Obesity and metabolic syndrome: Potential benefit from specific nutritional components

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Abstract The prevalence of metabolic syndrome (MetS) manifestations is rapidly increasing worldwide, and is becoming an important health problem. Actually, MetS includes a combination of clinical complications such as obesity (central adiposity), insulin resistance, glucose intolerance, dyslipidemia, non-alcoholic fatty liver disease and hypertension. All these alterations predispose individuals to type 2 diabetes and cardiovascular disease inducing earlier mortality rates among people.

In general terms, it is difficult for patients to follow a standard long-term diet/exercise regime that would improve or alleviate MetS symptoms. Thus, the investigation of food components that may deal with the MetS features is an important field for ameliorate and facilitate MetS dietary-based therapies. Currently antioxidants are of great interest due to the described association between obesity, cardiovascular alterations and oxidative stress. On the other hand, high MUFA and PUFA diets are being also considered due to their potential benefits on hypertension, insulin resistance and triglyceride levels. Mineral composition of the diet is also relevant since high potassium intake may improve hypertension and high calcium consumption may promote lipid oxidation. Thus, although nutritional supplements are at the peak of dietetic therapies, the consumption of some specific foods (legumes, fatty fish, vegetables and fruits, etc) with bioactive components within an energy-restricted diet is a promising approach to manage MetS manifestations. Therefore, the present review focuses on some of the most important food components currently investigated to improve and make easier the nutritional MetS treatment.

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Introduction

Metabolic syndrome (MetS) involves a combination of clinically specific risk features including obesity (central adiposity), insulin resistance, glucose intolerance, dyslipidemia, non-alcoholic fatty liver disease and hypertension [1], which is rising worldwide as a consequence of the continued obesity epidemic [2,3]. In 2005, the International Diabetes Federation (IDF) established the criteria of central obesity as (a) waist circumference \( \geq 94 \text{ cm for men, } \geq 80 \text{ cm for women and two of the following alterations: raised triglyceride level } \geq 150 \text{ mg/dl, or specific treatment for this lipid abnormality, (b) reduced HDL-c: } <40 \text{ mg/dl in males and } <50 \text{ mg/dl in females or specific treatment for this lipid abnormality, (c) raised blood pressure: systolic BP } \geq 130 \text{ or diastolic BP } \geq 85 \text{ mmHg, or treatment of previously diagnosed hypertension, (d) raised fasting plasma glucose } \geq 100 \text{ mg/dl or previously diagnosed type 2 diabetes.}

In addition to genetic predisposition, the physical inactivity as well as high-density food availability is among the main determinants of obesity, cardiovascular diseases [4] and metabolic syndrome, being important causes of mortality [5].

Dietary and physical activity advices are the first choice for treating these metabolic diseases [6]. In spite of the simplicity of the treatment, the success rate in the long term is poor. Lifestyle changes result very difficult in an obesogenic environment. Moreover, people who start losing weight believe that this lifestyle change is temporarily, since they use to return to their initial habits, which often make them put on more weight than they had initially. Overall, there is full agreement that lifestyle changes focused primarily on weight loss and exercise are the keys to success. However, contrary to what has been traditionally suggested, the success rate is poor. Weight loss as (a) waist circumference \( <94 \text{ cm for men, } <80 \text{ cm for women and two of the following alterations: raised triglyceride level } \geq 150 \text{ mg/dl, or specific treatment for this lipid abnormality, (b) reduced HDL-c: } <40 \text{ mg/dl in males and } <50 \text{ mg/dl in females or specific treatment for this lipid abnormality, (c) raised blood pressure: systolic BP } \geq 130 \text{ or diastolic BP } \geq 85 \text{ mmHg, or treatment of previously diagnosed hypertension, (d) raised fasting plasma glucose } \geq 100 \text{ mg/dl or previously diagnosed type 2 diabetes.}

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Antioxidants and metabolic syndrome

Antioxidants are of great interest by their positive effects against oxidative stress, which is a process closely related to obesity, cardiovascular alterations, some degenerative diseases and certain types of cancer [10]. Many nutritional intervention studies have been performed with antioxidant supplements, but finding controversial results [11–14]. However, current literature emphasizes on the potential therapeutic effects of micronutrients found in natural products, indicating positive applications for controlling the pathogenesis of chronic diseases [15].

Nutritional studies have obtained positive results on metabolic syndrome features using botanical or pharmaceutical antioxidants [16,17], however, the most healthy and advised compounds are those coming from the most popular antioxidant-rich foods such as fruits, vegetables, legumes, olive oil, red wine, green tea and nuts [13,18–20]. In this sense, the PREDIMED study, which assessed the adherence to the Mediterranean diet, found that consumption of legumes, olive oil and red wine (all antioxidant-rich foods) was associated with lower prevalence of MetS [21]. The SUVIMAX study examined the effect of an antioxidant supplementation on 5220 subjects showing no benefits on the incidence of MetS. However, baseline serum antioxidant concentrations of \( \beta\)-carotene and vitamin C were negatively associated with the risk of MetS [22]. Furthermore, it is known that antioxidant supplementation beyond critical concentrations might induce the contrary to awaited effects [23]. Positive results have been also described, concretely an individual flavonoid supplementation (quercetin) in 93 obese and overweight subjects with metabolic syndrome traits decreased systolic blood pressure, HDL-c concentrations and plasma oxidised LDL concentrations, while cholesterol, triglycerides and some inflammatory markers remained unaltered [24]. Although antioxidant supplementation should be considered with precaution, the consumption of foods with antioxidants properties should be considered as important components of a dietary programme in the treatment of cardiovascular diseases.

Fruits and vegetables

Consumption of fruits and vegetables has been associated with protection against various diseases, including cancer and cardiovascular and cerebral-vascular diseases. Fruits and fruit juices, vegetables and vegetable products, teas and dietary supplements are the major sources of dietary antioxidants [18]. An interventional study showed that consumption of strawberries, spinach or other fruits and vegetables rich in antioxidant phenolic compounds, increased the serum antioxidant capacity in humans [25]. Plasma carotenoid concentrations are negatively correlated with the risk for cardiovascular disease and cancer, and carotenoids may therefore in part mediate the protective effect of vegetables and fruits. Interestingly, in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study neither alpha-tocopherol nor beta-carotene serum levels were associated with lower risk of type 2 diabetes [26]. On the other hand, observational studies have reported inverse association between vitamin E and cardio-metabolic risks, but also, results from trials studying supplementation with antioxidant vitamins failed to confirm any protective effect of them on cardiovascular diseases [14,18,27,28]. Overall, Mediterranean diet has been proposed as a therapeutic approach in inflammatory and oxidative stress diseases including cardiovascular disease, obesity, type 2 diabetes and metabolic syndrome [9]. A nutritional intervention study was carried out in a group of obese men and women...
Table 1  Described beneficial effects on metabolic syndrome features through the inclusion of some Mediterranean foods in a dietary programme.

<table>
<thead>
<tr>
<th>Metabolic syndrome criteria</th>
<th>Mediterranean foods included as part of a dietary pattern</th>
<th>Putative functional components</th>
<th>Healthy benefits of its consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin resistance</td>
<td>Legumes</td>
<td>Complex carbohydrates and soluble fibre, magnesium, potassium</td>
<td>Decrease postprandial glycaemia, improve glycaemic control</td>
</tr>
<tr>
<td></td>
<td>Olive oil</td>
<td>Phenolic components, MUFAs</td>
<td>May exert beneficial effects on insulin sensitivity</td>
</tr>
<tr>
<td></td>
<td>Red wine</td>
<td>Antioxidants: Resveratrol</td>
<td>Decrease carbohydrate absorption and insulin levels and may reduce the lipid accumulation in the liver</td>
</tr>
<tr>
<td>Low HDL cholesterol</td>
<td>Fatty fish, olive oil</td>
<td>ω-3 fatty acids, fish proteins, MUFAs (ω-9)</td>
<td>Modestly improvement on HDL cholesterol levels</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>Fatty fish, fish oils, nuts</td>
<td>Omega-3 fatty acids</td>
<td>Stimulation of lipid oxidation, favouring the decrease of triglyceride level</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Fatty fish</td>
<td>Omega-3 fatty acids, fish proteins</td>
<td>May improve insulin and leptin levels, decreasing sympathetic nervous activity and arterial constriction</td>
</tr>
<tr>
<td></td>
<td>Legumes, fruits and vegetables</td>
<td>Potassium content</td>
<td>Increase sodium elimination, decreasing plasmatic volume</td>
</tr>
<tr>
<td></td>
<td>Fermented dairy products</td>
<td>Calcium, bioactive peptides</td>
<td>Angiotensin-converting enzyme inhibition, control of arterial dilation</td>
</tr>
<tr>
<td>Abdominal obesity</td>
<td>Legumes, vegetables, fruits</td>
<td>Low glycaemic index carbohydrates, soluble and insoluble fibre</td>
<td>Reduce gastric emptying, increase satiety and dietary adherence, which may improve weight reduction</td>
</tr>
<tr>
<td></td>
<td>Low-fat milk, dairy products</td>
<td>Calcium</td>
<td>May improve weight loss</td>
</tr>
<tr>
<td></td>
<td>Fish or fish oils</td>
<td>Omega-3 fatty acids</td>
<td>Modulate lipogenic enzymes and favour lipid oxidation, decreasing fat accumulation</td>
</tr>
<tr>
<td>Diet</td>
<td>Length</td>
<td>Subjects</td>
<td>Food and frequency</td>
</tr>
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<td>--------------------</td>
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<tr>
<td>17% P; 53% CHO; 30% L [36] Energy restricted</td>
<td>8 weeks</td>
<td>Obese n = 16</td>
<td>Legume restriction</td>
</tr>
<tr>
<td>20% P; 50% CHO; 30% L [106,114,131,132] Energy restricted</td>
<td>8 weeks</td>
<td>Overweight n = 80</td>
<td>Control: sunflower oil 6 capsules/day</td>
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<td></td>
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<td>Overweight n = 80</td>
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<td></td>
<td>Overweight n = 80</td>
</tr>
<tr>
<td>17% P; 50% CHO; 30% L [105] Energy restricted</td>
<td>8 weeks</td>
<td>Obese n = 16</td>
<td>Fatty fish restriction</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Obese n = 16</td>
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<tr>
<td>15% P; 55% CHO; 30% L [29,133] Energy restricted</td>
<td>8 weeks</td>
<td>Obese women n = 8</td>
<td>2–3 fruit servings/day</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Obese women n = 7</td>
</tr>
<tr>
<td>15% P; 50% CHO; 35% L [134] Without energy restriction</td>
<td>3 years</td>
<td>Overweight n = 59</td>
<td>Conventional low-fat diet</td>
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<tr>
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<td></td>
<td></td>
<td>Overweight n = 65</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Overweight n = 63</td>
</tr>
<tr>
<td>Duration</td>
<td>Group</td>
<td>Description</td>
<td>Energy Intake</td>
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<tr>
<td>8 weeks</td>
<td>Obese</td>
<td>Legume restriction</td>
<td>17% P; 53% CHO; 30% L</td>
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<td></td>
<td></td>
<td></td>
<td>Energy restricted</td>
</tr>
<tr>
<td>7.5 years</td>
<td>Subjects free of MetS</td>
<td>n = 2525 antioxidant supplementation</td>
<td>15-20% P; 50-60% CHO; &lt;30% L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n = 2695 placebo</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>Obese with MetS</td>
<td>Control diet without energy restriction</td>
<td>Dietary habits with antioxidant supplementation [22]</td>
</tr>
<tr>
<td></td>
<td>n = 40</td>
<td>Weight-reducing diet with an energy restriction of 500 kcal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 38</td>
<td>DASH diet with an energy restriction of 500 kcal</td>
<td></td>
</tr>
<tr>
<td>12 weeks</td>
<td>Obese with MetS</td>
<td>Control group</td>
<td>Dietary recommendations [122]</td>
</tr>
<tr>
<td></td>
<td>n = 25</td>
<td>Nut group</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 25</td>
<td>111 hypertriglyceridemic with untreated normal/ high blood pressure</td>
<td>2 g PUFA supplementation</td>
</tr>
</tbody>
</table>
who were assigned in two different dietary groups. Both groups followed an energy-restricted diet but one of them was enriched in fruits. After the 8-week nutritional intervention program both groups lost weight but the fruit enriched group showed more beneficial effects such as lower levels of oxidized LDL-cholesterol and higher total antioxidant capacity [29]. On the other hand, metabolic syndrome patients were instructed on the DASH diet (Dietary Approaches to Stop Hypertension) and randomized into three groups: 0, 8 or 16 fluid ounces of low sodium vegetable juice. At the end of the study the outcomes showed that those consuming juice lost more weight, and consumed more vitamin C, potassium, and dietary vegetables than individuals who were in the group that only received diet counselling [30] (Tables 1 and 2).

Legumes

Epidemiological studies have found inverse associations between legume consumption and cardiovascular diseases [31]. Legumes, besides a high nutritive value, contain significant quantity of polyphenolic compounds such as flavonoids, isoflavones, phenolic acids and lignans. In a nutritional intervention study, soya consumption reduced plasma malondialdehyde (MDA) levels and increased total plasma antioxidant capacity (TAC) in postmenopausal women with metabolic syndrome [19]. Likewise, several meta-analysis of randomized controlled trials concluded that soy isoflavones significantly reduce total and LDL-cholesterol [32-34]. However, not only soy consumption has interesting benefits on metabolic alterations, but also, more common legumes, such as beans, lentils, chickpeas etc, have improved cardiovascular risk factors and oxidative stress markers [35]. Likewise, an 8-week intervention study that included legume consumption (4 servings per week) in a weight reduction program showed that those patients following the legume diet lost more weight [36], improved their plasma antioxidant capacity and decreased the oxidized LDL concentration as well as cholesterol levels (total and LDL-cholesterol) [35].

On the other hand, besides the higher satiety effect, some authors have found that the inclusion of such foods in a weight loss program may reduce the negative effect of caloric restriction on lean mass loss and basal metabolic rate [7,36], which is an important factor to be taken into account due to the ease to put on weight after following a hypocaloric diet. Anderson et al. previously emphasized on the health benefits of consuming legumes such as lentils, chickpeas, peas and beans [37]. Thus, currently, these kinds of foods are considered relevant components of a healthy diet because of their important benefits on CVD manifestations.

Red wine

Resveratrol is another polyphenolic compound found in grapes and red wine, with potential therapeutic implications including anti-inflammatory, antioxidant, cardio-protective, anti-ageing actions and beneficial properties against metabolic diseases [38,39]. Studies in mice have shown that resveratrol is able to protect against the metabolic changes...
Nutritional components and obesity

associated with hypercaloric diets [38,40]. Resveratrol acts mimicking the action of SIRT1 and seems to be able to correct the prothrombotic state induced by metabolic syndrome [41,42]. In this sense, a study confirmed that resveratrol improved the left ventricular function of type 2 diabetics, who suffered recent acute myocardial infarction when a moderate red wine amount (containing resveratrol) was taken daily by patients receiving conventional anti-ischaemic therapy in comparison with another group treated alone with anti-ischaemic compounds [41]. It has been also suggested that resveratrol exerts its multiple protective effects against the MetS through stimulating AMP-activated protein kinase and promoting mitochondrial biogenesis [43]. A short intervention study was carried out to determine the in vivo effects of the red wine consumption (400 mL/day for 2 weeks) where increases in total plasma antioxidant capacity and decreases in oxidative stress markers (plasma MDA and glutathione) were found [44]. Another research evaluated the effect of grape polyphenols supplementation in a group of pre- and postmenopausal women. At the endpoint, the supplemented group showed beneficial effects on lipid and lipoprotein metabolism, oxidative stress and inflammatory markers in both pre- and postmenopausal women [39]. Another randomised crossover trial compared the effect of gin with red wine intake, showing greater antioxidant effect for the red wine consumption [45]. However, in spite of most findings about resveratrol are positive, a recent animal study showed that this micronutrient supplementation significantly increased homocysteine levels and negatively affected HDL metabolism [46].

Green tea
Green tea is naturally rich in a group of antioxidants known as catechins [47]. A number of studies including green tea and other foods with high antioxidant content indicate that their bioactive components confer a protective effect against coronary heart disease [48]. Tea catechins reduce the serum cholesterol concentrations and suppress post-prandial hypertriacylglycerolemia in animal and human experimental studies [49,50]. Thus, it has been suggested that green tea may contribute in the prevention of the metabolic syndrome [49,50] however, more interventional trials should be carried out to confirm it.

Overall, antioxidant supplementation is still a controversial issue, however, there is a full agreement that a high antioxidant (no supplemented) diet based on a combination of high antioxidant foods is able to improve the benefits of weight loss alone, and specially in those patients with cardiovascular alterations and people with metabolic syndrome features.

Other nutritional components and metabolic syndrome

Glycaemic index and fibre
The glycaemic index (GI) of carbohydrates as well as fibre consumption are important dietary factors that can influence on weight control and metabolic syndrome alterations [48]. Dietary fibre has been shown to have important health implications in the prevention of risks of chronic diseases [51]. It is known that fasting and postprandial triglyceride responses may depend upon the fibre content of the diet [48]. High carbohydrate/low fibre consumption increases fasting serum triglycerides [52], whereas high carbohydrate/high-fibre diets reduce triglycerides [53]. The cholesterol-lowering effects of soluble fibres often involve 5–10% reduction, but the mechanisms of these are not fully understood [48]. The comparison of a high-fibre Mediterranean diet with a low-carbohydrate diet for weight management led to similar weight losses, however, the high-fibre diet showed more favourable effects on lipids (LDL-c) [54].

On the other hand, inconsistent findings from observational studies have prolonged the controversy over the effects of dietary GI on the risk of certain chronic diseases [55]. Studies in animal models have shown that diets based on consuming high-GI starches promote weight gain, visceral adiposity and the activity of lipogenic enzymes than do not produce diets based on low-GI foods [56–58]. On the contrary, diets based on low-GI foods may enhance weight control, promoting satiety and minimizing post-prandial insulin secretion [59–61]. In this sense, a low-GI diet emphasising low-GI breads, cereals, parboiled rice, pasta, beans, peas and nuts was compared with a high cereal low-fibre diet with a similar energy intake. In addition to a more marked improvement in HbA1c levels, the low-GI diet increased HDL-c, compared with a reduction in the high-GI low-fibre group [62]. Fibre and whole cereal intakes may protect against hyperinsulinaemia and the risk of type 2 diabetes. A randomized crossover trial showed benefits of consuming high-fibre rye bread on insulin secretion, suggesting an improvement of beta cell function [63]. Interestingly, the form of the food and botanical structure may play a role in determining the postprandial insulin responses rather than the amount of fibre or the type of carbohydrate. In this sense, Juntunen et al. [64] determined the effect of rye fibre in containing these cereal breads on postprandial insulin and glucose responses. The findings showed that fibre content did not explain the lower postprandial insulin response to rye bread as compared to wheat bread, but structural differences were responsible of such differences. Thus, the characteristics of a starchy food are able to modify the postprandial glucose and insulin responses in humans.

On the other hand, the importance of the macronutrient composition of the diet for the prevention and management of obesity has been showed in the Diet, Obesity, and Genes (Diogenes) study [65]. This European study was designed to assess the efficacy of moderate-fat diets that vary in protein content and glycaemic index for preventing weight regain and obesity related risk factors after weight loss. Thus, it was found that a modest increase in the protein content and a reduction in the glycaemic index led to an improvement in study completion and maintenance of weight loss.

Magnesium
Low magnesium (Mg) intake and low Mg status have been associated with a higher prevalence of MetS [66–68] so
inadequate Mg consumption is related with glucose and insulin metabolism impairment [69]. The major dietary sources of Mg intake include whole grains, legumes, nuts, and green leafy vegetables [70]. Experimental and clinical studies suggest that Mg intake may be inversely related to the risk of hypertension and type 2 diabetes mellitus, and may decrease blood triglyceride and increase high-density lipoprotein cholesterol levels [71]. In patients with type 2 diabetes who had low Mg levels, randomization to an oral supplementation improved insulin sensitivity and glucose control after 16 weeks [72,73]. In this context, a meta-analysis of nine randomized double-blind controlled trials with a total of 370 patients with type 2 diabetes assessed the effect of oral magnesium supplementation (360 mg/day) during 4–16 weeks on glycaemic control, blood pressure and lipids. After the treatments, results showed that magnesium supplementation was effective in reducing fasting glucose levels and increasing HDL-c concentration. But, the magnesium addition had no effect on total cholesterol, LDL-c, triglyceride and blood pressure [74]. However, there is limited empirical data to evaluate whether magnesium supplements should or should not be recommended to patients with diabetes. Although it may be safe in selected patients at appropriate dosages, magnesium may cause adverse effects or death at high dosages [70]. Additional long-term controlled trials in diabetic as well as patients with MetS are warranted to assess the efficacy of magnesium supplementation.

**Calcium and dairy products**

Dietary calcium appears to play a pivotal role in the regulation of energy metabolism and obesity risk [75]. Initial studies by Zemel et al. (2000) [76] reported that those patients in the highest quartile of adiposity were negatively associated with calcium and dairy product intake. Another nutritional intervention trial also demonstrated that higher low-fat dairy intake among overweight type 2 diabetic patients on isocaloric-restricted regimes enhances the weight loss process [77]. Furthermore observational studies have presented inverse associations between dairy intake and the prevalence of insulin resistance syndrome and type 2 diabetes mellitus [78,79]. The Atherosclerosis Risk in Communities (ARIC) study also revealed that dairy consumption was inversely associated with incident MetS [80].

In a highly educated Mediterranean cohort (SUN), low-fat dairy consumption, but not whole-fat dairy consumption, was associated with a lower risk of incident hypertension, even after control for several potential confounders such as age, sex, physical activity, body mass index [81]. Indeed, a recent crossover study showed that dietary supplementation with whole-fat dairy products, compared to low-fat dairy, was associated with weight gain while no differential effects were observed for levels of blood pressure [82].

Dairy products are the main source of dietary calcium and different mechanisms have been proposed for explain the role of calcium in the risk for suffering MetS [78]. However, there are evidences that calcium provided as a food supplement or by fortification appears to decrease LDL-c and triglyceride concentrations, as well as to increase HDL-c concentrations [83]. The potential hypolipidemic mechanisms of calcium may occur via: (i) the inhibition of fat absorption accompanying an increased faecal fat excretion; (ii) inhibition of the absorption of bile acids; (iii) a calcium-induced increase in the conversion of cholesterol to bile acids [84].

In addition to the effects on lipid profile, an inverse relationship between the MS and dairy intake might have been mediated by calcium intake to some extent, mediated by its putative effect in reducing body weight and fat mass [85–87]. Dietary calcium could affect the body fat mass by increasing faecal fat excretion as well as by stimulating lipolysis and inhibiting lipogenesis, which is stimulated in high dietary calcium [88]. In addition, calcium could partly account for the observed inverse association between dairy consumption and the risk of hypertension [89]. The relationship between calcium intake and coronary artery disease or stroke, which are two major consequences of hypertension, could be presented only for calcium from dairy products but not from other sources [81]. Also, it has been suggested that some peptides (containing up to 10 amino acids) produced as a result of dairy fermentation or during the digestive process could have angiotensin-converting enzyme (ACE)-inhibitory and endothelin release-inhibitory activity [90]. However, the antihypertensive potential of the peptides requires that they reach target sites without being degraded and inactivated by intestinal or plasma peptidases.

Earlier intervention studies showed that skim milk or yogurt consumption might decrease plasma cholesterol levels, while whole milk had neither a hypo- nor hyper-cholesterolemic effect [90]. A possibility is that the intestinal bacteria can bind bile acids to cholesterol, resulting in an excretion of bile acid–cholesterol complexes in the faeces [90].

On the contrary, a multicenter study recruited middle-aged overweight subjects (n = 121) with traits of MetS, which were randomly assigned into milk or control group. After the 6-mo intervention study no differences were observed in body composition, blood pressure, markers of inflammation, endothelial function, adiponectin or oxidative stress between groups [91]. Many metabolic and dietary factors appear to influence the degree to which dairy affects metabolic syndrome parameters such as calcium and vitamin D, BMI and age. Very often calcium and vitamin D availability is also a controversial issue, since dairy products are a minimal source of vitamin D unless they were fortified, which have been related to adiposity reduction [85].

Milk and dairy products have been also inversely associated to homocysteine levels and positively with folate levels [92]. Moreover, the inclusion of milk in the diet could enhance the bioavailability of food folate, due to the whey protein fraction of milk, which contains a high-affinity folate-binding protein and protects folate from degradation [93].

Overall, in spite that many authors have found positive effects on weight loss and metabolic syndrome complications of increased intake of dairy products, more and long-term studies would be necessary confirm the hypothesis.
Selenium and zinc

In an observational study, dietary selenium intake was inversely related to sialic acid, an inflammatory marker, and to triacylglycerol levels, proposing selenium as a potential anti-inflammatory nutrient [94]. Moreover, a possible role of selenium intake in the modulation of serum complement 3, which may be an early marker of metabolic syndrome manifestations [95].

Many experimental and clinical studies have documented that zinc deficiency may predispose to glucose intolerance, diabetes mellitus, insulin resistance, atherosclerosis and coronary artery disease [96–98]. The effect of zinc on LDL-c and HDL-c has also been reported [97–99]. Moreover, supplementation with zinc provides a significant prevention of oxidative damage to the heart. Diabetes causes a significant systemic oxidative stress and also often is accompanied by zinc deficiency that increases the susceptibility of the heart to oxidative damage [98]. Therefore, there is a strong rationale to consider the strategy of zinc supplementation to prevent or delay diabetic complications [98].

On the other hand, high zinc levels have been also positively associated with MetS incidence [22]. A hypothesis about this epidemiological association of serum zinc and MetS is that could reflect less healthy eating habits such as high red meat consumption [22].

Fatty acids and metabolic syndrome

Regarding fatty acids, this part of the article has been focused on the most consumed foods in the Mediterranean region. Thus, fatty acids considered in this section have been fatty acids from fish, fish oil, nuts and olive oil consumption, excluding other types of vegetal fats.

Fish and fish oils

During the last century increasing evidences have suggested that the type of fat is more important than the amount of fat. A number of studies have clearly evidenced the nutritional benefits of fish consumption on several CVD [100]. It has been described that consumption of long-chain \( \omega_3 \)-FA from marine sources may improve certain MetS features, and thus may reduce risk for CVD [101]. Although bioavailability of the fatty acids is appreciably higher when ingested through fish, numerous studies have found advantages of using fish oil capsules or standardised preparations for long-lasting treatments [48]. As a consequence over the years, products enriched in \( \omega_3 \) long chain polyunsaturated fatty acid (PUFA) or fish oil capsules have been used for the prevention and treatment of coronary diseases [48].

In this sense, a retrospective study evaluated the effect of the long-term PUFA supplementation in 111 hypertriglyceridemic subjects with untreated normal-high blood pressure. Patients were prescribed to consume 2 g PUFA supplementation for 12 months in order to improve their plasma lipid pattern. After the treatment, results showed that PUFA long-term supplementation was associated with a significant reduction in systolic and diastolic blood pressure [102]. Several authors have suggested that the protective effect that these fatty acids produce against coronary heart disease is partly mediated by its effect decreasing blood pressure [102,103]. Also, the benefits could be likely mediated through the activity of transcription factors relating to expression of genes involved in lipid oxidation and synthesis.

Weight loss programs promoting fatty fish intake have shown increased benefits on lipid profile, blood pressure and insulin levels [48,100,102]. These health benefits were previously showed by Mori et al. [104], who found that a daily fish meal as part of a weight-reducing regimen was more effective than either measure alone at reducing leptin, insulin levels, as well as blood pressure. A subsequent study showed that three servings per week of fatty fish as part of an energy-restricted diet were enough to specifically improve insulin sensitivity and leptin levels in obese subjects [105]. In the same way, a balanced hypocaloric diet enriched in salmon resulted in a beneficial effect on the plasma lipid profile [106]. Likewise, the low prevalence of insulin resistance, metabolic syndrome and diabetes in Alaskan Eskimos compared to American Indians stimulated the need to study if the relatively low blood pressures, low serum triglycerides and high HDL cholesterol levels in Eskimos resulted from \( \omega_3 \)-FA consumption [107,108]. Thus, 447 Norton Sound Eskimos were evaluated and results showed that plasma \( \omega_3 \)-FA concentrations were highly correlated with dietary \( \omega_3 \)-FA and HDL levels and inversely associated with plasma levels of insulin, HOMA-I-IR, triglyceride levels and diastolic blood pressure. In the GOCADAN study [109], long-chain \( \omega_3 \)-FA, from fish and sea mammals, were associated with lower 2-h glucose, insulin and homeostasis model assessment, lower blood pressure, serum triglycerides and higher high-density lipoprotein cholesterol. On the other hand, saturated fat as well as \( \omega_3 \)-FA consumption was associated with higher triglyceride levels and blood pressure. In spite of increased intakes of fatty fish or supplements of \( \omega_3 \) marine FA could play a role on insulin sensitivity, it is a highly controversial issue [100,110]. Indeed, there are also several investigations where fish oil supplementation or fatty fish consumption did not change insulin levels. Thus, in a long-term study, diets enriched in SFA or MUFAs were compared [111]. Additionally, each diet was supplemented with fish oil or olive oil (placebo). Findings showed significant differences in insulin sensitivity when consuming SFA and MUFA diets. However, fish oil supplementation did not modify insulin sensitivity. Moreover, favourable effects of MUFA were only seen at a total fat intake below median (37E%), suggesting a maximum limit at which the quality of fat may involve benefits [111].

Currently, the recommendation of the Nutrition Committee of the American Heart Association specifies that patients without documented coronary heart disease should eat oily fish twice weekly. Patients with documented coronary heart disease should consume about 1 g EPA + DHA daily, preferably from oily fish, although supplements may be used, and individuals with hypertriglyceridaemia may be advised to receive 2–4 g EPA + DHA daily from capsules [112].

On the other hand, although more attention has been paid to \( \omega_3 \)-FAs, there are also evidences that not only the
fatty acid content of the fish is important, but also other nutrients in fish may influence on CVD. In this sense, Erkkilä et al. found that the intake of lean fish at least four times per week could reduce blood pressure levels in coronary heart disease patients [113]. Likewise, there are also some evidences that suggest benefits on body weight [114,115]. In young, overweight men, the inclusion of either lean or fatty fish, or fish oil as part of an energy-restricted diet resulted in approximately 1 kg more weight loss after 4 weeks, than did a similar diet without seafood or supplement of marine origin [114].

In this sense, although more and longer-term studies are needed, fish and fatty acids should be considered as part of an effective strategy in the treatment of cardiovascular diseases and metabolic syndrome.

Olive oil

Olive oil is considered a functional food, which besides having a high level of MUFA, the oleic acid, contains multiple minor components with potential biological properties [116]. In this context, scientific evidence has been accumulated in the last 2 decades about the beneficial role of diets with a relatively high MUFA content on cardiovascular risk factors, obesity, and DM [117]. These beneficial MUFAs are provided by the traditional Mediterranean food pattern and, specifically, by olive oil and most nuts [118].

When SFA is replaced by MUFA in the diet, two important effects are the decrease in LDL-c and maintaining the HDL-c at a higher level rather than SFA when is substituted by PUFA or carbohydrates [116]. In LDL-c particles rich in oleate have been shown to be less susceptible to oxidation than rich in linoleate. Moreover, olive oil-rich diets increase the LDL-c particle size more than carbohydrate-rich diets, being this effect influenced by the apo E genotypes [116]. Thus, a high-MUFA diet, such as a classical Mediterranean food pattern, may be a better substitute than the low-fat, high-carbohydrate diet for a Westernized diet that is rich in SFA, considering the improving in the HDL-c levels and inhibition in the LDL-c oxidation.

In addition, a moderate-fat diet rich in MUFA represents for some people a considerably more palatable alternative than low-fat approaches for promoting healthy eating and weight loss in the diabetics and obese individuals, thus making easier the adherence and the long-term compliance of participants [118]. The mechanisms of the improved glycaemic control associated with a high-MUFA diet remain undefined. There is some evidence that a proportion of total dietary fat in excess of 40% worsens insulin sensitivity, particularly when the diet includes high saturated fat [117]. Olive oil also contains hundreds of non-fat components with great biological potential, including: (i) polyphenolic compounds such as phenolic acids (e.g., 4-hydroxybenzoic acid, protocatechuic acid, gallic acid, etc.), tyrosol, hydroxytyrosol and derivatives; lignans and flavonoids (e.g., apigenin, luteolin, quercetin); (ii) chlorophyll and derivatives; (iii) hydrocarbon (squalene); (iv) carotenoids (e.g., β-carotene, lutein, neoxanthin) and; (v) tocochromanols (α-, β-, γ- and δ-) [119].

The content of the minor components of an olive oil varies, depending on the cultivar, climate, ripeness of the olives at harvesting, and the processing system employed to produce the types of olive oil [119]. In this context, the EUROLIVE study demonstrated that the consumption of medium- and high-phenolic content olive oil (25 mL/day) decreased lipid oxidative damage biomarkers such as plasma oxidized LDL-c, uninduced conjugated dienes, and hydroxy fatty acids, besides to increase HDL-c. This improvement in the lipid oxidative damage was linear with the phenolic content of the olive oil consumed, providing a relevant evidence that olive oil is more than a MUFA fat [120]. MUFA intake could be associated with an increased sensitivity to insulin, producing a reduction in blood pressure. However, the most accepted explanation is that other components of olive oil, such as the mentioned phenolics compounds could be associated with lower blood pressure and a reduced risk of hypertension.

Nuts

At the same time, nuts have been considered of interest since provide many bioactive compounds that may benefit metabolic syndrome components [121,122]. Several studies have investigated the possible effect of nut consumption on healthy humans, and patients with hypercholesterolaemia or high cardiovascular risk, which are often contradictory. In a randomized, parallel-group, 12-week feeding trial, 50 patients with MetS were given recommendations for a healthy diet with (Nut diet) or without (Control diet) supplementation with 30 g/day of raw nuts (15 g walnuts, 7.5 g almonds and 7.5 g hazelnuts). At the end of intervention, only people without supplementation reported a significant reduction in LDL-cholesterol. On the other hand, patients with daily nut consumption showed an insulin and HOMA-insulin resistance decrease [122]. A meta-analysis concerning several randomized trials suggested that almond consumption ranging from 25 to 168 g/day may decrease total cholesterol without changes on LDL or HDL cholesterol, triglycerides, or the LDL:HDL ratio [123]. Epidemiological studies suggest that frequent nut consumption is associated with a significant lower cardiovascular disease risk [124]. Likewise, different trials have consistently shown an association between nut consumption and reduced risk of CVD as well as an improvement in serum lipid and lipoprotein profiles [125], thus, the American Heart Association has recommended nut consumption since 2000 [126]. Particularly, nuts are high in unsaturated FA, especially oleic acid (MUFA) and linoleic acid (PUFA), which can vary their content according to types of nuts. Actually, several intervention studies have found a cholesterol-lowering effect in diets supplemented with walnuts, macadamia nuts, pecans, pistachio nuts, peanuts and almonds [127]. However, the decreased risk of CVD associated with nut consumption is not solely related to the FA profile, but may be due in part to the presence of other bioactive components (arginine, fibre, copper and magnesium). In addition, they also supply significant amounts of tocopherols, squalene and phytosterols that are relevant compounds with antioxidant properties.

Although the beneficial effects of nuts consumption on metabolic syndrome features are recognized, there is a continued concern that an increase in consumption of this
energy-dense, high-fat foods will lead to excessive weight gain. In this context, an evaluation of SUN cohort found that participants who ate nuts two or more times per week had a significantly lower risk of weight gain than those who never or almost never ate nuts, after adjusting for age, sex, smoking, leisure time physical activity, and other known risk factors for obesity [125].

Conclusions

The dietary treatment of the metabolic syndrome has achieved beneficial effects on specific metabolic features such as plasma lipids, blood pressure and plasma glucose. Indeed, a number of cross-sectional, epidemiological studies, prospective cohort studies, randomized intervention trials on human or research in animals have evidenced that substituting dietary saturated fat for MUFA improves insulin sensitivity (KANWU study) [111], that tocopherol supplementation influences the incidence of type 2 diabetes (ATBC study) [26], that weight loss and cardiovascular risk reduction based on nutrition induced healthy benefits in patients with metabolic syndrome (DPP) [128], that the adherence to the Mediterranean diet improves metabolic syndrome features (PREDIMED) [21] as well as the DASH eating pattern [129] or ARIC study [80]. The Finish Diabetes Prevention study also evidenced reduction in diabetes risk due to nutrition and lifestyle changes [130].

Interestingly, these healthy effects are often improved when specific foods are included in the nutritional treatment of the metabolic syndrome. Thus, it is evident that the inclusion of fruits, vegetables and legumes increases the consumption of fibre, antioxidants, low glycaemic index carbohydrates and minerals that produce a crucial effect on some metabolic syndrome manifestations by inducing blood pressure regulation, plasma lipid decrease and an insulin resistance improvement. In this sense, legumes consumption may contribute to the adherence to dietary recommendations due to their satiety capacity, which assures a success weight loss program. Fatty fish and nuts consumption also are important components of a nutritional treatment, increasing the ω3 fatty acids intake, which is related with the blood pressure regulation, blood lipids improvements and an insulin resistance decrease. Low-fat dairy products should be also considered in a dietary treatment, given that its consumption increase calcium content, which could produce important effects favouring weight loss and maintaining bone health. In addition, olive oil is one of the most important mono-unsaturated fatty acid sources, strongly related with improvements in insulin resistance and low plasma cholesterol concentrations, so, this type of fat could accompany most important meals.

In summary, a reduction in the daily energy intake is part of the dietary treatment in those subjects with metabolic syndrome, but increasing the consumption of all these natural foods in this treatment, the benefits could be increased, favouring the improvement of the metabolic syndrome features. There is sufficient evidence to recommend a diet rich in a variety of fruits, vegetables, whole grains, legumes, fish, oils, dairy product and nuts, for an improvement in the adverse MetS features.

References


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[125] Marques M, Parra D, Kiely M, Bandarra N, Thorsdottir I, Martinez JA. [Omega-3 fatty acids inclusion as part of an energy restricted diet to improve the effect on blood lipids]. Med Clin (Barc) 2008;130:10–2.


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