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The Ameliorating Effects of Garlic (Allium Sativum) on Blood Glucose Levels and Lipid-Related Indices

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Abstract
Garlic (Allium sativum L.), a culinary plant with medicinal properties, has been utilized as a traditional remedy by people worldwide for centuries. Garlic possesses a variety of health benefits, such as its antibacterial and anticancer properties, its capacity to slow the aging process and prevent obesity, its antihypertensive, antioxidative, and cardioprotective properties, and its capacity to reduce blood sugar and cholesterol. Garlic possesses organosulfur compounds, which have been associated with advantageous and favorable impacts on health. This review specifically examines the therapeutic potential and molecular mechanisms of Garlic in influencing important processes related to the control of glucose and lipid metabolism. These effects have been observed in both laboratory studies and clinical trials. The processes encompassed within this category entail the excretion of insulin, the absorption of glucose, the accumulation of glycogen, and the synthesis of lipids in the liver. The results of this study investigating the impact of Garlic on glucose and lipid regulation will deepen our comprehension of this fascinating natural compound. This information will be invaluable for healthcare professionals, researchers, and individuals seeking to prevent and treat metabolic disorders.

Keywords: Garlic, Organic sulfides, Blood glucose, Lipid profile, Health benefits

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Introduction

One of the main risk factors for the development of complications in diabetes is hyperglycemia, which can lead to retinopathy, neuropathy, nephropathy, and cardiovascular disease (1). In addition, dyslipidemia is a prevalent feature of several metabolic disorders, including obesity, diabetes, and fatty liver disease (NAFLD) (2,3). High triglycerides (TG) and total cholesterol (TC), a reduction in high-density lipoprotein cholesterol (HDL-c), a rise in the plasma level of low-density lipoprotein cholesterol (LDL-c), and very low-density lipoprotein (VLDL) are the most noticeable signs of dyslipidemia (4). An independent risk factor for atherosclerosis disease is elevated LDL-c levels (5). Time will reveal if hyperlipidemia can lead to catastrophic conditions including heart issues and stroke if left untreated (6).

As a result, several of these chemicals are used in the treatment and management of individuals with high blood sugar. Unfortunately, there aren't many therapy choices for these kinds of illnesses, and the majority of medications only address one specific issue. As a result, a number of medications that lower blood sugar and reduce cholesterol have been introduced to the market; however, these benefits are only momentary (7). These medications also cause adverse responses, which raise the possibility of hypoglycemic reactions and the accumulation of extra fat just for the purpose of temporarily relieving episodes related to diabetes and other metabolic problems (8). They have been studied and have received some notoriety lately because of their potential therapeutic efficacy when used to treat various illnesses. Modern traditional medicine uses the anti-inflammatory and antioxidant properties of garlic to treat a variety of ailments, including heart disease, cancer, diabetes mellitus, and infections like the common cold (9-11). This article provides a thorough analysis of these effects and the mechanisms involved in order to determine how garlic may affect the treatment of diabetes and/or metabolic syndrome.

Garlic as a therapeutic agent: unveiling the healing power

The Allium genus is well known for its garlic (Alluim sativum). It is a flowering plant with several uses. Renowned for its numerous medicinal benefits in addition to its unique flavor and scent, which are used in preparing food (12). A range of organosulfur compounds have been increasingly credited by the pharmaceutical industry with their therapeutic effectiveness. Garlic contains a variety of naturally occurring therapeutic qualities due to its sulfur and non-sulfur components (13).

S-allyl-cysteine sulfoxide, or alliin, is referred to as the active ingredient in garlic by one of the leading bioactive scientists (14). This chemical goes through several stages of processing. Alliinase catalyzes a series of transformational processes including chewing, crushing, cutting, and extracting. The enzymatic process known as alliinase converts alliin into allicin (diallyl thiosulfinate), a highly active compound that serves as a foundation for several health benefits (15). Ajoene, allyl sulfides, and vinyldithiines are among the other sulfur compounds produced during the transformation that are beneficial in medicine and together they contribute to the variety of biological activities of garlic (16).

Garlic (Allium sativum) contains a chemical called allicin, which gives it its distinct and strong smell. Attention is drawn to allicin because of its potential medicinal benefits and health benefits. Because of its potential medicinal benefits-such as its anti-oxidative (17), anti-microbial (18), and possible cardiovascular (19) and anticancer effects (20) researchers have shown interest in it. However, further clinical research has to be done to prove that Allicin can only be extensively utilized after patients are aware of the dosage, mode of administration, and potential adverse effects that are advised as a therapeutic drug.

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Numerous health advantages of garlic include its antibacterial and anticancer properties, its ability to prevent obesity and aging, its antihypertensive, antioxidative, and cardioprotective properties, and its ability to decrease blood sugar and cholesterol. As evidenced by the literature, they have been extensively researched to determine these impacts. It could occur from a diet high in garlic, which has anti-obesity properties (21-23). However, Mohammd et al. (2014) shown that garlic can inhibit pre-adipocyte maturation, which would slow the formation of adipose tissue and thus fight obesity (24). Moreover, administering garlic to humans orally also works well. Rats fed a high-fat diet and exhibiting signs of hyperlipidemia and epididymal obesity lost a significant amount of body weight. These findings thus suggest that garlic offers an option in the battle against obesity (25). Because it prevents angiotensin from being converted to angiotensin II, it further improves heart health (26). It decreases blood pressure since it is an antihypertensive agent (22). Garlic's antioxidants protect the blood vessels and the heart, avoiding atherosclerosis (27). Numerous studies highlight the benefits of reducing diabetes and associated consequences as well as the function that garlic plays in nutrition in preventing atherosclerosis (28-30). S-allyl cysteine sulfoxide, which has been identified in garlic, has been shown to act as an insulin secreting agents in diabetic rats (31). Additionally, garlic indirectly lowers the risk of atherosclerosis by lowering blood pressure, cholesterol, and maybe even diabetes mellitus. It also inhibits the production of thrombi (32, 33). Moreover, garlic may help decrease cholesterol and blood sugar levels. It may be able to help control hyperlipidemia and diabetes (28,34). Although the effects of garlic on blood lipids and glucose have been well studied, the origins of garlic and the evolution of animal trials are better understood. Our analysis looks at the data that is currently available on gap closure. These results demonstrate that garlic has several health benefits in addition to being a dietary ingredient. Thus, in order to provide a thorough understanding of the therapeutic implications of utilizing garlic in the treatment of metabolic health, this review incorporates findings from both animal and clinical investigations (Tables 1&2).

Underlying Mechanisms for the glucose and Lipid-Regulating Effects of Garlic

Rats with normal health showed significant changes in serum concentrations of total cholesterol (TC), triglycerides (TG), and blood glucose after receiving 0.5 g/kg/day of raw garlic for 4 weeks (34). Black garlic (1.5, 3, and 6 mg/200 g Bw/day) for 25 days substantially decreased blood glucose, TG, TC, and LDL-c levels in Alloxan-induced diabetic rats, according to Isninai et al.'s validation (35). In rats fed a fructose diet, Gargouri et al. observed that 8 weeks of exposure to raw garlic (250 mg/kg/day) significantly decreased plasma glucose, HbA1c, insulin resistance, and TG (36).

In Supakul L's experiment, rats that were obese and showed signs of insulin resistance were given dosages of 250 and 500 mg/kg/day of garlic extract for four weeks. Insulin levels, HOMA-IR (Homeostatic Model Assessment of Insulin Resistance), and total cholesterol (TC) were all significantly reduced by both garlic dosages (37). Another study showed that giving rats given high-cholesterol diets 5 grams of garlic per kilogram per day for 10 weeks significantly reduced their levels of TG, TC, and LDL-c (38). All of these results point to the effectiveness of garlic in raising insulin sensitivity as well as in lipid and glucose metabolism in animal models. Garlic significantly lowers fasting blood glucose (FBG) and HbA1c in diabetic individuals, according to research by Ebadi et al. The study's findings demonstrated the potential of garlic as a dietary supplement for the management and treatment of diabetes (39).

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Table 1. Animal studies of the glucose and lipid management of Garlic

Animal	Interventions	Dose of Garlic	Duration (Week or day)	Results	Ref.
High-fat fed rats	Black Garlic extract	(15g /kg/day)	5 w	↓TG, TC ↓mRNA of SREBP-1c, ACC, FAS, G6PDH, HMG-CoA reductase, ACAT	(55)
Normal rats	Raw Garlic	0.5 g/kg/day	4 w	↓Glucose, TG, TC	(34)
Alloxan induced diabetic rats	Black Garlic	1.5, 3, 6 mg/200 g Bw/day	25 d	↓Blood glucose ↓ TG, TC, LDL-c	(35)
Alloxan induced diabetic rats	Garlic extract	300 mg/kg/day	6 w	↓Blood glucose ↓Total lipid, TC	(57)
Rats fed a high fructose	Raw Garlic	250 mg/kg/day	8 w	↓Serum glucose, HbA1c, insulin resistance ↓TG	(36)
Insulin-resistant obese rats	Garlic extract	250 or 500 mg/kg/day	4 w	↓ Insulin, HOMA-IR ↓TC	(37)
Rats fed high cholesterol diets	High temperature- and high pressure-processed Garlic	5g /kg/day	10 w	TC, LDL-c, TG	(38)
NAFLD rarts induced long-term high-fat diet	Diallyl disulfide (DADS)	20 mg/kg/day	12 w	↓Body weight, Adipose tissue weight Down-regulation of SREBP-1c, ACC, FAS, and HMG-CoA reductase, Stimulation of PPARα and CPT-1	(56)
High-fat fed rats	Garlic oil	92.6 mg/kg/day	60 d	↓Body weight, Adipose tissue weight ↓TC, TG and LDL-c ↑ HDL-c	(58)
High-fat/sucrose fed rats	Aged black Garlic	250 mg/kg/day	8 w	↓Body weight, TG, LDL-c, ↑HDL-c ↓PPAR-γ, LPL, HSL expression ↑INSR, GLUT-4 expression	(59)

↓: significantly decrease, ↑: significantly increase in the experimental group compared to the control group)

Table 2. Clinical trials about Garlic and its beneficial effects on glucose and lipid parameters

Participants	N sample (Case: control)	Interventions	Dose of Garlic (mg/day)	Duration (week)	Results	Ref.
Subjects with type 2 diabetes	30: 30	Garlic + Allicin tablet Control: (Vit B1 tablet)	2406	12	↓ FBS ↓HbA1c	(39)
Subjects with type 2 diabetes and obesity	30: 30	Metformin + Garilic capsul Control: (Metformin)	500	12	↓FBS, TG, TC, LDL ↑HDL	(30)
Subjects with type 2 diabetes	30: 30	Garlic + Metformin Control: (Placebo+Metformin)	900	24	↓FBS, TG, TC, LDL ↑HDL	(40)
Women with GDM	26: 23	Garlic pill Control: Placebo	400	8	↓FBS	(41)
Obese patients	46: 46	Garlicin capsule Control: Placebo	400	12	↓TC, LDL	(60)
Subjects with type 2 diabetes and hyperlipidemia	40: 0	Garsin tablet Control: -	900	4	↓TC ↓LDL-c	(42)
Subjects with type 2 diabetes	20: 20	Allicore (Garlic powder) Control: placebo	600	1	↓FBS ↓TG ↓ Fructosamine	(43)
Patients with dyslipidemia	35:35	Garlic tablet Control: placebo	600	12	↓TC, LDL ↑HDL	(61)
Patients with NAFLD	45: 43	Garlic tablet Control: placebo	1600	12	↓TG, TC, LDL ↑HDL	(44)

↓: significantly decrease, ↑: significantly increase in the intervention group compared to the control group)

In comparison to the control group, Kumar and Ashraf showed that garlic dramatically decreased the blood levels of FBG, TG, TC, and LDL-c and increased the levels of HDL-c in people with T2DM. According to the findings of these research, people with diabetes can better control their blood sugar and hyperlipidemia by taking garlic with their regular anti-diabetic medications (30,40). According to research by Faroughi et al., giving women with gestational diabetes 400 mg of garlic daily for eight weeks lowers their diastolic blood pressure, prediabetes symptoms, and FBS levels (41). According to a research by Afkhami et al., supplementing with garlic lowers LDL-c and total cholesterol in

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those with Type 2 diabetes (T2DM). The results of this investigation showed no discernible variation between the levels of FBG and 2hpp glucose before and after garlic consumption. After consuming garlic, HDL-c levels increased, but not significantly (42). In the Sobenin research, FBG, serum triglyceride, and fructosamine levels decreased after a week of therapy with 600 mg/day of Allicore powder tablets. In addition to diet therapy, the study's findings suggest that Allicore Garlic powder pills can be helpful in the management and treatment of type 2 diabetes (43). A different investigation on NAFLD patients found that HDL-c increased while TG, TC, and LDL-c decreased (44).

Garlic could reduce blood sugar levels and enhance lipid profiles through a number of mechanisms, according to a number of pre-clinical and trial investigations, even if the exact mechanism behind its anti-glycemic and anti-lipidemic effects is unknown. Organosulfur compounds (OSC) from garlic may function like insulin, reduce insulinase activity, and enhance insulin sensitivity (45). Moreover, it boosts insulin release and promotes the growth and regeneration of pancreatic beta cells. One theory for the mechanism of action is that the allicin in garlic prevents insulin inactivation by reacting with molecules that include sulfhydryl groups that deactivate insulin (46,47). Additionally, it has been shown that garlic extract increases the amount of liver glycogen storage, stimulates insulin and Glut-4 expression, absorbs carbs, and lowers blood glucose levels (48). There hasn't been enough research done on the mechanism by which garlic decreases plasma lipids. However, studies on animals have shown that taking supplements containing garlic lowers the activity of hepatic lipogenic and cholesterogenic enzymes (49). Sterol Regulatory Element Binding Protein-1c (SREBP-1c), an essential transcription factor in lipid metabolism, is activated and blood lipid levels are raised by excessive fat ingestion. SREBP-1c suppresses the expression of lipolytic genes, such as Carnitine Palmitoyltransferase-1 (CPT-1) and Peroxisome Proliferator-Activated Receptor Alpha (PPARα), and activates a multitude of lipogenic genes involved in the synthesis of fatty acids, triglycerides, and cholesterol (3-Hydroxy-3-Methylglutaryl-CoA Reductase - HMG-CoA reductase and Acyl-CoA: Cholesterol Acyltransferase - ACAT)(50,51). Key adipogenic transcription factor peroxisome proliferator activated receptor γ (PPARγ) increases the transcription of genes involved in glucose and fatty acid absorption (52). Research has revealed that mice fed a high-fat diet (HFD) have elevated levels of PPARγ2 mRNA, which may indicate that HFD-induced adipocyte hypertrophy is related to it. Studies have shown that supplementing with garlic significantly reduces the expression of genes that accumulate fat, such as PPARγ, ACC, and adipocyte Protein 2 (aP2) mRNA (53,54). The expression of lipogenic enzymes, including ACC and glucose-6-phosphate dehydrogenase (G6PDH), was likewise decreased by garlic administration, indicating a possible function in preventing lipogenesis and thereby enhancing fatty acid oxidation. The decrease in plasma triglyceride and cholesterol levels that has been reported may be attributed to this mechanism, underscoring the medicinal potential of garlic in the management of hyperlipidemia (54).

A specific investigation found that giving rats black garlic extract reduced the expression of liver SREBP-1c and the target genes it is linked to (FAS, ACC, and G6PDH). As a consequence, the liver's ability to synthesize fat was decreased due to this downregulation. Moreover, a noteworthy reduction in the expression of ACAT and HMG-CoA reductase was seen in rats given black garlic supplements, which helped to significantly lower the blood cholesterol levels (55). A different investigation on the garlic component diallyl disulfide (DADS) showed a reduction in the mRNA expression of SREBP-1c, ACC, FAS, and HMG-CoA reductase. Concurrently, there was a rise in PPARα and CPT-1 mRNA expression. These results show that in rats given a high-fat diet (HFD), DADS

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substantially decreased the production of hepatic fatty acids and cholesterol while modulating lipid metabolism (56).

Conclusion

The findings of this study demonstrate that the compounds found in Garlic have a beneficial impact on lowering blood glucose and cholesterol in both animal and human subjects. Garlic components enhance blood glucose control by promoting the release of insulin and the absorption of glucose. Moreover, the protection it provides against changes in lipid metabolism mostly occurs through the SREBP-1c dependent route. Garlic components have no significant adverse effects, making it suitable for use as an herbal remedy to enhance glucose and lipid metabolism, particularly in those with diabetes and dyslipidemia. Garlic and its bioactive components show great potential as dietary supplements for preventing and treating many ailments. Further investigation is required to uncover the intricacies of the processes by which Garlic operates and its molecular pathways. Furthermore, it is imperative to conduct additional clinical trials in order to substantiate the physiological advantages of Garlic in the human population.

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Conflict of Interest

The authors have stated no conflict of interest.

Authors' contributions

Conceptualization: F.S, A.SR, F.Z and S.D. Data gathering and curation: N.H and M.S. Writing original draft preparation: F.S, A.SR, N.H, and N.N. Writing review and final editing: A.SR, S.D and M.AA. Visualization: M.S. Supervision: A.SR and M.AA. All authors have read and agreed to the published version of the manuscript.

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