Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

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REVIEW

Consumption of Cooked Common Beans or Saponins Could Reduce the Risk of Diabetic Complications

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Abstract: Several risks for diseases, such as atherosclerosis, renal diseases, and diabetes, have inextricably been linked with obesity. Nowadays, this health-risk-laden disease is being managed with assorted types of drugs, some of which guarantee modest benefits. The chronic inflammatory effect of obesity has a negative effect in insulin signaling, a situation attributable to insulin resistance that culminates in high blood sugar inputs seen in diseases such as type 2 diabetes and metabolic syndrome. Food such as beans with different bioactive compounds could reduce the risk of diabetic complications. Demand for bean products is growing because of its robust contents of several health-promoting components, eg, saponins. Saponins are characterized by containing lower glucose and cholesterol levels and have been doted with antioxidant activities, as well as anti-inflammatory and anti-diabetic effects. In this writing, the attributes of saponins in providing substantial health and nutritional benefits in humans, as well as in improving and ameliorating diabetic complications, were reviewed.

Keywords: beans, saponins, diabetes

Introduction

The health implications of obesity lie in triggering the risk of atherosclerosis, renal diseases, vesicular lithiasis, and diabetes. Diabetes mellitus (DM) is a complex metabolic disease, epidemically global with expected toll of 380 million patients by 2025.[1] In particular, type 2 diabetes mellitus (T2DM), due to generalized unhealthy lifestyles, has reached epidemic proportions in the last few decades.[2] Unfortunately, diabetic retinopathy is one of the secondary complications encountered by the patients suffering from chronic diabetes mellitus. The two major characteristic features of diabetic retinopathy are macular edema and angiogenesis. The properties of endostatin, a valuable substance employed in the treatment of cancer can be exploited as a potential antiangiogenic therapy agent.[3] In addition, diabetes is an important health load of obesity. Most patients with this disease require insulin for its control, with its consequent hypoglycemic effects that characterize a crucial point in the struggle for the containment of the pathology.[4] Currently, there are various types of drugs used for the management of obesity that guarantee modest benefits. Insulin resistance is a major risk factor for diseases such as T2DM and metabolic syndrome. Several clinical studies have shown that leguminous plants such as dried beans are able to reduce insulin resistance and other related T2DM parameters due to their antioxidant activities.[5]

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Carbohydrates and Diabetes

Food consumption with different bioactive compounds could reduce the risk of diabetic complications. Carbohydrates are an umbrella term that encompasses sugar, fruits, vegetables, fibers, and legumes. These substances act as an energy source, and help in the control of blood glucose and insulin metabolism. Besides, they are linked with cholesterol and triglyceride metabolism, and fermentation. Carbohydrates are one of the three macronutrients in the human diet, along with protein and fat. These molecules contain carbon, hydrogen, and oxygen atoms. In addition, they play an important role in the human body. Upon consumption, their breakdown into glucose is the sole responsibility of the digestive tract and this breakdown product is the source of energy for biological and physical activities.[6]

Saponins: Effects and Properties

Demand for bean products is growing because of their abundant content of several health-promoting components such as saponins, found in great amount in edible bean products. Saponins are naturally occurring compounds that are widely distributed in all cells of legume plants.[7] They contain a carbohydrate moiety attached to a triterpenoid or steroids. Moreover, they have been associated with upliftment of the immune system to protect the human body against cancers, and with lowering the glucose and cholesterol levels. Some saponins form an insoluble complex with cholesterol which prevents its absorption from the small intestine.[8] Others cause an increase in the fecal excretion of bile acids, an indirect route for elimination of cholesterol.[9] In general, the saponins are potential natural activators of AMPK; thus, a promising compound with the potential to serve as an antidiabetic substance.[10]

Legumes and Blood Glucose Levels

The association of legumes with low-glucose blood level is progressively being recognized. A 4-week treatment with a cooked bean supplemented (10%) diet, Flor de Mayo bean (FMB), was found to lower blood glucose levels, due to its ability to augment blood insulin levels; decrease urine albumin and urea levels; and increase creatinine clearance.[11] Beans (Phaseolus vulgaris L.) are common legumes, consumed worldwide. The wild beans contain more protein (25.5% vs. 21.7%), ash (5.15 vs. 4.15%) and crude fiber (7.08% vs. 5.04%) compared to cultivated beans. Also, they contain less fat (0.56 vs. 0.89%) and carbohydrates (61.64 vs. 68.05%). Sulfur amino acids were found to be limiting in both groups of beans, as expected; however, the cultivated beans had a higher content of the limiting amino acids.[12]

Green Vegetable Soya Beans

There are five triterpenoid saponins with different chemical structures (Table 1).[13] Saponins owe their name to the characteristic of forming foam. They are compounds that are found in various plants. Saponins come from the *Saponaria* plant that has formerly been used to form soap (sapon = soap).[14] In their chemical structure, they are glycosides with a polycyclic aglycone called sapogenin. The aglycone is the free part of a glucoside. It can be in the form of a steroid or a triterpenoid choline bound through C3.[15] Triterpenes can be subdivided into 20 different groups with particular chemical structures in each of them. The aglycone part is covalently attached to one or more glycones (sugar) and this can be glucose, galactose, glucuronic acid, or xylose.[16] There are reports that highlight the biological activities of saponins. For example, the sea cucumber *Holothuria thomasi* saponin is reported to have a hypoglycemic effect in diabetic rats,[17] by stimulating insulin secretion and regeneration of beta cells of the pancreas. Moreover, for its chemical structure and antioxidant properties, it activates responsible enzymes to use glucose. It is important to

Table 1 Triterpenoid Saponins and Their Chemical Structures

1.	3β,24-dihydroxy-22β,30-epoxy-30-oxoolean-12-en 3-O-α-l-rhamnopyranosyl-(1 → 2)-β-d-xylopyranosyl-(1 → 2)-β-d-glucuronopyranoside
2.	3β,24-dihydroxy-22β,30-epoxy-30-oxoolean-12-en 3-O-α-l-rhamnopyranosyl-(1 → 2)-β-d-(3″-O-formyl)-galactopyranosyl-(1 → 2)-β-d-glucuronopyranoside
3.	22-keto-3β,24-dihydroxy oleanane-12-ene 3-O-α-l-rhamnopyranosyl-(1 → 2)-β-d-(3″-O-formyl)-galactopyranosyl-(1 → 2)-β-d-glucuronopyranoside
4.	3β,22β,24-trihydroxy oxyolean-18(19)-ene-29-acid 3-O-α-l-rhamnopyranosyl-(1 → 2)-β-d-galactopyranosyl-(1 → 2)-β-d-glucuronopyranoside
5	Punicanolic acid 3-O-α-l-rhamnopyranosyl-(1 → 2)-β-d-galactopyranosyl-(1 → 2)-β-d-glucuronopyranoside

know the structure of saponins, because such knowledge can be used in making synthetic modifications of the substances through the insertion of functional groups that strengthen its activity or improve its affinity with the specific receptors (Figure 1). Some substances possess moderate anti-inflammatory activities. The bean hulls possess the most abundant phytochemical elements. The whole grain is a potent antioxidant with anti-inflammatory and anti-diabetic effects.[18] A study with 50 grams of available carbohydrate in a meal based on black beans and rice was performed in healthy adult women (n=12, 18–65 years). The meals were served in the mornings in different times and days for a minimum of 7 days. Blood samples were collected at time 0 (fasting), and at 30, 60, 90, and 120 minutes postprandial, and were subsequently analyzed for glucose and insulin concentrations. Glucose response based on the incremental area under the curve showed a significant difference by treatment (P=0.027). Changes in blood glucose concentrations were significantly different for the meals based on black bean in comparison to rice alone at 60 minutes (P=0.026 and P=0.024), 90 minutes (P=0.001 and P=0.012) and 120 minutes post prandial (P=0.024; black bean meal). This provides evidence that black bean improves glycemic response; and thus, its traditional inclusion in our daily food consumption is a promising indication for dietary guidance to reduce postprandial glucose and related health risks.[19] Blank bean seed coat is a rich source of natural compounds such as primary saponins and flavonoids.[20] Quercetin 3-O-glucoside and soya saponin Af, the principal contents of the coat, are respectively the sources of primary flavonoid and saponin. Their extracts significantly reduce the expression of SREBP1c, FAS, and HMGCR; and stimulate the expression of the reverse cholesterol transporters ABCG5/ABCG8 and CYP7A1 in the liver. In addition, they increase the expression of hepatic PPAR-α and consequently decrease hepatic lipid depots and promote a significant increase in bile acid secretion.[21] Flavonoids and saponins from common beans have been widely studied due to their bioactivity. These studies reported that total phenolic content and antioxidant capacity of the extracts were higher when obtained from seed coats, and that flavonoids and saponins were more related with hepatic and colon cancers.[22] These authors suggest that one-day germinated black beans could increase the concentration of saponins and non-glycosylated flavonoid in sprouts and seed coats.

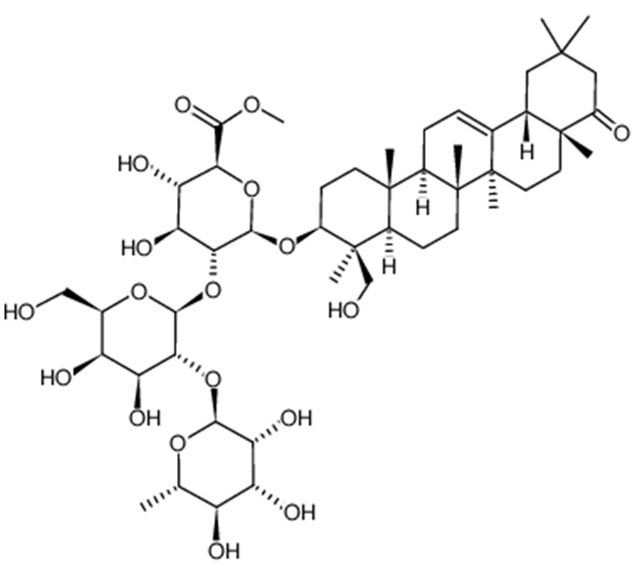

Figure 1 Base chemical structure of saponin.

Natural Products and Metabolic Actions

Tecoma stans has the potential for α-glucosidase inhibition and may provide an effective natural product to treat hyperglycemia and prevent subsequent diabetic complications.[23] Many of the natural products that have a direct or indirect effect on diabetic pathways as enzyme inhibitors are saponins (Table 2). The mechanisms associated with these effects pivot around their inhibitory action on intestinal alpha-glucosidase and alpha-amylase, lens aldose reductase, advanced glycation end-products formation, postprandial hyperglycemia, and aldose reductase. In addition, saponins can provide protection against oxidative stress, and lower the levels of plasma glucose and skeletal hexokinase, as well as alter the enzyme activity of hexokinases and glucose-6-phosphate. They have positive effects on the synthesis and release insulin, including the stimulation of GLUT-4, and decrease of G6P activity.[33] Likewise, they modulate the expression of enzymes involved in lipid metabolism, including peroxisome proliferator-activated receptor α (PPAR-α), sterol regulatory element-binding protein 1 (SREBP-1), fatty acid synthase (FAS), and stearoyl CoA desaturase-1 (SCD-1) mRNA in liver.[34]

Table 2 Saponins in Natural Products That Have a Direct or Indirect Effect on Diabetes Pathways

Type of Saponin	Tissue	Effect	Ref
Panax notoginseng saponins	Skeletal myoblast cell line	Increased insulin-induced glucose uptake, reduced blood glucose and serum insulin levels, and improved glucose tolerance	[24]
Saponins of *Momordica charantia*	Type 2 diabetic mice	Restored the body weight, reduced fasting blood glucose levels, ameliorated insulin resistance, and increased the proportion of hepatic phosphorylated adenosine monophosphate-activated protein kinase (p-AMPK)/total protein	[25]
Saponins of Stauntonia chinensis	Type 2 diabetic db/db mice	Exhibited hypoglycemic activities and modulated hyperlipidemia that was associated with type 2 diabetes	[26]
Saponins of *Boussingaultia gracilis*	Three-week old male mice	Reduced the hepatic damage underlying steatosis, modulated lipid metabolism, enhanced adipocyte thermogenesis, restored insulin sensitivity and glucose homeostasis, and alleviated inflammation status	[27]
Saponins of *Catharanthus roseus*	Streptozotocin-induced diabetic mice	Had a hypoglycemic effect that may be explained by an increase in insulin secretion	[28]
Panax noto ginseng saponins	Subunits of NF-κB p50 and p65 from macrophages in culture medium	Anti-inflammatory properties, inhibition of platelet aggregation, improvement of blood flow and insulin resistance	[29]
Saponin from sea cucumber	C57BL/6 mice fed with a high fat diet	Inhibited lipid synthesis and accelerated lipid β-oxidation and glycolysis in the liver	[30]
Balanites aegyptiaca Del. (Zygophyllaceae) fruits	Streptozotocin-induced diabetic male albino Wistar rats	Reduced the fasting plasma glucose level and total cholesterol	[31]
Saponin Extracts from *Dianthus basuticus*	α-amylase and α-glucosidase inhibitory activities in vitro	Exhibited a competitive mode of inhibition on α-amylase and promising antidiabetic and antioxidant activity	[32]

Conclusion

Indeed, control of blood glucose, plasma cholesterol, and nutrient absorption through dietary saponins could provide substantial health and nutritional benefits in humans, as well as reduce diabetic complications.

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Author Contributions

All authors made a significant contribution to the work reported, either in the conception, study design, execution, acquisition of data, analysis and interpretation or in all these areas. In addition, they took part either in drafting, revising, or critically reviewing the article, and gave their final approval of the version to be published; as well as agreed on the journal to which the article has been submitted; and accepted to be accountable for all aspects of the work.

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