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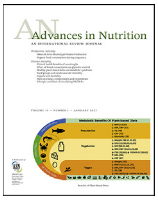

Review

Healthy plant-based diets improve dyslipidemias, insulin resistance, and inflammation in metabolic syndrome. A narrative review

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ABSTRACT

Plant-based diets (PBDs) have become very popular in recent years and have been identified as a dietary strategy associated with protection against chronic disease. However, the classifications of PBDs vary depending on the type of diet. Some PBDs have been recognized as healthful for their high content of vitamins, minerals, antioxidants, and fiber, or unhealthful if they are high in simple sugars and saturated fat. Depending on this classification, the type of PBD impacts its protective effects against disease dramatically. Metabolic syndrome (MetS), characterized by the presence of high plasma triglycerides and low HDL cholesterol, impaired glucose metabolism, elevated blood pressure, and increased concentrations of inflammatory biomarkers, also increases the risk for heart disease and diabetes. Thus, healthful plant-based diets could be considered favorable for individuals having MetS. The different types of plant-based diets (vegan, lacto-vegetarian, lacto-ovo-vegetarian, or pescatarian) are discussed with a focus on specific effects of dietary components in maintaining a healthy weight, protecting against dyslipidemias, insulin resistance, hypertension, and low-grade inflammation.

Keywords: Healthy plant-based diets, metabolic syndrome, dyslipidemia, insulin resistance, hypertension, waist circumference, inflammation

Statement of significance

This review evaluates the effects of different types of plant-based diets with a focus on being healthy in the parameters of metabolic syndrome. There is very little information on this topic as a narrative review. In addition, we are focusing on the last 10 y.

Introduction

There is an increased interest in the use of plant-based diets (PBDs) for various reasons, including the fact that they are more environmentally friendly, cause less pollution, and tend to protect our natural resources [1]. In addition, they provide multiple health benefits for the whole body and the brain [2].

Plant-based diets are considered the healthiest and the most popular trend in the US. They are nutrient-dense, rich in fiber, phytochemicals, and micronutrients, and low in calories and saturated fat [3]. The phytochemicals and fiber content in plant foods improve immune function and positively influence cardiometabolic function, promoting health. When appropriately administered, PBDs are healthful, with adequate nutrition for all age groups [3].

It is well-recognized that PBDs are associated with a lower risk of chronic diseases, including heart disease and diabetes [4,5]. However, diet quality can vary extensively depending on the concentration of antioxidants, fiber, vitamins, and minerals. Therefore, the quality of a plant-based diet is directly associated

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Abbreviations: ALA, alpha-linoleic acid; DBP, diastolic blood pressure; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FBG, fasting blood glucose; hPBD, healthful plant-based diet; hPVG, healthful provegetarian; HOMA, homeostatic model assessment; IR, insulin resistance; MCP-1, monocyte chemoattractant protein 1; MetS, metabolic syndrome; PBDs, plant-based diets; PON1, paraoxonase-1; SBP, systolic blood pressure; TC, total cholesterol; T2D, type 2 diabetes; TGF-β1, transforming growth factor-beta 1; TG, triglycerides; uPBD, unhealthful plant-based diet; ω-3, Omega 3; WC, waist circumference; uPVD, unhealthful provegetarian; WBC, white blood cells.

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with its ability to reduce the risk of chronic disease. A classification of PBD exists based on the dietary components that promote health compared with those that increase the risk for chronic disease [6,7]. Satija et al. [8] established an index method to classify PBDs into healthy and unhealthy index, leading to the nomenclature of healthful plant-based diets (hPBDs) and unhealthful plant-based diets (uPBDs) that are currently used by investigators in this area of research.

If PBDs are not well monitored, increased carbohydrate intake and foods rich in added sugars may displace more nutrient-dense foods, thus leading to both overfed and undernourished people, resulting in unhealthy weight loss or abdominal obesity [9]. Additionally, it is vital to have adequate amounts of protein, iron, calcium, and reliable sources of vitamin B-12 as fortified foods or supplements for optimal health while following PBD. About 50% of individuals with PBD are not consuming healthful diets and may not benefit from chronic disease risk reduction [3].

Plant-based diets are classified into 6 categories: vegan, raw vegan, vegetarian, lacto-vegetarian, ovo-vegetarian, and lacto-ovo-vegetarian [10]. A vegan diet abstains from all types of animal products [11]. Vegetarian diets are characterized by not having any animal products, including meat, poultry, fish, and seafood [12]. Lacto-vegetarian means the inclusion of dairy products, ovo-vegetarian refers to the inclusion of eggs in the diet, and raw vegan includes raw products with an average of 75%–85% raw food [10]. Other definitions of PBD are pescatarian diets that include the consumption of fish [1], and flexitarian is a semi-vegetarian diet in which animal products are limited to a few portions per week [13]. This review focuses on vegan, vegetarian (including ovo- and lacto-vegetarian), and pescatarian diets.

Metabolic syndrome (MetS), characterized by central obesity, dyslipidemias, insulin resistance, hypertension, and low-grade inflammation [14], significantly increases the risk for heart disease and diabetes. Most of the biomarkers of the disease can be stabilized with healthy diets, and several dietary strategies have been reviewed for patients with MetS [15]. Although one study reported that unhealthful plant-based diets rich in simple carbohydrates and salt are inversely related to the incidence of MetS [16]. The contribution of healthy plant-based diets in reversing dyslipidemia, insulin resistance, and inflammation associated with MetS has yet to be evaluated in detail.

The American Heart Association [17] and the American Diabetes Association [18] provide dietary guidelines for healthy eating. However, additional information related to dietary patterns such as PBD is needed, specifically for those individuals with metabolic disorders, including insulin resistance (IR), hypertension, obesity, and dyslipidemias. The purpose of this review is to summarize the positive effects of PBD on the MetS biomarkers in studies from the last 10 y, including inflammatory markers in individuals with MetS, to expand the current information on appropriate dietary regimes for those individuals who are at risk for heart disease and diabetes.

Beneficial Effects of Plant-Based Diets

CVD is the leading cause of mortality, attributing to one in 3 deaths globally [19]. The high prevalence of heart disease has been linked to lifestyle factors such as smoking, western diets high in animal fat, added sugars, and refined foods, and a lack of exercise [20]. A low-fat, vegetarian diet is the exclusive dietary pattern showing cessation and reversing atherosclerotic plaque in clinical trials when combined with exercise and stress management [20]. Vegetarian diets are associated with a reduced risk for CVD, ischemic heart disease, and cerebrovascular diseases [20]. Risk factors associated with heart disease are also less frequent among those following vegetarian diets [11,21]. Plant-based diets are cardioprotective as they are low in saturated fat and consist of advanced glycation end products, nitrosamines, and heme iron, commonly seen in meat products.

Plant-based diets may effectively reduce cardiometabolic risk factors, thereby preventing MetS [22]. The cross-sectional analysis of the Primary Prevention of Cardiovascular Disease with a Mediterranean diet (PREDIMED)-Plus study suggests that higher adherence to a healthful provegetarian food pattern (hPVG) was associated with lower cardiovascular risk when compared to an unhealthful provegetarian food pattern (uPVG) in MetS participants, as measured by the MetS z-score [23]. By affecting the individual components of MetS criteria, PBD may help attenuate the progression of MetS patients. When untreated, MetS raises the chance of developing type 2 diabetes (T2D) by 5 times and has twice the risk of developing CVD in the future. A meta-analysis of 7 randomized controlled trials and 32 observational studies concluded that vegetarian diets caused lower systolic (SBP) and diastolic blood pressure (DBP) when compared to omnivorous diets [24]. However, clinical trials in MetS providing similar results are scarce.

Effects of different types of PBDs on the parameters of MetS

In the following paragraphs, a comparison of different types of plant-based diets and their effectiveness in improving the biomarkers of MetS is reviewed.

Vegan diets and parameters of metabolic syndrome

Intervention studies among Seventh-day Adventists, a large cohort following vegetarianism, have shown lower concentrations of plasma triglycerides (TG), total cholesterol (TC), and LDL-cholesterol (LDL-C), plasma glucose, waist circumference (WC), and body mass index (BMI) but no effect on HDL cholesterol (HDL-C) [25]. Similarly, a study on an adult Indian population showed that vegans have a lower prevalence of T2D and obesity than omnivores [26]. This beneficial effect may be due to the presence of the phytonutrients of plant origin and the absence of animal fats, in addition to the increased consumption of low glycemic index foods. Data from a randomized controlled clinical trial in overweight adults suggest that increasing low-fat plant foods and minimizing high-fat and animal foods are associated with decreased body weight and fat loss and that a low-fat vegan diet can improve measures of diet quality and metabolic health [27]. Different protein concentrations fed to mice were used to determine improvement in MetS parameters [28]. Investigators concluded that low protein, a characteristic of vegan diets, was more effective in lowering plasma TG and glucose concentrations, 2 main components of MetS [28]. However, one drawback of vegan diets, as indicated above, is that they have been shown to lower HDL-C, which is one of the biomarkers of MetS [25].

Vegetarian diets (including ovo- and lacto-) and parameters of metabolic syndrome

In a cross-sectional study involving 146 omnivorous or vegetarian adults (18–65 y; self-reported diet adherence ≥6 mo), health biomarkers were identical between the groups matched for age, gender, and adiposity [29]. However, when regrouped by low versus high diet quality, the biomarkers differed significantly between groups for fasting insulin, HOMA (homeostatic model assessment)-IR, and TG/HDL-C ratio, with more favorable effects in the group with high diet quality scores, suggesting that diet quality attributes are more closely associated with health biomarkers than plant-based diet categories.

In a case-controlled study of female vegetarians (80% lacto-ovo-vegetarians), participants were associated with a reduced risk of developing MetS and IR [30]. The effect of vegetarianism on Taiwanese Buddhist vegetarian females in multivariate linear regression analyses was associated with a lower body mass index, smaller waist circumference with reduced risk for central obesity, and lower TC, LDL-C, and HDL-C (30). Despite having lower HDL-C, these vegetarians had significantly lower TC/HDL-C and LDL-C/HDL-C ratios [30]. The Tzu Chi Health study used a cohort of 6000 Taiwanese adults and compared the effects of insulin sensitivity in vegetarians to omnivores [31]. Vegetarians had a lower prevalence of diabetes when compared to omnivores, although the omnivores consumed a limited quantity of meat and fish, illustrating the contribution of meat to the development of IR [31].

In a matched cohort, cross-sectional and longitudinal study comparing the metabolic profiles of vegetarians with non-vegetarians, the authors observed lower values for WC, BMI, SBP, DBP, fasting blood glucose (FBG), TC, HDL-C, and LDL-C, along with lower TC/HDL-C ratios [32]. For the cross-sectional comparisons, all sub-types of vegetarians reduced each of the biomarkers compared with nonvegetarians, except for HDL-C and TG. The beneficial effects on the metabolic profiles of vegetarians were partially attributed to their lower BMI, which can be considered a confounding variable. The authors suggested that with proper management of TG and HDL-C, along with caution on maintaining a healthy plant diet index (hPDI) by reducing the intake of refined carbohydrates and fructose, a PBD may benefit all aspects of the biomarkers of disease [32].

A randomized controlled cross-over intervention in 24 habitual omnivores with MetS following a lacto-ovo-vegetarian diet and consuming 2 whole eggs with spinach daily for breakfast for 4 wk demonstrated that combining whole eggs with a PBD resulted in a protective effect for MetS participants [33]. Compared to an equivalent amount of egg substitute, whole egg intake resulted in a significant reduction in body weight and BMI, with increases in plasma HDL-C choline and zeaxanthin. Following a plant-based diet for 13 wk, this intervention highlighted the influence of diet quality on the health effects associated with PBD in MetS [6]. At baseline, when on a lacto-vegetarian diet, hPDI was inversely associated with weight ($r = -0.445$, $P < 0.05$), and unhealthy plant diet index (uPDI) was positively associated with weight ($r = 0.437$, $P < 0.05$). Follow-up data after 9 wk showed that HDL-C was positively associated with hPDI ($r = 0.411$, $P < 0.05$) and negatively associated with uPDI ($r = -0.411$, $P < 0.05$).

Mediterranean diet, Nordic diet, and parameters of MetS

Adherence to the Mediterranean diet is associated with better blood lipid profiles and reduced risk for MetS [34]. The Mediterranean is characterized by regular consumption of olive oil as the main source of added fat and plant-based foods, including whole grains, vegetables, legumes, fresh fruits, nuts and seeds, moderate amounts of fish, seafood, dairy and poultry, and low consumption of red and processed meat [35].

Oxidative stress is increased in the case of MetS due to dyslipidemia and insulin resistance. One way the Mediterranean diet protects against lipid peroxidation and oxidative stress is by increasing the activity of paraoxonase1 (PON1), a well-recognized antioxidant transported by HDL [36]. It has also been shown that PON1 has a role in preventing microvascular complications due to oxidative stress in individuals with MetS [36,37].

When low-calorie vegetarian and Mediterranean diets were compared in their efficiency in improving MetS profiles, both diets effectively reduced body weight, BMI, and fat mass, with no significant differences between diets. However, a low-fat vegetarian diet was more effective in lowering LDL-C concentrations, whereas the Mediterranean diet was more effective in reducing plasma TG concentrations [38]. Like the Mediterranean diet, a healthy Nordic diet (healthy pescatarian diet) improves the lipid profile and beneficially affects low-grade inflammation in MetS [39]. This diet focuses on seasonal plant-based whole foods (≥300 g/wk, including ≥200 g/wk fatty fish), whole-grain products, berries, fruits, vegetables, rapeseed oil, and low-fat dairy products), typically found in Nordic regions like Norway, Denmark, and Iceland. In contrast, greater adherence to diets consisting of a high intake of refined carbohydrates, sugars, and salty foods in PBD, that is, higher adherence to an unhealthful plant-based diet is associated with an increased risk of MetS [39]. These studies suggest that considering the quality of plant foods is critical for preventing MetS in a population that habitually consumes plant-based foods.

Plant-based diets index

There are, however, some discrepancies related to the effects of PBDs and MetS. A cross-sectional study of 270 Iranian adults with MetS showed that adherence to hPDI was associated with significantly better anthropometric measures such as a lower BMI, body weight, and WC (40). In this study, there was no significant relationship between the plant-based diet index (PDI) and the risk of obesity, hypertension, and dyslipidemia to confirm the relationship between PDI and MetS in this population group [40]. A similar cross-sectional investigation of 178 Iranian older adults showed that plant-based diets were not significantly associated with the risk of MetS [41]. There were no significant differences between the PDI, the hPDI, and uPDI for this population. The MASALA (Metabolic Syndrome and Atherosclerosis in South Asians Living in America) study compared the dietary pattern of South Asians living in the US, classifying 150 participants into 2 principal patterns: vegetarian ($n = 91$) and Western diet ($n = 59$) [42]. The vegetarian pattern was associated with lower fasting glucose, HOMA-IR, and HDL-C than the Western diet. This study suggests that both dietary patterns were associated with detrimental metabolic changes. Thus, healthful diet choices rather than dietary patterns may assist Asian Indians in maintaining lower levels of risk factors for CVD.

In contrast to the previous studies, an open prospective, population-based, longitudinal study using data from the China Health and Nutrition Survey (CHNS) suggests that adherence

Table 1

Positive effects of different types of plant-based diets on parameters of the metabolic syndrome. The type of study, the participants, the characteristics of the evaluated diet, the metabolic parameters, and the main results are presented[1]

Study Design/ Duration	Participants	Evaluation of Diets	Metabolic Parameters	Results	Ref
Prospective cohort, median follow-up 6 y	5646 (men and women) aged 40–60 y.	FFQ 4 plant-based diet indexes PDI, h-PDI, uPDI, and provegetarian index.	TG, HDL, FBG, BP, and WC.	The highest vs. lowest quintile of uPDI had a 50% higher risk of developing MetS after adjusting for demographic and lifestyle factors.	[16]
Cross-sectional matched cohort study	4415 lacto-ovo-vegetarians, 1855 lacto-vegetarians, and 1913 vegans; each vegetarian was compared with 5 nonvegetarians based on age, sex, and study site.	FFQ Questionnaire to classify participants into vegan, lacto-vegetarian, lacto-ovo-vegetarian, and omnivore.	WC, BMI, SBP, DPB, FBG, HDL, LDL, and TG.	After adjusting for confounding variables, vegetarians had lower WC, BMI, SBP, DPB, FBG, TC, and LDL-C. Each additional year of the vegan diet lowered the risk of obesity by 7%. Lacto-vegetarian diet reduced the risk of elevated SBP by 8% and elevated glucose by 7%.	[32]
Intervention Randomized cross-over	24 Participants with metabolic syndrome.	Lacto-ovo-vegetarian compared to a lacto-vegetarian.	Parameters of metabolic syndrome and body weight.	Lacto-ovo vegetarianism resulted in lower BMI and body weight and higher HDL-C.	[33]
Cross-sectional	6439 participants of the PREDIMED Plus study.	FFQ General Prove-vegetarian (gPVG), healthful (hPVG), and unhealthful (uPVG).	BMI, SBP, DBP, HDL-C, TG and FBG.	A higher adherence to the gPVH and hPVG was associated with lower cardiometabolic risk in multivariate models.	[23]
Cross-sectional	29 with MetS.	3-d food records. PBD and quintiles for h-PBD and U-PBD.	TG, HDL-C, FBG, BP, and WC.	At baseline, hPDI was inversely associated with weight, and uPDI and positively associated with weight. Using follow-up data, HDL-c was positively associated with hPDI and negatively associated with uPDI.	[6]
Cross-sectional case-control study	391 female vegetarians (compared with age-matched 315 female omnivores).	VEG status was determined from a self-reported questionnaire. Among the 391 vegetarians, 22 were pure vegetarians (5.6%), 20 were ovo-vegetarians (5.1%), and 33 were lacto-vegetarians.	TG, HDL, FBG, BP (systolic only), WC, BMI, smaller WC, lower concentrations of FBG, TC, LDL-C, and HDL-C compared to non-VEG female vegetarians were associated with	The VEG group was associated with lower BMI.	[30]

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Table 1 (*continued*)

Study Design/ Duration	Participants	Evaluation of Diets	Metabolic Parameters	Results	Ref
			reduced risk for MetS and IR.		
Cross-sectional	91 vegetarians compared to 50 omnivores (Western diet)	FFQ, Food group intake was collected with the Study of Health Assessment and Risk in Ethnic (SHARE) groups.	WC, TG, LFL, and FBG	Compared with the Western diet, the vegetarian diet was associated with lower HOMA-IR and HDL.	[42]

[1] DBP, diastolic blood pressure; FBG, fasting blood glucose; FFQ, food frequency questionnaire; gPVG, generally provegetarian; hPDI, healthy plant diet index; hPVG, healthful provegetarian; HOMA-IR, homeostatic model assessment for insulin resistance; PBD, plant-based diets; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; T2D, type 2 diabetes; uPDI, unhealthy plant dietary index; uPVG, unhealthful provegetarian; VEG, vegetarian; WC, waist circumference.

to an overall PD helps in reducing the risk of metabolic diseases such as T2D, obesity, and hypertension in Chinese adults who habitually consume plant-based foods, especially for those aged <55 y [43]. Furthermore, this study [43] points out that a PBD for a longer duration is more important than diet indices, which is in contrast to other observations in most reviewed studies [29–31,41,42]. Table 1 presents the beneficial effects of different types of PBDs on the parameters of metabolic syndrome.

Nutrients associated with beneficial effects of PBD on parameters of the metabolic syndrome

As mentioned earlier, PBDs include nutrients such as dietary fiber, polyphenols, carotenoids, and flavonoids, derived primarily from whole grains, fruits, and vegetables, as well as omega-3 (ω-3) fatty acids in the pescatarian diet. Some of these nutrients that promote cardioprotective effects and improve the biomarkers of MetS are described below:

- **Dietary fiber:** Dietary fiber has been shown to decrease plasma cholesterol by binding to bile acids and dietary cholesterol in the intestinal lumen, resulting in reduced cholesterol absorption [44]. Further, the loss of bile acids results in a compensatory mechanism by which bile acids are formed from hepatic cholesterol. The decrease in cholesterol results in the upregulation of the LDL receptor and the removal of LDL from plasma [45]. Dietary fiber has also been shown to decrease body weight, BMI, and WC [46] by providing a sensation of fullness and reducing caloric consumption. A meta-analysis of 21 controlled clinical trials demonstrated a significant reduction in body weight ($P = 0.03$) in those diets where pulses, high in dietary fiber, were used to replace other foods [47].
- ω-3 Fatty acids: The plant-derived ω-3 fatty acid, alpha-linolenic acid (ALA), is readily available from plant sources such as green leafy vegetables, walnuts, chia seed, flaxseed, and vegetable oils, including flaxseed, soybean, and canola

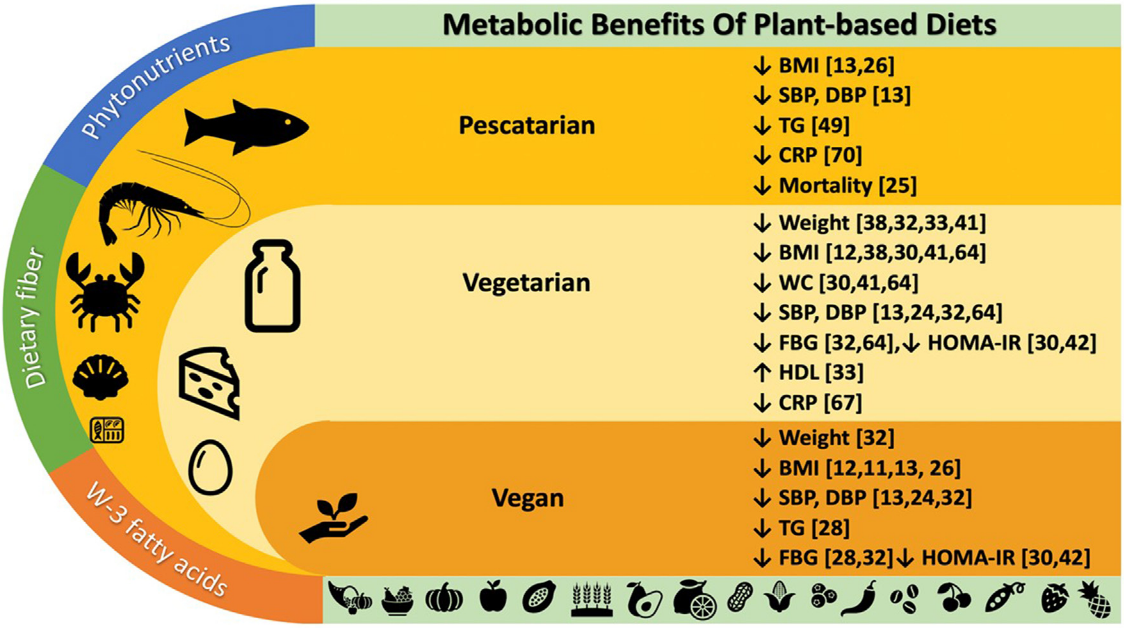

Fig. 1. Benefits of different plant-based diets: vegan, vegetarian (may include dairy and eggs), and pescatarian on the parameters of metabolic syndrome and inflammatory markers. The number in brackets is the corresponding reference. Abbreviations used: BMI, body mass index; CRP, C reactive protein; DBP, diastolic blood pressure; FBG, fasting blood glucose; IR, insulin resistance; SBP, systolic blood pressure; TG, triglycerides

oils. Alpha-linolenic acid is an essential omega-3 fatty acid metabolized to eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA). However, the effectiveness of converting alpha-linolenic to EPA and DHA appears to be unreliable and restricted, with severely restricted conversion in the case of DHA [48]. Therefore, fish oils are rich in EPA and DHA fatty acids, and fish has been demonstrated to possess cardioprotective and hypotriglyceridemic properties [49]. Dietary supplementation of ω-3 fatty acids may improve obesity-induced metabolic syndrome features, including insulin resistance, hypertension, and dyslipidemia, by lowering plasma triglycerides [50,51].

- **Polyphenols:** Healthy PBDs include a high intake of polyphenol-rich foods such as nuts, fruits, vegetables, spices, and olive oil, to mention a few. They may prevent the development and progression of MetS by lowering body weight, blood pressure, and plasma glucose and improving abnormal lipid metabolism [22,52].
- **Flavonoids:** Consumption of dietary flavonoids are associated with reduced risk for MetS. Isoflavones, present in soy, have anti-inflammatory properties and potentially protect against MetS by preventing the onset of hypertension, hyperglycemia, dyslipidemia, and arteriosclerosis [53]. A recent systemic review and meta-analysis demonstrated that dietary intake of soy products effectively improves the lipid profiles and glycemic parameters in MetS [54]. The isoflavones genistein and daidzein may improve cardiovascular health by increasing LDL oxidation resistance and inhibiting thrombus formation [55].
- **Carotenoids**: Dietary carotenoids are potent antioxidant nutrients that can alter the composition of lipoproteins, affecting the components of MetS. A systematic review and meta-analysis in middle-aged and older men evaluated the link between vitamin A and carotenoids and metabolic syndrome [56]. The authors reported a lower prevalence of MetS and reduced serum TG after higher total carotenoid intakes, mainly those of beta-carotene and lycopene [56]. Participants consuming a plant-based diet with 2 eggs (rich in bioavailable lutein and zeaxanthin) per day in combination with spinach as an omelet for breakfast have shown increases in plasma HDL-C [33]. Observational and interventional studies suggest that the intake of lutein and zeaxanthin is positively correlated with serum HDL-C but negatively correlated with serum LDL-C and TG [57,58]. Similarly, dietary lycopene may provide a protective role by its association with the individual parameters of MetS [59].

The Fig. 1 represents a summary of the nutrients involved in decreasing the MetS parameters.

PBD: Effects on Inflammation

Elevated WC is one of the features of MetS, and central obesity is a marker of low-grade systemic inflammation. People diagnosed with MetS commonly present low-grade systemic inflammation. The effect of diet on inflammation may differ between average weight and obese individuals with an unhealthy metabolic profile [60]. Data on how PBD specifically plays a role in inflammation for MetS-diagnosed individuals is less studied than the effects of PBD on the key parameters of MetS, such as dyslipidemia, glucose metabolism, and WC. The current literature focuses on how PBD affects the most common inflammatory markers, as discussed below.

The most commonly measured inflammatory markers in people with MetS are C-reactive protein (CRP), interleukin (IL)-6, IL-8, IL-10, IL-17, IL-18, tumor necrosis factor-alpha (TNFα), transforming growth factor-beta 1 (TGF-β1), IL-β1, monocyte chemoattractant protein (MCP)-1, serum amyloid A, and the anti-inflammatory adiponectin. Additionally, ferritin has been measured based on its role in insulin sensitivity and inflammation. Ferritin is found in all body cells but is in high concentrations in marrow macrophages, the spleen, and the liver [61]. It provides intracellular storage of bioavailable iron in a safe and readily accessible form. Ferritin tends to be elevated in people with MetS and correlates with increased hepcidin production and other inflammatory cytokines [61].

It is difficult to determine the effects of a PBD in observational studies, where there could be confounding factors that might not be accounted for including the fact that healthier lifestyle factors are commonly followed by individuals choosing a PBD.

The reviewed studies regarding inflammation and PBDs can be grouped into 2 categories: 1) examining the inflammatory markers and the incidence and/or prevalence of MetS in individuals following a PBD versus an omnivorous diet, and 2) examining individuals with MetS and how following a PBD may ameliorate inflammation, along with the well-studied key features of MetS.

Metabolic syndrome and low-grade inflammation

There is evidence that following a PBD is associated with lower markers of low-grade systemic inflammation and can be protective against developing MetS over time.

Park et al. [62] tested the association between participants' immunity by measuring plasma CRP and white blood cells (WBC) and different dietary patterns, including PBDs (n = 40, 764). A PBD, physical activity, and non-smoking were related to lower WBC counts and CRP. Additionally, those with the lowest plant-based dietary intake were 2 times more likely to develop MetS.

Data from a cross-sectional Brazilian study of overweight individuals showed that omnivores had 6 times higher odds of having MetS than those following a vegetarian diet [63]. There were no differences in CRP between the 2 groups. Increases in liver enzymes can also be considered a biomarker of inflammation and have been shown to be elevated in T2D patients [64]. Slywitch et al. [65] analyzed the association between biochemical markers of inflammation, liver function, IR, and BMI values in vegetarian and omnivore individuals. Vegetarian obese individuals had lower concentrations of gamma-glutamyl transferase, a marker of hepatobiliary disease and oxidative stress, and ferritin than omnivores in this cross-sectional study [65].

PBD, inflammation, and obesity

Results from a meta-analysis of PBDs and its relationship with inflammatory and immune markers showed that consumption of a vegetarian-based dietary pattern was associated with significantly lower CRP, fibrinogen, and leukocyte levels compared with those following a mixed omnivorous non-vegetarian diet [66]. However, the review did not discriminate among hPDB and uPBD nor people with and without MetS [66].

Table 2

Effects of healthful plant-based diets on inflammatory markers in population studies. The study design, duration, participants, characteristics of the evaluated diets, evaluated inflammatory markers, and results are presented[1]

Study Design/ Duration	Participants	Characteristics of the Evaluated Diet	Inflammatory Markers/ Adipokines	Results	Ref
Retrospective Cohort	40,768 adults aged over 40 y	SQFFQ PCA to determine: Korean balanced diet, PBD, Western-style diet & rice-based diet	CRP, WBC. Participants divided in quartiles	In the low PBD intake group, immunity status was associated with 2-fold risk for MetS. No associations in the high PBD group	[62]
Cross-sectional	88 "apparently healthy" men > 35 y.	44 Vegetarian (VEG) & 44 Omnivorous (OMN)	CRP and Framingham Risk score	Percentage of individuals with MetS was higher among OMN than among. No differences in CRP among groups.	[63]
Cross-sectional	1340 adults (422 men] and 918 women) aged 18-60 y.	(1) omnivores (2) semi-vegetarians (3) lacto-ovo-vegetarians and (4) vegans	hs-CRP Ferritin	No differences in CRP among diet groups A higher prevalence of obesity in omnivores when compared to lacto-ovo vegetarians semi-vegetarians and vegans Regardless of sex: vegetarian obese individuals had lower values of GGT and ferritin concentrations than omnivorous individuals	[65]
Cross-sectional	3690 Diabetes-free female participants in the Nurses' Health Study.	FFQ Red meat consumption divided into quartiles.	CRP, ferritin, and adiponectin.	Greater total and unprocessed red meat intakes were significantly associated with higher plasma ferritin concentration after adjustment for demographic, medical history, BMI, and lifestyle variables. BMI accounted for much of the associations of the total, unprocessed, and processed red meat intake with CRP.	[68]
Cross-sectional	240 obese adult women range of 18–48 y. (Mean BMI 30, WC 94 cm)	FFQ PDI, hPDI, and uPDI in quartiles.	hsCRP, IL-1β, and TGF-β.	By increasing the diet based on a healthy plant, the inflammatory factors of hsCRP and TGF decreased significantly.	[69]
Cross-sectional	289 overweight women aged over 18 y. Metabolically healthy and unhealthy phenotype (65).	FFQ Overall PDI and tertiles for h-PBD and uPBD.	CRP, TGF-β1, ILβ1, and MCP-1.	In the crude model, neither inflammatory markers nor phenotypes were associated with the tertiles of PDI, hPDI, or uPD. TGF-β1 had a significant inverse association with hPDI.	[72]

[1] CRP, C-reactive protein; FFQ, food frequency questionnaire; GGT, gamma-glutamyl transferase; hPDI, healthy plant diet index; hPBD, healthful plant-based diet; MCP-1, monocyte chemoattractant protein-1; OMN, omnivorous; PCA, principal component analysis; SQFFQ, semiquantitative food frequency questionnaire; TG, triglycerides; TGF, transforming growth factor; TGF-β1, transforming growth factor β-1; uPBD, unhealthful plant-based diet; VEG, vegans; WBC, white blood cells; WC, waist circumference.

Grosso et al. [67] reviewed the anti-inflammatory effects of nutrients to shed more light on the effect of diet components on inflammation. One example of this approach comes from the Nurses' Health Study data which showed that substituting unprocessed red meat with either fish or nuts and legumes was associated with lower ferritin and CRP in their sample [68]. A cross-sectional study in obese Iranian women also reported that higher hPBD adherence was associated with lower concentrations of CRP and TGF [69]. Similarly, another study using National Health and Nutrition Examination Survey (NHANES) data showed that the association between the Dietary Inflammatory Index and at least one CVD-Risk factor was dose-dependent [70]. This means that those participants in the 3rd and 4th quartile of this inflammatory index were 1.37 (95% CI: 1.11–1.68) and 1.50-fold (95% CI:1.19–1.90) more likely to have at least one CVD-Risk factor [70].

Mohamadi et al. [72] examined the association of hPBD and uPBD in Iranian women categorized into 2 groups: metabolically healthy obese and unhealthy obese phenotypes based on Karelis criteria [71]. The markers CRP, TGF-β1, IL-β1, and MCP-1, were not associated with the diets in the crude model, but researchers reported a significant inverse association between hPBD and TGF-β for the unhealthy metabolic phenotype [72]. A randomized control study was conducted in which participants were randomly assigned to follow a vegan, vegetarian, pesco-vegetarian, semi-vegetarian, or omnivorous diet for 6 mo. Improvements in dietary inflammatory index scores compared to diets containing meat were reported [73]. Other recent studies have also reported a lower CRP by vegetarian diets [74,75].

Table 2 reports recent information on the effects of a PBD on inflammatory markers.

Nutrients associated with beneficial effects of plant-based diets on inflammatory markers

Specific dietary components present in an hPBD can contribute to explaining how these diets can ameliorate low-grade systemic inflammation.

- **Dietary fiber**: hPBD are high in soluble and insoluble fiber. Fiber intake positively alters the microbiota and increases gut barrier function and anti-inflammatory biomarkers [76]. The low energy density of this nutrient is associated with lower BMI, so there is an indirect long-term effect on adiposity that also contributes to modulating the inflammatory response [77].
- **Phytochemicals**: hPBD are high in polyphenols, which are well-known for their anti-inflammatory and antioxidant capacity [78]. These compounds modulate inflammation by different mechanisms, such as inactivating nuclear factor kappa-B and modulating mitogen-activated protein kinase and arachidonic acids pathways [79].
- **ω-3 Fatty acids:** hPBD are high in the ω-3 linolenic and alpha-linoleic acid from vegetable oils such as canola, nuts, seeds, and soybeans and low in saturated fat. Consuming high-fat meals promote endotoxin (e.g., lipopolysaccharide) translocation into the bloodstream, stimulating innate immune cells and leading to a transient postprandial inflammatory response [80]. An increase in plant-derived ALA could potentially contribute to a decrease in inflammation observed in plant-based diets. An RCT to evaluate the effect of a hypo-energetic diet rich in ALA (3.4 g/d) in individuals with MetS showed decreases in CRP [81]. The high ALA intake led to a more pronounced reduction in the serum concentration of YKL-40 compared with the intake of the low-ALA control diet. YKL-40 is an inflammatory glycoprotein involved in endothelial dysfunction [72]. In addition, EPA and DHA contained in fish have shown a consistent effect in reducing inflammatory markers [49,67]. Monounsaturated fatty acids from olive oil and certain nuts can be anti-inflammatory in PBD, particularly by replacing saturated fat intake [82].

A summary of the nutrients that might affect inflammation in the different types of PBD is presented in the Figure.

Limitations

For the most part, in this review, it is clear that the different types of PBD have some benefits to improve the parameters of MetS and reduce inflammation. However, there are mixed results in studies where no significant differences were found in these parameters compared to omnivorous diets. These results were not unexpected, given the complexity related to the metabolic status, the breath of the inflammatory markers used, and the control of confounding factors (diet adherence, microbiota, genotype). Additionally, most of the studies analyzed were observational, preventing controlling for relevant variables. In the context of the COVID-19 pandemic, the potential anti-inflammatory and lipid-lowering effects of hPBD should also be considered as a preventative measure for a better immune reaction when affected with pathogens such as the severe acute respiratory syndrome coronavirus-2 [78].

Conclusions

Regarding the different types of PBDs discussed, we conclude that vegan diets are very effective in lowering body weight and reducing inflammatory markers; however, a consistent decrease in HDL-C is a drawback of these diets. The lack of a more efficient effect of these diets in improving metabolic parameters could be related to the dietary choices of individuals adhering to this dietary pattern. Lacto- and lacto-ovo-vegetarian diets, including dairy and eggs that contain nutrients and antioxidants that improve inflammation and dyslipidemia, appear to provide beneficial effects for MetS. Finally, pescatarian diets associated with decreases in plasma TG and inflammatory markers are another healthy option for PBDs.

Future Directions

Future directions should focus on precision nutrition and its applications to metabolic risk factors and PBDs. For example, caveolin-1 (CAV-1) is the major structural protein of caveolae, and it correlates with insulin resistance and MetS. A recent study evaluated the interactions between caveolin-1 (rs3807992) and PDI on metabolic and inflammatory markers in overweight and obese Iranian women [83]. Researchers have reported a gene-diet interaction between plant-based diets and CAV-1 polymorphism where the AA allele carriers who consumed a PBD with a higher dietary index had lower concentrations of liver enzymes, insulin, MCP-1, and hsCRP compared to GG homozygotes [83]. This suggests that certain genetic polymorphisms can make individuals more sensitive to a PBD. The future of individualized healthy diets is in clarifying the interactions between diet and genetics to have a better understanding of how a healthy PBD can improve the biomarkers of MetS.

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Authors contributions

MLF conceptualized the review, wrote part of the review, and was responsible for the final content. MST created the figure, wrote part of this review, and was responsible for Table 1. MC wrote part of this review and was responsible for the content of Table 2.

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