

PJN

ISSN 1680-5194

PAKISTAN JOURNAL OF
NUTRITION

ANSI*net*

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Effect of Various Doses of Cinnamon on Blood Glucose in Diabetic Individuals¹

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Abstract: The effect of cinnamon doses on blood serum glucose was studied in type 2 diabetic individuals for 60 days. Sixty type 2 diabetic individuals of both sexes and of age 48 ± 6.5 years were divided into 6 groups; each group was having 10 individuals. Groups 1, 2 and 3 were assigned for 1g, 3g and 6g cinnamon doses/day respectively. Groups 4, 5 and 6 were assigned for 1g, 3g and 6g placebo doses/day respectively. The doses were equally distributed over the day. Cinnamon and placebo were given in the form of capsules with breakfast, lunch and dinner. The doses were given for 40 days and after 40 days; there was a 20 days blank period. Fasting blood samples were taken on days 0 (starting day of the experiment) 20, 40 and 60 and blood serums were separated. The blood serum glucose of both the cinnamon and placebo groups were determined. The mean fasting serum glucose levels for cinnamon doses on days 0, 20, 40 and 60 were 208.7, 189.1, 156.5 and 176.6 mg/dl for 1 g cinnamon dose/day; 206.2, 178.4, 170.3 and 177.8 mg/dl for 3 g cinnamon dose/day and 233.9, 183.2, 166.4 and 205.7 mg/dl for 6 g cinnamon dose/day respectively. The cinnamon doses significantly ($P < 0.05$) reduced the mean fasting serum glucose levels while the placebo doses did not affect the serum glucose levels. In the light of this research, it is recommended that Type 2 diabetic individuals should use 1-3g cinnamon in their food preparations on regular basis. They can use cinnamon shakers for sprinkling of cinnamon powder on the curry in the plate. They can prepare cinnamon tea without sugar and can use it after meals. Also they can chew cinnamon bark after meals. This will keep their sugar level near to normal values.

Key words: Cinnamon, blood glucose, diabetic

Introduction

Diabetes mellitus is a chronic disorder of glucose metabolism resulting from dysfunction of pancreatic-beta cells and insulin resistance. It is still a serious health problem all over the world. Because the disease prevails in both genders and all age groups so, the general public has a concern about its control and treatment.

Natural products like spices have been used for taste and flavor development in food preparations. Some spices have an additional benefit of having role in carbohydrate metabolism (Khan *et al.*, 1990). Marles and Farnsworth (Marles and Fransworth, 1994) have reported that one- to two-thirds of the 1123 plants that affect blood glucose may be dangerous, and many of the phytochemicals are hypoglycemic due to metabolic or hepatic toxicity. However, medicinal plants have been used for diabetes safely and with reasonable success (Marles and Fransworth, 1994; Duke *et al.*, 1998).

Botanical products can improve glucose metabolism and over all condition of persons with diabetes not only by hypoglycemic effect but also by improving lipid metabolism, antioxidant status, and capillary function (Broadhurst, 1997). A number of medicinal/culinary herbs have been reported to yield hypoglycemic effects in subjects with diabetes. These include cinnamon, cloves, bay leaves, turmeric (Khan *et al.*, 1990), bitter

melon (Srivastava *et al.*, 1993; Raman and Lau, 1996), gurmar (Basakaran *et al.*, 1990; Shanmugasundaram *et al.*, 1990; Bishayee and Chatterjee, 1994), Korean ginseng (Sotaniemi *et al.*, 1995), onions and garlic (Koch and Lawson, 1996), holy basil (Rai *et al.*, 1997), and flaxseed meal (Cunnane *et al.*, 1993).

(Broadhurst *et al.*, 2000) re-evaluated the extract of cinnamon on insulin function in the insulin-dependent utilization of glucose using a rat epididymal adipocyte assay. Cinnamon was the most bioactive product. The glucose oxidation enhancing bioactivity was lost from cinnamon by polyvinylpyrrolidone (PVP) treatment, indicating that the active phytochemical were likely to be phenolic in nature. They concluded that the extract of cinnamon had improved the glucose and insulin metabolism.

Khan *et al.*, 1990 isolated an unidentified factor from cinnamon and termed this factor as insulin potentiating factor (IPF). They demonstrated that IPF increased the activity of insulin 3 fold in glucose metabolism in rat epididymal fat cells. (Anderson *et al.*, 2001) characterized this unidentified factor present in cinnamon as methyl hydroxy chalcone polymers (MHCP). They reported that MHCP found in cinnamon increased insulin dependent glucose metabolism roughly 20 fold *in vitro*. They explained that MHCP made fat cells more responsive to insulin by activating the

¹This project was funded by University Grants Commission/NWFP Agricultural University, Peshawar, Pakistan

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enzyme that causes insulin to bind to cells (insulin-receptor-kinase) and inhibiting the enzyme that blocks this process (insulin-receptor-phosphatase) leading to maximal phosphorylation of the insulin receptor, which is associated with increased insulin sensitivity.

However, those studies were conducted *in vitro*. There is a general view that the results of animal studies may not be applied to human. Therefore, this study was designed to see the effect of cinnamon on blood glucose in Type 2 diabetic individuals.

Materials and Methods

Location, sample size and criteria for registration of the study: The study was conducted in the department of Human Nutrition, NWFP Agricultural University Peshawar, Pakistan. Sixty type 2 diabetic individuals of both sexes and of age 40 years or older, who were residing in Peshawar city and its vicinity, were registered for the study. These diabetic individuals were registered at different times and at different locations, because diabetics were not available at one time. Only those diabetic subjects, who were not on insulin therapy, were not taking medicine for other health conditions and whose fasting blood glucose were in the range of 140-400mg/dl, were included in the study.

Preparation of cinnamon and placebo capsules:

Cinnamon and wheat flour were used for the preparation of cinnamon and placebo capsules. The required amount of cinnamon and wheat flour were purchased from the local market and ground finely. The ground cinnamon and wheat flour were given to Mehran Traders, Pharmaceutical Suppliers, Khalid Market, Charsadda Road, Peshawar for preparation of the capsules. Capsules were prepared and each capsule was having 500mg of cinnamon or wheat flour. Packages of 40 (1g or 2 capsules/day for 20 days), 120 (3g or 6 capsules/day for 20 days) and 240 (6g or 12 capsules/day for 20 days) of both the cinnamon and placebo capsules were prepared in plastic bags.

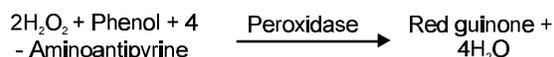
Protocol of the study: The study was conducted for 60 days. The 60 type 2 diabetic individuals were divided into 6 groups. Each group was having 10 individuals. Groups 1, 2 and 3 were assigned to cinnamon and groups 4, 5 and 6 were assigned to placebo. The individuals were allowed to take their routine diet and usual diabetic medicine. Groups 1, 2 and 3 were given 1g, 3g and 6g cinnamon/day respectively for 40 days. From day 41 to 60, no dose of cinnamon was given. On similar pattern, 1g, 3g and 6g placebo/day were given to groups 4, 5 and 6 respectively for 40 days. The 1g doses of cinnamon and placebo were spread over the day as 0.5g (1 capsule) at the time of lunch and 0.5g (1 capsule) at the time of dinner. The 3g and 6g doses of cinnamon and placebo were spread over the day as 1g (2 capsules) and 2g (4 capsules) at the time of breakfast, lunch and

dinner respectively. The individuals were told to take the capsules immediate after breakfast and meals.

Collection of blood samples and biochemical analysis Approximately 5ml fasting blood samples were taken from each individual on day 0, 20, 40 and 60. Blood samples were transferred to sterilized centrifuge tubes and allowed for clotting at room temperature. The blood samples were centrifuged for 10 minutes in a centrifuge at 4000 rpm for serum separation. Serum samples were stored in freezer at 0 °C for later analysis of glucose. These tests were done in the Main Laboratory, Hayat Abad Medical Complex by using auto analyzer (Express plus, Ciba coming USA).

Determination of Glucose: Glucose was determined by the enzymatic calorimetric method of Trinder (Trinder, 1969). Auto analyzer (Express plus, Ciba coming USA) and Elitech kit were used. In this method, the enzymatic reaction is in two steps. In the first step, glucose is oxidized to gluconic acid and hydrogen peroxide in the presence of glucose oxidase enzyme. In the second step, red quinone is formed in the presence of peroxidase enzyme. The absorbance of this colored substance is taken and the concentration of glucose is calculated.

The enzymatic reactions are as follow:



Reagents:

Reagent 1:

Phosphate buffer, pH 7.40 100 mmol/l
Phenol 10 mmol/l

Reagent 2:

Glucose oxidase $\geq 10\,000$ U/l
Peroxidase ≥ 600 U/l
4-Amino antipyrine 270 $\mu\text{mol/l}$

Sample:

Serum free of hemolysis

Procedure: The working reagent was prepared by dissolving reagent 2 in reagent 1. This working reagent is stable for 1 month at 20-25 °C and for 3 months at 2-8 °C. The reagent reservoir was kept in the auto analyzer chamber. The wavelength was adjusted at 546 nm and the temperature was set at 37 °C. Cuvette of 1cm light path was used. Before using the auto analyzer, it was calibrated and both normal and abnormal control ranges were given. If the sample reading falls between these two ranges and the auto analyzer shows the current calibration, then it is in a position to work properly and to give accurate results. 10 μl sample and 300 μl working reagent was sucked and mixed automatically and the analyzer gave the optical density (OD) after a short incubation period.

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Table 1: Effects of Different Doses of Cinnamon on Blood Glucose

Group* of Diabetics	Doses of Cinnamon (g/day)	Mean Fasting Blood Glucose (mg/dl)**	
		Before Cinnamon Intake	After Cinnamon Intake
1	1	208.7 ^a	172.8 ^a
2	3	206.2 ^a	174.4 ^a
3	6	233.9 ^a	174.8 ^a

* = 10 individuals in each group, **= The figures in column No. 4 are the average of values on days 20 and 40. Means followed by different letters in rows are significantly different at P < 0.05 as determined by analysis of variance and LSD test.

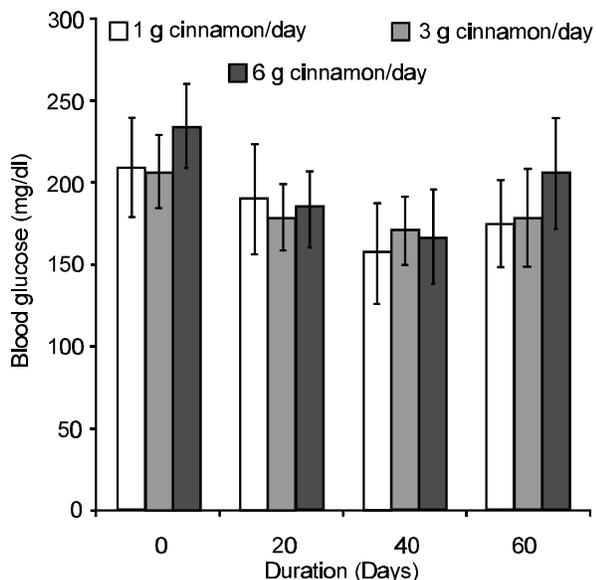


Fig. 1: Effect of cinnamon on blood glucose in diabetic individuals

Calculations:

Factor = n / OD

n = Standard concentration

n = 100 mg/dL

Glucose concentration = OD sample x factor

The calculations were done automatically.

Statistical Analysis: Two- way Analysis of Variance and Randomized Complete Block Design was used for statistical analysis (MSTAT-C).

Results and Discussion

Effect of cinnamon on blood glucose: The effect of various doses of cinnamon on the blood glucose levels of diabetic individual is given in Fig. 1. The glucose values on day 0 in Table 1 indicate the fasting blood glucose of diabetic individuals before the start of cinnamon capsules. So these glucose levels were control values for the study.

On the starting day of the experiment (day 0), the mean fasting blood glucose levels of the diabetic individuals of the 3 groups, assigned for 1g, 3g and 6g cinnamon

dose/day, were 208.7 mg/dl, 206.2 mg/dl and 233.9 mg/dl respectively. When the diabetic individuals of these groups used 1g, 3g and 6g cinnamon doses/day for 20 days, their mean fasting blood glucose level dropped to 189.1 mg/dl, 178.4 mg/dl and 183.2 mg/dl respectively. The data demonstrated that cinnamon doses had reduced the mean fasting blood glucose level in all the 3 groups. However, this reduction in glucose levels was not statistically significant (P<0.05) from the mean fasting blood glucose values on day 0. This was perhaps due to the large variability in the blood glucose levels of individuals in each group (Table 1). When the same individuals of the same groups used 1g, 3g and 6g cinnamon doses/day for another 20 days (total 40 days), their mean fasting blood glucose further dropped to 156.5 mg/dl, 170.3 mg/dl and 166.4 mg/dl respectively. Consumption of the various doses of cinnamon for 40 days significantly (P <0.05) lowered the mean fasting blood glucose levels of diabetic individual of all the 3 groups of cinnamon as compared to the mean fasting blood values of the diabetic individuals of the same groups at the start of the experiment (day 0). The mean fasting blood glucose levels of diabetic individuals of all the 3 groups were significantly (P<0.05) lower, when they used cinnamon doses for 40 days, than when they used cinnamon doses for 20 days, showing that longer use of cinnamon was more beneficial than shorter use of cinnamon.

It should be pointed out that 40 days consumption of cinnamon for treatment of diabetes is really a lengthy therapy and many diabetic individuals may not like such long treatment. Cinnamon is not a medicine but a spice and is used in food preparations for flavor and taste. So it is a part of food and one would not be tired of its use. The hypoglycemic effect of cinnamon is an additional benefit of cinnamon and is particularly important for type 2 diabetic individuals. In the light of this research, it is recommended that diabetic individuals should use cinnamon in their food preparations on regular basis. They can use cinnamon shakers for sprinkling of cinnamon powder on the curry in the plate. They can prepare cinnamon tea without sugar and can use it after meals. Also they can chew cinnamon bark after meals. This will keep their sugar level near to normal values. The mean fasting blood glucose levels of the diabetic

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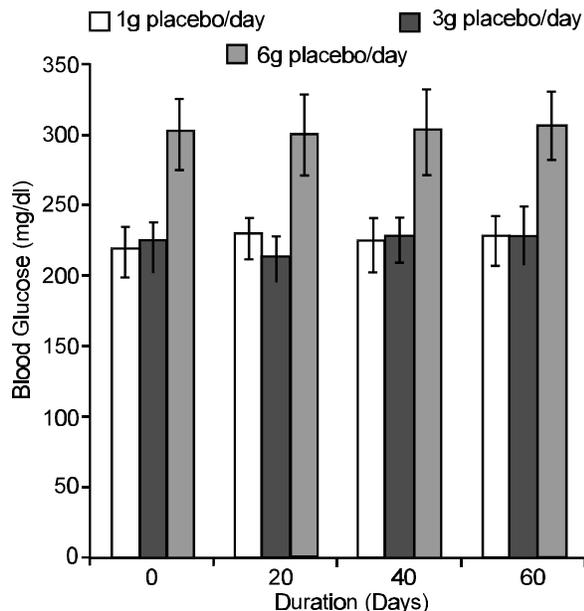


Fig. 2: Effect of placebo on blood glucose in diabetic individuals

individuals of all the 3 groups on day 60 (when they were not using cinnamon for the last 20 days) were 174.6 mg/dl, 177.8 mg/dl and 205.7 mg/dl respectively. The mean fasting blood glucose levels of the diabetic individuals of all the 3 groups on day 60 were significantly lower ($P < 0.05$) than the mean fasting blood glucose levels of the diabetic individuals of all the 3 groups on day 0, but were non-significantly higher than the mean fasting blood glucose levels of the diabetic individuals of the 3 groups on days 20 and 40. This trend was justified as cinnamon was potentiating the function of insulin in carbohydrate metabolism and when cinnamon was not present, then insulin was not oxidizing glucose at the same rate as it was oxidizing it in the presence of cinnamon. Khan *et al.*, 1990 has reported that an unidentified factor is present in cinnamon that potentiates the action of insulin in carbohydrate metabolism. They termed this factor as insulin potentiating factor (IPF). Broadhurst *et al.*, 2000 reconfirmed the presence of this factor in cinnamon. This hypoglycemic effect of cinnamon may or may not be like other hypoglycemic drugs.

The gradual increase in the mean fasting blood glucose levels of the individuals, who were not taking cinnamon doses for the last 20 days, indicated that cinnamon had lasting hypoglycemic effect in diabetic individuals. The cinnamon dose might have introduced some biochemical change at the cellular level and as a result the mean fasting blood glucose did not rise to the level where it was at the start of the experiment (day 0). We are not sure yet, but it seems that cinnamon might have

brought some biochemical/physiological changes in the sites of resistance to insulin, transfer of glucose through cell membrane, enzyme system of carbohydrate metabolism and receptor sites. If the assumption of the authors, that the biochemical/physiological changes in the sites of resistance to insulin or other parameter is true, then a permanent cure for diabetes mellitus is present in cinnamon therapy.

Symptoms of insulin resistance include a decreased stimulation of muscle glycogen synthesis, defects in glycogen synthase activity, hexokinase activity and glucose uptake (Cline *et al.*, 1999). In addition, altered enzymatic activities, such as an increased phosphatase activity and/or seryl phosphorylation of the insulin receptor substrate by glycogen synthase kinase 3 (GSK-3), have also been shown to be involved in some cases of type 2 diabetes mellitus (Begum *et al.*, 1991; Nativ *et al.*, 1994; Eldar and Krebs, 1997).

Dephosphorylation of the receptor β -subunit is associated with the deactivation of its kinase activity and therefore is associated with insulin signal down-regulation (King *et al.*, 1991). Jarvill-Taylor, *et al.*, 2001 concluded from their study that methylehydroxy chalcone polymers (MHCP) was an effective mimetic of insulin. MHCP might be useful in the treatment of insulin resistance and in the study of the pathways leading to glucose utilization in cells.

Cinnamon extracts have also been shown to improve insulin receptor function by activating insulin receptor kinase and inhibiting insulin receptor phosphatase, leading to increase insulin sensitivity (Imparl-Radosevich *et al.*, 1998). Khan *et al.*, 1990 isolated an insulin-potentiating factor (IPF) from cinnamon. This unidentified factor increased the activity of insulin 3 fold in glucose metabolism in rat epididymal rat fat cell. Anderson *et al.*, 2001 characterized this unidentified factor present in cinnamon as methylehydroxy chalcone polymers (MHCP). They explained that MHCP made fat cells more responsive to insulin by activating the enzyme that causes insulin to bind to cells (insulin-receptor-kinase) and inhibiting the enzyme that blocks this process (insulin-receptor-phosphatase) leading to maximal phosphorylation of the insulin receptor, which is associated with increased insulin sensitivity.

To verify that the drop in the mean fasting blood glucose level was not due to psychological effect of the cinnamon capsules, a parallel placebo trial where placebo capsules were given to the groups of diabetic individuals in the pattern of cinnamon trial. Blood samples were collected and analyzed. The doses of placebo did not affect the glucose level (Fig. 2).

The effect of different cinnamon doses on the mean fasting blood glucose is given in Table 1. There was no significant effect of cinnamon doses on the concentration of glucose in type 2 diabetic individuals. This indicated that small doses of cinnamon like 1-

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3g/day were as good as 6g/day in reduction of glucose level in diabetic individuals. The usual addition of cinnamon as a spice to food preparations was sufficient for the additional benefit of reducing glucose level in diabetic individuals.

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