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PRESENCE OF SALVIA HISPANICA L. SEED FROM WEANING IS ABLE TO MITIGATE AND PREVENT THE ALTERED LIPID METABOLISM AND GLUCOSE HOMEOSTASIS IN ADULT Off SPRING (EXPOSED TO A NUTRITIONAL CHALLENGE FROM UTERO TO ADULTHOOD)

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Abstract

Seed from Salvia hispanica L. or more commonly known as chia is a traditional food in central and southern America. Currently, it is widely consumed for various health benefits especially in maintaining healthy serum lipid level. Chia is a good source of polyunsaturated fatty acids: omega-3 and omega-6, soluble dietary fiber. It also contains appreciable amount of proteins and phytochemicals. Nutritional value of chia is the reason why it is used in prophylaxis of several non-infectious diseases such as obesity, hypertension, cardiovascular diseases (CVDs), cancer and diabetes. The present work analyzes the effects of dietary chia seeds during postnatal life in offspring exposed to a sucrose-rich diet (SRD) from utero to adulthood. Chia was able to prevent the development of hypertension, liver steatosis, hypertriglyceridemia and hypercholesterolemia. Normal triacylglycerol secretion and triacylglycerol clearance were accompanied by an improvement of de novo hepatic lipogenic and carnitine palmitoyl transferase-1 enzymatic activities, associated with an accretion of n-3 polyunsaturated fatty acids in the total composition of liver homogenate. Glucose homeostasis and plasma free fatty acid levels were improved while visceral adiposity was slightly decreased. These results confirm that the incorporation of chia seed in the diet in postnatal life may provide a viable therapeutic option for preventing/mitigating adverse outcomes induced by an SRD from utero to adulthood.

Keywords: *Chia-seed α-linolenic acid (ALA) Dyslipidemia Liver steatosis Glucose homeostasis*

INTRODUCTION

Salvia is a genus of about 900 species of green plants, shrubs, subshrubs and bushes of the *Salvia* L. family. Chia (*Salvia hispanica* L.) is a representative of the *Salvia* genus. Among the species of the *Labiatae* family chia is distinguished by both high nutritional and therapeutic potential. *Salvia hispanica* L. is an annual plant growing in an area stretching from western Mexico to northern Guatemala. The optimal development of the plant is guaranteed by the warm climate, high rainfall and temperatures of 15-30 °C (**Coates W. et.al 1996, Coates W. et.al 1996**). The maximum height of the plant is 1 m. It has opposite leaves, which are 4-8 cm long and 3-6 cm wide (**Nutritional Nutrient. et.al 2011**). The flowers are purple or white and sized 3-4 mm. They are gathered in whorls on top of shoots. The fruits (schizocarps) contain numerous oval seeds, which are about 2 mm long. The seeds are mottle-coloured with brown, grey, black and white (**Ixtaina. et.al 2011, Mohd Ali N. et.al 2012, Olovos-lugo. et.al 2010**). The word 'chia' derives from the Náhuatl word 'Chian', which means 'oily'. The other part of the name *Salvia hispanica* was given to the plant by *Carl Linnaeus* (1707-1778), who discovered the wild-growing plant in the new world and confused it with a native plant from Spain (**Edwards S.S. et.al 1819**). However, chia comes from Mexico and it was imported to Spain by *Hernán Cortés* (**Ortiz de. et.al 1978**).

Chia has a high nutritional potential due to the seed composition. The composition depends on genetic factors and on the effect of the ecosystems where the plants were grown (**Ayerza R. et.al 2011**). Chia seeds contain 16-26% of protein, 31-34% of fat, 37-45% of carbohydrates in total, 23-35% of total dietary fibre (Table 1). Apart from that, they are a source of minerals (calcium, phosphorus, potassium and magnesium), vitamins (thiamine, riboflavin, niacin, folic acid, ascorbic acid and vitamin A) and antioxidant compounds (**Ixtaina. et.al 2011, Mohd Ali N. et.al 2012, Olovos-lugo. et.al 2010**). The energetic value of chia seeds is 459-495 kcal/100 g (**Coelho M.S. et.al 2014, Fernandez. et.al 2008**).

The chemical composition of chia seeds

Component	**Content of nutrients in chia seeds [g/100 g d.w.]**				
	Nutritional Nutrient Database for Standard Reference, 2011	**Ayerza R. & Coates W., 2011**	**Sargi S.C., Silva B.C., Santos H.M.C., Montanher P.F., Boeing J.S., Santos Júnior O.O., Souza N.E., Visentainer J.V., 2013**	**Ayerza R. & Coates W., 2011**	**Monroy-Torres R., Mancilla-Escobar M.L., Gallaga-Solórzano J.C., Medina-Godoy S., Santiago-García E.J., 2008**
Protein	16.54	19.6	21.52	16.45-26.03	18.65
Fats	30.47	34.4	21.69	29.98-33.50	33.00
Ash	no data	4.6	3.63	no data	4.35
Carbohydrates	no data	41.4	45.30	no data	37.73
Dietary fibre	34.4	23.7	no data	no data	28.36

NUTRITIONAL PROPERTIES AND THERAPEUTIC, DIETETIC PROPERTIES OF CHIA SEEDS

The composition of fatty acids in chia seed oil and docosahexaenoic acid (DHA) [Flachs P., Rossmeis M., Bryhn M., Kopecky J., 2009]

Fatty acids	Content of individual fatty acids [% of total fat content]					
	Ciftci O.N., Przybylski R., Rudzińska M., 2012	Ayerza R. & Coates W., 2001	Álvarez-Cháveza L.M., Valdivia-Lópeza M.A., Aburto-Juárezb M.L., Tecantea A., 2008	Ixtaina V.Y., Martínez M.L., Spotorno V., Mateo C.M., Maestri D.M., Diehl B.W.K., 2011	Coelho M.S., Salas-Mellado M.M., 2014	Sargi S.C., Silva B.C., Santos H.M.C., Montanher P.F., Boeing J.S., Santos Júnior O.O., Souza N.E., Visentainer J.V., 2013
Palmitic acid 16:0	7.10	9.66	6.30	7.2	6.69	5.85
Stearic acid 18:0	3.24	4.34	3.10	3.8	2.67	2.49
Oleic acid 18:1	10.53	6.84	7.50	15.2	10.55	6.16
ω-6 α-linolenic acid 18:2	20.37	17.65	19.90	19.1	17.36	17.47
ω-3 α-linolenic acid 18:3	59.76	64.08	63.4	64.7	62.02	54.49

The percentage of polyunsaturated fatty acids [PUFAs] in chia oil vs. other vegetable oils and The content of indispensable amino acids in chia seeds

Type of oil	PUFAs (% of total fatty acids)			References
	ω-3	ω-6	Total	
Chia	59.76	20.64	80.40	Ciftci O.N., Przybylski R., Rudzińska M., 2012
Perilla	60.93	14.72	75.85	Ciftci O.N., Przybylski R., Rudzińska M., 2012
Flax	42.90	30.90	73.80	Łoźna K., Kita A., Styczyńska M., Biernat J., 2012
Wheat germ	2.90	56.60	59.60	Łoźna K., Kita A., Styczyńska M., Biernat J., 2012
Sunflower	0.50	55.90	56.40	Łoźna K., Kita A., Styczyńska M., Biernat J., 2012
Pumpkin seed	0.50	47.30	47.80	Łoźna K., Kita A., Styczyńska M., Biernat J., 2012
Rapeseed	9.80	20.30	30.20	Łoźna K., Kita A., Styczyńska M., Biernat J., 2012

Amino acid [g/100 g]	USDA[Nutritional Nutrient Database for Standard Reference, 2011]	Amino acid [mg/kg/day]	WHO data for 2002 [2002: Geneva, Switzerland).WHO Technical Report Series 2007; No. 935]	WHO data for 1985 [2002: Geneva, Switzerland).WHO Technical Report Series 2007; No. 935]

Argininea	2.14	Histidine	10	8-12
Lysine	0.97	Isoleucine	20	10
Histidine	0.53	Leucine	39	14
Phenylalanine	1.01	Lysine	30	12
Leucine	1.37	Methionine + cysteine	15	13
Methionine	0.59	Phenylalanine + tyrosine	25	14
Valine	0.95	Threonine	15	7.0
Threonine	0.71	Tryptophan	4.0	3.5
Total	8.27	Total	184	93.5

Content of minerals in chia seeds

Minerals	**Content of minerals (mg/100 g)**		
	Nutritional Nutrient Database for Standard Reference, 2011	**Bolaños D., Marchevsky E.J., Camiña J.M., 2016**	**Llorent-Martínez E.J., Fernández-de Córdova M.L., Ortega-Barrales P., Ruiz-Medina A., 2013**
Calcium	631	624	580
Phosphorus	860	799	696
Potassium	407	666	870
Magnesium	335	369	403
Iron	7.7	24.4	10.9
Zinc	4.6	6.9	6.0
Selenium*	55.2	78.0	no data

* µg/100 g

Content of antioxidants in chia seed extracts (mg/g)

Antioxidant	**Reyes-Caudillo E., Tecante A., Valdivia-López M.A., 2008**	**Álvarez-Chávez L.M.a, Valdivia-López M.A.a, Aburto-Juárez M.L.b, Tecantea A., 2008**	**Coelho M.S., Salas-Mellado M.M., 2014**
Polyphenols	0.511-0.881	0.914-0.975	0.641
Chlorogenic acid	0.0459-0.102	0.214-0.235	0.00468
Caffeic acid	0.003-0.0068	0.141-0.156	0.03089
Quercetin	0.15-0.268	0.006	0.17
Kaempferol	0.360-0.509	0.024-0.025	0.00017

Content of polyphenols in chia seed extracts (mg/g)

[Reyes-Caudillo E., Tecante A., Valdivia-López M.A., 2008]

Antioxidant	Crude extract	Hydrolised extract
Polyphenols	0.757-0.881	0.511-0.777

The nutritional properties of chia seeds, such as: high content of polyunsaturated fatty acids, vegetable protein, dietary fibre, vitamins, minerals and bioactive substances result in numerous studies on these seeds in order to prove their therapeutic properties. Hypotensive (**Vuksan V. et.al 2007**), antineoplastic, laxative and analgesic properties are attributed to chia seeds. They are said to protect the cardiovascular system (**Ayerza R. et.al 2005**), exhibit antiinflammatory properties, control lipid metabolism (**Brenna J.T. et.al 2009, Chicco A.G. et.al 1996, Rodea D.A. et.al 2012**), have anti-oxidative properties and increase the performance of athletes (**Ulbricht C. et.al 2009**). Studies in adult rats have reported that dietary fats rich in ALA decrease serum lipid concentration and improve insulin sensitivity and glucose tolerance (**Ayerza R. et.al 2005, Ayerza R. et.al 2007, Ayerza R. et.al 2011**). In an adult dyslipemic insulin-resistant rat model, different studies have described the capability of dietary chia seed in normalizing/improving altered glucose homeostasis, dyslipidemia, hypertension and liver steatosis (**Chicco A.G. et.al 2009, Ciftci O.N. et.al 2012, Coates W. et.al 1996, Coates W. et.al 1998**).

Predisposition to the development of the metabolic syndrome (MS) begins in utero as part of a broader life course perspective (**Coelho M.S. et.al 2014**). A deficient nutrition during the intrauterine environment as well as an excess of energy like "junk food" or high-fat diet during pregnancy and/or lactation have also linked with the development of exacerbated adiposity, dyslipidemia, hypertension and insulin resistance in the adult offspring (**Edwards S.S. et.al 1819, Fernandez. et.al 2008, Flachs P.et.al 2009**). Regarding the impact of a maternal sucrose feeding in utero and during suckling, Samuelsson et al. **(Guevaracruz. et.al 2012**) described altered glucose homeostasis in the female offspring weaned on a control diet at 3 months of age. In 100-day-old offspring from dams fed a sucrose-rich diet (SRD) during pregnancy and lactation, D'Alessandro et al. (**HoH. et.al 2013**) reported several metabolic changes which are exacerbated accompanied by an increase in the weight of adipose tissues regardless of the weaning diet **(Hou W.C. et.al 2003**). Reducing postnatal hostile exposures represents a potential opportunity to mitigate the adverse intrauterine effects under the "two-hit hypothesis" (**Ixtaina. et.al 2011**, **Ixtainaa V.Y. et.al 2008**). A postnatal supplementation with EPA and DHA from birth to adulthood rescued glucocorticoid-programmed hypertension, dyslipidemia, inflammatory state and can limit adverse fetal programming effects on the adipose tissue of adult offspring (**Jin F. et.al 2012, Kalanowski et.al 2007**).

Chemical composition of chia biscuits

Chemical properties of chia seeds

Parameters	Chia seeds
Moisture content	5.77
Fat content	30.56
Ash content	2
Carbohydrates	42.9
Crude fibre	27
Protein content	16.54

The ash content of biscuits increased with the addition of chia seeds. The increase in ash content may be due to the high dietary fiber and mineral content in the chia seeds i.e. iron, calcium, phosphorus and magnesium. The moisture content decreased from 3.43% (control biscuits) to 2.89% (20%chia biscuits). There was a change in ash from 1.43% to 1.72%, crude fiber from 1.07% to 3.17%, protein from 5.52% to 8.09% and carbohydrates from 70.86% to 64.29%. The decrease in moisture content may be due to the decrease in protein content an increase in moisture content of bakery products with increase in protein content. The fat content of control biscuits was 17.68% and it increased to 19.84% in 15% chia seed biscuits. Similarly the fiber content of control biscuits was 1.07 and it increased to 3.17 in 15% chia seed biscuits. This is due to the higher fiber content in chia seeds. The protein content of biscuits ranged from 5.52 (control) to 8.09(20%chia seed bread). The moisture, ash, protein, fat and total carbohydrate contents of biscuits were more or less similar to those reported by (Estefanía et.al,).

Chemical analysis of biscuit

Chia seeds level	**Moisture content**	**Carbohydrate**	**Protein**	**Crude Fiber**	**Fat**	**Ash Content**
Control	3.43	70.87	5.52	1.07	17.68	1.43
5%	3.30	68.26	6.90	1.90	18.17	1.47
10%	3.66	66.67	7.01	2.43	18.72	1.51
15%	2.46	66.34	7.48	2.94	19.13	1.65
20%	2.89	64.29	8.09	3.17	19.84	1.72

Chia seed included in the post-weaning diet was able to prevent the development of liver steatosis, hypertriglyceridemia and hypercholesterolemia and improved plasma FFA levels. Hypertension was also prevented. The incorporation of chia seed was also able to ameliorate glucose homeostasis: normal plasma glucose levels and K_{ITT} but an altered Kg.

The dietary LA: ALA relationship plays an important role in plasma lipid levels. M.A. Fortino et al., 2016 studied, this ratio is 0.42. The maximum hypotriglyceridemic effects in rats were observed with a ratio of 0.33, suggesting that the effect of ALA may be due to an increase of long-chain PUFA in membrane phospholipids (**N.M. Jeffery et.al 1996, M. Ihara et.al 1998**). Very low density lipoprotein assembly and secretion is a substrate-dependent process that is highly regulated by the availability of hepatic TAG (**S.H. Choi et.al 2011**) and this content reflects a balance between the uptake of circulating fatty acids, hepatic fatty acid synthesis and oxidation. It is also important to remark that the presence of chia seed from weaning improves the elongases and desaturases indexes and their relationship with liver TAG.

Hepatic steatosis in fetuses from fructose-fed dams were associated with a higher expression of genes related to lipogenesis (SREBP, ACC_2) and a lower expression of fatty acid oxidation genes (PPAR) (**Y. Mukai et.al 2013, R.H. Ching et.al 2011, L. Rodriguez et.al 2013**). M.A. Fortino et al., 2016 observed a high BP in addition to hypercholesterolemia in the SRD-SRD group. The observation that both hypercholesterolemia and hypertension never developed in SRD-SRDC suggests that the post weaning treatment completely suppress the effects of sucrose exposure in utero and suckling period, although sucrose was also present after weaning. Moreover, similar results were reported by Poudyal (**H.Poudyal et.al 2012**) suggesting that the hypotensive effect of chia seed in rats fed high-fructose high-fat diet was associated with increasing docosapentaenoic acid (DPA) and DHA contents in cardiac phospholipids.

A protein fraction of chia has the capacity to act as antioxidant and could be considered as a novel hypotensive source (**D. Orona-Tamayo et.al 2015**). At this point, it is important to notice that Yamamoto (Y Yamamoto et.al 2006) showed an antihypertensive effect of quercetin (flavonoid included in chia seed) in rats fed a high-fat high-sucrose diet, suggesting that the increased nitric oxide availability is one of the main factors of quercetin effect on blood pressure. Between the long-chain n-3 PUFAs, EPA and DHA seem to exert a more pronounced effect than their precursor ALA (**S. Lorente-Cebrian et.al 2013**).

5. Conclusion

As it has been reported by various researchers that chia seeds helps in reducing diabetes and helps in maintaining healthy levels of cholesterol. Chia sees decreases postprandial blood glucose and insulin levels in humans. This study may help to generate technology to diversify the use of chia seeds in the food processing enterprises, specially baking industries. After incorporation of 10% chia seeds in wheat flour it was observed that protein, crude fiber, ash content and fat was increased. From this study can be concluded that development and utilization of chia seeds will not only improve the nutritional status of the population but also helps those suffering from degenerative diseases. The study of M.A. Fortino et al., 2016 provides new information regarding the possible beneficial effect of dietary chia seed given to offspring exposed to a nutritional challenge from utero to adulthood. The presence of chia seed from weaning was able to mitigate and/or prevent the altered lipid metabolism and glucose homeostasis in adult offspring although visceral adiposity was slightly modified.

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