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Comprehensive REVIEWS in Food Science and Food Safety

Chia Seed (*Salvia hispanica* L.) as a Source of Proteins and Bioactive Peptides with Health Benefits: A Review

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Abstract: The consumption of chia seed (*Salvia hispanica* L.) has increased in recent years due its high content of omega-3 fatty acids and dietary fiber. This seed also has a high concentration of proteins and essential amino acids, becoming a promising source of bioactive peptides. The objective of this review was to identify the composition and the beneficial effects of chia seeds (*S. hispanica* L.), their proteins, peptides, and their potential impact on human health. The UniProt database was used to identify the chia proteins and their amino acid sequences. The BIOPEP database was used to analyze the peptides's bioactive potential. A total of 20 proteins were cataloged in chia seed, 12 of those were involved in the regular metabolic processes of the plant cells. However, eight proteins were specifically related to production and storage of plant lipids, thus explaining the high concentration of lipids in chia seeds (around 30%), especially omega-3 fatty acids (around 20%). The analyses of amino acid sequences showed peptides with bioactive potential, including dipeptidyl peptidase-IV inhibitors, angiotensin-converting enzyme inhibitors, and antioxidant capacity. These results correlated with the main health benefits of whole chia seed in humans such as antioxidant capacity, and hypotensive, hypoglycemic, and anticholesterolemic effects. Such relation can be associated with chia protein and peptide compositions and therefore needs further investigation *in vitro* and *in vivo*.

Keywords: antioxidant, bioactive peptides, chia seed, linolenic acid, linoleic acid, protein

Introduction

History, classification, and botanical description of chia

Chia (*Salvia hispanica* L.) is an herbaceous plant that belongs to the order Lamiales, family Lamiaceae, subfamily Nepetoideae, and genus *Salvia* (Arctos Specimen Database, 2018). The *Salvia* genus is considered the most numerous in the family Lamiaceae. It consists of approximately 900 species widely distributed throughout several regions of the world, including Southern Africa, Central America, North America, South America, and South-East Asia (Takano, 2017). The chia plant is native to northern Guatemala and southern Mexico and today is cultivated in Australia, Bolivia, Colombia, Guatemala, Peru, Argentina, and Mexico, the latter being the world's largest producer (Busilacchi et al., 2013).

Pre-Columbian populations consumed chia in the 16th century to provide energy, endurance, and strength. During the battles and expeditions, Aztec soldiers consumed chia to meet their nutritional needs. The oil extracted from the seeds has been used to produce cosmetics. In addition, chia seed was an offering to the gods in religious ceremonies or used as a form of payment of taxes (Ayerza, 2009). Other parts of the plant, such as the branches, leaves and roots, were used less commonly to fight respiratory infections (Sosa, 2016).

The chia plant is about 1 m tall and has simple leaves, which measure 4 to 8 cm long and 3 to 5 cm wide, oval-elliptical shape, pubescent, and with acute apex. A chia seed is quasi-oval, with a length between 1 and 2 mm, a diameter between 0.8 and 1.3 and a width between 0.8 and 1.4 mm. It has a smooth and shiny peel and coloring that can be black, brown, gray, black-spotted, or white. The mucilage is present inside the epidermal cells of mature chia seeds and when they come into contact with water it immediately expands rupturing the primary cell layer that protrudes from these epidermal cells thus surrounding the seed, which increases its size and imparts a characteristic gel appearance to chia (Figure 1) (Muñoz, Cobos, Diaz, & Aguilera, 2012).

The largest cultivation of seeds of this genus occurs in mountainous regions from temperate to subtropical (Capitani, Spotorno, Nolasco, & Tomás, 2012). The chemical composition and nutritional value of chia seed may vary according to climatic conditions, geographic location, nutrients, and soil conditions, as well as year of cultivation (Ayerza, 2009; Ayerza & Coates, 2009; da Silva et al., 2017). For example, the composition of fatty acids varies according to climate and the altitude of the plant; the colder and higher the region, the higher the content of omega-3 unsaturated fatty acids (Ayerza h & Coates, 2011).

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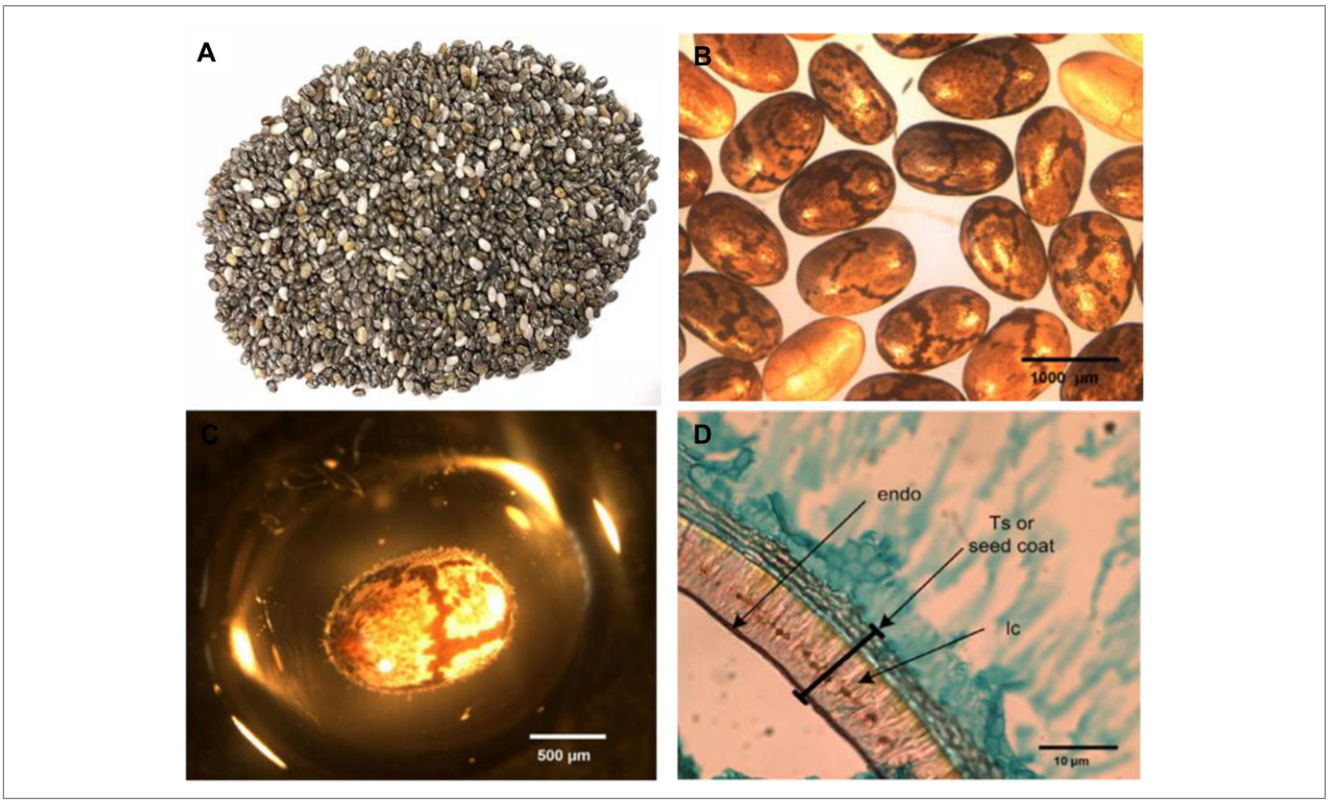

Figure 1–Chia seed. (A) Seeds in full-size; (B) whole dry seed (approximate image); (C) whole seed hydrated with mucilaginous capsule around; (D) inside the seed: the three layers of rectangular cells forming the seed shell are observed; endo: endocarp layer; lc: sclereid layer. Source: Adapted from Muñoz et al. (2012) with permission from Elsevier.

Chia seed uses

The consumption of chia has been increasing over the years, given its health benefits related to chronic diseases such as obesity, cardiovascular diseases, diabetes, and cancer (Ixtaina, Nolasco, & Tom, 2008; Poudyal, Panchal, Ward, & Brown, 2013; Vázquez-Ovando, Rosado-Rubio, Chel-Guerrero, & Betancur-Ancona, 2010). These benefits result mainly from the high concentrations in chia seeds of essential fatty acids, dietary fibers, proteins, antioxidants, vitamins, carotenoids, and minerals (Ayerza & Coates, 2011; Reyes-Caudillo, Tecante, & Valdivia-López, 2008). Today, the chia seed is consumed whole or in the form of flour, alone (*in natura*), added to other foods, such as yogurts, salads, and fruits (Cahill, 2004; Vuksan et al., 2007), in preparations such as breads, cakes, granola bars, beverages, and others (Figure 2).

In general, the incorporation of chia in foods improve their physicochemical and sensory characteristics, especially their nutritional properties. The incorporation of chia seeds in tortillas reduces the rate of enzymatic hydrolysis of starch and the glycemic index (Rendón-Villalobos, Ortíz-Sánchez, Solorza-Feria, & Trujillo-Hernández, 2012). The chia seeds in bakery products increase their concentrations of proteins, unsaturated fatty acids, antioxidants, and dietary fiber (Iglesias-Puig & Haros, 2013; Segura-Campos, Salazar-Vega, Chel-Guerrero, & Betancur-Ancona, 2013). The gum present in chia seed has the ability to hold water and oil as well as having emulsifier and stabilizer potential (Segura-Campos, Ciau-Solís, Rosado-Rubio, Chel-Guerrero, & Betancur-Ancona, 2014). Furthermore, chia seed when added to wheat bread increases its antioxidant activity, nutritional content, textural properties (higher moisture content and lower hardness), color, and sensory profiles with 3.7 points in global acceptability score (1 to 5) (Sayed-Ahmad et al., 2018). Similarly, the use of 10% of chia flour in gluten-free bread received an overall acceptability scores of 8.1 on a 10 cm scale, and increased the levels of lipid, protein and dietary fiber in comparison with white gluten-free bread (Sandri, Santos, Fratelli, & Capriles, 2017). The use of 30% chia seed flour (w/w) in a gluten-free noodle formulation increased the content of protein, fat, antioxidant activity and total phenolic compounds in comparison to the control sample. Phytic acid and phytate phosphorus increased 889.39 and 250.81 mg/100 g, respectively. In this study, the content of Ca, P, K, Mg, Fe, and Zn increased in noodles containing chia seed and there was a decrease of surface smoothness, appearance and chewiness score of raw and cooked noodle samples (Levent, 2017).

The protein-rich fraction obtained from the seeds has shown high thermal stability, between 70.4 and 125.0 °C, and good water-holding (4.06 g/g) and oil-holding (4.04 g/g) capacities (Olivos-Lugo, Valdivia-López, & Tecante, 2010). This high stability is associated with hydrophobic interactions between amino acids (Olivos-Lugo et al., 2010). The protein-rich fraction has high emulsifying activity independent of pH, but at pH 8 and 10 the emulsion stability has been shown to be the highest, about 92%. These protein fractions also had good foam stability and viscosity (Vázquez-Ovando, Betancur-Ancona, & Chel-Guerrero, 2013). Furthermore, due to the ability of the fractions to form a gel, chia proteins are promising for food processing by providing consistency and thickening to various foods (Borneo, Aguirre, & León, 2010). These characteristics indicate that the proteins from chia seed are promising food additives that can help improve food quality and extend the shelf-life of foods (Valdivia-López & Tecante, 2015).

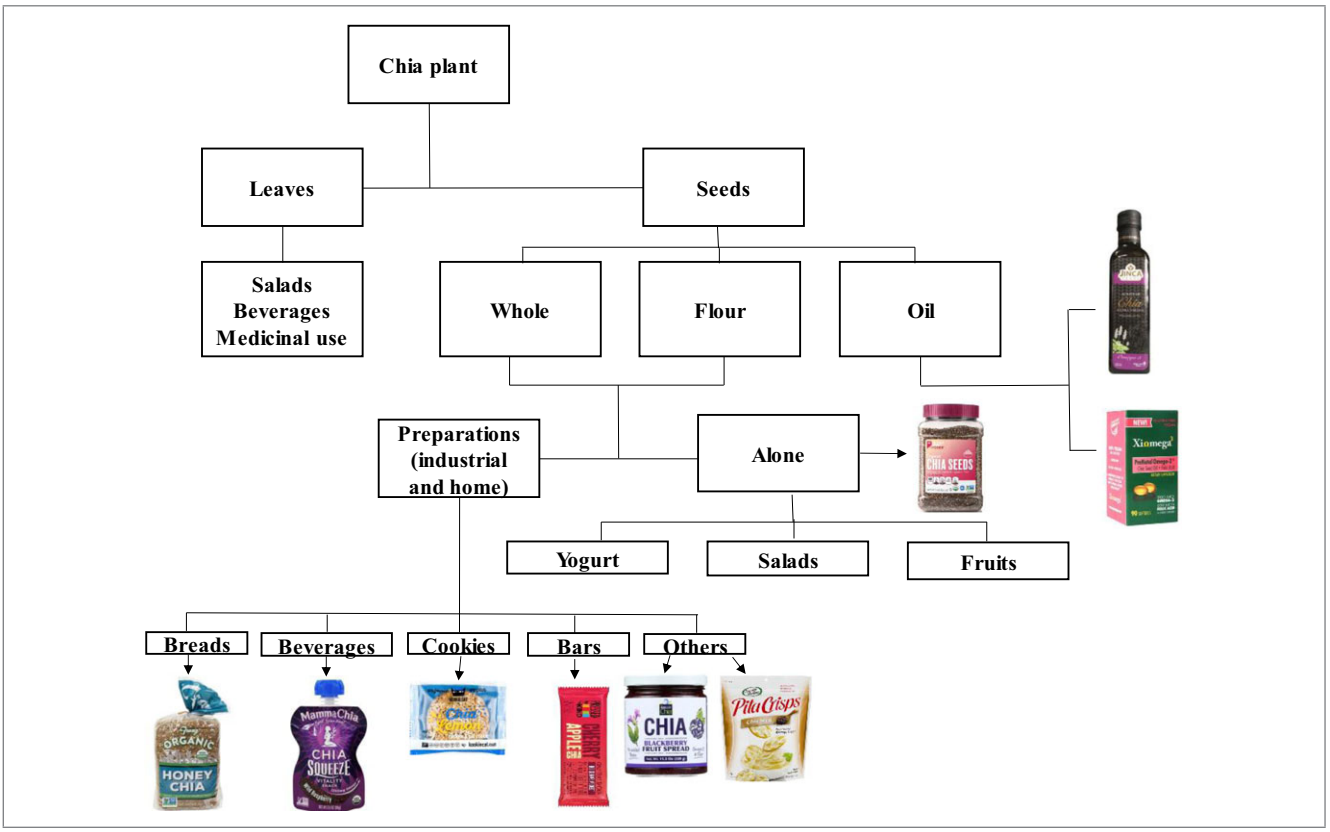

Figure 2–Uses of chia plant and some products obtained from chia seed.

Chia seed oil is also commercially exploited because of its rich content of essential fatty acids, such as alpha-linolenic (omega-3 or n-3) and alpha-linoleic acids (omega-6 or n-6) (Mohd Ali et al., 2012). The residual content of the oil extraction process is a source of dietary fiber (36.97 to 39.94 g/100 g) and polyphenolic compounds [chlorogenic acid (0.05 to 0.102 g/100 g), caffeic acid (0.01 to 0.003 g/100 g), phenolic glycoside-Q (0.25 to 0.31 g/100 g), and phenolic glycoside-K (0.40 to 0.50 g/100 g)] with antioxidant activity. In this way, chia seed can be used as a source of natural antioxidants with commercial applications (Reyes-Caudillo et al., 2008).

The objective of this review was to identify the composition and the beneficial effects of chia seeds (*Salvia hispanica* L.), their proteins, peptides, and their potential impact on health.

As a descriptive review, the information presented is related mainly to protein and bioactive peptides from chia seed only. Scopus and PubMed databases were used to locate publications with the descriptors: "chia seed," "*Salvia hispanica*," "chia seed" AND either "composition," "health benefits," "cholesterol," "oxidative stress," "hypertension," "glycemia," "protein," "bioactive peptides," "amino acids," or "simulated digestion"; "Salvia hispanica" AND either "composition," "health benefits," "cholesterol," "oxidative stress," "hypertension," "glycemia," "protein," "bioactive peptides," "amino acids," or "simulated digestion." Furthermore, Uniprot database was used to identify proteins using "*Salvia hispanica* L." as a keyword. BIOPEP database was used to identify the bioactive potential of amino acid sequences from each identified protein. In the topic "Benefits of chia seed," research on chia seed from human studies were included. Studies about chia oil were excluded.

Bioactive Compounds of Chia

Although the nutritional composition of chia depends on the cultivation conditions, it has, in general, a good nutritional value and promising bioactive compounds for human health (Table 1). Chia seed has low amounts of carbohydrates (3.4%) and high protein (18.9%) and lipid (31.2%) contents. There are high contents of alpha-linolenic (omega-3 or n-3) (19.5%) and alpha-linoleic acids (omega-6 or n-6) (around 5.2%), both essential nutrients since the human organism cannot synthesize them. The proportion n-6/n-3 in Brazilian chia seeds has been reported as 1:3 (da Silva et al., 2017). This high concentration of n-3 is associated with reduced risk of coronary artery disease, hypertension, type 2 diabetes, rheumatoid arthritis, autoimmune diseases, and cancer (Meyer & Groot, 2017).

In addition, chia seed is rich in vitamins such as riboflavin (0.17 mg/100 g), niacin (8.83 mg/100 g), and thiamine (0.62 mg/100 g) at levels above those of other seeds (Muñoz et al., 2012). Chia also has high concentrations of calcium (455 mg/100 g), phosphorus (585 mg/100 g), potassium (585 mg/100 g), magnesium (340 mg/100 g), iron (8.54 mg/100 g), and zinc (3.70 mg/100 g) (da Silva et al., 2017). The concentration of calcium in chia seeds is higher than that found in milk, as well as the concentration of iron, which is higher than found in good sources of this mineral such as liver (Ullah et al., 2016).

Despite the high concentration of minerals in chia seed, its consumption by Wistar rats for 35 days revealed lower calcium balance and lower calcium absorption and retention rates in comparison with the group of animals that received calcium carbonate (control group) (da Silva et al., 2019). However, male Sprague-Dawley rats fed a longer term (13 month) with 10% chia seed,

Table 1–Composition of Brazilian chia seeds.

Components	Content in Brazilian chia seeds[a]	Content in Mexican chia seeds[b]
Total dietary fiber (g/100g)	33.37 ± 0.26	41.41 ± 0.2
Soluble dietary fiber (g/100g)	2.89 ± 0.09	6.84 ± 0.9
Insoluble dietary fiber (g/100g)	30.47 ± 0.35	34.90 ± 0.9
Lipids (g/100g)	32.16 ± 0.29	35.13 ± 0.04
18:2 (n-6) (g/100g)	5.69 ± 0.42	58.07
18:3 (n-3) (g/100g)	20.37 ± 1.38	68.52 ± 0.02
Proteins (g/100g)	18.18 ± 1.20	24.11 ± 0.43
Moisture (g/100g)	7.14 ± 0.26	6.82 ± 0.13
Carbohydrates (g/100g)	4.59 ± 0.34	1.51 ± 0.08
Total phenolics compounds (mg GAE)	0.97 – 0.99	0.757
Tannins (mg GAE/g)	14.93 – 19.08	n.d
Phytates (g 100 g^{-1})	0.96 – 1.16	n.d
Carotenoids (μg 100^{-1})	57.01	n.d
Flavones (μg 100^{-1})	6.07 – 16.03	n.d
Flavanones (μg 100^{-1})	4.39 – 9.34	n.d
Vitamin E (μg 100^{-1})	8169.50 – 8237.64	n.d

[a] Adapted from Silva et al. (2017).
[b] Adapted from Segura-Campos et al. (2014) and Reyes-Caudillo, Tecante, Valdivia-Lopez (2008). n.d: not determined.

versus a conventional isocaloric diet, showed higher bone mineral content and improved morphology of hepatocytes and gut tissue (Montes Chañi et al., 2018). This study provided new data suggesting the potential benefits associated with the long-term intake of chia seed. Furthermore, the consumption of chia showed an iron bioavailability similar to ferrous sulfate (control group) (da Silva et al., 2016a).

Another characteristic of chia seed is its high concentration of antioxidant compounds, mainly phenolic acids and flavonoids. It is now known that rosmarinic acid is the phenolic compound present in the greatest amount (0.927 mg/g), followed by protocatechuic acid (0.747 mg/g), caffeic acid (0.027 mg/g), and gallic acid (0.012 mg/g) (Martínez-Cruz & Paredes-López, 2014). Flavonoids are present, in great number, as flavones and flavanones. Tannins and phytates are present in small quantity, but other antioxidant compounds such as carotenoids and vitamin E appear in high amounts (da Silva et al., 2017; Oliveira-Alves et al., 2017) (Table 1).

Chia seed is also a source of dietary fiber (35%) (da Silva et al., 2017) in higher levels than other seeds, such as amaranth (7.3%), quinoa (7.0%), and corn (8.3%) (Srichuwong et al., 2017). Insoluble fiber is also present in greater quantity in chia (Table 1). It is primarily composed of lignin, cellulose, and hemicellulose, whereas mucilage is the main type of soluble fiber of the seed (Reyes-Caudillo et al., 2008). This mucilage has high capacity for water absorption and can absorb about 27 times its own weight (Muñoz et al., 2012).

Benefits of Chia Seeds

Despite the existence of some chia protein studies that include bioactive peptides, most investigations have been focused on research regarding the whole seed. As described in Table 2, several beneficial effects to living organisms, including humans, have been reported when consuming chia seed.

Antioxidant capacity

Chia seeds have numerous antioxidant compounds, such as vitamins, polyphenols, and peptides. These compounds can inhibit the activation of the NF-κB transcription factor *in vitro*, thus reducing the inflammatory and carcinogenic processes (Aggarwal & Shishodia, 2006; Ellulu, 2017; Rahman, Biswas, & Kirkham, 2006) and protecting against the attack of reactive oxygen species or nitrogen (ROS) (Kampa et al., 2002). These antioxidant actions can protect the organism from pathologies, like neurological diseases, inflammation, immunodeficiency, ischemic heart disease, strokes, Alzheimer's and Parkinson's diseases, and cancer (Marcinek & Krejpcio, 2017).

It has been demonstrated that rats fed a high-fat diet including chia seeds for 6 or 12 weeks experienced a decrease of thiol levels and plasma catalase and glutathione peroxidase activities, while liver levels of the glutathione reductase became enhanced (Marineli, Lenquiste, Moraes, & Maróstica, 2015a). Rats that received a long-term sucrose-rich diet and were fed chia seeds, returned to the same activities of antioxidant enzymes catalase, superoxide dismutase, and glutathione reductase as control values (de Souza Ferreira, dd Sousa Fomes, da Silva, & Rosa, 2015). In addition, increases in superoxide dismutase and IL-10 plasma concentrations were observed when Wistar rats consumed chia seed flour plus a high-fat diet for 35 days in comparison with a control group (calcium carbonate) (da Silva et al., 2019). In healthy humans who had received chia seeds (12 weeks) a better plasma antioxidant activity was observed compared to hypertensive (Toscano et al., 2014) or overweight patients (Nieman et al., 2009).

It has been demonstrated that germinated chia showed increased protein quality, as measured by protein efficiency ratio (PER). The amount of the γ-aminobutyric acid (GABA), total phenolic content, and antioxidant activity increased even more in the flour of germinated seeds (Gómez-Favela et al., 2017), as well as in normal chia flour (da Silva et al., 2017; Martínez-Cruz & Paredes-López, 2014; Sargi et al., 2013). The albumin and globulin fractions showed a high antiradical activity against DPPH and prolamin as well as globulin ability to chelate ferrous ions (Orona-Tamayo, Valverde, Nieto-Rendón, & Paredes-López, 2015).

Anticholesterolemic

High concentrations of blood serum HDL-cholesterol (HDL-c) are directly associated with the development of cardiovascular disease (CVD) in humans (Rasheed & Cummins, 2018). The consumption of chia seed has shown promise for reducing the levels of serum cholesterol, since it has high concentrations of dietary fiber and unsaturated omega-3 fatty acids (da Silva et al., 2017). Most recently, it has been demonstrated that chia proteins and chia bioactive peptides can block key markers of cholesterol synthesis, such as 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase) (Coelho et al., 2018).

Table 2–Health benefits of whole chia seeds in humans.

Population	Age (years)	Dose	Duration (weeks)	Effects	Reference
Antioxidant capacity					
29 hypertensive and overweight	35-65	35 g/day	12	↓ plasma MDA ↓ plasma nitrite	(Toscano et al., 2014)
76 overweight	20-70	50 g/day	12	No effects	(Nieman et al., 2009)
Anticholesterolemic					
10 postmenopausal women	53-60	25 g/day	7	↑ ALA ↑ EPA	(Jin et al., 2012)
29 overweight and obesity participants	35-65	35 g/day	12	↓ TC ↓VLDL-c ↑ HDL-c	(Toscano et al., 2015)
76 overweight	20-70	50 g/day	12	No effects	(Nieman et al., 2009)
62 postmenopausal women	53-60	25 g/day	10	↑ ALA ↑ EPA	(Nieman et al., 2012)
Anti-hypertensive					
29 Hypertensives and overweight	35-65	35 g/day	12	↓ MBP ↓ DBP ↓ SBP	(Toscano et al., 2014)
76 Overweight	20-70	50 g/day	12	No effects	(Nieman et al., 2009)
20 participants with type-2 Diabetics	18-75	37 g/day	12	↓ DBP ↓ SBP	(Vuksan et al., 2007)
Anthropometrics					
77 overweight or obese participants with type 2 diabetes	35-75	30 g/1000 kcal	24	↓ body weight ↓ waist circumference ↑ adiponectin	(Vuksan et al., 2017b)
29 overweight and obese participants	35-65	35 g/day	12	↓ body weight ↓ % body fat	(Toscano et al., 2015)
76 overweight	20-70	50 g/day	12	No effects	(Nieman et al., 2009)
29 hypertensive and overweight	35-65	35 g/day	12	No effects	(Toscano et al., 2014)
62 postmenopausal women	53-60	25 g/day	10	No effects	(Nieman et al., 2012)
20 participants with type-2 diabetics	18-75	37 ± 4 g/day	12	No effects	(Vuksan et al., 2007)
Hypoglycemic					
13 healthy participants	–	7, 15 or 24 g	acute	↓ iAUC	(Ho et al., 2013)
11 healthy participants	–	7, 15 or 24 g	acute	↓ iAUC ↓ blood glucose	(Vuksan et al., 2010)
15 healthy participants	23.9 ± 3	25 g	acute	↓ AUC ↓ glucose peak ↑ time to glucose peak	(Vuksan et al., 2017a)
62 postmenopausal women	53-60	25 g/day	10	No effects	(Nieman et al., 2012)
29 overweight and obese patients	35-65	35 g/day	12	No effects	(Toscano et al., 2015)
76 overweight	20-70	50 g/day	12	No effects	(Nieman et al., 2009)
77 overweight/obese patients with type 2 diabetes	35-75	30 g/1000kcal	24	No effects	(Vuksan et al., 2017b)

MDA: malondialdehyde; ALA: alpha-linolenic acid; EPA: docosahexaenoic acid; TC: total cholesterol; VLDL-c: very low-density lipoprotein cholesterol; HDL-c: high-density lipoprotein cholesterol; MMP: mean blood pressure; DBP: diastolic blood pressure; SBP: systolic blood pressure; iAUC: incremental area under the curve; AUC: area under the curve.

In a clinical study, 10 postmenopausal women who ingested 25 g/day of milled chia seed over a 7-week period showed increased plasma levels of alpha-linolenic acid (ALA) and docosahexaenoic acid (EPA) by 138% and 30%, compared to baseline levels, respectively (Jin et al., 2012). Also, the consumption of 35 g of chia flour/day by overweight and obese adults resulted in a reduction in total cholesterol and very-low-density lipoprotein cholesterol (VLDL-c), and an increase in HDL-c (Toscano, Toscano, Tavares, Oliveira, & Silva, 2015). Furthermore, 62 postmenopausal women had increased plasma levels of ALA and EPA after ingestion of 25 g/day milled chia for 10 weeks (Nieman et al., 2012).

In animal studies, chia consumption has resulted in better lipid redistribution associated with cardioprotection and hepatoprotection. This was observed in rats receiving a hyperlipidic and hyperglycemic diet, who also presented an inhibition of enzyme stearoyl-CoA 9-desaturase index in liver and heart (Poudyal, Panchal, Waanders, Ward, & Brown, 2012). Another investigation with rats also found improvement in dyslipidemia and insulin resistance induced by the consumption of a sucrose-rich diet (62.5%) after ingestion of chia seeds (Chicco, D'Alessandro, Hein, Oliva, & Lombardo, 2009). Wistar rats fed both conventional and thermally treated chia, had lower glucose concentrations, triacylglycerides, LDL-c, VLDL-c, and increased levels of HDL-c, hypertrophy of intestinal muscle layers, and good protein digestibility (da Silva et al., 2016b). Another study evaluated the effect of chia seed on rats fed a sucrose-rich diet in the long-term with consequent adipose tissue dysfunction. The authors observed that chia reduced epididymal fat and normalized dyslipidemia and insulin sensitivity induced by sucrose (de Souza Ferreira et al., 2015). In a separate study, a sucrose-rich diet and containing chia seed fed to Wistar rats for either 3 or 5 weeks reduced the epididymal fat, normalized dyslipidemia and insulin sensitivity (Rossi, Oliva, Ferreira, Chicco, & Lombardo, 2013). In this study, the consumption of chia by the animals prevented (3 months) or normalized (5 months) dyslipidemia, liver TAG, FAS, ACC (acetyl-CoA carboxylase), and G-6-PDH (glucose-6-phosphate dehydrogenase) activities and PPARa and SREBP-1 proteins levels. Also, chia seed increased fatty acid oxidase (FAO) and CPT-1 activities (carnitine-palmitoyl-transferase-1).

In a pregnant rats study in which corn oil was replaced by chia seed in a sucrose-rich diet, the offspring showed lower liver steatosis, hypertriglyceridemia, and hypercholesterolemia. Furthermore, CPT-1 and ACC enzyme activities and free fatty acid were reduced in the plasma of offspring from progenitors fed the chia seed containing diet (Fortino, Oliva, Rodriguez, Lombardo, & Chicco,

2017). Similarly, male rats that received chia seed instead of corn oil in the sucrose-rich diet improved heart lipotoxicity, increased FAT/CD36 (fatty acid transporter) proteins levels and M-CPT1 (muscle-type carnitine palmitoyltransferase 1) activity. In addition, there was a reduction in the PPARα proteins and plasma fatty acids (FAs) levels. Authors suggested that the normalization of dyslipidemia by chia was due to the prevention of translocation of FAT/CD36 that reduced the influx of FAs, decreasing elevation of M-CPT1 activity and lipid storage, thus improving glucose oxidation in cardiac muscles (Creus, Ferreira, Oliva, & Lombardo, 2016). Furthermore, the consumption of chia seed flour for 35 days reduced TC, LDL-c, and VLDL-c, but increased PPAR-α protein levels in Wistar rats fed with a high-fat diet (da Silva et al., 2019).

Antihypertensive

Together with dyslipidemias, hypertension or high blood pressure (BP) is one of the most important risk factors for CVDs (Fowokan et al., 2018). Some studies have shown a promising potential of chia seeds to reduce BP. In hypertensive adults, the consumption of 35 g/day of chia flour for three months reduced BP, lipid peroxidation, and plasma nitrite concentrations. These effects were attributed to a large amount of n-3 fatty acids in chia that exerted antioxidant and antiinflammatory effects (Toscano et al., 2014). Also, patients with type-2 diabetes had a reduction of systolic and diastolic pressure after consumption of 35 g/day of chia for a period of 12 weeks (Vuksan et al., 2009). However, some studies have not found a change in BP after treatment with chia seeds in humans (Nieman et al., 2009; Toscano et al., 2015).

In a study with pregnant rats in which corn oil was replaced by chia seed in a sucrose-rich diet, the offspring showed a lower incidence of hypertension, liver steatosis, hypertriglyceridemia, and hypercholesterolemia. These results were associated with a high concentration of the omega-3 in chia seeds (Fortino et al., 2017). Similarly, male rats that received chia seeds instead of corn oil in the sucrose-rich diet had, among other effects, normalization of blood pressure after 3 months of treatment (Creus et al., 2016). Male rats that received a high-fat and high-fructose diet, for 8 weeks plus 8 weeks with 5% of the diet with chia seeds as treatment, showed several benefits regarding markers of CVDs. In addition, there were improvements in insulin sensitivity and glucose tolerance, reduced visceral adiposity, decreased hepatic steatosis and reduced cardiac and hepatic inflammation and fibrosis, but there was no change in blood pressure (Poudyal et al., 2012).

Furthermore, chia seeds have shown a hypotensive effect by enzymatic analysis. The chia protein hydrolysate has the same blocking activity of angiotensin-converting enzyme I (ACE-I) as done by synthetic ACE-I inhibitors. The authors of this study observed that the hydrophobic residues of chia protein had a similar action to that of synthetic ACE-I inhibitors, likely because they block the production of angiotensin II (Segura Campos, Peralta González, Chel Guerrero, Betancur Ancona, & Betancur Ancona, 2013). In addition, the C-terminal amino acids were believed to be responsible for the higher inhibitory ACE activity (Segura-Campos et al., 2013).

Anthropometrics

Due to the composition of chia, high in dietary fiber and low in carbohydrates, this seed has demonstrated the ability to increase satiety and reduce the desire to eat (Ayaz et al., 2017; Vuksan et al., 2017a). These observations can be associated with other results that have demonstrated that the consumption of 30 g/1000 kcal of chia seed during six months by overweight and diabetic adults resulted in weight loss, reduction of waist circumference and C-reactive protein and increase in adiponectin (Vuksan et al., 2017b). Moreover, overweight and obese adults who received 35 g/day for 12 weeks had reductions in weight and percent fat (Toscano et al., 2015).

However, in one other study, overweight adults who consumed 25 g/day of chia did not have a reduction in their body mass index, waist circumference, or insulin resistance (Nieman et al., 2009). Also, the consumption of 35 g/day of chia seed by overweight adults for 12 weeks did not promote any significant change in body mass index or waist circumference (Toscano et al., 2014). Similarly, individuals with type 2 diabetes who consumed 37 g/day chia did not have changes in body weight (Vuksan et al., 2007). Furthermore, 62 postmenopausal women had no changes in their body composition after consumption of 25 g/day milled chia for 10 weeks (Nieman et al., 2012).

In a Wistar rat experiment in which soybean oil and cellulose contained in a standard basal diet were replaced by chia flour and heat-treated or untreated chia seeds, experienced weight loss as compared to the group of animals consuming the standard control diet (da Silva et al., 2016b). However, in another investigation, chia flour did not reduce the weight of Wistar rats fed with a high-fat diet (HFD) (da Silva et al., 2016a; Marineli et al., 2015a). It has also been reported that chia seed consumption for 13 months increased the body weight in rats as compared to a control group (Montes Chañi et al., 2018; Poudyal et al., 2012). Although chia seeds increased the weight in rats fed a HFD, it also reduced the visceral adiposity index and decreased the retroperitoneal and omental fat depositions (Poudyal et al., 2012).

Hypoglycemic

High levels of glycemia in blood can activate pathways related to overproduction of reactive oxygen species that induce a biochemical cascade resulting in increased inflammation and endothelial dysfunction. These conditions are associated with the development of diseases such as diabetes and cardiovascular problems (Nazarian-Samani, RDE, Lorigooini, & Rafieian-Kopaei, 2018).

In an acute study, healthy adults who consumed 25 g of ground chia, together with a glucose challenge, had a reduced blood glucose area under the curve (AUC) over 120 min and a reduction of peak glucose and increased time to peak compared with the control (Vuksan et al., 2017a). Also, ground and whole chia were incorporated in bakery products (7, 15, and 24 g) and consumed by healthy individuals after 10 to 12 hr of fasting, and there were reduced blood glucose incremental areas under the curve (iAUC) as compared to the control (Ho et al., 2013) and postprandial glycemia (Vuksan et al., 2010). However, individuals with type 2 diabetes who consumed 30 g/100 kcal chia for 6 months did not experience changes in glycated hemoglobin or fasting glucose (Vuksan et al., 2017b). Similar results were observed in overweight or obese individuals who ingested, for 12 weeks, 35 g/day chia flour (Toscano et al., 2015) or 25 g/day chia seeds (Nieman et al., 2009). Furthermore, consumption of 25 g/day of chia seed by postmenopausal women over 10 weeks did not show any effects on serum glucose (Nieman et al., 2012). These results demonstrate a positive action of chia in acute studies, but not in chronic studies in humans.

In animal studies, both, chia seed and chia flour (heat-treated and untreated), reduced plasma glucose in normal Wistar rats after 14 days of treatment (da Silva et al., 2016b). In one of these

studies, a group of animals received a HFD together with chia flour for 12 weeks (prevention group). The other group was fed initially only a high-fat and high-fructose (HFF) diet for 6 weeks, followed by an additional 6 weeks with HFF diet containing chia seed (treatment group). On the final day of the study, the consumption of chia seeds had improved glucose and insulin tolerance for both groups, prevention and treatment (Marineli et al., 2015b). These results may be associated with the expression of HSP70, HSP25 (heat shock proteins) and peroxisome proliferator-activated receptor-g coactivator-1a (PGC-1a) in skeletal muscle. Both of these proteins protect against insulin intolerance, increase control of energy homeostasis and glucose metabolism (Marineli et al., 2015b). Similar results were observed in Wistar rats fed with a high-fat and high-carbohydrate diet and 5% of chia seeds during 8 weeks in comparison with a control group (Poudyal et al., 2012).

Proteins from Chia (*Salvia hispanica* L.)

Nutritional quality

Proteins from animal sources are of good quality, but costly, and in some individuals can cause allergies or intolerances, such as egg or milk proteins. Plant proteins can be a good source of essential amino acids, complementing or even replacing animal sources (Montoya-Rodríguez, Gómez-Favela, Reyes-Moreno, Milán-Carrillo, & González de Mejía, 2015; Sandoval-Oliveros & Paredes-López, 2013). The chia seed contains around 19% protein, and therefore it is considered a good source of this nutrient (Table 1). The protein concentration is greater than that found in other traditional grains, such as wheat (14%), barley (9.2%), oats (15.3%), corn (14%), and rice (8.5%) (Monroy-Torres, Mancilla-Escobar, Gallaga-Solórzano, Medina-Godoy, & Santiago-García, 2008).

Moreover, chia protein has a good digestibility (78.9%), similar to that of casein (88.6%) (Sandoval-Oliveros & Paredes-López, 2013) and beans (77.5%), and higher than maize (66.6%), rice (59.4%), and wheat (52.7%) proteins (Betancur-Ancona, Gallegos-Tintoré, & Chel-Guerrero, 2004), but less than amaranth (90%) (Grobelnik-Mlakar, Turinek, Jakop, Bavec, & Bavec, 2009). The digestibility value of chia protein is a general indicator of the nutritional quality of its proteins, and it may be associated with their chemical structures which make them more or less susceptible to proteolytic enzymes (López, Galante, Robson, Boeris, & Spelzini, 2018).

Chia seeds contain all essential amino acids for human nutrition: isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, histidine, and valine (Sandoval-Oliveros & Paredes-López, 2013). Among all amino acids, glutamine is in highest concentration and histidine is the least present. The chemical score of chia seeds is 100% satisfactory for the sulfur amino acids and the coverage for the remaining essential amino acids ranges from 52% to 76%. The content of essential amino acids in seed flour varies from 66% to 126%. Lysine is the limiting amino acid with the lowest coverage of requirement (Table 3) (FAO/WHO/UNU, 2008; Sandoval-Oliveros & Paredes-López, 2013).

Seed proteins can be classified based on different criteria such as function and differential solvent solubility, among others. The storage proteins are those proteins which are present to supply intermediary nitrogen compounds for biosynthesis at a metabolically active stage of seed development (López et al., 2018). The main storage proteins present in chia are prolamins, glutelins, albumins, and globulins, the latter two are found in greater quantity than the others (Kačmárová, Lavová, Socha, & Urminská, 2016; Orona-Tamayo et al., 2015; Sandoval-Oliveros & Paredes-López, 2013).

Table 3–Amino acid composition of chia seed and contribution of essential amino acids with requirement patterns for infants and adults.

Amino acid	Content in the seed flour (mg/g raw protein)	Contribution of essential amino acids (%)			
		Infants (0.5-1 year)		Adults (>18 years)	
		RP	% CR	RP	%CR
Aspartate	47.3 ± 0.9				
Glutamine	70.8 ± 1.1				
Serine	26.2 ± 0.3				
Glycine	22.8 ± 0.7				
Arginine	42.3 ± 0.4				
Alanine	26.8 ± 0.3				
Proline	19.9 ± 0.7				
Histidine	13.7 ± 0.1	20	69	15	91
Threonine	18.0 ± 0.2	31	58	23	78
Valine	25.5 ± 0.4	43	66	39	73
Methionine + cysteine	27.8 ± 0.5	28	99	22	126
Isoleucine	24.2 ± 0.4	32	76	30	81
Leucine	41.5 ± 0.6	66	63	59	70
Phenylalanine + tyrosine	38.8 ± 0.5	52	75	38	102
Lysine	29.9 ± 0.5	57	52	45	66

RP = requirement patterns (mg/g raw protein) (FAO/WHO/UNU, 2008); CR = coverage of requirement for that specific essential amino acid in percentage according of age. Source: Adapted by Sandoval-Oliveros, Paredes-Lopéz, 2013.

The amount of protein may vary according to the botanical source, plant variety, preparation of the meal, extraction method, and other factors (Vázquez-Ovando et al., 2010). The protein fractions in chia seed have been shown to contain mostly 11S and 7S proteins whose molecular sizes range from 15 to 50 kDa, under native conditions. The presence of the globulins 7S and 11S in ingredients may confer nutritional and physiological characteristics to foods that are dependent on their structural sequence and physicochemical properties (Sandoval-Oliveros & Paredes-López, 2013).

The denaturation temperatures of crude albumins, globulins, prolamins, and glutelins are 103, 105, 86, and 91 °C, respectively, thus indicating an excellent thermal stability for albumins and globulins (Sandoval-Oliveros & Paredes-López, 2013). The stability at high temperatures can be an indicator of hydrophobic bonds between the amino acids that make up the proteins, since hydrophobic interactions are entropy-driven and endothermic; they are stabilized at a high temperature (60 to 70 °C), but destabilized at a low temperature (Olivos-Lugo et al., 2010). Moreover, the denaturation peak temperature (T_d) has been reported as single and high (97°C), but the thermal stability of chia proteins was improved (108.6°C) when it interacted with chia seed gum by complex coacervation (Timilsena, Adhikari, Barrow, & Adhikari, 2016).

Chia protein isolates showed a good water-holding capacity, which is the amount of water withheld by the hydrated protein after having applied an external force. Isolates also have an excellent oil-holding capacity, which is the union of fat by means of the lateral nonpolar protein chains. These characteristics indicate the presence of hydrophobic amino acids and demonstrate the possibility of using chia in emulsions and bakery products (Olivos-Lugo et al., 2010).

Identified proteins from chia seeds

Twenty proteins from chia seeds have been identified in the literature based on their amino acids sequences (www.uniprot.org). Twelve of these proteins are responsible for the metabolic functions needed for the existence of the seed: as metabolism, cell division, and pathways. Eight proteins are related to lipid

Table 4–Proteins identified from chia seed (*Salvia hispanica*).

Protein	ID	Sequence	AAR	MW
Ribulose bisphosphate carboxylase large chain	Q36769	MSPQTETKASVGFKAGVKEYKLTYYTPEYETKDTDILAAFRVTPQPGVPPEEAGAAV AAESSTGTWTTVWTDGLTSLDRYKGRCYHIEPVPGEKDQYICYVAYPLDLFEEGSVT NMFTSIVGNVFGFKALRALRLEDLRIPVAYVKTFQGPPHGIQAERDKLNKYGRPLLG CTIKPKLGLSAKNYGRAVYECLRGGLDFTKDDENVNSQPFMRWRDRFLFCAEAIYKS QAETGEIKGHYLNATAGTCEEMMKRAIFARELGVPIVMHDYLTGGFTANTSLAHYCR DNGLLLHIHRAMHAVIDRQKNHGMHFRVLAKALRLSGGDHIHSGTVVGKLEGERDIT LGFVDLLRDDFVEKERSRGIYFTQDWVSLPGVIPVASGGIHVWHMPALTEIFGDDSV LQFGGGTLGHPWGNAPGAVANRVAVEACVLARNEGRDLAAEGNAIIREACKWSPELA AACEVWKEIKFEFPAMD	473	52,390
Oleosin	A0A0F6PN28	MADQHYGQFQSRPHHLQQHHPRSHQMVKAATAVTAGGSLLVLSGLTLAATVIALTIAT PLLVIFSPVLVPAALAVFALAGGFLASGGFGVAALSVLSWIYKYMTGKHPVGADQLDT ARTKLAGKARDMKDRVDHNVSVAQSS	142	14,894
Fatty acid desaturase 3 isoform 2	A0A1Z1EC60	MAVSSGADAEHHGHAQYEHLGKRAADKFDPAAPPPFKIADIRAAIPPHCWVKDPLRSL SYVAWDVFVVAALLAAAAFFDSWIFWPIYWAAQGTMFWALFVLGHDCGHGSFSDNTTL NNVVGHVLHSSILVPYHGWRISHRTHHQNHGHVENDESWVPLTENLYKQLDFSTKFLR YKIPFPMFAYPLYLWYRSPGKSGSHFNPYSSLFKPNERDLVITSTICWAAMVACLLYA STIVGPTMLFKLYGVPYLIFVVWLDTVTYLHHHGYDKKLPWYRSKEWSYLRGGLTTVD QDYGIFNKIHHDIGTHVVHHLFPQIPHYHLVEATREAKRVLGNYYREPRKSGAVPFHL VPTLLKSLSRDHYVSDNGDIVYYQTDGELFSSKEI	386	43,983
Fatty acid desaturase 3 isoform 1	A0A1Z1EC53	MAVSSGARLSESGAEGGEPYAGQCEHLEGIGKRAADKFDPAAPPPFKIADIRAAIPPH CWVKDPLRSLSYVAWDLIAVAALLAAAAYFDSWIFWPIYWAAQGTMFWALFVLGHD CGHGSFSDSTTLNNVVGHILHSSILVPYHGWRISHRTHHQNHGHVEKDESWVPLPE NLYKQLDFSTKFLRYKIPFPMFAYPLYLWYRSPGKTGSHFNPDSSLFKPNERDLVI TSTVCWAAMVAFLLYASTIVGPTMLFKLYGVPYLIFVVWLDTVTYLHHHGYDKKLP WYRSKEWSYLRGGLTTVDQDYGIFNKIHHDIGTHVIHHLFPQIPHYHLVEATREAK RVLGNYYREPRKSGPVPFHLIPTLLKSLSRDHYVSDNGDIVYYQTDSQLFSS KEI	393	44,873
Fatty acid desaturase 7 isoform 1	A0A1Z1EC64	MASWVLSGCGLKPLPRIYPMPRTVSSPNPSKLRISTADFSSDSSSLCSVGRGRNWGL NVSAPLRFQEVGEEENEERESEVVNGFGGGDGFDPGAPPPFKLADIRAAIPKHCWVK NPWKSMSYVVRDVAVVFGLAAAAAYLNNWAVWPLYWFAQGTMFWALFVLGHDC GHGSFSNDPKLNSVAGHLLHSSILVPYHGWRISHRTHHQNHGHVENDESWHPLSEK IYKQLDFVTKKLRFTLPFPMLAYPIYLWSRSPGKKGSHFHPDSDLFVPNERKDVIT STVCWTAMVAILAGLSFVMGPLQLLKLYGIPYFGFVAWLDLVTYLHHHGHEDKLPW YRGKEWSYLRGGLTTLDRDYGWINNIHHDIGTHVIHHLFPQIPHYHLIEATEAAKP VLGKYYKEPQKSGPLPLYLLGVLAKSMKKDHYVSDTGDI VYYQTDPKLN	440	49,789
Fatty acid desaturase 8	A0A1Z1EC52	MASFVISGCGLKPLPRIYPKPRSVQNSFSTSNLRISRPNQFSSSSIGINQKRNWGLGVSAP LRIQPLEEENEEFDPAAPPPFKLSDIKAAIPKHCWVKDPWRSVGYVVRDVVAVLGMA AAAAYFNSWIVWPLYWFAQSTMFWALFVLGHDCGHGSFSNNPKLNSVFGHFLHSSIL VPYHGWRISHRTHHQNHGHVENDESWHPMPEKIYNSLDSMAKKLRFTLPFPMLAYPI YLWTRSPGKKGSHYHPDSDLFVPAERKDVITSTVCWTAMAALLVGLSFVMGPIQLLK LYGIPYLGFVAWLDTVTYLHHHGHEDKLPWYRGKEWSYLRGGLTTLDRDYGLINNIH HDIGTHVIHHLFPQIPHYNLIEATEAAKGVLGKYYREPKKSGPLPLHLLGDLVRSLK KDHYVSDTGDVVYYQTDPQLNGGQKS	429	48,721
Fatty acid desaturase 2 isoform 2	A0A1Z1EC55	MGAGGRMSVPPAEKAAKSDIVQRVPHTKPPFTLGDIKKAIPPHCFKRSIPRSFSYVVY DLVFASLFYYVATNYIHQLPHPLSYPAWILYGICQGCILTGVWVIAHECGHHAFSDYQ WLDDTVGLILHSFLLVPFFSWKYSHRRHHSNTGSLERDEVFVPKVKTGVSWAAKYMNN PPGRLITLVVQLTLGWPLYLMFNVSGRPYDRFACHFDPNSPIYSDRERAQIFISDAGI LAVTYGLYRLSVAKGLAWVLCVYGGPLLVVNGFLVLITFLQHTHPSLPHYDSSEWDWL RGALSTVDRDYGILNTVFHNITDTHVAHHLFSTMPHYHAMEATKVIKPILGKYYQFDG TPVFKAMFREVK ECIYVEPDEG EENKGVFWYN NKL	383	43,717
Fatty acid desaturase 2 isoform 1	A0A1Z1EC46	MGAGGRMSVPPADKKAKSDVIQRVPHAKPPFTLG EIKKAIPPHCFKRSIPRSFSYVVYDLIIASLFYYVATNYIHQLPQPLSYLAWTLYG ICQGCILTGVWVLAHECGHHAFSDYQWLDDTVGLILHSFLLVPYFSWKYSHRRHHS NTGSLERDEVFVPKVKSGVSWTAKYMNNPPGRVITLIVQLTLGWPLYLMFNVSGRP YDRFACHFDPKSPIYSDRERAQIFISDAGILAVLYGLYRMSVAKGLAWVLCVYGGP LLVVNGFLVLITFLQHTHPALPHYDSSEWDWLRGALATVDRDYGILNTIFHNITDT HVAHHLFSTMPHYHAMEATKAIKPILGKYYQLDETPVFKAMFREVK E CIYVEPDEG EENKGVFWYN NKL	383	43,788
Monoacylglycerol acyltransferase	AJW67342.1	MSPENPSNFWGDTPEEEYYASQGVRNSKSYFDSP HGRLFTQSFLPLDPTRPVKASVFMTHGYGSDSSWMFQKFCISYAAWGYAVFAADML GHGRSDGIRCYMGDLPKVAAASLAFFRSVRVSDEYKDLPAFLVGESMGGLATLLMY FQSEKDLWTGLIFSAPLFVIPESMMPSKVHLFAYGMLFGLADTWAAMPDNKMVGKA IKDPEKLKVIASNPMRYTGKPRVGTMRELLRQTEYAQNNFDKVTIPFFTAHGTSDG LAEWSGSQMLYDKASSEDKTLKLYEGMYHSLIQGEPDENANLVLADMRAWIDERVE RYGKKN	320	36,009
Eukaryotic translation initiation factor 3 subunit E	A0A2R4LNR4	MASKYDLTPRIAPNLDRHLVFPLLEFLQERGLYPE EDILKAKIELLNHTNMVDYAMDIHKSLYHSDDVPQDMIDRRAEVVGRLKALEDGAAP LIGFLQNPNAVQELRADKQYNLQMLKDRYQIGPEQIDALYDYAKFQFECGNYSGAAD YLYQYRALCTNSDKSLSALWGKLAAEVLMQNWDIALEELNRLKEIIDSKNFSSPLNQ VQSRIWLMHWSLFIFFNHDNGRTQIIDLFNQDKYLNAIQTNAPHLLRYLATAFIVNK RRRPQFKEFIKVIQQEQYSHEDPITEFLACIYVNYDFDGAQKKMKECEEVILNDPFL GKRIEEGNFTTVPLRDEFLEPSYTNVYEQLIDHTKALSTRTYKIVHQLLENAPGQTA RCRIHQRIDMGVLADKLNLNYEEAERWIVNLIRTSKLEAKIDSKLGTIIME N ARLFIFETY	438	51,240

(*Continued*)

Table 4–Continued.

Protein	ID	Sequence	AAR	MW
S-adenosylmethionine decarboxylase proenzyme	A0A2R4LNQ8	MDMPVSAIGFEGYEKRLEISFVEPGVFADPDGYG LRALTKAQLDEILDPAQCTIVASLKNDDVDSYVLSESSLFVYSYKIILKTCGTTKL LLSIPPILRLADGLGLTVSSVRYSRGSFIFPGAQPFPHRSFNEEVAVLDDHFSKLG LMSEAYVMGDADEHEKWHVYSAYLEPSSDVEPVYTLEMCMTNLDQKKASVFFKNQS SSATIMTDASGIRNILPESEICDFDFDPCGYSMNSIEGGAVSTIHVTPEDGFSYAS FETGGYDFEKVDLTQLVERVLACFNPAKFSVAVRASIAGKELDSAFKLDIAKYGCA GRRCEVLGDGGSVIYCNFTSATGCGSPRSTLHLCWSESEDEEIEKK	360	39,453
Tubulin beta chain	A0A2R4LNR5	MREILHIQGGQCGNQIGSKFWEVICDEHGVDPTG RYKGDGSESDTQLERINVYFNEASGGRYVPRAVLMDLEPGTMDSIRSGPYGQIFRP DNFVFGQSGAGNNWAKGHYTEGAELIDSVLDVVRKEAENCDCLQGFQVCHSLGGGT GSGMGTLLISKIREEYPDRMMLTFSVFPSPKVSDTVVETYNATLSVHQLVENADEC MVLDNEALYDICFRTLKLSTPSFGDLNHLISATMSGVTCCLRFPGQLNSDLRKLAV NLIPFPRLHFFMVGFAPLTSRGQHYISLTVPELTQQMWDSKNMMCAADPRHGRYLT ASAMFRGKMSTKEVDEQMLNVQNKNNVKSSVCDIPPTGLKMSSTFVGNSTSIQEMF RRVSEQFTAMFRRKAFLHWYTGEGMDEMEFTEAESNMNDLVAEYQQYQD A TADEEEDYE EDGAEGEYEDSSYFVEWIPN	450	50,485
Peptidyl-prolyl cis-trans isomerase	A0A2R4LNR0	MSGNHMISIVIAMVCIGVFRGSITAIATVPELGS ARVVFQTNYGDIEFGFYHSVAPKTVEHIFKLVRLGGYNTNHFFRVD K GFVAQVADVGGGRTAPMNE VQRLEAEKTV VGEFSDV KHV RGILSMGRYSDPDSAQSSFSILLGDAPHLDGQYAIFGKVTKGD ETLSKMEEVPTRKEGIFVMPTERITIFSTYYYDTETESCEDDRLELKRRILASAVE I EKQRMKCFP	229	25,507
Serine/threonine-protein phosphatase	A0A2R4LNQ7	MPGHGDLDRQIEQLMECKPLSEAEVKILCDQARA ILVEEWNVQPVKCPVTVCGDIHGQFYDLIELFRIGGNAPDTNYLFMGDYVDRGYYS VETVTLLVALKVRYRDRITILRGNHESRQITQVYGFYDECLRKYGNANVWKFFTDL FDYLPLTALIESQVFCLHGGLSPSLDTLDNIRALDRMQEVPHEGPMCDLLWSDPDD RCGWGISPRGAGYTFGQDIAAQFNHTNGLTLISRAHQLVMEGFNWCQEKNVVTVFS APNYCYRCGNMAAILEIGEHME QNFLQFDPAP RQIEP DTTRK TPDYFL	306	35,001
Elongation factor 1-alpha	A0A2R4LNQ6	MGKEKIHISIVVIGHVDSGKSTTTGHLIYKLGGIDK RVIERFEKEAAEMNKRSFKYAWVLDKLKAERERGITIDIALWKFETTKYYCTVIDAPG HRDFIKNMITGTSQADCAVLIIDSTTGGFEAGISKDGQTREHALLAFTLGVKQMICCC NKMDATTPKYSKARYDEIIKEVSSYLKKVGYNPEKIPFVPISGFEGDNMIERSTNLDW YKGPTLLEALDAVQEPKRPSDKPLRLPLQDVYKIGGIGTVPVGRVETGVIKPGMVVTF GPTGLTTEVKSVEMHHEALQEALPGDNVGFNVKNVAVKDLKRGFVASNSKDDPAKEA ANFTSQVIIMNHPGQIGNGYAPVLDCHTSHIAVKFSELMTKIDRRSGKELEKEPKFLKN GDAGMVKMIPTKPMVVETFSQYPPLGRFAVRDMRQTVAVGVIKSVEKKDPSGAKV TKAAAKKGAK	449	49,408
Glyceraldehyde-3-phosphate dehydrogenase	A0A2R4LNR9	MAKIKIGINGFGRIGRLVARVALQRDDVELVAVN DPFITVDYMTYMFKYDSVHGQWKHHELKVKDEKTLLFGEKPVTVFGFRNPEEIPWA STGAEYIVESTGVFTDKDKAAAHLKGGAKKVVISAPSKDAPMFVVGVNEKSYTPDL DIVSNASCTTNCLAPLAKVINDRFGIVEGLMTTVHSITATQKTVDGPSAKDWRGGR AASFNIIPSSTGAAKAVGKVLPALNGKLTGMAFRVPTVDVSVVDLTVRLEKEATYD EIKAALKEESEGNLKGILGYTEDDVVSTDFVGDNRSSIFDAKAGIALSKNFVKLVS WYDNEW GYSTRVVDLI KHIHSTQ	337	36,706
Actin	A0A2R4LNQ3	MADAEDIQPLVCDNGTGMVKAGFAGDDAPRAVF PSIVGRPRHTGVMVGMGQKDAYVGDEAQSKRGILTLKYPIEHGIVSNWDDMEKIW HHTFYNELRVAPEEHPILLTEAPLNPKANREKMTQIMFETFNTPAMYVAIQAVLS LYASGRTTGIVLDSGDGVSHTVPIYEGYALPHAILRLDLAGRDLTDSLMKILTER GYMFTTTAEREIVRDIKEKLAYIALDYEQELETAKTSSAVEKNYELPDGQVITIG AERFRCPEVLFQPSMIGMEAAGIHETTYNSIMKCDVDIRKDLYGNIVLSGGSTMF PGIADRMSKEITALAPSSMKIKVVAPPERKYSVWIGGSILASLSTFQQMWIAKAE YDESGPS IVHRKCF	377	41,738
Clathrin adaptor complex	A0A2R4LNR7	MPLAASAIYFLNLRGDVLINRLYRDDVGGNMVD AFRVHIMQTKELGTCPVRQIGGCSFFYMRISNVYIVIVVSSNANVACAFKFVVEA VTLFKSYFGGSFDEDAIRNNFVLIYELLDEIMDFGYPQNLSPEILKLYITQEGVR SPFSSKTADKPVPNATLQVTGAVGWRREGLVYKKNEVFLDIVESVNLLMSSKGSV LRCDVTGKILMKCFLSGMPDLKLGLNDKIGLEKESQLKSRPAKSGKTIELDDVTF HQCVNLTRFNSEKTVSFVPPDGEFELMKYRITEGVNLPFRVLPTIKELGRTRMEV NVKVKSVFGAKMFALGVVIKIPVPKQTAKTSFQVTSGKAKYSPSIDCLVWKIRKF PGQTEPTLSAEVELISTITEKKSWTRPPIQMEFQVPMFTASGLRVRFLKVWEKSG YNTVEWVRYITK AGSYEVRC	438	49,311
Alpha-tubulin	A0A2R4LNS8	MISNNTAVAEVFSRIDHKFDLMYSKRAFVHWYV GEGMEEGEFSEAREDLAALEKDYEEVGAEGVDDEDDE GEDY	74	8,488
FtsH protease	A0A2R4LNS4	FDRNIVVPNPDVEGRRQILESHMSKVLKGEDVDIE IIARGTPGFSGAELANLVNVAAIKAAMDGAKAVSMADLEHAKDKIVMGSERKSAVIS DESRRNTAYHEGGHALVAMFTDGALPVHKATIVPRGNALGMVSQLPDKDQTSVSRKQ MLARLDVCMGGRVAEELIFGESEVTSGASSDLESATRMARSMVTRYGMSKQLGFVSH DYNDNGRSMSTETRLLIEQEVKDLLEKAYNNAKTILTTHSKELHALANELLDKETLT GAQVKALLENVKAQNTQ QQKQQQIVT	289	31,473

AAR = Amino acid residues; MM = Molecular mass (Da). Amino acid nomenclature: C, cys; cysteine; H, his; histidine; I, ile; isoleucine; M, met; methionine; S, ser; serine; V, val; valine; A, ala; alanine; G, gly; glycine; L, leu; leucine; P, pro; proline; T, thr; threonine; F, phe; phenylalanine; R, arg; arginine; Y, tyr; tyrosine; W, trp; tryptophan; D, asp; aspartic acid; N, asn; asparagine; B, asx; either of D or N; E, glu; glutamic acid; Q, gin; glutamine; Z, glx; either of E or Q; K, lys; lysine; X, undetermined amino acid. Protein sequence was obtained from UniProt database (http://www.uniprot.org).

production and storage (Table 4). The main functions of these proteins are described below.

Fatty acid desaturases. The desaturase enzymes are responsible of dehydrogenation reactions, they introduce a double bond between defined carbons of fatty acyl chains. These enzymes can be soluble and are found in the plant plastid acting as acyl–acyl carrier protein desaturases (Dar, Choudhury, Kancharla, & Arumugam, 2017; Sharma & Chauhan, 2012).

The seed-specific delta-12 fatty acid desaturase 2 (FAD2) is a bifunctional hydroxylase/desaturase and tri-functional acetylenase

responsible for inserting a double bond at the delta-12 position of oleic acid, thereby producing linoleic acid (omega-6). The FAD2 is a multifunctional enzyme that acts in the biological membrane systems: signaling, energy storage, thermal adaptation, and resistance to biotic and abiotic stresses in plants (Sharma & Chauhan, 2012). The fatty acid desaturases 3, 7, and 8 (FAD3, FAD7, FAD8) are key enzymes responsible for producing α-linolenic acid (ALA), also called omega-3 in plants. The FAD3 catalyzes the introduction of a third double bond at the delta-15/ omega-3 carbon position of linoleic acid in the endoplasmic reticulum, and the FAD7 and FAD8 in plastids (Xue et al., 2018). Fatty acid desaturases 2 (FAD2) and 3 (FAD3) are the main enzymes responsible for the delta-12 and delta-15 desaturation in plants (Radovanovic, Thambugala, Duguid, Loewen, & Cloutier, 2014). The FAD 2, 3, 7, and 8 are different by nucleotide and amino acid sequences of the conserved region (Dehghan Nayeri & Yarizade, 2014).

Monoacylglycerol acyltransferase (MGAT). The lipids produced by FAD are organized into molecules as triacylglycerol (TAG) formed by several enzymes. First, the glycerol-3-phosphate is acylated by G3P acyltransferase (GPAT) in two free hydroxyl positions to produce lysophosphatidic acid (LPA). This one is acylated by LPA acyltransferase (LPAT), producing phosphatidic acid (PA). Both, LPA and PA, can be dephosphorylated to monoacylglycerol (MAG) and diacylglycerol (DAG). MAG is converted to DAG by MAG acyltransferase (MGAT) that transfers an acyl moiety from acyl-CoA to MAG. Finally, DAG is then acylated by DAG acyltransferase (DGAT) to produce TAG (Sreedhar, Priya, Sunny, Ram, & Malathi, 2015; Vijayaraj et al., 2012).

The MGAT can be soluble, as above, or associated with oleosin. In this case, MGAT has a role to form TAG that will be stored in oleosin (Sreedhar et al., 2015). Because of this, MGAT can have a role in preserving unsaturated fatty acids in plants, such as *Ricinus communis, Brassica napus*, and maize (Baud & Lepiniec, 2010). While DAG is a signaling molecule and an intermediate for the synthesis of neutral and membrane lipids, the MGAT pathway may operate for storage purposes. Also, it has been demonstrated that MGAT activity is more evident with unsaturated than saturated fatty acids (Vijayaraj et al., 2012).

Oleosin. In plants, more specifically in seeds, the triacylglycerol (TAG) is typically stored in lipid droplets that are stabilized by associated proteins, as oleosins (Winichayakul et al., 2013). Oleosins contain the amphipathic N- and C-terminal domains exposed to cytosol, and a hydrophobic central domain formed by a long chain of non-polar amino acids. This structure stabilizes the lipids inside the cells, protecting, for example, against phospholipases and desiccation (Huang, 2017).

Chia seeds have a high concentration of lipids, on average 31%, and the main type of fatty acid found in chia seed is the omega-3 (around 20%), followed by omega-6 (about 6%) (da Silva et al., 2017). This seed is one of the most efficient omega-3 sources for enriching foods, its proportion of omega-3:omega-6 is the highest among crop sources (Segura-Campos et al., 2014). The high concentration of omega-3 fatty acid desaturases (FAD3, FAD7, and FAD8) and the presence of oleosin and MGAT may be responsible for the elevated production and storage of omega-3 in chia seed.

Ribulose bisphosphate carboxylase large chain. Ribulose-1,5-bisphosphate carboxylase/oxygenase (RuBisCO) is a bifunctional multimeric plant metabolic enzyme that converts carbon dioxide from the biosphere into organic carbon in a rate-limiting step of the Calvin cycle and photorespiration, depending on its affinity for carbon dioxide or molecular oxygen (Andersson & Backlund, 2008). The RuBisCO structure is a heterohexadecamer with eight large subunits with high molecular weight, and eight small subunits with low molecular weight. In chia, only large chains have been detected (Table 4) (Udenigwe et al., 2017). This enzyme is made up of about 50% soluble proteins in the plant leaf and can be found in autotrophs, including bacteria and algae; RuBisCO is the most abundant protein on earth (Andersson & Backlund, 2008).

RuBisCO is a good source of bioactive peptides that have demonstrated beneficial effects for health promotion both *in vitro* and *in vivo* (Udenigwe et al., 2017). Rubiscolin, a δ-opioid peptide with sequence YPLDLF shows a memory-consolidating effect, since it is blocked by naltrindole and raclopride, antagonists of the δ-opioid receptor and dopamine D2-receptor, respectively (Yoshikawa, 2015). Rubiscolin also shows anorexigenic effects (Kaneko et al., 2014).

Eukaryotic translation initiation factor 3 subunit E. This protein is required for some steps in the initiation of protein synthesis and it is required for the disassembly and the recycling of post-termination ribosomal complexes. Also, the "eukaryotic translation initiation factor 3 subunit E" is involved in the pathway of cell proliferation (Consortium, 2017)

S-adenosylmethionine decarboxylase proenzyme. It is a key rate-limiting enzyme in the polyamine biosynthesis required for plant growth, development, and protection in response to stress (Gupta, Yadav, Raj, Freilich, & Varadwaj, 2017).

Alpha and beta tubulin chain. This protein is the major constituent of microtubules, responsible of several cell functions, such as mitosis, cell expansion and division, and movement of organelles and vesicles. It binds two moles of GTP, one at an exchangeable site on the beta chain and one at a non-exchangeable site on the alpha chain (Chu et al., 2018).

Peptidyl-prolyl cis-trans isomerase. This ubiquitous enzyme is found in all kingdoms of life, responsible for catalyzing a rate-limiting step in the protein-folding by *cis-trans* isomerization of proline peptide bonds (Consortium, 2017; Thongnak et al., 2017).

Serine/threonine-protein phosphatase. In plants, many cellular functions are controlled by the phosphorylation and dephosphorylation of target proteins by the serine/threonine-protein phosphatase family. These proteins are involved in a variety of biological processes, such as transcriptional control, cell cycle regulation, and signal transduction (Park et al., 2011).

Elongation factor 1-alpha. During protein biosynthesis, this protein promotes the GTP-dependent binding of aminoacyl-tRNA to the A-site of ribosomes. Also, this protein can be part of messenger ribonucleoprotein particle (mRNP) complexes, part of the valyl-tRNA synthetase complex, bind to actin, to be associated with the endoplasmic reticulum or the mitotic apparatus, and to be involved in protein degradation or ribosome association (Consortium, 2017).

Glyceraldehyde-3-phosphate dehydrogenase. This protein is involved in the glycolysis pathway by synthesis of pyruvate from D-glyceraldehyde 3-phosphate. Also, GAPDH has roles in plant development, abiotic stress, and immune responses in plants (Zeng et al., 2018).

Actin. This protein is part of the cellular cytoskeleton and acts in cell division and expansion, vesicle trafficking, organelle movement, and cell growth (Paez-Garcia, Sparks, de Bang, & Blancaflor, 2018).

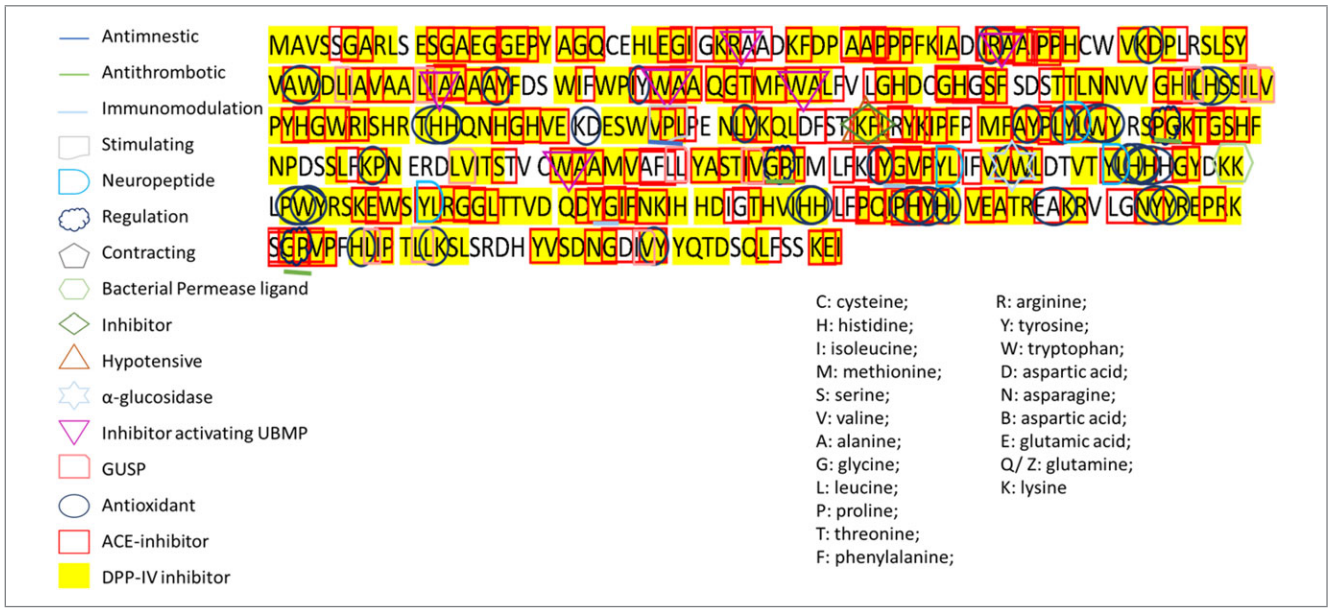

Figure 3–Bioactivity effect map of FAD3i.

Clathrin adaptor complex. This is a complex of proteins that regulates of the movement of proteins and lipids between the cellular membranes and has a role in the signaling and homeostasis, defining the interactions of cells with their surroundings (Jackson et al., 2010).

FtsH protease. It is an inner membrane-embedded zinc-dependent metalloprotease, involved in the egradation and assembly of protein complexes in the photosynthetic electron-transport pathways, and it acts on chloroplast manutention (Kato & Sakamoto, 2018).

Analysis of Bioactive Peptides from Chia Seed Proteins

Bioactive peptides are inactive within the sequence of the parent protein from plants, animals, or marine foods. However, after fermentation, enzymatic, chemical hydrolysis, or gastrointestinal digestion, peptides can be released (Meisel, 1997; Udenigwe & Aluko, 2012). On the other hand, peptides formed by gastrointestinal digestion, may act as regulatory compounds with hormone-like activity, as well as hypotensive, hypocholesteremic, anticancer, immunomodulatory agents, among others (Cicero, Fogacci, & Colletti, 2017). Thus, peptides represent potential health-enhancing nutraceuticals for food and pharmaceutical applications (Meisel, 1997).

For this review, all protein sequences, including the protein related to lipid and general metabolism in chia seed had their profile of active peptides evaluated using the database BIOPEP (http://www.uwm.edu.pl/biochemia). Each protein showed many effects and, as an example, Figure 3 shows the bioactivity effect map of FAD3i1. The results presented in Figure 4 were calculated as follows:

$$\%\,\text{occurrence of frequency} = \frac{\text{n° amino acids of each bioactive effects}}{\text{total n° of amino acids with bioactive effects}}$$

The peptides found demonstrated mainly hypoglycemic and hypotensive activity, since most of them presented dipeptidyl peptidase IV (DPP IV inhibitor) and angiotensin-converting-enzyme (ACE) inhibitor activities, respectively (Figure 4, Tables 5 and 6).

The antioxidant effect and the glucose uptake stimulating peptide (GUSP) had a high occurrence of frequency (5.9 and 2.7%, respectively). The other effects, for example, antimnestic, stimulating vasoactive substance release, neuropeptides, and immunomodulating had a frequency of occurrence of less than 1% (Figure 4).

The number of studies using isolated peptides from chia are limited but show beneficial promising health effects. A protein hydrolysate from chia seed, produced by enzymatic hydrolysis, with alcalase and/or Flavourzyme, demonstrated antibacterial activity, reducing the velocity of enzymatic reaction of and 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase) (Coelho et al., 2018). The chia protein hydrolysate has also shown ACE-inhibitory and antioxidant activities (Chim-Chi, Gallegos-Tintoré, Jiménez-Martínez, Dávila-Ortiz, & Chel-Guerrero, 2018; Segura Campos et al., 2013; Segura-Campos et al., 2013). In another study, peptides with molecular weight <15 kDa were produced from a chia seed coproduct, generated during oil production, by digestion with papain. Peptides showed a potent radical scavenging effect against 1,1-diphenyl-2-picrylhydrazyl (DPPH) and 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS) radicals in comparison with non-digested samples (Cotabarren et al., 2019).

The simulated digestion of chia to produce protein hydrolysates and, consequently, peptides, can be performed with such enzymes as alcalase and Flavourzyme. These are commercial enzymes obtained from bacteria, for example, *Bacillus amyloliquefaciens.* They act by interacting with peptide bonds through a serine residue at the active site (Ottesen & Svendsen, 1970). However, digestion with the enzymes trypsin, chymotrypsin, and pepsin demonstrates a hydrolytic physiological process, since the human gastrointestinal system produces such enzymes. This allows to evaluate the production of the bioactive peptides after normal consumption of food proteins (Udenigwe & Aluko, 2012). These enzymes, under optimum pH and temperature conditions, break the bonds between specific amino acids and release peptides and free amino acids that can be absorbed (Gardner, 1984).

Table 5—Identification of peptides in metabolic proteins from chia seed.

Bioactive Potential	RuBisco	ELF-3e	AdoMetDC	TBc	PPctl	STPp	EF1a	GAPH	Actin	CAdC	a-tubulin	Ftsh
Antiamnestic	PG, GP	VPL, PG, GP	PG	PG, GP	–	PG	PG, GP	GP	PG, GP	PG	–	PG
Antithrombotic	GP, PG	GP, PG, NQDK	PG, DEE	GP, PG, DEE	–	PG	GP, PG	GP	GP, PG	PG	–	–
Immunomodulating	YG	EAE	YG	YG, EAE	YG, EAE	YG, EAE	KRP	–	YG	–	–	YG
Stimulation	EEE, SSS, EE	VPL, EE	SSS, EE, SE	EEE, EE, SE	–	EE, SE	SE	EE, SE	EE	SE	EE, SE	EE, SE
Neuropeptide	GQ	GQ, YL	YL	GQ, YL	GQ	GQ, YL	GQ, YL	GQ	GQ	GQ	–	–
Regulation	DY, GP, PG	GFL, GLY, DY, GP, PG	PG	DY, GP, PG	–	DY, PG	GP, PG	LGY, DY, GP	DY, PG, GP	PG	DY	DY, PG
Contracting	PLRP	–	–	–	–	–	–	–	–	–	–	–
Bacterial permease ligand	KK	KK	KK	–	–	–	KK	KK	–	KK	–	–
Inhibitor	EF	IR, KF, EF	IR, KF	IR, KF	EF	IR, KF	KF	–	IR	IR, KF, EF	KF, EF	–
Hypotensive	EF	IR, KF, EF	IR, KF	IR, KF	EF	IR, KF	KF	–	IR	IR, KF, EF	KF, EF	–
α-glucosidase inhibitor	VW	–	–	–	–	VW	–	–	VW	VW	–	–
activating UBMP	LA, WA	RA, LA	RA, LA	RA, LA, WA	LA	RA	LA	RA, LA, WA	LA	LA	RA, LA	LA
GUSP	VL, LV, IV, IL, LI, LL	VL, LV, IV, IL, LI, II, LL	VL, LV, IV, IL, LL	VL, LV, IL, LI, LL	LV, IV, IL, LL	LV, IL, LI, LL	VL, LI, II, LL	VL, LV, IV, IL, LI, II, LL	VL, IV, IL, LL	VL, LV, IV, IL, LI, LL	–	VL, LV, IV, IL, LI, II, LL
Antioxidant	LHH, LH, HL, HH, AY, LY, IY, WY, IHH, HYH, THH, YYQ, VYY, LHL, LWT, PHY, PWY, KD, PW, LKP, LK, KP, TY, VY, VW, LW, WG	HL, LY, IY, EL, YDY, YQY, LWG, RHL, RWI, EAK, KVI, KD, RW, IR, LK, TY, VY, LW, LLR, GAA, WG, LAC	LH, HL, AY, IY, EL, YSY, LHL, PHR, YVL, IR, LK, VY	LH, EL, LHF, LHI, LHW, IR, LK, TY, VY, MM	HL, EL, YYD, YYY, TYY, PHL, LK, TY	LH, GYY, AH, EL, YYS, YCY, LHG, LWS, PHE, IR, KP, VY, VW, LW, WG, FC	HL, HH, IY, EL, MHH, KYY, YYC, LWK, KD, LK, KP, VY, AW, LW, QYP	HL, HH, AH, EL, WY, HIH, KHH, PWA, KVI, KD, PW, LK, KP, TY, GAA	HH, AY, LY, IY, EL, WHH, PHA, RHT, MY, KD, IR, LK, TERGY, WDDMEK, LDY, VW, YVGD	LY, IY, EL, IR, LK, KP, VY, VW, CLV	WY, MY, KD	LH, AY, EL, LARL, KD, LK
ACE inhibitor	IYP, PLP, LKL, AAP, AKK, LY, IY, VF, LW, VW, YW, VY, HY, FP, LVR, GY, PR, YL, LF, YG, LAY, AY, LA, KR, VP, AA, GF, VG, IG, GI, GM, GL, GH, HL, KG, FG, GS, GV, MG, GQ, GK, WG, HG, GG, SG, LG, GF, TG, EA, NG, PG, VR, VAV, GHF, QK, SY, SF, KY, KL, KA, IPY, KP, RIY, IE, VE, LN, PPPQ, EW, EK, KE, HP, PH, IQP, FVP, AV, LEE, GSH, LPF, AVL, DY, YV, IL, YH, WA, WL, MGP, SGP, RG, ST, YN, GHG, LR, LGV	RL, IR, RY, LY, IY, LW, VY, FP, PR, LAA, YL, LF, FNQ, YP, GP, PL, IW, LYP, YQY, PSY, IA, LKA, RW, RP, AF, AP, LA, KR, VP, RA, YA, AA, GF, IF, IG, GA, GL, HL, GR, DA, MG, GQ, GK, GT, WG, SG, LG, EG, EA, NG, PG, LRY, QK, DG, NY, NF, SY, KY, KF, KL, YK, NK, RR, AR, KA, IAP, EI, IE, EV, LQ, LN, TQ, PQ, ME, KE, PH, HK, AI, LEF, AV, LNY, LEE, GLY, DY, TP, DF, DM, FQ, YV, YE, IL, YH, WL, ST, YN, LR, RRR	NILP, ILP, RL, IR, RY, IY, VF, KW, VY, FP, GGY, IPP, GY, PR, YL, LF, YG, AY, YGL, IA, IP, AF, LA, KR, RA, YA, GF, IF, IG, GI, GA, GL, AG, HL, GR, DA, GS, GV, MG, GK, GT, GG, SG, LG, GD, TG, EG, PG, IAK, VR, VAV, QK, DG, NF, SY, SF, KF, KL, YK, RR, KA, LVE, VIY, CF, EI, IE, EV, VE, TQ, PP, EK, KE, PH, AI, VRY, AV, ASL, FNE, AQL, DGL, AVL, TP, DF, DM, YV, YE, IL, RG, ST, LR	RL, IR, LKL, RY, VF, MF, FAP, RF, VY, HY, FP, PR, YL, YG, YP, GP, PL, VFPS, VK, IP, RP, AF, AP, LA, VP, RA, AA, GF, FR, IF, VG, IG, GM, GA, GL, GH, GR, KG, FG, GS, GV, GQ, GK, GT, HG, GE, GG, QG, SG, LG, GD, TG, EG, EA, PG, VR, YVP, LTF, DG, NF, SY, SF, KF, KL, YK, NK, RR, KA, LVE, CF, EY, EI, EV, VE, TE, LQ, LN, PT, TQ, EW, ME, KE, TF, AV, FNE, AFL, AVL, DY, TP, FQ, YV, YE, IL, MM, AEL, WA, MW, SGP, RG, GTG, ST, YN, LR	VMP, RL, FGK, RY, VF, TAP, GDAP, FP, VAP, LVR, YG, VK, IA, AP, LA, VP, YA, GF, FR, IF, VG, IG, GI, HLGR, KG, FG, DA, GS, GV, MG, GQ, GK, GE, GG, SG, LG, GD, EG, EA, VR, IFG, NY, SF, KL, RR, AR, CF, EI, IE, EV, VE, TE, PT, ME, EK, KE, PH, AI, AV, GKV, VVF, FQ, IL, YH, TLS, RG, ST, YN	IR, RY, VF, LW, VW, VY, GY, LSP, IRA, YL, LF, YG, FY, TQVY, PL, VK, IA, GW, AP, VP, RA, AA, GF, FR, IG, GI, GA, GL, AG, GH, FG, GQ, WG, HG, GE, GG, GD, EG, EA, NG, PG, VR, PAP, NY, NF, KY, KF, AR, LVE, KP, EI, IE, EV, VE, LQ, TQ, AH, EW, ME, PH, EP, TF, AI, VRY, DY, TP, YV, IL, RG, GHG, LFR, LR	RL, AKK, RY, IY, LW, RF, VY, GY, YL, YP, PLG, LPG, GP, PL, AW, VK, IA, LKA, IP, RP, AP, LA, KR, VP, YA, AA, GF, VG, IG, GI, GM, GA, GL, AG, GH, HL, GR, KG, FG, DA, GV, MG, GQ, GK, GT, GG, SG, LG, GD, TG, EG, EA, NG, PG, VR, VAV, KYY, IYK, LIY, NF, SY, SF, KY, KF, KL, YK, NK, RR, AR, KA, KP, EI, IE, EV, VE, TE, LQ, PT, PP, EK, KE, HP, TF, AV, TKY, AVL, LEK, TP, DF, DM, KGP, RG, ST, YN, LR	VLP, RL, AKK, VF, MF, RF, GY, GP, PL, VK, IA, IP, AF, AP, LA, VP, RA, AA, FR, IF, VG, IG, GI, GM, GA, GL, AG, HL, GR, KG, FG, DA, GV, GQ, GK, HG, GE, GG, LG, TG, EG, EA, NG, VR, VAV, TTN, QK, DG, NF, SY, SF, KY, KL, AR, KA, EY, KP, EI, VE, TE, LQ, LN, PT, TQ, AH, EW, EK, KE, AV, LEK, VSW, DY, TP, DF, IL, WA, RG, ST	RL, IR, FQP, ALPHA, YALPHA, GRP, LY, IY, VF, MF, MY, VW, RF, FP, VAP, GY, PR, LNP, LF, YG, FY, LAY, AY, YP, GP, PL, IW, IWH, VFPS, VK, IA, LAP, RP, AP, LA, KR, VP, YA, AA, GF, FR, VG, IG, GI, GM, GA, AG, GR, DA, GS, GV, MG, GQ, GT, HG, GG, SG, GD, TG, EG, EA, NG, PG, VR, QK, DG, NY, KY, KL, KA, CF, EY, VWIG, EI, IE, EV, VE, TE, LN, TQ, PP, ME, EK, KE, HP, PH, IQP, TF, AI, AV, ALP, YVA, FYN, DY, TP, DM, FQ, YV, YE, IL, MW, SGP, RG, GTG, ST, YN, LR, LDY	VLP, RL, IR, LKL, RY, LY, IY, VF, VW, RF, VY, FP, VPP, GY, LAA, LSP, LF, FY, YP, VPK, PL, VK, GW, IP, RP, AF, LA, VP, AA, FR, VG, IG, GM, GA, GL, AG, GR, KG, FG, DA, GS, GV, GQ, GK, GT, GE, GG, SG, LG, GD, TG, EG, EA, PG, VR, LIY, DG, NF, SY, SF, KY, KF, KL, YK, RR, KA, CF, KP, FAL, EI, IE, EV, VE, TE, LN, PT, TQ, PP, PQ, EW, ME, EK, KE, TF, AI, VRSP, VRY, LVY, AV, DF, FQ, YE, IL, RG, ST, YN, AGS	VF, MY, AF, LA, KR, RA, VG, GM, GV, GE, EG, EA, KF, AR, EV, ME, EK, HK, AV, LEK, DY, YV, YE	RL, RY, MF, VAA, PR, YG, AY, VK, IA, LA, VP, AA, GF, IF, GM, GA, GH, GR, KG, FG, GS, MG, GE, GG, SG, LG, TG, EG, NG, PG, IFG, QK, DG, RR, AR, KA, EI, IE, EV, VE, TE, TQ, EK, KE, AI, AV, ALP, LEK, VTR, DY, TP, IL, YH, AEL, RG, ST, YN

(*Continued*)

Table 5–Continued.

Bioactive Potential	RuBisco	ELF-3e	AdoMetDC	TBc	PPctl	STPp	EF1a	GAPH	Actin	CAdC	a-tubulin	Ftsh
DPP- IV inhibitor	GP, PP, MP, VA, MA, KA, LA, FA, AP, PA, LP, VP, LL, VV, GQ, IP, SP, FP, RP, KP, HP, YP, WA, EP, NP, TA, QP, FL, WV, HL, EK, AL, SL, GL, VR, WRS, WRI, AA, PL, WR, WL, WI, WY, WT, WS, LW, WF, IQP, VGL, WG, AE, AS, AT, AV, AY, DP, DR, ES, EW, FN, GF, GG, GH, GI, GV, GY, HD, HE, HF, HH, HR, HS, HV, HY, IH, IL, IQ, KE, KG, KH, KI, KK, KR, KS, KY, LH, LI, LN, LT, LV, MG, ML, ND, NE, NG, NH, NL, NN, NQ, NW, PF, PG, PH, PI, PK, PM, PN, PQ, PW, PY, QL, QN, QS, QT, RG, RI, RK, RN, SF, SH, SI, SV, SW, SY, TD, TG, TH, TL, TM, TR, TS, TT, TV, TY, VE, VF, VG, VI, VK, VL, VM, VQ, VS, VT, VW, VY, WH, YF, YG, YH, YL, YN, YQ, YR, YV, YW, YY	GP, MA, KA, LA, AP, VP, LL, VV, VPL, GQ, APG, TP, SP, FP, RP, YP, GA, IA, RA, NP, TA, FL, HL, AL, SL, GL, AA, PL, WL, WI, WS, LW, YT, WG, AD, AE, AF, AS, AT, AV, DN, DP, DR, EG, EI, ET, EV, FN, FQ, GF, HD, HE, HS, HT, HW, IH, II, IL, IM, IQ, IR, IW, KE, KF, KI, KK, KR, KS, KV, KY, LI, LM, LN, LT, LV, ME, MG, MH, MI, MK, ML, MQ, MV, NA, ND, NF, NG, NH, NL, NQ, NR, NV, NY, PF, PG, PH, PI, PN, PQ, PS, QD, QE, QF, QI, QL, QN, QQ, QS, QT, QV, QY, RH, RI, RL, RR, RW, SH, SK, SY, TE, TI, TK, TN, TQ, TR, TS, TV, TY, VD, VH, VI, VL, VN, VQ, VY, WD, YA, YD, YE, YH, YK, YL, YN, YQ, YR, YS, YV	PP, MP, VA, KA, LA, FA, PA, LP, LL, IP, TP, FP, GA, IA, RA, EP, NP, QP, HL, EK, AL, SL, GL, VR, WS, AD, AF, AG, AS, AT, AV, AY, DP, EG, EH, EI, ES, EV, FN, GF, GG, GI, GV, GY, HF, HR, HV, IH, IL, IM, IR, KE, KF, KI, KK, KR, KT, KV, KW, LH, LM, LT, LV, MG, MN, NE, NF, NL, PF, PG, PH, PI, PS, PV, QL, QS, RG, RL, RN, RR, SF, SI, SK, SV, SY, TD, TG, TI, TK, TL, TN, TQ, TS, TT, TV, VD, VE, VF, VI, VL, VM, VS, VT, VY, WH, YA, YD, YE, YG, YK, YL, YS, YV	GP, VA, KA, LA, FA, AP, VP, LL, VV, GQ, IP, TP, SP, FP, RP, YP, GA, RA, WA, EP, TA, FL, AL, SL, GL, VR, AA, PL,WI, MW, WE, YT, AD, AE, AF, AS, AT, AV, DN, DP, DR, EG, EH, EI, ES, ET, EV, EW, EY, FN, FQ, FR, GE, GF, GG, GH, GV, HF, HI, HW, HY, IL, IQ, IR, KE, KF, KG, KI, KS, KV, LH, LI, LM, LN, LT, LV, ME, MF, ML, MM, MN, MR, MV, NA, ND, NE, NF, NH, NL, NM, NN, NQ, NV, NW, PF, PG, PK, PN, PS, PT, PY, QD, QE, QF, QG, QH, QI, QL, QN, QQ, QS, QV, QY, RG, RH, RI, RK, RL, RM, RR, SF, SI, SK, SV, SY, TE, TF, TG, TK, TL, TM, TQ, TS, TV, TY, VD, VE, VF, VG, VH, VI, VK, VL, VN, VQ, VS, VT, VY, WD, YD, YE, YF, YG, YI, YK, YL, YN, YQ,	MP, VA, LA, AP, VP, LL, VV, GQ, FP, IA, TA, HL, EK, VR, AD, AE, AS, AT, AV, DP, DR, EG, EI, ET, EV, FQ, FR, GE, GF, GG, GI, GV, HF, HI, HS, HV, IL, KE, KG, KH, KT, KV, LV, ME, MG, MI, MK, MN, MV, NE, NH, NT, NY, PH, PK, PM, PT, QS, QV, QY, RG, RI, RK, RL, RM, RR, SF, SI, SK, SV, TE, TI, TL, TN, TR, TV, TY, VD, VE, VF, VG, VK, VM, VQ, VT, YA, YD, YG, YH, YN, YS, YY	MP, VA, MA, AP, PA, VP, LL, VV, GQ, TP, SP, KP, GA, IA, RA, EP, TA, QP, FL, AL, GL, VR, AA, PL, WC, WS, LW, YT, WG, AE, AG, AH, DN, DP, DR, EG, EH, EI, ES, ET, EV, EW, FN, FR, GE, GF, GG, GH, GI, GW, GY, HE, HT, IH, IL, IR, KF, KI, KV, KY, LH, LI, LM, LT, LV, ME, MQ, NA, NF, NG, NH, NM, NV, NW, NY, PG, PH, PM, PS, PV, QA, QD, QE, QF, QI, QL, QN, QV, RG, RI, RK, RM, TD, TF, TI, TL, TN, TQ, TR, TT, TV, VD, VE, VF, VK, VM, VQ, VT, VW, VY, YD, YF, YG, YL, YR, YS, YV, YY	GP, PP, VA, KA, LA, FA, AP, PA, LP, VP, LL, VV, HA, GQ, APG, IP, TP, RP, KP, HP, YP, GA, IA, EP, NP, FL, WV, HL, EK, AL, GL, VR, LPL, AA, PL, PPL, WK, LW, AW, AD, AE, AG, AS, AT, AV, DN, DP, DR, EG, EH, EI, ET, EV, FN, GF, GG, GH, GI, GV, GY, HE, HH, HI, HR, HT, HV, IH, II, IM, KE, KF, KG, KI, KK, KR, KS, KV, KY, LI, LM, LT, MG, MH, MI, MN, MR, MV, NF, NG, NH, NL, NM, NV, PF, PG, PI, PK, PM, PS, PT, PV, QA, QD, QE, QT, QV, QY, RG, RL, RR, SF, SH, SI, SK, SV, SY, TE, TF, TG, TI, TK, TL, TN, TR, TS, TT, TV, VD, VE, VG, VI, VK, VL, VQ, VS, VT, VY, YA, YD, YK, YL, YN, YS, YY	GP, VA, MA, KA, LA, AP, PA, LP, VP, LL, VV, GQ, IP, TP, KP, GA, IA, RA, WA, NP, TA, HL, EK, AL, GL, VR, WRG, AA, PL, WR, WK, WY, YT, AE, AF, AG, AH, AS, AT, AV, DN, DP, DR, EG, EI, ES, EW, EY, FN, FR, GE, GG, GI, GV, GY, HE, HH, HI, HS, IH, II, IL, IN, KE, KG, KH, KI, KK, KT, KV, KY, LI, LM, LN, LT, LV, MF, NA, ND, NE, NF, NG, NL, NR, PF, PM, PS, PT, PV, PW, QW, RG, RI, RL, RN, SF, SI, SK, SV, SW, SY, TD, TE, TG, TL, TN, TQ, TR, TT, TV, TY, VD, VE, VF, VG, VH, VI, VK, VL, VN, VS, VT, YD, YI, YM, YS	GP, PP, VA, MA, KA, LA, FA, AP, PA, LP, VP, LL, VV, HA, GQ, TP, FP, RP, HP, YP, GA, IA, NP, TA, QP, EK, AL, SL, VR, AA, PL, WI, MW, IQP, AD, AE, AG, AS, AV, AY, DN, DR, EG, EH, EI, ES, ET, EV, EY, FN, FQ, FR, GF, GG, GI, GV, GY, HE, HH, HR, HT, IH, IL, IM, IQ, IR, IW, KE, KI, KR, KT, KY, LM, LN, LT, ME, MF, MG, MI, MK, MV, MY, NE, NG, NR, NY, PG, PH, PI, PK, PS, QA, QE, QI, QQ, QS, QV, RG, RH, RK, RL, RM, SH, SI, SK, TD, TE, TF, TG, TI, TL, TM, TQ, TS, TT, TV, VD, VE, VF, VG, VH, VI, VK, VL, VM, VS, VW, WD, WH, YA, YD, YE, YG, YN, YS, YV	PP, MP, VA, KA, LA, FA, PA, LP, VP, LL, VV, GQ, IP, SP, FP, RP, KP, YP, GA, EP, TA, FL, WV, EK, AL, GL, VR, WRR, AA, PL, WR, WK, WT, WE, AD, AE, AF, AG, AS, AT, AV, EG, EI, ES, EV, EW, FN, FQ, FR, GE, GG, GV, GW, GY, HI, IL, IM, IN, IQ, IR, KE, KF, KG, KI, KK, KS, KT, KV, KY, LI, LM, LN, LT, LV, ME, MK, MR, MV, NA, ND, NE, NF, NL, NN, NV, PF, PG, PI, PK, PM, PN, PQ, PS, PT, PV, QE, QI, QL, QN, QT, QV, RG, RI, RK, RL, RM, RN, RR, SF, SI, SK, SV, SW, SY, TE, TF, TG, TI, TK, TL, TQ, TR, TS, TV, VD, VE, VF, VG, VH, VI, VK, VL, VN, VS, VT, VW, VY, YE, YF, YI, YK, YN, YR, YS	VA, LA, RA, TA, EK, AL, WY, AE, AF, AV, EG, EV, GE, GV, KF, KR, LM, ME, MI, MY, NN, NT, RI, SK, VD, VF, VG, VH, YE, YS, YV	VA, MA, KA, LA, LP, VP, LL, VV, HA, TP, GA, IA, NP, TA, EK, AL, AA, AD, AE, AS, AT, AV, AY, DQ, DR, EG, EH, EI, ES, ET, EV, GE, GF, GG, GH, HD, HE, HS, II, IL, KE, KG, KI, KS, KT, KV, LH, LI, LT, LV, MF, MG, MV, NA, ND, NE, NG, NL, NN, NT, NV, PG, PN, PV, QE, QI, QL, QN, QQ, QT, QV, RG, RK, RL, RM, RN, RR, SH, SK, SV, TD, TE, TG, TH, TI, TL, TQ, TR, TS, TT, VD,VE, VH, VK, VL, VM, VN, VS, VT, YG, YH, YN

Sequences identified in BLAST tool ® Program and analyzed in BIOPEP® database. ACE inhibitor: angiotensin-converting-enzyme inhibitor; DPP IV inhibitor: dipeptidyl peptidase IV inhibitor; Activating UBMP: Activating ubiquitin-mediated proteolysisç GUSP: Glucose uptake stimulating peptide; SVSR: Stimulating vasoactive substance release; Regulation: peptide regulating the stomach mucosal membrane activity. RuBisCO: ribulose-1,5-bisphosphate carboxylase/oxygenase large subunit; ELF-3e: eukaryotic translation initiation factor 3 subunit E; AdoMetDC: S-adenosylmethionine decarboxylase; TBc: Tubulin beta chain; PPcti; Peptidyl-prolyl cis-trans isomerase; STPp; Serine/threonine-protein phosphatase; eEF1a: elongation factor 1-alpha; GAPDH: glyceraldehyde-3-phosphate-dehydrogenase; CAdC: clathrin adaptor complex.

Table 6–Identification of peptides in protein related to lipids metabolism from chia seed.

Biologic activity	Oleosin	FAD2i1	FAD2i2	FAD3i1	FAD3i2	FAD7i1	FAD8	MGAT
Antiamnestic	–	PG, GP	PG, GP	VPL, PG, GP	VPL, PG, GP	PG, GP	PG, GP	
Antithrombotic	–	GP, PG	GP, PG	GP, PG	GP, PG	GP, PG	GP, PG	
Immunomodulating	YG	YG, YGG	YG, YGG	YG	YG	YG	YG	YG
Stimulating	–	EE, SE	EE, SE	VPL	VPL	EE, SSS, SE	EEE, EE, SSS	EEE, EE, SE
Neuropeptide	GQ	YL	YL	GQ, YL	YL	YL	GQ, YL	
Regulation	–	GLY, DY, GP, PG	GFL, GLY, DY, GP,	GP, PG	GP, PG	DY, GP, PG	GP, PG	
Contracting	–		–	–		PLPR	PLPR	
Bacterial permease ligand	–	KK	KK	KK	KK	KK	KK	KK
Inhibitor	–	–	–	PPPF, IR, KF	PPPF, IR, KF	PPPF, IR	EF	IR, KF
Hypotensive	–	–	–	IR, KF	IR, KF	IR	EF	LW, FT, LR, IR, KF
α-glucosidase inhibitor	–	–	–	VW	WW	VW	VW	
Activating UBMP	–	RA, LA	RA, LA, WA	RA, LA, WA	RA, LA, WA	RA, LA, WA	LA, WA	RA, LA
GUSP	VL, LV, LL	VL, LV, IV, IL, LI, II	VL, LV, IL, LI, LL	LV, IV, IL, LI, LL	VL, LV, IV, IL, LL	VL, LV, LI, LL	VL, LV, IL, LI, LL	
Antioxidant	PHH, HL, HH, IY, QHH, KD	LH, HL, HH, IKK, LY, IY, AH, WY, AHH, HYH, GHH, KYY, YYV, YYQ, FYY, RHH, LHS, PHA, PHY, KAI, KP, VY, AW, YQLD, YQL, YVE	LH, HL, HH, IKK, LY, IY, AH, WY, AHH, HYH, GHH, KYY, YYV, YYQ, FYY, RHH, LHS, PHT, PHY, KAI, KVI, KP, TY, VY, AW, YVE	LHH, LH, HL, HH, AY, LY, IY, WY, IHH, HYH, THH, YYR, NYY, HHH, LHS, LWY, PHY, PWY, GGE, EAK, KD, PW, IR, LK, KP, VY, AW, VW	LHH, LH, HL, HH, VHH, AY, LY, IY, EL, WY, HYH, THH, YYR, NYY, HHH, LHS, LWY, PHY, PWY, EAK, KD, PW, IR, LK, KP, VY, AW, VW, LW	LHH, LH, HL, HH, AY, ADF, LY, IY, WY, IHH, HFH, THH, KYY, YYK, YYQ, VYY, HHH, LHS, PHY, PWY, KD, WPL, PW, IR, LKP, LK, KP, TY	LHH, LH, HL, HH, AY, LY, IY, WY, IHH, HYH, THH, YYQ, VYY, LHL, LWT, PHY, PWY, KD, PW, LKP, LK, KP, TY, VY, VW, LW, WG	HLAY, LY, AH, EYY, YYA, LWT, PHG, MY, KAI, KD, IR, LK, KP, TW, AW, LW, LLR, FC
ACE inhibitor	IY, HY, PR, LAA, YG, LQQ, HHL, PL, VK, IA, RP, LA, VP, AA, GF, IF, VG, GL, AG, HL, FG, GS, GV, GQ, GK, GG, SG, TG, KY, AR, KA, FAL, LQ, HP, PH, LSW, AV, TP, DM, FQ	LY, IY, VF, MF, LVL, RF, VY, HY, YL, LF, YG, FY, YGL, VPK, HHL, VFK, GPL, GP, PL, IKP, AW, VK, IA, GW, IP, RP, AF, LA, KR, VP, RA, GF, FR, IF, VG, GI, GA, GL, AG, GH, HL, GR, KG, DA, GS, GV, MG, GK, GE, GG, QG, SG, LG, TG, EG, EA, NG, PG, NPP, YGG, KYY, NKL, NY, SY, SF, KY, KL, NK, RR, KA, CF, KP, EI, EV, VE, LQ, LN, AH, PP, PQ, EW, HP, PH, AI, RPY, FVP, AV, ASL, ALP, GLY, YVA, IVQ, VLY, AVL, VSW, DY, TP, YV, IL, YH, WL, RG, ST, YN, FKR	RL, IKP, LY, IY, VF, MF, LVL, RF, VY, HY, YL, LF, YG, FY, YP, YGL, VPK, HHL, VFK, GPL, GP, PL, AW, VK, IA, GW, IP, RP, AF, LA, KR, VP, RA, AA, GF, FR, IF, VG, GI, GA, GL, AG, GH, HL, GR, KG, DA, GS, GV, MG, GK, GT, GG, QG, SG, LG, GD, TG, EG, EA, NG, PG, NPP, YGG, KYY, NKL, DG, NY, SY, SF, KY, KL, NK, RR, KA, CF, KP, EV, VE, LQ, LN, AH, PP, EW, EK, HP, PH, VIKP, AI, RPY, FVP, AV, ASL, GLY, YVA, VSW, DY, TP, YV, IL, YH, WA, WL, RG	PLP, RL, IR, AAP, RY, LY, IY, MF, LW, VW, YW, VY, HY, FP, VAA, IPP, GY, PR, LAA, IRA, YL, LF, YG, AY, AIP, YP, GP, PL, IVY, AW, GPV, GEP, VK, IA, GW, IP, AF, AP, LA, KR, VP, RA, YA, AA, IF, VG, IG, GI, GA, GL, AG, GH, HL, GS, GV, GQ, GK, GT, HG, GE, GG, QG, SG, LG, GD, TG, EG, EA, NG, PG, LRY, AIPP, NY, SY, SF, KF, KL, YK, NK, AR, KP, EI, VE, LN, PT, PP, PQ, EW, KE, PH, VAF, AI, AFLL, GSH, AFL, VGP, DY, DF, YV, IL, YH, WA, WL, SGP, PPP, RG, ST, GHG	IR, VP, AAP, RY, LY, IY, VF, MF, LW, VW, YW, VY, HY, FP, VAA, IPP, GY, PR, LAA, IRA, YL, LF, YG, AY, AIP, YP, GP, PL, IVY, AW, VK, IA, GW, IP, AF, AP, LA, KR, VP, RA, YA, AA, IF, VG, IG, GI, GA, GL, GH, HL, DA, GS, GV, GK, GT, HG, GE, GG, QG, SG, LG, GD, EA, NG, PG, LRY, AIPP, DG, NY, SY, SF, KF, KL, YK, NK, KP, EI, VE, TE, LN, PT, PP, PQ, EW, KE, PH, AI, AV, GSH, VGP, DY, DF, YV, YE, IL, YH, WA, WL, PPP, RG, ST, GHG, LR	IYP, PLP, IR, LKL, LY, IY, MF, VW, YW, RF, VY, HY, FP, PR, LAA, IRA, YL, LF, YG , LAY, AY, AIP, YP, HHL, HLL, GPL, GP, PL, AW, LKP, VK, GW, IP, AP, LA, VP, RA, AA, GF, VG, IG, GI, GA, GL, AG, GH, HL, GR, KG, FG, GS, GV, MG, GK, GT, WG, HG, GE, GG, QG, SG, LG, GD, TG, EA, NG, PG, VR, VAV, KYY, IYK, QK, DG, SY, SF, KY, KL, YK, KP, RIY, IE, EV, VE, TE, LQ, LN, PP, PQ, EK, KE, HP, PH, AI, VWP, AV, DY, DF, FQ, YV, YH, WA, WL, MGP, SGP, PPP, RG, ST, GHG, FGG, AVV, LR, LGV	IYP, PLP, LKL, AAP, AKK, LY, IY, VF, LW, VW, YW, VY, HY, FP, LVR, GY, PR, YL, LF, YG, LAY, AY, YP, HHL, HLL, GPL, GP, PL, LKP, VK, IP, RP, AP, LA, KR, VP, AA, GF, VG, IG, GI, GM, GL, GH, HL, KG, FG, GS, GV, MG, GQ, GK, WG, HG, GG, SG, LG, GD, TG, EA, NG, PG, VR, VAV, GHF, QK, SY, SF, KY, KL, KA, IPY, KP, RIY, IE, VE, LN, PP, PQ, EW, EK, KE, HP, PH, IQP, FVP, AV, LEE, GSH, LPF, AVL, DY, YV, IL, YH, WA, WL, MGP, SGP, RG, ST, YN, GHG, LR, LGV	RL, IR, RY, LY, VF, MF, MY, LW, GKP, VAA, GY, PR, LF, YG, AY, PL, DLP, AW, GEP, VK, IA, IP, AF, AP, LA, RA, YA, AA, FR, IF, VG, GI, GM, GL, GH, HL, GR, FG, GS, GV, MG, GK, GT, HG, GE, GG, QG, SG, GD, TG, EG, VR, QK, DG, NF, SY, SF, KF, KL, YK, NK, KA, EY, KP, VE, TE, PT, AH, EW, EK, PH, AI, AV, ASL, FDK, DGL, TP, DM, FQ, YE, YH, WM, GHG, LR,

(*Continued*)

Table 6–Continued.

Biologic activity	Oleosin	FAD2i1	FAD2i2	FAD3i1	FAD3i2	FAD7i1	FAD8	MGAT
DPP- IV inhibitor	VA, MA, KA, LA, FA, VP, LL, GQ, TP, SP, RP, HP, IA, TA, FL, HL, AL, SL, GL, AA, PL, ALAV, WI, AD, AG, AS, AT, AV, DQ, FQ, GF, GG, GV, HH, HY, KH, KY, LT, LV, MK, MV, NV, PH, PV, QF, QH, QL, QQ, SH, SV, SW, TG, TI, TK, TL, VD, VF, VG, VI, VK, VL, VS, VT, YG, YM	LA, GP, PP, MP, VA, KA, LA, FA, PA, LP, VP, LL, VV, HA, IP, TP, SP, RP, KP, HP, GA, IA, RA, EP, NP, TA, QP, FL, WV, HL, AL, SL, GL, PL, PPG, WK, WL, WY, WT, VGL, AW, AD, AF, AG, AH, AS, AT, AV, DP, DR, EG, EI, ET, EV, EW, FN, FR, GE, GF, GG, GH, GI, GV, GW, HE, HF, HH, HR, HS, HT, HV, HY, IH, II, IL, IQ, KG, KK, KR, KS, KY, LH, LI, LM, LN, LT, LV, MF, MG, MN, NG, NN, NT, NV, NY, PG, PH, PI, PK, PQ, PY, QG, QH, QI, QL, QW, RG, RH, RM, RR, SF, SI, SV, SW, SY, TD, TG, TH, TI, TK, TL, TM, TN, TV, VD, VE, VF, VG, VI, VK, VL, VN, VQ, VS, VY, WD, YD, YF, YG, YH, YI, YL, YM, YN, YQ, YS, YV, YY, LPQ	GP, PP, MP, VA, KA, LA, FA, PA, LP, VP, LL, VV, HA, IP, TP, SP, RP, KP, HP, YP, GA, IA, RA, WA, EP, NP, FL, WV, HL, EK, AL, SL, GL, AA, PL, PPG, WK, WL, WI, WY, VGL, AW, AE, AF, AG, AH, AS, AT, AV, DP, DR, EG, EV, EW, FN, GF, GG, GH, GI, GV, GW, HE, HF, HH, HR, HS, HT, HV, HY, IH, IL, KG, KK, KR, KS, KT, KV, KY, LH, LI, LM, LN, LT, LV, MF, MG, MN, NG, NN, NT, NV, NY, PF, PG, PH, PI, PK, PN, PS, PY, QF, QG, QH, QI, QL, QW, RG, RH, RL, RM, RR, SF, SI, SV, SW, SY, TD, TG, TH, TK, TL, TM, TN, TV, TY, VD, VE, VF, VG, VI, VK, VL, VN, VQ, VS, VT, VY, WD, YD, YG, YH, YI, YL, YM, YN, YQ, YS	GP, PP, VA, MA, LA, FA, AP, LP, VP, LL, VV, VPL, GQ, IP, WP, SP, FP, KP, YP, GA, IA, RA, WA, EP, NP, FL, WV, HL, AL, SL, GL, WRI, AA, PL, WR, WL, WI, WY, WS, LW, AW, AD, AE, AF, AG, AS, AT, AV, AY, DN, DP, EG, EH, EI, ES, FN, GE, GG, GH, GI, GV, GW, GY, HD, HF, HH, HI, HR, HS, HV, HY, IH, IL, IR, KE, KF, KI, KK, KR, KS, KT, LH, LI, LN, LT, LV, MF, MV, NG, NH, NL, NN, NV, NY, PF, PG, PH, PI, PN, PQ, PT, PV, PW, PY, QD, QG, QI, QL, QN, QT, RG, RI, RK, RL, SF, SH, SI, SK, SW, SY, TD, TG, TH, TI, TL, TM, TR, TS, TT, VD, VE, VG, VI, VK, VS, VT, VW, VY, WD, YA, YD, YF, YG, YH, YK, YL, YQ, YR, YV	GP, PP, VA, MA, LA, FA, AP, LP, VP, LL, VV, HA, VPL, IP, WP, SP, FP, KP, YP, GA, IA, RA, WA, EP, NP, FL, WV, HL, AL, SL, GL, WRI, AA, PL, WR, WL, WI, WY, WS, LW, AW, AD, AE, AF, AS, AT, AV, AY, DN, DP, EH, EI, ES, EW, FN, GG, GH, GI, GV, GW, GY, HD, HF, HH, HR, HS, HV, HY, IH, IL, IR, KE, KF, KI, KK, KR, LH, LN, LT, LV, MF, MV, ND, NG, NH, NL, NN, NT, NV, NY, PF, PG, PH, PI, PN, PQ, PT, PW, PY, QD, QG, QI, QL, QN, QT, QY, RG, RI, RK, SF, SH, SI, SK, SW, SY, TD, TE, TH, TI, TL, TM, TR, TS, TT, TV, VD, VE, VF, VG, VH, VI, VK, VL, VS, VT, VW, VY, WD, YA, YD, YE, YG, YH, YK, YL, YQ, YR, YS, YV, YW, YY	GP, PP, VA, MA, LA, FA, AP, LP, VP, LL, VV, IP, WP, SP, FP, KP, HP, YP, GA, RA, WA, EP, NP, TA, WV, HL, EK, AL, SL, GL, VR, WRI, LPL, AA, PL, WR, WK, WL, WI, WY, WT, WS, AW, WG, AD, AG, AS, AT, AV, AY, DP, DR, ES, EV, FQ, GE, GF, GG, GH, GI, GV, GW, HD, HE, HF, HH, HR, HS, HV, HY, IH, IN, IR, KE, KG, KH, KI, KK, KS, KY, LH, LI, LN, LT, LV, MF, MG, MK, ML, MV, ND, NE, NG, NH, NN, NV, NW, PF, PG, PH, PI, PK, PM, PN, PQ, PS, PV, PW, PY, QE, QG, QI, QL, QN, QT, RG, RI, RK, RN, SF, SI, SV, SW, SY, TD, TE, TG, TH, TK, TL, TM, TR, TS, TT, TV, TY, VE, VG, VI, VK, VL, VM, VN, VS, VT, VW, VY, WH, YF , YG, YH, YK, YL, YQ, YR, YV, YW, YY	GP, PP, MP, VA, MA, KA, LA, FA, AP, PA, LP, VP, LL, VV, GQ, IP, SP, FP, RP, KP, HP, YP, WA, EP, NP, TA, QP, FL, WV, HL, EK, AL, SL, GL, VR, WRS, WRI, AA, PL, WR, WL, WI, WY, WT, WS, LW, WF, IQP, VGL, WG, AE, AS, AT, AV, AY, DP, DR, ES, EW, FN, GF, GG, GH, GI, GV, GY, HD, HE, HF, HH, HR, HS, HV, HY, IH, IL, IN, IQ, KE, KG, KH, KI, KK, KR, KS, KY, LH, LI, LN, LT, LV, MG, ML, ND, NE, NG, NH, NL, NN, NQ, NW, PF, PG, PH, PI, PK, PM, PN, PQ, PW, PY, QL, QN, QS, QT, RG, RI, RK, RN, SF, SH, SI, SV, SW, SY, TD, TG, TH, TL, TM, TR, TS, TT, TV, TY, VE, VF, VG, VI, VK, VL, VM, VQ, VS, VT, VW, VY, WH, YF, YG, YH, YL, YN, YQ, YR, YV, YW, YY	MP, VA, KA, LA, FA, AP, PA, LP, LL, IP, TP, SP, KP, IA, RA, EP, NP, TA, FL, HL, EK, SL, GL, VR, LPL, AA, PL, WI, WM, WT, WS, LW, AW, YT, AD, AF, AH, AS, AT, AV, AY, DN, DP, EG, ES, EW, EY, FQ, FR, GE, GG, GH, GI, GV, GY, HS, IR, KF, KK, KS, KT, KV, LI, LM, LV, MF, MG, ML, MR, MV, MY, NA, NF, NL, PF, PH, PK, PM, PS, PT, PV, QG, QN, QS, QT, RL, RN, SF, SK, SV, SW, SY, TE, TG, TH, TI, TL, TM, TR, TS, TW, VE, VF, VG, VH, VI, VK, VL, VS, VT, YA, YD, YE, YF, YG, YH, YK, YM, YY

Sequences identified in BLAST tool ® Program and analyzed in BIOPEP® database. ACE inhibitor: angiotensin-converting-enzyme inhibitor; DPP IV inhibitor: dipeptidyl peptidase IV inhibitor; Activating UBMP: Activating ubiquitin-mediated proteolysis; GUSP: Glucose uptake stimulating peptide; SVSR: Stimulating vasoactive substance release; Regulation: peptide regulating the stomach mucosal membrane activity. FAD3i1: fatty acid desaturase 3 isoform 1; FAD3i2: fatty acid desaturase 3 isoform 2; FAD7i1: fatty acid desaturase 7 isoform 3; FAD2i2: fatty acid desaturase 2 isoform 2; FAD8: fatty acid desaturase 8; MGAT: monoacylglycerol acyltransferase.

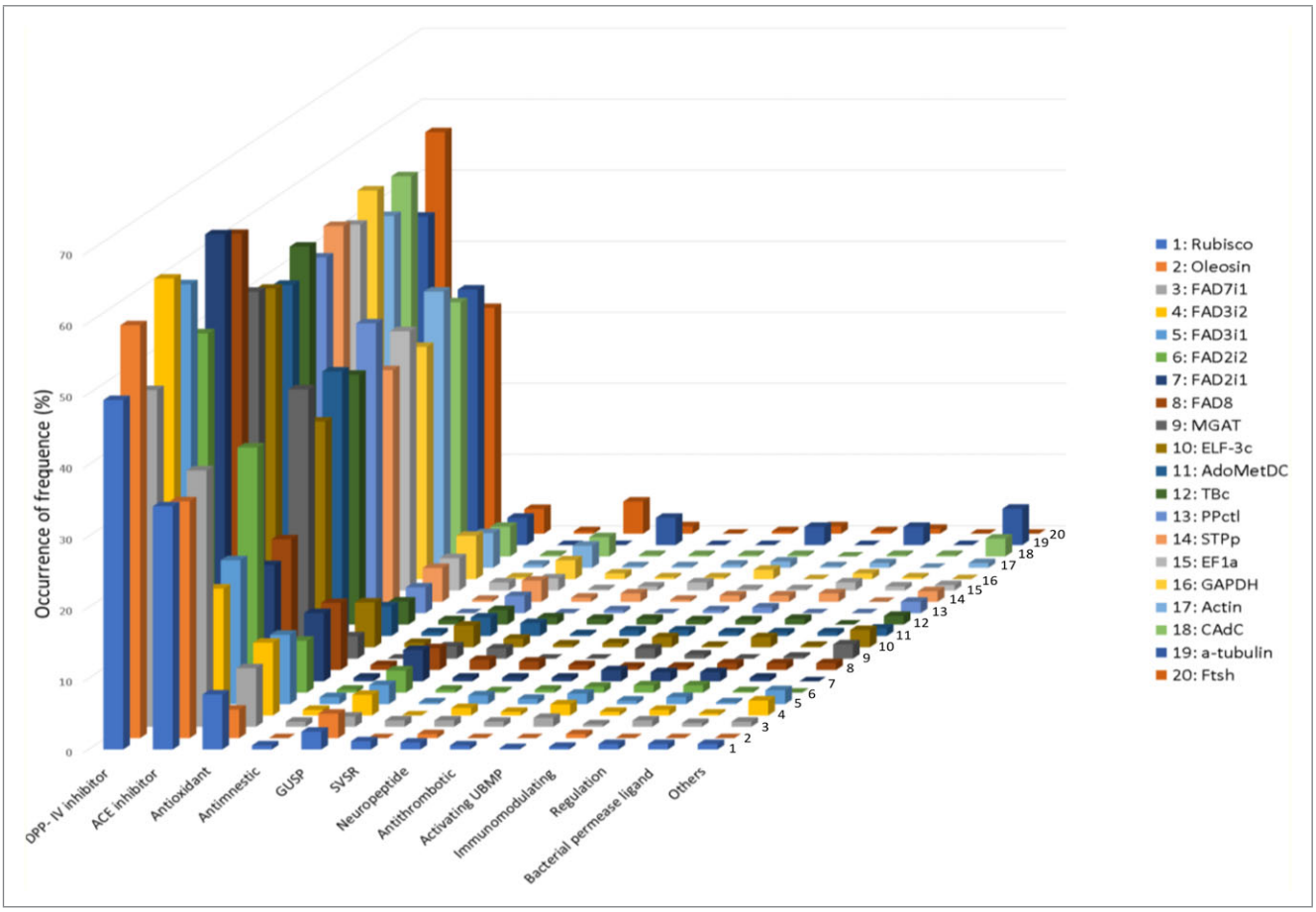

Figure 4–Bioactive potential of peptides sequenced found in chia protein. Sequences identified in BLAST tool ® Program and analyzed in BIOPEP® database. DPP IV inhibitor: dipeptidyl peptidase IV inhibitor; ACE inhibitor: angiotensin-converting-enzyme inhibitor; GUSP: Glucose uptake stimulating peptide; SVSR: Stimulating vasoactive substance release; Activating UBMP: Activating ubiquitin-mediated proteolysis; Regulation: peptide regulating the stomach mucosal membrane activity; RuBisCO: ribulose-1,5-bisphosphate carboxylase/oxygenase large subunit; FAD7i1: fatty acid desaturase 7 isoform 1; FAD3i2: fatty acid desaturase 3 isoform 2; FAD3i1: fatty acid desaturase 3 isoform 1; FAD2i2: fatty acid desaturase 2 isoform 2; FAD2i1: fatty acid desaturase 2 isoform 1; FAD8: fatty acid desaturase 8; MGAT: monoacylglycerol acyltransferase; ELF-3e: eukaryotic translation initiation factor 3 subunit E; AdoMetDC: S-adenosylmethionine decarboxylase; TBc: Tubulin beta chain; PPcti; Peptidyl-prolyl cis-trans isomerase; STPp; Serine/threonine-protein phosphatase; eEF1a: elongation factor 1-alpha; GAPDH: glyceraldehyde-3-phosphate-dehydrogenase; CAdC: clathrin adaptor complex.

The processing conditions, as hydrolysis time, degree of hydrolysis of the proteins, kind of enzyme, enzyme–substrate ratios, and pretreatment of the protein prior to hydrolysis can influence the bioactive properties of the peptides. Peptide properties can also be influenced by net charge, hydrophobicity and the size of the peptide, which are factors that affect their absorption across the enterocytes (Udenigwe & Aluko, 2012).

Chia protein fractions have been also separated and hydrolyzed with pepsin and pancreatin. Each of the resulting fractions, after gastrointestinal digestion, presented different compositions of bioactive peptides with different physiological actions (Orona-Tamayo et al., 2015). In this study, the highest antiradical activity against 2,20-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) and angiotensin-converting enzyme (ACE) was by peptides from albumin and globulin. Moreover, prolamin and globulin fractions showed the most potent ability to chelate ferrous ion. These results highlight the antioxidative and antihypertensive potential of peptides from chia (Orona-Tamayo et al., 2015).

Conclusions

This review shows that all proteins identified in chia seeds (*Salvia hispanica* L.) and their peptide sequences have auspicious biological potentials, mainly antioxidative, antihypertensive, and hypoglycemic properties. Among other bioactive compounds that may exert biological functions, these peptides can be responsible for the positive effects found in research studies in humans that consumed the whole chia seed; although, many results are still inconclusive. New investigations that focus on chia proteins and their bioactive peptides are necessary to demonstrate specifically the mechanisms of action that contribute to the observed health benefits.

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Author Contributions

Mariana Grancieri: compiled data and prepared the initial draft; Hercia Stampini Duarte Martino: critical analysis; Elvira de Mejia: overall concept, editing of the manuscript, and critical analysis. All authors critically revised the manuscript and gave their attention, conclusions, and final approval for submission.

Nomenclature

ACE inhibitor	angiotensin-converting enzyme inhibitor
Activating UBMP	activating ubiquitin-mediated proteolysis
AdoMetDC	S-adenosylmethionine decarboxylase
ALA	alpha-linolenic acid
AUC	area under the curve
CAdC	clathrin adaptor complex
DBP	diastolic blood pressure
DPP IV inhibitor	dipeptidyl peptidase IV inhibitor
eEF1a	elongation factor 1-alpha
ELF-3e	eukaryotic translation initiation factor 3 subunit E
EPA	docosahexaenoic acid
FAD2i2	fatty acid desaturase 2 isoform 2
FAD3i1	fatty acid desaturase 3 isoform 1
FAD3i2	fatty acid desaturase 3 isoform 2
FAD7i1	fatty acid desaturase 7 isoform 3
FAD8	fatty acid desaturase 8
GAPDH	glyceraldehyde-3-phosphate-dehydrogenase
GUSP	glucose uptake- stimulating peptide
HDL-c	high-density lipoprotein cholesterol
iAUC	incremental area under the curve
MDA	malondialdeyde
MGAT	monoacylglycerol acyltransferase
MBP	mean blood pressure
Omega-3	acid alpha-linolenic
Omega-6	acid linoleic
PPcti	peptidyl-prolyl cis-trans isomerase
Regulation	peptide regulating the stomach mucosal membrane activity
RuBisCO	ribulose-1,5-bisphosphate carboxylase/oxygenase large subunit
SBP	systolic blood pressure
STPp	serine/threonine-protein phosphatase
SVSR	stimulating vasoactive substance release
TBc	tubulin beta chain
TC	total cholesterol
VLDL-c	very-low-density lipoprotein cholesterol.

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