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To cite this article: Ana Paula Silva Caldas, Larissa Oliveira Chaves, Letícia Linhares Da Silva, Dayane De Castro Morais & Rita de Cássia Gonçalves Alfenas (2017) Mechanisms involved in the cardioprotective effect of avocado consumption: A systematic review, International Journal of Food Properties, 20:sup2, 1675-1685, DOI: [10.1080/10942912.2017.1352601](https://doi.org/10.1080/10942912.2017.1352601)

To link to this article: <https://doi.org/10.1080/10942912.2017.1352601>



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Accepted author version posted online: 20 Jul 2017.  
Published online: 21 Dec 2017.



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## Mechanisms involved in the cardioprotective effect of avocado consumption: A systematic review

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### ABSTRACT

The objective of this review was to verify the effects of avocado consumption on cardiovascular diseases (CVDs) risk factors. A systematic search was conducted in electronic databases using the descriptor avocado, combined with CVD, monounsaturated fat, antioxidant, lipoprotein, and inflammation, and their respective terms in Spanish. The review was carried out in pairs, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) recommendations. Initially, 234 studies were identified. After selection, eight articles were included. All the studies were randomized, most were crossover studies, and involving adult subjects. Total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-c), triglycerides (TG), platelet aggregation, and apolipoproteins reductions; besides high-density lipoprotein-cholesterol (HDL-c) and serum lipid peroxidation increases; IκB protein (IκB-α) protein preservation; and NF-κB (NFκB) inactivation were observed. Thus, avocado consumption exerts a beneficial effect on CVDs prevention, which can be attributed to its monounsaturated fatty acids (MUFA) content, especially oleic fatty acid. However, there is no consensus on the amount of avocado needed to confer such benefits.

### KEYWORDS

Cardiovascular disease;  
Dyslipidemia; Inflammation;  
Oxidative stress; *Persea  
americana*

### Introduction

Cardiovascular diseases (CVDs) affect thousands of people, and represent the leading cause of mortality worldwide.<sup>[1]</sup> The consumption of high-fat diets is one of the factors that favor the manifestation of these diseases. However, recent studies indicate that the dietary fat quality can exert a protective effect.<sup>[2]</sup> The consumption of foods rich in monounsaturated fatty acids (MUFA), dietary fibers, and antioxidants has been associated with lipid profile improvement and body weight loss.<sup>[3–6]</sup>

Avocado is a fruit that contains about 2.11 g of soluble fiber and 2.7 g of insoluble fiber per 100 g, with an energy density of 1.7 calories/g, and approximately 15% of fat, of which 63% are represented by MUFA, mainly oleic fatty acid (C18: 1n9). Furthermore, avocado has antioxidants and phytosterols.<sup>[4,7,8]</sup> It is believed that the beneficial effect of avocado, contributing to the reduction of cardiovascular risk factors, is associated with these nutritional compounds.<sup>[9–11]</sup>

However, there are only a few studies that discuss the mechanisms by which antioxidant compounds, phytosterols, fibers, and MUFA present in avocado exert their beneficial effects. Thus, the objective of this review was to verify the effects of the components originated from avocado on the cardiovascular risk factors, as well as to elucidate the involved mechanisms.

## Methodology

A systematic search in the electronic databases Lilacs, Medline, Scopus, and Science Direct was performed. We included in this review only original articles involving humans, with no publication date restriction. The search terms used were avocado combined with CVD, monounsaturated fat, antioxidant, lipoprotein, and inflammation, and their respective terms in English and Spanish.

For the selection of the studies, initially the titles and abstracts were evaluated, and subsequently, the entire articles were read. A reverse search was conducted in the reference section of the selected studies in order to identify relevant studies that had not been included. Initially, 234 studies were identified. After the selection steps, eight studies were included. Review articles, studies in which only the chemical composition was analyzed, or characterization studies, animal studies, and those not related to CVD were excluded (Fig. 1). In all the selection stages, each article was read by two researchers, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) recommendations, to ensure that the review protocol and the inclusion and exclusion criteria were followed.<sup>[12]</sup>

## Results

Eight studies were selected for this systematic review. All the studies were randomized, and most were crossover studies.<sup>[4,9,10,13,14]</sup> Subjects were adults<sup>[4,9,10,13-16]</sup> or adults and the elderly<sup>[17]</sup>, presenting some types of illness in 75% of the studies.<sup>[4,9,14-17]</sup> The duration of intervention adopted in the studies varied from 1 day (acute)<sup>[10]</sup> to 6 weeks<sup>[16]</sup>, with an average time duration of four weeks.<sup>[9,14,15,17]</sup> The amount of avocado ingested ranged from 68<sup>[10]</sup> to 500 g.<sup>[13]</sup> Only one study evaluated avocado consumption included in a meal.<sup>[10]</sup> In the others, the fruit was ingested fresh, and in one of these studies avocado was consumed with olive oil<sup>[17]</sup> (Table 1).

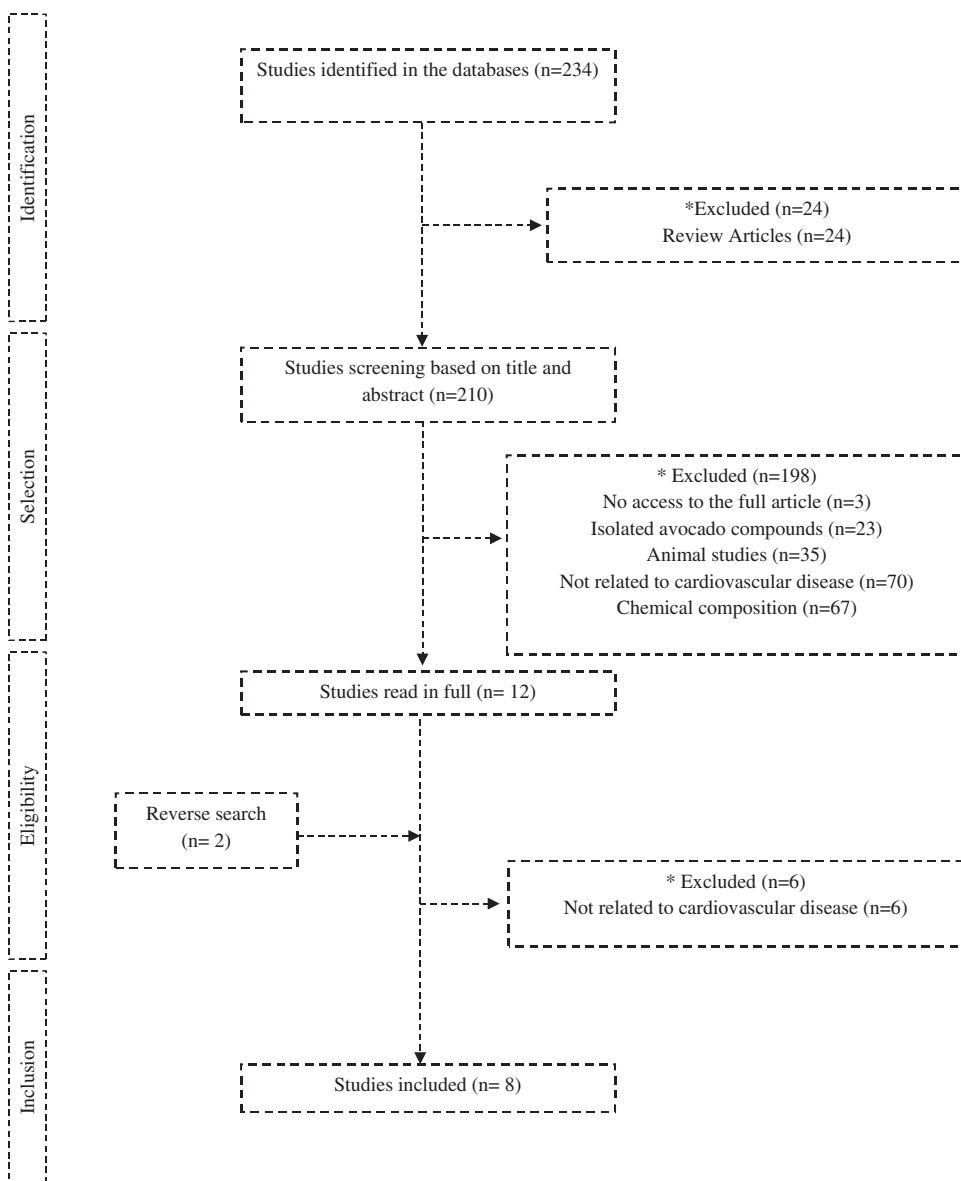
Reductions in total cholesterol (TC)<sup>[4,13-15,17]</sup>, low-density lipoprotein (LDL-c)<sup>[4,13,15,17]</sup>, triglycerides (TG)<sup>[14,15]</sup>, apolipoproteins A and B,<sup>[4,13]</sup> and platelet aggregation were observed.<sup>[9]</sup> There was an increase in high-density lipoprotein (HDL-c)<sup>[15,17]</sup> and serum lipid peroxidation.<sup>[9]</sup> Preservation of Ikappa-B protein (IkB) and inactivation of NF-kappa B (NFkB)<sup>[10]</sup> were observed. Pieterse et al.<sup>[16]</sup> observed only reduction in body weight after avocado consumption for 6 weeks (Table 1). MUFA<sup>[4,13,15,16]</sup>, phytosterols<sup>[4,13]</sup>, and fibers<sup>[4]</sup> were considered responsible for the improvement on CVD, due to lipid profile improvement, inflammation inhibition, reduction of proinflammatory cytokines, and vasoconstrictor effect reduction.<sup>[10]</sup> However, most of the authors attributed the observed beneficial effects to MUFA present in the avocado (Table 1).

## Discussion

The consumption of avocado, a source of antioxidants, fiber, and MUFA, was able to reduce body weight, control dyslipidemia, and reduce the plasma concentrations of proinflammatory markers, acting in the prevention and control of CVD<sup>[10,13-17]</sup> (Fig. 2).

### Excess body weight

Excess body weight has been considered one of the risk factors for CVD manifestation.<sup>[18]</sup> Since 1980, the prevalence of excess body weight more than doubled globally and heart diseases were the leading cause of death in 2012.<sup>[19]</sup> Therefore, the search for dietary strategies capable of promoting a healthy body weight has received attention in the scientific media. Regardless of its relatively high energy density, avocado consumption can favor body weight control, due to its fiber content and the quality of fats present.<sup>[20,21]</sup>



**Figure 1.** Flow chart of studies selection.

Among the studies selected for this review, only one assessed the influence of avocado intake on body weight. The consumption of hypocaloric diet containing 200 g of avocado instead of 30 g of fat (margarine, mayonnaise, or oil) resulted in weight loss ( $-2.13$  kg) similar to that observed after consumption of the same diet containing other sources of fat ( $-2.65$  kg).<sup>[16]</sup>

Other authors also verified a reduction in body weight after the consumption of 225 g<sup>[9]</sup> and 200–500 g<sup>[13]</sup> of avocado for 4 and 9 weeks, respectively. On the other hand, weight loss was not observed<sup>[15]</sup> or there was weight gain in two other studies in which a whole unit<sup>[14]</sup> and 250 g<sup>[17]</sup> of the avocado were ingested during 16 and 4 weeks, respectively. The results of these studies suggest that, in order for weight loss to occur in response to avocado consumption, the fruit should be consumed for at least three weeks, in association with a controlled diet. In other words, the calories from avocado should be included in the total calories consumed.

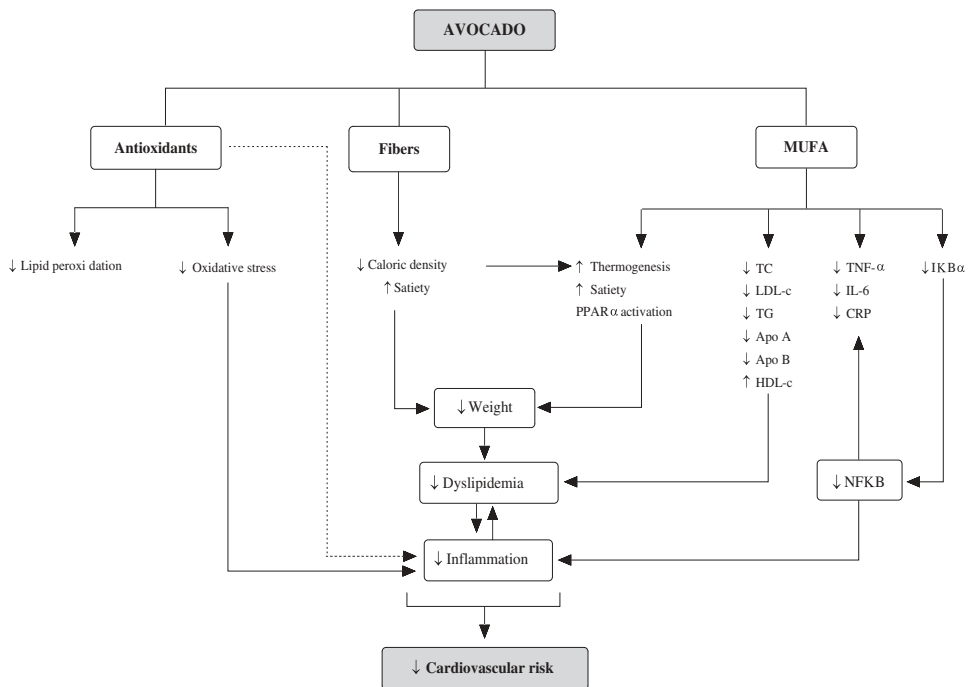
**Table 1.** Effect of avocado consumption on cardiovascular risk factors.

Study type	Sample characteristics	Intervention	Duration	Main results	Main nutrients	Reference
Crossover	15 F 37–58 years Sedentary	Group 1: low fat (20–25% reduction of usual fat) Group 2: Addition of 200 to 500 g of avocado (20–25% of daily energy needs) Avocado cultivar: <b>Hass avocado</b>	9 weeks	↓ TC ↓ Apo B ↓ LDL-c	MUFA Phytosterols	[13]
Crossover	12 M 48–64 years DM2	Group 1: MUFA-rich diet (1 avocado plus 4 teaspoons of olive oil/day) Group 2: 60% carbohydrate diet Avocado cultivar: <b>Hass avocado</b>	16 weeks	↓TC ↓TG	MUFA	[14]
Cross-sectional	30 F/M 30–65 years Dyslipidemic	Usual diet plus 250 g of avocado/day Avocado cultivar: ND	4 weeks	↓ TC ↓ LDL-c ↑ HDL-c ↑ TG ↑ Body weight	MUFA	[17]
Case-control	21 F/M 48–64 years DM2	Group 1: 1700 kcal/day Group 2: 1700 kcal/day plus 225 g of avocado Avocado cultivar: <b>Hass avocado</b>	4 weeks	↑ Serum lipoperoxidation ↓ Platelet aggregation	MUFA	[9]
Case-control	14 M 27–57 years Dyslipidemic Overweight	Group 1: usual diet plus 30 g of corn oil Group 2: usual diet plus 30 g avocado fat (200g of avocado/day) Avocado cultivar: <b>Hass avocado</b>	4 weeks	↓ TC ↓ TG ↓ LDL-c ↓ HDL-c	MUFA	[15]
Crossover	11 M 19–31 years Healthy	Group 1: 250g of traditional hamburger (436 kcal and 25 g of fat) Group 2: 250 g of traditional hamburger plus 68 g of avocado (550 kcal and 36 g of fat) Avocado cultivar: <b>Hass avocado</b>	Acute	Inhibition of vasoconstriction Inhibited degradation of IκB; ↓Activation of NFκB	Oleic acid	[10]
Crossover, randomized, controlled	45 F/M 32–58 years Overweight	Group 1: low fat (24%) Group 2: moderate in fat (34%) Group 3: moderate in fat (34%) plus 136 g of avocado Avocado cultivar: <b>Hass avocado</b>	21 weeks	↓LDL-c ↓TC ↓ApoB-100 ↓ApoA1	MUFA Phytosterols Fibers	[4]
Randomized, controlled	55 F/M 21–57 years Overweight	Group 1: caloric restriction Group 2: caloric restriction plus 200 g of avocado Avocado cultivar: ND	6 weeks	↓Body weight	–	[16]

LDL-c, low-density lipoprotein; HDL-c, high-density lipoprotein; TC, total cholesterol; TG, triacylglycerol; ApoB100, apolipoprotein B-100; ApoA1, apolipoprotein A1; MUFA, monounsaturated fatty acid; DM2, diabetes mellitus type 2; NFκB, factor nuclear kappa B; ND, not declared; IκB, inhibitory protein kappa B; M, male; F, female.

Fibers in general are directly involved in the mechanisms of satiety and nutrient absorption.<sup>[22]</sup> Through water absorption, soluble fibers promote an increase in food bolus volume, gastric fullness, and thus being able to reduce hunger.<sup>[22,23]</sup> In addition, the probiotic role of these fibers has been recently discovered, and they are capable of modulating the intestinal microbiota, causing changes in the energy metabolism favoring body fat reduction.<sup>[24]</sup> On the other hand, insoluble fibers, which represent more than 70% of the fibers in avocado<sup>[25,26]</sup>, have a laxative effect, increasing motility and reducing intestinal transit time, which may result in decreased absorption of the ingested calories<sup>[27]</sup> (Fig. 2).

The type of fat consumed can also affect body composition, because they present different metabolic behaviors.<sup>[28]</sup> There are evidences that MUFA, which represent 64% of avocado fat, favor weight loss by stimulating the expression of leptin mRNA. The maintenance of the normal



**Figure 2.** Possible mechanisms involved in the beneficial effect of avocado on cardiovascular diseases prevention and control. ApoA, apolipoprotein A; ApoB, apolipoprotein B; CRP, C-reactive protein; HDL-c, high-density lipoprotein; IκB, inhibitory protein kappa B; IL-6, interleukin 6; LDL-c, low-density lipoprotein; MUFA: monounsaturated fatty acid; NFκB: factor nuclear kappa B; PPARα, peroxisome proliferator-activated receptor alpha; TC, total cholesterol; TG, triacylglycerol; TNF-α, tumor necrosis factor alpha.

levels of this hormone favors satiety and food intake reduction.<sup>[29]</sup> Once leptin is stimulated, it also regulates energetic homeostasis, since it exerts lipolytic effect by increasing the mRNA expression of the hormone-sensitive lipase and inhibits lipogenesis by preventing the expression of acetyl-CoA carboxylase.<sup>[30]</sup> In addition, it promotes greater mitochondrial beta-oxidation and increases the expression of peroxisome alpha proliferators (PPARα).<sup>[30]</sup> PPARα regulates cell differentiation and lipid metabolism by controlling the synthesis of adipose tissue.<sup>[31]</sup>

In addition, MUFA, compared with saturated fatty acids, increase thermogenesis and are preferentially oxidized in the body, promoting greater energy expenditure and lower fat storage-<sup>[29,32]</sup> (Fig. 2). This increase in thermogenesis may occur as a function of a stimulus to the sympathetic nervous system, by MUFA, capable of stimulating the hormone-sensitive-lipase complex, which hydrolyzes fat present in the adipocytes and promotes body weight reduction.<sup>[33]</sup> Thus, it seems that the fibers and MUFA present in avocado increase satiety signaling, lipolysis, and thermogenesis, contributing to reduce caloric intake and the storage of adipose tissue, and thus reducing the risk of CVD. Although not discussed by the authors, the oils, fibers, and antioxidants contents of avocado may vary in accordance with the cultivars, region of origin, or climatological conditions. This difference in the nutrients content may interfere directly in the results of studies.<sup>[34–36]</sup>

### Dyslipidemia

A balanced and adequate dietary intake can play a beneficial role when blood lipid profile is unfavorable.<sup>[37]</sup> The results of some studies suggest that the risk of dyslipidemia can be modified according to the type of fat ingested.<sup>[37,38]</sup> The authors of a meta-analysis study conducted in the

United States concluded that the consumption of avocado, instead of saturated fats, decreases CT, LDL-c, and TG concentrations in healthy eutrophic adults.<sup>[37]</sup> Other authors also highlighted an increase in the concentration of HDL-c, due to the high content of MUFA in avocado.<sup>[39–41]</sup>

The first clinical intervention study with avocado showed that the consumption of 0.5–1.5 avocados a day may help control TC in men.<sup>[40]</sup> A review carried out by Dreher & Davenport (2013) showed that in hypercholesterolemic individuals, consumption of diets enriched with avocado can reduce LDL-c and TG and increase HDL-c compared with diets high in carbohydrate or in avocado-free diets. In subjects presenting blood lipids within the normal range, the addition of that fruit to the diet reduced LDL-c without reducing HDL-c.<sup>[26]</sup>

Among the studies analyzed in the present review, the intake of at least 136 g of avocado for 5 weeks showed a positive impact on blood lipid profile, reducing the concentrations of CT, apolipoproteins A and B, LDL-c, and TG and increasing the concentration of HDL-c.<sup>[4,13–15]</sup> In one of the studies evaluated, there was an increase in plasma TG after the consumption of 250 g of avocado during 4 weeks.<sup>[17]</sup> However, a high carbohydrate intake by the subjects was observed, which may have led to an increase in plasma TG.<sup>[42]</sup> In addition, although the amount of avocado to be consumed was predetermined, the subjects consumed it under free living conditions. Therefore, the authors of that study failed to ensure adequate intake.

A possible mechanism involved is the degradation of TG by the lipoprotein lipase enzyme (LPL) that preferentially degrades TG containing long-chain unsaturated fatty acids.<sup>[43,44]</sup> Then, the fatty acids released from the TG are incorporated into HDL-c particles, raising the concentration of this lipoprotein in the plasma.<sup>[45,46]</sup> Therefore, the oleic fatty acid, present in avocados, can play an active role in reducing plasma TG and elevating HDL-c.<sup>[43,44]</sup>

Oleic fatty acid can reduce the plasma concentration of LDL-c, without causing its oxidation. This fatty acid is the main substrate for acyl-CoA: cholesterol acyltransferase (ACAT), a liver enzyme that catalyzes the formation of cholesterol esters from cholesterol. Thus, the presence of excess cholesterol in the free form is rapidly esterified, it does not lead to LDL-c receptors suppression, and it favors the uptake of LDL-c, decreasing its plasma concentration. In addition, oleic acid can induce lower endogenous CT synthesis when compared with polyunsaturated fatty acids (PUFA).<sup>[47,48]</sup> Therefore, the fatty acids present in avocado also interfere in key mechanisms promoting CT and LDL-c reduction.

Although the authors of only one study attributed improved blood lipid profile to fiber intake<sup>[4]</sup>, it has been shown that the consumption of diets rich in fiber promotes a significant reduction in plasma TC and LDL-c concentrations in hypercholesterolemic individuals.<sup>[49]</sup> This effect is mainly attributed to soluble fiber, which is approximately 30% of the fiber content of avocado, and which increases bile acids synthesis and reduces cholesterol absorption, decreasing blood cholesterol.<sup>[50,51]</sup> In addition, propionate, the product of the fermentation of these fibers, inhibits cholesterol hepatic synthesis.<sup>[51]</sup> The results of all these studies show that avocado consumption should be encouraged to improve blood lipid profile and cardiovascular health.

### **Inflammation and oxidative stress**

Inflammation and oxidative stress are interrelated and are processes involved in the main mechanisms that lead to the manifestation of chronic non-communicable diseases, including CVD.<sup>[52]</sup> Inflammation favors the development of CVD, especially in the process of atherosclerosis, which predisposes to most of these diseases.<sup>[18]</sup> LDL-c continuously deposited in the subendothelial layer is exposed to agents that transform LDL-c into oxidized forms of LDL (LDL<sub>ox</sub>) with strongly immunogenic potential.<sup>[53]</sup> Once formed, LDL<sub>ox</sub> activates the atherosclerotic process and simultaneously induces the inflammatory process, with the subsequent release of cytokines, chemokines, and the activation of T cells.<sup>[54]</sup>

Moreover, in the last few decades, strong evidences have emerged that oxidative stress is one of the most potent inducers of endothelial dysfunction and is involved in all of the development stages

of the atherosclerotic process.<sup>[55]</sup> Therefore, it has been verified that the intakes of MUFA food sources and bioactive compounds, such as avocado, are associated with the reduced risk of CVD, by increasing the concentration of HDL-c and acting as antioxidants, thereby preventing LDL-c oxidation.<sup>[56]</sup> Furthermore, avocado also contains lipophilic phytochemicals, including vitamin E, carotenoids, and sterols, which have antioxidant activity, thus exerting anti-inflammatory and anti-atherogenic effects.<sup>[57]</sup>

In the present review, only one study evaluated the anti-inflammatory effect of avocado after the acute consumption of beef burger containing approximately 70 g of avocado.<sup>[10]</sup> In the aforementioned study, there was postprandial reduction on the plasma concentration of IL-6 and IκBα preservation, followed by the lower activation of NFκB, considered the main transcription factor capable of inducing inflammatory response by stimulating the expression of proinflammatory cytokines, chemokines, and adhesion molecules.<sup>[56,58–61]</sup> Although the amount of avocado ingested was small compared with other intervention studies (200–250 g)<sup>[15,17]</sup>, it was sufficient to promote a positive effect on postprandial inflammatory status. This result was associated with avocado's fatty acid profile and antioxidant content, which likely interfered in the regulatory mechanisms of inflammation.

Oleic fatty acid is the MUFA present in greater quantity in avocado and potentially responsible for most of the beneficial effects attributed to its consumption. Although the exact mechanism has not yet been elucidated, it has been suggested that oleic acid can reduce the concentrations of inflammatory markers such as interleukin-6 (IL-6), C-reactive protein, and tumor necrosis factor-α (TNF-α), exerting anti-inflammatory and vascular-protective properties.<sup>[60,62]</sup>

Mediterranean diet, consisting essentially of vegetables, whole grains, nuts, fish, and olive oil, is widely associated with the improvement of inflammatory status.<sup>[63,64]</sup> This effect is mainly attributed to the presence of oleic fatty acid that is able to modulate the expression of pleiotropic genes involved in signal transmission pathways and the production of proinflammatory cytokines.<sup>[65]</sup> In rats, the administration of oleic acid reduced the production of proinflammatory mediators such as IL-1β and IL-6, and induced an improvement in the neutrophils function.<sup>[66]</sup>

Excess free radicals in the body lead to oxidative stress with consequent modification of the redox status of the cell, a powerful stimulus for inflammatory pathways, among them is NFκB.<sup>[52]</sup> Cells cultured in the presence of oleic fatty acid showed reduced concentrations of IL-6, IL-1β, and TNF-α, subsequent to lower expression of NFκB.<sup>[67,68]</sup> This study exemplifies what has been proposed as a mechanism for the anti-inflammatory effect of MUFA. These fatty acids, among them oleic acid, are able to interfere in the NFκB pathway, preventing the onset of inflammatory cascade in an AMPK-dependent manner<sup>[69]</sup> (Fig. 2). Moreover, the anti-inflammatory capability of oleic acid can also contribute to CVD reduction.

Furthermore, although avocado is a source of antioxidants, Li et al. (2013) did not suggest any possible mechanism to try to explain the influence of these components on the observed anti-inflammatory effect.<sup>[10]</sup> There is evidence that bioactive compounds act directly to reduce proinflammatory cytokines by interfering in the expression of proinflammatory genes, even when they are used in small quantities.<sup>[70]</sup> In addition, these compounds can also reduce oxidative stress by promoting the elimination of free radicals or by stimulating an increase in the endogenous antioxidant capacity. Lower concentration of free radicals results in lower stimulus for proinflammatory gene expression.<sup>[70]</sup> Therefore, although there are no studies in the literature in which the effect of the bioactive compounds of avocado on inflammatory markers were assessed, such compounds can prevent inflammation and oxidative stress, and exert cardioprotective function.<sup>[71,72]</sup>

Even though physiologically, there are evidences for the possible anti-inflammatory and antioxidant mechanisms of oleic fatty acid, there is still no consensus in the literature regarding the minimum amount of this fatty acid necessary to promote such benefits. Nuts were the first food source of MUFA, especially oleic fatty acid, to receive the title of cardioprotector by the Food and Drug Administration (FDA, USA).<sup>[73]</sup> The consumption of approximately 30 g per day of nuts is

associated with cardiovascular events reduction.<sup>[73,74]</sup> However, the recommendation on the amount to be consumed or the frequency of consumption of any MUFA food source has not been established yet.

## Conclusion

Consumption of avocado, a fruit source of MUFA, especially of oleic fatty acid, fiber, and antioxidants, plays a beneficial role on body weight, plasma lipid profile, oxidative stress, and inflammation. These effects have been observed in response to both acute and chronic ingestions. However, there is no consensus regarding the amount of avocado to be included in a diet. Therefore, more studies should be conducted in order to establish the minimum effective amount for CVD prevention.

## Declaration of interest

The authors declared no conflict of interest.

## Author contributions

All authors participated in the different steps of elaboration of this present article, including selection, reading, and critical analysis of all articles used as reference. Moreover, all authors contributed greatly to the writing of this article.

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