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Review Article

Chemical composition, nutritional characteristics and benefits associated with the consumption of Chia (*Salvia hispanica L.*)

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ABSTRACT

Chia (Salvia hispanica L.) is a seed native to the southern part of Mexico and Guatemala, which has spread to other Latin American countries. This seed has been used for different purposes throughout history, where it stands out as a food product due to its great versatility, since it can be used as a seed, wholemeal flour, fiber and/or protein fractions and oil. Currently, the investigation of new food sources that provide health benefits has managed to collect information on the chemical composition and nutritional value of this seed and its derivatives (flour and oil). For polyunsaturated fatty acid content, n-3 is found, highlighting alpha linolenic acid (C18:3n-3, ALA), which is proposed as an alternative source of this nutrient to foods of other origins. In addition, the fiber content of chia is mainly insoluble fiber. Regarding the benefits associated with chia consumption, it is closely related to chronic non-communicable diseases such as dyslipidemia, type 2 diabetes, hypertension, and cancer, among others, managing to attract the attention of researchers to control and prevent these pathologies that are increasing in the world population. Therefore, it is relevant to deepen the knowledge available about this seed and its by-products in order to establish the possible molecular mechanisms that are involved in generating health benefits. The objective of this review is to present an update on the benefits associated with consumption of chia seed and its derivatives.

Keywords: α-linolenic acid; Antioxidants; Chia seeds; Dietary fiber; Salvia hispanica L.

INTRODUCTION

Salvia hispanica L., commonly known as chia, is a seed of the *Lamiaceae* family, native to southern Mexico and southern Guatemala, which was heavily explored and used by the Aztecs[1]. After Spanish colonization, the seed stopped being cultivated for many years, and was resumed in 1991, thanks to a regional project in northern Argentina. Later, it also began to be cultivated again in Mexico, on a small scale, in cities such as Jalisco, Morelos and Guerrero, and in other South and Central American countries such as Ecuador and Guatemala[1,2]. It has been used for nutritional, medicinal and aesthetic/recreational purposes, the latter to improve the quality of the paint[3]. The versatility of this seed in the food industry has managed to capture the attention of many people, since it can be consumed as the whole seed, its oil extracted, or as different flours (whole grain, dietary fiber fraction, or protein fraction), which can be used for different preparations, such as cookies, bread, juice, or salads[4,5].

At present, more and more people worldwide are searching for foods that provide health benefits. This has led to research into the high nutritional value of the chia seed, mainly associated with its n-3 polyunsaturated fatty acid content (n-3 PUFA), especially α-linolenic acid (C18:3n-3, ALA), which make it a good alternative to animal sources[6], in addition to its high protein content (even higher than that of other seeds such as flaxseed and rosehip)[6,7], dietary fiber, and antioxidants. Due to these characteristics, its consumption has been found to have positive results at the metabolic level in the prevention and/or resistance against diseases such as dyslipidemia, hypertension, diabetes, cancer, among others[4].

The consumption of chia and the benefits associated with its nutritional contribution have been an area of interest, since it has been found that the n-3 PUFAs in it produce lipid redistribution, decreasing plasma levels of triglycerides, total cholesterol, LDL cholesterol and VLDL, while also increasing HDL cholesterol levels, which has cardioprotective and hepatoprotective effects[8]. Another nutritional contribution is its fiber content, soluble and insoluble, which helps to increase the volume of stools and decrease the speed of digestion, exerting an effect at the level of peristaltic movements and glucose release, in addition to reducing the bioaccessibility of lipids and cholesterol, helping to prevent colon cancer, diabetes and dyslipidemia[8,9]. The antioxidant compounds found in this seed are associated with a decrease in the amount of reactive oxygen species, reducing inflammatory processes; and the isoflavones, specifically, have an anticarcinogenic effect[10]. On the other hand, studies have shown that chia consumption decreases postprandial glucose levels with incidence in the dose-response relationship, in addition to a decrease in appetite indices, associating these effects specifically to dietary fiber[11]. In addition, it has been reported that in subjects with type 2 diabetes, chia consumption was associated with a decrease in systolic blood pressure and c-reactive protein levels, reducing cardiovascular risk, maintaining good control of glucose and lipid levels[12]. An increasing number of benefits associated with the consumption of chia are being discovered, thanks to its content of polyunsaturated fatty acids, proteins, fiber and antioxidants, which have various impacts such as lipid redistribution, glucose tolerance, insulin sensitivity, dyslipidemia, and hypertension, as seen in rats supplemented with chia oil[13]. Based on all of the above, the objective of this article is to present an update of the benefits associated with the consumption of chia seed and its derivatives.

METHODOLOGY

This review included studies conducted under three different models: *in vitro*, animal, and human, where the effect of treatment with chia or its derivatives was analyzed in order to elucidate the benefits associated with its consumption. The literature was reviewed on the PubMed database (of the National Institutes of Health's National Library of Medicine), Web of Science, and the *Revista Chilena de Nutrición* platform. Experimental studies in English and Spanish were included, published from 2013 to date, that included the terms: *"Salvia hispanica L."* OR "Chia seeds" OR "Chia oil" OR "Chia flour". The main inclusion criterion was the presence, in each article, of an association between chia consumption (seed, oil and flour) and potential beneficial effects. Articles that could additionally explain the mechanisms associated with these benefits were also considered.

Chemical composition and nutritional value of chia seed, oil and flour

In the last decade, the nutritional value of various seeds has been extensively explored. Among them, chia stands out for its high lipid, protein and fiber content, which varies depending on the geographical location where it is grown, seasonality and other environmental factors[14].

Chemical composition of chia seed

The chemical composition of the chia seed is characterized by its low humidity, containing mostly lipids and presenting a high content of dietary fiber (Table 1). Most notable among its components is the high value of fatty acids (30%), mainly polyunsaturated, where 60% of the fatty acids correspond to ALA, followed by linoleic acid (C18:2n-6, LA) with 20%. Chia seeds also contain a high percentage of proteins (16-26%) that include essential amino acids such as arginine, leucine, phenylalanine, and others. Thanks to its protein content, it can provide approximately 3.61 g of nitrogen per 100 g of seed[15]. 20-40% corresponds to fiber found in the chia seed, composed mainly of cellulose, pectin, hemicellulose, lignin, polysaccharides and oligosaccharides. The fiber fraction is made up of 85-93% insoluble fiber and 7-15% soluble fiber[7]. The vitamins contained in the seed correspond mainly to B complex vitamins, such as thiamin (B_1), riboflavin (B_2), niacin (B_3) and folic acid, and minerals such as calcium, phosphorus, magnesium, potassium, selenium, iron, copper and zinc. Another important element are antioxidant compounds such as polyphenols, tocopherols, sterols, isoflavones, and flavonoids such as daidzin, genistein, glycitin, quercetin, and kaempferol[16].

Chemical composition of chia oil

The oil obtained from the chia seed is characterized by a high content of polyunsaturated fatty acids, in addition to providing essential fatty acids. Table 2 shows the content of fatty acids in chia oil, with a predominance of ALA followed by LA[7].

Chemical composition of chia flour

The chemical composition of whole chia flour (Table 3) is similar to that of the seed. The fiber found is 91.3% insoluble fiber and 8.7% soluble fiber. There are also phenolic compounds (0.97 ± 0.07 g/100 g) and phytates (0.96 ± 0.11 g /100 g)[8].

Table 1. Chemical composition of chia seed.

	Jiménez et al.[7] g / 100 g	**USDA**
Humidity	6.2 ± 0.0	6.96
Protein	19.9 ± 0.2	18.29
Fats	27.9 ± 0.4	42.16
Carbohydrates	8.6 ± 0.3	28.88
Fiber	33.0 ± 0.5	27.3

Data expressed in grams per 100 g of chia seeds.
* USDA: United States Department of Agriculture.

Table 2. Fatty acid composition of chia oil.

Main fatty acids	**% methyl esters**
Alpha linolenic acid (C18:n3, ALA)	51,82 ± 1,49
Linoleic acid (C18:n2)	19,36 ± 0,16
Oleic acid (C18:n1)	8,91 ± 0,30
Palmitic acid (C16:n0)	7,29 ± 0,17
Stearic acid (C18:n0)	3,84 ± 0,09

Source: Adaptation of Jiménez et al.[7]

Table 3. Chemical composition of chia flour.

	g/100g
Humidity	7,14 ± 0,26
Protein	18,18 ± 1,20
Fats	32,16 ± 0,29
Carbohydrates	4,59 ± 0,34
Fiber	33,37 ± 0,26

Data expressed in grams per 100 g of chia seeds.
Source: Adaptation of Da Silva et al.[8]

Chia and benefits in humans

Cardiovascular health and metabolic disorders

Cardiovascular diseases are the most prevalent worldwide, and there are ongoing efforts to find effective treatments and prevention. Some of the cardiovascular risk factors in the population are arterial hypertension, dyslipidemia, diabetes, or fasting hyperglycemia[17]. In this regard, patients with mild hypercholesterolemia who consumed a diet with chia seeds (4 g/day for 2.5 months) experienced a significant decrease in serum levels of LDL cholesterol (-18%) and triglycerides (-17.1 %), achieving a change in the lipoprotein profile and reducing the risk of cardiovascular events[18]. In another experimental study, a single group of patients with non-alcoholic fatty liver disease (NAFLD) consumed ground chia seed (25 g/day) for 8 weeks, and showed an increase in plasma ALA and greater fiber consumption. In addition, total cholesterol, non-HDL cholesterol, free fatty acids, body weight and visceral abdominal fat were significantly reduced, resulting in a regression of the disease in a considerable percentage of patients[19].

In another randomized clinical trial, in 42 patients with type 2 diabetes mellitus (T2DM), the intake of chia seeds (40 g/day for 12 weeks) significantly decreased systolic pressure, while the lipid profile, body weight, inflammatory markers and glycemia did not change significantly[20]. Similarly, in a double-blind randomized clinical trial, where 44 patients with T2DM were supplemented with a capsule containing viscous fiber, chia, and American and Korean ginseng extract for 24 weeks, glycemic control improved, attenuating the increase in glycosylated hemoglobin (HbA1c) and the insulinemic profile[21]. In another study, healthy patients who took 50 g of glucose together with 25 g of chia seed on three occasions, experienced a reduction in the glycemic peak, increasing the time it took to reach it, possibly mediated by the viscosity of the fiber. In addition, the consumption of chia increased the perception of satiety, decreasing the desire to eat and appetite in general[22]. Along the same lines, in a randomized controlled dose-response relationship clinical trial conducted in 13 healthy subjects who were given white bread alone or with the addition of 7, 15 or 24 g of chia seeds, whole or ground, it was found that the chia in either form and regardless of the dose is effective in reducing blood glucose, as in the study mentioned above, due to its fiber content[23]. Patients with arterial hypertension with and without treatment who consumed 35 g/day of chia flour for 12 weeks showed a decrease in pressure at the clinical and outpatient level[24].

Body weight

Another important factor in the development of diseases is malnutrition due to excessive food consumption, which has been increasing in recent years, affecting people of all ages[25]. Two studies have shown that chia consumption is associated with a reduction in body weight. For example, in overweight and obese patients who ingested 35 g/day of chia flour for 12 weeks, there was a significant reduction in body weight, with a greater impact in obese subjects, where waist circumference and cholesterol (total and VLDL) decreased, and HDL cholesterol increased, but only in patients with an altered lipid profile. On the other hand, blood glucose, triglycerides and LDL cholesterol did not show differences[26]. In addition, in a double-blind randomized clinical trial, patients with T2DM who consumed a low-calorie diet with chia seeds (30 or 36 g/1,000 kcal/day for 6 months) showed greater weight loss, as well as smaller waist circumferences, and lower plasma levels of C-reactive protein[27]. On the other hand, in a double-blind randomized clinical trial conducted in 30 prepubertal children with nutritional status of overweight and obese who were subjected to daily treatment with 25 g of ground chia seeds or cornstarch placebo for 75 days, no significant differences were found in body weight or biochemical parameters, but there was a statistically significant correlation between the inflammatory biomarkers, nuclear factor κB (NF-κB) and tumor necrosis factor α (TNF-α), and the presence of fiber from ground chia seeds, indicating that they may have an anti-inflammatory effect attributable to fiber in patients with excess weight[28].

Fatty acid composition of breast milk

The consumption of ALA and docosahexaenoic acid (C22:6n-3, DHA) is essential for the brain and visual function, but in the Western diet, it is below recommended levels. Therefore, as a precursor of DHA in humans, ALA can be used to increase the contribution of DHA, and reduce the consequences of its deficiency. In this sense, a randomized clinical trial carried out on 40 healthy pregnant women, where 19 received 16 ml/day of chia oil from the third trimester of pregnancy until the sixth month of lactation, found a significantly higher ALA consumption and a lower LA consumption, without significant changes in arachidonic acid (C20:4n-6, AA), eicosapentaenoic acid (C20:5n-3, EPA) and DHA. The same occurred in the content of breast milk, except for the DHA, which increased only in the first three months of lactation.

Animal model

Several studies conducted under animal (or *in vivo*) models have found links between the intake of chia seeds and health benefits. For example, in a study carried out in Wistar rats where six study groups were used (control group with casein, control group without protein content, untreated chia seed, heat-treated chia seed, untreated chia flour, and heat-treated chia flour), the rats fed with chia, in any form, had lower levels of glucose, triglycerides, VLDL, LDL, liver weight and liver fat percentage compared to the control groups; while good protein digestibility and an increase in circulating levels of HDL cholesterol were also observed[8]. In another study conducted on *Caenorhabditis elegans* that were fed with chia oil obtained by two methods (methanol/chloroform extraction and hexane extraction) at different concentrations (1, 1.5, 2, 2.5 and 3%), it was observed that low concentrations of oil reduced triglyceride levels and fat reserves in an obese model[30]. On the other hand, in the study by Fernández et al.[31], conducted on Wistar rats of both sexes that were fed for 10 days with diets based on different lipid sources (soybean oil, lard, lard supplemented with n-3 PUFA from fish oil, or lard supplemented with n-3 PUFA from chia oil), no significant differences were found in triglyceride levels and serum cholesterol levels. In contrast, it showed that n-3 PUFAs from chia oil are more beneficial than those from fish, because they not only increase serum levels of EPA and DHA, but also increase ALA values. Furthermore, lipid profile, glucose, biochemical markers of liver damage, and inflammatory factors were evaluated in non-obese rats with dyslipidemia and induced acute steatohepatitis fed with 15% chia for 4 weeks. Rats on a chia diet had less or no cholestasis, inflammation, necrosis, and oxidative stress, while in rats with dyslipidemia and non-alcoholic steatohepatitis, total cholesterol and triglycerides decreased[32].

Chia seed has also been shown to have an effect on inflammatory processes in rats. In a study conducted by Da Silva et al.[33], a high-fat diet with the addition of chia flour was administered for 35 days, obtaining a reduction in inflammatory processes, a decrease in saturated fatty acids, and an increase in PUFA due to the nutritional composition of the seed, without significant differences in terms of oxidative stress and production of reactive oxygen species. In another study conducted on Wistar rats, where one group was fed a high-fat, high-fructose diet supplemented with 13.3% chia seeds, and another group with a high-fat, high-fructose diet supplemented with 4% chia oil, increased levels of reduced glutathione (GSH), plasma catalase (CAT) and glutathione peroxidase (GPx) were obtained, while in the liver, glutathione reductase (GRd) activity increased, and plasma thiobarbituric acid reactive substances (TBARS) were reduced, showing that chia seed and chia oil have a similar antioxidant capacity[34].

Regarding the effect produced on glucose metabolism, much remains to be elucidated, since in a study carried out in diabetic rats with acute administration of a peptide fraction obtained from chia seeds in two concentrations, no significant differences were found in terms of decreasing or delaying glucose absorption, independent of the content of the administered sample. This could be due to the fact that the consumption was in a single dose and the quantity or frequency of consumption was not increased[35]. In addition to effects on lipid and glucose metabolism, chia has also been shown to affect the musculoskeletal system. This was observed in a study carried out in Sprague-Dawley rats fed a diet with 10% chia evaluated at 10 and 13 months, where it was found that the rats fed a diet that included chia had a significantly higher bone mineral content in the long term[36]. Finally, a study conducted on female Wistar rats exposed to a sucrose-rich diet in utero evaluated the effect of a sucrose-rich diet supplemented with chia seeds (20 g per 100 g of food) for 150 days after birth. The consumption of chia beginning at weaning managed to prevent the alteration in the metabolism of lipids and glucose, in addition to slightly reducing visceral adiposity[37].

In vitro model

In addition to *in vivo* studies, several *in vitro* studies have corroborated the beneficial effects. In this regard, the effect of total protein and fractions of digested chia seed proteins on the inflammatory response and atherosclerosis was evaluated in macrophages, which generated a decrease in the activation of NF-κB, in the secretion of nitric oxide (NO), in the secretion of proinflammatory cytokines (such as TNF-α) and inhibition of 5-lipooxygenase (5-LOX), cyclooxygenase 1 and 2 (COX-1-2) and inducible nitric oxide synthase (iNOS), with an increase in interleukin 10 (IL-10). Furthermore, digested proteins decreased the production of reactive oxygen species (ROS). This indicates that the digested proteins were effective in modulating inflammatory processes and atherosclerosis[38].

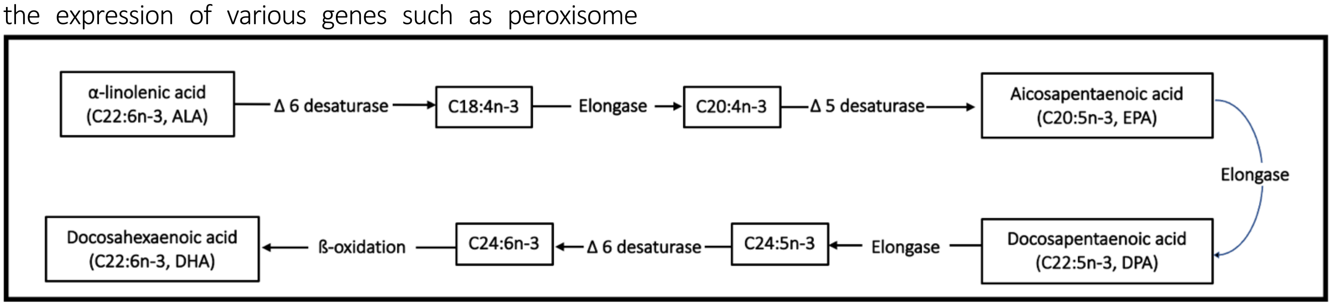
In epidermal melanocytes, the effect of chia seed extract with pomegranate on melanin production was evaluated, resulting in an 80% decrease in its production mediated by the reduction in the expression of genes associated with melanogenesis (Tyr, Tyrp1 and Mc1r). These results were obtained when the PUFAs were supplied in their entirety, since they did not show an effect separately[39].

Different cancer cell lines (MCF-7, Caco2, PC3, HepG2) and human fibroblasts were exposed to a protein fraction of chia seed at different concentrations (0.25, 0.5, 0.75, and 1 mg/ml) to assess toxicity, and it was found that this protein fraction showed a significant inhibition of all cancer cells, without being toxic[40]. Starting from a similar protein fraction, human microglia cell lines (HMC3) were treated with different concentrations of peptide fraction, showing neuroprotective activity, with anti-inflammatory and antioxidant action after damage induction[41]. The antioxidant action could possibly work as a mechanism to protect against neuronal damage, since according to Zhang et al.[42], the excessive production of free radicals leads to neuronal damage to the point of necrosis, while the anti-inflammatory action could be caused by the modulation of pathways that inhibit the production of proinflammatory cytokines.

Molecular mechanisms

Various studies have suggested that n-3 PUFAs exert their action at the metabolic level, providing health benefits such as the regulation of glycemic control and lipid profile, among others[6,8,43]. As a result, various plant sources, such as chia seed, have been widely investigated, since they are rich in ALA that can be metabolized and converted into long-chain PUFA (Figure 1) such as EPA and DHA, and several studies showed that a higher content of ALA increased the concentration of these fatty acids[44,45,46,47]. In this sequence of reactions, the n-3 PUFAs synthesized in the liver can be incorporated into membrane phospholipids or can be transported through lipoproteins to various organs, where they can modulate the expression of various genes such as peroxisome proliferator-activated receptor γ (PPAR-γ), IL-6, IL-1 and TNF-α, among others, reducing the risk of chronic non-communicable diseases[48]. Along these same lines, dietary chia helps to normalize the levels of proinflammatory cytokines such as IL-6 and TNF-α, and increase the levels of PPAR-γ in adipose tissue[49].

In rats fed a diet rich in sucrose, it has been shown that the administration of chia was able to prevent the development of dyslipidemia due to a lower hepatic secretion of VLDL and an increase in the uptake of plasmatic triglycerides, which improved the action of insulin[50]. In addition, another study indicates that the effect exerted by ALA is due to an increase in long-chain n-3 fatty acids in membrane phospholipids, modifying their fluidity[51]. At the hepatic level, chia seed, by increasing the concentration of EPA, manages to influence the hepatic synthesis of fatty acids, through the action of enzymes such as acetyl CoA carboxylase, fatty acid synthase and glucose 6-phosphate dehydrogenase. In addition, chia seed prevents the decrease in the protein mass of PPAR-α and the activities of carnitine palmitoyl transferase-1 and fatty acid oxidase and regulates the mechanism of the binding protein to sterol regulatory elements (SREBP-1c), with a metabolic change in the processing of lipids, favoring their oxidation[52]. The chia seed's more viscous fiber slows down the release of its glucose molecules, helping to control blood glucose levels[9]. At the muscular level, fatty acids interfere with the transport of glucose mediated by insulin, but some researchers postulate that the consumption of chia reduces the triglycerides and free fatty acids in plasma, which decreases lipotoxicity and restores the translocation of Glut4 to the cell membrane, normalizing the oxidation processes and glucose phosphorylation, in addition to increasing IRS-1 phosphorylation and normalizing the serine/threonine kinase pathway[53].



In adipose tissue, chia has been shown to reduce adipose tissue mass and adipocyte hypertrophy through the binding of n-3 PUFA ligands to PPAR-γ and their activation in adipose tissue, as well as a reduction in the enzyme xanthine oxidase (XO). As for oxidative stress, excessive consumption of fats or sugars increases the production of reactive oxygen species (ROS), which is reversed by the consumption of chia due to the activation of enzymes in the adipose tissue such as CAT, SOD and GPx, in addition to an increased expression of erythroid nuclear transcription factor 2 (Nrf2), protecting cells from damage caused by free radicals and decreasing lipid peroxidation levels (TBARS)[49]. Finally, one flavonoid found in chia seeds, quercetin, presents antioxidant and anti-inflammatory activity since it activates mitogen-activated protein kinases (MAPKs), preventing a decrease in PPAR-γ activity[54]. As is widely known, peroxisome proliferator-activated receptors (PPARs) act as transcription factors that can be activated by fatty acids, where they are specifically capable of binding long-chain n-3 PUFAs, triggering cascades of metabolic processes such as b-oxidation of fatty acids (PPAR-α) and adipogenesis (PPAR-γ)[55]. These nuclear receptors are responsible for lipid homeostasis, in addition to working in conjunction with other mediators, such as insulin-like growth factor 1 (IGF-1), improving insulin sensitivity and deactivating NF-κB, reducing pro-inflammatory factors and inflammation, thus helping to prevent chronic diseases[56,57].

CONCLUSIONS

Chia, in its different forms (seeds, oil, and whole or fractionated flour), shows potential benefits in humans, *in vivo* and *in vitro*, suggesting a positive effect for the prevention and treatment of chronic diseases (Table 4). Its benefits are associated with its high content of ALA, which can act mainly by regulating lipid metabolism, also influencing glycemic control in conjunction with insoluble dietary fiber. In addition, its antioxidant components, such as quercetin and genistein, play a fundamental role in reducing oxidative stress. Because of this, chia (seed, flour and oil) has been widely explored in terms of its composition, but there are still action mechanisms to be explored through which this seed could contribute positively to the control or prevention of alterations at the metabolic level (Figure 2). Finally, according to the current available evidence, the consumption of chia in all its presentations could be recommended, but the quantities necessary to produce an effect in the general population still need to be calculated, since according to studies in humans, the recommended consumption ranges between 4 and 40 g/day, and there are differences in the models of the studies reviewed. In addition, the economic cost associated with the acquisition of this seed must be evaluated, so that in the near future healthy foods of plant origin may be subsidized, in the context of a sustainable and healthy diet.

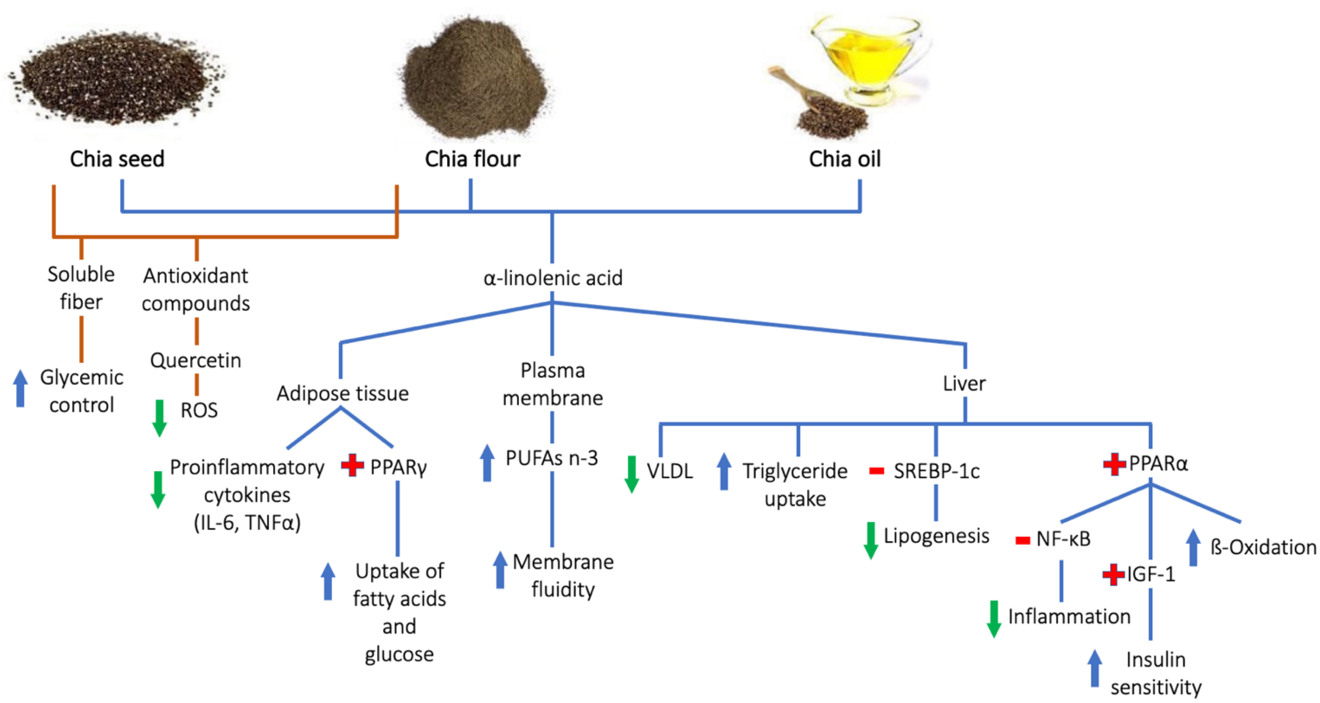


Figure 2: Molecular mechanisms of the benefits of chia.

Table 4. Summary of the methodology of the main articles reviewed.

Study design/model	n	Cell type and/or condition	Intervention	Duration	Outcomes	Reference (First author, year)
Humans						
Randomized trial	62 (47 women and 15 men)	Mild hypercholesterolemia	Diet low in saturated fat + 25 g of soy protein + 14 g of dehydrated cactus + 4 g of chia seeds + 14 g of oats + 4 g of inulin + 0.02 g of sweetener and 0.15 g of flavoring	2.5 months	Reduction of total cholesterol and LDL producing a change in the lipoprotein profile	Vázquez-Manjarrez, et al.[18]
Experimental	25 (10 women and 15 men)	Non-alcoholic fatty liver	25 g per day of ground chia	8 weeks	Increased plasma ALA concentration and dietary fiber intake and decreased total cholesterol, non-HDL cholesterol, free fatty acids, body weight, and visceral abdominal fat	Medina-Urrutia, et al.[19]
Experimental/ Controlled trial	42 adults	Diabetes mellitus type 2	40g/day of chia seeds	12 weeks	Significant reduction in random systolic blood pressure	Alwosais, et al.[20]
Experimental/ Randomized, double-blind, controlled trial	104 adults	Diabetes mellitus type 2	10 g of viscous fiber, 60 g of seeds, 1.5 g of extracts of American red ginseng and 0.75 g of Korean or 53 g of oats bran, 25 g of inulin, 25 g of maltodextrose and 2.25 g of wheat bran	24 weeks	Better glycemic control with the administration of seeds and herbs	Zurbau, et al.[21]
Experimental/ Randomized, controlled, crossover trial	15 adults (10 women and 5 men)	Healthy	50 g of glucose + 25 g of ground chia or 31.5 g of flax	3 samples	Chia showed better glycemic control due to fiber content and improved satiety	Vuksan, et al.[22]
Experimental	26 adults	Hypertension	35 g/day of chia flour	12 weeks	Decreased blood pressure in hypertensive individuals with or without treatment	Tavares, et al.[26]
Animal model						
Experimental	36 male Wistar rats	-	Control diet Protein free diet Chia seed diet Heat treated chia seed diet Chia flour diet Heat treated chia flour Diet	14 days	The rats treated with chia (in any of its forms) had lower levels of glucose, triglycerides, VLDL, LDL, liver weight, and percentage of liver fat, compared to the control groups.	Da Silva, et al.[8]
Experimental	2,000 worms *Caenorhabditis elegans* per treatment	Obese model tub-1	Chia oil extract in concentrations of 1, 1.5, 2, 2.5 and 3%	30 minutes	Low concentrations of extract produced a reduction in triglyceride levels and fat reserves in an obese model.	Rodrigues, et al.[30]
Experimental	Male Wistar rats	Non-obese model with induction of dyslipidemia and/or steatohepatitis	15% chia added	4 weeks	In rats with 15% added chia, less or no cholestasis, inflammation, necrosis and oxidative stress were observed, while total cholesterol and triglycerides decreased in rats with dyslipidemia and non-alcoholic steatohepatitis.	Fernández, et al.[32]
In vitro model						
Experimental / Cell culture	2.7×10^4 cells/plate (96 plates) 2.5×10^5 cells/plate (6 plates)	Macrophages	0.1 – 0.5 - 1 mg mL^{-1} of total protein digest and fractionated protein digest of chia seed	-	Chia seed digested protein achieved a reduction in the secretion and expression of markers associated with inflammation pathways and atherosclerosis	Grancieri, et al.[38]
Experimental / Cell culture	5×10^4 cells/plate (24 plates)	Epidermal melanocytes	100 µg/ml chia seed extract with linoleic and α-linolenic acid concentrations of 0.5% and 1.2%, respectively + pomegranate extract with 20% punicalagins	4 days	The combination of chia seed and pomegranate extracts caused a reduction of melanin in epidermal melanocytes.	Diwakar, et al.[39]

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