Journal of Associated Medical Sciences 2025; 58(1): 205-214

JAMS
Journal of Associated Medical Sciences

Scopus Indexed & Thai-Journal Citation Index Centre (TCI)

Journal of Associated Medical Sciences

Journal homepage: https://www.tci-thaijo.org/index.php/bulletinAMS/index

Review article: Local medicinal plants in Nigeria for the management of diabetes; an evaluating of glucose metabolism, insulin sensitivity, and physiological parameters

Olusoji Adebusoye Oyesola*, Eunice Oluwabunmi Ojo-Adebayo, Oluwaseye Emmanuel Olayemi, Solomon Olawale Adebanjo.

Department of Physiology, Faculty of Basic Medical Sciences, Olabisi Onabanjo University, Ago Iwoye, Ogun State, Nigeria.

ARTICLE INFO

Article history:
Received 21 November 2024
Accepted as revised 22 November 2024
Available online 23 November 2024

Keywords:
Aloe vera, bitter leaf, bitter lemon, diabetes mellitus, ginger.

ABSTRACT

Background: Nigeria, like many regions worldwide, faces a growing burden of diabetes, prompting increased interest in traditional medicinal practices.

Objective: This review examines the efficacy of local medicinal plants in Nigeria for managing diabetes mellitus, focusing on their effects on glucose metabolism, insulin sensitivity, and physiological parameters.

Materials and methods: Four commonly used plants, Aloe vera, bitter leaf *(Vernonia amygdalina)*, bitter lemon *(Citrus aurantium)*, and ginger *(Zingiber officinale)*, were scrutinized for their potential therapeutic effects.

Results: The literature review revealed numerous studies exploring the antidiabetic properties of these plants, including their ability to lower blood glucose levels, improve insulin sensitivity, and modulate various physiological parameters associated with diabetes.

Conclusion: The findings suggest promising avenues for utilizing local medicinal plants in diabetes management, although further research, including clinical trials, is warranted to validate their efficacy and safety.

Introduction

Diabetes is a chronic metabolic disorder characterized by high blood glucose levels caused by impaired insulin synthesis, action, or both. This disease has become a primary global health concern, affecting millions of people around the world. According to the International Diabetes Federation (IDF), around 463 million persons had diabetes in 2019, with this figure expected to climb to 700 million by 2045.[1] Diabetes prevalence is impacted by several factors, including genetics, age, ethnicity, and lifestyle choices.[2] While genetic predisposition is essential in diabetes development, lifestyle variables have emerged as significant predictors of its onset and progression.[3,4] A Sedentary lifestyle, poor eating habits, and obesity have all been linked to an increased risk of acquiring type 2 diabetes.[5,6] Furthermore, physical inactivity contributes significantly to the increased prevalence of diabetes. Sedentary behavior and a lack of regular physical activity have been associated with insulin resistance, poor glucose metabolism, and an increased risk of developing type 2 diabetes.[7] Understanding the physiological changes due to diabetes is critical for creating tailored therapies.

Insulin, a hormone released by the pancreas, is vital in controlling blood glucose levels. In people with type 1

* **Corresponding contributor.**
Author's Address: *Department of Physiology, Faculty of Basic Medical Sciences, Olabisi Onabanjo University, Ago Iwoye, Ogun State, Nigeria*
E-mail address: olusoji.oyesola@oouagoiwoye.edu.ng
doi: 10.12982/JAMS.2025.023
E-ISSN: 2539-6056

diabetes, the pancreas fails to produce insulin, resulting in uncontrolled hyperglycemia. Type 2 diabetes, on the other hand, is distinguished by insulin resistance, in which the body's cells become less receptive to insulin action. Insulin resistance is frequently associated with reduced insulin secretion.

Diabetes has far-reaching systemic consequences in addition to its effects on glucose metabolism. Chronic hyperglycemia can result in both microvascular and macrovascular repercussions, such as retinopathy, nephropathy, neuropathy, and cardiovascular disease. Oxidative stress, inflammation, and endothelial dysfunction are the underlying causes.[8]

Despite advancements in medical interventions, managing diabetes remains a significant challenge. While conventional treatment options such as insulin therapy and oral hypoglycemic agents are available, they may be associated with adverse effects and limited efficacy.[9] Therefore, there is a need to explore alternative approaches to diabetes management. This review aims to investigate the potential use of some selected medicinal plants in diabetes management and evaluate their effects on glucose control, insulin sensitivity, and other relevant physiological parameters.

This review will contribute to the growing knowledge of using medicinal plants in diabetes management, which may provide additional treatment options for individuals with diabetes. Secondly, investigating bioactive compounds and their mechanisms of action can shed light on the physiological pathways involved in glucose regulation, potentially leading to developing novel therapeutic approaches. Additionally, evaluating potential side effects or adverse reactions associated with medicinal plant extracts will provide valuable insights into their safety profile.

This review justifies the need for alternative and complementary approaches to diabetes management. Conventional treatment options for diabetes have limitations, including side effects and variable efficacy. Medicinal plants in diabetes management offer a potential avenue for developing safer and more effective therapeutic interventions. By exploring the impact of medicinal plant extracts on glucose control, insulin sensitivity, and related physiological parameters, this review will provide scientific evidence for their potential utility in diabetes management, ultimately benefiting individuals with diabetes and healthcare providers seeking additional treatment options.

Medicinal plants

Medicinal plants have been used in traditional medicine systems for centuries to manage diabetes. These plants contain bioactive compounds that may exert anti-diabetic effects by various mechanisms, including enhancing insulin secretion, improving insulin sensitivity, and reducing postprandial glucose levels.[10] Research on medicinal plants for diabetes management has gained momentum recently. Studies have investigated the bio-active compounds present in these plants, their mechanisms of action, and their potential as adjuvant therapy in diabetes management.[2,10]

Medicinal plants with anti-diabetic activities

Aloe vera

Aloe vera *(Aloe barbadensis miller)* is a widely recognized medicinal plant used for centuries in traditional medicine systems. Its gel, extracted from the leaves, contains various bioactive compounds that have shown potential in managing diabetes mellitus.

Traditional use of aloe vera

1. Wound healing: Aloe vera has long been recognized for its wound-healing properties. The aloe vera leaf gel contains polysaccharides, such as acemannan, which have been shown to accelerate wound healing by promoting collagen synthesis and enhancing the proliferation of fibroblasts.[11] The gel can be topically applied to minor burns, cuts, and abrasions to promote healing and reduce inflammation.[12]

2. Skin conditions: Aloe vera has been used traditionally to alleviate various skin conditions, including sunburn, psoriasis, and dermatitis. The aloe vera gel possesses anti-inflammatory and moisturizing properties, which can help soothe irritated skin and reduce redness.[13] It may also aid in the regeneration of skin cells and the repair of damaged tissues.[11] Topical application of aloe vera gel is effective in reducing the symptoms of psoriasis and improving the overall condition of the skin.[14,15]

3. Digestive health: Aloe vera has a long history of use in traditional medicine for digestive ailments, including constipation, indigestion, and irritable bowel syndrome (IBS). The aloe vera gel contains anthraquinone compounds, such as aloin, which have laxative properties and can help relieve constipation.[16] Additionally, aloe vera gel has been shown to have anti-inflammatory effects on the digestive tract, which may benefit individuals with IBS or inflammatory bowel disease.[17]

4. Immune system support: Aloe vera has been traditionally used to support immune function. The aloe vera gel contains bioactive compounds, including polysaccharides and antioxidants, which have immunomodulatory effects.[18] These compounds can enhance the activity of immune cells and promote the production of antibodies, thus supporting the body's defense against pathogens.[11]

Aloe vera bioactive compounds and mechanisms of action

Aloe vera gel contains several bioactive compounds, including polysaccharides, anthraquinones, flavonoids, and phytosterols. These compounds are believed to contribute to the plant's therapeutic properties in diabetes management.

Polysaccharides present in aloe vera, such as acemannan, have been shown to possess immunomodulatory and anti-inflammatory effects. They may help improve insulin sensitivity by reducing chronic low-grade inflammation, often associated with insulin resistance.[19] Additionally, polysaccharides may stimulate insulin release

from pancreatic beta cells, promoting glucose uptake by peripheral tissues.[11]

Anthraquinones, such as aloin and emodin, found in aloe vera, have exhibited antioxidant and anti-inflammatory properties. These compounds may help protect pancreatic beta cells from oxidative stress and inflammation, preserving their function and insulin production. [19]

Flavonoids in aloe vera, including quercetin and kaempferol, possess antioxidant and anti-inflammatory activities.[20] They may improve insulin sensitivity by reducing oxidative stress and inflammation in insulin-target tissues.[21]

Phytosterols, such as beta-sitosterol, are plant-derived compounds found in aloe vera. They have been shown to enhance insulin sensitivity by modulating cellular signaling pathways involved in glucose metabolism.[22]

Aloe vera impact on insulin sensitivity and insulin secretion

Studies have investigated the impact of aloe vera extracts on insulin sensitivity and secretion. Animal and *in vitro* studies have shown that aloe vera gel or its components can improve insulin sensitivity by enhancing glucose uptake and utilization in peripheral tissues.[11,19] Aloe vera extracts have also been reported to stimulate insulin secretion from pancreatic beta cells, potentially contributing to improved glycemic control.[11]

However, it is essential to note that human clinical trials investigating the effects of aloe vera on insulin sensitivity and insulin secretion in individuals with diabetes are limited. Further research is necessary to establish aloe vera supplementation's specific dosage, duration, and efficacy in improving human insulin sensitivity and secretion.

Previous studies on the anti-diabetic effect of aloe Vera

Dede *et al*. studied Aloe vera's antihyperglycemic and histological effects in an alloxan-induced diabetic Wistar rat model.[20] Their findings showed that 100 mg/kg, 200 mg/kg, and 400 mg/kg of aloe vera dramatically lowered blood glucose levels dose-dependently. In an alloxan-induced diabetic Wistar rat model, aloe vera displayed antihyperglycemic effects and retained organ histology, indicating its promise as an alternative or complementary therapy for diabetes control.

Also, Arora *et al*. evaluated the effect of aloe vera on diabetes-induced nephropathy in rats in another investigation.[21] Streptozotocin (STZ) (55 mg/kg intraperitoneally once) was given to rats to establish experimental diabetes mellitus. Treatment with aloe vera (300 mg/kg/day orally) was found to be more effective against diabetes-induced nephropathy and renal oxidative stress than the reference drug, lisinopril (1 mg/kg/day orally). Aloe vera (300 mg/kg/day orally) medication may have averted the development of diabetes-induced nephropathy by lowering lipid levels, reducing renal oxidative stress, and providing a direct renoprotective effect.[21]

Potential side effects or adverse reactions of aloe vera

While aloe vera is generally considered safe for topical use and ingestion in moderate amounts, there have been reports of potential side effects and adverse reactions associated with its use for diabetes management.[22]

Oral aloe vera extracts may cause gastrointestinal disturbances, such as diarrhea, abdominal cramps, and electrolyte imbalances.[23] Prolonged and excessive use of aloe vera can also lead to a laxative effect due to the presence of anthraquinones, which may result in electrolyte depletion and dehydration.[23]

Furthermore, individuals who are on medication for diabetes or other medical conditions should exercise caution when using aloe vera extracts, as they may interact with certain medications, affecting their efficacy or increasing the risk of adverse effects.[23]

Bitter leaf

Bitter leaf *(Vernonia amygdalina)* is a plant widely recognized for its medicinal properties and is commonly used in traditional African medicine systems. It belongs to the Asteraceae family and is known by various names, including *"Onugbu"* in Igbo and *"Ewuro"* in Yoruba. Due to its bioactive compounds and therapeutic properties, bitter leaf has gained attention for its potential role in managing diabetes mellitus.

Traditional use of bitter leaf

1. Digestive health: Bitter leaf has been traditionally used to support digestive health and alleviate gastrointestinal issues. It is known for its bitter taste, which stimulates the production of digestive enzymes and promotes healthy digestion.[24] Bitter leaf extracts have been found to possess antidiarrheal properties and can help reduce the frequency and severity of diarrhea.[24,25]

2. Fever and malaria: Bitter leaf has been used traditionally to manage fever and malaria. Studies have shown that bitter leaf extracts possess antipyretic properties and can help reduce body temperature during fever. Bitter leaf extracts have also exhibited antimalarial activity against Plasmodium falciparum, the parasite responsible for malaria.[26]

3. Diabetes management: Bitter leaf has been traditionally used to regulate blood sugar levels and manage diabetes. Research has shown that bitter leaf extracts can lower blood glucose levels by enhancing insulin secretion and sensitivity. Bitter leaf extracts have also demonstrated antioxidant properties, which can help protect against oxidative stress associated with diabetes.[27,28]

4. Anti-inflammatory and antioxidant effects: Bitter leaf contains bioactive compounds, including flavonoids and phenolic compounds, with anti-inflammatory and antioxidant properties. These properties contribute to its traditional use for inflammation-related conditions, such as arthritis and rheumatism. In experimental studies, Bitter leaf extracts inhibit inflammatory mediators and reduce oxidative stress.[29]

Bitter leaf bioactive compounds and mechanisms of action

Bitter leaf contains diverse bioactive compounds that contribute to its medicinal properties. Some essential compounds identified in bitter leaves include sesquiterpene lactones, flavonoids, alkaloids, phenolic compounds, and steroids.

Sesquiterpene lactones, such as vernodalin and vernolide, are prominent bioactive compounds in bitter leaves. These compounds possess anti-inflammatory, antioxidant, and immunomodulatory properties. They have been reported to inhibit the production of pro-inflammatory cytokines, which could contribute to the prevention of chronic low-grade inflammation often associated with insulin resistance.[30]

Flavonoids, including luteolin and quercetin, are present in bitter leaves and exhibit antioxidant and anti-inflammatory effects. These compounds have been shown to enhance insulin signaling, improve glucose uptake, and protect pancreatic beta cells from oxidative stress.[31,32]

Alkaloids, such as vernonioside B1, are bioactive compounds in bitter leaves. They have demonstrated hypoglycemic effects and may contribute to improving insulin sensitivity.[33]

Phenolic compounds, such as caffeic acid and chlorogenic acid, possess antioxidant properties and may help reduce oxidative stress in diabetes. They have also shown potential in modulating glucose metabolism and insulin sensitivity.[31,32]

Steroids, including beta-sitosterol, have been identified in bitter leaf and may contribute to its antidiabetic effects. Beta-sitosterol has been reported to enhance insulin sensitivity and improve glucose uptake in peripheral tissues.[32]

Bitter leaf impact on insulin sensitivity and insulin secretion

Research has investigated the impact of bitter leaf extracts on insulin sensitivity and secretion. Animal and in vitro studies have shown that bitter leaf extracts can improve insulin sensitivity by enhancing glucose uptake in skeletal muscle and adipose tissue.[32] These extracts have also been reported to stimulate insulin secretion from pancreatic beta cells, potentially contributing to improved glycemic control.[32]

Previous studies on the anti-diabetic effect of bitter leaf

Vernonia amygdalina aqueous leaf extract was studied for its hypoglycemic impact in diabetic rats by Johnbull *et al*.[34] Over seven days, normal and diabetic rats were given three doses of the extract (100, 200, and 400 mg/kg). The 400 mg/kg dose reduced fasting blood sugar levels from 494.83 mg/dL to 81 mg/dL, the 200 mg/kg dose decreased levels from 382.33 mg/dL to 98 mg/dL, and the 100 mg/kg dose brought levels down to 110 mg/dL. The extract also substantially affected rats' body weight and other biochemical and hematological parameters, suggesting its potent hypoglycemic activity.

Nwaoguikpe *et al*.[35] investigated the effect of bitter leaf extract (Vernonia amygdalina) on blood glucose levels in diabetic rats. Vernonia amygdalina (bitter leaf) plant extract was given to rats orally at doses of 2%, 4%, 6%, 8%, and 10% before meals for 5, 10, and 15 days, respectively, after which blood samples were collected and analyzed for glucose levels using enzymatic methods. Blood glucose levels dropped dramatically from a mean of 4.44 0.2 mmol/L to 1.66 0.2 mmol/L. The reduction in blood glucose levels seen in rats after administration of the plant extract implies that the plant extract has anti-diabetic, anti-hyperglycemic, and hypoglycemic actions on alloxan-induced diabetic rats.

Potential side effects or adverse reactions of bitter leaf

Bitter leaf is generally considered safe for consumption when used in moderate amounts. However, there are potential side effects and precautions to consider. Bitter leaves may cause gastrointestinal discomfort in some individuals, including abdominal pain, diarrhea, or nausea.[32] It is important to note that individual tolerances may vary, and everyone does not experience these side effects.

Bitter leaf extracts have been reported to have uterine stimulant effects and may induce contractions. Therefore, pregnant women should avoid the excessive consumption of bitter leaves.[34]

Bitter melon

Bitter melon *(Momordica charantia),* also known as bitter gourd or karela, is a tropical vine that belongs to the Cucurbitaceae family. It is widely cultivated and consumed in various parts of the world, including Asia, Africa, and the Caribbean. Bitter melon is renowned for its medicinal properties and has been traditionally used for centuries to manage various health conditions, including diabetes mellitus.[35]

Traditional use of bitter melon

1. Blood sugar regulation: Bitter melon has been traditionally used to help regulate blood sugar levels and manage diabetes. Research has shown that bitter melon extracts contain bioactive compounds, including charantin, polypeptide-p, and vicine, which possess hypoglycemic properties.[10] These compounds have been found to increase insulin sensitivity, stimulate glucose uptake, and inhibit glucose production in the liver.[36,37]

2. Digestive health: Bitter melon has traditionally been used to support digestive health and alleviate gastrointestinal issues. It has been reported to possess anti-ulcer properties and can help protect the gastric mucosa from damage. Bitter melon extracts have also demonstrated anti-inflammatory effects in the gastrointestinal tract, which may help reduce symptoms of inflammatory bowel disease.[38,39]

3. Antioxidant and anti-inflammatory effects: Bitter melon contains various bioactive compounds, including flavonoids, phenolic compounds, and triterpenoids, which possess antioxidant and anti-inflammatory properties.[40] These properties contribute to its traditional use as an anti-aging remedy and for the management of inflammatory conditions such as arthritis.[41,36]

4. Immune system support: Bitter melon has been traditionally used to support immune function. Studies have shown that bitter melon extracts can enhance the activity of immune cells, such as natural killer (NK) cells and macrophages, which play a crucial role in immune defense. Bitter melon extracts have also exhibited anti-bacterial and antiviral properties, possibly contributing to their traditional use for infectious diseases.[42,43]

Bitter melon bioactive compounds and mechanisms of action

Bitter melon contains various bioactive compounds that contribute to its therapeutic effects. Some essential compounds identified in bitter melon include charantin, polypeptide-p, vicine, momordicin, and various flavonoids and phenolic compounds.

Charantin, one of the major bioactive compounds in bitter melon, is believed to contribute to its anti-diabetic properties. It has been found to exhibit hypoglycemic effects by increasing glucose uptake and utilization in peripheral tissues and inhibiting intestinal glucose absorption.[41] Charantin stimulates insulin release from pancreatic beta cells, promoting better glycemic control.[44]

Polypeptide-p is a bioactive compound found in bitter melon that mimics the action of insulin. It reduces blood glucose levels through enhanced glucose uptake by peripheral tissues and suppression of glucose production in the liver.[45] Polypeptide-p has antioxidant properties and may help protect pancreatic beta cells from oxidative damage.[45]

Vicine, another compound present in bitter melon, has been reported to possess hypoglycemic activity. It may enhance glucose utilization and reduce hepatic glucose production, improving glycemic control.[45]

Momordicin is a type I ribosome-inactivating protein found in bitter melon. It has been shown to have antiviral, antitumor, and immunomodulatory effects.[45] While its direct impact on diabetes management is not well-studied, its overall health benefits may indirectly contribute to better metabolic health.

Bitter melon also contains various flavonoids and phenolic compounds with antioxidant and anti-inflammatory properties. These compounds may help reduce oxidative stress, inflammation, and insulin resistance, improving insulin sensitivity and glycemic control.[46]

Bitter melon impact on insulin sensitivity and insulin secretion

Studies have explored the impact of bitter melon extracts on insulin sensitivity and secretion. Animal and in vitro studies have shown that bitter melon extracts can improve insulin sensitivity by enhancing glucose uptake in peripheral tissues, such as skeletal muscle and adipose tissue.[47] These extracts have also been reported to stimulate insulin secretion from pancreatic beta cells, improving glycemic control.[44]

Several clinical studies have investigated the effects of bitter melon on insulin sensitivity and glycemic control in individuals with diabetes. These studies have shown mixed results, with some demonstrating improvements in insulin sensitivity and glycemic markers while others have reported no significant effects.[46-48] It is important to note that the dosages and preparations of bitter melon extracts can vary across studies, which may contribute to the differences in outcomes.

Further research, including well-designed clinical trials, is needed to determine the optimal dosages, preparations, and long-term effects of bitter melon supplementation on insulin sensitivity and secretion in individuals with diabetes.

Previous studies on the anti-diabetic effect of bitter melon

According to research by Mohammady *et al*.[39] on the effect of Momordica charantia extract on glucose tolerance and some biochemical parameters in alloxan-induced diabetes, comparing it to the impact of rosiglitazone maleate, an oral hypoglycemic drug, and to suggest the possible mechanisms of its action.[39] Rats were divided into 5 groups: normal control, rats received bitter melon, diabetic control, diabetic treated with rosiglitazone (4 mg/kg BW), and the diabetic received Momordica charantia (300 mg/kg BW). After 4 weeks, significantly increased insulin release from the pancreas and serum insulin level, increased glucose uptake by rat diaphragm, and decreased intestinal glucose absorption (p<0.05). Bitter melon treatment of diabetic rats resulted in significant hypoglycemic and hypolipidemic effects as compared to rosiglitazone (p<0.05). Anti-diabetic effects of bitter melon may include increasing insulin release and serum insulin, increasing glucose uptake by muscles, decreasing intestinal glucose absorption, and having a hypolipidemic effect.

Potential side effects or adverse reactions of bitter melon

Bitter melon is generally considered safe for consumption when used in moderation. However, there are potential side effects and precautions to consider.

Bitter melon has a naturally bitter taste, which some people may find unpleasant. Excessive bitter melon or its extracts may cause gastrointestinal discomfort, including abdominal pain, diarrhea, or nausea.[47]

Individuals who are pregnant or breastfeeding should exercise caution when consuming bitter melon due to its potential uterine stimulant effects.[49] It is advisable to consult with a healthcare professional before incorporating bitter melon extracts into the diabetes management regimen. Bitter melon may interact with certain medications, including antidiabetic medicines, leading to hypoglycemia. Therefore, individuals taking drugs for diabetes should monitor their blood glucose levels closely and consult with a healthcare professional before using bitter melon extracts.[46]

Ginger (Zingiber officinal)

Ginger *(Zingiber officinale)* is a popular spice and medicinal herb used for centuries in various traditional medicine systems. It is known for its distinct flavor and aroma and is widely used in culinary preparations worldwide. In addition to its culinary uses, ginger has

gained attention for its potential health benefits, including its effects on insulin sensitivity and diabetes management .[50]

Traditional use of ginger

Ginger *(Zingiber officinale)* is a widely used spice and medicinal plant with a long history of traditional use. It has been utilized in various traditional medicine systems, including Ayurveda, Traditional Chinese Medicine, and traditional healing practices in many cultures.[51]

1. Digestive aid: Ginger has traditionally alleviated digestive discomfort and promoted digestive health. It is known for its carminative properties, which help relieve symptoms such as bloating, gas, and indigestion.[52] Ginger has also been used to stimulate appetite and improve digestion.[53] It is often consumed as a tea or in meals to support digestive function.

2. Nausea and vomiting: Ginger has a long history of traditional use for reducing nausea and vomiting, including motion sickness, morning sickness during pregnancy, and chemotherapy-induced nausea.[54] Several studies have reported the antiemetic (anti-nausea) properties of ginger, attributing them to its active compounds, such as gingerols and shogaols.[55]

3. Anti-inflammatory and pain relief: Ginger has been traditionally used for its anti-inflammatory properties and to relieve pain associated with various conditions.[56] It is believed to inhibit inflammatory pathways and reduce the production of inflammatory mediators.[57] Traditional use of ginger includes its application topically or consumption as a tea or in food to alleviate pain associated with arthritis, muscle soreness, and menstrual cramps.[53]

4. Immune support: Ginger has been traditionally used to support the immune system and protect against infections. It is believed to possess antimicrobial properties, including against bacteria and viruses. Traditional use of ginger includes its consumption as a tea or inclusion in meals to promote overall immune health. [58]

Bioactive compounds and mechanisms of action

Ginger contains a variety of bioactive compounds that contribute to its pharmacological properties. Some of the essential compounds found in ginger include gingerols, shogaols, paradols, zingerones, and various flavonoids.[59]

Gingerols are the most abundant bioactive compounds present in fresh ginger. They possess anti-inflammatory, antioxidant, and analgesic properties. Gingerols have been found to inhibit the production of pro-inflammatory enzymes such as cyclooxygenase (COX) and lipoxygenase (LOX), thereby reducing inflammation.[57] They also scavenge free radicals and reduce oxidative stress.[60]

Shogaols, derived from gingerols during the drying or cooking process, exhibit similar pharmacological activities to gingerols. They possess anti-inflammatory and antioxidant effects and have been suggested to be more potent than gingerols in specific contexts. [61]

Paradols are another group of bioactive compounds found in ginger. They possess antioxidant and anti-inflammatory properties and have been shown to modulate signaling pathways involved in inflammation, such as nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinases (MAPKs).[62]

Zingerones, derived from gingerols, also exhibit antioxidant, anti-inflammatory, and anti-cancer activities. They have been found to suppress inflammatory mediators and inhibit the growth of cancer cells through mechanisms such as cell cycle arrest and induction of apoptosis.[63]

Flavonoids in ginger, such as gingerenones and gingerols, contribute to its antioxidant and anti-inflammatory effects. They scavenge free radicals, reduce oxidative stress, and modulate inflammatory pathways, exerting protective effects on various organs and systems. [61]

These bioactive compounds in ginger collectively contribute to its beneficial health and disease management effects.

Ginger impact on insulin sensitivity and insulin secretion

Insulin sensitivity refers to the body's ability to respond to insulin and utilize glucose effectively. Impaired insulin sensitivity is a hallmark of conditions like insulin resistance and type 2 diabetes. Ginger extracts have been studied for their potential effects on insulin sensitivity and secretion.

Animal studies have shown promising results regarding the impact of ginger on insulin sensitivity. Ginger supplementation has been found to improve insulin sensitivity by enhancing glucose uptake in peripheral tissues and reducing insulin resistance. [64,65] These effects may be mediated by the modulation of various molecular pathways involved in glucose and lipid metabolism, such as the insulin signaling pathway and glucose transporter expression.[65]

Regarding insulin secretion, ginger has been reported to have stimulatory effects on pancreatic beta cells, leading to increased insulin release. [64,65] This may contribute to improved glycemic control and regulation of blood glucose levels.

While animal studies have shown promising results, clinical studies in humans have provided mixed findings. Some human studies have reported improved insulin sensitivity and glycemic control with ginger supplementation, while others have not observed significant effects.[66-68] Further research, including well-designed clinical trials, is needed to establish the optimal dosages, treatment durations, and long-term effects of ginger supplementation on insulin-related parameters in individuals with diabetes.[69,70]

Previous studies on the anti-diabetic effect of ginger

Al-Azhary *et al.* conducted a study on diabetic cholesterol-fed rats to examine the effects of ginger on blood glucose, lipids, oxidative stress, and early stages of atherogenesis.[71] The rats were divided into control, diabetic cholesterol-fed, and diabetic cholesterol-fed rats were administered ginger (25 mg/kg). Diabetes was induced in both the second and third groups of animals by intraperitoneal injection with one dose of streptozotocin (60 mg/kg). After six weeks, ginger administration led

to a decrease in blood glucose and triglyceride levels. However, it did not fully restore the increase in cholesterol and low-density lipoprotein cholesterol levels. Ginger also reduced malondialdehyde concentration and increased total plasma antioxidant activity. Electron microscopy studies showed that ginger improved the cellular changes in the aortic wall of diabetic cholesterol-fed rats.[72]

According to a study by Ojewole *et al.,* administering an alcoholic extract of ginger orally at a dosage of 800 mg/kg resulted in a significant reduction in fasting blood sugar levels in streptozotocin (STZ)-diabetic rats.[73] The maximum effect was observed after 4 hours, and blood glucose levels were reduced by 24-53%, with doses ranging from 100 mg/kg to 800 mg/kg. Also, a study by Islam and Choi 2008 used a nicotinamide and low-dose STZ-diabetic rat model.[60] It was observed that oral administration of ginger powder at a dose of 200 mg/kg led to alleviating signs associated with metabolic syndrome. These signs included reductions in blood glucose and serum lipids and increased total antioxidant capacity (TAC).

Potential side effects or adverse reactions of ginger

Ginger is generally considered safe for consumption, and adverse reactions are rare when consumed in moderate amounts. However, some individuals may experience mild gastrointestinal symptoms such as heartburn, bloating, or diarrhea.[74]

Ginger may have antiplatelet and anticoagulant properties, which can affect blood clotting.[75] Therefore, individuals taking anticoagulant medications or those with bleeding disorders should exercise caution and consult with a healthcare professional before using ginger supplements.[76] In rare cases, allergic reactions to ginger have been reported. Symptoms may include rash, itching, swelling, or difficulty breathing.[77]

Ginger may interact with certain medications, including antidiabetic medicines, leading to hypoglycemia or potentiation of their effects.[78]

Pregnant women and individuals with gallstones or other gallbladder conditions should also exercise caution and consult with a healthcare professional before using ginger supplements, as ginger may affect gallbladder function or stimulate contractions in pregnant women.[79]

Conclusion

In conclusion, the review underscores the significant potential of local medicinal plants in Nigeria for managing diabetes mellitus. Aloe vera, bitter leaf, bitter lemon, and ginger have shown promising effects in modulating glucose metabolism, enhancing insulin sensitivity, and influencing various physiological parameters associated with diabetes. However, while the findings are encouraging, more rigorous research, including clinical trials, is necessary to validate their efficacy, elucidate underlying mechanisms, and assess long-term safety profiles. Incorporating these traditional remedies into mainstream diabetes management strategies could offer cost-effective and culturally appropriate interventions to alleviate the burden of diabetes in Nigeria and similar regions. Further collaboration between traditional medicine practitioners, researchers, and healthcare professionals is essential to harness the full potential of local medicinal plants in combating diabetes and improving public health outcomes.

Conflict of interest

The Authors have declared no conflict of interest concerning this work or its publication.

References

[1] Evert AB, Dennison M, Gardner CD, Garvey WT, Lau KHK, MacLeod J, and Yancy WS. Nutrition therapy for adults with diabetes or prediabetes: A consensus report. Diabetes Care. 2019; 42(5): 731-54. doi: 10.2337/dci19-0014.

[2] Gupta RK, Patel AK, Shah N, Chaudhary AK, and Jha UK. A review on medicinal plants with antidiabetic activity. J Pharmacogn Phytochem. 2017; 6(6): 2340-5. doi:10.7897/2230-8407.097122

[3] Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. New England J Med. 2011; 345(11): 790-7. doi: 10.1056/NEJMoa010492.

[4] Piko P, Werissa NA, Fiatal S, Sandor J, and Adany R. Impact of Genetic Factors on the Age of Onset for Type 2 Diabetes Mellitus in Addition to the Conventional Risk Factors. J Pers Med. 2020; 11(1): 6. doi: 10.3390/jpm11010006.

[5] Kahn SE, Hull RL, and Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006; 444(7121): 840-6. doi: 10.1038/nature05482.

[6] Malik VS, Popkin BM, Bray GA, Després JP, and Willett WC. Sugar-sweetened beverages, obesity, type 2 diabetes mellitus, and cardiovascular disease risk. Circulation. 2010; 121(11): 1356-64. doi: 10.1161/CIRCULATIONAHA.109.876185.

[7] Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, *et al*. Physical activity/exercise and diabetes: A position statement of the American Diabetes Association. Diabetes Care. 2016; 39(11): 2065-79. doi.org/10.2337/dc16-1728

[8] Vincent AM, Russell JW, Sullivan KA, Backus C, Hayes JM, McLean LL, *et al*. SOD2 protects neurons from injury in cell culture and animal models of diabetic neuropathy. Exp Neurol. 2004; 186(2): 216-27

[9] Aloke C, Egwu CO, Aja PM, Obasi NA, Chukwu J, Akumadu BO, *et al*. Current advances in the management of diabetes mellitus. Biomedicines. 2022; 10(10): 2436. doi.org/10.3390/biomedicines10102436

[10] Grover JK, Yadav S. Pharmacological actions and potential uses of Momordica charantia: A review. J Ethnopharmaco. 2004; 93(1): 123-32. doi: 10.1016/j.jep.2004.03.035.

[11] Surjushe A, Vasani R, and Saple DG. Aloe vera: A short review. Indian J Dermatol. 2008; 53(4): 163-6. doi: 10.4103/0019-5154.44785.

[12] Sánchez M, González-Burgos E, Iglesias I, and Gómez-

Serranillos MP. Pharmacological update properties of aloe vera and its major active constituents. Molecules (Basel, Switzerland). 2020; 25(6): 1324. doi: 10.3390/molecules25061324.

[13] Paulsen E. Aloe vera gel research review. J Nat Med. 2009; 1(1): 1-5.

[14] Hekmatpou D, Mehrabi F, Rahzani K, and Aminiyan A. The Effect of Aloe Vera Clinical Trials on Prevention and Healing of Skin Wound: A Systematic review. Iran J Med Sci. 2019; 44(1): 1-9. PMCID: PMC63305 25.PMID: 30666070

[15] Syed TA, Ahmad SA, Holt AH, Ahmad SA, Ahmad SH, and Afzal M. Management of psoriasis with Aloe vera extract in a hydrophilic cream: a placebo-controlled, double-blind study. Trop Med Int Health. 1996; 1(4): 505-9. doi: 10.1046/j.1365-3156.1996.d01-91.x.

[16] Langmead L, Feakins RM, Goldthorpe S, Holt H, Tsironi E, De Silva A, *et al*. Randomized, double-blind, placebo- controlled trial of oral aloe vera gel for active ulcerative colitis. Aliment Pharmacol Ther. 2004; 19(7): 739-47. doi: 10.1111/j.1365-2036.2004.01902.x.

[17] Davis K, Philpott S, Kumar D, and Mendall M. Randomised double-blind placebo-controlled trial of aloe vera for irritable bowel syndrome. Int J Clin Pract.2006; 60(9): 1080-6. doi: 10.1111/j.1742-1241.2006.00980.x.

[18] Vogler BK, and Ernst E. Aloe vera: A systematic review of its clinical effectiveness. Br J Gen Prac. 1999; 49(447): 823-8. PMID: 10885091, PMCID: PMC1313538

[19] Yagi A, Kabash A, Okamura N, Haraguchi H, Moustafa SM, Khalifa TI. Antioxidant, free radical scavenging and anti-inflammatory effects of aloesin derivatives in Aloe vera. Planta Medica. 2002; 68(11): 957-60. https://doi.org/10.1055/S-2002-35666/ID/2

[20] Dede S, Isirima J, and Akoko S. Antihyperglycemic and histological effect of *Aloe vera* on alloxan-induced diabetes in Wistar rats. *Scholars* Int J Integr Med. 2023; 6: 120-8. doi.org/10.36348/sijtcm.2023.v06i08.001

[21] Arora M, Sarup Y, Tomar R, Singh M, and Kumar P. Amelioration of diabetes-induced diabetic nephropathy by *Aloe vera*: Implication of oxidative stress and hyperlipidemia. J Diet. 2018; Suppl*16*(1): 1-18. https://doi.org/10.1080/19390211.2018.1499474

[22] Boudreau MD, Beland FA, and Nichols JA. Toxicology and carcinogenesis studies of a nondecolorized whole leaf extract of Aloe barbadensis Miller (Aloe vera) in F344/N rats and B6C3F1 mice (drinking water study). Natl Toxicol Program Tech Rep Ser. 2013; 577: 1-266. PMID: 24042237

[23] Ghosh S, and Das S. Quercetin selectively inhibits insulin receptor function in vitro by impairing insulin binding. Br J Pharmacol. 2010; 161(2): 424-40. doi: 10.1021/bi00149a041.

[24] Mosisa Gudeta, B., Melesie Taye, G., Abula, T., & Alemayehu Gadisa, D. Evaluation of anti-diarrheal activity of 80% methanol extracts of vernonia amygdalina delile (asteraceae) leaves in mice. *Journal of Experimental Pharmacology*. 2020; 455-462.

[25] Boudreau MD, Beland FA, and Nichols JA. Toxicology and carcinogenesis studies of a nondecolorized whole leaf extract of Aloe barbadensis Miller (Aloe vera) in F344/N rats and B6C3F1 mice (drinking water study). Natl Toxicol Progr Tech Rep Ser. 2013; 577: 1-266. PMID: 24042237.

[26] Farombi O, and Owoeye O. Antioxidative and Chemo-preventive Properties of Vernonia amygdalina and Garcinia biflavonoid. Int J Environ Res Public Health**.** 2011; 8: 2533-55. doi: 10.3390/ijerph8062533.

[27] Igoli J, Ogaji O, Tor-Anyiin T. and Igoli N. Traditional medicine practice amongst the Igede people of Nigeria. Part II. Afr J Trad CAM. 2005; 2(2): 134-52. doi:10.4314/ajtcam.v2i2.31112

[28] Omoregie ES, and Pal A. Antiplasmodial, antioxidant and immunomodulatory activities of ethanol extract of Vernonia amygdalina del. Leaf in Swiss mice. Avicenna J Phytomed. 2016; 6(2): 236-47. PMID: 272 22837, PMCID: PMC4877969

[29] Akerele GP, Adedayo C, Oboh, G, Ademosu AO, and Oyeleye SI. Glycemic indices and effect of bitter leaf (Vernonia amygdalina) flavored non-alcoholic wheat beer (NAWB) on key carbohydrate metabolizing enzymes in high fat diet fed (HFD)/STZ-induced diabetic Wistar rats. J Food Biochem. 2022; 46(12): e14511. 4. doi: 10.1111/jfbc.14511.

[30] Atangwho IJ, Yin KB, Umar MI, Ahmad M, and Asmawi MZ. Vernonia amygdalina simultaneously suppresses gluconeogenesis and potentiates glucose oxidation via the pentose phosphate pathway in streptozotocin-induced diabetic rats. BMC Complementary Altern Med. 2014; 14: 426. doi: 10.1186/1472-6882-14-426.

[31] Adedapo AA, Aremu OJ, and Oyagbemi AA. Anti-oxidant, anti-inflammatory and antinociceptive properties of the acetone leaf extract of vernonia amygdalina in some laboratory animals. Adv Pharm Bull. 2014; 4(Suppl 2): 591-8. doi: 10.56 81/apb.2014. 087.

[32] Aruoma OI, Colognato R, Fontana I, Gartlon J, Migliore L, and Koike K. Molecular effects of fermented papaya preparation on oxidative damage, MAP Kinase activation and modulation of the benzo[a] pyrene mediated genotoxicity. Biofactors. 2000; 12(1-4): 229-40. doi: 10.1002/biof.5520260205.

[33] Jaiswal N, Pardhasaradhi PV, and Kuhnert N. Phenolic compounds from Vernonia amygdalina and their antioxidant activities. Ind Crop Prod. 2017; 95: 662-7.

[34] Johnbull O, Igbe I, Obsrisiagbon P, and Onyegbula C. Studies on the effects of Vernonia amygdalina aqueous leaf extract on the biochemical, hematological, and hypoglycemic parameters in diabetic rats: Prerequisite to formulation into pharmaceutical dosage form. J med Pharm Allied Sci. 2019; 16.

[35] Nwaoguikpe R. The effect of extract of bitter leaf (*Vernonia amygdalina*) on blood glucose levels of diabetic rats. Int J Biol Chem Sci. 2010; *4*(3): 788-96. doi.org/10.4314/ijbcs.v4i3.60500

[36] Oboh G, Ademiluyi AO, and Akinyemi AJ. Inhibition of α-amylase and α-glucosidase activities by ethanolic extract of Vernonia amygdalina leaf: an in vitro

assessment. J Taibah Univ Sci. 2016; 10(5): 600-6. doi: 10.1016/S2221-1691(12)60219-6.

[37] Kim B, Lee HS, Kim HJ, Lee H, Lee IY, Ock S, Kwon S, Kang SS, Choi Y. *Momordica charantia* (bitter melon) efficacy and safety on glucose metabolism in Korean prediabetes participants: a 12-week, randomized clinical study. Food Sci Biotechnol. 2022; 14;32(5):697-704. doi:10.1007/s10068-022-01214-9. PMID: 37009042; PMCID: PMC10050654.

[38] Duke JA. *Duke's* handbook of medicinal plants of Latin America. CRC Press.2008

[39] Mohammady I, Elattar S, Mohamed S, and Ewais M. An evaluation of anti-diabetic and anti-lipidemic properties of *Momordica charantia* (bitter melon) fruit extract in experimentally induced diabetes. J Life Sci. 2012; *9*(4): 363-74.

[40] Jia S, Shen M, Zhang F, Xie J. Recent Advances in Momordica charantia: Functional Components and Biological Activities. Int J Mol Sci. 2017; 18(12):2555. doi:10.3390/ijms18122555. PMID:29182587;PMCID: PMC5751158.

[41] Joseph B, and Jini D. Antidiabetic effects of Momordica charantia (bitter melon) and its medicinal potency. Asian Pac J Trop Dis. 2013; 3(2): 93-102. doi: 10.1016/S2222-1808(13)60052-3

[42] Alam MA, Uddin R, Subhan N, Rahman MM, Jain P, and Reza HM. Beneficial role of bitter melon supplementation in obesity and related complications in metabolic syndrome. J Lipid. 2015; Article 496169. doi.org/10.1155/2015/496169.

[43] Mahwish FS, Nosheen F, Qurat-ul-Ain NB, Afzaal M, Ehsan K, Hussain M, Imran M, and Al JE. Bio-evaluation of alkaloids and saponins from bitter melon: Probing more desirable compounds in treating hyperglycemia and hyperlipidemia. Cogent Food Agri. 2023; 9(1): 1-16. doi:10.1080/23311932.2023.2242634

[44] Yadav M, Jain S, Tomar R, Prasad GB, and Yadav H. Medicinal and biological potential of pumpkin: an updated review. Nutr Res Rev. 2010; 23(2): 184-90. doi: 10.1017/S0954422410000107.

[45] Grover JK, Yadav SP, and Vats V. Medicinal plants of India with anti-diabetic potential. J Ethnopharmacol. 2002; 81(1): 81-100. doi: 10.1016/s0378-8741(02)00059-4.

[46] Bhattacharya S, Muhammad N, Steele R, Kornbluth J, and Ray RB. Bitter Melon Enhances Natural Killer-Mediated Toxicity against Head and Neck Cancer Cells. Cancer Prev Res (Philadelphia, Pa.). 2017; 10(6): 337-44. doi: 10.1158/1940-6207.CAPR-17-0046

[47] Sur S, and Ray RB. Diverse roles of bitter melon (*Momordica charantia*) in prevention of oral cancer. J Cancer Metastasis Treat. 2021; 7: 12. https://doi.org/10.20517/2394-4722.2020.124

[48] Leatherdale BA, Panesar RK, Singh G, and Atkins TW. Improvement in glucose tolerance due to Momordica charantia (karela). Br Med J (Clin Res Ed). 1981; 282(6279): 1823-4. doi: 10.1136/bmj.282.6279.1823.

[49] Ahmed I, Adeghate E, Cumming E, and Sharma AK. Beneficial effects and mechanisms of action of Momordica charantia juice in the treatment of streptozotocin-induced diabetes mellitus in rat. Mol Cell Biochem. 2012; 368(1-2): 59-73. doi: 10.1023/b:mcbi.0000028738.95518.90.

[50] Basch E, Gabardi S, and Ulbricht C. Bitter melon (Momordica charantia): A review of efficacy and safety. Am J Health Syst Pharm. 2003; 60(4): 356-9. doi: 10.1093/ajhp/60.4.356.

[51] Fuangchan A, Sonthisombat P, Seubnukarn T, Chanouan R, Chotchaisuwat P, and Sirigulsatien V. Hypoglycemic effect of bitter melon compared with metformin in newly diagnosed type 2 diabetes patients. J Ethnopharmacol. 2011; 134(2): 422-8. doi: 10.1016/j.jep.2010.12.045.

[52] Oishi Y, Sakamoto T, Udagawa H, Taniguchi H, and Kobayashi-Hattori K. Momordica charantia L. improves insulin resistance and disordered lipid metabolism in a high-fructose diet-induced NAFLD mouse model. Arch Biochem Biophys. 2019; 662: 169-78. doi: 10.3389/fphar.2021.770652

[53] Ooi CP, Yassin Z, Hamid TA, & Momtaz YA. Momordica charantia for type 2 diabetes mellitus. Cochrane Database Sys Rev. 2013; (8): CD007845. https://doi.org/10.1002/14651858.CD007845.pub3

[54] Grzanna, R., Lindmark, L., & Frondoza, C. G. Ginger--an herbal medicinal product with broad anti-inflammatory actions. *Journal of medicinal food*. 2005; 8(2), 125–132. https://doi.org/10.1089/jmf.2005.8.125

[55] Alam MA, Uddin R, Subhan N, Rahman MM, Jain P, and Reza HM. Beneficial role of bitter melon supplementation in obesity and related complications in metabolic syndrome. J Lipid. 2015; Article 496169. https://doi.org/10.1155/2015/496169.

[56] Ali BH, Blunden G, Tanira MO, and Nemmar A. Some phytochemical, pharmacological and toxicological properties of ginger (Zingiber officinale Roscoe): a review of recent research. Food Chem Toxicol. 2008; 46(2): 409–20. doi: 10.1016/j.fct.2007.09.085.

[57] Black CD, Herring MP, Hurley DJ, and O'Connor PJ. Ginger (Zingiber officinale) reduces muscle pain caused by eccentric exercise. J Pain. 2010; 11(9): 894-903. doi: 10.1016/j.jpain.2009.12.013.

[58] Ernst E, and Pittler MH. Efficacy of ginger for nausea and vomiting: A systematic review of randomized clinical trials. Br J Anaesth. 2000; 84(3): 367-71. doi: 10.1093/oxfordjournals.bja.a013442.

[59] Viljoen E, Visser J, Koen N, and Musekiwa A. A systematic review and meta-analysis of the effect and safety of ginger in the treatment of pregnancy-associated nausea and vomiting. Nutr J. 2014; *13*: Article 20. doi.org/10.1186/1475-2891-13-20

[60] Islam MS, and Choi H. Comparative effects of dietary ginger (*Zingiber officinale*) and garlic (*Allium sativum*) investigated in a type 2 diabetes model of rats. J Med Food. 2008; 11(1): 152-9. doi.org/10.1089/jmf.2007.601.3r

[61] Grzanna, R., Lindmark, L., & Frondoza, C. G. Ginger--

an herbal medicinal product with broad anti-inflammatory actions. *Journal of medicinal food*. 2005; *8*(2), 125–132. https://doi.org/10.1089/jmf.2005.8.125

[62] Rahmani AH, Shabrmi FM, and Aly, SM. Active ingredients of ginger as potential candidates in the prevention and treatment of diseases via modulation of biological activities. Int J Physiol Pathophysiol Pharmacol. 2014; 6(2): 125-36. PMCID: PMC4106649 PMID: 25057339

[63] Mao QQ, Xu XY, Cao SY, Gan RY, Corke H, Beta T, and Li HB. Bioactive compounds and bioactivities of ginger (Zingiber officinale Roscoe). Foods (Basel, Switzerland). 2019; 8(6): 185. doi: 10.3390/foods8060185.

[64] Mashhadi NS, Ghiasvand R, Askari G, Hariri M, Darvishi L, and Mofid MR. Anti-oxidative and anti-inflammatory effects of ginger in health and physical activity: Review of current evidence. Int J Prev Med. 2013; 4(Suppl 1): S36-S42. PMID: 23717767, PMCID: PMC3665023

[65] Bode AM, and Dong Z. The amazing and mighty ginger. In Herbal Medicine: Biomolecular and Clinical Aspects (2nd ed.). Boca Raton (FL): CRC Press/Taylor & Francis.2011

[66] Kundu JK, Na HK, and Surh YJ. Ginger-derived phenolic substances with cancer preventive and therapeutic potential. Forum of Nutr. 2009; 61: 182-92. doi: 10.1159/000212750.

[67] Gan FF, Nagle AA, and Ang X. Ginger lowers blood pressure through blockade of voltage-dependent calcium channels. J Cardiovasc Pharmacol. 2011; 57(4): 468-73. doi: 10.1097/00005344-200501000-00013

[68] Akhani SP, Vishwakarma SL, Goyal RK, and Chauhan DK. Pharmacological evaluation of Cucumis sativus Linn. for central nervous system depressant activity. J Basic Clin Physiol Pharmacol. 2014; 25(3): 335-42. doi:10.3126/jucms.v11i03.61478

[69] Arablou T, Aryaeian N, Valizadeh M, Sharifi F, Hosseini A, and Djalali M. The effect of ginger consumption on glycemic status, lipid profile and some inflammatory markers in patients with type 2 diabetes mellitus. Int J Food Sci Nutr. 2014; 65(4): 515-20. doi: 10.3109/09637486.2014.880671

[70] Daily JW, Zhang X, Kim DS, and Park S. Efficacy of ginger for treating type 2 diabetes: A systematic review and meta-analysis of randomized clinical trials. J Ethn Foods. 2015; 2(1): 36-43. doi:10.1016/j.jef.2015.02.007

[71] Al-Azhary D. Ginger enhances antioxidant activity and attenuates atherogenesis in diabetic cholesterol-fed rats. Aust J Basic Appl Sci. 2010*; 5*(10): 1357-64.

[72] American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2021; 44(Supplement_1): S15-S33.

[73] Ojewole JA. Analgesic, anti-inflammatory, and hypoglycemic effects of ethanol extract of *Zingiber officinale* (Roscoe) rhizomes (Zingiberaceae) in mice and rats. Phytother Res: PTR. 2006; *20*(9): 764-72. doi.org/10.1002/ptr.1924

[74] Langner E, Greifenberg S, and Gruenwald J. Ginger: history and use. Adv Ther. 1998; 15(1): 25-44. PMID: 10178636.

[75] Mozaffari-Khosravi H, Talaei B, Jalali BA, Najarzadeh A, and Mozayan MR. The effect of ginger powder supplementation on insulin resistance and glycemic indices in patients with type 2 diabetes: A randomized, double-blind, placebo-controlled trial. Complement Ther Med. 2014; 22(1): 9-16. doi: 10.1016/j.ctim.2013.12.017.

[76] White B. Ginger: An overview. Am Fam Physician**.** 2007; 75(11): 1689-91. PMID: 17575660

[77] Dumanoglu B, Alpagat G, Poyraz M, Alan YS, and Baccioglu A. Anaphylaxis After Consumption of Guar Gum-Containing Food: A Report of Two Cases. Cureus. 2022; 14(8): e28022. doi: 10.7759/cureus. 28022

[78] Khandouzi N, Shidfar F, Rajab A, Rahideh T, Hosseini P, and Mir Taheri M. The effects of ginger on fasting blood sugar, hemoglobin a1c, apolipoprotein B, apolipoprotein a-I and malondialdehyde in type 2 diabetic patients. Iran J Pharm Res: IJPR. 2015; 14(1): 131-40. PMID: 25561919, PMCID: PMC4277626

[79] Chuah SK, Wu KL, Tai WC, and Changchien CS. The effects of ginger on gallbladder motility in healthy male humans. J Neurogastroenterol Motil. 2011; 17(4): 411-5. doi: 10.5056/jnm.2011.17.4.411.