http://www.herbmedpharmacol.com doi: 10.34172/jhp.53271

Journal of Herbmed Pharmacology

Bioactive components, mechanisms, and applications of functional seeds (Flaxseed, chia, pumpkin, hemp, and sesame) in insulin resistance: A mini-review

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ARTICLE INFO

Article Type:
Mini-Review

Article History:
Received: 11 Jul. 2025
Revised: 13 Nov. 2025
Accepted: 13 Nov. 2025
epublished: 1 Jul. 2026

Keywords:
Functional seeds
Lignans
Polyphenols
Insulin sensitivity
Diabetes mellitus

ABSTRACT

Insulin resistance is a significant metabolic dysfunction that contributes to the pathogenesis of type 2 diabetes mellitus (T2DM). As interest grows in functional foods for chronic disease management, seeds of various plants, such as *Linum usitatissimum* (flaxseed), *Salvia hispanica* (chia), *Cucurbita pepo* (pumpkin), *Cannabis sativa* (hemp), and *Sesamum indicum* (Sesame) have gained prominence due to their rich profile of bioactive compounds. These seeds contain polyunsaturated fatty acids (PUFAs), dietary fibre, lignans, polyphenols, and key micronutrients that act synergistically to enhance insulin sensitivity. The mechanisms by which these components exert their effects include modulation of insulin signaling pathways, activation of AMP-activated protein kinase (AMPK), enhancement of adiponectin secretion, and improvement of gut microbiota composition. For instance, chia and pumpkin seed extracts have shown reductions in serum glucose and hemoglobin A1C (HbA1c) in diabetic rodent models. Though little evidence from both animal and human studies suggests that some seed extracts and oils can lower blood glucose, reduce insulin resistance, and improve lipid profiles. This review summarises the mechanistic insights, preclinical and clinical evidence, and functional food applications of these seeds, while highlighting current research gaps. Incorporating functional seeds into dietary interventions may offer a sustainable and accessible approach for managing insulin resistance and preventing T2DM. Despite promising findings, more robust and long-term human clinical trials are required to validate these effects and establish standardized dosages.

Implication for health policy/practice/research/medical education:
Incorporating functional seeds into dietary recommendations offers a low-cost, scalable strategy for managing insulin resistance, particularly in regions with limited access to pharmaceuticals. For health professionals and educators, this highlights the importance of food-based approaches in managing chronic diseases.

Please cite this paper as: Ndlovu N. Bioactive components, mechanisms, and applications of functional seeds (Flaxseed, chia, pumpkin, hemp, and sesame) in insulin resistance: A mini-review. J Herbmed Pharmacol. 2026;15(3):293-302. doi: 10.34172/jhp.53271.

Introduction

The incidence of diabetes has been increasing worldwide, contributing to approximately 425 million cases, more commonly among people between the ages of 20–79 years (1). Meanwhile, the World Health Organization (WHO) predicted a further increase in the number of people with diabetes, possibly reaching 463 million by 2030 (1,2). This is attributable to risk factors such as being overweight or obese, elevated blood pressure and glucose levels, age, high-fat and high-sugar diets, an inactive lifestyle, and urbanization (3,4). Obesity is the major risk factor, playing a significant role in increasing the risk of type 2 diabetes (T2D) and insulin resistance (IR) (5). Insulin sensitivity refers to the body's effectiveness in responding to insulin, a hormone critical for glucose regulation. Impaired insulin sensitivity, or insulin resistance, is a characteristic of type 2 diabetes mellitus (T2DM) and metabolic syndrome (6). Although there is a lot of evidence on the existing

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association between obesity and insulin resistance, several studies have reported the possibility of the development of T2D and IR even among healthy non-obese individuals (7). Similarly, insulin resistance in non-obese subjects is linked to several factors, namely genetics, lifestyle, metabolic anomalies in glucose and lipid metabolism as well as inflammatory pathways (6). Thus, any preventive strategies of T2DM are focused mainly on adjusting individuals' lifestyles, specifically physical activity and food choices, whether a person is already obese or not.

Currently, pharmacological solutions to T2DM rely largely on metformin, pioglitazone, sulfonylureas, and thiazolidinediones (8). These medications have, however, been reported to have adverse reactions, including hypoglycemia, lactic acidosis, peripheral oedema, severe hepatotoxicity, and gastrointestinal complications due to prolonged administration (8). Thus, there is a need for alternative hypoglycemic agents with minimal adverse effects.

Functional foods, defined by the Functional Food Centre (FFC) as foods that provide health benefits beyond basic nutrition, are being increasingly explored for their therapeutic potential in addressing metabolic disorders, particularly T2DM (9,10). Extensive research indicates that regularly incorporating functional foods, such as legumes, spices, and whole grains, in appropriate amounts can help reduce the risk of complications associated with T2D (11-14). Recent studies have shown that combining functional foods can accelerate recovery, improve overall treatment effectiveness, and reduce endothelial dysfunction and microvascular complications associated with diabetes, offering promising and affordable strategies for diabetes management (11). Functional foods provide health benefits through their rich content of bioactive compounds, including omega-3 fatty acids, antioxidants, probiotics, prebiotics, and phytochemicals (15,16). Antioxidants abundant in fruits, vegetables, and whole grains help the body neutralize damaging free radicals, thereby mitigating oxidative stress and reducing the risk of chronic diseases (T2DM, cancers, and heart diseases) (17). Among functional foods, seeds stand out as nutrient-dense, plant-based options with a unique combination of bioactive compounds (18). Flaxseed, chia, pumpkin, hemp, and sesame seeds are among the top five common functional seeds (18,19). These five seeds were selected because they represent some of the most widely consumed and researched functional seeds globally. They are not only easily accessible and incorporated into a range of traditional and modern diets, but they also contain diverse bioactive compounds that have been consistently linked with metabolic health. Importantly, insulin resistance is not only a precursor to T2DM but also underlies a wide range of metabolic complications, including cardiovascular disease, non-alcoholic fatty liver disease (20,21), polycystic ovary syndrome (22), and cognitive decline (21,22). The bioactive components of functional seeds may therefore play both therapeutic and preventive roles. Through their antioxidant, anti-inflammatory, and lipid-modulating effects, these compounds have the potential to reduce the onset and progression of such comorbidities, highlighting the importance of functional seeds as a preventive dietary strategy. Their prominence in functional food formulations, coupled with a growing body of experimental and clinical evidence supporting their roles in glycemic regulation, makes them particularly relevant candidates for a focused synthesis on insulin sensitivity.

While several reviews have explored the general health benefits of functional seeds, few have focused specifically on their mechanistic roles in insulin resistance. This mini-review provides a comparative synthesis of bioactive components across flaxseed, chia, pumpkin, hemp, and sesame, linking each to specific molecular pathways, including AMP-activated protein kinase (AMPK) activation, peroxisome proliferator-activated receptor (PPAR) modulation, and gut microbiota regulation. By integrating recent animal and clinical data, this paper highlights translational opportunities for developing seed-based interventions in metabolic disorders.

Overview of the functional seeds

Linum usitatissimum is commonly referred to as flaxseed when used for human consumption and as linseed when used for industrial purposes (23). Flaxseed comes from a blue-flowering annual herb of the *Linaceae* family, typically growing between 12 and 40 inches tall. The plant features a slender, fibrous stem and striking blue flowers, approximately 3 cm in diameter. The seeds themselves are flat, oval-shaped with pointed ends, and have a smooth, glossy surface. Their colour ranges from dark brown to yellow, and they have a crispy, chewy texture with a mild, nutty flavour (23). The potential health benefits of flaxseed and its oil are attributed to their rich content of bioactive compounds and elements such as linolenic acid, linoleic acid, lignans, cyclic peptides, polysaccharides, alkaloids, cyanogenic glycosides, and cadmium (23).

Chia seeds are edible seeds derived from *Salvia hispanica*, a plant species in the mint family (*Lamiaceae*) (24). These seeds are oval-shaped, predominantly grey in colour with black and white speckles, and measure approximately 2 millimetres (0.08 inches) in width (25,26). It is native to Mexico, northern regions, and Guatemala (27). *Salvia hispanica L.* belongs to the *Labiatae* family and is an annual flowering plant (28). Historically consumed as a food source, chia seeds are typically cultivated in mixtures containing both white and black varieties (29). Presently, black chia seeds, distinguished by their spiral and striped patterns, are more commonly grown (30). Chia seeds are particularly rich in dietary fibre (about 34–40 g/100 g), omega-3 fatty acids (especially alpha-linolenic acid

[ALA]), and plant-based proteins (approximately 16–24%) (31). They also contain beneficial antioxidants, phenolic compounds (like quercetin and caffeic acid), and essential minerals such as calcium, magnesium, phosphorus, and manganese (31,32). Additionally, chia seeds provide B vitamins (e.g., niacin and folic acid) and vitamin E (32,33). This nutrient composition contributes to their functional benefits in supporting cardiovascular health, glycemic control, digestive function, and antioxidant defence (25).

Pumpkin seeds (*Cucurbita pepo* L*)* are flat, oval-shaped seeds typically green in colour once the white outer hull is removed (34,35). They are native to the Americas and have been consumed both as food and medicine for centuries. Nutritionally, pumpkin seeds are rich in protein (approximately 30%), healthy fats including linoleic and oleic acids, and micronutrients such as magnesium, zinc, and iron (34). They also contain bioactive compounds such as phytosterols, flavonoids, and phenolic acids, which contribute to their antioxidant and anti-inflammatory properties (35). These attributes make pumpkin seeds an important functional food, with growing evidence supporting their role in cardiometabolic health and glycemic regulation.

Hemp seeds are small, oval-shaped seeds derived from *Cannabis sativa* L., and unlike other parts of the plant, they are non-psychoactive. They are highly nutritious, containing about 25–30% protein with a complete amino acid profile, and an optimal ratio of omega-6 to omega-3 fatty acids (approximately 3:1) (36). In addition, hemp seeds are rich in dietary fibre, vitamin E, and essential minerals such as magnesium, phosphorus, potassium, and zinc (36). Bioactive peptides, polyphenols, and phytosterols further contribute to their antioxidant, anti-inflammatory, and cardiometabolic benefits (19). Due to this unique nutrient profile, hemp seeds are increasingly recognized as a functional food capable of supporting metabolic health and insulin sensitivity (36).

Sesame seeds are tiny, flat, and oval-shaped seeds that come in white, brown, yellow, or black varieties. They have been cultivated for thousands of years and are valued both as food and medicine across many cultures. Nutritionally, sesame seeds are abundant in healthy fats, high-quality protein, dietary fibre, and minerals such as calcium, iron, and zinc (37). Their bioactive profile is dominated by lignans, particularly sesamin and sesamolin, which exhibit strong antioxidant, lipid-lowering, and anti-inflammatory properties (19,37). Sesame seeds also contain tocopherols and phytosterols that contribute to their health-promoting effects (38). Increasing evidence suggests that sesame seed consumption supports glucose regulation, improves lipid metabolism, and may help counteract insulin resistance, making it a valuable contributor to functional seed-based strategies for maintaining metabolic health (39,40).

Despite the growing interest in these functional seeds, several challenges limit their clinical translation. The nutrient composition of seeds is highly variable, depending on genetic, agronomic, and processing factors, which complicates standardization in research and practice (41). In addition, many of the bioactive compounds present in seeds, such as polyphenols and lignans, exhibit poor bioavailability, raising questions about their effective physiological concentrations in humans (42). Most available evidence is derived from preclinical studies, while human trials remain limited in number, scale, and duration. Addressing these gaps is critical to advancing seeds from promising dietary adjuncts to evidence-based interventions for insulin resistance.

Bioactive components of functional seeds

Preparation and isolation methods

The health benefits of seeds are closely influenced by the methods used for their preparation and extraction of bioactive constituents. Common techniques include cold-pressing to obtain oils rich in polyunsaturated fatty acids (PUFAs), as well as aqueous and alcoholic extractions to isolate polyphenols and lignans, and enzymatic or fermentation-based methods to enhance the release of bioactive peptides (43,44). These approaches not only improve yield but also affect the stability, bioavailability, and physiological potency of the isolated compounds (43).

Omega-3 and omega-6 fatty acids

Seeds are rich in health-promoting unsaturated fats, particularly PUFAs and, to a lesser extent, monounsaturated fatty acids (MUFAs) (18,19). Flaxseeds and chia seeds are notable for their high content of ALA, an essential omega-3 fatty acid (45). These fatty acids have been shown to positively influence lipid metabolism by lowering total cholesterol, reducing triglyceride levels, and improving the ratio of HDL to LDL cholesterol (46). Moreover, PUFAs play a vital role in maintaining membrane fluidity, which supports the optimal function of insulin receptors, ion channels, and membrane-bound enzymes (47). Enhanced membrane dynamics are essential for cell signalling and systemic metabolic regulation. The regular consumption of ALA-rich seeds may reduce the risk of cardiovascular disease, improve insulin sensitivity, and modulate inflammatory pathways (45). Flaxseed and chia are among the richest plant sources of ALA (48), an omega-3 fatty acid known to enhance insulin sensitivity by modulating lipid metabolism and reducing inflammation (19). Similarly, chia seeds are a rich plant-based source of omega-3 fatty acids, mainly ALA, and offer a healthy ratio of omega-3 to omega-6 fats (29). These seeds are associated with several potential health benefits, such as aiding digestion and contributing to weight management (48). The overall impact of omega-6 fatty acids on T2DM may depend on their ratio to omega-3 intake, emphasizing the need for balanced dietary strategies (49). Hemp seeds offer a balanced omega-6 to omega-3 ratio, making it an excellent seed oil for maintaining metabolic health.

Lignans and phytosterols

Phytoestrogens are a group of naturally occurring compounds derived from plants (50). They are widely distributed in nature and can be found in foods such as vegetables, grains, nuts, olive oil, legumes, cereals, and leaves, as well as in wood pulp (50). Common dietary phytosterols include sitosterol, stigmasterol, and campesterol, which exist in free form or bound as esters with fatty or cinnamic acids, or as glycosides that are broken down by pancreatic enzymes (1). These compounds have garnered increasing attention for their potential to improve overall health and metabolic function. Due to their structural resemblance to estrogen, they have been widely studied for their diverse therapeutic effects, including lipid-lowering, anti-inflammatory, antioxidant, antiproliferative, and blood sugar-regulating properties (1). A growing body of research suggests that phytosterols and diets rich in them may help regulate glucose and lipid metabolism, as well as reduce insulin resistance (50). For example, a study reported that a daily dose of 2 g decreases cholesterol absorption by 30–40% and LDL cholesterol by 10% on average (50). Flaxseed is particularly rich in lignans such as secoisolariciresinol diglucoside (SDG), which exhibit antioxidant and estrogenic properties (51). These compounds may improve insulin action and reduce oxidative stress. Sesame seeds contain sesamin, another lignan with lipid-lowering and anti-inflammatory effects (52).

Dietary fibre

Many edible seeds are excellent sources of dietary fibre, including both soluble and insoluble fractions (19). Seeds like chia and flaxseeds form viscous gels when hydrated, which can slow gastric emptying, enhance satiety, and contribute to glycemic control (18,29). More importantly, the fibre content in these seeds acts as a prebiotic substrate for beneficial gut microbiota. Fermentation of these fibres in the colon leads to the production of short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate. SCFAs help regulate inflammation, improve gut barrier function, and stimulate the secretion of glucagon-like peptide-1 (GLP-1), a hormone involved in appetite regulation and glucose homeostasis (53,54). Thus, seed-derived fibre not only improves digestive health but also influences metabolic processes beyond the gut.

Polyphenols and antioxidants

Seeds contain a diverse array of polyphenolic compounds and flavonoids, including catechins, quercetin, ellagic acid, and lignans (55). For instance, flaxseeds are especially rich in lignans, while pumpkin seeds contain quercetin and phenolic acids that contribute to their functional profile (56). Sesame seeds also provide lignans such as sesamin, and chia seeds contain caffeic and rosmarinic acids. These compounds, along with antioxidant vitamins such as vitamin E, have been linked to protective effects against oxidative stress and chronic inflammation. Their presence highlights the potential of functional seeds to provide bioactive compounds that impact metabolic health.

Mechanisms of action

Insulin signalling

Phytosterols, such as β-sitosterol, stigmasterol, and campesterol, play a central role in modulating insulin signaling (57). These plant-derived sterols enhance the expression and activation of insulin receptors (IR), initiating a cascade that involves insulin receptor substrate-1 (IRS-1), phosphoinositide 3-kinase (PI3K), and protein kinase B (Akt) (1,57). The activation of this signalling pathway promotes the translocation of glucose transporter type 4 (GLUT4) to the plasma membrane, thereby facilitating glucose uptake into insulin-sensitive tissues, such as skeletal muscle and adipose tissue (1). This mechanism underlies the improvement in glycemic control and the reversal of insulin resistance observed in both in vivo and in vitro models supplemented with phytosterols (58).

AMPK activation

Lignans found in seeds enhance insulin sensitivity by activating the AMPK pathway (55). AMPK is a key energy sensor that regulates cellular metabolism. Activation of AMPK by lignans stimulates GLUT4 expression and translocation, increases fatty acid oxidation, and improves mitochondrial efficiency. These metabolic improvements collectively enhance glucose uptake and utilization, reducing insulin resistance at the cellular level. Certain seed components, such as ALA and polyphenols, have also been shown to activate AMPK pathways (55).

PPAR/Adiponectin and lipid metabolism

Seeds influence the peroxisome proliferator-activated receptor gamma (PPARγ) pathway, which regulates lipid storage and insulin signalling (59). Enhanced adiponectin levels, associated with seed intake, further contribute to improved glucose metabolism (55). Phytosterols also influence lipid metabolism in a manner that supports insulin sensitivity. These compounds reduce hepatic lipid accumulation by downregulating the expression of lipogenic genes, including sterol regulatory element-binding protein-1c (SREBP-1c) (1). By lowering lipid levels and altering the composition of circulating lipids, phytosterols prevent ectopic fat deposition in the liver and skeletal muscle, which are key sites of insulin action (1). Improved lipid profiles are associated with better insulin sensitivity and a reduced risk of metabolic syndrome (60).

Gut microbiota modulation

Fibre and polyphenols in seeds act locally in the gut as prebiotics, influencing the composition and activity of the gut microbiota (61). These shifts in microbial ecology promote the production of SCFAs, improve gut barrier function, and lower systemic endotoxemia (62). These changes are increasingly recognized as important contributors to improved insulin sensitivity and metabolic homeostasis, demonstrating the integrative role of lignans in modulating host-microbe interactions for better glucose regulation (61).

Anti-inflammatory and antioxidant effects

The bioactive compounds present in seeds exert significant effects on inflammatory and oxidative stress pathways that contribute to insulin resistance (63). Lignans, omega-3 fatty acids, and phenolic compounds suppress pro-inflammatory cytokines such as tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), largely through inhibition of the nuclear factor kappa B (NF-κB) signalling cascade (64). Antioxidant constituents, including vitamin E and flavonoids, neutralize reactive oxygen species (ROS), thereby preventing oxidative damage to insulin signalling proteins and cellular structures (63). The anti-inflammatory and antioxidant actions help restore insulin sensitivity and protect tissues from chronic metabolic stress and degeneration (5). Furthermore, phytosterols act as scavengers of ROS, thereby protecting insulin receptors and related intracellular molecules from oxidative degradation (1). This preservation of redox balance enhances cellular insulin responsiveness and mitigates the metabolic dysfunction associated with hyperglycemia (65). These compounds downregulate key inflammatory cytokines, including TNF-α, IL-6, and resistin, which are known to impair insulin receptor function and downstream signalling (64). In animal models of insulin resistance, β-sitosterol has been shown to inhibit inflammatory pathways, including the c-Jun N-terminal kinase (JNK), inhibitor of nuclear factor kappa-B kinase (IKK), and NF-κB (57). By suppressing these pathways, phytosterols reduce chronic inflammation in adipose tissue and other metabolic organs, thereby restoring insulin responsiveness (57).

In addition to these effects, seed-derived polyphenols and lignans influence apoptotic signalling, regulating Bcl-2 family proteins and caspase activity (66). This confers cytoprotective benefits, preserving β-cell survival and mitochondrial integrity under conditions of metabolic stress (66). By acting at the intersection of inflammatory, oxidative, and apoptotic pathways, seed bioactives provide multilayered protection that supports insulin responsiveness and metabolic homeostasis.

Figure 1 summarises the major mechanisms through which seed-derived bioactive compounds modulate insulin resistance. These compounds act at multiple levels, enhancing insulin signalling, activating AMPK, modulating gut microbiota, improving lipid metabolism, suppressing inflammation and oxidative stress, and protecting β-cells, ultimately converging to improve insulin sensitivity and delay the onset of T2DM.

Evidence from animal and human studies

A synthesis of experimental studies highlights the insulin-sensitizing potential of various functional seeds, particularly chia, pumpkin, and flaxseeds (Table 1). Among these, chia seeds emerge as the most extensively researched, supported by at least four independent rat model studies examining different extracts, bioactive compounds, and metabolic outcomes. The wide range of chia seed studies may be attributed to their rich and diverse composition, including ALA, fibre, antioxidants (such as quercetin, caffeic acid, and rosmarinic acid), and sterols, which collectively influence multiple metabolic pathways. In streptozotocin-induced diabetic rats, 100 mg/kg of chia seed aqueous extract administered for 15 days significantly enhanced glucose metabolism and

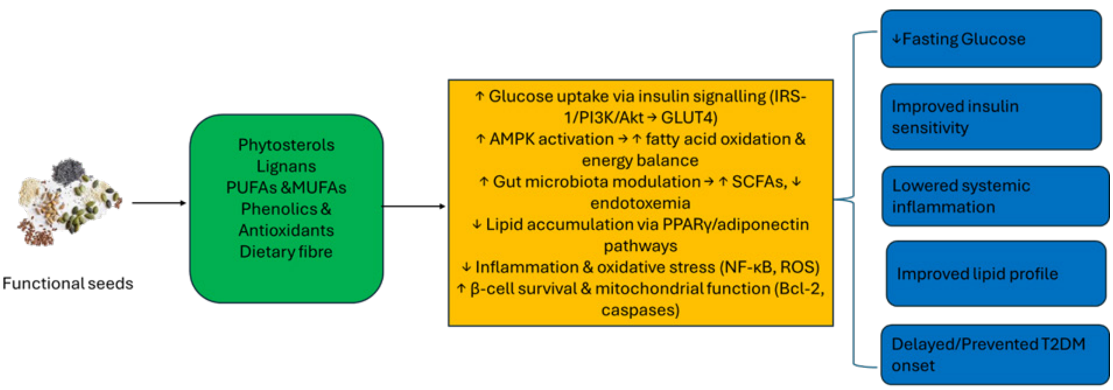

Figure 1. Summary of mechanisms and pathways of seed-derived bioactive compounds in managing insulin resistance. PUFAs: Polyunsaturated fatty acids; MUFAs: Monounsaturated fatty acids; SCFAs: Short-chain fatty acids; AMPK: Adenosine monophosphate-activated protein kinase; GLUT 4: Glucose Transporter 4; ROS: Reactive oxygen species; T2DM: Type 2 diabetes mellitus; PPARγ: Peroxisome proliferator-activated receptor gamma.

Table 1. Evidence of studies on the hypoglycaemic and insulin-sensitizing effects of seeds

Seed	Bioactive compounds	Dose	Model	Extract	Mechanism	Reference
Chia	Caffeic acid, chlorogenic acid, carotenoids, sterols, gallic acid, rosmarinic acid	100 mg/kg for 15 days	Streptozotocin-induced diabetic rat	Seed aqueous extract	↑Blood glucose metabolism and insulin production	(26)
Pumpkin	Flavonoids	3%	Alloxan-induced diabetic rats	Oil extract	↓Serum glucose, cholesterol, and triglyceride	(68)
Black Chia	Linoleic acid, quercetin	1 ml (20%, w/w)	Diabetic, male rats	Seed extract	↓Serum glucose ↓HbA1c ↓HOMA-IR ↓Serum LDL-c ↑insulin level ↑QUICKI	(67)
Chia	Antioxidants	4.5 mg/kgBW and 13.5 mg/kgBW	Male Wistar Rats	Seed extract	↓Blood sugar	(27)
Chia seeds	Fibre	1.5 g	Rats	Seed extract	↓Blood glucose	(69)
Flaxseeds	SDG	1.5 g	Rats	Seed extract	↓Blood glucose	(69)

HbA1c: Haemoglobin A1c; HOMA: Homeostatic model assessment of insulin resistance; QUICKI: Quantitative insulin sensitivity check index; SDG: Secoisolariciresinol diglucoside.

insulin production, suggesting its capacity to restore pancreatic function and glycemic control (26). Another study using black chia extract rich in linoleic acid and quercetin showed reductions in serum glucose, HbA1c, HOMA-IR, and LDL-c, while simultaneously increasing insulin levels and the QUICKI index, a marker of insulin sensitivity (67). Additional investigations using chia seed fibre and antioxidant extracts further confirmed their hypoglycemic effects, demonstrating significant reductions in blood glucose levels in both moderate and high dosages (27).

Beyond chia and flaxseed, pumpkin has been extensively studied in animal models for its anti-hyperglycemic potential. In alloxan- and streptozotocin-induced diabetic rats, pumpkin seed and fruit extracts significantly lowered fasting blood glucose, improved insulin production, and reduced postprandial glycemic excursions (34). Protein-bound polysaccharides (PBPP) demonstrated dose-dependent effects, while pumpkin polysaccharide hydrolysates (PPe-H) not only improved glucose control but also reduced oxidative stress and enhanced GLP-1 secretion (34). Pumpkin seed oil also showed promising results in alloxan-induced diabetic rats (68). Its flavonoid-rich profile contributed to significant reductions in blood glucose, cholesterol, and triglyceride levels, indicating its potential in lipid and glycemic regulation. These findings suggest that pumpkin exerts multifaceted benefits through both pancreatic and extra-pancreatic pathways, although confirmation in well-designed clinical trials remains limited.

One study demonstrated a similar capacity for flaxseed in reducing blood glucose levels, primarily through its abundant SDG content, a lignan known for its antioxidant and insulin-enhancing properties (69). Notably, as reported in an updated systematic review by Kavyani et al in 2023, some human clinical trials report no significant improvement in HbA1c or fasting glucose with flaxseed supplementation, highlighting variability in human outcomes and the need for larger, well-controlled trials (70).

Across all seed types, the most common mechanism reported was enhancement of glucose uptake and insulin production, typically mediated through modulation of insulin signalling pathways and activation of AMPK (Table 1). Several studies also observed anti-inflammatory and antioxidant effects, supporting improved β-cell function and reduced insulin resistance. These findings consistently emphasize that the bioactive components in seeds, particularly polyphenols, omega-3 fatty acids, lignans, and dietary fibre, target inflammatory pathways, oxidative stress, and metabolic enzyme regulation to restore insulin sensitivity.

While animal studies dominate the literature, human clinical data remain limited and often inconclusive, with small sample sizes and short intervention periods restricting interpretation.

Applications and functional food innovations

Functional seeds are increasingly being used in the development of health-promoting foods (34). Examples include seed-enriched breads, snack bars, seed butters, and dairy alternatives (71,72). These formulations offer a convenient way to incorporate bioactive compounds into daily diets. Ground or cold-pressed forms may enhance bioavailability. Flaxseeds are commonly incorporated into foods such as breads, cereals, and smoothies, and are also found in dietary supplements because of their reputed health-promoting effects, particularly for heart health and inflammation reduction (73). Chia seeds are used in a variety of forms in the food industry, including whole, ground, and roasted (74). Their adaptability allows them to be mixed into a range of meals, including yogurts, salads, and baked items, to enhance nutritional quality (74). Oil extracted from chia seeds is also commonly used in food products. In 2017, the European Food Safety Authority (EFSA) introduced regulations outlining the acceptable levels of chia seed inclusion in different dietary items (75). According to these guidelines, chia seed content should not exceed 5% in bread, 10% in breakfast cereals, baked goods, and fruit and seed mixtures, 1% in fruit pastes, 1.3 g per 100 g or 4.3 g per 330 g in yogurt, 15 grams of whole or ground seeds in vegetable and fruit juices or drinks, and 5% in ready-to-eat foods, as reported by Turck and colleagues in 2019 (75). Recognized as a health-promoting food, chia seeds are widely available in packaged form and are sold in different quantities. Chia seeds can be added to a broad range of food products, including juices, yogurt, cakes, cookies, pasta, baked goods, ice cream, desserts, breakfast cereals, and even processed meats such as sausages and hams, to enhance their nutritional profile (74). Food-grade chia seed oil is also available commercially and can be used in various applications such as sandwiches, salads, cottage cheese, and spreads (74). Furthermore, due to their high water-binding capacity, chia seeds can serve as a natural substitute for eggs or oils in baked goods (74). In addition to chia and flaxseed-based formulations, pumpkin powders and extracts have been incorporated into functional food products, with studies indicating their ability to enhance insulin secretion and protect against renal complications associated with diabetes (34). The potential for developing pumpkin seed-enriched foods or supplements highlights their value as a cost-effective dietary adjunct for glycemic management.

Challenges and future perspectives

Although growing evidence supports the role of functional seeds in improving insulin sensitivity, several challenges hinder their clinical application. Variability in nutrient composition due to genetic, agronomic, and processing factors complicates standardization, while poor bioavailability of certain compounds, such as lignans and polyphenols, raises concerns about achieving effective physiological concentrations in humans. In addition, the lack of well-designed, long-term clinical trials limits the strength of current evidence, particularly regarding optimal dosage and formulation.

Another important gap is the limited number of in vitro studies that systematically investigate the biological activities of seed-derived compounds. Dose-dependent studies in adipocytes, hepatocytes, and pancreatic β-cell models are needed to clarify mechanistic pathways, establish efficacy thresholds, and identify potential toxicities. Such work will provide a stronger foundation for translational studies and inform safe clinical application. Addressing these gaps through integrated in vitro, preclinical, and clinical research will be critical for advancing functional seeds from promising dietary adjuncts to evidence-based interventions for insulin resistance and related metabolic disorders.

Conclusion

Functional seeds present a compelling, food-based solution for enhancing insulin sensitivity and managing T2DM. Their rich array of bioactive compounds, including PUFAs, lignans, fibre, and antioxidants, supports multiple metabolic pathways involved in glucose regulation. Preclinical studies confirm their potential in improving insulin signalling, modulating gut microbiota, reducing inflammation, and enhancing lipid profiles. Despite promising findings, more robust human clinical trials are needed to establish standardized dosages and formulations. As part of a holistic dietary strategy, functional seeds offer a safe, cost-effective, and accessible adjunct to conventional therapies for insulin resistance and T2DM prevention.

Declaration of AI-assisted Tools in the Writing Procedure

To improve the readability and language of this manuscript, the author used ChatGPT (OpenAI, San Francisco, USA) and Grammarly for grammar refinement and phrasing. These tools were applied solely for language editing.

Conflict of interests

The author declares no conflict of interest.

Funding/Support

No external funding was received for this work.

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