Nutrición Hospitalaria

Revisión

Effect of chia seed (*Salvia hispanica L.*) consumption on cardiovascular risk factors in humans: a systematic review

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Abstract

Introduction: chia is a seed rich in such nutrients as proteins, n-3 fatty acids and especially alpha-linolenic acid (ALA), minerals, fibers and antioxidants. Efforts have been made to assess whether human consumption of chia can reduce cardiovascular risk factors; however, it has not been established as effective and the findings of the few studies to have looked into the matter are inconsistent.

Aim: to systematize the findings of studies assessing the effect the consumption of chia seed, either milled or whole, has in the prevention/control of cardiovascular risk factors in humans.

Methods: this is a systematic literature review (SLR) with no meta-analysis. The articles scrutinizedwere identified in the electronic databases Lilacs, Medline (PubMed version), Cochrane, Scielo, Scopus, and Web of Science under the keywords"dyslipidemia" or "*dislipidemia*", "hyperlipidemia" or "*hiperlipidemia*", "obesity" or "*obesidade*", "salvia"or"*salviahispanica*", "Lamiaceae" or "chia", "hypertension" or "*hipertensão*", "hypertrygliceridemia" or "*hipertrigliceridemia*", and "*riscocardiovascular*" or "cardiovascularrisk." We chose for our selection English-, Portuguese- or Spanish-language articles about clinical trials on humans and published within the last ten years. The biases of risk analysis were carried out considering 6 of the 8 criteria of the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.

Findings: seven studies (n = 200) fit our inclusion criteria. Of the chosen clinical trials, only one was not randomized. Five of the studies were blind experiments. Two of the studies were acute trials, both of them randomized. Of the chia seed interventions, one study showed a significant drop in systolic blood pressure (SBP) and inflammatory markers, yet there was no change in body mass, lipid profile or blood sugar. In four of the studies reviewed there was a significant spike in ALA and eicosapentaenoic acid (EPA), with no significant change to other parameters. In the acute trials, post-prandial blood

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EFECTOS DEL CONSUMO DE LA SEMILLA DE CHÍA (*SALVIA HISPANICA L.*) EN LOS FACTORES DE RIESGO CARDIOVASCULAR EN HUMANOS: UNA REVISIÓN SISTEMÁTICA

Resumen

Introducción: la chía es una semilla rica en nutrientes tales como proteínas; ácidos grasos omega 3, especialmente ácido alfa-linolénico (ALA); minerales; fibras y antioxidantes. Se han hecho esfuerzos para evaluar si el consumo humano de chía puede reducir los factores de riesgo cardiovascular; sin embargo, no se ha establecido como eficaz y los resultados de los pocos estudios que han examinado la cuestión son incompatibles.

Objetivo: sistematizar los hallazgos de los estudios que evaluaron el efecto del consumo de la semilla de chía, ya sea molida o entera, tiene en la prevención/control de los factores de riesgo cardiovascular en los seres humanos.

Métodos: se trata de una revisión sistemática de la literatura (SLR), sin metaanálisis. Los artículos escrutados eran identificados en las bases de datos Lilacs electrónicos, Medline (PubMed versión), Cochrane, Scielo, Scopus y Web of Science bajo la palabra clave "dyslipidemia" o "dislipidemia", "hyperlipidemia" o "hiperlipidemia", "obesity" o "obesidade", "salvia" o "salviahispanica", "Lamiaceae" o "chia", "hypertension" o "hipertensão", "hypertrygliceridemia" o "hipertrigliceridemia" y "riscocardiovascular" o "cardiovascularrisk". Elegimos para nuestra selección artículos en inglés, portugues o español sobre ensayos clínicos en seres humanos publicados en los últimos diez años. Los sesgos de análisis de riesgo se realizaron considerando seis de los ocho criterios del Manual Cochrane para Revisiones Sistemáticas de Intervenciones Versión 5.1.

Resultados: siete estudios (n = 200) encajan con los criterios de inclusión. De los ensayos clínicos seleccionados, solo uno no fue aleatorio. Cinco de los estudios fueron experimentos ciegos. Dos de los estudios eran ensayos agudos, ambos asignados al azar. De las intervenciones de semillas de chía, un estudio mostró una disminución significativa de la presión arterial sistólica (PAS) y los marcadores de inflamación; sin embargo, no hubo cambios en la masa corporal, el perfil de lípidos o el azúcar en sangre. En cuatro de los estudios revisados no había un pico significativo en ALA y ácido eicosapentaenoico (EPA), ni ningún cambio significativo en otros parámetros. En los ensayos agudos, el nivel postprandial de azúcar en sangre fue significativamente menor. Solo un estudio mostró un

sugar was significantly lower. Only one study showed a significant drop in triglycerides (TG), body mass and inflammatory markers; however, the chia seed in that case was mixed with other foods. Most of the studies showed unclear or low risk of bias. Two studies showed a high risk of bias because not all the pre-specified primary outcomes were reported in the findings.

Conclusion: most of the studies did not demonstrate statistically significant results in relation to cardiovascular disease (CVD) risk factors. The evidence regarding the relationship between chia seed consumption and cardiovascular risk factors are insufficient, and the studies included in this review present numerous limitations. Further research is hence needed.

descenso significativo de los triglicéridos (TG), la masa corporal y los marcadores inflamatorios; sin embargo, la semilla de chía en ese caso se mezcló con otros alimentos. La mayoría de los estudios mostraron riesgos claros o bajo sesgo. Dos estudios mostraron un alto riesgo de sesgo, porque no todos los resultados primarios preespecificados fueron reportados en los hallazgos.

Conclusión: la mayoría de los estudios no demostraron resultados estadísticamente significativos en relación con los factores de riesgo cardiovascular (ECV). La evidencia sobre la relación entre el consumo de semillas de chía y los factores de riesgo cardiovascular son insuficientes, y los estudios incluidos en esta revisión presentan numerosas limitaciones. Por lo tanto, se necesita más investigación.

Introduction

Salvia hispanica L., commonly known as chia, is an annual plant belonging to the Lamiaceae family. Originating in such countries as Guatemala, Mexico and Colombia, chia seed was used and consumed as a source of energy and incorporated into a number of foods in the diet of the indigenous Aztec civilization (Ulbricht *et al.*, 2009).

The lipid content in chia seeds varies from 25% to 40%, with 60% of the total lipids made up of ALA (n-3) and 20% composed of linoleic acid (n-6) (Bresson *et al.* 2009). When the oil is extracted from the chia seed, what remains is a significant concentration of dietary fiber (33.9g/100g) and protein (17g/100g). (Ayresa& Coates 1999; Craig & Sons 2004).

Of total dietary fiber, the greatest fraction (53.45g/100g) comprises insoluble fiber, which plays a role in satiety and proper bowel function (Vázquez *et al.* 2008). Rich in magnesium and phenolic compounds (mainly quercetin and kaempferol), chia seed offers significant antioxidant capacity (Lee A.S. 2009; Caudillo *et al.* 2008), while its calcium and potassium content suggests it may be helpful in controlling high blood pressure (HBP) (Vuksan *et al.* 2007).

According to the World Health Organization (WHO 2013), CVD is the world's number one cause of mortality, with approximately 17 million deaths per year. In Brazil, CVD causes 21.1% of all deaths (Datasus 2012), as well as being responsible for a great number of hospitalizations, which results in higher health care and socioeconomic costs (Schmidt *et al.* 2011; Brazilian Cardiology Society 2010).

Among the cardiovascular risk factors that can be modified, controlled or treatedare excess weight (overweight or obesity), hypertension, dyslipidemia and diabetes mellitus, with approximately 5% of worldwide deaths attributed to excess weight (World-Heart Federation 2012).

When added to the diets of pigs and chickens, chia seed boosted the levels of n-3 fatty acids and reduced the amount of cholesterol found in the meat and eggs (Ayerza *et al.* 2002; Azeona *et al.* 2008; Coates *et al.* 2009). In rats, use of the seed lowered plasma LDL cholesterol and triglycerides while it elevated plasma HDL cholesterol (Ayerza *et al.* 2007) levels.

Most of the studies conducted on humans using chia seed looked at the relationship between its consumption and the possible effect it could have on cardiovascular risk factors, by examining such data as body composition and mass, lipid profile, blood pressure, blood sugar and inflammatory markers (Nieman 2009; Vuksan 2007; Nieman 2012). However, the findings of the few available studies are controversial, with little evidence to prove chia seed's efficacy, and furthermore, most of the studies presenting positive results were conducted on animals.

Thus, our aim with this SLR is to synthesize the findings regarding the human use of chia seed and assess its possible benefits in the prevention/reduction of cardiovascular risk factors.

Methods

For this SLR we used the current guidelines for systematic reviews (Liberatti 2009).

We carried out our search from May to July 2014 in the databases Lilacs, Medline (PubMed version), Cochrane, Scielo, Scopus, and Web of Science by consulting the following keywords in English and Portuguese: *dislipidemias* (dyslipidemias), *salvia*, *salvia hispanica*, *obesidade* (obesity), *hipertensão arterial sistêmica* (systemic arterial hypertension), *hipertrigli-*

ceridemia (hypertrigliceridemia), *risco cardiovascular* (cardiovascular risk), chia andLamiaceae. We used the conjunction "And" to associate the use of chia with cardiovascular risk factors, for example "SALVIA [descriptor of subject] and DYSLIPIDEMIAS [descriptor of object]" (Table I). Two researchers (CSF and LFSG) analyzed the articles yielded by the search, independently of each other.

Our inclusion criteria were that the articles had to be less than 10 years old, written in English, Spanish or Portuguese, clinical trials on humans, and not literature reviews. We excluded animal studies, studies that weren't clinical trials, and duplicate articles.

Assessment of risk of bias

To assess risk of bias we used Cochrane Handbook for Systematic Reviews of Interventions Version 5.1 (Higgins 2011), which has areas with ratings "low risk", "high risk" and "unclear risk". The selection of the 6 criteria was based on the applicability to the selected types of study for this paper.

Collaboration's tool thereby performing a critical appraisal of each aspect of the risk separately. The tool assesses bias according to seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcomes, selective outcome reporting, and other sources of bias. Each of the domains appraised can be classified into three categories: low risk of bias, high risk of bias or unclear risk of bias (Fig. 1).

Assessing outcomes of interest

The outcomes we assessed from the studies were total cholesterol, high-density lipoprotein (HDL-c),
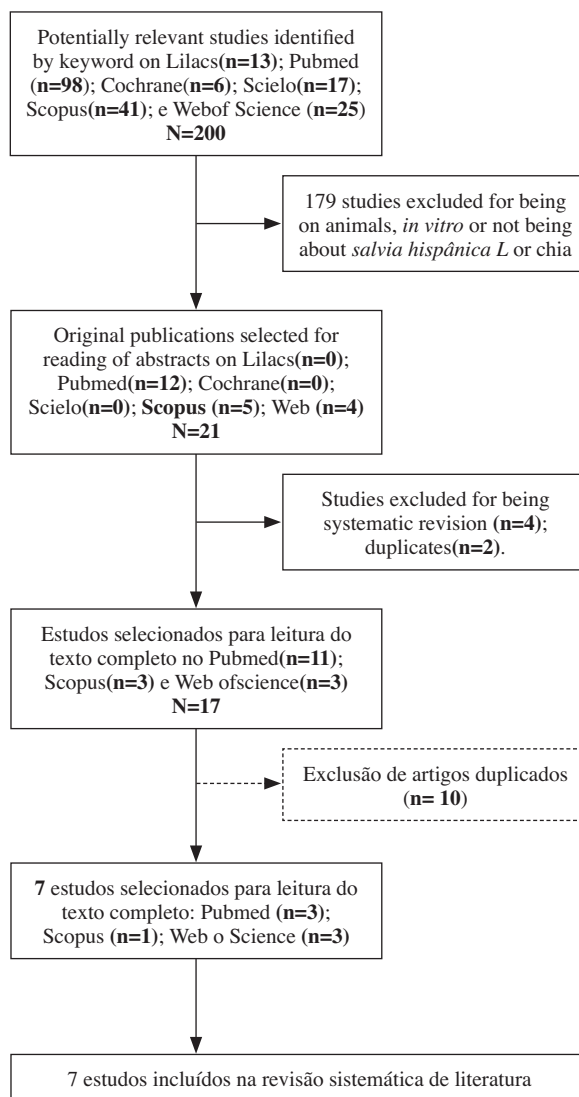
Potentially relevant studies identified by keyword on Lilacs(**n=13**); Pubmed (**n=98**); Cochrane(**n=6**); Scielo(**n=17**); Scopus(**n=41**); e Webof Science (**n=25**)
N=200

179 studies excluded for being on animals, *in vitro* or not being about *salvia hispânica L* or chia

Original publications selected for reading of abstracts on Lilacs(**n=0**); Pubmed(**n=12**); Cochrane(**n=0**); Scielo(**n=0**); **Scopus (n=5**); Web (**n=4**)
N=21

Studies excluded for being systematic revision (**n=4**); duplicates(**n=2**).

Estudos selecionados para leitura do texto completo no Pubmed(**n=11**); Scopus(**n=3**) e Web ofscience(**n=3**)
N=17

Exclusão de artigos duplicados (**n= 10**)

7 estudos selecionados para leitura do texto completo: Pubmed (**n=3**); Scopus (**n=1**); Web o Science (**n=3**)

7 estudos incluídos na revisão sistemática de literatura

Fig. 1.—*Flowchart illustrating study search and selection process.*

Table I Descriptors and concepts used in LRS				
Concepts in português	Concepts in english	Descriptors in portuguese	Descriptors in english (mesh)	Synonyms
Dislipidemia		-	Dyslipidemias	Dislipoproteinemias
Hiperlipidemia		-	Hyperlipidemias	Hyperlipemia
Hipertrigliceridemia	-	Hipertrigliceridemia		
Obesidade		-	Obesity	-
SalviaHispanica				
Hipertensão	Hypertension	Hipertensão	Hypertension	
Chia	-	-		-
Salvia	Salvia	Salvia	Salvia	-
Lamiaceae	Lamiaceae	Lamiaceae		
Risco cardiovascular	Cardiovascular Risk		-	-

Table II

General characteristics of clinical trials included in the selected studies

Clinical trial (author, year)	Chia dosage reported	Design/ follow-up	Population sex/age	Population profile (Metabolic/ pathological)	Duration	Diet/Medications	Statistics	Outcomes of interest	Principal findings
Vuksan et al. 2007.	37 g/d ± 4 g of milled chia seed added to white bread	Randomized, placebo-controlled, single-blind clinical crossover trial	20 teenagers, adults and senior citizens of both sexes. Age: 18-75	Type-2 controlled diabetics	12 weeks	Diet: Recommended by Canadian Diabetes Association Medication: Individuals maintained usual treatment (type and dosage) of oral hypoglycemic, antihypertensive and antilipidemic medication.	NCSS 2000 (NCSS statistical Software Kaysville, UT) Significance $p < 0.05$	-Fasting blood glucose and insulin -Blood pressure (systolic and diastolic) -Lipids (Total, LDL, HDL, TG) Inflammatory markers (CRP, fibrinogen, Von Willebrand Factor VIII).	Compared with control group, chia treatment lowered SBP 6.3 ± 4.2 mmHg ($P < 0.001$); CRP (mg/l) 40 ± 1.6% ($P < 0.04$); Von Willebrand Factor 21 ± 0.3% ($P < 0.03$), ALA and EPA increased with chia consumption ($P < 0.05$)
Vuksan et al. 2010	0, 7, 15 or 24 g/d of chia seed added to white bread	Acute, randomized, placebo-controlled, double-blind clinical crossover	11 adults of both sexes Age?	Healthy, eutrophic individuals	120 minutes. Capillary blood collection 15, 30, 60, 90 and 120 min. after ingestion	Diet and medication not reported	NCSS 2000 (NCSS statistical Software Kaysville, UT) Significance $p < 0.05$	Post-prandial blood sugar	Significant reduction in post-prandial blood sugar with all doses ($P = 0.002$, $r^2 = 0.203$)
Nieman et al. 2009	25 g/d of chia seed mixed with 0.25 L of water – twice daily (50 g/d)	Randomized, placebo-controlled, single-blind clinical trial	76 adults of both sexes Age: 20-70 years	Healthy individuals with excess body fat ($\geq$ 25 Kg/m²).	12 weeks	Diet: individuals oriented to maintain standard diet Medications: none reported	T-Student test- Significance $p < 0.05$	Body composition and mass, inflammatory markers (CRP, Interleukin-6, Monocyte-Chemotactic Protein, TNF Alpha); Oxidative Stress Markers, PA; Lipid Profile; Blood glucose, analysis of fatty acid in plasma	Compared to control group, plasma ALA increased 24.4% (67.3 ± 5.6 to 83.7 ± 8.5 μg/Ml) $P = 0.012$ No significant difference between groups in reduction of body mass or composition, blood sugar, lipid profile, PA or inflammatory markers

Table II (cont.)

General characteristics of clinical trials included in the selected studies

Clinical trial (author, year)	Chia dosage reported	Design/ follow-up	Population sex/age	Population profile (Metabolic/ pathological)	Duration	Diet/Medications	Statistics	Outcomes of interest	Principal findings
Nieman et al. 2012	25 g/d of milled or whole chia seed	Randomized, double-blind, placebo-controlled clinical trial	56 adult and elderly women; Age 49-79 years	Healthy with excess body fat (≥ 25 Kg/m^2), post-menopausal, non-smokers	10 weeks	Diet: individuals oriented to maintain standard diet Medications: none reported	Anova T-Student test Mann-Whitney test and Wilcoxon test. MATLAB R2010a (MathWorks, Inc., Natick, MA) Significance $p < 0.05$	Body mass and composition, inflammatory markers (PCR, Interleucine-6, Monocyte Chemoattractive Protein, TNF Alpha); Oxidative Stress Markers, PA; Lipid Profile; Blood glucose, analysis of fatty acid in plasma	Significant increases in serum concentrations of ALA (58.4% $p = 0.002$) and EPA (38.6% $p = 0.016$) in the group given milled chia compared to that given whole chia or placebo. No significant difference in body mass or composition, blood pressure, lipid profile or inflammatory markers between whole-seed, milled or placebo groups.
Jin et al. 2012	25 g/day of milled chia	Individual, self-reported clinical trial. Six blood extractions	10 women Age 52-60 years	Post-menopausal, healthy. BMI-17 to 29 Kg/m	7 weeks	Diet: individuals oriented to maintain standard diet Medications: none reported	Anova T-tests-Bonferroni Significance $p < 0.05$	Plasma concentrations of ALA, EPA and DHA	No significant change in body mass.(Pre-study 69.4 ± 13.8 Kg; three weeks 69.3 ± 13.7 Kg; seven weeks 60.1 ± 13.4 Kg) - p value not mentioned ALA - 138% increase ($p < 0.001$) EPA- 30% increase ($p = 0.019$) DHA-decrease ($p=0.030$)

Table II (cont.)

General characteristics of clinical trials included in the selected studies

Clinical trial (author, year)	Chia dosage reported	Design/ follow-up	Population sex/age	Population profile (Metabolic/ pathological)	Duration	Diet/Medications	Statistics	Outcomes of interest	Principal findings
Guevara-Cruz et al. 2012	4 g of chia seed mixed with palm, oats and soy powder diluted in 250 mL of water/2 per day	Randomized, double-blind, placebo-controlled clinical trial	67 adults of both sexes Age 20-60 years	Individuals with excess body mass and metabolic syndrome	2 months	Diet: 500 kcal reduction from usual diet, reduction in saturated fat and cholesterol for 2 weeks before randomization, and after randomization reduction of 500 kcal in diet and further 235 kcal in complement Medications: none reported	Kolmogorov-Smirnov Z test Anova T-Student Significance $p < 0.05$	Body mass, waist perimeter, body composition, PA, blood sugar, insulin, lipid profile, leptin, adiponectin, CRP	Significant decrease in body mass and composition, BMI and waist circumference in both groups ($p < 0.0001$). Significant decrease in TG ($p = 0.05$), CRP (0.01) and insulin resistance (0.001) only in group with diet + complement. No significant difference found in blood sugar or total plasma insulin, cholesterol, HDL-c or LDL-c in either group ($p > 0.05$) No change in leptin or adiponectin.
Ho et al. 2013	0, 7, 15 or 24 g of whole or milled chia added to white bread	Acute, randomized, crossover clinical trial	13 individuals of both sexes	Eutrophic, healthy individuals	Capillary blood collection 15, 30, 45, 60, 90 and 120 min following ingestion	Diet: not reported Medications: individuals using blood sugar-metabolization-altering medications excluded from study	Anova NCSS 2000 (NCSS statistical Software Kaysville, UT) Significance $p < 0.05$	Post-prandial blood sugar represented by area under curve (IAUC))	Decrease in post-prandial blood sugar significantly related to dosage of chia ($p = 0.004$); however, not related to form—milled/whole seed ($p = 0.74$) when compared to placebo group

PAS = systolic blood pressure, EPA = eicosapentaenoic acid, DHA = docosahexaenoic acid, BMI = body mass index, TG = triglycerides; CRP = C-reactive protein

low-density lipoprotein (LDL-c), triglycerides (TG), blood sugar, body mass, systolic and diastolic blood pressure (SBP, DBP), inflammatory markers, and ALA and EPA concentrations.

Data extraction

The data we extracted from the articles in our LRS were: author and year of publication; how chia seed was administered and dose; design\follow-up; study population (sex\age); population profile (metabolic\pathological); exposure\duration; diet\medications; statistics, outcomes of interest, and principal findings. (Table II).

Findings

Study selection

Figure 1 is a flowchart that describes the process of selecting the studies. The search turned up 200 articles, of which 13 references were from Lilags, 98 from Pubmed, six from Cochrane library, 17 from Scielo, 41 from Scopus, and 25 from Web of Science.

We made our initial selection based on title and abstract, which were read by two reviewers independently of each other. Divergences between the reviewers in selecting the studies were resolved by consensus. Upon analyzing the inclusion and exclusion criteria, seven studies were included in the LRS.

Description of studies in systematic review

Table II highlights the principal characteristics of the studies included in our review. Sever articles published between the years 2007 and 2013 met the inclusion criteria and were selected for the LRS. All the studies are clinical trials, six are randomized (Vuksan 2007; Vuksan 2010; Nieman 2009; Nieman 2012; Guevara-Cruz 2012; HO 2013), and five are placebo controlled (Vuksan 2007, Vuksan 2010, Nieman 2009, Nieman 2012, Guevara-Cruz 2012). Three of the articles cover double-blind clinical trials (Vuksan 2007; Nieman 2012; Guevara-Cruz 2012), two are single-blind, and three are crossover trials (Vuksan 2007; Vuksan 2010; Ho 2013). Two of the studies are acute trials (Vuksan 2010; HO 2013). In one of the studies chia seed was added to other foods (Guevara-Cruz 2012).

The amount of the chia seed used in the different studies varied from 4 to 50g, with some of the trials using milled chia (Vuksan 2007; Jin 2012), while others used whole chia seed (Vuksan 2010; Nieman 2009; Guevara-Cruz 2012) or both (Nieman 2012; Ho 2013). In some of the studies, the chia, in either whole or milled form, was added to bread (Vuksan 2007; Vuksan 2010; Ho 2013) or diluted in water (Nieman 2009). In Guevara-Cruz *et al*.'s 2012 study, the chia, along with palm, oats and soy protein, were diluted in water. The studies where milled chia (Vuksan 2007; Nieman 2012; Jin 2012) was used obtained the most positive results, as these found an association with lowered blood sugar levels (Vuksan 2010; Ho 2013).

Study-participant age varies from 18 to 79 years of age. Sample size was a factor that varied a great deal, with the smallest sample group composed of 10 individuals (Jin 2012), and the largest 76 (Nieman 2009). Study duration varied as well, the average being approximately 10 weeks.

The study populations' metabolic profiles varied as well, with one study involving people with type 2 diabetes (Vuksan *et al*. 2007), and another dealing with metabolic syndrome (Guevara-Cruz *et al*. 2012). The rest of the studies selected individuals showing no signs of disease, all of them being either healthy (Vuksan *et al*. 2010; Jin *et al*. 2012; Ho *et al*. 2013) or overweight (Nieman *et al*. 2009; Nieman *et al*. 2012).

Only two of the studies involved dietary intervention (Vuksan *et al*. 2007; Guevara-Cruz *et al*. 2012). The findings from these are significant for outcomes relating to CVD risk, such as SBP, inflammation marker (Vuksan *et al*. 2007), body mass, waist circumference, body composition, TG and C-reactive protein (CRP) (Guevara-Cruz *et al*. 2012; Jin *et al*. 2012). The studies that did not involve dietary intervention (Nieman *et al*. 2009; Nieman *et al*. 2012; Jin *et al*. 2012) and did maintain the dietary profile of the individual participants, did not obtain results significant for said outcomes. The acute trials (Vuksan 2010; Ho 2013) sought to assess only post-prandial blood sugar levels in relation to chia seed consumption.

The CVD-risk outcomes of interest assessed in the studies varied. Although most of the outcomes were not significant for such data as body mass, body composition, inflammatory markers, blood sugar, and lipid profile (Chart 2), there was consensus in regard to the increase in ALA and EPA seen with chia ingestion (Vuksan *et al*. 2007, Nieman *et al*. 2009, Nieman *et al*. 2012, Jin *et al*. 2012). The acute studies did not look at ALA or EPA (Vuksan *et al*. 2010, Ho *et al*. 2013); only at post-prandial blood sugar.

Cochrane Collaboration bias assessment

Cochrane Collaboration's bias- or systematic error-assessment tool aims to determine whether a study was executed properly, that is, without bias. For a study to be valid one needs to determine whether the design, data collection and analysis were done correctly. Chart 3 shows the summarized bias risk according to the authors regarding each of the articles in this LRS selection. Graph 1 shows the bias risk for all the articles assessed.

Six of the articles included (Table II) are randomized clinical trials, widely regarded as the gold standard among all clinical research methods, as they are able to produce direct scientific evidence with a low probability of error and thus shed light on a cause-effect relationship between two events (de Carvalho 2013).

Though almost all the studies selected are said to have included randomization, most of them were assessed to have an unclear risk of bias for not providing data as to how the randomization was conducted. Therefore, we were unable to ascertainwhether there had been any criteria for randomization that would minimize the risk of bias.

As far as blinding of study participants, personnel and outcome evaluators, there was a more homogeneous percentage between low and unclear risk of bias in the studies (Fig. 1). One reason for this is the fact that there was no report as to how the blinding was obtained. It must be stressed that bias or systematic error represents a flaw in the collection, analysis, interpretation, publication or review of data, leading to conclusions that systematically tend to depart from the truth (de Carvalho 2013). As most of the studies we looked at were of unclear risk of bias for lack of information, this risk seems inflated.

In regard to the reporting of selective outcomes, the results described in both the studies by Nieman *et al*. (2009 and 2012) showed high risk of bias. This is because in these studies not all the primary outcomes were reported, which may compromise the quality of the study. In this respect the other studies were found to have a low risk of bias.

Discussion

Most of the studies investigating chia seed consumption, both by animals and humans, looked at the effect on cardiovascular risk factors, excess body mass and serum concentrations of ALA and EPA. The interest in this seed arose, mainly, due to its high levels of ALA, fiber, proteins, minerals (calcium, magnesium and potassium) and antioxidants (chlorogenic, caffeic, quercetin and kaempferolacids) (Norlaily 2012).

Although not common in studies on humans, some research points to the consumption of chia having a positive effect on health. However, these studies vary a great deal in both sample size and the profiles of the individuals in the sample group, which may have created a discrepancy in the findings. Furthermore, the quantities and forms of chia seed —ie, milled, whole-seed, baked in bread— were different in the different studies.

In Viksan *et al*.'s 2007 study, although it was one of the few with significant findings (lowered blood pressure and inflammatory markers) the sample size was small (20 individuals) and the participants' ages varied from teenage to old age (18 to 75 years old). Hence, having individuals in such distinct physiological conditions may have affected the results, with no significant difference found in lipid profile or body mass. However, it was one of the few studies that took into account the positive effect the nutritional intervention had on the study outcomes.

Nieman *et al*. (2009) had the largest sample size in their study (76 individuals of both sexes), but their selection also had a broad age range, with both adults and senior citizens (20-70 years old); they used chia seed diluted in water, and their study had the largest amount of chia (50g). There was no significant difference in reduction of body mass or composition, plasma lipoprotein concentrations, blood pressure or inflammatory markers.

Nieman *et al*. (2012), so as to minimize the differences between individuals, selected 56 women who were healthy, post-menopausal (49-79 years old), non-smokers and who consumed 25g of milled chia seed per day. They noted a significant increase in serum

Table III
Summary of risk of bias. Review judgment by authors on each bias-risk item for each study in selection

Articles	Other sources of bias	Selective outcome reported	Incomplete outcome	Researcher blinding	Participant blinding	Allocation concealment	Random-sequence generation
Vuksan 2007	+	+	+	+	+	+	+
Vuksan 2010	?	?	?	?	?	+	?
Nieman 2009	?	?	?	?	?	-	?
Nieman 2012	?	?	?	?	+	-	?
Jin 2012	?	?	+	+	+	+	+
Guevar 2012	?	?	?	?	+	+	?
Ho 2013	+	?	+	+	+	+	?

Key: + low risk
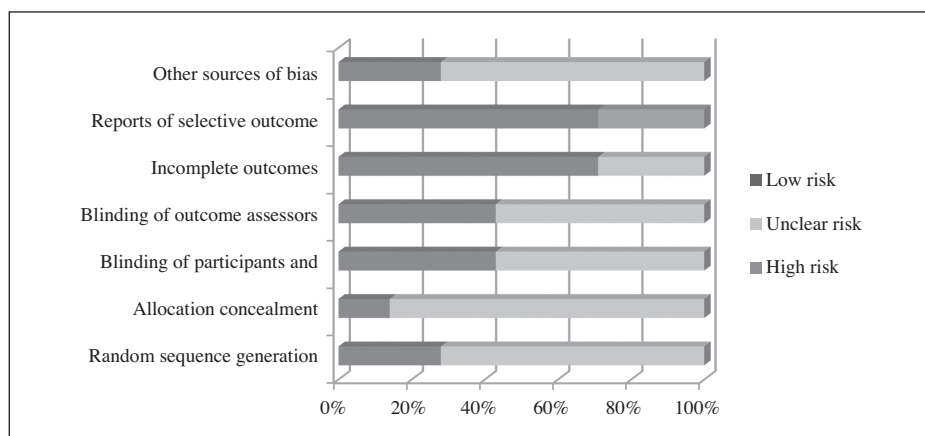- high risk
? unclear risk

Fig. 2.—Frequency of risk of bias in studies assessed.

ALA and EPA levels in the group given milled chia, but no change was found in the other study parameters.

The acute trials of Vuksan *et al.* (2010) and Ho *et al.* (2013) involved a small number of individuals, 11 and 13 respectively, and used milled and/or whole-seed chia to investigate only post-prandial blood sugar levels. Both studies demonstrated chia seed to lower blood sugar.

Jin *et al.* (2012) assessed 10 post-menopausal women using 25g of milled chia per day over a seven-week period, and found a significant increase in serum ALA and EPA concentrations. Now, the study by Guevara-Cruz *et al.* (2012), where they used a mixture of palm, oats and soy powder diluted in 250 mL of water in conjunction with a dietary intervention, demonstrated a significant decrease in body mass, BMI, waist circumference, TG, CRP and insulin resistance.

In experimental studies, chia seed supplementation attenuated metabolic, cardiovascular and hepatic alterations in rats subjected to a diet heavy in fat and carbohydrates over an eight-week period. They noted improved insulin sensitivity and glucose tolerance, and a reduction in visceral fat, fatty liver and heart and liver inflammation. No change was found in plasma lipid concentrations or blood pressure (Poudyal 2012, Chicco 2008). In another study on rats ingesting chia seed, a significant drop was found in TG and LDL concentrations and a spike in HDL and polyunsaturated fatty acids (Ayerza 2007).

All the studies show a certain risk of bias in some respect, according to Cochrane Collaboration's tool. Mainly for the omission of details regarding study design, how the randomization and blinding was done, and often the description of the outcomes proffered in the study. Hence the quality of methodology in the studies on human chia consumption was compromised, producing inconclusive results where the efficacy of consuming chia to prevent/control cardiovascular risk is concerned.

In spite of the many shortcomings of the studies we selected, the strength of this LRS is the fact that the research consists in two authors, independently of each other, thoroughly searched six distinct databases. This means there is a good likelihood that the all the publications relating to the subject were identified and included in the review. However, the findings are contradictory, probably due to the methodological shortcomings identified in the selected studies.

Conclusion

The studies investigating the effect the consumption of chia seed has on cardiovascular risk present inconclusive results. We underscore the need for randomized, double-blind, placebo-controlled clinical trials in order to obtain results that are more reliable.

Conflict of interest

The authors declare that there is no conflict of interest.

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