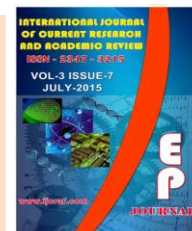




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Evaluation effect of Cinnamon-Plus on HbA1C of patients with Diabetes

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A B S T R A C T

Diabetes is a metabolic disease affecting the metabolism of glucose, lipid and protein and a major health problem with increasing prevalence in the world. Inadequate response to conventional treatment of diabetes has promoted the use of herbal medicines. The aim of this study was determine of Cinnamon plus on HbA1C and BMI of patients with diabetes. In clinical trial study that performed in internal medicine of Tabriz University of Medical Sciences on patients with diabetes, the effects of Cinnamon plus on HbA1C and BMI of patients with diabetes type 2 evaluated. In 70 studied patients in both group, significant difference was not found secondary FBS and HbA1C level in case group into primary level of them. significant difference was not found secondary FBS and HbA1C level in control group into primary level of them. In our study, in patients underwnt Cinnamon plus, we found decrease in FBS and HbA1C level in after treatment than before treatment, but this difference was not statistically significant. In contrast, in the control group patients, level of FBS and HbA1C increased at after treatment than before treatment, but this difference was not statistically significant, which represents a beneficial effect of Cinnamon Plus on patients.

Introduction

Diabetes is a metabolic disease, affecting glucose metabolism, body fat and protein. With an increasing prevalence rate throughout the world, it is considered a major health issue, causing such complications as nephropathy, neuropathy, retinopathy, and loss of vision (1-3). In 2000, DM-2 had a global prevalence rate of

approximately 2% for all ages. It is now estimated that, by 2003, this figure would reach to 4.4%, equaling to a total number of 366 million individuals suffering from DM-2 (4-5).

Among the matters that need to be taken into account in diabetes management are:

changing lifestyle, including the adoption of healthy diets, doing exercises, and the consumption of oral hypoglycemic drugs (6).

Although oral hypoglycemic drugs and insulin are regarded as the pillars of diabetes treatment, their side effects, inefficacy in the adequate prevention and control of the disease complications, as well as their reduced effectiveness over time has prompted researchers to investigate and develop more modern and promising approaches to controlling this disease and its prospective complications (7).

In the United States, about 2-3.6 million individuals use complementary and alternative medicine (CAM) due to the inadequacy of some of the conventional methods for treating diabetes. Of the various methods of CAM therapy for treating diabetes, the most amount of attention is being paid to herbal and nutritional therapies (8).

The Iranian traditional medicine, which was disregarded for a period of time, is a holistic medical approach with a centuries-old history. Today, this approach has been revived by the efforts of its admirers and on account of the recommendation put forward by the World Health Organization to the effect that, indigenous knowledge be developed and national methods of CAM therapy be utilized. To this end, the country's reputable universities are engaging in the training of medical specialists dedicated to this field.

Cinnamon, with the scientific name *Cinnamomum zeylanicum*, is among the plants with seemingly hypoglycemic properties. It was demonstrated that, cinnamon extracts resulted in increased glucose consumption, glycogen

accumulation, and phosphorylation on the part of insulin takers, all of which contributes to an increased sensitivity to insulin (9). Furthermore, Sheng et al. (10) demonstrated that, cinnamon lowered blood lipids and glucose levels in laboratory mice. Cinnamon has long been applied in Asian and European herbal medicine. It has been demonstrated in some studies that, the insulin-like effect of this plant can potentially lower blood glucose levels (11-14). Yet, there are some debates with regards to this claim.

Studies have shown that, condiments such as cinnamon, cloves, nutmeg, green tea, and oregano produce insulin-like effects, with cinnamon being the most effective one (15). Various studies within the laboratory environment have shown that, a water-soluble polyphenol polymer known as methyl hydroxychalcone is released from cinnamon, producing an effect similar to that obtained by antioxidants in environments outside the human body (15). For years, researchers have concentrated on discovering chemical compounds that prevent non-enzymatic glycosylation of proteins, and that lack disturbing side effects. To this end, specific attention has been paid to medicinal plants. The use of plants in treating diabetes is an old-age practice. Researchers have been attracted by the use of plants in the prevention and control of diabetes, especially in individuals with high levels of blood sugar and those with glucose intolerance (16). Today, special consideration is being given to different food additives. The reason why these compounds are deemed fascinating is that, they are herbally grounded and have a wide range of applications in different diets. Cinnamon is a pleasant, aromatic plant with such chemical compounds as volatile oils, cinnamaldehydes, terpenes, cinnamyl alcohol, limonenes, phellandrenes, and

safroles (17). This plant has various medicinal properties such as, antispasmodic, anti-tympanites, anti-diarrheal, antioxidant-like, and antibacterial (18). Some studies have suggested that the existing polyphenols in cinnamon prevent the formation of (advanced) glycation end products within the blood serum (19). Conventional condiments such as cinnamon, turmeric, clove, and tea displayed insulin-like properties in laboratory studies (19-20). It has been demonstrated in animal and laboratory studies that, cinnamon acts as an insulin stimulant (21). In 1990, it was reported that cinnamon compounds enhanced insulin action and reduced insulin resistance (22). Cinnamon extracts enhance insulin action up to 20 times. The existing polyphenols in cinnamon increase glucose metabolism in mice fat cells up to several times (23). Strong evidence suggests that polyphenols in cinnamon stimulate insulin-like activity in animal and human cells (24). Several clinical studies have been published on the effects of cinnamon, with contradictory results.

Studies have shown that the daily consumption of three different amounts of cinnamon, i.e. 1, 3, and 6 grams, respectively, for 60 days reduces the mean levels of fasting blood sugar (FBS) (25). While, another study concluded that the daily consumption of 1 gram of cinnamon for 3 months did not cause any significant change in the fasting blood sugar or glycosylated hemoglobin levels (26). Researchers point to an unknown factor existing in cinnamon which, they believe, enhances insulin action in carbohydrate metabolism (25).

Broadhurst et al. verified the existence of such a factor in cinnamon. This unknown factor enhances insulin action in glucose metabolism of epidermal adipose cells in

mice up to 3 times (21). The existing polyphenols in cinnamon have been identified as being regulators of insulin receptors in mice fat cells (23).

It has been confirmed in laboratory studies that, cinnamon extracts increase the phosphorylation activity of beta-cell insulin receptors, while simultaneously decreasing tyrosine phosphatase activity; hence, displaying insulin-like properties (27). Some studies have demonstrated that, similar to insulin, the existing polyphenols in cinnamon stimulate glucose uptake and glycogen biosynthesis by activating the glycogen synthase enzyme and preventing the activities of glycogen synthase kinase (28).

Since the identification of practical medicinal plants in treating DM-2 could result in a more widespread adoption of them by diabetic patients, determining such plants could promote a desirable evolution in treating DM-2. Therefore, the present study was designed and conducted with the objective of comparing the effects of cinnamon and placebo on the glycosylated hemoglobin (HbA1c) levels in patients with DM-2. The purpose behind the present study was to determine the effects of cinnamon on a more desirable control of HbA1c in patients with DM-2.

Materials and Methods

In a clinical trial carried out on patients with diabetes in Tabriz, the effects of Cinnamon-Plus on the HbA1c levels in patients with DM-2 was investigated.

Considering the 4.4% prevalence rate and the 95% diagnostic accuracy degree, 64 individuals were selected as the sample size of the present study using the related formula, which was ultimately expanded to

include 70 individuals so as to increase the degree of accuracy.

In this double-blind clinical trial conducted in Tabriz, the effects of Cinnamon-Plus in treating patients with diabetes, as well as its effects on the HbA1c and blood sugar levels in these patients were studied. A group of patients (the case group) were treated by Cinnamon-Plus 1g tablets (Manufactured by Borner Co, Germany) twice a day, and the control group patients were given placebos. The effects of the treatments were studied after 3 months of administration. Cinnamon-Plus tablets were given to patients in the intervention group alongside the specified routine treatments for them, i.e. they were not deprived of receiving necessary treatments.

Before the initiation of the treatment, necessary information, such as laboratory parameters and HbA1c levels were examined. Subsequently, the patients in the case group were treated by cinnamon extracts, and the ones in the control group received placebos.

Furthermore, both groups were homogenous in terms of the received treatments, and were homogenized at the beginning of the study in terms of the parameters under study.

The patients were, first, grouped randomly by a third party, with both the patients and the researcher being unaware of the specific group in which individual patients were placed.

Exclusion Criteria

Pregnant women, patients with DM-1, patients with Chronic Renal Failure (CRF), under-18 and above-65 individuals, patients with higher-than-8 HbA1c levels, and those with higher-than-140/90 blood pressure.

This clinical trial has been registered on IRCT.ir with the number IRCT2015010713612N4.

Ethical Considerations

No aggressive action was performed on the patients under study. In addition, no alteration was made in the treatment process of the patients, and no additional cost was enforced on them for Cinnamon-Plus tablets. Cinnamon-Plus tablets were made available to the patients by the researcher free of charge, and all information about the patients will be kept confidential.

Informed consents were obtained from the patients after providing them with the necessary information and a full explanation of the study and its objectives, using a clear, intelligible language. In the case of unlettered patients, informed consents were obtained with the assistance of their literate escorts. The patients were assured that participation in the present study was completely optional, and that they could withdraw from it at any time.

Results and Discussion

In this study, the effects of cinnamon extracts on FBS and HbA1C levels in patients with diabetes were investigated, yielding the following results:

The mean age of the patients in the case and control groups were 57.10 ± 0.80 and 58.87 ± 7.91 years, respectively ($P=0.473$).

20 patients from the case group and 18 others from the control one were males. 15 patients from the case group and 17 others from the control one were females ($P=0.243$). The results obtained from the laboratory findings at the beginning and end of the study are presented in tables 1 to 3.

The mean levels of primary and secondary FBS in the case group patients were 134.71±44.49 mg/dl and 132.03±30.24 mg/dl, respectively (P=0.448).

The mean levels of primary and secondary HbA1c in the case group patients were 7.25±1.01 and 7.06±0.85, respectively (P=0.207). The mean levels of primary and secondary FBS in the control group patients were 120.85±31.19 mg/dl and 129.82±42.28 mg/dl, respectively (P=0.283).

The mean levels of primary and secondary HbA1c in the control group patients were 7.28±1.40 and 7.47±1.43, respectively (P=0.361).

In some studies, stimulation of insulin secretion and prevention of cellular resistance increase to insulin have been identified as the effects of cinnamon. Furthermore, it has been demonstrated that cinnamon could stimulate glucose uptake

and glycogen synthesis. With respect to the effects of cinnamon on blood glucose levels, however, various trials have yielded dissimilar results, in a way that, the debates on this matter are still ongoing.

Cinnamon has long been applied in Asian and European herbal medicine. It has been demonstrated in some studies that, the insulin-like effect of this plant can potentially lower blood glucose levels (11-14). Yet, there are some debates with regards to this claim.

Sheng et al. demonstrated that, cinnamon could lower blood fat and glucose levels in mice (10). In another study conducted by Khan et al. in Pakistan, it was revealed that the daily consumption of 1, 3, and 6 grams of cinnamon for a period of 40 days could significantly lower glucose, cholesterol, triglyceride, and LDL levels in patients with DM-2 compared to the control group (11).

Table.1 Laboratory parameter of patients between two groups

	Group		P
	Case	Control	
FBS Before	134.71 ± 44.49	120.86 ± 31.19	0.136
HbA1C Before	7.25 ± 1.02	7.29 ± 1.40	0.907
FBS After	132.03 ± 30.25	129.83 ± 42.28	0.807
HbA1C After	7.06 ± 0.85	7.48 ± 1.44	0.157
TG	174.00 ± 68.82	175.43 ± 93.32	0.946
Choll	178.00 ± 48.31	172.47 ± 45.20	0.649
HDL	43.83 ± 10.34	46.10 ± 9.14	0.273
Cr	1.20 ± 0.72	0.97 ± 0.19	0.093

Table.2 Laboratory Findings of Intervention Group

	Intervention Group		P
	Before	After	
FBS	134.71 ± 44.49	132.03 ± 30.25	0.448
HbA1C	7.25 ± 1.02	7.06 ± 0.85	0.207

Table.3 Laboratory Findings of Control Group

	Control Group		P
	Before	After	
FBS	120.86 ± 31.19	129.83 ± 42.28	0.283
HbA1C	7.29 ± 1.40	7.06 ± 0.85	0.361

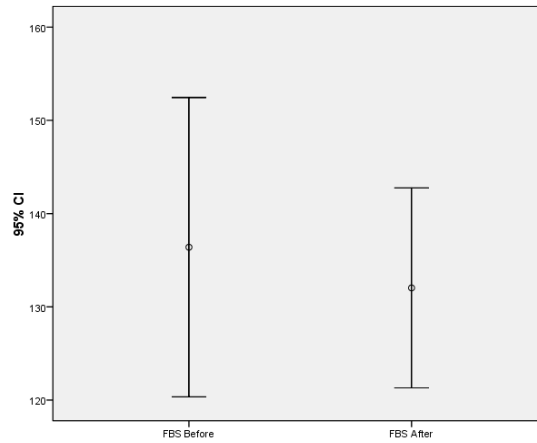


Chart.1 Distribution of FBS level in intervention group at before and after of treatment

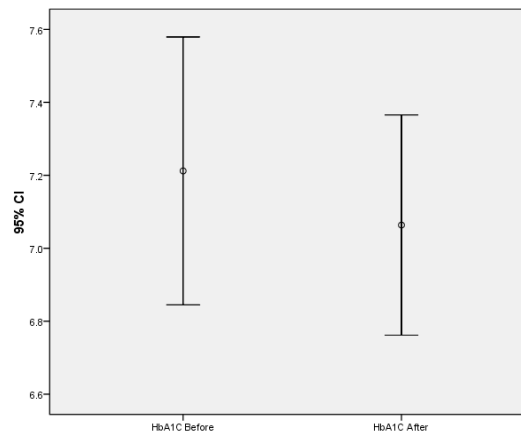


Chart.2 Distribution of HbA1C level in intervention group at before and after of treatment

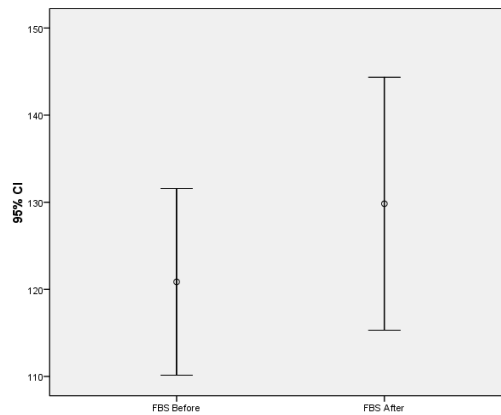


Chart.3 Distribution of FBS level in Control group at before and after of treatment

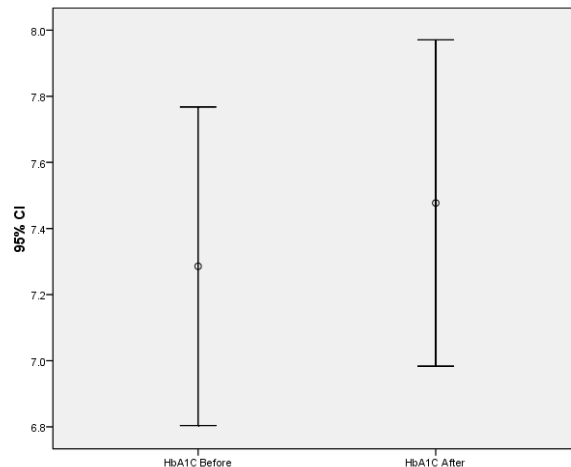


Chart.4 Distribution of HbA1C level in Control group at before and after of treatment

In a study carried out by Mang et al, the consumption of 3 grams of cinnamon per day for a period of 4 months merely lowered blood glucose levels, with no effect on HbA1c and blood fat levels. They concluded that, the consumption of cinnamon in diabetic patients with poor glycemic control is averagely effective on blood glucose levels (29).

In another research conducted by Blevins et al, the effects of consuming 1 gram of cinnamon per day for a period of 3 months on HbA1c, fat, and blood sugar levels were studied, with no statistically significant reduction observed in these indicators (30). No significant change was also noticed in our study in the levels of HbA1c and FBS in both the case and control group patients.

In a meta-analysis of several studies undertaken by Baker et al, it was determined that cinnamon failed to reduce the levels of blood glucose, lipid, and HbA1c more than placebos did (31). In a study carried out by Altschuler et al. on patients with insulin-dependent diabetes mellitus (IDDM), the consumption of cinnamon did not leave any beneficial effect on HbA1c levels compared to the control group (32). However, Crawford et al. reported the daily

consumption of 1 gram of cinnamon to be beneficial in lowering HbA1c levels in patients with DM-2 (33).

In our study, a decrease in the levels of FBS and HbA1c in the patients treated with cinnamon extracts was observed, although the difference was not statistically significant. Peng et al. realized that the existing polyphenols in cinnamon prevent the formation of (advanced) glycation end products within the blood serum (19).

Anderson et al. described the existing unknown factor in cinnamon as methyl hydroxychalcone polymer (MHCP). They went on to explain that, MHCPs sensitize fat cells to insulin by activating the tyrosine kinase of the insulin receptor and preventing the activities of the tyrosine phosphatase of the insulin receptor, leading to a blockage of insulin action. This, in turn, results in the phosphorylation of insulin receptor, and consequently, the increase of insulin sensitivity (34).

It has been confirmed in laboratory studies that cinnamon extracts increase the phosphorylation activity of beta-cell insulin receptors, while simultaneously decreasing tyrosine phosphatase activity; hence, displaying insulin-like properties (35).

Some studies have demonstrated that, similar to insulin, the existing polyphenols in cinnamon stimulate glucose uptake and glycogen biosynthesis by activating the glycogen synthase enzyme and preventing the activities of glycogen synthase kinase (36).

Blevins et al. studied the effects of cinnamon on the levels of blood sugar, lipid, and HbA1c in 58 patients with DM-2. The results suggested that, the consumption of 1 gram of cinnamon per day for a period of 3 months did not produce a significant change in the levels of blood sugar, lipid, and glycosylated hemoglobin (37), corresponding to the findings of the present study.

Altschuler et al. studied the effects of cinnamon on HbA1c levels in 72 adolescent patients with DM-1. The results suggested that, the consumption of a gram of cinnamon per day for a period of 90 days did not bring about a significant change in the levels of glycosylated hemoglobin in both the cinnamon and placebo groups (38).

In the study conducted by Haghghian in Tabriz, the daily consumption of 1.5 grams of cinnamon for 60 days lowered the mean glucose and glycosylated hemoglobin levels to a significant degree (39). Yet, in the study conducted by Zahmatkesh in Yazd, the daily consumption of 1 gram of cinnamon for 60 days did not significantly reduce the mean glucose and glycosylated hemoglobin levels (40).

In our study, a post-treatment decrease in HbA1c and FBS levels in patients treated with cinnamon extracts was observed, yet the difference was not statistically significant. On the other hand, an increase in HbA1c and FBS levels in the control group patients was noticed after the conclusion of the study, which was also not statistically significant. This is an indicator of the

beneficial effects of cinnamon extracts for patients with DM-2.

Conclusion

No significant difference was noticed in the secondary mean levels of FBS and HbA1c in the case group patients, compared to their primary mean levels. Furthermore, no significant difference was noticed in the secondary mean levels of FBS and HbA1c in the control group patients, compared to their primary mean levels. In our study, a post-treatment decrease in HbA1c and FBS levels in patients treated with cinnamon extracts was observed, yet the difference was not statistically significant. On the other hand, an increase in HbA1c and FBS levels in the control group patients was noticed after the conclusion of the study, which was also not statistically significant. This is an indicator of the beneficial effects of cinnamon extracts for patients with DM-2.

Suggestions

Considering the obtained results, the consumption of Cinnamon-Plus in diabetic patients is advisable. Moreover, it is suggested that other studies be carried out with larger sample sizes and longer consumption periods.

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