Effects Of Raw Garlic (*Allium Sativum*) On Hyperglycemia In Patients With Type 2 Diabetes Mellitus

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Summary

Diabetes mellitus is a group of metabolic disorders that results in hyperglycemia due to insufficient insulin utilization or decreased insulin production. *Allium sativum,* commonly known as "Garlic", belongs to the family Lilliaceae, an indigenous antidiabetic plant popularly used in South India for diabetes mellitus. They possess antimicrobial, hypolipidemic, antihyperglycemic, antioxidant, antineoplastic and antithrombotic effects. Garlic has been claimed to be an excellent remedy for cancer and heart disease. This clinical trial was conducted on newly diagnosed type 2 diabetic patients (n=20). Diabetic patients were selected from Ehrlich laboratory, Chennai and were divided in to two groups each comprising of 10 patients. An equal number of healthy groups were also investigated. The subjects were male ranging in age from 40-60 years. Diabetic patients were received raw garlic 3 small sized raw garlic cloves (1 clove = 1.2g) once orally daily in the morning in fasting condition (12-14 hrs) for 30 days. After 30 days of treatment, the blood samples were obtained from all groups of subjects by venous arm puncture into heparinised tubes from all groups of subjects. The serum was separated and the biochemical factors were measured. The results showed a significant reduction in blood glucose level, lipid metabolism and significant improvement in Superoxide dismutase (SOD), Catalase (CAT) and Glutathione peroxidase (GPx) in erythrocytes of diabetic patients when compared with normal. Garlic decreases the serum cholesterol, triglyceride (TG) and low-density lipoprotein (LDL) while increasing the high-density lipoprotein (HDL) fraction. The results of the present study suggest that raw garlic exerts its antidiabetic effect through its potent antioxidant agents (gallo-ellagi) tannoids. Based on these results it is concluded that garlic is a more potent antidiabetic effect.

Key words: Antioxidants, Garlic, Antidiabetic, Lipidperoxidation.

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Introduction

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia and associated with increased free-radical activity. The mechanisms of free-radical production include glucose autoxidation, protein glycation, advanced glycated end products formation, and activation of polyol pathway, ultimately resulting in oxidative stress in a variety of tissues[1]. Reactive oxygen species (ROS) are produced continuously in living cells as byproducts of normal cellular metabolism of xenobiotics as well as during exposure to high temperature or radiation. Over production of ROS are implicated in the pathophysiology of various diseases including cancer[2]. The presence of oxygen free radicals and the simultaneous decline of antioxidant defence mechanisms observed in diabetic patients could promote the development of late diabetic complication. Elevated lipid peroxidation byproducts and declined antioxidants were reported in both human and experimental diabetes[3]. Certain natural substances have the potential to reduce the detrimental effect of a number of cardiovascular risk factors.

Garlic (Allium sativum) has been found to have a wide range of medicinal properties ranging from antibacterial to anticancer effects[4,5]. Garlic was known to be effective in decreasing cholesterol[6,7] and can inhibit LDL oxidation[8]. Garlic has also shown to have antioxidant properties, which could have a protective nature against gastrointestinal neoplasias, against blood clots (antiplatelet action) due in part to the compounds alliin and ajoene, which have fibrinolytic activity[9]. S-allyl cysteine Sulphoxide (SACs), a sulphur containing amino acid of garlic which is the precursor of allicin and garlic oil has antidiabetic effects in alloxan diabetic rats. It decreased concentration of serum lipids, blood glucose and activities of serum enzymes, like alkaline phosphatase (ALP), acid phosphatase and lactate dehydrogenase and liver glucose-6-phosphatase[10]. It protects DNA against free radical-mediated damage and mutations. Lipid peroxides, uric acid, blood glucose, total lipid, triglycerides and cholesterol were decreased significantly after treatment with garlic oil, also on liver and kidney lipid peroxides decreased significantly after garlic oil treatment[11]. Hence, in this study, we have evaluated the hypoglycemic effects of garlic in patients with type 2 diabetes mellitus.

Material and Methods

Twenty newly diagnosed diabetic patients, ranging in age from 40-60 years from Ehrlich laboratory Chennai, were chosen for this study. An equal number of healthy subjects (volunteers) were also investigated. Diabetic patients were received 3 small sized raw garlic cloves (1 clove = 1.2g) once orally daily in the morning in fasting condition (12-14 hrs) for 30 days. After 30 days of treatment, the blood samples were obtained from healthy individuals and diabetic patients before and after the treatment with raw garlic by venous arm puncture into heparinised tubes. Heparinised blood samples containing serum and plasma were separated by centrifugation at 3000 rpm for 5min and buffy coat was removed and packed cell washed three times with physiological saline. Serum was separated and analysed for the biochemical parameters: Triglyceride, HDL, cholesterol and LDL. Enzymatic antioxidants and TBARS were estimated in plasma and erythrocytes in all groups.

Biochemical analysis

Blood glucose, Triglyceride, cholesterol, HDL and LDL were estimated by the method of Autoanalyser. Lipid peroxides in plasma were assayed by the method of Yagi[12]. TBARS in plasma and erythrocytes membrane was estimated by the method of Donnan[13]. Superoxide dismutase activities were estimated by the method of Kakkar[14]. Catalase and

Glutathione activities in erythrocyte hemolysate were estimated by the method of Sinha and Rotruck [15,16].

Statistical analysis

All quantitative measurements were expressed as means ± SD for healthy and normal subjects. The data were analyzed using one way analysis of variance (ANOVA) followed by students 't' test by using statistical package of social sciences (SPSS) version 10.00 for windows.

Results

Effect of garlic on TBARS, blood glucose levels

The clinical parameters of the controls and the type 2 diabetics were shown in table 1. There was a significant increase in blood glucose and TBARS levels in diabetic patients. Administration of raw garlic significantly decreased blood glucose and TBARS levels in diabetic treated patients.

Table 1: Effect of garlic on TBARS, Blood glucose levels in Diabetic patients and Diabetic patients treated with raw Garlic.

Parameter	Healthy subjects	Diabetic patients	Diabetic patients treated with raw garlic
Blood glucose (mg/dL)	99.8 ± 8.3[a]	243.3 ± 23.9[b]	107.3 ± 9.7[ac]
Plasma TBARS (nmol/ml)	2.19 ± 0.16 [a]	4.30 ± 0.34 [b]	2.34 ± 0.20 [ac]
Erythrocyte TBARS (nmol/ml)	0.30 ± 0.02 [a]	1.53 ± 0.11 [b]	0.31 ± 0.03 [ac]

TBARS - Thiobarbituric acid reactive substances.
Values are expressed as mean ± SD; n=20.
a, c – significantly different from normal subjects is ap <0.001, cp< 0.005
b – significantly different from diabetic patients

Action of garlic on lipid profiles

Table 2 shows the effect of raw garlic on lipid profile in diabetic patients. There was a significant elevation of cholesterol, LDL, triglyceride and reduction of HDL were observed in diabetic patients. Supplementation of raw garlic significantly decreased cholesterol, triglyceride, LDL and increased HDL levels.

Table 2: Effect of raw Garlic on lipid profile Diabetic patients and Diabetic patients treated with raw Garlic

Parameter	Healthy subjects	Diabetic patients	Diabetic patients treated with raw garlic
Serum cholesterol (mg/dL)	149.5 ± 11.8 [a]	208.3 ± 28.00 [b]	173.4 ± 8.9 [ac]
Triglycerides (mg/dL)	140.6 ± 11.5 [a]	167.5 ± 27.80 [b]	153.6 ± 15.00 [ac]
HDL (mg/dL)	64.00 ± 9.30 [a]	53.00 ± 8.00 [b]	60.00 ± 9.00 [ac]
LDL (mg/dL)	81.00 ± 24.40 [a]	118.00 ± 23.30 [b]	93.40 ± 18.3 [ac]

HDL – High density lipoprotein; LDL – Low density lipoprotein.
Values are expressed as mean ± SD; n=20.
a, c – significantly different from normal subjects is ap <0.001, cp< 0.005
b – significantly different from diabetic patients

Influence of garlic on antioxidants status

The activities of SOD, CAT, and GPx in erythrocytes of diabetic patients have been summarized in Table 3. There was a significant reduction in the activity of SOD, CAT and GPx in erythrocytes during diabetes when compared with normal group. By administration of raw garlic increased the activity of SOD, CAT and GPx in erythrocytes to near normal.

Table 3: Effect of raw Garlic on Enzymatic Antioxidants in erythrocytes of Diabetic patients.

Parameter	Healthy subjects	Diabetic patients	Diabetic patients treated with raw garlic
CAT (U^A /mg Hb)	2.01 ± 0.11 [a]	1.24 ± 0.11 [b]	1.91 ± 0.14 [ac]
SOD (U^B/mg Hb)	1.54 ± 0.16 [a]	1.01 ± 0.16 [b]	1.42 ± 0.15 [ac]
GPx (U^C/mg Hb)	17.2 ± 1.1 [a]	10.3 ± 0.8 [b]	16.07 ± 1.40 [ac]
Plasma GPx (U^A/L)	140.6 ± 10.7 [a]	101.8 ± 12.9 [b]	130.9 ± 10.90 [ac]

SOD – Superoxide dismutase; CAT – Catalase; GPx – Glutathione peroxidase.
Values are expressed as mean ± SD; n=20.
a, c – significantly different from normal subjects is ap <0.001, cp< 0.005
b – Significantly different from diabetic patients

Discussion

Diabetes mellitus has been known to be a state of excess generation of free radicals contributed by several mechanisms, including hyperglycemia and antioxidant status, causing oxidative stress. This oxidative stress exacerbates the development and progression of diabetes and its complications. Excessive production of free radicals observed both in type 1 (insulin-dependent) and types 2 (non insulin dependent) diabetes and its insufficient removal results in damage to cellular proteins, membrane lipids, and nucleic acids[17]. In the present study, we have evaluated the efficacy of garlic on hyperglycemia in patients with type 2 diabetes in comparison to normal. According to our study, treatment with raw garlic significantly reduced the levels of blood glucose, triglyceride, LDL and increases HDL level. Increased blood glucose level suggests that pancreatic β-cells were severely damaged in type 2 diabetic patients. Reversal of blood glucose after treatment with raw garlic in type 2 diabetic patients indicates that the garlic induced insulin secretion from undamaged pancreatic β-cells and stimulated glucose utilization by hepatic and extra hepatic tissues.

The hypoglycemic action of garlic could possibly due to an increase in pancreatic secretion of insulin from β-cells, release of bound insulin or enhancement of insulin sensitivity. It has been previously suggested that garlic (allicin) can enhance serum insulin by effectively combining with compounds like cysteine, which would spare insulin from SH group which are common cause to insulin inactivation[18]. Glucose concentration in blood reduced significantly in garlic treated patients compared to diabetic patients. This condition was attributed to improving of the antioxidant system in cells of the pancreas to produce insulin. Kumar and Thomson[19,20] found that feeding mice with garlic induced significant, decrease of serum glucose levels. The lower levels of plasma glucose in human have also been reported in the biochemical effect of Allium sativum.

One of the end products of lipid peroxidation is malondialehyde (MDA). It showed a significant decrease in garlic treated diabetic patients compared to diabetic patients. In the study performed 60 patients with type 2 diabetes mellitus received garlic daily, and their total serum cholesterol and LDL decreased after 5 weeks and HDL cholesterol increased after 7 weeks. Mechanism of action in lowering serum lipids includes the garlic delayed lipid absorption from the gastrointestinal (GI) tracts and diminished LDL cholesterol synthesis by liver[21.] There is no change in serum cholesterol levels in patients with hypercholesterolemia after 12 weeks of treatment with garlic powder 900mg per day, while significant reduction in total cholesterol and LDL cholesterol as well as moderate increase in HDL cholesterol but no change in triglyceride levels was observed in our study[22].

SOD scavenges the superoxide ions produced as cellular byproducts. SOD is a major defence for aerobic cells in combating the toxic effects of superoxide radicals[23]. In erythrocytes, SOD activity was increased in garlic treated group compared to normal. Garlic extract exerts antioxidant action by scavenging ROS, enhancing the cellular antioxidant enzymes SOD in the cells[24]. Catalase is rich in eukaryotes and peroxisomes and serves to degrade H_2O_2 produced by peroxisomal oxidases to water and oxygen. CAT activity in erythrocytes showed significant increase in garlic treated group compared to normal. Its oil enhanced CAT activity in the cells. Garlic powder increases the antioxidant capacity in hamsters [25]. Glutathione peroxidase (GPx) is selenium dependent enzyme found primarily in the cytoplasm but found also in the mitochondria. GPx activity showed significant increase in garlic treated group compared to normal. Garlic extract increases antioxidant action by scavenging ROS, enhancing the cellular antioxidant

enzymes, GPx and increasing glutathione in the cells. Garlic oil and diallyldisulfide increased glutathione levels in red blood cells [26].

Conclusion

In conclusion, it can be suggested that, administration of garlic to diabetic patients can decrease the blood glucose level and increase the antioxidant activity in humans. Garlic has been used as food additive and can be recommended as a dietary supplement for long term use without toxic effects. We certainly believe that garlic overall is a magical medicinal herb and if consume as much as possible has got the prophylactic effect in all people.

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Abbreviations

ALP	-	Alkaline phosphatase
ANOVA	-	Analysis of variance
CAT	-	Catalase
GI	-	Gastrointestinal
GPx	-	Glutathione peroxidase
HDL	-	High density lipoprotein
LDL	-	Low density lipoprotein
MDA	-	Malondialdehyde
ROS	-	Reactive oxygen species
SOD	-	Superoxide dismutase
TBARS	-	Thiobarbituric acid reactive substances