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The Active Ingredients and Antidiabetic Effects of *Zingiber Officinale*: A Review Article

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ABSTRACT: Zingiber officinale Roscoe (Ginger) a genus classified within the family "Zingiberaceae". This family is known because of its high content of dietary and biochemical components, especially the impacts against diabetes mellitus and inflammation. Ginger, perform the antihyperglycemic activity by causing restoration for β-cells in pancreas, providing protection for the morphology of β-cells, amelioration of the pathological injuries of kidneys, control of the concentration of pro-inflammatory cytokines, regulation of hepatic gene expression of enzymes associated with glucose metabolism, inhibition oxygen free radicles caused during glucose metabolism, translocation of GLUT4, inhibition of liver glucose production, stimulation of pancreatic insulin release, inhibition of carbohydrate metabolizing enzymes, high production of hepatic glycogen through the improvement of glycogen synthesis in the liver, and decreasing insulin resistance, and peripheral consumption of blood sugar as well as its antioxidant activity. This review cast a brief light on the active ingredients and the activity of cinnamon in the reduction of high blood glucose.

1. INTRODUCTION

Ginger, scientifically known as Zingiber officinale, is a perennial plant belonging to the Zingiberaceae family. It is renowned worldwide for its distinct aroma and potent flavor, making it a popular spice and seasoning. Ginger is not only a culinary herb of great value but also has been highly treasured in herbal medicine in India as well as in China for years. Its curative properties have been found useful in the treatment of various conditions, such as nausea in pregnancy as well as that which results from chemotherapy drugs, primary dysmenorrhoea, hypertension, nonalcoholic fatty liver disease, migraines, arthritis, stomachache, nausea and colds (Attyah and Ismail, 2012; Zhu et al., 2018) . The Food and Drug Administration considers ginger a safe food additive; it has been used for hundreds of years in cooking and herbal medicine to remedy many health problems (Aderonke Otunola & Jide Afolayan, 2020).

The interest in ginger is due to its many benefits on health, which have led to several research works to study its pharmacological and physiological effects. Regarding clinical research, evidence favoring the efficacy of ginger on human health has been increasing. Many randomized controlled trials (RCTs) have investigated the potential benefits of ginger in symptom reduction. Examples include RCTs that assessed the usefulness of ginger supplementation in controlling chemotherapy-induced nausea and vomiting among cancer patients and those that investigated dysmenorrhea. Several systematic reviews with meta-analyses (SR-MA) have also addressed clinical effectiveness. One of them is Chen et al.'s work on oral ginger intake, which proved effective in relieving menstrual pain among women suffering from dysmenorrhea. In another SR-MA, it was exhibited that supplementation of ginger has improved the lipid profile and in a positive way influenced insulin sensitivity plus glucose control and HbAc1 (glycosylated hemoglobin) levels among patients with insulin-independent diabetes mellitus (Chen et al., 2016 ; Zhu et al., 2018).

ACTIVE INGREDIENT

Ginger is known to contain over a hundred compounds (more than 100 have been identified so far). Major classes are zingerone, zingiberene, shogaols, and gingerol, along with other trace components like minerals, vitamins, and terpenes. among these gingerols are the major constitutes and have been reported to show a wide variety of bioactivities. Therefore, several extensive research studies were performed on the bioactivities of ginger, including anti-neuroinflammatory and antimicrobial antioxidant

activity, among other properties. Moreover, it has exhibited promise in the reduction of chemotherapy-induced vomiting and nausea as well as fatigue with possible anticancer effects. Further evidence has highlighted the contribution of ginger toward better daily human activity in terms of improving quality of life (Al-Saigh and Dakheel, 2012 ; Anh et al., 2020).

Terpenes and oleoresin (ginger oil) are the most important of these active components in ginger. Volatile oils are the other components of ginger, making up about 1%–3% of its composition, apart from water, fiber, and proteins. The other nonvolatile pungent compounds belonging to oleoresin are known as gingerols. Sesquiterpene hydrocarbons and phenolic compounds are the primary components found in terpenes, which are lipophilic extracts from the rhizome; these extracts may contain potentially active gingerols, which under certain conditions may be transformed to paradol, zingerone, and shogaols (Rahmani et al., 2014).

The ginger root plants belong to a diverse family of over 1300 species. The strong smell and taste of the root are due to the presence of gingerols, ketones that belong to a class of compounds known as polyphenols and which serve as their major constituents. It is a major source of essential nutrients — vitamin C, vitamin B6 — and micronutrients: water, fiber, manganese plus copper, potassium, and magnesium. Also, it contains large quantities of polyphenols and phytochemicals. Among the terpenes found in ginger, the three major active components are paradols, shogaols, and gingerols. The recommended daily serving size of ginger powder ranges from 170mg to 1g. One notable primary metabolite of gingerol is (S)-[6]-gingerol-4'-0-β-glucuronide. Ginger and its components have a tendency to be accumulated in the gut, where they perform their impacts by alleviating pain through anti-inflammatory properties, addressing nausea, and soothing the digestive system with carminative effects. Recent research has been dedicated to exploring the mode of action of ginger and its different constituents (Modi and Modi, 2022).

REDUCTION OF BLOOD GLUCOSE LEVEL

Despite the significant advancements achieved in the control of diabetes using various management techniques and traditional medications, diabetes and its associated complications remain a significant medical challenge and a growing burden on healthcare systems. Many synthetic oral hypoglycemic agents used to treat diabetes have certain drawbacks, such as severe side effects, drug resistance, inapplicability during pregnancy, toxicity, and high costs. Numerous experimental investigations have demonstrated that the administration of ginger extracts leads to a dose-dependent decrease in blood sugar levels in both insulin-dependent and insulin-independent diabetic animals (Aderonke Otunola & Jide Afolayan, 2020).

The antidiabetic properties of bioactive ginger compounds have been demonstrated to potentially improve insulin secretion by affecting KATP channels. Additionally, the pathway of insulin secretion in beta cells in the pancreas may be stimulated by 6-Gingerol. Another suggested mode of action proposes that the stimulation of Rab27a GTPase in isolated islets could contribute to the release of insulin-containing dense core granules. This increase in Rab27a GTPase may also promote the movement of glucose transporter 4 (GLUT4) vesicles to the membrane of skeletal muscle cells (Samad et al., 2017).

Conversely, there are encouraging indications of the advantageous characteristics of ginger extract, which appears to be successful in reducing blood sugar concentrations. In a study performed by Zhu et al., it was found that ethanolic ginger extract exhibited a noteworthy antihyperglycemic impact on streptozotocin (STZ)-induced diabetic rats over a duration of 20 days. Additionally, ginger aqueous extract demonstrated a significant decrease in blood glucose levels on the 8th day comparing to the baseline in rats with diabetes induced by alloxan (Bhandari et al., 2005 ; Jafri et al., 2010).

Conflicting results have been observed in previous human studies regarding the impact of ginger on blood glucose control. One study found that consuming a ginger supplement for 21 days did not lead to significant changes in blood glucose levels comparing to a placebo. However, another study revealed that taking a ginger capsule for over 2 months resulted in a significant reduction of fasting blood glucose levels by up to 20% in non-diabetic adults. On the contrary, a separate study conducted by Bordia et al. showed that consuming 5 grams of ginger powder (4 grams per day) for 3 months did not have any effect on fasting and postprandial blood sugar concentrations in non-diabetic patients (Bordia et al., 1997 ; Imani et al., 2015).

In the study by Lamuchi-Deli et al., the impacts of the hydroalcoholic extract of ginger on arginase I activity and expression in the retina of rats with diabetes induced by streptozotocin were assessed. There was a marked decrease in blood glucose concentration with a high significant downregulation ($P < 0.05$) of arginase I activity and expression. In comparison with untreated diabetic controls, it also effectively reduced body weight to near-normal levels after the significant increase observed in diabetic rats ($P < 0.01$). The serum insulin levels of diabetic rats were also significantly increased when compared with diabetic controls, although they did not attain normal values ($P < 0.05$) based on this evidence, it could be hypothesized that ginger might have a role in the treatment of vascular disorders related to diabetes by influencing some metabolic abnormalities present in this experimental model (Lamuchi-Deli et al., 2017).

The antidiabetic and nutritional potentials of ginger powder, its watery and alcoholic extracts, as well as its essential oil, were assessed in rats with diabetes induced by streptozotocin. The results indicated a significant decline in the levels of serum alanine aminotransferase (AST and ALT) activities, alkaline phosphatase (ALP), aspartate, and, liver total cholesterol, and lipids in diabetic rats. Also, there was an increase in hepatic triglyceride and glycogen levels comparing to the normal group. Among the ginger components, ginger oil demonstrated the most effective antidiabetic activity, followed by the ginger extracts. Furthermore,

study performed in 2014 found that the administration of ginger extract to male Sprague-Dawley diabetic rats for a duration exceeding two months exhibited a protective effect against insulin resistance (Anfenan, 2014)

In a previous investigation, it was discovered that extracts derived from fresh ginger had the ability to lower the levels of serum low density lipoprotein (LDL) and cholesterol levels in the blood of rats with diabetes induced by alloxan. This reduction was observed when comparing the diabetic rats to the control groups. Furthermore, the ginger extracts were able to decrease LDL levels to a level similar to that of the normal group, demonstrating an effect equivalent to the administration of atorvastatin at a dosage of 10 mg/day. Additionally, when diabetic rats induced by streptozotocin were orally administered aqueous ginger extract for a duration of 30 days, it was found that the antihyperglycemic effect was dose-dependent, resulting in a 68% decrease in plasma glucose levels at a daily dose. These results indicate that ginger holds promise as a natural remedy for the treatment of diabetes. Moreover, Iranloye et al. conducted a study that demonstrated the effectiveness of ginger in reducing fasting malondialdehyde levels and blood glucose, while also decreasing insulin resistance in rats with alloxan-induced diabetes and insulin resistance, when comparing to control rats (Iranloye et al., 2011 ; Abdulrazaq et al., 2012; Al-Noory et al., 2013) .

There have been numerous suggestions put forth regarding the glucose-lowering effects of medicinal herbs. These proposals encompass a range of mechanisms, such as hindering the production of glucose in the liver, mimicking the actions of insulin, promoting the secretion of insulin from the pancreas, impeding the activity of enzymes involved in carbohydrate metabolism, bolstering the synthesis of glycogen in the liver through the upregulation of glycogen regulatory enzymes, and enhancing the utilization of glucose in peripheral tissues (Aderonke Otunola & Jide Afolayan, 2020).

The antidiabetic properties of ginger have been linked to its bioactive components, specifically gingerol and shogaol. These compounds have been found to improve glucose entry into skeletal muscle cells of rats and increase the expression and translocation of GLUT-4 glucose transporter to the cell membrane, thus removing excess glucose from circulation effectively. Ginger also inhibits essential enzymes of sugar metabolism (α-amylase and α-glucosidase) in addition to phenolic compounds such as shogaols and gingerols. Consequently, more recent research has revealed that ginger increases the uptake of glucose by peripheral tissues, which is related to increased storage of glycogen in the liver and muscles. This peripheral consumption of glucose further curtails gluconeogenesis in the hepatic tissue and kidneys by limiting precursors (such as lactate and amino acids) for glucose production, as insulin does (Sattar et al., 2012).

CONCLUSION

Ginger, perform the antihyperglycemic activity by causing restoration for β-cells in pancreas, providing protection for the morphology of β-cells, amelioration of the pathological injuries of kidneys, control of the concentration of pro-inflammatory cytokines, regulation of hepatic gene expression of enzymes associated with glucose metabolism, inhibition oxygen free radicles caused during glucose metabolism, translocation of GLUT4, inhibition of liver glucose production, stimulation of pancreatic insulin release, inhibition of carbohydrate metabolizing enzymes, high production of hepatic glycogen through the improvement of glycogen synthesis in the liver, and decreasing insulin resistance, and peripheral consumption of blood sugar as well as its antioxidant activity.

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