal cholesterol may reduce by the inhibition of HMG-CoA reductase, it stimulates the production of additional LDL receptors (Bishop, 2010). Control of dietary intake is one of the easiest and least cost intensive means to achieve reductions in cholesterol (Henry's, 2011). However in this study, to test the effectivity of Ashitaba within seven (7) days, we didn't control the diet of the participants who have elevated blood cholesterol. We obtained a result that the intake of Ashitaba didn't lower the blood cholesterol. Therefore, the Ashitaba didn't exhibited inhibitory behavior against HMG-CoA reductase, a rate limiting enzyme in cholesterol biosynthesis. Thus, these findings suggest that while taking Ashitaba it is necessary to maintain low-fat and low-cholesterol diet and control the lifestyle to lower blood cholesterol. We concluded that Ashitaba is more potent in lowering blood glucose level than the blood cholesterol level.

CONCLUSION AND RECOMMENDATION

The present study was designed to compare the potency of *Angelica keiskei* (Ashitaba) on Anti-hypercholesterolemic and Anti-hyperglycemic effect on blood levels in Barangay Trapiche, Tanauan City Batangas. Ashitaba intake helps to lower the blood glucose level, although the opposite could be said for its effects on the blood cholesterol. In addition, the intake of Ashitaba within a short period did not appear to have any adverse effects on the blood glucose level. Although further research is needed to shed light on its other effects, these results indicate that Ashitaba may be a helpful and safe food. Ashitaba can also be tested on a bigger number of subjects to validate the current findings.

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