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FOOD SCIENCE & TECHNOLOGY | REVIEW ARTICLE

Phytochemical profile, nutritional composition, and therapeutic potentials of chia seeds: A concise review

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Abstract: Chia (Salvia hispanica) seeds are oilseeds, often known as pseudo-cereals, which contain a variety of nutrients, including macro and micronutrients, as well as health aids; consequently, they could be classified as a nutraceuticals food. The seeds are a wonderful source of phenolic compounds like rosmarinic acid, caffeic acid, protocatechuic acids, quercetin, and myricetin. According to studies, chia seeds have a high nutritious content of protein (18–24%), fiber (30–34%), and a variety of fatty acids. Chia seeds also have a variety of minerals and vitamins and shown to have beneficial effects in the treatment of hypertension, diabetes, and dyslipidaemia, as well as acting as an antioxidant, anti-anxiety, laxative, anti-

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PUBLIC INTEREST STATEMENT

Chia seeds, produced by the *Salvia hispanica L* plant, have been used for over 5,500 years. Chia seeds' strong nutritional and therapeutic value has led to a dramatic increase in their popularity in recent years. Chia seeds include several beneficial nutrients, including omega-3 fatty acids, polyunsaturated fatty acids, fiber, protein, vitamins, and minerals. The seeds have abundant polyphenols and antioxidants such as caffeic acid, rosmarinic acid, myricetin, quercetin, and others. Chia has been studied recently in several academic disciplines. Researchers from all around the globe have been looking at the potential health advantages of chia seeds for years. Human-controlled studies and systematic scientific literature reviews have revealed that chia seeds positively affect cardiovascular risk factors, including body weight, blood pressure, lipid levels, blood sugar, and inflammation. Nutrients including phytochemicals and the potential therapeutic effect of chia seeds have been described in detail in this paper.

depressant, analgesic, and strengthen the immune system. Due to its presence of minerals, lipids (omega-3), fibers, proteins, and antioxidants in chia seed and its health benefits, it has now grabbed the attention of many food industries and educators. The present review article highlights the nutritional composition, phytochemical profile, and therapeutic potentials like cardio-protective, diabetes-controlling, immune boosting, and antioxidant action in detail.

Subjects: Food Additives & Ingredients; Food Chemistry; Food Engineering; Food Laws & Regulations

Keywords: chia; phytochemical; nutritional; therapeutics

1. Introduction

The "Chia" and "Chia sage" seeds of *Salvia hispanica* L. were a significant staple food. Chia, seeds are tasty and come from Central America's lowlands, southern Mexico, and northern Guatemala (Grancieri et al., 2019). Chia seeds are from the *Lamiaceae* family and the genus *Salvia*. The ancient Mayas and Aztecs used chia seeds for nourishment, folk medicine, and painting. Chia seeds are becoming increasingly popular in Mexico, Chile, Japan, Argentina, the United States, Canada, and Australia. Chia has been consumed as food since 3500 BC, and central Mexico has long recognized it as a viable food crop (Özcan et al., 2019b). It is utilized in a range of food products throughout the world (Porras-Loaiza et al., 2014). The plant is tolerant of a wide spectrum of well-drained silt and saline soils, as well as salinity and acid. It can generate 500–600 kg of seed per acre, but under optimal agronomic conditions, a yield of 2,500 kg per acre has been reported (Cahill, 2003). Chia farming is gaining status in East Africa because of its low cost and nutritional benefits (Kibui et al., 2018). Chia is described as "the seed of the 21st century", "new gold", "superfood" or "super nutrient" (Segura-Campos et al., 2014). Chia seeds are smooth, glossy, and oval, measuring 1 to 2 mm in size. The seed coat can be grey, black-spotted, or white-spotted. In contrast, black chia seeds are more common, and white chia seeds are slightly larger than black chia seeds (Dinçoğlu & Yeşildemir, 2019). In latest years, there has been an increase in attention to the nutritional potential of chia seeds. This little seed has become a favorite of athletes due to its nutritious benefits. It contains ω-3 fatty acids, a significant amount of dietary fiber, high-quality protein, minerals, vitamins, and a large number of antioxidant compounds including chlorogenic acid, quercetin, kaempferol, and myricetin (Cahill, 2003). When the oil content of the raw and roasted chia seeds was compared for various qualitative attributes, it was discovered to be 35.83% and 37.7%, respectively. Chia seeds' respective raw and roasted total phenol concentrations were found to be 3.07 and 3.43 mg GAE/g reported by Ghafoor et al. (2018). Chia seed oil's linoleic acid concentration varied between 19.21% (900W) and 21.17% (control) when cooked in a microwave (p0.05). Chia seed oils that had been heated ranged in linolenic acid concentration from 66.84% (900W) to 68.71% (control). The concentrations of the chia oil samples of -tocopherol and -tocopherol ranged from 47.71 mg/100 g (900W) and 51.17 mg/100 g (control) to 62.58 mg/100 g (900W) and 67.81 mg/100 g (control), respectively reported by Özcan et al. (2019a). While, the oils' caffeic acid concentrations range from 0.27 mg/g (900W) to 3.84 mg/g (control), the chia seed oils' rosmarinic acid contents were found to range from 1.32 mg/g (900W) to 3.17 mg/g (control). According to current research, chia contains various beneficial effects on blood lipid profile, hypoglycemic, hypotension, antibacterial, and immunological response. For thousands of years, chia seeds have been largely consumed in many countries because of their huge nutritional and therapeutic potential. The nutritional and chemical composition of the seed makes it a potential crop for commercialization, and technological advancements have developed outstanding opportunities to establish an agricultural sector that can simultaneously contribute a new and an old crop to the world. Different studies have revealed the excellent nutritional and medicinal potential of these seeds, describing a diversity of possible applications for this remarkable food constituent (Timilsena et al., 2017). In this regard, the current review aims to characterize the full content of chia seeds, including the nutritional and functional effects of these compounds, as well as their potential medical applications.

2. Nutritional composition

The benefits of chia seed as a nutritional supplement and nutraceutical food cannot be inflated (M. S. Coelho & Salas-Mellado, 2014). Climate, provenance, and extraction techniques all have an impact on the quantity and amount of therapeutic components (Reyes-Caudillo, Tecante, & Valdivia-Lo´pez, 2008). Chia seeds provide dietary fiber (30-34 g), among which (85–93%) is an insoluble fraction and (7–15%) is soluble fiber (Capitani et al., 2012). It consists of approximately 25%-40% of polyunsaturated fatty acids (PUFA) which includes 55%-60% ω-3 fatty acids. Primarily stimulating the fatty acid profile through PUFA, especially linolenic acid, which accounts for approximately 60% of total fatty acids decrease concentrations of oleic, palmitic acid, linoleic acids and eicosapentaenoic acid (EPA) are present (Ghafoor et al., 2018; Özcan et al., 2019b). The highest percentage of α-linolenic acid (18%-20%) is exhibited by chia seeds in comparison with any of the other plant sources, and it is the precursor of the long-chain unsaturated fatty acids. These seeds have higher ω-3 fatty acids than flaxseed. Furthermore, Villanueva-Bermejo et al. (2019) showed a favorable ω-3 to ω-6 fatty acids 0.35:0.3 ratio. The seed is appropriately known as an ω-fatty acid powerhouse. Seeds also contain a lot of protein, which makes up 18–24% of their bulk (Nitrayova et al., 2014). The amino acid (AA) profile of chia seeds revealed the presence of 10 exogenous AAs with leucine, lysine, valine, phenylalanine, and arginine having greater quantities. They contain a lot of endogenous amino acids in their proteins, including aspartic acids, glutamic, serine, glycine, and alanine (Munoz et al., 2013). It's critical to keep in consideration that chia seeds are gluten-free, which may be consumed by persons suffering from celiac disease (Grancieri et al., 2019). Additionally, these seeds include a variety of minerals, with the highest concentrations of K^+ (0.407–0.726 g/100 g), Mg^+ (0.335–0.449 g/100 g), P (0.860–0.919 g/100 g) and CA^+ (0.456–0.631 g/100 g). According to research, a few vitamins, including niacin (0.0088 g/100 g), Vit.B1 (0.0006 g/100 g), and Vit.B2, were also discovered (Jin et al., 2012). Furthermore, these seeds are an excellent source of numerous phytochemical components with distinct biological actions (Rahman et al., 2017) (Figure 1). Cinnamic, chlorogenic, caffeic, gallic, ferulic acids, epicatechin, quercetin, rutin, kaempferol, apigenin, and p-coumaric acid, are some of the polyphenols that are particularly noteworthy. Stigmasterol (1.248 g/kg lipids), campesterol (0.472 g/kg lipids), 5-avenasterol and sitosterol (2.057 g/kg lipids). Tocopherols were also been detected in chia seeds, including -tocopherol (0.422 g/kg lipids), tocopherol (0.015 g/kg lipids), and -tocopherol (0.008 g/kg lipids) according to Ciftci et al. (2012).

3. Phytochemical profile

3.1. Flavonoids

Flavonoids are widely distributed chemicals found in plants. They are part of the polyphenolic subclass and have a 15C chain made up of 2-benzene rings (A & B) linked by a heterocyclic pyrane ring (C). They are mostly responsible for food's colour, flavour, and fat oxidation prevention (Zhu et al., 2012). Numerous biochemical functions of flavonoids include anti-inflammatory, antibacterial, hepato-protective, antioxidant, anti-cancer, and antiviral properties (Yao et al., 2004). These are extensively dispersed and microbial infections cause a rise in their production. Taga et al. (1984) reported that Quercetin, kaempferol, and myricetin were found in methanol hydrolyzed extracts of chia seeds and assessed their antioxidant properties. Reyes-Caudillo, Tecante, and Valdivia-Lo´pez (2008) examined chia seeds' natural and hydrolyzed isolates from two locations in Mexico (Figure 2). They determined that kaempferol phenolic glycosides and quercetin phenolic glycosides were the two main substances in the raw extract. Authors measured active aglycon components in Sinaloa and Jalisco seeds as kaempferol 0.509 mg/g and 0.360 mg/g and quercetin 0.268 & 0.150 mg/g, respectively, following hydrolyzing the extracts. In contrast, R. Ayerza (2013) found that myricetin, followed by quercetin kaempferol, was the main flavonol in Iztac and Tzotzol chia seeds genotypes which mainly differ in seed color among all genotypes (0.121 mg/g & 0.115 mg/g, accordingly). Martı´nez-Cruz and Paredes-Lo´pez (2014) conducted another study on the seeds

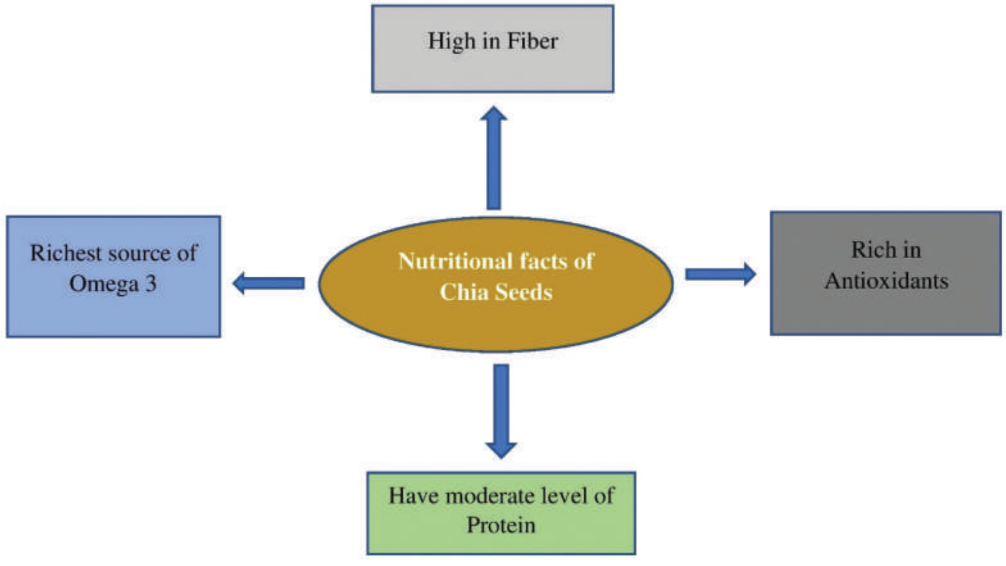


Figure 1. Nutritional facts of chia seeds.

variety Chionacalyx harvested from Mexico and found that the predominant phytoconstituents within phenol isolate were genistin, glycitin, genistein, daidzin, and glycitein. Daidzin was discovered within the specimen at 0.066 mg/g.

3.2. Phenolics

In seed isolate, caffeine plays a significant function from a biological and chemical aspect. That phenolic acid, made up of an acrylic acid-linked dihydroxyphenyl group, serves as the molecular framework for several metabolites found within the *Lamiaceae f*amily. Caffeoylquinic acids, of which chlorogenic acid is the most numerous inside the polar isolation of Chia seeds, are formed when caffeine, also known as hydroxycinnamic acid, binds to quinic acid in various locations. Polymers produced during precipitation are also found in the metabolism of chia seeds and the monomers that make up the building blocks of caffeic acid. In Mexico, Colima, Ultra-high-performance-liquid chromatography was used to identify monomeric compounds from chia seeds reported by Ixtlahuacan Martı´nez-Cruz and Paredes-Lo´pez (2014). These compounds include ferulic acid and caffeic-acid. Balasundram et al. (2006) described that the amount of caffeic acid (0.0274 mg/g) was lower than that found in peach (0.0371 mg/g) but greater than that found in blueberry (0.0216 mg/g), papaya (0.0159 mg/g) and mango (0.0077 mg/g). According to Craig (2004), the presence of polyphenols in chia seeds protects them from oxidative deterioration. Crosby (2005) discovered that chia seeds included significant levels of chlorogenic acid, caffeic acid, quercetin, phenolic glycoside k, and glycoside Q. It is well documented that these phenolic compounds possess antioxidant properties. Table 1.

4. Therapeutic perspectives

Chia seeds have also been linked to therapeutic benefits. Chia seed contains a high concentration of antioxidants such as kaempferol, caffeic-acid, myricetin, chlorogenic-acid, and quercetin that are known to have anti-hepatic, anti-cardiovascular, anti-aging, and anti-carcinogenic qualities. Chia seeds have high dietary fibre content aids with diabetes management and digesting. Ullah et al. (2016) revealed that gluten free protein and vitamins in its PUFA have therapeutic effects in the control of hypertension, diabetes, and dyslipidaemia, as well as acting as an anti-oxidant, anti-blood clotting, anti-inflammatory, anti-anxiety, anti-depressant, laxative, analgesic, immune system, and vision improver.

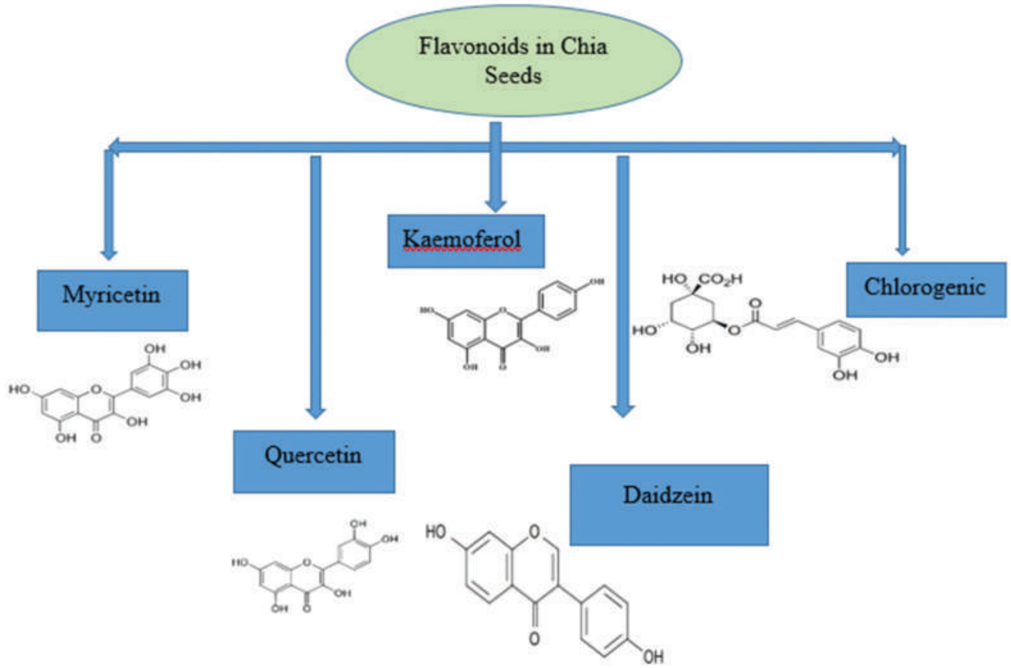


Figure 2. Depicts the flavonoids present in chia seeds.

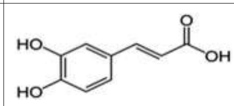
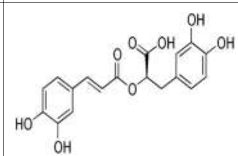
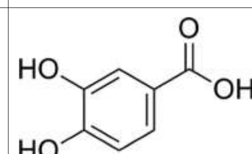
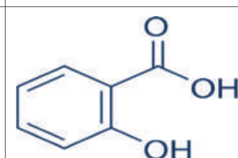
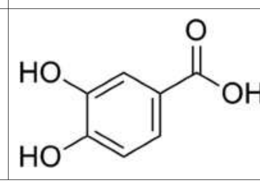
4.1. Cardio-protective Effects

Eicosapentaenoic acid and linolenic acid are essential in the formation of beneficial biological molecules (such as leukotriene, prostaglandin, and thromboxane) responsible for many physiological functions (Leaf & Kang, 1998). Omega-3 fatty acids contribute to heart health by improving heart rate fluctuations, parasympathetic tone, and abnormal heartbeats (Pawlosky et al., 2003). A higher intake of alpha-linolenic acid reduces the risk of heart failure considerably. An investigation conducted at St. Michael Hospital in Toronto, Canada, discovered that chia seeds had numerous health benefits, including higher iron, fiber, magnesium, and calcium content than milk, gluten-free and blood glucose levels in diabetic patients were stabilized by taking 37 g seeds daily, an excellent source of ω-3 fatty acids, reduced systolic blood pressure up to 6 mmHg and prevented myocardial infarction and strokes by suppressing aggregation of platelets Vuksan et al. (2010). Some excellent medicinal properties have also been encountered in chia seeds, including inhibiting blood clotting, preventing neurological disorders such as epilepsy and stress, decreasing blood cholesterol, and boosting the immune system. It has been proved that consuming chia seeds during pregnancy can be beneficial since it improves the development of the fetus's retina and brain (Vuksan et al., 2007). Fernandez et al. (2008b) also observed in a study that feeding chia seed to male Wistar rats showed enhancement of the good high-density lipoprotein cholesterol and a significant reduction in triglycerides another advantage of chia seed consumption was a decrease in ω-6 in plasma and a decrease in the ω-6: ω-3 ratio, which has a cardio-protective impact (R. J. Ayerza & Coates, 2007). Alwosais et al. (2021) investigated the impact of chia seed supplementation on blood pressure indicators in persons (21–65 years old) with type 2 diabetes. Long-term dietary supplementation with chia seeds decreases systolic blood pressure by 13 mmHg compared to baseline in persons with type 2 diabetes, according to research. (Table 2).

4.2. Diabetes Controlling Effect

Several research works have proved that chia seeds possess a hypoglycaemic effect. The research results indicate that mice fed chia oil or chia flour reduced adiposity but only chia oil could improve glucose tolerance and restore the energy fuel system in the liver (Ho et al., 2013). Both black and

Table 1. Phenolic substances present in chia seeds

Phenolic Compounds in Chia Seeds	Biological Activity	Chemical Structure	Reference
Caffeic Acid	• hypoglycemic activity • Effective against epilepsy		(Chang et al., 2015; V. R. Coelho et al., 2015)
Rosmarinic acid	• Immuno-regulatory, • Anti-microbial, anti-oxidant and anti-inflammatory activities		(Jayanthy & Subramanian, 2014)
Protocatechinic acids	• Have antioxidant activity		(Alcântara et al., 2019)
Salicylic acid	• Peeling agent • Its peels have therapeutic effects		(Arif, 2015)
Protocatechuic acids	• Have anti-mutagenic and anti-inflammatory properties		Tunçil and Çelik (2019)

white chia seeds dramatically lower fasting blood glucose, triglycerides, liver enzymes low-density-lipoprotein, and total cholesterol like alanine-aminotransferase and aspartate-aminotransferase (Almri, 2019). Research workers established that chia seeds have the ability to exhibit a hypoglycaemic effect due to the main presence of high dietary fiber content (Enes et al., 2020).

4.3. Immune System Impact

Researchers discovered that it has a strategic edge over other omega-3 PUFA products in treating ailments such as diarrhea, allergies, fishy flavor, weight loss, and digestive issues. This study was sole in its emphasis on the immune system, and a significant gap in our understanding of chia immune-stimulant properties is that none of the findings have been repeated. Fernandez et al. (2008b) discovered that the concentration of IgE (immunoglobin E) was considerably greater with the chia diet compared to the control in research on weaning Winstar rats. The trial lasted one month, and thymus and serum IgE concentrations were used as markers of immunity. It was also observed that there were no symptoms of diarrhea, abnormal behavior, dermatitis, or any other allergy to chia seeds or oil, whereas fishy flavor, diarrhea, allergy, or problems with the gastro-intestinal tract were observed with supplementation with different sources of ω-3 fatty acids like marine products or flaxseeds (R. Ayerza & Coates, 2005). In terms of food intake, body weight, thymus weight, thymocyte number, and IgE, chia was shown to be equivalent to fish oil (Parker et al., 2018).

Table 2. Potential therapeutic functions of Chia seed

Experiment details	Main Results	References
36 young obese rats supplemented with 0.133 kg chia seeds or chia oil 0.04 kg/kg diet	lipid peroxidation was reduced in oxidative stress, also improved antioxidant status.	Marineli et al. (2015)
20 male Wistar rat 20 g chia seed extract/ground chia seeds supplemented to 90 g rat pellet	A progressive increase in body weight and an increase in postprandial blood glucose levels were noted	Mihafu et al. (2020)
Hypercholesterolemia rabbits were given 10 g chia oil [CD] or 10 g chia oil +1 g cholesterol/kg diet	In the HD-Ch group, triacylglycerol concentrations were lowered while linolenic acid content was increased	Sierra et al. (2015)
18 male rats were fed 150 g chia seeds or chia oil 50 g/kg diet	Certainly not significant influence was observed on IgE concentration.	Fernandez et al. (2008b)
26 aged 45–55 years obese or overweight men and women were given chia flour 35 g/d	BW was observed to be lower in the chia flour group. The supplemented group had lower total cholesterol and higher LDL cholesterol.	Toscano et al. (2015)
13 healthy persons were chia seeds supplemented with 0 g, 7 g, 15 g and 24 g, which were then put to 50 gm bread.	Postprandial glycaemia reduction was found.	Ho et al. (2013)
Twenty type 2 diabetic men and women were given 37 g ground chia seeds mixed into bread each day	Chia supplementation reduced systolic blood pressure and CRP concentrations while increasing eicosapentaenoic acid and linolenic acid concentrations by a factor of two.	Vuksan et al. (2007)
15 healthy adults were given 0.025 kg ground chia seeds to 0.050 kg glucose, 0.025 kg flax to 0.050 kg glucose, or 0.050 kg glucose alone	Appetite score and prospective consumption were significantly reduced compared with flax	Vuksan et al. (2016)
All extracts were assessed against oral microorganisms	Ethanolic and aqueous extract of Chia seeds (S.hispanica) showed its anti-microbial activity against actinomycetemcomitans, P. gingivalis A. and F.nucleatum	Divyapriya et al. (2016)
Ethanol extract of Chia seeds were tested against Aeromonas hydrophila, Staphylococcus aureus, Escherichia coli, Bacillus subtilis, Candida albicans, Candida tropicalis, Acinetobacter baumannii, and Candida glabrata	Ethanol extract of Chia seeds was showed its more effectiveness against A. baumannii (MIC: 62.5 µg/mL) compared to reference drug Ampicillin	Güzel et al. (2020)
76 obese people took 25 g chia seeds in 250 mL water/twice a day	Concentration of serum α-linolenic acid of the group was increased. No influence was found in seeds on inflammatory markers, body composition and blood pressure.	Nieman et al. (2009)
10 women after menopause took 25 g ground chia seeds/day	Concentration of α-linolenic and eicosapentaenoic acids was increased.	Jin et al. (2012)
11 healthy men and women supplemented their bread with 0, 7, 15, and 24 g chia seeds each day	Postprandial glycaemia was significantly reduced in chia feed group.	Vuksan et al. (2010)

4.4. Effect as Antioxidant

Several research works have documented the higher antioxidant activity of chia seeds. V. R. Coelho et al. (2015) confirmed that the enzymatic oxidation of guaiacol was inhibited by the extracts of chia seeds. Marineli et al. (2015) performed an experiment with obese rats on diet with chia seeds at 133 g/kg for 6 weeks and chia oil at 40 g/kg for 12 weeks. A few days after consumption, the activity of antioxidant enzymes (catalase, glutathione reductase, glutathione, and glutathione peroxidase) was increased significantly in animals fed on seeds or oil compared to animals consuming a high fructose diet without chia supplement. Several studies have found that chia seeds have a strong antioxidant ability. Sargi et al. (2013) showed that chia seeds can deactivate ABTS cation radicals. Chia seeds can also scavenge synthetic DPPH radicals and reduce iron ions, according to the study. The result of the study showed that chia seeds have more antioxidant activity than flaxseed. However, Segura-Campos et al. (2013) validated the antioxidant activity of chia seeds. They demonstrated that chia seed extracts can quench DPPH radicals and neutralize them by more than 70%. They also discovered that these extracts block guaiacol enzymatic oxidation. The ORAC value is a primary indicator of the antioxidant potential of biological material (Oxygen Radical Absorbance Capacity). Reyes-Caudillo, Tecante, and Valdivia-Lo´pez (2008) studied the influence of chia seed extract incorporation on beta-carotene breakdown rate in a linoleic acid/beta-carotene model system heated to 50 C. They discovered that chia seed extracts have antioxidant activity ranging from 73.50% to 79.30% in the model emulsion. Additionally, they demonstrated that chia seeds can prevent lipid peroxidation.

4.5. Anti-obesity Effect

Obesity-relieving effects of chia seed and its oil have been investigated in animal studies. The treatment of obesity rodents with chia seed and chia seed oil produced similar effects with minor variations. According to Poudyal et al. (2012), chia seed administration enhanced insulin and glucose tolerance, visceral obesity, hepatic steatosis, cardiac and hepatic fibrosis, and inflammation. Stearoyl-CoA desaturase (SCD) activity, which converts elaidic acid to conjugated linolenic acid, is inhibited by chia seed. According to this research, C18:2n-6 is oxidized and transferred into the mitochondria, where it lowers *n*-6/n-3 levels. SCD inhibition protects mice against obesity, cellular lipid build-up, and insulin resistance.

4.6. Other Therapeutic Effect

Soluble extracts derived from the seeds of plants high in dietary fiber, such as chia seeds, may improve gastrointestinal motility by enhancing vitamin and mineral salt absorption (Miśta et al., 2017). Chia seeds include insoluble dietary fiber, which prolongs digestion, expands defecations and prevents blockage. They also provide solid lipids, proteins, and cancer-prevention chemicals that protect cells (Tan & Seow-Choen, 2007). Pereira da Silva et al. (2019) investigated the effects of soluble chia seed extracts on Fe and Zn levels and intestinal brushtail functioning in vivo. Chia seed extract was shown to enhance intestinal function by increasing the area, thickness, and breadth of intestinal villi, as well as enterocyte proliferation and mucus production. The scientists also discovered that chia seed extract improved the intestinal microbiota by boosting enterocyte proliferation and the number of mucus-producing cells, which may improve the digestive and absorptive ability of the intestinal brush-border membrane.

The enzymatic activity of *S. hispanica* seed peptides to slow skin aging processes and enhance skin condition was investigated in a study by Aguilar-Toala and Liceaga (2020). The research demonstrated that all skin aging-related enzymes that lead to the breakdown of the skin protein matrix were inactivated by the peptide fraction with a total mass density of less than 3 kDa (at 1 mg/ml). In this study chia seed, peptides inhibited collagenase and tyrosinase in a direct pattern and hyaluronidase and elastase in a mixed pattern. The findings imply that peptide sequences may enhance skin look and condition by guarding against enzymes linked to skin aging.

5. Conclusion

Chia (*Salvia hispanica*) seeds have long been utilised as a staple meal in Aztec and Mayan diets. Because of the existence of bioactive chemicals with health advantages, chia seeds have rising potential as a source of nutrients and nutraceuticals important to technology, science, medicine, and engineering. Chia seeds are also high in phytochemicals (caffeic acid, quercetin, myricetin, kaempferol and chlorogenic acid, among others), fatty acids, dietary fibres, proteins (including important amino acids), vitamins, and minerals. Chia seeds can be added to food to improve nutritional quality, and a diet rich in chia seeds can help prevent disease owing to its phytochemical profile, high nutritional value and great therapeutic potential.

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Corresponding and all the co-authors are willing to participate in this manuscript.

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Even though adequate data has been given in the form of tables and figures, however, all authors declare that if more data required then the data will be provided on request basis.

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