



Chia (*Salvia hispanica* L.) Seeds: Nutritional composition and biomedical applications

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1. Introduction

Medicinal plants showed potential biomedical and pharmaceutical applications (El-Naggar et al., 2016; El-Said et al., 2019; El-Sawy et al., 2023). Chia (*Salvia hispanica* L.) is a plant. It belongs to Lamiaceae family and vegetates annually. Fig (1) illustrates chia plant and seeds shape. About 900 species of the genus *Salvia* are found. Chia height is 1 meter. Chia leaves width is 3 to 5 cm and length are 4 to 8 cm. Leaves are elongated, serrated, and placed in opposition. Bisexual flowers are white or purple. Flowers size is 3 to 4 mm. Seeds are oval, 1 to 2 mm length and white to black in color (depending on specific species and cultivation area). White chia seeds contain higher omega-3 fatty acids on comparison with darker ones. Southern Mexico and Guatemala are chia home, but it is grown both in Egypt and throughout the world (Motyka et al., 2022). Chia is a promising plant approved by the Authority of European Food Safety in 2019.

ABSTRACT

Chia (*Salvia hispanica* L.) herb plant grows annually and belongs to *Lamiaceae* family. Its impressive health and biological benefits are due to its nutritional and phytochemical composition. Previous research has been done on chia seeds, protein hydrolysates and oil to evaluate their beneficial role in nutritional and health aspects. Chia can be incorporated in diet, food synthesis, and different industries. It can also be encapsulated to maximize its usefulness to incorporate in regular diets to enhance overall health and battle various illnesses. This review will discuss the recent findings about the nutritional values and the biomedical applications of chia seeds. Throughout this review chia source, constituents, biological activities, beneficial dosage, how to impart in our diet? and possible side effects of overconsumption will be referred. This review will also provide a comparison between the nutritional composition of Egyptian chia seeds and imported seeds.

Keywords: Chia, Seeds, Health Benefits, Nutritional factors, Biomedical applications.

Chia seeds approval permitted its inclusion in various foods as well as cosmetics. They hold many nutritional and active components (Motyka et al., 2022).

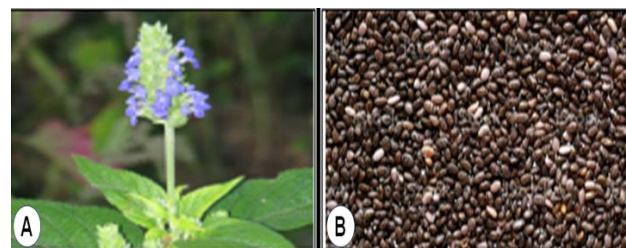


Fig. 1. (A): Chia plant with large leaves and purple flowers. **(B):** Chia seeds (Mohammed et al., 2019).

The origin and type of soil in which chia is grown are the primary determinants of its makeup. Because chia seeds have been used traditionally in food and medicine, they have been well studied. In contrast, hardly much research has been done on the chemical makeup of chia leaves. This section will compare and illustrate the valuable contents of Egyptian chia seeds with those imported from the United

States. The composition of chia leaves will also be investigated.

2. Chia seeds composition

2.1. Chia seeds macronutrients and caloric content

After investigation, it was shown that Egyptian dried chia seed was a valuable source of the three primary nutrients: proteins, lipids, and carbohydrates with the highest concentration of fat, protein, and fiber. Accordingly, chia is a rich source of nutrients (Mohammed et al., 2019). Chia seeds with low moisture content are protected from microbiological development and biochemical reactions, maintaining their quality while being stored properly.

2.2. Chia seeds active ingredients

It was discovered that chia seeds contain a variety of active components with numerous beneficial effects on human health. There are free polyphenolic or sugar-bounded fractions bound by glycosidic linkages. The polyphenols compartments included the following: depsides (rosmarinic and chlorogenic) acids; phenolic acids (ferulic, caffeic, gallic, and p-coumaric); flavonoids (apigenin, rutoside, myricetin, kaempferol, and quercetin); isoflavones (daidzein, genistin, genistein, glycitin); and epicatechin, a type of catechin (Motyka et al., 2022). Rosmarinic acid is the primary phenolic acid, with protocatechuic, caffeic, and gallic acid coming in order of preference. Low concentrations of phytates and tannins are present. There is also a very little amount of carotenoids, or carotenes and xanthophylls. According to Grancieri et al. (2021), there are trace levels of campesterol, β -sitosterol, stigmasterol, and Δ^5 -avenasterol. Chia seeds are an ideal supply of fats and play a variety of biological purposes, including forming lipid membranes, storing fuel, and regulating several physiological functions. The percentage of fat ranged from 36.57 to 37.2%. Essential fatty acids (EFAs), primarily polyunsaturated fatty acids (PUFA), are implicated in chia seeds. α -linolenic acid (ALA), an omega-3 fatty acid, makes up 60% of all fatty acids. 20% of it is linoleic acid (LA), an omega-6 fatty acid. As a result, the ratio of omega-six

to omega-three fatty acids in chia seeds is very beneficial (between 0.30 and 0.35). Chia seeds contain 10% monounsaturated fatty acids, or omega 9, at most oleic acid. Saturated fatty acids, primarily palmitic and stearic acids, make up the remaining 10% (Melo et al., 2019). There were noticeable differences in the fatty acid makeup of local and imported chia seed oil. According to fig. (2), which depicts the metabolic pathways of fatty acids, ALA can be transformed into EPA and DHA, or eicosapentaenoic and docosahexaenoic acids. In vivo, ALA plays several advantageous functions, including decreasing blood pressure, the risk of heart disease, cholesterol and triacylglycerol levels, and blood pressure. ALA has anti-inflammatory and conservative effects on the liver and heart. Lipids throughout the body can be redistributed by ALA, moving them away from the liver and visceral fat. The anti-diabetic properties of ALA have been demonstrated before. It also guards against cancers, arthritis, and autoimmune disorders. Conversely, LA behaves in the opposite way as ALA. Increased levels of LA cause thrombosis, hypertension, and inflammation. Therefore, for human welfare, the specific fatty acid composition found in Chia is preferred. Eicosanoids generated by LA are linked to cardiovascular and cancer risks (Ali et al., 2012). According to Ullah et al. (2016), ALA and EPA play a critical role in the production of leukotrienes, prostaglandins, and thromboxane, all of which have positive effects on health. The percentage of protein was 26.1–27.89%. The primary protein is globulin, which is followed by prolamins, albumins, and glutelins. As chia seeds lack gluten proteins, they are suitable for those with celiac disease. Chia protein digests more easily than wheat, rice, or maize proteins, but nevertheless has a similar level of digestibility to casein. When it comes to cereals, chia seeds have more protein than quinoa, maize seeds, rice, and wheat. Most essential and non-essential amino acids are compromised by chia seeds. The predominant amino acid is glutamic acid; other amino acids are present in smaller concentrations, but arginine and aspartic acid are also found in high values (US Department of Agriculture, 2021).

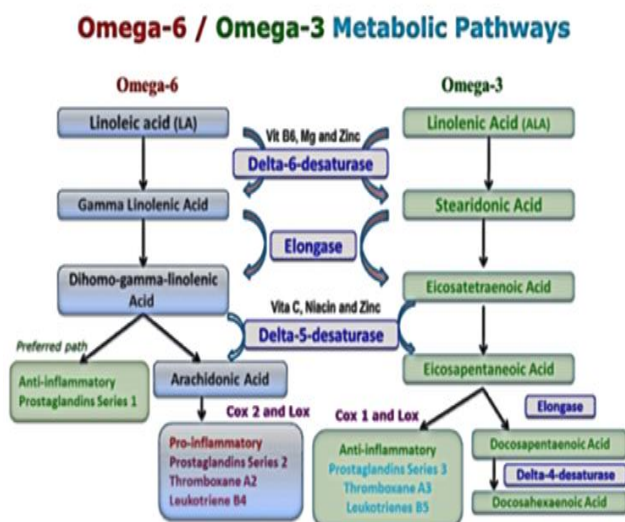


Fig. 2. Metabolic fate of omega-six/omega-three fatty acids (Saini and Keum, 2018)

2.3. Ash, fiber, and carbohydrates contents

There was a 4.8–5.15% ash value. Both local and foreign chia seeds had crude fiber contents ranging from 22.22 to 24.31% and other carbohydrates from 5.8 to 9.96%, respectively. There are oligosaccharides and polymeric dietary fibers. Gums, pectin, cellulose, and hemicelluloses make up the fiber compartments, which can link to lignin and other non-carbohydrate substances. Chia seeds have a higher percentage of insoluble fiber than soluble fiber. According to Peláez et al. (2019), chia seeds have more dietary fiber than cereals, nuts, and dried fruits. According to earlier research, lipid was the primary component of chia seeds, which was followed by proteins, fibers, nitrogen-free extracts, and ash (Table 1). The imported seeds contained higher lipid, protein, and crude fibers values. While Egyptian one had a larger ash and nitrogen free extracts. Therefore, chia seed can be included as a new oil seed source.

Broadly, the data of proximate composition of either local or imported chia seeds were linked with those reported by previous investigators (Fernandes and Salas-Mellado, 2017).

A high intake of fiber is linked to numerous beneficial effects (fig. 3); these include improved intestinal function, glycemic and insulinemic responses, and antioxidant activity associated with lowered cholesterolaemia. Thus, it helps reduce the risk of diabetes, heart disease, and tumors. Dietary fiber reduces hunger, promotes satiety, and aids in weight loss (Ullah et al., 2016). Insoluble fiber is the main dietary fiber that promotes satiety and healthy bowel functions (Ferreira et al., 2015). Additionally, it confers gel-forming, fat-binding properties, and functions as a chelating and texturizing agent.

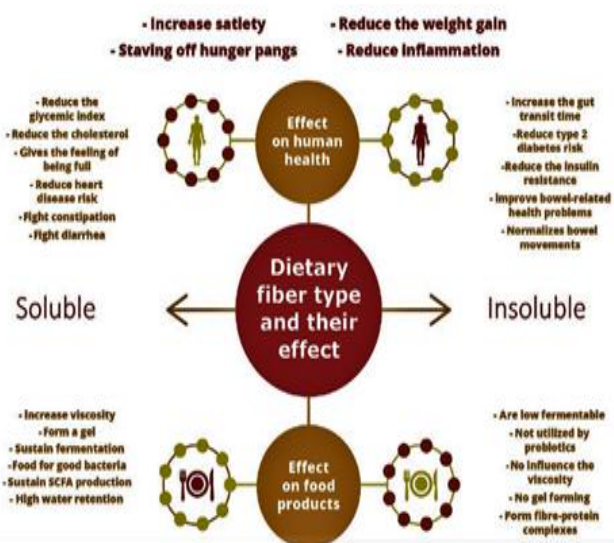


Fig. 3. Soluble and insoluble fiber beneficial effect (Weickert and Pfeiffer, 2018).

2.4. Mineral and vitamin content of chia seed

Micronutrients, which are necessary for hormone synthesis, growth regulation, and defense against oxidative stress, are abundant in chia seeds. They were high in calcium, potassium, magnesium, and phosphorus, in that order. Table (2) assigned a low score to salt, iron, zinc, manganese, and copper. Among the macro elements, phosphorus was found in the highest concentration, followed by calcium and potassium. Only substantial levels of magnesium were discovered; trace amounts of the other microelements were detected. Potassium and calcium content are crucial for promoting healthy bones and lowering high blood pressure. Antioxidant capability is also increased by magnesium (Ferreira et al., 2015). When compared to Egyptian chia seeds, imported chia seeds had lower levels of sodium, calcium, zinc, manganese, magnesium, and iron and greater levels of potassium, phosphorus, and copper. Chia seeds have a high nutritional content. Chia seeds are primarily rich in vitamins C, B-complex, A, and E. According to Da Silva et al. (2017), seeds can hold 8.83 mg, 1.6 mg, 0.62 mg, 0.50 mg, 0.17 mg, and 54 µg of niacin (B3), vitamin C, thiamine (B1), vitamin E, riboflavin (B2), and vitamin A in 100 g.

2.5. Chia leaves chemical composition.

Research on chia has focused primarily on the seeds. Very few researchers examined the

chemical compartments in leaves. Studies have been conducted on the antioxidant and antibacterial properties of chia leaves. Chia leaves were shown to contain flavonoids and derivatives of hydroxycinnamic acid (Amato et al., 2015). Chia leaves contain derivatives of hydroxycinnamic acid, specifically rosmarinic, caffeic, and p-coumaric acids. The portions of flavonoids are flavones and flavonols. Flavones such as myricetin, vitexin, luteolin, orientin, and apigenin. Quercetin and kaempferol are examples of flavonols. Furthermore, the acetyl derivatives of vitexin and orientin have been separated and identified as two unique components. Higher bioactive compartment concentrations were found using ethanol and ethyl acetate extraction. The most prevalent ones include kaempferol, protocatechuic genistein, rosmarinic, p-coumaric, caffeic acids, and coumaric acid-O-hexose (Elshafie et al., 2018).

3. Biomedical effects of chia seeds verified by scientific investigations

Because of its nutritive and active ingredients, chia is regarded as a functional food. This has sparked curiosity among academics throughout the world to investigate the potential biological benefits of chia on human health and as a treatment for prevalent public health issues. This section will highlight a few of the health benefits of chia.

Table 1. Chia seeds composition and total caloric content (Mohammed et al., 2019)

| Ingredient | Egyptian chia seeds | Imported chia seeds |
|----------------------------|---------------------|---------------------|
| Lipid% | 36.57 ± 0.17 | 37.2 ± 0.02 |
| Protein% | 26.1 ± 0.6 | 27.89 ± 0.16 |
| Crude fiber% | 22.22 | 24.31 |
| Nitrogen free extract% | 9.96 | 5.8 |
| Ash% | 5.15 ± 0.1 | 4.8 ± 0.1 |
| Caloric value (kcal/100 g) | 562.25 | 566.8 |

Table 2. Chia seeds mineral content (Mohammed et al., 2019).

| Mineral (mg/100g) | Egyptian chia seeds | Imported chia seeds |
|-----------------------|---------------------|---------------------|
| Macro-elements | | |
| Phosphorus (P) | 796 | 814 |
| Calcium (Ca) | 592 | 574 |
| Potassium (K) | 323.79 | 535 |
| Sodium (Na) | 34.7 | 25.5 |
| Micro-elements | | |
| Magnesium (Mg) | 296 | 287.4 |
| Iron (Fe) | 7.1 | 5.39 |
| Zinc (Zn) | 5.19 | 3.76 |
| Manganese (Mn) | 1.65 | 1.55 |
| Copper (Cu) | 0.748 | 0.936 |

3.1 Antioxidant and anti-inflammatory activities of chia seeds

Biomolecules known as antioxidants have the power to fend off free radicals and prevent the development of oxidative stress. Chia seeds have been found to contain vitamins and biomolecules that are antioxidants. This encouraged researchers to appreciate chia seeds' potent antioxidants. The ability of chia seeds to inactivate ABTS (2,20-azinobis-3-ethylbenzothiazoline-6-sulfonic acid) was used to measure their potency as in vitro antioxidants. The test known as FRAP (ferric reducing antioxidant power) is used to calculate the reduction power of iron (III) ions. A test for the removal of DPPH (2,2-diphenyl-1-picrylhydrazyl) radicals was also conducted. According to Sargi et al. (2013), the reference antioxidant Trolox/g sample was defined by the ABTS, FRAP, and DPPH tests, respectively, and the antioxidant intensity of the tested samples was 2.56, 2.86, and 1.72 mmol antioxidant. Marineli et al. (2015) estimated the impact of chia seed and oil diet on the plasma and liver oxidative status of obese rats. Comparing the complemented groups to the control group, the former displayed increased antioxidant activity and concentration associated with oxidants at lower levels in both plasma and liver, by 35% and 47%, respectively. When compared to common and fava beans, chia seeds exhibit a greater capacity to function as an electron donor or scavenger for free radicals. According to Parker et al. (2018), chia protein isolates had a limited

impact on angiotensin-converting enzymes. The antioxidant defense of chia seeds and its subsequent antihypertensive effects were reported in the results.

Inflammation is a biological restraint to tissue harm either placed by free radicals or other stimuli. Polyphenols, tannins, and flavonoids inhibit inflammatory cascades. Because they naturally contain anti-inflammatory properties, chia seeds have been found to have such properties. In 2019, Da Silva et al. (2017) examined the impact of chia intake on the lipid fractions, oxidative status, and inflammation of adult Wistar female rats who had undergone ovariectomy. For eighteen weeks, rats were divided into sections and given one of three diets: standard; chia plus standard; high-fat; or chia + high-fat. Measurements of oxidative stress and inflammation were unaffected by ovariectomies. Chia seeds improved the metabolic effects of a high-fat diet. Dietary chia complementation to rats mended antioxidant activity via raising catalase activity, high density lipoprotein cholesterol (HDL-c) value and messenger ribonucleic acid (mRNA) expressions of peroxisome proliferator-activated receptor (PPAR)-alpha and superoxide dismutase (SOD). Contrary, chia intake lowered thiobarbituric acid reactive substances (TBARS), low density lipoprotein cholesterol (LDL-c), inflammatory indicators as interleukin-1 beta (IL-1 β) levels and mRNA expressions of nuclear factor kappa beta (NF κ B) and tumor necrosis factor alpha (TNF- α).

Chia seed oil remedies for inflammation ALA, DHA, and EPA, the omega-three poly unsaturated fatty acid components found in chia seeds, compete with arachidonic acid, the omega-six fatty acid, for incorporation into cellular membranes. As a result, the production of inflammatory prostaglandin and leukotriene (PGE₂, LTB₄, and LTE₄) changes to anti-inflammatory ones (PGE₃, LTB₅, and LTE₅) with decreased cyclooxygenase-2 (COX-2) induction and efficacy as well as protein expression, favoring a reduced initiation of inflammatory responses (Gazem and Chandrashekariah, 2016).

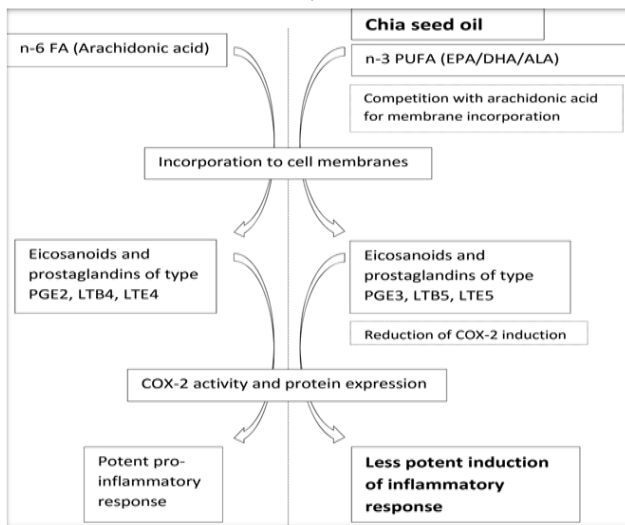


Fig. 4. Anti-inflammatory techniques of chia seed oil (Gazem and Chandrashekariah, 2016).

3.2. Chia seeds impact on metabolic syndrome, hyperlipidemia, obesity, hypertension, and non-alcoholic fatty liver disorder

Metabolic syndrome is characterized by high blood sugar, cholesterol, blood pressure, obesity (especially visceral obesity) and fatty liver. Diets rich in sugar and/or fat consumption linked with sedentary lifestyle are the main causes of metabolic syndrome. It became widespread among kids, teens, and adults alike. Thus, it is critical to find safe, affordable, and helpful herbal plants that can regulate and control these changes in metabolism. Chia seeds are being examined under a microscope to assess the effects of their active ingredients and nutrients. To determine the precise mechanism of action of chia seeds against metabolic

illnesses, research on animals as well as humans was carried out.

3.2.1. Animal model studies

Rats fed a meal high in sucrose along with 2.6% chia seeds were used to investigate the beneficial effects of chia seeds on the lipid fractions. Rats fed a high-sucrose diet had a worse lipid profile than rats fed chia seeds because the chia seeds reduced the concentrations of non-esterified fatty acids, triacylglycerol (TAG), and total cholesterol (TC). Chia seeds feeding improved the glucose metabolic pathway and caused collagen deposition to resume rat's heart tissues with decreased visceral fat tissue density (Chicco et al., 2009).

Marineli et al., 2015 evaluated the impact of chia seed consumption on the metabolic outcomes of feeding experimental rats a high-fat/high-fructose diet. Rats fed either a high-fat/high-fructose diet with replacing soybean oil with chia seed oil or supplementing with 13.3% chia seeds for six to twelve weeks displayed higher insulin levels and greater tolerance to elevated glucose when soybean oil was swapped out for chia seed oil. The amount of non-esterified fatty acids in the blood was lower in rats that ate chia seeds. Furthermore, the benefits of chia containing high-fat/high-fructose meals were offset by a decrease in the activity of the liver function indicators aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in contrast to high fat /fructose diets effects.

An additional experiment aimed to ascertain the impact of adding chia seeds and seed oil to a high-fat/high-fructose diet for 6 or 12 weeks on the total liver and plasma antioxidant levels in obese rats. Consuming chia seeds or oil significantly increased the activity of the antioxidant plasma enzymes, catalase (CAT) and glutathione peroxidase (GPx). In addition, a higher reduced glutathione (GSH) level was observed compared to the group that was fed a high-fat and sugar diet. Rat livers showed enhanced activity of glutathione reductase (GR). Additionally, mice treated with chia showed a decrease in blood indicators of lipid peroxidation, such as TBARS and 8-

isoprostane. In comparison to the control group, hepatic and plasma antioxidant capacity rose by 47% and 35%, respectively, in chia seeds and oil (Marineli et al., 2015).

Da Silva et al., (2016) discovered that, as compared to rats given non-protein or casein diets, rats given chia seed or seed flour supplementation for 14 days had higher levels of HDL-c and lower blood concentrations of TAG, TC, LDL-c, and very-low-density lipoprotein cholesterol (VLDL-c). Liver weight was decreased by chia eating compared to the control group. Chia seeds also showed hypoglycemic properties.

Mahfouz, (2020) investigated the effects of giving bread enriched with chia seeds to rats suffering from non-alcoholic fatty liver disease (NAFLD). For eight weeks, drinking water with 25% dissolved sugar was used to cause NAFLD. For 28 days, 300g of bread supplemented with varying amounts of chia seed powder (4%, 6%, and 8% per kilogram of diet) was given to rats with fatty liver disease. The findings showed that, in comparison to fatty liver diseased rats fed a basal diet, rats fed chia substituted bread had a significant increase in body weight and food intake along with a significant decrease in serum liver function enzymes, bilirubin, glucose, total lipids, TC, TAG, LDL-c, urea, creatinine, and TNF- α . Because chia seeds are high in protein, dietary fiber, and unsaturated fatty acids, feeding them to rats with fatty liver disease improved their condition.

3.2.2. Clinical trials

Tavares et al., (2014) studied the effects of chia seed flour supplementation on blood pressure and other cardio-metabolic parameters in people treated or not from hypertension. Three sets of patients were created: one with no treatment, one with medication treatment, and one with a placebo. For three months, the test subjects were given a daily dose of 35 grams of flour or a placebo. A diet supplemented with chia seed flour together with medication showed a decrease in mean blood pressure. The consumption of a diet enriched with flour alone resulted in a mean decrease in systolic blood pressure. In the placebo group, there was no change in blood pressure. Chia protein hydrolysates have an inhibitory impact on the

angiotensin-converting enzyme, which lowers blood pressure. (Orona-Tamayo et al., 2015). Vuksan et al., (2017) studied the effects of chia seed supplements on body weight, visceral obesity, and obesity-related risk factors in type 2 diabetics who were overweight or obese. People continued to follow a low-calorie diet. The participants were split into two groups, one was given 30 g of chia seeds and 1000 kcal per day, whereas the control group was given 36 g of wheat bran and 1000 kcal per day. Over a six-month period, weight loss was noted. Improvements were also seen in the levels of C-reactive protein, waist circumference, glycemic management, and hormones linked to satiety. The chia group lost more weight (1.9 kg) than the control group (0.3 kg) after six months, which was correlated with a greater decrease in waist circumference (3.5 and 1.1 cm), respectively. Feeding chia seeds accelerates the reduction of intrahepatic fat in NAFLD patients. Waist circumference and body weight decreased by 1.4% after feeding crushed chia seeds (25 g/day) to 25 insulin resistance and non-alcoholic fatty liver disease patients for two months. There was also a decrease in TAG (from 1.9 to 1.6 mmol/L) and TC (from 4.8 to 4.6 mmol/L) in the supplemented group. Patients with NAFLD may benefit from chia seeds' omega-3 fatty acids, fiber, and polyphenols (Medina-Urrutia et al., 2020). Da Silva et al., (2020) investigated the effects of feeding chia seeds on obese kids. For a period of seventy-five days, thirty pre-pubertal children, aged five to ten, of various genders, with body mass indices equal to or higher than the 95th percentile, were given 25 grams of crushed chia seeds or corn starch every day. Chia seeds, rich in omega-3 fatty acids and fiber, may help reduce inflammation linked to pediatric obesity by lowering TNF- α and NF- κ B levels. Based on all of the prior research and trials conducted on humans and experimental animals, it can be concluded that chia nutritional compartments, particularly fiber and omega-3 fatty acids, when combined with polyphenolics, improved and controlled metabolic syndrome, obesity, hypertension, and NFALD caused by consuming high-sugar or high-fat diets by adjusting synthesis of hepatic lipid and fatty acid oxidation. (Fig. 5).

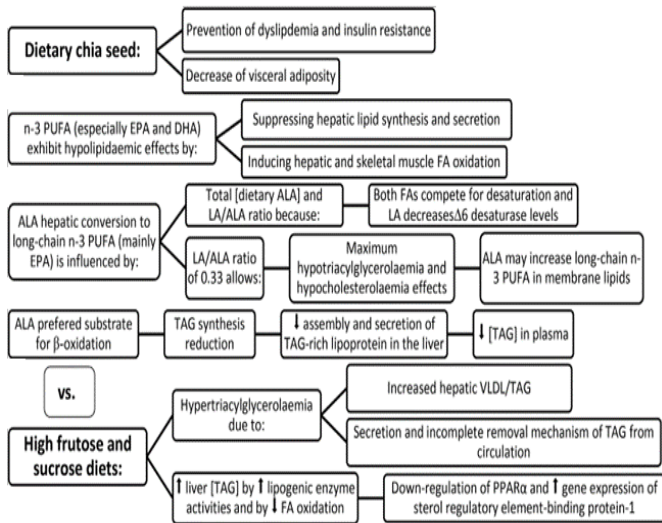


Fig. 5. Chia seed mechanistic against high-fat/high-sugar diets (Melo et al., 2019).

3.3. Hypoglycemic and anti-diabetic chia seeds efficacy

Diabetes mellitus is a metabolic disruption which outcomes from the pancreas’s loosened ability to generate appropriate insulin quantity for the body (type1) or the body failure to employ the secreted insulin effectively (type2). Uncontrolled creation typically leads to high blood sugar amount or hyperglycemia, resulting in body’s systems serious harm. The quantity of diabetic individuals is increasing globally. Chia and chia ingredients were looked over to battle with diabetes and hyperglycemia. HO et al. (2013) evaluated the impact of chia seed eating on the decrease of postprandial blood glucose levels in well individuals. The impact of chia seeds on the dose was examined in the study findings. On consuming chia seeds - including bread, postprandial glycemia declined as opposed to regular bread eating. The investigators speculated that the hypoglycemic effect of chia seeds stems from their high fiber content. Further investigation explored the impact of chia seed oil on body weight composition and insulin signaling in the skeletal muscles of obese mice. Mice fed a diet enriched with chia seed oil showed elevated lean mass and minimized fat buildup. Likewise greater amounts of HDL-c and enhanced insulin tolerance were identified (Fonte-Faria et al., 2019). The benefits of eating chia seeds on blood pressure in patients with type 2 diabetes

(T2-DM) were demonstrated by Alwosais et al. (2021). 42 T2DM patients were divided evenly into two groups: the chia seed set, which consumed 40 grams of chia seeds per day for three months, and the control set, which did not consume any supplements. After consuming 40 grams of chia seeds per day for three months, T2-DM patients who were maintained on a normal diet, exercise regimen, and medication showed a significant drop in systolic blood pressure, comparable to the control group.

The underlying techniques of chia and its products on diabetes after the *in vivo and in vitro* research models are illustrated in Fig. (6). Chia oil's lipid components, particularly ALA, were found to have the greatest effects on glucose and insulin tolerance. The underlying methods that were altered by chia oil included the mRNA up-regulation of the insulin receptor (INSR), which raised the insulin affinity of the hepatocyte membrane receptor, phosphorylating serine/threonine protein kinase (AKT), and starting the uptake and oxidation of glucose as the primary energy source (as indicated by the mRNA expression of the glycolysis enzymes pyruvate kinase (PK), phosphofructo kinase (PFK), and glucokinase (GK)). P-AKT limits the migration of fork head box protein O1 (FOXO1) to the nucleus, as well as the development of gluconeogenic enzymes and, ultimately, the dominant glucose synthetase.. Chia flour and oil similarly increased the expression of the adenosine monophosphate-activated protein kinase (AMPK) gene, which may indicate an insulin-independent mechanism for controlling glucose metabolism. Chia phenolics may also have an effect via down-regulating the amounts of glucose 6-phosphatase (G6Pase) mRNA and gluconeogenesis activity, which are linked to phosphor-enolpyruvate carboxykinase (PEPCK). (Fig. 6) (Enes et al., 2020).

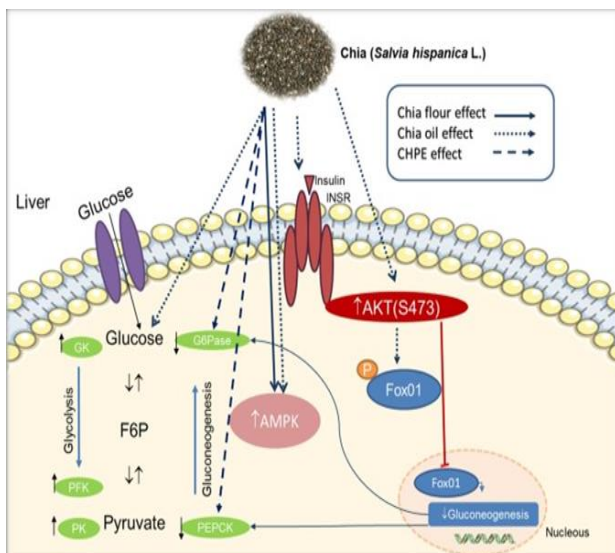


Fig. 6. Chia's potential impact on glucose homeostasis (Enes et al., 2020).

3.4. Chia's protection against cardio and hepatic-toxicities

Since the liver and heart are the two main organs in the human body, research has been done on the protective effects of chia and its components against items that are hepatic and cardiotoxic.

Apoorva et al., (2020) determined how chia seeds (250, 500, and 1000 mg/day/orally) affected the liver damage caused by anti-tubercular medications (100 mg/kg of isoniazid and rifampicin intraperitoneally) over the course of 21 days. When compared to a normal control group, the hepatotoxicated rats clearly had higher levels of total bilirubin and liver enzymes linked to histopathological illness. By maintaining the structure of the hepatic tissues and the activity of liver function enzymes, chia seeds provide protection against drug-induced liver damage. Its antioxidant activity can be attributed to a potential mechanism.

Chia seed oil's capacity to prevent cardiotoxicity caused by the anti-cancer and antibacterial medication doxorubicin in female Wistar rats was assessed. Rats were given 2.5 and 5 ml/kg/day of chia seed oil orally as a preventative measure for seven days. On the seventh day, rats were given a single intraperitoneal dosage of doxorubicin (25 mg per kg) to induce cardiotoxicity. According to the study, pretreatment with chia seed oil improves electrocardiogram (ECG)

analysis, regulated blood creatine kinase (CK), AST, and creatine kinase-MB (CK-MB) elevated activities, extending cardio-protection against cardiotoxicity in female Wistar rats. Chia oil also notably prevented the glutathione depletion and rise in malondialdehyde (MDA) content brought on by doxorubicin.

In rats that were cardiotoxicated, chia seed oil mitigated histopathological damage. Chia seed oil is a powerful nutraceutical that protects against chemotherapy. To reduce their cardiotoxicity, it is advised to be used in conjunction with chemotherapy drugs such doxorubicin (Ahmed et al., 2021). Based on the aforementioned information, chia's strong antioxidant activity makes it a hepatoprotective and cardioprotective agent.

3.5. Effects of chia seeds on the brain

Chia seeds are nutrient-dense seeds that contain a variety of physiologically active ingredients. Depending on the seed fraction utilized, the conditions of the experiment, and the length of the trial, each component's impact on the brain may differ. Rats were given chia seed extract along with 200 mg/kg of aluminum chloride (AlCl₃) for 60 days to assess the preservative effect of the extract against the development of Alzheimer's disease. The treatment of chia seed extracts orally reduced the histological and biochemical changes caused by AlCl₃ in the cortex and hippocampal regions of the brain. In the areas of the brain under investigation, chia seeds reverse the levels of aluminum, acetylcholinesterase (AChE) activity, and amyloid precursor protein (APP) molecules. Moreover, the extract from chia seeds lessened behavioral deficits. It was clear that chia seeds could reverse memory loss caused by aluminum intoxication by regulating the amyloidogenic pathway and AChE activity. Leo and Campos (2020) investigated the potential neuroprotective function of fractions containing chia peptides. Enzymatic hydrolysis of the chia protein produced three tested fractions of peptide (1, 1–3, and 3–5 kDa). The human microglial clone 3 cell line was used to test the anti-inflammatory and protective properties of the tested peptides. The highest level of protection was demonstrated by the 1–3 kDa peptide. Reduction of the levels of

inflammatory mediators, such as TNF- α , IL-6, NO, and H₂O₂, and of reactive oxygen species (ROS). The authors proposed that the antioxidant and anti-inflammatory properties of bioactive chia seed peptides could be beneficial in mitigating neurodegenerative diseases.

3.6. The preventive role chia seeds against kidney stones (urolithiasis)

In albino rats, urolithiasis was induced by administering ethylene glycol and ammonium chloride for three days. The methanolic extract of chia seeds was tested against this condition. Oral administration of cysteine medication (750 mg/kg) or methanolic extract of chia seeds (100, 300, and 700 mg/kg) was administered to urolithiatic rats. When compared to reference control values, the injection of methanolic extracts from chia seeds lowered the serum levels of urea, creatinine, urea nitrogen, albumin, and total protein. Urine also included lower amounts of phosphate, calcium, and oxalate. In vitro tests showed that the tested extract inhibited the primary steps of calcium oxalate crystal formation—nucleation, aggregation, and growth phases—thereby avoiding the development of stones. This action is mostly attributed to quercetin, one of the flavonoids found in chia seeds that could serve as an antioxidant and prevent kidney stones from forming (Saleemnazir et al., 2020).

3.7. Chia anti-tumor, anti-carcinogenic, anti-proliferative, and apoptotic actions

Due to the rising frequency of cancer worldwide and the unfavorable effects of its therapy, scientists have been looking at natural anticancer agents that may have less side effects. The active components in chia seeds were studied for potential anticancer properties. Three groups of 30 male and 30 female mice were used: the first group was fed a commercial meal as a control, the second group got 6% chia seed oil, and the third group got 6% safflower oil. After three months of being fed the experimental diets, a subcutaneous transplant of metastatic mouse mammary gland cancer was given to each of the three groups. Supplementing with chia oil significantly reduced tumor weight. Additionally, it hindered mitosis and promoted apoptosis. The increased membrane content of EPA could be the

mechanism. According to Espada et al. (2007), EPA has direct apoptotic activity, triggering caspase and programmed cell death in addition to providing anti-tumor affinity. In vitro cancer cytotoxic bioactivity of chia seed oil, either by itself or in combination with soybean and palmolein oils, against MCF-7 breast cancer cells and chronic myelogenous leukemia was studied by Gazem et al. (2017). Based on cytotoxic and cell growth suppression on malignant cells, the results showed that chia seed oil, either alone or in combination with other oils, has anticancer action due to its anti-inflammatory and anti-lipoxygenase properties. The ethanolic extract of chia seeds (25, 50, 100, and 200 μ g/mL) was tested against human lung cancer cell lines, A549. According to the results, polyphenol extraction inhibited the growth of tumors, cell mitosis, and spread of neoplastic tissue. It also increased apoptosis, particularly at the highest dose (Güzel et al., 2020).

3.8. How does chia affect the digestive tract function?

Plant-based soluble extracts, such as those found in high-fiber chia seeds, may have a positive impact on gastrointestinal motility and improve the absorption of vitamins and minerals (especially the improved bioavailability of iron and zinc). These advantageous effects are caused by changes in the expression of intestinal brush-border membrane proteins combined with an increase in the surface area of the intestinal villi, which is associated with an increase in the formation of mucilage. Making soluble extracts by separating prebiotics from food that primarily consists of water-soluble fiber (Mi'sta et al., 2017; Sarao and Arora, 2017). When seed extracts are administered, intestinal bacteria increase their fermentation activities and produce short-chain fatty acids, which lower pH and create an environment that is unfavorable for pathogenic intestinal bacteria (Weinborn et al., 2017).

To study the effects of soluble methanolic prebiotic chia extracts intra-amniotic administration on iron and zinc levels, intestinal shape and bacterial populations, as well as on in vivo membrane brush-border functions, Da

Silva et al. (2019) designed an experiment. Evaluations were conducted on treatment sets that included non-injected, H₂O (highly oxygenated water), 40 mg/ml inulin, and 5, 10, 25, and 50 milligram/ml soluble chia seed extracts. The villus surface area, length, width, and quantity of goblet cells were all raised by the extracts, according to the study's findings. Moreover, elevated duodenal cytochrome b and zinc transporter 1 protein gene expression. Chia seeds could improve the health and function of the intestines. By boosting *Lactobacillus* and *Bifidobacterium* populations, it may help enhance intestine absorption of zinc and iron. By generating short-chain fatty acids, these bacteria reduce the pH of the intestines and create conditions that facilitate the absorption and solubility of minerals.

3.9. Chia's contribution to better bone health

Chia seeds are rich in α -linolenic acid, which when consumed over time has positive health effects. Despite this, Chañi et al. (2018) investigated the long-term consumption of plants high in omega-3 fatty acids like chia on 20 rats. For ten to thirteen months, the effects of a 10% chia seed-containing diet were compared to an isocaloric diet. Long-term consumption of chia seeds in the diet of Sprague-Dawley rats was associated with an increase in bone mineral content (BMC) and an improvement in the morphology of the intestines and liver. Weights and parameters were similar during the first ten months of the diet. At the thirteenth month, the total and proximal areas of the left tibia BMC in the rats fed chia were significantly higher than in the control group. Furthermore, chia set improvements were observed in BMC, bone mineral density, musculoskeletal system, final skin, and body weights. The chia set showed improved liver and intestinal architecture, including reduced hepatocyte lipid deposits, and expanded intestinal muscle layers. A study revealed potential advantages associated with consuming chia seeds over time.

The effects of supplementing osteoporotic rats with chia seeds, calcium, and vitamin D were studied by Abd El Mejid et al. (2022). Eight sets of 48 female albino rats (Sprague Dawley strain) were created. To cause osteoporosis, 42 rats were given oral prednisone acetate (4.5 mg/kg

body weight/day) twice a week. The rats were also fed either a basic diet or one supplemented with 5% chia, 1% calcium, and 400 mg vitamin D for a period of four weeks. The negative control group was fed a basic diet. The use of prednisone acetate led to a noteworthy ($P \leq 0.05$) increase in liver enzymes, hyperglycemia, and hyperlipidemia, along with a reduction in HDL-c levels. These measurements were significantly improved in osteoporotic rats given 400 mg of vitamin D, 1% calcium, and 5% chia. When osteoporotic rats were given 400 mg of vitamin D and 5% of chia, their levels of calcium, phosphorus, bone mineral density, and concentration in the right femur increased. Because of their high calcium concentration and the omega-3 fatty acids that improve calcium absorption and bioavailability, chia seeds are therefore particularly useful for bone health.

3.10. Immunity and chia

Chia seeds' antioxidants and omega-3 fatty acids can protect cell membranes and structure, avoiding oxidative stress and inflammation. This often enhances immune response and occurs after immunity. The effect of chia seeds on immunological responses was investigated in two trials.

Fernandez et al. (2008) investigated and contrasted the effects of oil supplementation and pulverized chia seeds on a well-balanced diet to provide weanling male Wistar rats with similar levels of α -linolenic acid from the chia for a month. According to study findings, chia supplements can help reduce weight loss, allergies, diarrhea, and digestive issues just like fish oil without the fishy smell. There was no improvement in the IgE level, thymus gland weight, or total thymocyte count with either chia oil or ground chia seeds.

Another study by Villanueva-Lazo et al., (2022) used biochemical, enzyme-linked immunoassay, and reverse transcription polymerase chain reaction assays to evaluate the impact of chia protein hydrolysates on human monocyte-macrophage plasticity response. Monocytes play an anti- and pro-inflammatory role in the polarization of the M1 and M2 phenotypes. The activity of monocytes is essential for illnesses related to oxidative stress and inflammation. The findings demonstrated that chia protein

hydrolysates start the synthesis and release of anti-inflammatory cytokines while simultaneously reducing pro-inflammatory cytokine secretion via reducing ROS and nitrite output. Furthermore, lipopolysaccharide associated with M1 polarization is reversed into M2 by protein hydrolysates. Chia is a food that exports bio-peptides to promote post-immune function and prevent inflammatory and oxidative illnesses.

3.11. Potential anti-microbial action of chia

Because various microbes are responsible for the spread of infectious diseases, the antimicrobial activity of chia seed extracts has been investigated. Chia seed protein fractions have been shown to have antibacterial activity against both Gram-positive and Gram-negative bacteria (Coelho et al., 2018). According to Güzel et al. (2020), the ethanolic extract of chia seeds exhibited antibacterial, antifungal, and antimycobacterial properties against several infections. The antibacterial properties of the methanolic extract of germinated Egyptian chia seeds were also investigated by Abdel-Aty et al. (2021). In comparison to dried seeds, the germination of chia seeds boosted their polyphenol levels and improved their antibacterial action against specific pathogenic bacterial species, such as *Salmonella typhi*, *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. The extract from germinated seeds caused the bacteria to die by producing H₂O₂ molecules that affected the proteins in the bacteria and killed them.

4. Chia and cosmetics

Phenolic acids found in chia seeds have antimicrobial and antioxidant qualities that have an impact on dermatology and cosmetics. Chia phenolic acids reduce the signs of acne and atopic dermatitis and prevent skin photoaging and depigmentation by regulating tyrosinase activity, which oversees maintaining skin's even pigmentation (Przybylska-Balcerak and Stuper-Szablewska, 2019)

The two primary chia components found in cosmetics are oil and extract from chia seeds table (3). One can purchase chia oil as a cosmetic item. In various cosmetics, chia oil

and extract serve as nourishing and moisturizing ingredients.

For two months, Jeong et al. (2010) investigated the effects of an oil/water emulsion containing 4% chia seed oil on patients with diabetes or renal illness who experienced xerotic pruritus. Tested emulsions reduced itching without having any negative side effects and increased skin hydration and epidermal function by decreasing epidermal water waste.

5. How can chia seeds be used in the food and nutrition industries?

Chia seeds are widely employed in the creation of food, particularly functional food, because of its nutritional components and biomolecule makeup (Rabail et al., 2021). Chia seeds are safe to use in food production, according to the European Food Safety Authority. According to Turk et al. (2020), no mycotoxins or dangerously high quantities of heavy metals were found in chia seeds. Chia seeds are used in flour, seed oil, and whole or crushed form in the food sector. It can be included in a variety of dishes, including meat products, yogurts, juice, cookies, cakes, spaghetti, bread, desserts, ice cream, and breakfast cereals (Das, 2017).

When seed oil hit the market, it was utilized as a spread and as an ingredient in salad dressings, cottage cheese, and sandwiches. Chia seeds are hydrophilic, which means they can be used in place of fat and eggs. A seed's ability to absorb water up to twelve times its own weight gives meals a unique mucilaginous texture. The chia seed mucilage's high polysaccharide content, primarily cellulose, helps in the manufacture of edible coatings and films (Muñoz et al., 2012; Segura-Campos et al., 2014). Chia seeds are popular among vegetarians due to their high amount of omega-3 fatty acids (Sebastiani et al., 2019). Furthermore, because chia seeds are gluten-free, they have a higher nutritional value for those with celiac disease and those following a gluten-free diet. Chia seed flour might be a viable substitute for regular wheat flour because it contains protein, dietary fiber, and bioactive components. On contrasting the nutritional and sensory qualities of regular wheat biscuits with those that have chia, sesame, linseed, or poppy seeds. Compared to biscuits made of regular

wheat, those produced with seeds had twice as much protein. Additionally, the highest levels of protein and dietary fiber were found in cookies made with chia seed flour (Martinez et al., 2021). Chia seeds are added throughout the sausage-making process to improve both the nutritional and technological aspects of the product. Because chia seeds include a variety of polyphenolic chemicals that contribute to their antioxidant activity, adding 0.5 to 1% of them to meat products lowers the amount of fat peroxidation (Fernández-López et al., 2020).

6. Chia applications at the nanoscale

Scientists started looking into and examining the benefits of encapsulating chia seeds, seed oils, and seed mucilage as a nano-encapsulation material because of the active composition and biological impacts of chia.

Table 3. Chia components and their cosmetic applications (Motyka et al., 2022)

| Chia component | Application |
|--------------------|-----------------------------------|
| Seed | Scrubbing agent |
| Seed oil | Moisturizing and nourishing agent |
| Seed extract | Emollient and nourishing agent |
| Herb oil / extract | Perfumes and aromas production |

The use of chia seed mucilage as a wall material in the nano-encapsulation of chia seed oil was studied by De Campo et al. (2017). It was discovered that chia oil nanoparticles were more stable against oxidation and thermally inert at temperatures as high as 300 °C than non-encapsulated oil. Furthermore, chia mucilage serves as a practical stand-in for artificial polymers that are nano encapsulated. According to Krolevets et al. (2019), chia seed nanoparticles—chia seed nanostructures in different carbohydrate shells—had supramolecular properties and were soluble in water. The size range of a nano-capsule was 214–291 nanometers. Utilizing nano-structured chia seeds is beneficial for producing functional foods with improved nutrient and bioactive component absorption and digestion. According to Kuznetcova et al. (2020), oil and chia phospholipid-rich residue can both be utilized to

create settled nanoliposomes or nano emulsions, which have potential uses in the pharmaceutical, cosmetic, and healthcare industries. All that was needed to create nanostructures was spontaneous emulsification during lipid hydration. The effects of utilizing chia seeds or chia seeds given by nanoparticles (Poly(lactide-co-glycolide)-Poly (ethylene glycol)-nanoparticles) on breast cancer cell culture were compared by Shaer and Al-Abbas (2022). Compared to regular chia seeds, chia seed nanoparticles have a more cytotoxic effect, stop cell migration, and cause apoptosis in breast cancer cells. Thus, chia seed nanoparticles can be used as a supplemental therapy and have anticancer properties.

7. Recommended dosage for chia seeds

The UK's Novel Foods and Processes Advisory Committee suggested the following daily intake of chia seeds based on age groups: children ages 1.5 to 4.5 should take an average of 1.1 grams (not more than 3.2 grams), while adults ages 4.5 to 19 should not take more than 4.3 grams. Adults should eat 2.1 grams of chia seeds on average every day, with a daily maximum of 12.9 grams (about one tablespoon) (Melo, et al., 2019).

8. Chia seeds possible adverse effects

The 2000 US dietary standards advise against taking more than 48 grams of chia seeds per day (Norlaily et al., 2012). A 2017 upgrade noted the extraordinary amount of whole chia seed that may be added to breakfast cereals, baked goods, fruit and seed mixes (10%), yogurts (1.3 g /100 g), fruit drinks (15 g/day), fruit spreads (1%), bread and ready-to-eat items (5%), and yogurts (1.3 g /100 g). Overconsumption of chia seeds might result in the following health issues:-

Allergy: In certain populations, eating chia seeds may result in an IgE-mediated anaphylactic reaction. Some people may report allergic contact dermatitis in response to chia extract. Most people who may or may not ordinarily consume these seeds do not fit the profile of allergic patients, who typically have a personal history of ongoing allergies and sensitization to allergens (Tomas-Pérez et al., 2018).

Low blood pressure: Because chia seeds have an anti-hypertensive effect, people with hypotension or those on blood pressure medication should consume them with caution (Ulbricht et al., 2009).

Hypoglycemia: Because chia seeds lower blood glucose levels, those with type 2 diabetes should consume them under supervision to prevent hypoglycemia stroke (Ulbricht et al., 2009).

Discomfort and Bloating: Because chia has a high fiber content, eating a lot of it slows down digestion because fiber is difficult to digest and can lead to bloating and indigestion (Ulbricht et al., 2009).

In summary

Chia is a gorgeous plant with a wide range of biological effects because of its nutritional value and unique phytochemical makeup. Chia seeds offer several intriguing biological impacts on human health and appearance, however further research is advised to fully understand all these advantages. It is important to consider any potential negative consequences of chia consumption while evaluating its long-term impact. To determine their potential benefits, the other parts of the chia plant need to be researched and analyzed. It is advised to educate people about the health advantages of chia and how to utilize it in regular recipes in moderation. It is recommended that Egypt increases the amount of chia cultivated and consumed in the diet to manage and combat public health issues and malnutrition.

Conflicts of interest

here are no conflicts of interest to declare.

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