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Synergistic effect of metformin combination with garlic on anti-diabetic activity: A review

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Abstract
Diabetes mellitus (DM) is a disorder in which patients have high blood sugar levels and is a major health concern all over the world. Recent advances in the pharmacology of diabetes mellitus have resulted in the identification of multiple therapeutic medication targets for effectively lowering glucose levels, with Metformin with garlic being the most successful of these. In the treatment of diabetes, anti-diabetic medications are employe. Metformin has become the most often prescribed glucose-lowering medication in the world. Metformin is a biguanide that decreases blood glucose concentration by mechanisms different from those of insulin secretagogues, such as sulphonylureas, or exogenous insulin therapy. Along with pharmacological treatment represented by oral hypoglycemic medications (For type 2), and non-pharmacological treatment, represented by exercise and diet; natural herbal extracts such as Garlic also showed an additional reduce in blood glucose level in these patients. Garlic contains diverse bioactive compounds, such as allicin, alliin, diallyl sulfide, diallyl disulfide, diallyl trisulfide, ajoene, and S-allyl-cysteine. Substantial studies have shown that garlic and its bioactive constituents exhibit antioxidant, anti-inflammatory, antibacterial, antifungal, immunomodulatory, cardiovascular protective, anticancer, hepatoprotective, digestive system protective, anti-diabetic, anti-obesity, neuroprotective, and renal protective properties.
To assess the efficacy of Garlic plus Metformin and Garlic has a beneficial effect on blood glucose level, and can be administered to diabetic patients, in the absence of contraindications.

Keywords: Diabetes, garlic, metformin

Introduction

Diabetes mellitus (DM) is a condition in which people have high blood sugar levels. It is a common and serious health concern around the world, characterized by hyperglycemia caused by problems with insulin secretion, action, or both [1]. According to the World Health Organization's official 2016 estimates, around 422 million adults worldwide have diabetes mellitus. Diabetes mellitus is becoming more common, with type 2 diabetes accounting for up to 85-90 percent of all cases. Increases in total diabetic mellitus prevalence rates are largely due to an increase in type 2 diabetic mellitus risk factors, particularly being fat or overweight [2].
According to the International Diabetes Federation, there are 415 million diabetics worldwide, with more than 35.4 million in the MENA (Middle East and North Africa) region; this number is expected to rise to 72.1 million by 2040.
According to estimates from the International Diabetes Federation (IDF), the global prevalence of diabetes among people aged 20 to 79 years is 8.8%. Type I diabetes (insulin dependent) and Type II diabetes (Non-insulin-dependent) account for 90% of all diabetics [1, 2]. The American Diabetes Association (ADA standard) 's classification of diabetes as type 1, type 2, and gestational diabetes mellitus (GDM) published in 1997 is still the most widely recognised and implemented [4]. Type 1 diabetic mellitus (accounts for less than 10%), is attributed to destruction of the beta-cells of the pancreas that produce insulin4 leading to deficiency of insulin secretion absolutely [5]. Type 2 diabetic mellitus (accounts for about 90%), attributed to lack of enough insulin production and/or absence of sensitivity to the effect of insulin (resistant to insulin) [4].

Type 1 diabetic mellitus is a chronic disease characterized by the inability of the body to make insulin due to the autoimmune destruction of the pancreatic beta cells. The condition usually begins in childhood, although it can also strike people in the early 40s or late 30s. Type 2 diabetes mellitus composed of an array of malfunctions characterized by hyperglycemia and attributed the combination of resistance to the action of insulin, insufficient secretion of insulin, and excessive or inadequate glucagon secretion.

The loss of the pancreatic beta cells that generate insulin4 results in a complete lack of insulin secretion in type 1 diabetes (which affects less than 10% of persons) [5]. Type 2 diabetes is caused by a lack of insulin production and/or a loss of sensitivity to the effects of insulin (which accounts for about 90% of cases) (insulin resistance) [4]. Type 1 diabetes is a chronic disorder in which the pancreatic beta cells are destroyed by the immune system, preventing the body from producing insulin. The illness mainly strikes children, although it can also afflict adults in their early 40s or late 30s. Type 2 diabetes mellitus is a category of diseases marked by hyperglycemia and induced by a combination of insulin and other hormones. Maturity-onset diabetes in children and adolescents, as well as hereditary abnormalities in beta-cell activity. Gestational diabetes mellitus is a kind of diabetes that is diagnosed during the second or third trimester of pregnancy, when it is not yet obvious that the patient has diabetes) [6, 7].

Diabetic retinopathy is one of the microvascular consequences of diabetes. Diabetic neuropathy is the leading cause of blindness in working-age adults. About 70% of people with diabetes exhibit symptoms of peripheral and/or autonomic neuropathy. Serious peripheral neuropathy, in combination with immune system deficiencies, is expected to contribute to a higher prevalence of lower extremity amputations in people with diabetes, as diabetic nephropathy is the leading cause of end-stage renal disease. Complications of diabetes mellitus; diabetes mellitus is one of several risk factors for macrovascular diseases (peripheral vascular disease, cardiovascular disease and stroke). The high risk of macrovascular complications, including cardiovascular disease (congestive heart disease and stroke) and peripheral vascular disease is 2-4 times higher for individuals with diabetic mellitus [8]. Maturity-onset diabetes in children and adolescents, as well as hereditary abnormalities in beta-cell activity. Gestational diabetes mellitus is a kind of diabetes that is diagnosed during the second or third trimester of pregnancy, when it is not yet obvious that the patient has diabetes) [6, 7]. Diabetic retinopathy is one of the microvascular consequences of diabetes. Diabetic neuropathy is the leading cause of blindness in working-age adults. About 70% of people with diabetes exhibit symptoms of peripheral and/or autonomic neuropathy. Serious peripheral neuropathy, in combination with immune system deficiencies, is expected to contribute to a higher prevalence of lower extremity amputations in people with diabetes, as diabetic nephropathy is the leading cause of end-stage renal disease. Complications of diabetes mellitus; diabetes mellitus is one of several risk factors for macrovascular diseases (peripheral vascular disease, cardiovascular disease and stroke).

Diabetes mellitus (DM) is a disorder in which patients have high blood sugar levels and is a major health concern all over the world [2]. The majority of antidiabetic medications in clinical use have different methods of action, but they all have adverse effects suchnutritional problems, weight gain, hypoglycaemia, liver damage, and allergic reactions [3]. Because of the increased occurrence of side effects, researchers and corporations are looking for new anti-diabetic drugs with fewer adverse effects. Recent advances in the pharmacology of diabetes mellitus have resulted in the identification of multiple therapeutic medication targets for effectively lowering glucose levels, with Metformin with garlic being the most successful of these. In the treatment of diabetes, anti-diabetic medications are employed.

Metformin is an antidiabetic drug that works by inhibiting hepatic glucose synthesis and increasing muscle glucose uptake to maintain glucose homeostasis. Metformin (a iguanid derivative) reduces these problems by regulating blood glucose levels. It works by assisting in the restoration of the body's insulin response. It reduces the quantity of blood sugar produced by the liver and absorbed by the intestines or stomach [9]. Metformin also inhibits the liver's endogenous glucose synthesis, owing to a decrease in the rate of gluconeogenesis and a little effect on glycogenolysis. Metformin is the most extensively prescribed diabetes medication in the world, and there is mounting evidence that it can also be used to treat cancer.

Herbal formulations are used as a dietary supplement, a nervine tonic, or a hypolipdemic agent [10]. Despite the fact that these herbal supplements are touted to have no negative effects, they must be approved by the FDA. According to a worldwide survey, diabetes affects about 10% of the population (Siddharth, 2001). Oral hypoglycemic medicines and insulin are used to treat diabetes.

Through additive or synergistic activities, positive interactions between herbs and medicines may lead to increased effectiveness of antidiabetic medications. HDIs may develop from the co-administration of antidiabetic herbs and pharmaceutical medicines, leading to improved effects (Which may be desired therapeutically), decreased pharmacological effects, or adverse medication events like hypoglycemia. The medicinal plants that are included are chosen based on their long-term use and the strength of available research on effectiveness or adverse/synergistic effects.

Traditional medicinal herbs should be researched further for the treatment of diabetes mellitus, according to the World Health Organization's Expert Committee on Diabetes [12]. *Allium sativum* (garlic), Ginseng species, Momordica charantia (bitter melon), Trigonella foenum-graecum (fenugreek), and A. cepa are the most commonly used medicinal herbs (onion).

Allium sativum, more often known as garlic, is a popular culinary and medicinal herb that has been utilised by humans for over 7,000 years. Garlic has recently been used for therapeutic purposes in the form of garlic oil, garlic powder, and tablets [13, 14].

Garlic has a particularly enviable image due to its widespread use as a dietary and therapeutic supplement around the world [15, 16]. Garlic includes a number of beneficial components, including allicin, a sulfur-containing substance with anti-cholesterolemic, [17] antioxidant, [18, 19] hypotensive, anticoagulant, and antithrombotic properties. Garlic has a variety of characteristics, including immunological modulation and hepatoprotection [20]. Garlic extracts are thought to be helpful in the prevention of cardiovascular disease [21]. Garlic, particularly salt and potassium, aids in electrolyte balance [22]. It has been discovered that eating 10 gm of raw garlic twice a day for six weeks will lower blood glucose and HbA1c levels in diabetic people [23]. Other studies have shown that taking 40 milligrammes of garlic every day will help you feel better.

Since 1993, 44 percent of clinical trials have shown a reduction in total cholesterol, with the capacity of garlic to prevent platelet aggregation being the most significant benefit. In the areas of blood pressure and oxidative stress reduction, mixed findings have been reported. Because there have been so few trials on these topics, the conclusions are limited. Negative results in some clinical trials could possibly be due to the use of diverse garlic preparations, unknown active components, and their interactions.

Thus, although garlic appears to have promise in decreasing characteristics related with cardiovascular disease, more in-depth relevant research are needed, according to evaluations of these *in vitro* and *in vivo* studies published since 1993.

Historical development

It's estimated that 16 million Americans have diabetes, but only half of them have been diagnosed. Diabetics with type I or IDDM must take insulin in some form to live. Type II diabetes, also known as NIDDM, affects a higher number of Americans, and many can be managed with a mix of diet and exercise.

Banting, Best, Collin, and Macleod successfully lowered blood glucose levels and glycosuria in a patient treated with a material extracted from bovine pancreatic in the early 1920s, demonstrating the important role of insulin in glucose metabolism regulation. Lisper, the first fast-acting human insulin analogue, was approved in 1996 [25].

Metformin is the world's most extensively used ant hyperglycemic drug and the only clinically important biguanide [26]. Metformin (Dimethylbiguanide) has supplanted insulin as the preferred first-line oral blood glucose-lowering medication in the treatment of type 2 diabetes. *Galega officinalis* (also known as goat's rue) is a traditional European herbal medicine that was identified to be high in guanidine, a substance that has been shown to lower blood glucose levels, in 1918. In 1927, Muller and Reinwein published a paper about their early clinical experience with galegine sulphate.

Galegine, also known as isoamylene guanidine, is the active ingredient in the French lilac. Metformin has become the most often prescribed glucose-lowering medication in the world, and it is currently listed as an essential medicine by the World Health Organization (WHO) [27, 28, 29].

Kidney disease, blindness, nerve disorders, limb loss, and sexual function issues can all be prevented with good blood sugar control.

Metformin has improved prognosis in a variety of insulin-resistant conditions, including polycystic ovarian syndrome (PCOS), HIV-associated lipodystrophy, acanthosis nigricans, and probably dementia-type neurodegenerative disorders [30, 31, 32, 33].

Garlic was used as a treatment by physicians from several countries in the ancient and middle eras, as well as for a long time during the modern period. Garlic has recently been the subject of scientific investigation, with promising findings in the treatment of a variety of ailments from which nations from many continents have been protecting and healing for thousands of years.

The Sumerians (2600–2100 BC) were known to use garlic for its medicinal properties, and it is thought that they took garlic to China, from where it spread to Japan and Korea. Garlic expansion most likely began in the ancient world and continued in the new world. Despite this, some historians believe garlic originated in China [34].

Since 2700 BC, garlic has been one of the most widely utilized treatments in ancient China. It was then included in yang because of its heating and energizing properties (the yin yang concept, according to which in the good there is bad and in the bad there is good). Garlic has been suggested as a treatment for depression. As a result of these stimulating properties of garlic, the Japanese Buddhist tradition does not include garlic. Garlic is disliked in Japanese cuisine as well [35].

Garlic was a valuable therapy in ancient Indian medicine, used as a tonic, roborans, to treat a lack of appetite, common weakness, cough, skin disease, rheumatism, haemorrhoids, and other ailments. Garlic was referenced in the Vedas, India's holy book, along with other therapeutic plants. The first physicians and pharmacists were Indian priests, and healing was accompanied and complemented by a variety of spells and rituals, prayers, and hidden and exquisite rites [34].

Drug Profile

Name: Metformin

Synonyms

Table 1: Metformin

Metformin 657-24-9
1,1-Dimethylbiguanide
N, N-dimethylimidodicarbonimidic diamide
Metformine

Biological source of metformin

Metformin is derived from *Galega officinalis*, often known as French lilac, goat's herb, or goat's rue. It is a herbaceous plant belonging to the Faboideae subfamily of the Fabaceae legume family [36].

Molecular formula: C4H11N5

Molecular weight: 165.62 g/mol

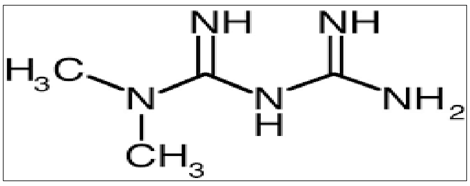
Solubilit

In 20 mL of water, metformin hydrochloride, USP 2.0 g dissolves. Metformin has a pKa of 12.4. A 1% aqueous solution of metformin hydrochloride has a pH of 6.68. Water is easily soluble; alcohol is somewhat soluble; acetone and methylene chloride are essentially insoluble.

Taste

Due to the prolonged presence of metformin in the saliva, patients on metformin medication frequently notice a lasting metallic taste in their mouth [35, 36]. Metformin is easily detected in the saliva of humans following either oral or intravenous administration [37].

Structure



Chemical constituents of Metformin
G. officinal is high in galegine, a blood glucose-lowering substance that laid the groundwork for the development of metformin, an Italian fitch [38] treatment for diabetes mellitus symptoms [39].

Cultivation and collection
It is native to regions of northern Africa, western Asia, and Europe, but it has been widely grown and naturalised throughout the world [40, 41, 42]. The plant has been used extensively as a feed crop, ornamental, bee plant, and green manure [42].

Metformin mechanism of action
The mechanisms of action of metformin are distinct from those of other oral ant hyperglycemic medications. Metformin lowers blood glucose levels by reducing hepatic glucose synthesis (Also known as gluconeogenesis), lowering glucose absorption in the intestine, and improving insulin sensitivity by enhancing peripheral glucose uptake and utilization [43]. Metformin is widely known for inhibiting mitochondrial complex I activity, and it has long been assumed that this is how it achieves its effective anti-diabetic effects [44, 45].

Name: Garlic

Synonyms of Garlic

Table 2: Garlic:

Poor Man's Treacle Star of Envy
Stinking Rose
The Bulb of the Tree of Life
The Fragrant Pear

Biological source of garlic
Garlic (*Allium sativum*), a perennial amaryllis (Amaryllidaceous) family plant valued for its flavorful bulbs. The plant is native to Central Asia, but it grows wild in Italy and southern France and is a staple in many national dishes.

Botanical classification of garlic

Table 3: Botanical classification of garlic

1	Kigdom	Plantae
2	Order	Asparagales
3	Family	Amaryllidacea
4	Subfamily	Allioideae
5	Genus	Allium
6	Species	A.Sativum

Molecular Formula: C18H32OS7

Molecular Weight: 488.9

Solubility
It is formed by the fast lysis of alliin by alliinase in crushed garlic cloves or wetted garlic powder. Allicin is 2% soluble in water, moderately soluble in hexane, and extremely soluble in organic solvents that are more polar than hexane. Garlic quality is generally measured by allicin production.

Taste
Garlic has a strong flavour and odour when chopped raw. When whole cloves are boiled or roasted, however, the heat changes the alliin into new, larger molecules before it comes into contact with the alliinase. This new structure provides garlic a smooth, sweet buttery flavour that many first-time garlic eaters are surprised by.

Structure of garlic

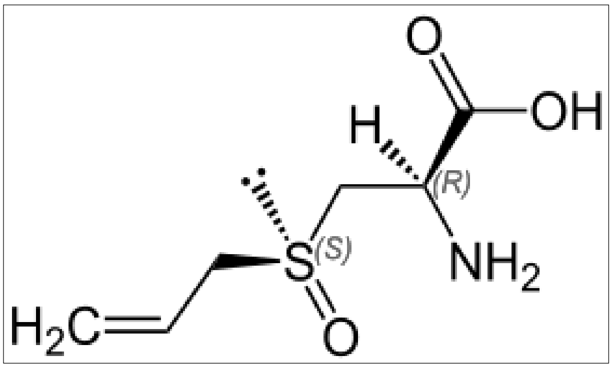


Fig 1: Garlic

Chemical constituents of garlic
The primary odoriferous compounds in freshly milled garlic homogenates are S propyl-cysteine-sulfoxide (PCSO), allicin, and S-methyl cysteine sulfoxide (MCSO) [46].

Garlic is high in sulphur compounds, enzymes, and minerals such as germanium, calcium, copper, iron, potassium, magnesium, selenium, and zinc, as well as vitamins A, B1, and C, fibre, and water. Lysine, histidine, arginine, aspartic acid, threonine, swine, glutamine, proline, glycine, alanine, cysteine, valine, methionine, isoleucine, leucine, tryptophan, and phenylalanine are among the 17 amino acids present in garlic (Josling, 2005) [49]. It has more sulphur compounds than any other Allium species, which are responsible for garlic's pungent odour as well as many of its medical properties. Effects of 402 Int. J. Med. Med. Sci. Modes:

One of the most biologically active compounds in garlic is allicin (Diallyl thiosulfinate or diallyldisulfide). The most abundant sulfur compound in garlic is alliin (S-allylcysteine sulfoxide), which is present at 10 and 30 mg/g in fresh and dry garlic, respectively. Typical garlic food preparation such as chopping, mincing and crushing disturbs S-allyl cysteine sulfoxide and exposed it to the allinase enzymes, then quickly converted it to diallyl thiosulfinate, which give off garlic's characteristic aroma. The allinase enzyme responsible for diallyl thiosulfanate conversion becomes inactivated below a pH of 3.5 or with heating. Although allicin is considered the major antioxidant and scavenging compound, recent studies showing that other compounds may play stronger roles; such as polar compounds of phenolic and steroidal origin, which offer various pharmacological properties without odor and are also heat stable [46, 47, 48, 49, 50].

Allicin is one of garlic's most biologically active components (Diallyl thiosulfinate or diallyldisulfide). Alliin (S-allylcysteine sulfoxide) is the most prevalent sulphur component in garlic, with concentrations of 10 and 30 mg/g in fresh and dry garlic, respectively. Typical garlic food preparation methods such as chopping, mincing, and crushing disrupt S-allyl cysteine sulfoxide, exposing it to allinase enzymes, which swiftly convert it to diallyl thiosulfinate, which gives garlic its distinctive scent. Below a pH of 3.5, or when heated, the allinase enzyme responsible for diallyl thiosulfanate conversion becomes inactive. Despite the fact that allicin is the most important antioxidant and scavenging component, recent research suggests that other chemicals, such as phenolic and polar phenolic compounds, may be more important.

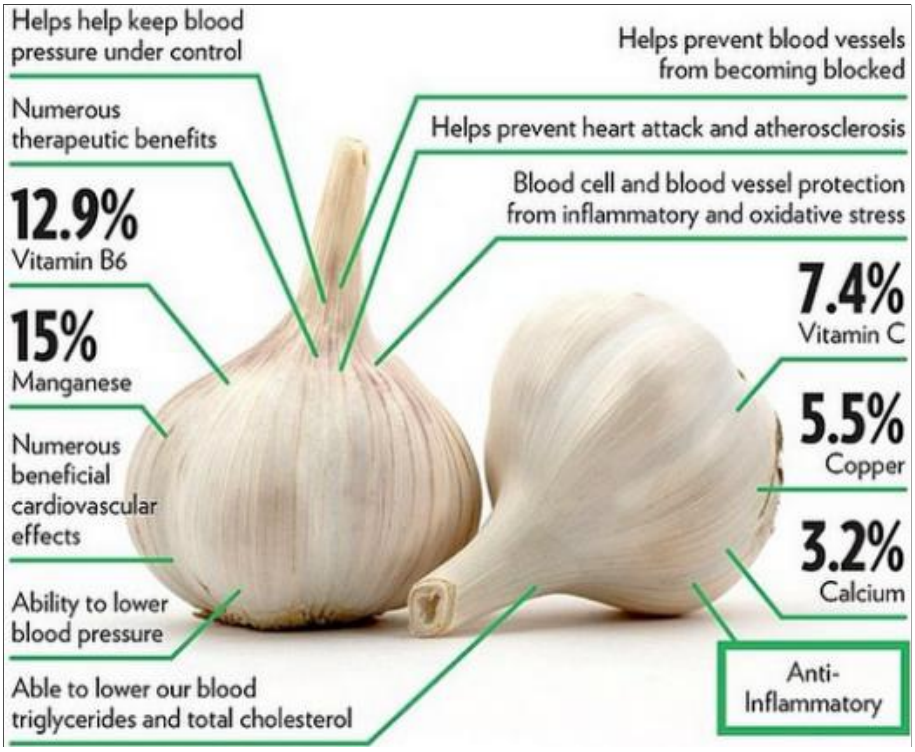


Fig 2: Health Benefits of Garlic

Cultivation and collection

Garlic is grown in the same way that onions are. It's usually grown as an irrigated crop all year round. It can be grown in a variety of settings, but thrives best in mild regions with few extremes of heat and cold. It may be grown in a range of soils. It grows well in a rich, well-drained clay loam. The land has been ploughed to a fine tilth, and beds and channels have been constructed. Garlic is grown on the lowlands in October-November and in the hills in February-March. Separate the cloves and lightly push them into the soil. Garlic necessitates a lot of manuring.

Prevent diabetes

A number of animal experiments have shown that garlic can lower blood glucose levels in mice with diabetes mellitus caused by streptozotocin or alloxan. Garlic has been shown to lower blood glucose levels in diabetic mice and rabbits in the majority of investigations. The effects of 14 days of oral garlic extract treatment on serum glucose, total cholesterol, triglycerides, urea, and uric acid in normal and streptozotocin-induced diabetic mice were investigated. The study found that diabetic mice had much lower serum glucose, total cholesterol, triglycerides, urea, uric acid, aspartate amino transferase, and alanine amino transferase levels, while normal mice had significantly higher serum insulin levels.

In streptomycin-induced type 1 diabetic mice, garlic has been demonstrated to prevent pancreatic cell injury, oxidative stress, and pathological alterations [51]. In diabetic rats, garlic also exhibited a protective effect against diabetic retinopathy. After 7 weeks of gastric gavage of raw garlic extract in rats, the weight, blood glucose, and morphological changes in retinal tissue in the garlic-treated group improved [52]. Furthermore, in streptomycin-induced diabetic rats, AGE demonstrated a dose-dependent anti-diabetic effect [53]. Furthermore, a meta-analysis of 768 patients with type 2 diabetes mellitus who participated in nine randomised controlled studies revealed that garlic supplements lowered fructosamine and glycosylated haemoglobin considerably. Garlic supplements were found to be beneficial in the treatment of type 2 diabetes mellitus in this investigation [54]. As a result, garlic and its bioactive components could be useful in the treatment of diabetes and diabetic complication.

Metformin combination with garlic and its mechanism of action

For many years, traditional medicine has used a wide range of plants and herbs to treat diabetes mellitus in Mexico and other nations. These plants are thought to have a critical role in providing alternative medicine, preventative agents, and as a source of novel leads in the drug discovery and development process. Metformin, derived from the *Galega officinalis* plant, is one of the most extensively used natural therapeutic medications to manage blood glucose levels in diabetes mellitus [55], and oral dose of metformin increases incretin effects by blocking the DPP-4 enzyme [56].

DPP-4 has emerged as a key therapeutic drug target for the treatment of diabetes mellitus in recent years, and significant effort by academia and the pharmaceutical industry has inevitably led to the creation of DPP-4 inhibitors with fewer adverse effects than currently approved FDA treatments. Garlic was determined to be more appealing throughout the plant screening process because of its antidiabetic potential, despite the fact that the mechanism of action is unknown. The DPP-4 inhibitory activity of garlic bulb extract was determined using a highly specific fluorometric technique in this study. Figure 3 depicts the DPP-4 inhibitory activity of produced garlic bulb extract in this investigation. At 100 g/mL, the garlic extract inhibited DPP-4 by 60.5 percent, indicating that the inhibitory capacity is concentration dependent. The results showed that produced garlic bulb extract, with an IC50 value of 70.9 g/mL, had a higher activity in inhibiting DPP-4. Free radicals, on the other hand, are well known for oxidising numerous biological components of cells, such as proteins, DNA, and lipids, resulting in cell death [57] and tissue damage [58]. Free radicals are neutralised by antioxidant activity, which avoids pathogenesis and diabetic complications [59, 60]. As a result, the capacity of garlic bulb extract to scavenge the DPPH radical was studied. The produced garlic bulb extract was shown to have a scavenging activity of 20%, which is equivalent to 10 g/mL ascorbic acid.

The goal of this study was to see how adding garlic to the antidiabetic drug metformin affected fasting blood glucose levels in patients with type 2 diabetes. Metformin was chosen because it is considered a first-line antidiabetic drug for the treatment of type 2 diabetes. It is safe to use regardless of age, body weight, or the severity of hyperglycemia, and it provides a handy pharmacological foundation for combined therapy with other anti-diabetic medications. In people with type 2 diabetes, metformin has a lower mortality and cardiovascular risk than most insulin secreting drugs such glimepiride, glibenclamide, glipizide, and tolbutamide. Metformin also has the advantage of not causing hypoglycemia because it does not enhance insulin secretion when used alone in patients with type 2 diabetes. Metformin is also known for assisting type 2 diabetic individuals in losing a small amount of weight. Garlic was added to the antidiabetic drug metformin with the hope of improving not only glycemic control but also lipid profile, which is a common occurrence in people with type 2 diabetes. When comparing baseline data at week 0 to week 12 and week 24, the results show a statistically significant decrease in fasting blood glucose and serum lipids in the garlic treated group as compared to the placebo treated group. Our findings back up prior preclinical research that garlic has hypoglycemic properties. Garlic was also reported to inhibit adrenal hypertrophy, corticosterone elevation, and blood glucose elevation in diabetic rats (Kasuga *et al*., 1999). Sallyl cysteine sulfoxide (Alliin), a sulfur-containing amino acid found in garlic, has been shown to have comparable efficacy in reducing hyperglycemia in diabetic rats to traditional antidiabetic medications like glibenclamide and insulin.

The alterations seen in this investigation are consistent with the findings of Eidia *et al*., 2006, who showed that administration of both garlic extract and glibenclamide tends to bring serum glucose and insulin levels closer to normal. Garlic (*Allium sativum*) human studies are insufficient and show conflicting results, despite many previous animal studies showing significant hypoglycemic effects of garlic. Some human clinical trials on garlic demonstrated hypoglycemic effects, but they were conducted in healthy people. The current study differs from earlier clinical trials in that garlic's hypoglycemic effects were detected in individuals with type 2 diabetes mellitus who were also taking the conventional anti-diabetic drug metformin. Although the exact mechanism for garlic's hypoglycemic effects is unknown, some research have suggested that garlic operates as an insulin secretagogue. It's also been suggested that the hypoglycemic impact of garlic is due to the presence of allylepropyldisulphide or diallyle disulphide. Garlic's antioxidant properties are another potential route for its use as an anti-diabetic medication. S-allyl cysteine sulfoxide, an isolated substance from garlic, is thought to have antioxidant and antiglycation activities. Garlic was also discovered to have hypoglycemic effects by preventing sulphydryl group insulin inactivation (Banerjee *et al.*, 2002). Patients with diabetes are more likely to develop coexisting hyperlipidemia, also known as diabetic dyslipidemia, which has been linked to an increased risk of cardiovascular disease. Patients with diabetes frequently require a combination of antidiabetic and antilipidemic medications to protect them from cardiovascular disease morbidity. In comparison to the placebo group, garlic had significant antilipidemic effects on all lipid markers. The shift in lipid profile found in this investigation is consistent with earlier clinical trials. Allicin inhibition of hydroxymethylglutaryl-CoA reductase (HMGCoA reductase) is thought to be the mechanism for garlic's antilipidemic actions. Garlic is thought to lower total cholesterol mostly through lowering LDL-C levels. The current study contrasts prior trials that found garlic to be ineffective. The most likely cause of this discrepancy is due to differences in garlic preparation, dose, and research period. Garlic has long been thought to be safe and suggested for a variety of common ailments, but too much of it might cause issues. Garlic breath and an uncommon allergic reaction are also expected side effects. Raw garlic and garlic powder formulations have also been linked to gastrointestinal adverse effects such as nausea and diarrhea. The enteric coated, odourless garlic tablet preparation used in this study did not cause any significant problems in patients with type 2 diabetes mellitus, and only one patient complained of gastric discomfort. This good tolerance could be due to the enteric coated, odourless garlic tablet preparation used in this study.

Activity Shown By Garlic

1. Antibacterial [bactericide] is a substance that kills bacteria.
2. Antibiotic [a substance that kills or inhibits the growth of microorganisms] (a highly effective natural antibiotic that does not harm the body's natural flora)

3. Anthelmintic [a substance that kills or expels worms and parasites in the intestine; vermicide; vermifuge]
4. Antioxidant [aids in the oxidation of free radicals, which are thought to play a role in premature ageing and dementia] (a really strong one)
5. Antispasmodic [a substance that relieves muscle spasms, cramps, and convulsions]
6. It thins the blood
7. Carminative [an agent that relieves griping pains, colic, and helps the intestines expel gas]
8. Anti-cancer activities
9. Anticoagulant [a substance that prevents clots from forming in a liquid, such as blood]
10. Antiseptic [a substance that prevents microorganisms from growing on living things]
11. Anti-tumor medication is number 11 on the list (inhibits tumour cell formation)
12. Antiviral (a substance that kills viruses)
13. Increases the flow of bile into the intestines by acting as a cholagogue fan agent.
14. Perspiration-inducing diaphoretic fan agent]
15. Digestive [addresses the gastrointestinal system]
16. Diuretic (a substance that cleanses the urinary system by increasing the volume and flow of urine)
17. Expectorant lan agent that promotes mucous and secretion discharge from the respiratory passages]
18. 16. Febrifuge [a substance that reduces or eliminates the effects of favours]
19. Stomachic [a stomach-strengthening, stimulating, or toning agent] 20. Stimulant [a substance that stimulates or accelerates the functional activity of tissues, resulting in increased energy]

Garlic's remarkable biological functions, including antioxidant, cardiovascular protective, anticancer, anti-inflammatory, immunomodulatory, anti-diabetic, anti-obesity, and antibacterial properties, have been demonstrated in numerous studies in recent decades [61, 62, 63, 64, 65, 66, 67, 68]. In comparison to fresh garlic, studies have increasingly concentrated on black garlic, a processed garlic product with higher polyphenol and flavonoid content as well as stronger antioxidant characteristics [69, 70].

Past, present and future aspect

Diabetes mellitus treatment necessitates medication intervention at some point throughout the disease's progression. According to their development history, antidiabetic drugs are divided into three parts: I, II, and III. Part I includes insulin, sulfonylureas, metiglinides, insulin sensitizers, biguanides, and -glucosidase inhibitors, which were all developed in the early twentieth century. Part II includes GLP-1 analogues, DPP-VI inhibitors, amylin analogues, and SGLT2 inhibitors, which were all created in the first decade of the twenty-first century. Part III identifies prospective targets for the development of innovative anti-diabetic medicines with fewer side effects than those already available.

In both the industrialised and developing worlds, diabetes has reached epidemic proportions. Because there have been numerous new improvements in the area in the previous several years, a new and up-to-date assessment of these advancements, as well as their rigorous appraisal, will aid both clinical and research diabetologists in better understanding where the profession is now headed.

Various attempts to control/check it have been done in the recent past. Natural antidiabetic medications are becoming increasingly popular. The literature on anti-diabetic plants is fragmented.

Endophytic fungus live inside plants and causes no harm to the host plant. They are a less well-known source of bioactive metabolites like anticancer, antioxidant, antibacterial, antidiabetic, and industrial enzymes.

There are specific features of garlic enhancement in general, and long-day garlic in particular, that are unique to the Indian and global garlic research communities. By the year 2050, India would need to grow 30 lakh tone of garlic to meet its ever-increasing population, export, and processing demands [71]. Increased production from the current 12.5 lakh tone level will necessitate genetic enhancement through the establishment of diversity and improved plant protection measures. Improvements in industrial technology, molecular knowledge, and explorations and introductions are all on the horizon.

Although garlic is thought to be a safe ingredient, long-term studies of a fair length of time would shed light on the potential adverse effects of various garlic extracts. Garlic's safety should be investigated in pregnant or breastfeeding women, as well as small children. Long-term and large trials are also needed to assess the differences in cancer and cardiovascular disease mortality, major adverse events, and morbidity after garlic therapy.

Conclusion

- Oral hypoglycemic medicines and insulin are used to treat diabetes. Through additive or synergistic activities, positive interactions between herbs and medicines may lead to increased effectiveness of anti-diabetic medications.
- Based on the results of our study, we conclude that as this drug has minimal complications and useful effects on blood glucose levels, it can be used as a supplementary drug for treatment of patients with diabetes mellitus.

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