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Original Research Article

Reduction of Cholesterol and Fasting Blood Sugar Levels by One Month Supplementation of Fresh Garlic in Diabetic Libyan Patients: A Double Blind, Baseline Controlled Study.

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ABSTRACT:

Background: The therapeutic effects of fresh garlic remain controversial. The aim of this study is to investigate whether supplementation of fresh garlic could improve blood glucose and cholesterol profile in Libyan diabetic patients with moderate blood cholesterol.

Methods: Forty-six diabetic patients were randomly assigned to either fresh garlic alone (≈ 2 grams/day), or fresh garlic in combination with glibenclamide taken on an empty stomach every morning for a month. Serum blood glucose, cholesterol and blood pressure were measured before starting treatment and after the end of the treatment period.

Results: Fresh garlic alone was able to decrease the mean serum cholesterol levels by 26 mg/dl (84% of the original base values), while the combination of fresh garlic and glibenclamide produced a 28 mg/dl decrease in the mean serum cholesterol (85% of the original base values). Fresh garlic alone was able as well to decrease the mean blood glucose levels by 20 mg/dl (85% of the original base values), while the combination of fresh garlic and glibenclamide produced a 60 mg/dl decrease in the serum glucose levels (72% of the original base values). Neither treatment had a significant effect on the mean systolic or diastolic blood pressures after 30 days of treatment.

Conclusion: Administration of fresh garlic every morning for a month significantly reduced the blood cholesterol and fasting blood glucose levels in diabetic patients. Thus administering dietary fresh garlic daily to diabetic patients might have cardio-protective effects on diabetic patients.

Keywords: garlic, cholesterol, blood glucose, diabetes mellitus, Libya.

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INTRODUCTION

Reducing the burden of cardiovascular mortality and morbidity in diabetic patients should begin with treatment of elevated blood cholesterol levels and high blood pressure (BP) [1]. Diabetes, lipid metabolism disturbances and/or hypertension [2] are risk factors for cardiovascular disease (CVD) [3]. CVD remains the leading cause of death in the United States [1]. Potentially many of these CVD risk factors are partially remediable or preventable with treatment, education and dietary intervention [4]. In animal models of diabetes, hypercholesteremia and hypertension, life style changes particularly dietary intervention have been shown to have protective effects [5-8].

In hypercholesteremic mice, allicine, one of the active ingredients of garlic, reduced blood cholesterol and triglycerides [8-10]. This demonstrates the potential value of garlic as a candidate in protecting against atherosclerosis. The therapeutic effect of garlic could be, at least partially, due to attenuation of oxidative stress [10].

In the two-kidney-one-clip (2K-1C) Goldblatt model (a type of unilateral reno-vascular stenosis hypertension), garlic (aqueous extract) fed female Sprague Dawley (SD) rats experienced lower systolic BP when compared with water vehicle-fed animals [11, 12]. Moreover, in hypertensive rats, a daily dose of alcohol garlic extract for 18 weeks has been shown to attenuate systolic BP (132-145 mmHg vs. 186 mmHg in control) [13]. Although the mechanism(s) of the beneficial effects of garlic have not yet been fully explained, the antioxidant properties of garlic seem to be involved in these effects [12].

Consistent with the in-vivo studies, in-vitro evidence suggested that garlic extract decreases reactive oxygen species generation [14], while it increases glutathione synthesis [15]. Consequently, garlic reduces methylglyoxal formation [16] and lipid oxidation [17]. Therefore, in many pathological conditions such as diabetes, atherosclerosis and hypertension, phase II protein inducers, such as ellagic acid, increase phase II

proteins (cytoprotective proteins), ameliorating conditions associated with oxidative stress [18, 19].

The in-vitro and in-vivo studies taken together strongly suggest that the bioactive compound in garlic can be a good candidate in reducing cardiovascular complications in humans. This work attempts to compare the therapeutic benefits of fresh garlic regarding blood glucose, cholesterol levels and blood pressure in diabetic patients with moderate hypercholesteremia.

METHODS AND MATERIALS

Study design

This is a one-month randomized baseline-controlled study. The participants were out-patients at Benghazi-Diabetic Center. The participants were selected, if they met the entry criteria. During the participants' visit to the out-patient diabetic clinic, informed consent was reviewed and signed. Forty-six diabetic patients were randomly assigned to either fresh garlic alone (n=23), or fresh garlic in combination with glibenclamide (Daonil®) (n=23). Serum blood glucose, cholesterol and blood pressure (systolic and diastolic) were measured before starting treatment and after the end of the treatment period. Thus, the pre-treatment values served as baseline for comparison. A clove of fresh garlic (2 grams/day) was consumed on an empty stomach by each patient every morning for a month. During the study, some of the participants (n=4) dropped out of each group.

Before the start of the study, the participants were instructed to report any adverse effects, non-compliance, i.e., missing doses, or changes in their life style. The participants were also followed up by home phone calls.

Participants

Participants gave written informed consent. The study was approved by the Benghazi Diabetic Center ethical committee. The study participants were recruited at Benghazi Diabetic Clinic by personal interview from out-patients at Benghazi



Diabetic Clinic. The inclusion criteria were: male, between 30 to 71 years old, has been diabetic for at least three months, has a plasma LDL-C level ≥ 130 mg/dl at the time of screening and has a fasting blood sugar level ≥ 130 mg/dl at the time of screening. The exclusion criteria were: any of the above criteria not met, history of malignancy, current active liver disease, using lipid-lowering drugs, or using antihypertensive agents.

Test compound

A clove of fresh garlic (2 grams), purchased from the vegetable market in Benghazi, was chewed by the participant once daily every morning on an empty stomach for one month. The participants were instructed to report any adverse effects from taking the garlic.

Biochemical analysis

Fasting blood samples were collected from the participants at the beginning and at the end of the study. Fasting blood glucose level and total blood cholesterol were determined, using the standard hospital assays. In addition, blood pressure in sitting position was measured at the beginning and at the end of the study using adult automated sphygmomanometers.

STATISTICAL ANALYSIS

Statistical analysis was performed using Graphpad Prism version 6.05 (Graph pad Software Inc., CA, USA). Variables were compared by using paired t-test (two-tailed) and data are presented as the mean $\pm$ SE. The level of significance was set at $P < 0.05$.

RESULTS

The effect of raw garlic on blood glucose level, alone or in combination with glibenclamide is shown in Figure 1. A drop in blood glucose levels was observed, and this decrease was statistically significant in both groups ($*P < 0.05$), as compared to control values measured at zero time.

Figure 2 shows the effect of raw garlic on blood cholesterol levels. It is evident that raw garlic alone and raw garlic with glibenclamide, over 30

days, significantly attenuates the higher cholesterol level in both groups ($*P < 0.05$).

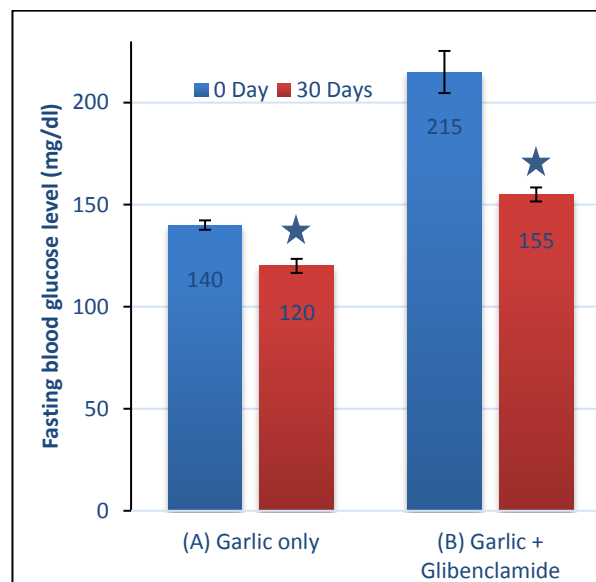


Figure 1: Effect of raw garlic alone or in combination over 30 days on blood glucose level. ($*P < 0.05$) from base-line values. Values are Mean $\pm$ SE.

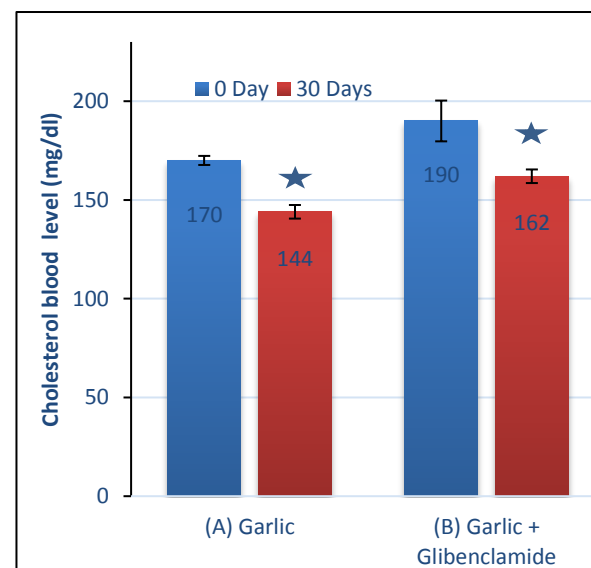


Figure 2: Effect of raw garlic alone or in combination over 30 days on serum cholesterol levels. ($*P < 0.05$) from base-line values. Values are Mean $\pm$ SE.

Table 1 shows the effects of raw garlic on systolic and diastolic blood pressure, respectively.

Garlic alone or with glibenclamide did not produce any change in the systolic or diastolic blood pressures.

Table 1: Effect of raw garlic alone or its combination with glibenclamide on blood pressure over 30 days. Values are presented as Mean±SE.

Treatment	Systolic B.P (mmHg)		Systolic B.P (mmHg)	
	0 TIME	After 30 days	0 TIME	After 30 days
Garlic alone	128±3.9	127±2.3	75±3.2	75±1.3
Garlic + Glibenclamide	130±2.7	130±1.8	80±3.0	76±2.5

DISCUSSION

In this baseline-controlled study, administration of 2 grams fresh garlic (*Allium sativum*) alone daily on an empty stomach to an adult diabetic patient reduced the mean fasting blood glucose level by 20 mg/dl (85% of the original values) when compared with the baseline pre-treatment control value. When compared with the pre-treatment control value, fresh garlic plus glibenclamide reduced fasting blood glucose by about 60 mg/dl (72% of the original pre-treatment control values, $P<0.05$). This is very important because strictly controlling hyperglycemia decreases the high burden of CVD in diabetic patients. Combination of garlic with metformin improves glycemic control in addition to antihyperlipidemic activity in diabetic patients [20].

For reducing blood total cholesterol, we establish that oral administration of fresh garlic to diabetic patients with hypercholesteremia reduced the mean blood cholesterol levels by 26 mg/dl ($P<0.05$), while when co-administered with glibenclamide, garlic reduced cholesterol by 28 mg/dl ($P<0.05$). Consistent with our study, combination of garlic with metformin improves glycemic control in addition to antihyperlipidemic

activity in diabetic patients [21]. Furthermore, a significant reduction of cholesterol (28 mg/dl) was observed when diabetic patients with dyslipidemia were given garlic twice daily for 12 weeks [22].

The results of previous studies have varied widely, ranging from no significant to very significant cholesterol lowering effects. In 2007, a study reported that a modest blood cholesterol reduction of 15.7 mg/dl compared with placebo when garlic was given over a treatment period of 8 to 24 weeks [23]. Consistent with the previous study, in 2014 other researchers reported that garlic intake reduces blood cholesterol by 16 mg/dl [24, 25]. In contrast, others have shown that garlic did not influence serum lipid of hyperlipidemic patients. Systematic reviews and recent studies provide evidence that garlic intake exhibited no significant effect on blood level of cholesterol [26, 27]. The heterogeneity of the results are partly due to the variety of garlic preparations used, poor standardization of products tested, the diversity of study designs employed and/or not publishing little effects or no effects observed [28, 29].

Diabetes like many other human diseases (e.g., obesity and atherosclerosis) is linked to oxidative stress modifications of biological molecules such as DNA, protein and lipids by reactive oxygen species, among them free radicals. Increased consumption of fruits and vegetables ameliorates cardiovascular diseases [30]. Meta-analysis shows that garlic preparation may lower blood pressure in hypertensive patients [31]. However, in this study we did observe no significant reduction of systolic or diastolic BP in the garlic and garlic + glibenclamide groups. Although different mechanisms may be involved in attenuating BP, an increase in cellular thiols, such as cysteine and glutathione [15], may induce smooth muscle relaxation and BP reduction. It has been reported that garlic intake enhances the activity of antioxidant enzymes [32], such as glutathione reductase (GR), glutathione-s-transferase (GST), glutathione peroxidase (GP) [33], catalase and superoxide dismutase (SOD) [34] in addition to



other mechanism(s) [35, 36]. Therefore, the antioxidant ability of garlic may be, at least partly, leading to reduction of hyperglycemia and suppression of lipid oxidation.

CONCLUSION

This study demonstrated that compared with baseline, fresh garlic was effective in reducing hyperglycemia and hypercholesterolemia in diabetic patients. Moreover, combination of fresh garlic with glibenclamide improves glycemic control. This is very important as the high burden of CVD may be reduced through simple diet intervention. Further studies should be conducted to explore the effect of fresh garlic as an adjunctive therapy in diabetic patients and as adjunctive therapy with statin in hyperlipidaemia patients.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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ملخص باللغة العربية

الحد من الكوليسترول ومستويات السكر في الدم بواسطة العلاج لمدة شهر بالثوم الطازج للمرضى الليبيين المصابين بداء السكري

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خلفية الدراسة: الآثار العلاجية للثوم الطازج لا تزال مثيرة للجدل. الهدف من هذه الدراسة هو التحقق من أن العلاج بالثوم الطازج يمكن أن يحسن مستوى الجلوكوز والكوليسترول في الدم لدى مرضى السكري الليبيين الذين يعانون من ارتفاع معتدل للكوليسترول في الدم. **طرق الدراسة:** تم علاج ستة وأربعين مريضاً مصاباً بمرض السكري عشوائياً إما بالثوم الطازج وحده (2 غرام / يوم)، أو الثوم الطازج في تركيبة مع غليبينكلاميد تؤخذ على معدة فارغة كل صباح لمدة شهر. وتم قياس مستوى الجلوكوز والكوليسترول في الدم وكذلك ضغط الدم قبل بدء العلاج وبعد انتهاء فترة العلاج.

نتائج الدراسة: كان الثوم الطازج وحده قادراً على خفض متوسط مستويات الكوليسترول في الدم بكمية 26 ملغ/لتر (84% من القيم الأساسية الأصلية)، في حين أن الجمع بين الثوم الطازج وغليبينكلاميد نتج عنه نقص في محتوى الكوليسترول في الدم بقيمة 28 ملغ/لتر (85% من القيم الأساسية الأصلية). وكان الثوم الطازج وحده قادراً أيضاً على خفض متوسط مستويات الجلوكوز في الدم بنسبة 20 ملغ/لتر (85% من القيم الأساسية الأصلية)، في حين أن الجمع بين الثوم الطازج و غليبينكلاميد أنتج نقصاً في كمية الجلوكوز في الدم بقيمة 60 ملغ/لتر (72% من القيم الأساسية الأصلية). لم يكن للعلاج بالثوم وحده أو الثوم الطازج وغليبينكلاميد أي تأثير على متوسط ضغط الدم الانقباضي أو الانبساطي بعد 30 يوماً من العلاج.

الاستنتاج: تناول الثوم الطازج كل صباح لمدة شهر خفض بشكل ملحوظ نسبة الكوليسترول ومستويات السكر في الدم لمرضى السكري. وبالتالي فإن تناول الثوم الطازج يومياً لمرضى السكري قد يكون له آثار وقائية على مرضى السكري.

الكلمات المفتاحية: الثوم، الكوليسترول، الجلوكوز في الدم، داء السكري، ليبيا.