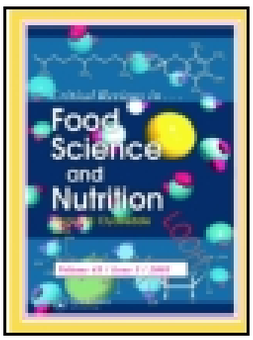

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Running title: sesame and lipid profile and blood pressure.

The effect of dietary intake of sesame (*Sesamumindicum L.*) derivatives related to the lipid profile and blood pressure: a systematic review

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ABSTRACT

In this Systematic Review we discuss the scientific evidence about the effect of dietary intake of seeds and sesame derivatives on lipid profile and blood pressure (BP) of hypertensive and dyslipidemic individuals. Clinical trials published in English, Portuguese or Spanish were

searched on databases Lilacs, PubMed, Isi Web of Knowledge, Cochrane Library, Scopus, Trip Data Base and Scielo. The bibliographic search period was started in September 2013 and ended in January 2014.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. Of the 7 clinical trials included, five evaluating individuals with hypertension observed a significant reduction in systolic and / or diastolic blood pressure. The two articles that evaluated individuals with dyslipidemia, showed improvement in lipid profile. The mechanisms of action are still being studied. Regarding the bias risk analysis, clinical trials included showed few descriptions of the methods applied. There are few studies about sesame ingestion, and it was observed high risk for bias in the selected studies. More standardized methods with attention to the design of studies are needed to improve the level of the evidence.

Keywords

sesamum, risk factors, hypertension, dyslipidemia, cardiovascular disease, sesame oil

INTRODUCTION

Sesame (*Sesamumindicum L.*) belongs to *Pedaliaceae* family and is a plant grown by small farmers in both tropical and subtropical countries, intercropped with other crops (Ricci et al. 1999).

It is a food widely used in Middle Eastern cuisine, in bakery products, pastes, vinaigrettes for salads and vegetarian preparations. Sesame can be found in the form of whole or ground seeds, oil or flour (Zoumpoulakis et al. 2012).

Sesame has high nutritional value and its main components are oil (54.08%) and protein (21.83%) (Beltrão and Vieira, 2001).The seeds contain calcium, phosphorus, vitamins A, E, B_1, B_2 and B_3(Namiki, 1995). It is also rich in phytosterols, lecithin, unsaturated fatty acids and lignans(Zoumpoulakis et al. 2012).

On the potential health benefits, depending on the variety of available nutrients, as well as specific lignanssuch as sesamin and sesamolin (Namiki, 2007), clinical trials with seeds and sesame derivatives have been conducted on its possible effects on blood pressure (BP) and modulation of the lipid profile.

The objective of this article is to discuss the scientific evidence available in the literature about the effect of dietary intake of sesame seeds and derivatives on the lipid profile and blood pressure of hypertensive and dyslipidemic individuals.

METHODOLOG**Y**

Qualitative systematic review of clinical trials was performed.

The question that guided this review was: "What is the effect already described in the literature of consumption of seeds and sesame derivatives in blood pressure and lipid profile?"

The search strategy and the bias risk analysis were performed by two evaluators who carried out the research of articles separately, in order to increase the capture range and minimize publication bias.

The two examiners reached a consensus about which items would be exploited in the systematic review and followed the methods described below.

Research strategies

In order to carry out the literature research, seven sources were used: Lilacs, PubMed, ISI Web of Knowledge, Cochrane Library, Scopus, Trip Data Base and Scielo. The literature search period started in September of 2013 and ended in January of 2014.

In the research strategy, the descriptors were surveyed through the website of *Biblioteca Virtual em Saúde* (BVS) (Biblioteca Virtual emSaúde, 2013), in English, Portuguese and Spanish using the following key words in Portuguese: sesame, flour, risk, dyslipidemia, cardiovascular, seed, oil, sesame oil and capsule. The descriptors found in Portuguese for the keywords were: *sesamum*, flour, risk factors, dyslipidemia, cardiovascular disease, seeds, oils, sesame oil and capsules.

In a second strategy, the following key words and their synonyms (if present) were researched in the database fields "title" and "abstract": *sesamum brasiliense*, sesame-of-Brazil, sesame, flour, risk factors, cardiovascular disease, lipids and dyslipidemia.

Then, tables were compiled for each source of research to catalog searches – untilthe depletion of sources. These tables contain the Descriptors column (when the source contemplated them), *MESH Terms* (when the source contemplated them), Keywords (when the source did not include the descriptors or *MESH terms*) and number of articles found.

Upon completion of the searches in the sources, the relevant articles to the topic of interest were selected for reading and analysis.

Study selection

In this article, we used various combinations of keywords described previously directed to our topic of interest with the widest search as possible to obtaining an overview of the publications in relation to sesame consumption. We'd reached the goal on studying the relation between sesame ingestion and cardiovascular disease. After having the panoramic view of our widest search, we judged that relation between sesame ingestion, hypertension and dyslipidemia would be very important to the current knowledge.

The criteria for the inclusion of papers were: studies describing clinical trials, which were in English, Portuguese or Spanish and analyzed the outcomes of interest "lipid profile" and "blood pressure", which populations contemplated individuals with hypertension or dyslipidemia, mainly they are comorbidities with a high prevalence in the world population.

Exclusion criteria were: records of the genre letter and annals of congress; interventions that were composed of mixtures such as cakes or cereal barsand articles with outcomes or languages different than the inclusion criteria.

Risk analysis of biases

Risk analysis of biases held by both evaluators considered 6 of the 8 criteria of Cochrane Handbook for Systematic Reviews of Interventions Version 5.1 (Shuster, 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.

The inclusion and exclusion of articles was discussed between the two evaluators, who reached a consensus to determine which studies would be explored.

Data extraction

After selected, the articles were arranged in tables according to the populations diagnosed with hypertension or dyslipidemia.

The outcome measures of the studies included: systolic blood pressure (SBP) and diastolic blood pressure (DBP), serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) and triglycerides (TG).

The realization of the meta-analysis was disregarded as a result of heterogeneity found on the populations, interventions and experimental design of the trials.

RESULTS

Search for articles and data extraction

Seven clinical trials published in the last nine years were included. The interval of publication of studies ranged from 2005 to 2012.

The search strategy allowed finding titles in English, Portuguese, Spanish, French, Dutch, German, Chinese and Russian. Papers in English and Portuguese were included.

In a total of seven databases searched, 3.417 abstracts were found. Excluding duplicate abstracts, the remaining total was of 1.432 (Figure 1).

After the abstracts were read by both evaluators, 38 were selected by consensus. Of these, 21 papers were excluded (9 owing to the different outcomes of the proposed; 1 owing to being in different language from those of the inclusion criteria; 2 due to insufficient data; 5 due to

intervention composed of mixtures; 4 owing to being population that didn't present hypertension and dyslipidemia) (Figure 1).

From 7 clinical trials included, 5 evaluated populations diagnosed with hypertension and 2 with dyslipidemia (Table 1).

Risk analysis of biases

Most clinical trials were not randomized, presenting high risk of selection bias. Furthermore, in the three studies that were randomized, it was not possible to identify the description of the generation of the randomization sequence, besides the hidden allocation of participants (Figure 2).

The studies that were randomized also did not describe the blinding of participants and personnel, presenting a high risk of performance bias. Two non-randomized studies have examined this area, but it was not possible to identify the description of blinding of the outcome assessors specifically, presenting a high risk of detection bias (Figure 2).

There was no information about the item *Incomplete Outcome Data* on selected papers, resulting in undefined risk for attrition bias (Figure 2).

All clinical trials evaluated the proposed outcomes, representing low risk of information bias (Figure 2).

Effects of sesame in individuals with hypertension

All five clinical trials which used interventions derived from sesame and evaluated individuals with hypertension found significant results for the reduction in SBP and / or DBP (Table 2). Among them, 3 studies also evaluated the lipid profile outcome, 2 of them having

found significant reduction for TC and LDL-c, 1 having found a significant increase in HDL-c and 2 having found significantly reduced TG (Table 2).

The amounts of sesame seeds and derivatives used in clinical trials varied as shown in Table 4. Of these, the low amount, if compared to other studies, used by Wichistrainoi et al (2011), of 7.6g / day of black sesame flour in capsules, administered for 4 weeks in pre-hypertensive population, with a mean age of 49.3 ± 7.7 years stood out. The result in the reduction of SBP was significant, and of DBP not significant (Table 2).

Three studies –Sankar et al (2005), Sankar et al (2006a) and Sankar et al (2006b)–that used sesame oil as intervention ranging from 45 to 60 days, in medicated hypertensive subjects (mild to moderate), aged between 35 and 64 years old, male and female – found significant results in reduction of SBP and DBP (Table 2).

A study in adults, which used sesamin capsules for 4 weeks in medicated mild hypertensive individuals, also found significant reduction of ~3% and ~2%, SBP and DBP, respectively (Alipoor et al., 2012).

The effect of sesame oil on the lipid profile of hypertensive individuals was observed in studies of the research group of Sankar et al 2005 and 2006. A significant decrease of ~ 18% TG (Alipoor et al., 2012) of ~ 18% and ~ 24% in TC and LDL-c, respectively (Sankar et al., 2006a) and ~ 16%, ~ 24% and ~ 19% TC, LDL-c and TG, respectively, with the significant increase of ~ 9% in HDL-c (Sankar et al., 2005) was observed (Table 2).

Effects of sesame in individuals with dyslipidemia

The two articles that evaluated the effect of seeds and sesame flour in individuals with dyslipidemia found positive results in the lipid profile (Table 3).

Chen et al (2005), using sesame flour and standardized diet for 4 weeks (with 6 of the 21 subjects of both sexes with a mean age of 50.9 ± 3.7 years in use of lipid-lowering medications), observed a significant reduction of ~6% and ~9% in TC and LDL-c, respectively. After 4 weeks of the end of the intervention, there was significant decrease of 4% in HDL-c and significant increase of ~8% in LDL-c (Table 3).

Alipoor et al (2012), using white sesame seeds for 60 days in individuals of both sexes, aged between 50 and 70 years, observed a significant reduction of ~8% and ~10% in TC and LDL-c, respectively (Table 3).

DISCUSSION

Diet can be either a risk or a protection factor for the development of cardiovascular disease (OPAS, 2003). Some dietary components are associated with decreased risk, like the polyunsaturated and monounsaturated fatty acids, dietary fiber, antioxidants and phytochemicals – also found in foods containing vegetable oils, such as sesame seeds (Chen et al., 2005).

The effect of the reduction of BP through the consumption of seeds and sesame derivatives may be related both to their antioxidant lignans (sesamin, episesamin, sesamol and sesamolin) and to their content of polyunsaturated fatty acids and vitamin E (Sankar et al., 2006b). However, some studies related to vitamin E do not corroborate this result (Ward et al., 2007; Economides et al., 2005; Palumbo et al., 2000).

Miyawakiet al (2009) attributed BP reduction to the effect of sesamin contained in their capsules (Table 2). In this study, in humans with mild hypertension, decrease in average of 3.5 mmHg in SBP and DBP of 1.9 mmHg after ingestion of 60 g of sesamin per day for 4 weeks was observed (Table 2).

The antihypertensive effects of sesamin have been demonstrated in previous studies, in which experimental models of hypertension suggest an antagonistic activity to Ca^{2+} channels (Nakano et al., 2003; Kita et al., 1995; Matsumura et al., 1998; Lee et al., 2004). One of the studies in which sesamin performed this activity – having as object the aortic ring of hypertensive rats fed with lignan– histological renal damage has been effectively reduced, as well as an attenuation of the rigidity of the intimate layer, and fibrinoid degeneration of the arterial wall could be observed. The intention would be to favor the treatment of hypertension and cardiovascular hypertrophy (Matsumura et al., 1998). The pharmacological effect of sesamin from sesame oil may have been responsible for the reduction in BP in hypertensive and diabetic patients treated in the study of Sankar et al (2006a) (Table 2). In Sankar et al (2005), this same action may also have been supported together with nifedipine. This study found that sesame oil would offer better protection to the level of blood pressure, lipid profile and lipid peroxidation compared to other oils such as peanut and sunflower.

The improvement in the balance between contraction and relaxation factors in the endothelium of blood vessels may be a mechanism responsible for the antihypertensive effect of black sesame flour found by Wichistranoi et al (2011). In this study, pre-hypertensive individuals did not use antihypertensive drugs (Table 1). Thus, black sesame flour could have increased relaxation factor, resulting in increased endothelium-dependent vasodilation related to oxidative stress. Karatziet al (2012), for example, showed improvement in endothelial function and reduction of BP, with acute and long-term use of 35g sesame oil in hypertensive individuals, male, with a mean age of 52.7 ± 10.4 years.

In addition, other factors that could influence the BP reduction mechanisms, through the intake of seeds and sesame derivatives, would be related to increased intake of vitamin E provided by these foods (Karatzi et al., 2012). Wichistranoi et al (2011) found an increase in serum levels of vitamin E, linking it to increased inhibition of their catabolism or their own intake. Another study suggested the hypothesis that the increase in bioavailability of vitamin E has occurred through interactions between sesame lignan and tocopherol (Kamal-Eldin et al., 2000).

The accumulation of vitamin E acts by detoxification of hydroxyl and proxy radicals, leading to reduction of lipid peroxidation or reducing the excess of aldehyde tissues (Sankar et al., 2005). Previous studies have shown this fact by showing inhibition of lipid peroxidation by supplementation of either vitamin E or sesamin and sesamolin (Cooney et al., 2001; Ikeda et al., 2003; Kang et al., 1998; Nakai, et al., 2003; Yamashita et al., 1995; Ikeda et al., 2007). Probably, this antioxidant effect contributes to the improvement of endothelial dysfunction by free radicals (Ito and Suzuki, 1995), resulting in an increase of the vasodilator factor, nitric oxide (Thomas et al., 2003).

In an experimental study, it was shown that the sesamin induced increase in the concentration of nitric oxide and inhibited the production of endothelin-1 by endothelial cells (Lee et al., 2004). These results indicate increased endothelial capacity for expansion.

Wichistranoi et al (2011) point out that the discussion of the assumptions that justify the reduction of BP through the use of sesame flour are still based on the evaluation of a few parameters, such as the reduction of malondialdehyde and the increase in plasma vitamin E found in their study. Other possible mechanisms related to antioxidants such as vitamin C, and

also nitric oxide, which together can determine the endothelium-dependent vasodilation have not been measured. They also emphasized that the potential effect of vitamin E in humans, on membrane fluidity and ability to inhibit the synthesis of 20-HETE by sesame lignan in kidney and liver microsomes, were not investigated by them. This calls for further investigation of these variables in order to explain how the sesame seeds and derivatives can act in the prevention of hypertension.

Another factor that may ultimately contribute to reduced BP of individuals pre- or already hypertensive would be the loss of weight with concomitant intake of sesame derivatives, observed by the same research group of the year 2006 (Sankar et al. 2006a). The reduction of body weight (Mori et al., 1999; Prisco et al., 1998) may have been the principal factor responsible for the reduction of blood pressure in individuals of Sankar studies (Sankar et al., 2006a; Sankar et al., 2006b). A mechanism that could explain these findings, is about the polyunsaturated fatty acids (PUFA) present in sesame oil, that would increase plasma levels of lepitin(Hynes et al., 2003). The PUFA supply arised from sesame oil, the reduction of serum sodium and potassium increase, may have favored the reduction in BP (Mori et al., 1999; Priscoet al., 1998). However, these mechanisms are not clear. Since were not reported sufficient data on the usual diet held by individuals and data on the chemical composition of sesame oils used, it is not possible to discuss what dietary factors may influence weight loss observed.

In general, the clinical trials reviewed in this study, which used seeds or sesame derivatives and rated the outcome "lipid profile", finding significant results in modification, point to benefits over TC parameters, HDL-c, LDL-c and TG levels (Tables 2 and 3).

The hypocholesterolemic effect of intake of polyunsaturated fatty acids has been widely described in the literature, but the mechanisms, still uncertain, permeate some of the following theories: reduced absorption and synthesis of cholesterol; increased excretion of neutral sterols; changes in the synthesis and catabolism rate of lipoproteins; and changes in fatty acid composition of the lipid membrane (Goodnight et al., 1982).

Thus, other food components such as dietary fibers (Chen et al., 2005; Hirata et al., 1996), sesamin (Dobiásová and Frohlich, 2001), vegetable protein and phytochemicals (Chen et al., 2005)– presentin oil seeds and sesame – seem to contribute significantly to the lipid-lowering effect.

It is believed that the mechanism of hypocholesterolemic effect of the sesamin in rats is related to reduction in serum and liver cholesterol concentrations. These reductions take place through the inhibition of intestinal absorption and synthesis of cholesterol, increasing the excretion through the bile and decreasing the activity of 3-hydroxy-3-methylglutaryl-CoA reductase inhibitors (Hirose et al., 1991; Ogawa et al., 1995; Kang et al., 2000; Noguchi et al., 2004). The decrease in this activity is one of the target pathways of the lipid-lowering drug treatment, with the limiting of enzyme rate in cholesterol biosynthesis, and the inhibition of the activity of acyl-CoA cholesterol acyltransferase. The sesame lignans may also induce a moderate increase in the activity of the enzyme 7-α-hydroxylase (Kamal-Eldin et al., 2011; Umeda-Sawada et al., 1994).

In an experimental study in rats, in which were added to the diet sesame seed with high concentrations of lignans sesamin and sesamolin (at 200g / kg), an increase in the activity of fatty acid oxidation enzymes such as acyl-CoA-oxidase, carnitinepalmitoyltransferase, 3-

hydroxy-CoA dehydrogenase and 3-quetoacil-CoA thiolase, an increase in hepatic mitochondrial and peroxisomal fatty acid oxidation was observed. In contrast, there was a decrease in the synthesis of enzymes that produce fatty acids such as fatty acid synthase, glucose-6-phosphate dehydrogenase, ATP-citrate lyase and pyruvate kinase (Sirato-Yasumoto et al., 2001).

Sankaret al (2005) observed a significant reduction in TC parameters, LDL-c and TG and increased HDL-c levels after the use of sesame and sunflower oil. In this study, peanut oil, rich in monounsaturated fatty acids, increased HDL-c levels, despite having high triglyceride levels also. In the following year, 2006, the same research team observed reduction of TC, LDL-c and TG (Sankar et al., 2006a) and also found a reduction in TG levels in another study (Sankar et al., 2006b), after the use of sesame oil. The reduction of these parameters may be related to the composition, rich in fatty poly and monounsaturated acids, of sesame oil. Lignans present in sesame oil may also have played a role in the modification of lipid profile (Sankar et al., 2006b). However, despite being of the same manufacturer, it has not been reported chemical composition of sesame oils used in these studies. The chemical composition of sesame oil used may help to explain the positive results obtained regarding lipid profile, since the amount of polyunsaturated fatty acids, the presence of sesamin and antioxidants, could be associated with reduction of cholesterol levels.

Based on the concepts of food analysis, the sesame samples used in these seven researches were varied in functional composition. Therefore, these clinical trials represented different mechanisms in improving lipid profiles and blood pressure. The functions of sesame oil may contribute due to its high PUFA content, and sesame seeds may contribute due to lignans and sesame peptides, for example.

The variability of interventions of the papers analysed in this study such as sesame oil, sesamin capsules,black sesame flour capsules, white sesame seeds and sesame flour are different products and must have different properties on its composition, because of its different levels of nutrients such as lignans, PUFA, diet fibers and vitamin E, for example. This could influence the mechanism of action of sesame derived to improve blood pression and dyslipidemia. The way that sesame in the studies were produced and processed can also contribute to this difference, such as the color of the sesame seed. However we excluded papers that presented sesame composed of mixtures such as cakes or cereal bars because its variability could be greater due to the use other ingredientes. We search for a purest form of sesame because we believed that minimize other effect of any ingredient in its composition.

Regarding the risk analysis of bias, in general, the clinical trials included showed few descriptions in relation to proceedings in which such methods were applied. As well as the three articles that underwent randomization, we could not identify its description clearly.

In carrying out this review we have a wide systematic search of studies in 7 databases. However, three (Sankar et al., 2005; Sankar et al., 2006a; Sankar et al., 2006b) of the seven studies included, were of the same authorship as met the eligibility criteria.

The study Wu et al (2009), did not observe significant results in lowering blood pressure and in the modification of the lipid profile and has not been included in the current review, because it fits in our exclusion criteria to use sesame seeds in bar.

There are few randomized clinical trials on the topic and this impaired differentiated point of view by other authors in this study. However, the bias risk analysis, in general, was

unsatisfactory. In addition, the use of antihypertensive medications and lipid-lowering in some of the selected studies may have influenced the results in favor of intervention.

On the theme that says about what is being studied worldwide on functional foods, that are important aids in nutritional interventions, it is necessary to carry out more controlled clinical trials on the effects of sesame derivatives consumption.

LIMITATIONS OF EVALUATED STUDIES

Through this study, we observed few randomized studies using derivatives of sesame in humans, as well as heterogeneous profile of participants of the study – not leading to a more incisive analysis of the results presented.

The sample size of the studies can be a limiting factor.

The use of drugs, concomitant with intervention may also be a confounding factor, since the analysis is not performed in a conjugated form.

Other important factor to be considered in this analysis regard the variable bioavailability of the chemical composition between the types of seeds and the metabolic pathways used by the components of the different presentations of sesame.

Clinical trials comparing the groups of operations parallel to sesame, or with other types of oil appear to be interesting in order to exclude possible mechanisms of action, considering the diversity of chemical components of the diet as a whole.

In some studies it was observed that, with regard to the diet, only general guidelines were scored individuals. However, in no study has been reported performing analysis or diet prescription for the study participants. There were no considerations for feeding, separately from

the use of drugs intake and sesame derived in these studies. Thus, the analysis of the influence of diet in the results was not possible.

CONCLUSION

Studies have been conducted to show the effects of consumption of seeds and sesame derivatives on variables that directly affect cardiovascular health such as blood pressure and lipid profile parameters. The mechanisms involved in this process are still being studied. Although the results available in the literature pointing to positive effects in improving blood pressure parameters and lipid profile - in people with hypertension or dyslipidemia - these results demonstrate inconclusive on the high risk of bias to which few clinical trials have conducted seem to have been submitted. To obtain more conclusive results, it is necessary to carry out more controlled studies with low risk of bias.

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Table 1. General characteristics of clinical trials included in the analysis.

Population profile	Clinical trial (author, year)	Design / follow-up	Population (sex, age)	Presentation of sesame	Exposition/Time	Diet/Medications	Statistics	Outcomes of interest
Hypertensive (mild to moderate)	Sankar et al (2005)	Interventional Controlled Randomized 2 months	Middle age n = 530	Sesame oil	GI: duration of 60 days with 35g oil per day per person: Sesame oil (n = 356) Sunflower oil (n = 87) Peanut oil (n = 47) GC (n = 40):	Usual diet. GI: were instructed to use their oil as sole oil (for cooking or other). Treated with nifedipine (20-30mg / day)	ANOVA Duncan Test	Lipid profile Blood pressure

					nifedipine with sunflower oil, sesame or peanut randomly / 60 days			
Hypertensive and diabetic (~2-3 years)	Sankar et al (2006a)	Interventional Controlled Randomized 90 days	18 (F) 22 (M) n = 40 49-64 years	Sesame oil	I: 4-5kg of sesame oil (such as cooking oil and salad seasoning) per month for each group of 4 family members (~ 1 kg of oil per person per month; ~ 35g of oil per person per day) / 45 days	Usual diet. Beta-blocker use (atenolol 50-100mg / day) and sulfonylurea (glyburide 10 mg / day).	Student's T Test	Lipid profile Blood pressure

					C: use of palm or peanut oil randomly / 45 days			
Hypertensive (mild to moderate)	Sankar et al (2006b)	Interventional Controlled 90 days	18 (F) 32 (M) n = 50 35-60 years	Sesame oil	I: 4-5kg of sesame oil (such as cooking oil and salad seasoning) per month for each group of 4 family members (~ 1 kg of oil per person per month; ~ 35g of oil per person per day) They were	Usual diet. They were instructed to continue the use of antihypertensive drugs. Use of diuretics or beta-blockers - hydrochlorothiazide or atenolol - 1 year ago.	Student's T Test	Lipid profile Blood pressure

					instructed to use sesame oil only/ 45 days C: return to habitual oil/45 days			
Population profile	Clinical trial (author, year)	Design / follow-up	Population (sex, age)	Presentation of sesame	Exposition/Time	Diet/Medications	Statistics	Outcomes of interest
Hypertensive (mild)	Miyawaki et al (2009)	Crossed Placebo-controlled Double-blind 12 weeks	2 (F) 23 (M) n = 25 49.1±1.8 years	Sesamin capsules	IG (n=12): 6 capsules per day with sesamin (10mg sesamin e 180mg wheat	Usual diet. Instructed not to modify the diet (including the number of daily meals, salt	Student's T Test Student's Paired T Test	Blood Pressure

					germ oil/capsule)/4 weeks PG (n=13): 6 capsules per day of placebo (180mg wheat germ oil/capsule)/4 weeks WD: 4 weeks	intake) and exercise routine. Treated with glyburide and metformin or a combination of both.		
Pre-hypertensive	Wichistrainoi et al	Placebo-controlled	8 (F) 22 (M) n = 30	Sesame flour capsules	IG (n=15): 18	Usual diet. Instructed not to	ANCOVA	Blood Press

	(2011)	Double-blind 4 weeks	49.3±7.7 years 50.3±5.6 years		capsules of black sesame powder (0.42g sesame/capsule) per day/4 weeks PG (n=15): 18 capsules (same chemical composition of black sesame capsule, but	change the diet and exercise routine and not to ingest vitamin or dietary supplements during the study. They did not use any dietary supplement or drugs that would affect the PA.	Pearson correlation Student's Paired T Test	ure

					without this element) per day / 4weeks			
Hyperlipidemic	Alipoor et al(2012)	Interventional Controlled Randomized 2 months	30 (F) 8 (M) n = 38 50-70years	Sesame seeds	IG (n=19): 40g White sesame seed/60 days CG (n=19): maintained the same pharmacological treatment (not	GI instructed by an expert on diets, to remove 240kcal of the daily diet.	T Test Paired T Test	Lipid Profile

					mentioned) that the GC / 60 days			
Hyperlipidemic and 1 obese individual	Chen et al (2005)	Interventional 10 weeks	15 (F) 6 (M) n = 21 50.9±3.7 years	Sesame flour	I: sesame flour 40g in prepared mixture / 4 weeks R: standardized diet / 2 weeks WE: removal of sesame flour and returned to usual	Instructed to keep dietary patterns according to the guidelines of the National Cholesterol Education Program Step I diet. Six individuals were using	Linear mixed-effects model	Lipid Profile

					diet / 4 weeks	lipid-lowering drugs.		

Legend: ; n = sample size; F = female; M = male; I = intervention; C = control; GI = intervention group; GC = control group.

Legend: n = sample size; F = female; M = male; I = intervention;IG = intervention group; CG = control group; R = run-in; WD = washout during the study; WE = washout at the end of the study.

Table 2.Results on the consumption of sesame derivatives in patients with systemic hypertension.

Sesame presentation	Clinical trial (Author, year)	SBP	DBP	TC	HDL-c	LDL-c	TG
Sesame Oil	Sankar et al (2005)	↓~19% ↓31.8 mmHg p<0.05 After 60 days	↓~16% ↓16.4mmHg p<0.05 After 60 days	↓~16% ↓33 mg/dL p<0.05 After 60 days	↑~9% ↑4.13 mg/dL p<0.05 After 60 days	↓~24% ↓30.1 mg/dL p<0.05 After 60 days	↓~19% ↓35.04 mg/dL p<0.05 After 60 days
Sesame Oil	Sankar et al (2006a)	↓~14% ↓20.4 mmHg p<0.001 After 45 days	↓~19% ↓18.3 mmHg p<0.001 After 45 days	↓~18% ↓44.9 mg/dL p<0.001 After 45 days	↑~1% ↑0.5 mg/dL NS After 45 days	↓~24% ↓37.66 mg/dL p<0.001 After 45 days	↓~23% ↓54.84 mg/dL NS After 45 days
Sesame Oil	Sankar et al (2006b)	↓~13% ↓19.37 mmHg	↓~14% ↓14.1 mmHg	↓~1% ↓3 mg/dL	↑~2% ↑1 mg/dL	↑~1% ↑2 mg/dL	↓~18% ↓35.8 mg/dL

		p<0.001 After 45 days	p<0.001 After 45 days	NS After 45 days	NS After 45 days	NS After 45 days	p<0.001 After 45 days
Sesame flour capsules	Wichistrainoi et al (2011)	↓~6% ↓ 8.3 mmHg p<0.05 After 4 weeks	↓~5% ↓ 4.2 mmHg NS After 4 weeks	NA	NA	NA	NA
Sesamin capsules	Miyawaki et al (2009)	↓~3% ↓3.5 mmHg p<0.044 After 4 weeks	↓~2% ↓1.9 mmHg p<0.04 After 4 weeks	NA	NA	NA	NA

Legend: percentages only for the differences between the means related to the before and after interventions with sesame; SBP = systolic blood pressure; DBP = diastolic blood pressure; TC = total cholesterol; HDL-c = HDL cholesterol; LDL-c = LDL cholesterol; TG = triglycerides; NA = not assessed; NS = not significant.

Table 3. Results regarding the use of sesame seeds and derived products in individuals with dyslipidemia.

Sesame presentation	Clinical trial (Author, year)	SBP	DBP	CT	HDL-c	LDL-c	TG
Sesame flour	Chen et al (2005)	NA	NA	↓~6% ↓16.7mg/dL p<0.05 After 4 weeks ↑~4% ↑9.7 mg/dL NS AfterWE	↑↓ 0% ↑↓0 mg/dL NS After 4 weeks ↓ 4% ↓2.5 mg/dL p<0.05 AfterWE	↓~9% ↓17.3 mg/dL p<0.05 After 4 weeks ↑~8% ↑13.9 mg/dL p<0.05 AfterWE	↓~0.1% ↓0.1 mg/dL NS After 4 weeks ↑~19% ↑20 mg/dL NS AfterWE
Sesame seeds	Alipoor et al (2012)	NA	NA	↓~8% ↓19.7 mg/dL p<0.05 After 60	↓~0.1% ↓0.4 mg/dL NS After 60	↓~10% ↓15.7 mg/dL p<0.05 After 60	↓~8% ↓12.8 mg/dL NS After 60

				days	days	days	days

Legend: percentages only for the differences between the means related to the before and after interventions with sesame; SBP = systolic blood pressure; DBP = diastolicblood pressure; TC = total cholesterol; HDL-c = HDL cholesterol; LDL-c = LDL cholesterol; TG = triglycerides; WE = washout at the end of the study; NA = not assessed; NS = not significant.

Table 4. Clinical trials, interventions derived from sesame and their quantities populations.

Individuals with hypertension		Individuals with dyslipidemia	
Clinical trial	**Quantity/Intervention**	**Clinical trial**	**Quantity/Intervention**
Sankar et al (2005)	35g/day ofSesame Oil	Chen et al (2005)	40g/day of sesame flour
Sankar et al (2006a)	35g/day ofSesame Oil	Alipoor et al (2012)	40g/day ofWhite sesame seeds
Sankar et al (2006b)	35g/day ofSesame Oil		
Miyawaki et al (2009)	60mg/day ofsesamin capsules		
Wichistrainoi et al (2011)	7.56g/day ofblack sesame flour in capsules		

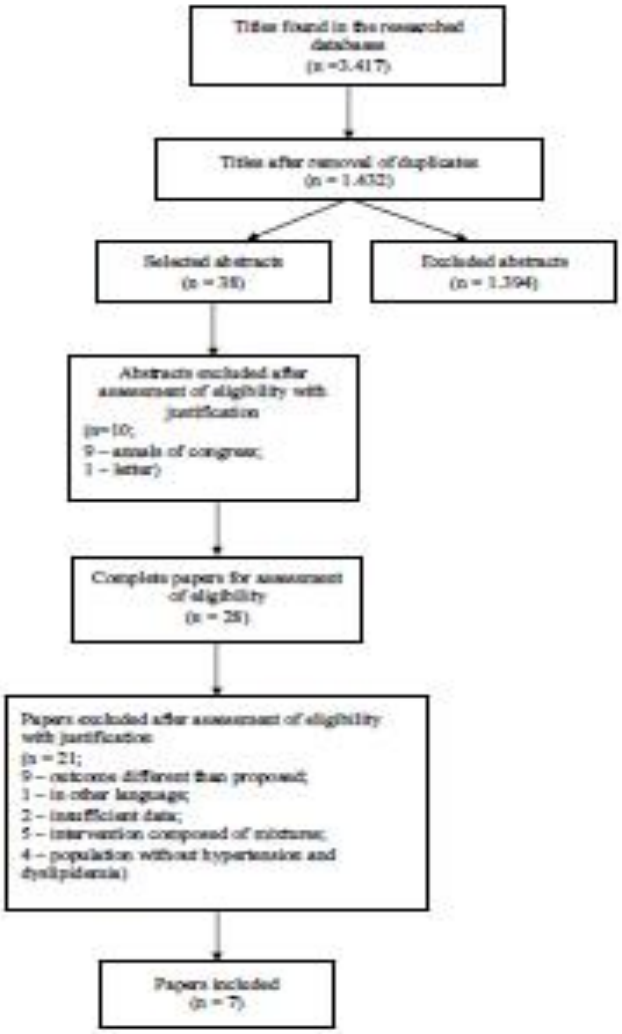

Figure 1. Prisma Flow Diagram - Selection, exclusion and inclusion of papers.

Clinical trial (author, year)	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
Chen et al (2005)	-	-	-	-	?	+
Sankar et al (2005)	?	?	-	-	?	+
Sankar et al (2006a)	?	?	-	-	?	+
Sankar et al (2006b)	-	-	-	-	?	+
Miyawaki et al (2009)	-	-	+	?	?	+
Wichistranoi et al (2011)	-	-	+	?	?	+
Alipoor et al (2012)	?	?	-	-	?	+

- Low risk

+ High risk

? Unclear risk

Figure 2.Biases risk analysis according to Cochrane Handbook for Systematic Reviews of Interventions Version 5.1. Judgment of the authors of this systematic review of each bias risk item for each item included.