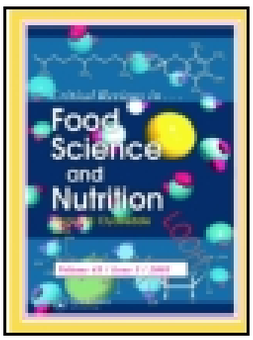

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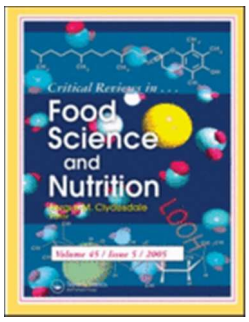

Effect of chronic consumption of pistachios (Pistacia vera L.) on glucose metabolism in pre-diabetics and type 2 diabetics: a systematic review

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ABSTRACT

Pistachio is a nut with high polyunsaturated fatty acids (PUFA), monounsaturated fatty acids (MUFA), polyphenols and carotenoids content, and the synergism between these compounds appears to affect glucose metabolism. In this systematic review we analyzed studies in which the effect of chronic consumption of pistachio on markers of glucose metabolism was evaluated in pre-diabetic and type 2 diabetics. We used the PubMed, Scopus, Cochrane and Lilacs databases. The research terms used were pistachio, pre-diabetes, type 2 diabetes mellitus, insulin resistance, blood glucose, hyperglycemia and glycated hemoglobin (HbA1c). Four articles were selected, of which three tested the intake of 50 to 57 g of pistachio/day and one 20% of the daily caloric intake, for a period of 1 to 4 months. Studies reported a decrease in fasting blood glucose, insulinemia, HOMA-IR, and fructosamine, but no change in HbA1c. Lower concentrations of miR-192 and miR-375 were also found, which correlated positively with HOMA-IR. The synergism between PUFA, MUFA, polyphenols and carotenoids present in pistachios can modulate specific miRNA, increasing insulin sensitivity through the PI3K-AKT signaling pathway. This modulation can be used as a tool to monitor the response to interventions, favoring the prevention and treatment of complications related to diabetes.

Keywords: Unsaturated fatty acids; Carotenoids; MicroRNAs; Pistachio; Polyphenols; Insulin resistance.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic disease characterized by hyperglycemia and corresponds to more than 90% of DM cases (ADA, 2014).Pre-diabetics have glycated hemoglobin (HbA1c) between 6 and 6.4%, in addition to altered glucose and glucose tolerance, making them more likely to develop DM and its complications (Perreault & Færch, 2014). The International Diabetes Federation (IDF) has shown that the number of adults affected by the disease in 2013 was 382 million, estimated to be 592 million cases in 2035 (Guariguata et al., 2014). Thus, the increase of this disease imposes high costs on the health system and the global economy (Seuring, Archangelidi & Suhrcke, 2015).

The diet has a central role in the prevention and control of T2DM (Danaei et al., 2009). In this sense, the benefits of regular nut consumption in relation to chronic diseases have been amply demonstrated in an epidemiological study (Sabaté& Ang, 2009) and clinical (Jenkins et al., 2011; Estruch et al., 2013). Among the nuts, pistachios stand out because they have lower concentrations of fat and calories. However, unsaturated fatty acids correspond to the majority of lipids, with 53.5% coming from monounsaturated fatty acids (MUFA) and 29.1% from polyunsaturated fatty acids (PUFA). In addition, pistachios have higher concentrations of fiber (soluble and insoluble), potassium, phytosterols, γ-tocopherol, vitamin K, polyphenols and carotenoids than the other nuts (Bulló et al., 2015; USDA, 2017).

Daily consumption of pistachios has been associated with improved glycemic control in pre-diabetic and type 2 diabetics (Hernández-Alonso et al., 2014; Parham et al., 2014; Sauder et al., 2015; Hernández-Alonso et al., 2016), and a better lipid profile in individuals with metabolic syndrome (Sari et al., 2010), besides reducing inflammation, oxidative stress and improving endothelial function in healthy young adults (Kasliwal et al., 2015).

However, evidences regarding the molecular mechanisms exerted by pistachios on glucose metabolism have not established yet. Therefore, the objective of this systematic review was to critically analyze the studies that evaluated the effect of chronic consumption of pistachios on glucose metabolism in pre-diabetics and type 2 diabetics, in addition to identifying possible molecular mechanisms related to the effects of unsaturated fatty acids (PUFAs and MUFAs) and bioactive compounds (polyphenols and carotenoids) from pistachios, on glucose metabolism.

METHODS

1.1 Protocol and Registration

This systematic review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2009)(Appendix I-Checklist), and was registered in PROSPERO (registration number: CRD42017067208).

1.2 Literature Search

Three authors (PVMR, AS and APA) independently researched original articles on the effect of chronic pistachio consumption on glucose metabolism in pre-diabetic and type 2 diabetics in the following electronic databases: MEDLINE (PubMed, www.pubmed.com), Cochrane (www.cochrane.org), Scopus (www.scopus.com) e Lilacs (www.lilacs.bvsalud.org). Keywords were chosen from the Medical Subject Headings (MeSH) and Descriptors in Health Sciences (DeHS),using the following search strategy: (Pistachio (s) OR “Pistachio nut (s)” OR “nut (s) pistachio” OR “nut, pistachio”) AND

("Diabetes Mellitus, Type 2" OR "Diabetes Mellitus" OR Prediabetes OR "Insulin Resistance" OR "Blood Glucose" OR "Glucose Metabolism Disorders" OR Hyperglycemia OR 'Hemoglobin A, Glycosylated").

The search strategy was not restricted by date, and articles published in English. Last search date was May 4, 2017. We also perform the reverse search of the relevant articles cited in the selected articles.

1.3 Studies Selection

The selection of the studies was performed in the three phases described below, by three authors (PVMR, AS e APA): analysis of titles, abstracts and full texts. We included all published clinical trials in which the effects of chronic consumption of pistachios on glucose metabolism in pre-diabetic and type 2 diabetic subjects.

Comments, reviews, letters, case reports, abstracts and unpublished articles were excluded. Studies involving animals, studies *in vitro*, epidemiological studies involving individuals with systemic diseases other than diabetes (e.g. metabolic syndrome, hypertension, dyslipidemias) and studies in which the markers of glucose metabolism was not been evaluated were also excluded.

1.4 Data extraction

After reading all the full articles, the comparison of the data between the researchers was conducted to guarantee the integrity and reliability. The divergent decisions were settled by consensus. For each included article, we extracted information about the title, authors,

year of publication, type of study, study objective, sample size, study design, intervention (dose), duration, country in which the study was conducted, and glucose metabolism markers.

1.5 Assessment of risk of bias

We assessed the risk of bias in clinical trials using Cochrane Collaboration (Higgins & Green, 2011).We judged the studies in three levels of bias - high risk, low risk and unclear (when the information provided was not sufficient to make a clear judgment). We consider the following biases: random sequence generation and allocation concealment (selection bias); Blinding of participants and staff (performance bias); Blindness of results evaluation (detection bias) and selective reporting (notification bias) (Higgins &Green, 2011).

1.6 Data analyses

We summarized all studies reviewed in this article in a table according to the main characteristics and results concerning markers of glucose metabolism. The studies were arranged chronologically by year of publication, starting with the first published study. We considered changes in glucose metabolism as the main variable. Secondary outcomes were: changes in insulinemia, plasma miRNAs, HbA1c, fructosamine, and GLP-1, HOMA-IR, SLC2A4 expression, and the glucose transport into lymphocytes; all of them related to pre-diabetes and diabetes risk. In addition, we analyzed the effect of the tested dose *versus* duration of the studies.

RESULTS

1.1 Study selection

We have identified 83 studies after the survey in all four databases (PubMed, SCOPUS, Cochrane e Lilacs). A total of 29 duplicates were removed resulting in 54 articles, after which 37 studies were excluded based on their titles, since they were considered irrelevant to the topic of interest. After reading the summary of the remaining 17 studies, 4 met all criteria for the systematic review. The most common reasons for exclusion were duplicate, *in vitro*, animal studies that did not mention glucose metabolism and the presence of subjects without pre-diabetes or T2DM (Figure 1).

1.2 Description of included studies

The four studies included in the present review (Table 1) contained data from a total of 177 subjects (103 pre-diabetics and 74 T2DM) (Hernández-Alonso, Giardina, Salas-Salvadó, Arcelin, & Bulló, 2016; Parham et al., 2014). These studies had sample sizes varying from 30(Sauder, McCrea, Ulbrecht, Kris-Etherton, & West, 2015) to 54(Hernández-Alonso, Salas-Salvadó, Baldrich-Mora, Juanola-Falgarona, & Bulló, 2014) participants. Two studies included pre-diabetics (Hernández-Alonso et al., 2016; Parham et al., 2014) and two included T2DM (Hernández-Alonso et al., 2016; Parham et al., 2014), all of which included individuals of the sex female (51.28%, n = 80) and male (48.72%, n = 76). The mean age was 55.35 ± 0.49 years for pre-diabetics and 54.50 ± 2.12 years for subjects with T2DM. In terms of geographic distribution, two studies were conducted in Spain, one in Iran and one in the USA. All studies were randomized, controlled, crossover and duration ranged from 4 weeks (Sauder et al., 2015)to 4 months (Hernández-Alonso et al., 2016; Parham et al., 2014). As for the dose of pistachios tested, two studies used 57 g/day (Hernández-Alonso et al., 2016; Parham et al., 2014), one 50g/day (Parham et al., 2014) and another 20% of the total calories (59 to 128g/day) (Sauder et al., 2015) (Table 1). In all studies the roasted pistachios with or

without salt were ingested without the addition of other foods. Isocaloric diets to the pistachio diet, but without the presence of the nut, were administered to the control groups.

1.3 Main results of individual studies

Consumption of 57 g of pistachios per day for 4 months resulted in reduced fasting glucose and insulin concentrations, HOMA-IR, and glucose transport into lymphocytes. The control diet resulted in a significant increase of 69% in SLC2A4 expression compared to the pistachio-containing diet (Hernández-Alonso et al., 2014). In another randomized clinical trial involving type 2 diabetics, the reduction of fasting glucose and HbA1c was observed in response to the intake of 50 g of pistachio for three months of intervention (Paham et al., 2014).

On the other hand, dietary intake of 20% of calories from pistachios by individuals with type 2 diabetes for 1 month led to a decrease in the concentration of fructosamine in relation to the control group (Sauder et al., 2015).

In another study involving subjects with pre-diabetes, the effects of regular consumption of pistachios (57 g/day) on the concentrations of seven circulating miRNAs (hsamiR-15a-5p, hsa-miR-21-5p, hsa-miR-29b-3p, hsa-miR-126-3p, hsa-miR-192-5p, hsa-miR-223-3p, hsa-miR-375) related to glycemia and insulinemia. After 4 months, the diet containing pistachios (PD) resulted in lower concentrations of miR-192 and miR-375 compared to the control diet (CD), while miR-21 concentrations increased after PD compared to CD. In addition, changes in circulating miR-192 and miR-375 were positively correlated with plasma glucose, insulin and HOMA-IR . Thus, authors concluded that the chronic consumption of pistachios positively modulated the expression of some miRNAs implicated in insulin sensitivity (Hernández-Alonso et al., 2016).

Thus, consumption of 50-57 g of pistachios per day or 20% of daily calorie needs in the form of pistachios for 1 to 4 months resulted in positive effects on glucose metabolism in all four studies included in this review. Of the 3 studies in which fasting glucose and insulin, HbA1c and HOMA-IR were evaluated, 2 of them(Hernández-Alonso et al., 2014; PARHAM et al., 2014) reported a reduction in fasting blood glucose and HOMA-IR (Hernández-Alonso et al., 2014; Parham et al., 2014)after ingestion of at least 50 g/day of pistachios for 3 months (Parham et al., 2014). Insulinemia decreased with 4 months of intervention but no changes in HbA1c (Hernández-Alonso et al., 2014). Markers such as fructosamine and miRNAs were not evaluated in all studies. However, reductions in the concentrations of these markers were observed in the 2 studies after the effect of pistachio consumption (Sauder et al., 2015; Hernández-Alonso et al., 2016).

1.4 Risk assessment of bias

We judged that the domains of major importance assessed in the present study were random generation of allocation sequences and incomplete outcome data, and all studies were at low risk of bias. All studies were randomized, the missing data were balanced between the intervention groups, and the ratios between the groups were similar. In addition, all the excluded data were justified by the authors. However, secrecy in treatment allocations was not clearly presented in two studies (Hernández-Alonso et al., 2014; Hernández-Alonso et al., 2016). Only the study of Sauder et al. (2015) presented low risk of bias for blinding of the participants, personnel and evaluation of results. In addition, only the Parham et al. (2014) did not clearly define the selective reporting of outcomes (Figure 2).

DISCUSSION

1.1 Nutritional composition of raw and roasted pistachio

Pistachio can have positive effects on the prevention and control of T2DM due to its high fiber concentrations, healthy fats, antioxidants and anti-inflammatory content of this food (Hernández-Alonso et al., 2016). In 100g of the roasted pistachio there is 45.32 g of total fat, being 5.90 g of saturated fatty acids (SFA), 14.38 g of PUFA and 23.25 g of MUFA (Table2). That is, of the 72% of lipids, 82.7% are from the MUFA and PUFA (USDA, 2016). In fact, oleic and linoleic fatty acids represent more than 60% of the total fat content in pistachios, and both are recognized by their cardioprotective properties (Bulló et al., 2015).

The roasted pistachio has in its composition carotenoids such as β-carotene, lutein and zeaxanthin. The composition in relation to the polyphenol group (cyanidin, catechin, epigallocatechin, epicatechin, quercetin and genestein) was performed only on the raw pistachio base, as these data are not available for the roasted pistachio (Table2).

Each pistachio contains 2.8g of fiber, about 80% of which are insoluble fiber (USDA, 2016). Fiber improves postprandial glucose control by increasing chyme viscosity, resulting in decreased glucose absorption. In the short term this mechanism reduces the peak of postprandial glucose (Lambeau& Mcrorie, 2017). In addition, the fibers are also associated with a dose-dependent control of satiety and food intake, being an important tool in weight control(Clark& Slavin, 2013).

Lutein is the main carotenoid present in pistachios (USDA, 2016). It is known that lutein has great antioxidant activity offering great benefits to cardiovascular health (Bolling et al., 2010). β-carotene is also present in pistachios, it is known that low serum concentrations of this compound may favor the occurrence of insulin resistance (Ärnlöv et al., 2009). In addition, a prospective 10-year study, including 37,846 men and women, also revealed an

inverse association between dietary intake of β-carotene and the risk of T2DM(Sluijs et al., 2015). Thus, the consumption of fiber and antioxidants present in pistachios may play an important role in the prevention and treatment of T2DM.

The pistachio also shows a good concentration of γ-tocopherol, about 6.64 mg per nut (USDA, 2016). γ-tocopherol recovers reactive nitrogen species and also exerts an anti-inflammatory role (Dreher, 2012). The pistachio has a higher concentration of isoflavones than the nuts (3.63 mg/100 g), the concentrations are 100 times higher than in other nuts (Bolling et al., 2010). In addition, pistachios are considered, among the nuts, the richest source of phenolic compounds (470 mg / walnut), which exert antioxidant and anti-inflammatory activities (Dreher, 2012).

The tocoferol and carotenoid intake was evaluated in a cohort of 2,285 men and 2,019 women (40-69 years) without diabetes for 23 years. Intake of vitamin E, α-tocopherol and γ-tocopherol were associated with a reduced risk of onset of T2DM. Among carotenoids, β-cryptoxanthin intake was associated with a lower risk of T2DM (Montonen et al., 2004). Thus, the results of this study suggest that the development of T2DM can be reduced by the dietary intake of antioxidants (Montonen et al., 2004).

Methylglyoxal is considered to be an important precursor of the Advanced Glycation End Products (AGEs), considered as one of the main causes of diabetes and its complications. Genistein and quercetin are capable of destroying and neutralizing methylglyoxal (Grzebyk&Piwowar, 2016; Shay et al., 2015). Thus, it is possible that these phenolic compounds present in pistachios may also promote the prevention of diabetes.

Analyzing the roasting process the composition of fatty acids and lutein/zeaxanthin were not altered (Schlörmann et al., 2015), but the concentration of γ-tocopherol showed a significant increase after the processing (raw: 30,6mg; after 140ºC: 35,9mg; p=0.033) (Wolfgang et al., 2016). However, the β-carotene concentration in the roasted pistachio

decreased significantly after a temperature of 160°C (raw: 204 µg; after 160ºC: 164; p <0.001) (Wolfgang et al., 2016). It is possible to note that the temperature used in the roasting process has an influence on the nutrient concentration of this food, observing that at higher temperatures (160ºC) there was a loss of important nutrients. Another aspect that should be considered is that the pistachios submitted to the roasting process in medium temperatures (140 to 159ºC) presented higher scores in sensorial analysis (Schlörmann et al., 2015).

1.2 Possible mechanisms exerted by pistachio on glucose metabolism

1.2.1 microRNAs as biomarkers of the risk of type 2 diabetes mellitus

Biochemical variables (fasting glucose or oral glucose tolerance test, HbA1c, triglyceride, cholesterol, lipoprotein concentrations) and nutritional variables (eating habits and anthropometry) have been used to predict the risk of T2DM (Guay & Regazzi, 2013). However, biomarkers lacking with high specificity and sensitivity to predict the risk of diabetes and complications related to this disease (Banerjee et al., 2017). Blood, saliva, urine, or feces can be sources of these biomarkers (Etheridge et al., 2013; Banerjee et al., 2017).

The miRNAs were recently recognized as being a new class of biomarkers highly specific for the disease state, being a good indicator of its pathogenesis and progression (Banerjee et al, 2017). The miRNAs appear as powerful regulators for various metabolic pathways, including insulin secretion, glucose homeostasis, and carbohydrate and lipid metabolism (Honardoost et al., 2014).

The miRNAs are a group of small non-coding 21-23 nucleotide RNAs that regulate the expression of the target gene, especially through post-transcriptional gene regulation. The miRNAs control gene expression through the transcriptional deletion of their target genes messenger RNAs (mRNAs) or degradation primarily by cleavage of the mRNA (Grosshans

& SLACK, 2002; Ambros, 2004; Shukla, Singh & Barik, 2011). Although miRNAs originate in the cell nucleus, they have been detected in fluids such as blood, urine, saliva, or breast milk (Weber et al., 2010). Their high stability and availability in plasma and other fluids and the ability to detect and analyze small interindividual variations make circulating miRNAs potentially new sources of noninvasive biomarkers and targets in different diseases (Zampetaki et al., 2010; Zampetaki et al., 2012).

To date, more than 2,500 human miRNAs have been deposited in the latest version of miRBase (disponível online: www.mirbase.org). In turn, more than 60% of the protein coding transcripts are regulated by one or more miRNAs (Kellis et al., 2014). Recently the profile of circulating miRNA in patients with DM2 has been characterized, providing consistent evidence that several miRNA in plasma are regulated in individuals with metabolic disorders (Chakraborty et al., 2014; Ortega et al., 2014; He et al., 2017).

Previous studies have indicated the involvement of several miRNA in protein cascades, especially in the insulin signaling pathway. The miRNA regulate insulin secretion, the insulin receptor (IR) expression, as well as control different proteins involved in the cascade of the insulin signaling pathway, such as insulin receptor substrate 1 (IRS-1), phosphatidylinositol 3 kinase (PI3K), protein kinase B (AKT / PKB) and glucose transporter 4 (GLUT4) (Chakraborty et al., 2014).

miR-375 was one of the first miRNA identified in the pancreas, being able to regulate insulin secretion (Poy et al., 2004; Poy, Hausser & Trajkovski, 2009). Serum miR-375 concentrations were higher in patients with T2DM than in normoglycemic or pre-diabetic subjects (Higuchi et al., 2015). Its overexpression appears to suppress glucose-induced insulin secretion, while the inhibition of the endogenous function of miR-375 increases insulin secretion (Poy et al., 2004; El Ouaamari et al., 2008; Xia et al., 2011). In contrast, miR-15a regulates the expression of pancreatic transcription factors that favor insulin

synthesis (Joglekar et al., 2007), and there are lower plasma concentrations in T2DM (Zampetaki et al., 2010).

Expression of some miRNA may also control the expression of IR. Insulin binding to IR is suppressed by Protein Tyrosine Phosphatase, Non-Receptor Type 1 (*PTPN1*). In this sense, miR-146a can act as a suppressor of PTPN1 to allow insulin signaling (Karolina et al., 2011). miR-192 also seem to reach IR (Karolina et al., 2011), and it is in high concentrations in pre-diabetic individuals and rats with glucose intolerance (Párrizas et al., 2015) and diabetics.

In turn, some miRNA are promoter to insulin resistance. miR-126 and miR-144 lead to insulin resistance by reducing the target protein IRS-1 (Ryu, Park& Ma, 2011; Karolina et al., 2011). miR-29a upregulates the expression of the p85α regulatory subunit of PI3K in adipose tissue and skeletal muscle (Park et al., 2009). The overexpression of miR-143 induced by obesity leads to hyperglycemia, inactivating the AKT signaling pathway (Jordan et al., 2011). miR-133a-1, miR-133a-2 and miR-133b reduce insulin-stimulated glucose uptake upon reaching GLUT4 (Horie et al., 2009). Overexpression of miR-21 largely improved insulin-induced phosphorylation in AKT and GLUT4 in adipocyte-insulin resistance (Ling et al., 2012).

1.2.2 Potential effect of bioactive compounds from pistachio on glucose metabolism, including miRNA regulation

The pathogenesis of diabetes is complex and the underlying molecular mechanisms are only partially understood (Wu & Miller, 2017). Thus, understanding the molecular mechanisms capable of explaining how diet influences health and disease is an area of active research. One of these mechanisms concerns the role of diet in modulating the activity and

function of miRNAs (Ross & Davis, 2014; Wu & Miller, 2017). Pistachios are dense foods with a complex array of nutrients and other bioactive compounds) that synergistically contribute to their beneficial role in the prevention and control of different metabolic diseases such as T2DM and cardiovascular diseases (Ros, 2009; Tan, Dhillon & Mattes, 2014).

The quality of lipids influences insulin sensitivity. Partial replacement of SFAs by MUFAs in the diet favors glucose control and insulin sensitivity in humans and animals (Paniagua et al., 2007; Shah et al., 2007; Moon et al., 2010; Yang et al., 2011) The beneficial effects of MUFAs and PUFAs as anti-inflammatory, cardioprotective as well as in reducing insulin resistance have been consistent (Due et al., 2008; Gillingham, Harris-Janz & Jones, 2011).In a randomized, single-blind, placebo-controlled pilot study, 54 patients with T2DM received 520 mg of fish oil (EPA + DHA) daily for 6 months. The glycemia of these patients reduced significantly compared to control. Hb1Ac, leptin and leptin / adiponectin significantly decreased in both groups after 6 months. Serum resistin, insulin and HOMA-IR increased significantly in both groups. Considering that 100 g of pistachio contains 212 mg of omega-3, it would be necessary to consume approximately 245g of pistachios to match what was ingested in that study (USDA, 2016; Jacobo-cejudo, Vald, & Guadarrama-l, 2017). In another study the consumption of pills containing 2g of PUFA per day for 3 months was able to reduce fasting glucose, HbA1c and HOMA-IR in Asian subjects with overweight and T2DM compared to the control group who took pills containing 2g of corn oil (Sarbolouki et al., 2013). Taking into account the amount of PUFA present in the pistachio, 940.0 g of pistachios would be necessary to achieve the effects shown by pills. In addition, the consumption of PUFA has been associated with inhibition of inflammatory signaling pathways mediated by TLR and TNF-a, also decreasing the expression of inflammatory genes such as IL-6, TNF-a, MCP-1, IL-1b, CD11c and increasing the expression of inflammatory people in adipose tissue such as IL-10, MGL1, YM-1, MMR (Lalia & Lanza,

2016; Rocha et al., 2017). It is believed that omega-3 PUFAs activate receptors such as G protein-coupled receptors, especially GPR040 and GPR120, and consequently stimulate insulin secretion and glucose uptake via GLUT4 in adipocytes (Coelho et al., 2016).

In T2DM an increase in oxygen reactive species and a decrease in antioxidant defense capacity result in oxidative stress. Hyperglycemia can lead to glucose auto-oxidation forms hydroxyl radicals and activates the polyol pathway (sorbitol), increasing the production of free radicals. In decompensated diabetes macrophages and neutrophils activation occurs frequently, leading to free radical production, resulting in oxidative damage to cellular components such as proteins, lipids and nucleic acids, besides inducing chronic inflammatory responses. In addition, oxidative stress can impair insulin secretion and / or increase insulin resistance. Some natural antioxidants such as carotenoids may exert positive effects in reducing the oxidative stress caused by T2DM (Roohbakhsh et al., 2017). Since pistachio contains a good concentration of bioactive compounds, such as carotenoids and polyphenols, which have antioxidant activity, the neutralization of oxidative stress in T2DM could be another mechanism of action against insulin resistance.

Polyphenols present in pistachios may also influence glucose metabolism by stimulating peripheral glucose uptake in insulin-sensitive and non-insulin-sensitive tissues. The most studied insulin signaling pathway leading to increased glucose uptake in muscle involves binding of insulin to GLUT4, phosphorylation of IRS and activation of various signaling enzymes such as PI3K and AKT. In this sense, polyphenol-rich foods and plant extracts have been the object of extensive research in recent years, since they are potential compounds capable of stimulating the uptake of glucose by this pathway (Hanhineva et al., 2010).

However, few studies have evaluated the effect of a nutritional intervention on the modulation of miRNA concentration (Tomé-Carneiro et al., 2013; Ortega et al., 2015;

Hernández-Alonso et al., 2016). In two recent studies, chronic consumption of pistachios (57 g / day for 4 months) of almonds and walnuts (30 g / day for 2 months) positively modulated the expression of some miRNAs implicated in insulin sensitivity (Ortega et al., 2015; Hernández-Alonso et al., 2016). Likewise, Tomé-Carneiro et al. (2013), observed that consumption of grape extract rich in resveratrol and vitamins modulate specific miRNAs. However, the possible molecular mechanism responsible for the effect of these foods on the modulation of circulating miRNAs has not been proposed in any of these studies.

Thus, based on the KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway, miRBase (available online: www.mirbase.org) and the literature (Chakraborty et al., 2014; He et al., 2017), we hypothesized in the present study that the synergism between the unsaturated fatty acids and bioactive compounds from pistachio can modulate specific miRNAs through the insulin signaling pathway (via PI3K-AKT), favoring glycemic control.

Thus, we believe that the synergism between unsaturated fatty acids (AGMIs and PUFAs) and bioactive compounds (carotenoids and polyphenols) with their effects on improving insulin sensitivity, anti-inflammatory effect and antioxidants, as mentioned previously, will modulate miR375 miRNAs, MiR15a, miR146a, miR192, miR126, miR144, miR29a, miR143, miR133 and miR21. These miRNAs will positively regulate the insulin signaling pathway. Thus, the insulin will bind to its receptor, resulting in the phosphorylation of the beta portion of said receptor and activating the signaling protein cascade. It begins with the activation of IRS1, PI3K, AKT and translocation of GLUT 4, with consequent normal uptake of glucose. Therefore, these miRNAs can regulate the expression of these proteins at different stages of the insulin signaling pathway (via PI3K-AKT), thereby controlling the signal transduction process (Figure 3).

1.3 Limitations

There are some limitations in this study. Not all studies selected for this review have evaluated the same markers of glucose metabolism as, for example, fructosamine, GLP-1, miRNAs. Despite this, the results of these studies indicated the existence of a positive effect of pistachio on glycemic control. We also observed a similar age of participants in these studies (non-young adults), making it limited to extrapolating the results to other age groups. Finally, the lack of data regarding the composition of polyphenols in the roasted pistachio allowed us to make inferences only in relation to the raw pistachio composition.

CONCLUSION

The results of the studies selected for the present review indicated that consumption of 50-57 g of pistachios per day or 20% of daily caloric intake from pistachios for 1 to 4 months resulted in positive effects on glucose control. We believe that this result is due to the synergistic effect exerted by unsaturated fatty acids (MUFA and PUFA) and bioactive compounds (carotenoids and polyphenols) in the modulation of specific miRNAs, improving insulin sensitivity through the PI3K-AKT signaling pathway. This modulation of circulating miRNAs can be considered as a new tool to be used to monitor the response to dietary interventions used in individuals with T2DM. Considering the scarcity of studies portraying the effect of diet on miRNAs modulation, the investigation of the effect of different food matrices on the modulation of the activity and concentration function of different miRNAs should be stimulated aiming at the identification of effective therapeutic strategies to be used in the prevention and control of this metabolic disease.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGMENTS

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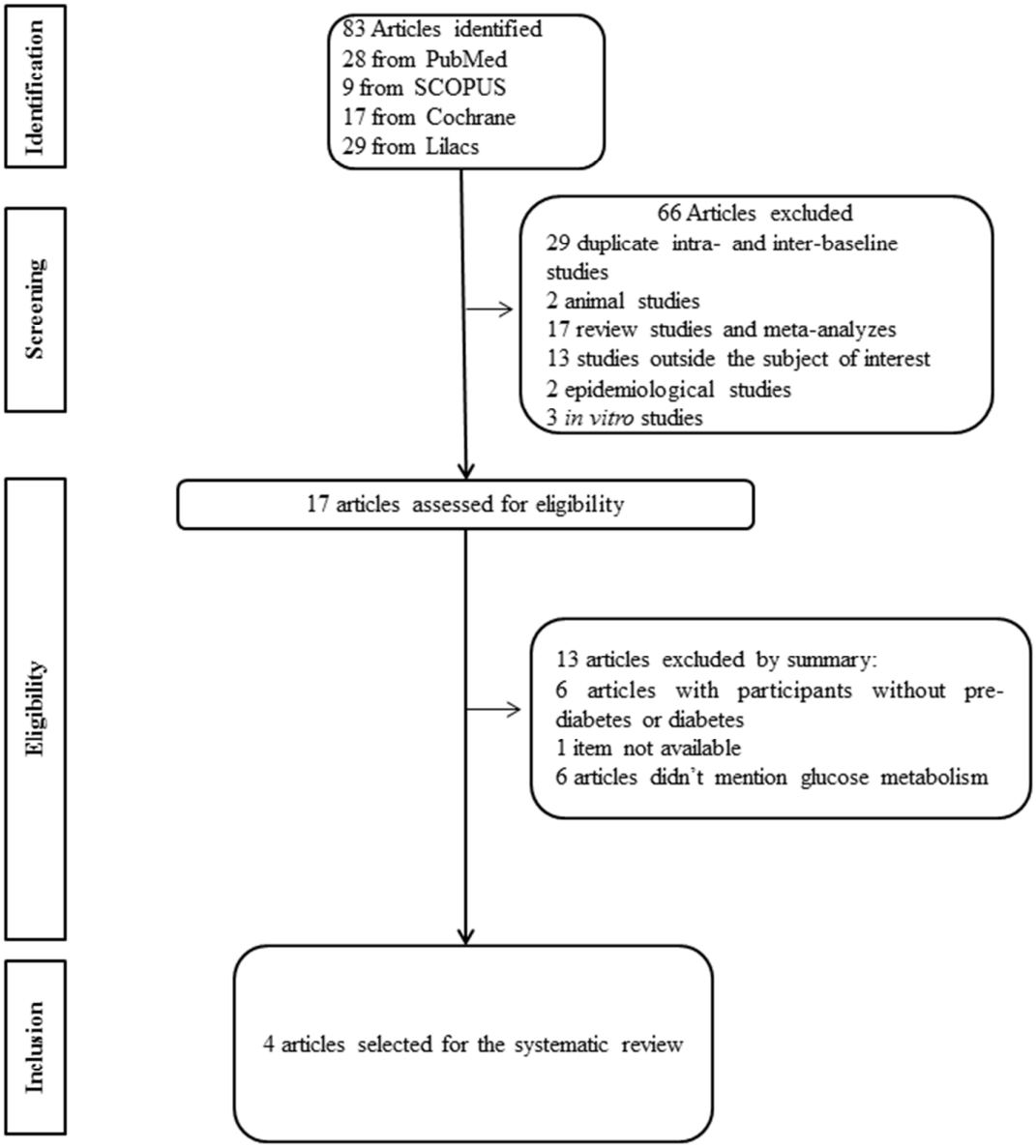

Figure 1: Flowchart of the process of selection of the studies

Table 1: Studies in which the effect of chronic consumption of pistachios on glucose metabolism in subjects with pre-diabetes and type 2 diabetes was evaluated

Reference	Sample	Intervention	Country where the study was conducted	Study Design	Duration	Main Results
Hernández-Alonso et al. (2014)	54 individuals with pre-diabetes Age: 55 (53.4-56.8) years. Sex: 25 women and 29 men	Test: Diet supplemented with pistachios (57g / day of pistachios) - 50% CHO, 35% LIP, 7% SFA, 20% MUFA, 5% PUFA and 15% PTN. Control: Diet without pistachios - 55% CHO, 30% LIP, 7% SFA, 16% MUFA, 3% PUFA and 15% PTN	Spain	Randomized, controlled and crossover	4 months (2 weeks *washout*)	Test group: ↓ Fasting glycemia, insulin and HOMA-IR; ↑ GLP-1, ↓ Expression of interleukin-6 and resistin genes in lymphocytes ↓ Cellular glucose uptake by lymphocytes compared to control and ↓ SLC2A4 (GLUT4) ↔ HOMA-BCF and HbA1c
Parham et al. (2014)	44 subjects with type 2 diabetes Age: 53.0 ± 10 years. Sex: 6 women and 17 men	* Test: 50g / day of pistachio (2 Snack of 25g 2x / day). Control: Diet without pistachios.	Iran	Randomized, single blind, controlled and crossover	3months (8 weeks *washout*)	Test group: ↓ HbA1c and fasting glycemia compared to control. In the first phase (Group A: pistachio x Group B: control): ↓ HbA1c, fasting glycemia and CRP compared to control. In the second phase (Group A: Control x Group B: Pistachio): ↓ HbA1c, fasting glycemia and HOMA-IR compared to control ↔ insulin
Sauder et al.(2015)	30 subjects with type 2 diabetes Age: 56.1 ± 7.8 years. Sex: 15 women and 15 men	Test: Diet with pistachio (contributing 20% of total energy - range: 59-128g / day) - 50.7% CHO, 33.2% LIP, 6.8% SFA, 13.1% MUFA, 10.4 % PUFA and 16.6% PTN. Control: Diet without	USA	Randomized, controlled and crossover	1 month (2 weeks *washout*)	↓ Fructosamine in the test group compared to control ↔ Fasting glucose, insulin, HbA1c and HOMA-IR

		pistachios - 55.1% CHO, 26.9% LIP, 6.7% SFA, 10.9% MUFA, 7.1% PUFA and 18.1% PTN.				
Hernández-Alonso et al. (2016)	49 individuals with pre-diabetes Age: 55.7 (53.9-57.4) years Sex: 23 women and 26 men	Test: Diet supplemented with pistachios (57g / day of pistachios) - 50% CHO, 33% LIP and 17% PTN. Control: Diet without pistachios - 55% CHO, 30% LIP and 15% PTN.	Spain	Randomized, controlled and crossover	4 months (2 weeks *washout*)	Test group: ↓ circulating levels of miR-192 and miR-375 compared to control ↔ miR-21 Changes in miR-192 and miR-375 circulation correlated positively with glycemia, insulinemia and HOMA-IR

Age data presented in median (minimum - maximum) or mean ± (standard deviation). * Macronutrient content of diets not available. CHO: carbohydrates; LIP: lipids; PTN: protein; SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids; GLP-1: Glucagon-like peptide-1; HbA1c: glycated hemoglobin. ↑ Increase; ↓ Decrease and ↔Iterminate.

	Randomization of the allocation sequence (Selection bias)	Allocation secrecy (Selection bias)	Blinding of participants and staff (Performance bias)	Result evaluation blinding (Detection bias)	Incomplete Outcome Data	Selective reporting of outcomes
Parham et al., 2014	+	+	?	?	+	?
Hernandez-Alonso et al., 2014	+	?	?	?	+	+
Sauder et al., 2015	+	+	+	+	+	+
Hernandez-Alonso et al., 2016	+	?	?	?	+	+

Figure 2: Risk assessment of bias. + Low Risk of Bias; ? Unclear.

Table 2: Chemical composition of Pistachio (100g)

Composition	Raw Pistachio	Salted pistachios without salt
Calories (kcal)	560.00	572.00
Protein (g)	20.16	21.05
Carbohydrates (g)	27.17	28.28
Fiber (g)	10.60	10.30
Total Lipids (g)	45,32	45.82
SFA (g)	5.90	5.64
MUFA (g)	23.25	24.53
PUFA (g)	14.38	13.35
β-Carotene (µg)	305.00	159.00
Lutein + Zeaxanthin (µg)	2903.00	1160.00
γ-Tocopherol (mg)	21.41	23.42
Cyanidin (mg)	7.33	-
Catechin (mg)	3.60	-
Epigallocatechin (mg)	2.00	-
Epicatechin (mg)	0.80	-
Quercetin (mg)	1.50	-
Genestein (mg)	1.75	-

Base: Table of Chemical Composition of Foods. United States Department of Agriculture (USDA). National Nutrient Database for Standard Reference.

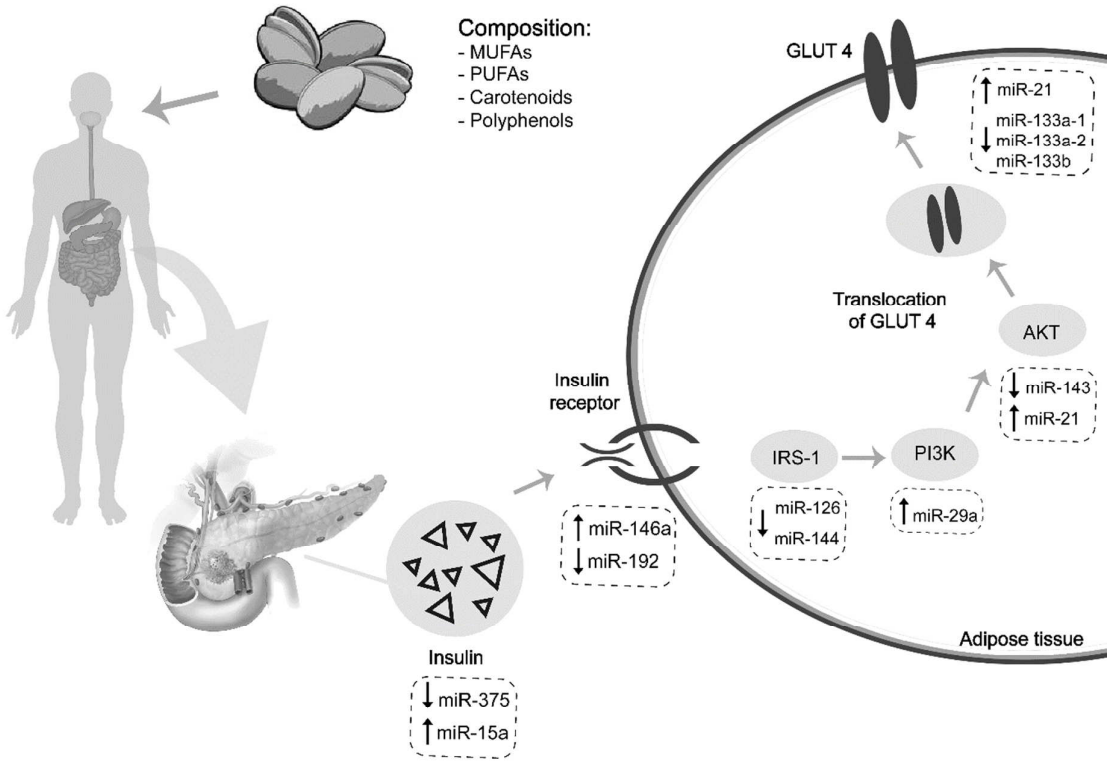

Figure 3: Mechanism related to the synergism between the unsaturated fatty acids and bioactive compounds from the pistachio, on the miRNAs, resulting in the modulation of different stages of the insulin signaling pathway.

ANNEX I- CHECK LIST PRISMA

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Yes
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Pg.1 Yes
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Pg. 2 and 3 Yes
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Pg. 3 Yes
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Pg. 4 Yes
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Pg. 5 Yes
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Pg. 4 Yes
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Pg. 4 Yes
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Pg. 5 Yes
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Pg. 6 Yes

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Pg. 6 Yes
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Pg. 5 and 6 Yes
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Not applicable
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Not applicable

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Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Pg. 5 and 6 Yes
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Pag. 7 and 10 Yes
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Pg. 7 Yes
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Pg. 10 and 13 Yes
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Pg. 8 Yes
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Pg. 11 Yes
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Pg. 10 and 13 Yes
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Pg. 12 and 13 Yes
DISCUSSION			

Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Pg. 14 and 15 Yes
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Pg. 26 Yes
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Pg. 26 Yes
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Not applicable

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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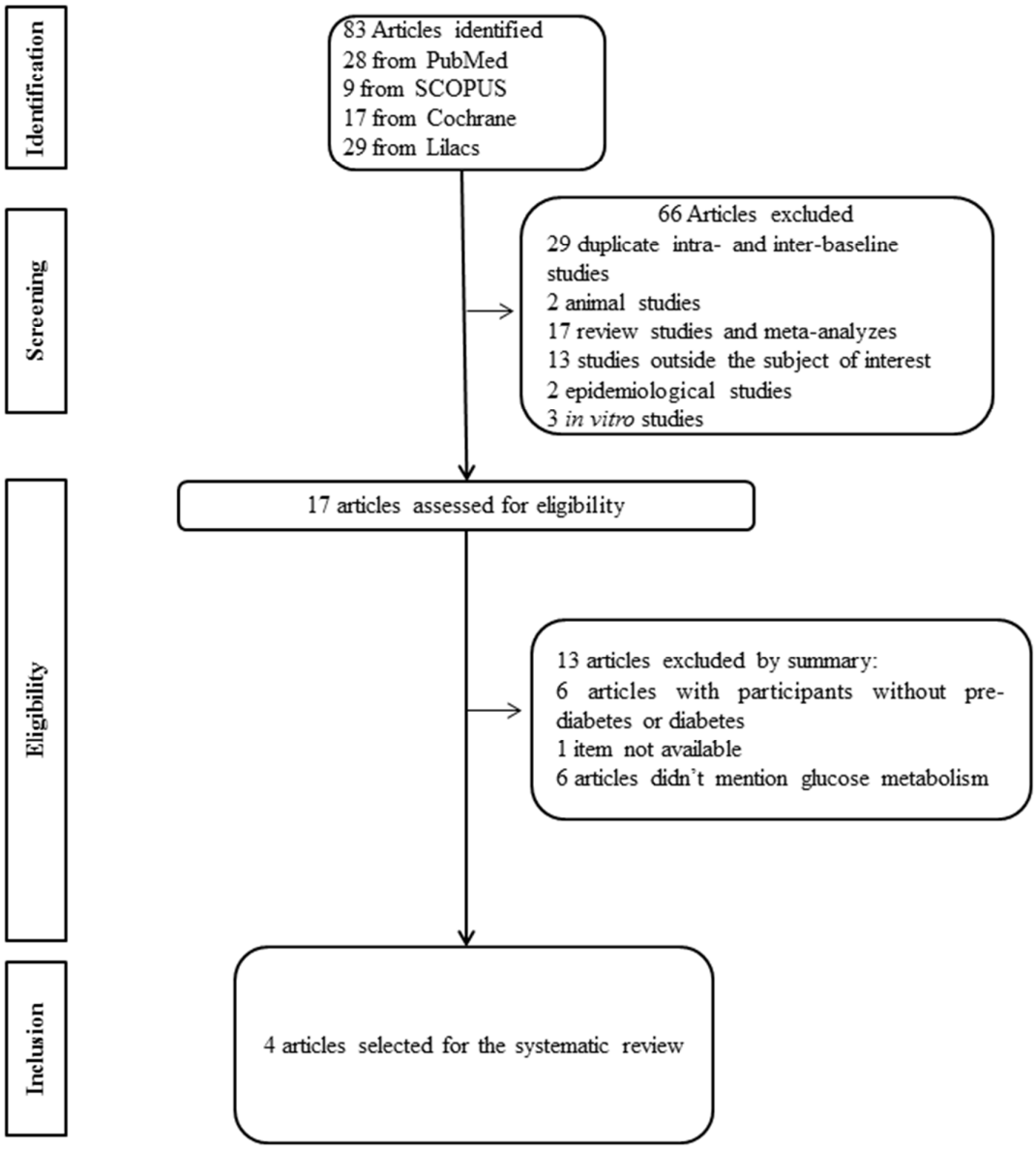
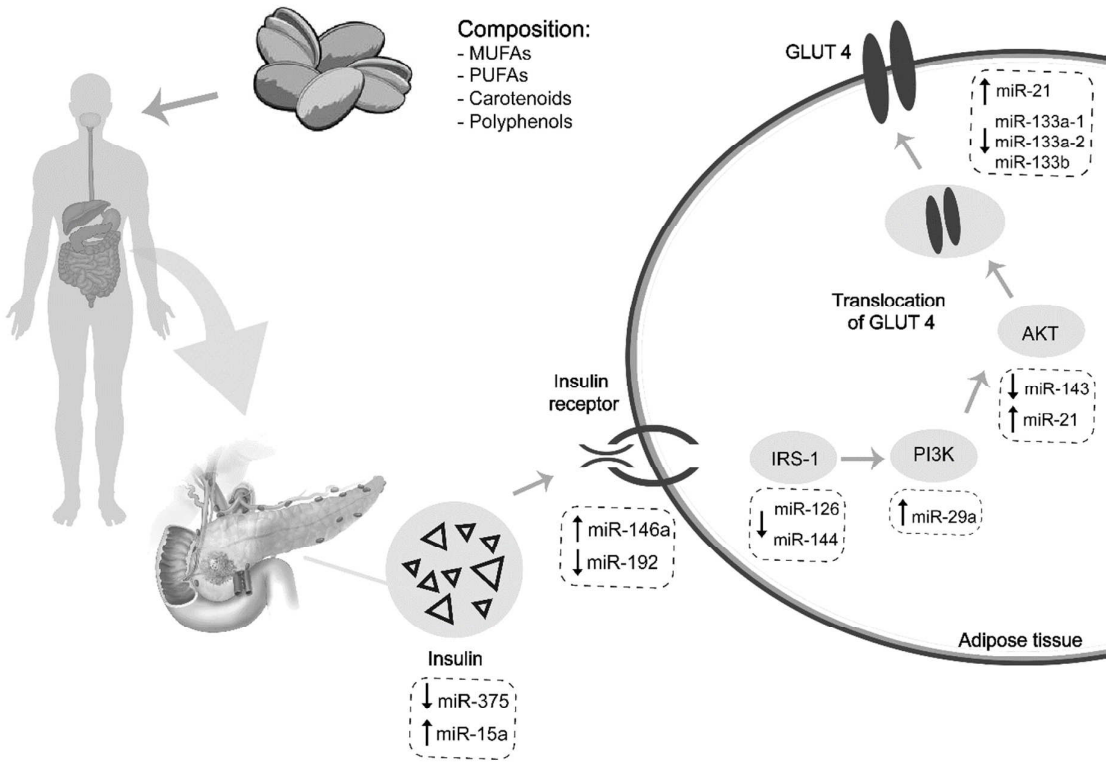


Figure 1: Flowchart of the process of selection of the studies

	Randomization of the allocation sequence (Selection bias)	Allocation secrecy (Selection bias)	Blinding of participants and staff (Performance bias)	Result evaluation blinding (Detection bias)	Incomplete Outcome Data	Selective reporting of outcomes
Parham et al., 2014	+	+	?	?	+	?
Hernandez-Alonso et al., 2014	+	?	?	?	+	+
Sauder et al., 2015	+	+	+	+	+	+
Hernandez-Alonso et al., 2016	+	?	?	?	+	+

Figure 2: Risk assessment of bias. + Low Risk of Bias; ? Unclear.



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Title	1	Identify the report as a systematic review, meta-analysis, or both.	Yes
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Pg.1 Yes
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Pg. 2 and 3 Yes
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Pg. 3 Yes
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Pg. 4 Yes
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Pg. 5 Yes
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Pg. 4 Yes
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Pg. 4 Yes
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Pg. 5 Yes

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Pg. 6 Yes
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Pg. 6 Yes
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Pg. 5 and 6 Yes
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Not applicable
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Not applicable

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Pg. 5 and 6 Yes
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Pag. 7 and 10 Yes
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Pg. 7 Yes
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Pg. 10 and 13 Yes
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Pg. 8 Yes
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Pg. 11 Yes
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Pg. 10 and 13 Yes

Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Pg. 12 and 13 Yes
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Pg. 14 and 15 Yes
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Pg. 26 Yes
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Pg. 26 Yes
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Not applicable

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit:**www.prisma-statement.org**.

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Table 1: Studies in which the effect of chronic consumption of pistachios on glucose metabolism in subjects with pre-diabetes and type 2 diabetes was evaluated

Reference	Sample	Intervention	Country where the study was conducted	Study Design	Duration	Main Results
Hernández-Alonso et al. (2014)	54 individuals with pre-diabetes Age: 55 (53.4-56.8) years. Sex: 25 women and 29 men	Test: Diet supplemented with pistachios (57g / day of pistachios) - 50% CHO, 35% LIP, 7% SFA, 20% MUFA, 5% PUFA and 15% PTN. Control: Diet without pistachios - 55% CHO, 30% LIP, 7% SFA, 16% MUFA, 3% PUFA and 15% PTN	Spain	Randomized, controlled and crossover	4 months (2 weeks *washout*)	Test group: ↓ Fasting glycemia, insulin and HOMA-IR; ↑ GLP-1, ↓ Expression of interleukin-6 and resistin genes in lymphocytes ↓ Cellular glucose uptake by lymphocytes compared to control and ↓ SLC2A4 (GLUT4) ↔ HOMA-BCF and HbA1c
Parham et al. (2014)	44 subjects with type 2 diabetes Age: 53.0 ± 10 years. Sex: 6 women and 17 men	* Test: 50g / day of pistachio (2 Snack of 25g 2x / day). Control: Diet without pistachios.	Iran	Randomized, single blind, controlled and crossover	3months (8 weeks *washout*)	Test group: ↓ HbA1c and fasting glycemia compared to control. In the first phase (Group A: pistachio x Group B: control): ↓ HbA1c, fasting glycemia and CRP compared to control. In the second phase (Group A: Control x Group B: Pistachio): ↓ HbA1c, fasting glycemia and HOMA-IR compared to control

						↔ insulin
Sauder et al.(2015)	30 subjects with type 2 diabetes Age: 56.1 ± 7.8 years. Sex: 15 women and 15 men	Test: Diet with pistachio (contributing 20% of total energy - range: 59-128g / day) - 50.7% CHO, 33.2% LIP, 6.8% SFA, 13.1% MUFA, 10.4 % PUFA and 16.6% PTN. Control: Diet without pistachios - 55.1% CHO, 26.9% LIP, 6.7% SFA, 10.9% MUFA, 7.1% PUFA and 18.1% PTN.	USA	Randomized, controlled and crossover	1 month (2 weeks *washout*)	↓ Fructosamine in the test group compared to control ↔ Fasting glucose, insulin, HbA1c and HOMA-IR
Hernández-Alonso et al. (2016)	49 individuals with pre-diabetes Age: 55.7 (53.9-57.4) years Sex: 23 women and 26 men	Test: Diet supplemented with pistachios (57g / day of pistachios) - 50% CHO, 33% LIP and 17% PTN. Control: Diet without pistachios - 55% CHO, 30% LIP and 15% PTN.	Spain	Randomized, controlled and crossover	4 months (2 weeks *washout*)	Test group: ↓ circulating levels of miR-192 and miR-375 compared to control ↔ miR-21 Changes in miR-192 and miR-375 circulation correlated positively with glycemia, insulinemia and HOMA-IR

Age data presented in median (minimum - maximum) or mean ± (standard deviation). * Macronutrient content of diets not available. CHO: carbohydrates; LIP: lipids; PTN: protein; SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids; GLP-1: Glucagon-like peptide-1; HbA1c: glycated hemoglobin. ↑ Increase; ↓ Decrease and ↔Iterminate

Table 2: Chemical composition of Pistachio (100g)

Composition	Raw Pistachio	Salted pistachios without salt
Calories (kcal)	560.00	572.00
Protein (g)	20.16	21.05
Carbohydrates (g)	27.17	28.28
Fiber (g)	10.60	10.30
Total Lipids (g)	45,32	45.82
SFA (g)	5.90	5.64
MUFA (g)	23.25	24.53
PUFA (g)	14.38	13.35
β-Carotene (µg)	305.00	159.00
Lutein + Zeaxanthin (µg)	2903.00	1160.00
γ-Tocopherol (mg)	21.41	23.42
Cyanidin (mg)	7.33	-
Catechin (mg)	3.60	-
Epigallocatechin (mg)	2.00	-
Epicatechin (mg)	0.80	-
Quercetin (mg)	1.50	-
Genestein (mg)	1.75	-

Base: Table of Chemical Composition of Foods. United States Department of Agriculture (USDA). National Nutrient Database for Standard Reference.

UNIVERSIDADE FEDERAL DE VIÇOSA
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Viçosa, October 11, 2017.

To: Editorial Board, Critical Reviews in Food Science and Nutrition

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Dear editor,

First, we welcome comments and considerations regarding the manuscript entitled "**Effect of chronic consumption of pistachios (pistacia vera l.) on glucose metabolism in pre-diabetics and type 2 diabetics: a systematic review**".
Thus, in this second version of the manuscript, we believe that we have examined all the comments and suggestions made and we have made the considerations suggested by the reviewer. Below are all the considerations and their corrections. These corrections have also been made in the original file, being in red.

Considerations- Reviewer 1

1) Toasted should be changes as "roasted in the manuscipt".
The word toasted was changed to roasted throughout the manuscript.

2) More papers can be added particularly roasted and unroasted pistachios and other.
We have added more papers comparing the effect of roasting on the nutritional composition of the pistachio.

Analyzing the roasting process the composition of fatty acids and lutein/zeaxanthin were not altered (Schlörmann et al., 2015), but the concentration of γ-tocopherol showed a significant increase after the processing (raw: 30,6mg; after 140ºC: 35,9mg; p=0.033) (Wolfgang et al., 2016). However, the β-carotene concentration in the roasted pistachio decreased significantly after a temperature of 160°C (raw: 204 µg; after 160ºC: 164; p <0.001) (Wolfgang et al., 2016).

It is possible to note that the temperature used in the roasting process has an influence on the nutrient concentration of this food, observing that at higher temperatures (160ºC) there was a loss of important nutrients. Another aspect that should be t considered is that the pistachios submitted to the roasting process in medium temperatures (140 to 159ºC) presented higher scores in sensorial analysis (Schlörmann et al., 2015).

Regards,

Master Priscila Vaz de Melo Ribeiro