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Review

Animal vs Plant-Based Meat: A Hearty Debate

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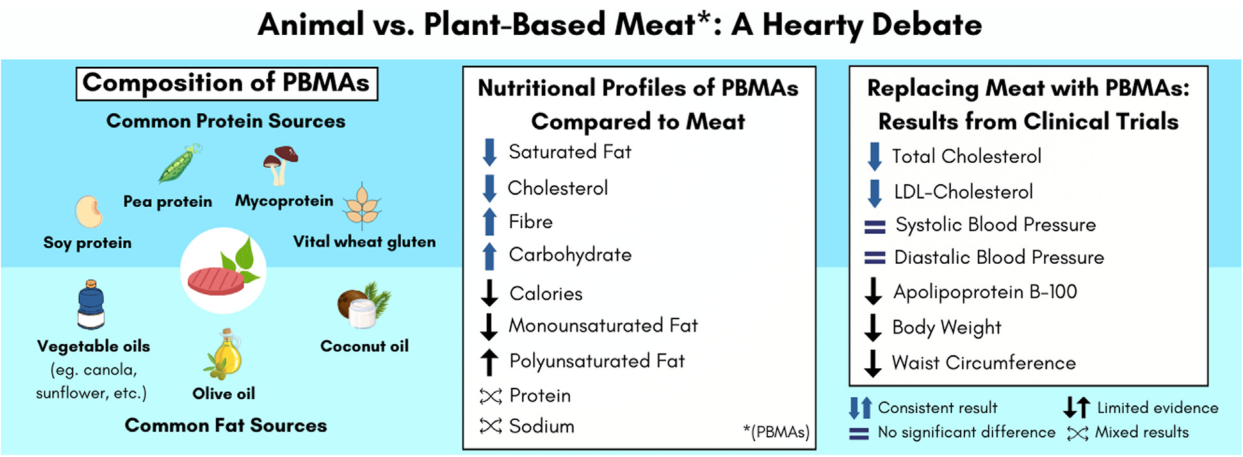
See editorial by Spence, pages 1210-1212 of this issue.



ABSTRACT

Plant-based meat alternatives (PBMAs) are highly processed food products that typically replace meat in the diet. In Canada, the growing demand for PBMAs coincides with public health recommendations to reduce ultra-processed food consumption, which prompts the need to investigate the long-term health implications of PBMAs. This review assesses the available literature on PBMAs and cardiovascular disease (CVD), including an evaluation of their nutritional profile and impact on CVD risk factors. Overall, the nutritional profiles of PBMAs vary considerably but generally align with recommendations for improving cardiovascular health; compared with meat, PBMAs are usually lower in saturated fat and higher in polyunsaturated fat and dietary fibre. Some dietary trials that have replaced meat with PBMAs have reported improvements in CVD risk factors, including total cholesterol, low-density lipoprotein cholesterol, apolipoprotein B-100, and body weight. No currently available evidence suggests that the concerning aspects of PMBAs (eg, food processing and high sodium content) negate the potential cardiovascular benefits. We conclude that replacing meat with PBMAs may be cardioprotective; however, long-

RÉSUMÉ

Les substituts de viande végétaliens sont des aliments hautement transformés qui remplacent habituellement la viande dans l'alimentation. Au Canada, la demande croissante pour ces substituts coïncide avec les recommandations de la santé publique de réduire la consommation d'aliments ultratransformés, d'où le besoin d'étudier les effets à long terme sur la santé associés à la consommation des substituts de viande végétaliens. Cette analyse vise à évaluer la littérature publiée sur les substituts de viande végétaliens et les maladies cardiovasculaires (MCV), et notamment à étudier leur bilan nutritionnel et leur effet sur les facteurs de risque cardiovasculaire. Dans l'ensemble, le bilan nutritionnel des substituts de viande végétaliens varie considérablement, mais correspond généralement aux recommandations visant à améliorer la santé cardiovasculaire. Comparativement à la viande, les substituts de viande végétaliens sont habituellement plus faibles en gras saturés et plus riches en gras polyinsaturés et en fibres alimentaires. Dans certaines études nutritionnelles où l'on a remplacé la viande par des substituts végétaliens, des améliorations ont été observées en ce qui concerne les facteurs de

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term randomised controlled trials and prospective cohort studies that evaluate CVD events (eg, myocardial infarction, stroke) are essential to draw more definitive conclusions.

risque cardiovasculaire, comme le cholestérol total, le cholestérol à lipoprotéines de basse densité (LDL), l'apolipoprotéine B-100 et le poids corporel. Actuellement, aucune donnée probante ne laisse croire que les aspects préoccupants des substituts de viande végétaliens (p. ex., la transformation alimentaire et la forte teneur en sodium) annulent les bienfaits cardiovasculaires potentiels. Nous concluons que le remplacement de la viande par des substituts végétaliens peut avoir un effet cardioprotecteur. Cependant, il est essentiel de mener des essais contrôlés randomisés à long terme ainsi que des études de cohortes prospectives qui évaluent les événements de MCV (p. ex., infarctus du myocarde, accident vasculaire cérébral) pour pouvoir tirer des conclusions plus formelles.

Plant-based meat alternatives (PBMAs) are foods that mimic their meat-based counterparts with numerous ingredients, including protein derivatives from soy, pea, wheat, and fungi (mycoprotein). The main consumers of PBMAs have not been specified but likely include the growing number of Canadians following a diet limiting or excluding meat, which was estimated to be 6.4 million in 2018, as well as the 25.7% of surveyed Canadians who were considering reducing their meat intake in 2020.[1,2] In years to come, the PMBA market is expected to grow. The Government of Canada invested $153 million into plant-based protein development in 2018, and a 2022 analysis estimated 12% growth in the Canadian PBMA market by 2024.[3,4] Consumers are now more aware of the potential health, environmental, and ethical benefits of eating more plant-based foods.[5-8]

According to Nova classification, most PBMAs are ultra-processed foods (UPFs): foods produced primarily from substances extracted from whole food sources (eg, sugar, salt, oil, protein) or synthesized in a laboratory (eg, flavour enhancers, food colouring, etc).[9,10] For this reason, the potential health implications of PBMAs have been questioned by the public and health professionals. The latest Canadian dietary guidelines state that highly processed foods should be limited because they are not part of a healthy dietary pattern.[11] A recent meta-analysis of prospective cohort studies found that higher UPF consumption was associated with a 21% higher risk of total mortality and a 35% higher risk of cardiovascular disease (CVD) events.[12] Each additional daily serving of UPF was associated with 2% and 4% higher risks of mortality and CVD events, respectively.

However, UPF is a heterogeneous category that can encompass a wide range of nutritionally diverse foods, including sugar-sweetened beverages, pizza, chocolate bars, almond milk, flavoured yoghurt, whole wheat bread, processed meat, and PBMAs. To the best of our knowledge, no study has delineated which types of UPFs are mostly responsible for the increased risk of CVD, and which are not. A broad analysis of the literature on UPFs would suggest that individual UPFs affect the risk of CVD differently. For example, sugar-sweetened beverages and processed meat have been associated with an increased risk of CVD,[13-17] but whole wheat bread and whole grain cereal have been associated with a reduced risk.[14-16,18,19] Whether PBMAs pose a health concern similar to some other UPFs, if at all, is a nutrition question without a clear answer. In this review, we assess the nutritional profile of PBMAs and consider the relevant clinical studies to try to answer the question: Are PBMAs cardioprotective as a replacement for meat?

The literature search was limited to publications discussing the nutritional composition of PBMAs, dietary trials using PBMAs as the intervention, and reviews of common ingredients in PBMAs on CVD risk factors and outcomes. Peer-reviewed literature published in the English language from January 1970 to August 2023 were identified with the use of Pubmed and Google Scholar. Search terms included the following: plant-based meat, meat alternative, nutrition, soy protein, pea protein, plant protein, gluten, mycoprotein, coconut oil, olive oil, canola oil, vegetable oil, cardiovascular disease, cholesterol, LDL, ApoB, triglycerides, blood pressure, body weight, BMI, C-reactive protein, and inflammation. When applicable, references included in the publications identified via the literature search were also investigated. We prioritised the inclusion of studies that compared PBMAs or their components vs meat, particularly when analysing their nutritional composition or how these foods affect CVD risk factors and outcomes. Moreover, relevant prospective cohort studies and randomised controlled trials (RCT) were prioritised for inclusion over other types of studies with a greater risk of bias.

Nutritional Composition of PBMAs

Adding to the difficulty in determining the long-term health impact of PBMAs is the diversity of available products. From one PBMA to another there is considerable variability in the nutrient profile that may affect CVD risk, including sodium and saturated fatty acid (SFA), which can increase risk, and polyunsaturated fatty acid (PUFA) and fibre, which can decrease risk via mechanisms as detailed elsewhere.[20-26] Even 2 seemingly similar PBMAs ("burgers") can differ substantially regarding these nutrients. The current formulation of the plant-based burger patty from Impossible Foods contains 6 g SFA, 370 mg sodium, and 5 g fibre, whereas Dr Praeger's Perfect Burger contains 1 g SFA, 530 mg sodium, and 3 g fibre per serving (Figs. 1 and 2).[27,28]

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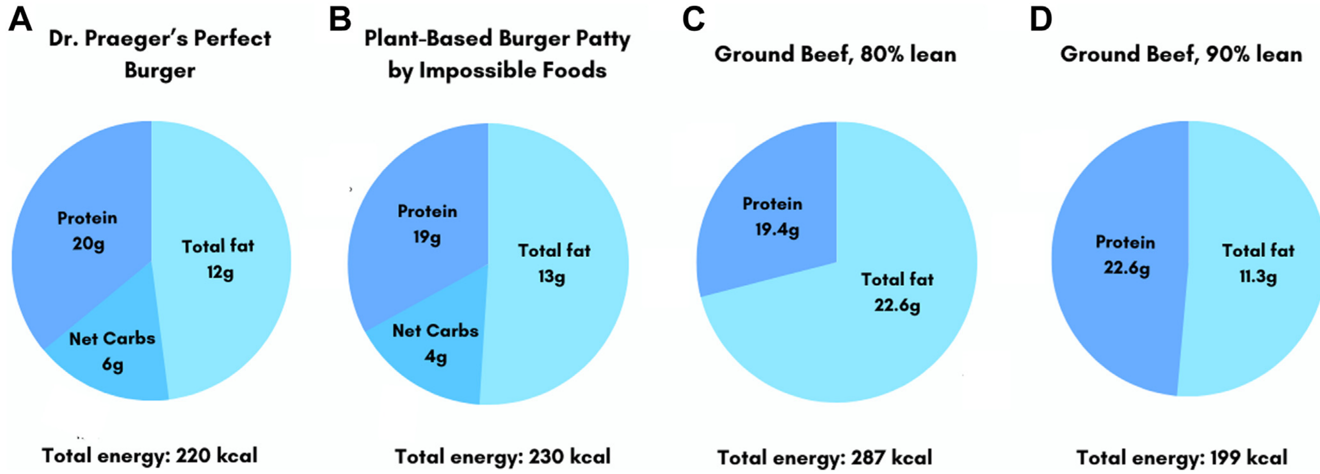

Figure 1. Macronutrient information for a 113 g serving of (**A**) Dr Praeger's Perfect Burger, (**B**) Impossible Foods Plant-Based Burger Patty, (**C**) 80% lean beef, and (**D**) 90% lean beef. Percentage of energy provided by protein, net carbohydrates, and total fat were obtained from the Cronometer Community Database and are depicted in pie charts. All other nutritional data for Dr Praeger's and Impossible Foods were obtained from their respective Nutrition Facts labels, and data for 80% lean beef (raw) and 90% lean beef (raw) were obtained from the USDA's FoodData Central. Net carbohydrates (carbs) calculated as grams of fibre subtracted from grams of total carbohydrates.

Despite the variability among PBMAs, according to a 2022 review, several analyses conducted in different international markets have suggested that they generally have a more favourable nutrient profile for reducing the risk of CVD compared with meat while also being more environmentally sustainable protein sources.[29] Alessandrini et al. analysed 207 PBMAs and 226 meat products from 14 UK retailers and found that PBMAs had lower energy density, total fat, SFA, and protein but higher sodium and fibre content than meat on average.[30] Only 14% of the PBMAs were classified as "less healthy" according to the UK Nutrient Profiling Model, much less than the 40% of meat products. Similarly, an analysis of products available in Germany found that PBMAs tend to have lower Ofcom A-scores, which reflects lower amounts of "nutrients to limit," such as total calories, SFA, and sodium.[31] Another study of 125 PBMAs available in Brazil found that PBMAs tended to have calorie, protein, SFA, and sodium content similar to meat products overall but contained more fibre.[32] However, there were differences depending on which types of products were being compared. The SFA content of plant-based meatballs, breaded chicken, and sausages was lower than their animal-based counterparts.

Analyses of products available in the USA have displayed similar findings. Harnack et al. evaluated 37 plant-based ground beef alternatives and found that they tended to be low in SFA and provided a median of 15% of the daily value for fibre.[33] They did, however, tend to be higher in sodium and lower in protein than ground beef. As for micronutrients, most ground beef alternatives were considered to be good sources of folate, niacin, iron, phosphorus, manganese, and copper but contained less zinc and vitamin B_{12} than beef. A similar analysis evaluating 6 plant-based burgers in the USA found that they tend to have similar amounts or more protein, more fibre, and less SFA but more sodium than beef burgers.[34]

Nonetheless, 2 analyses out of the USA did emphasise that leaner cuts of meat may provide similar or less SFA per serving compared with certain PBMAs while also providing less total calories and sodium.[35,36] However, the researchers did not account for sodium commonly added in preparation, which is a concern that can apply to nearly every study on this topic. Of note, the PBMAs in both analyses also contained 2-3 g fibre per patty whereas the beef options contained none. There were additional differences in the types and amounts of metabolites found in each product, but the relevance of those differences to human health are unclear.

One detailed analysis of plant-based burgers evaluated 27 samples of PBMAs from 3 brands and 24 samples of meat-based burgers from 4 brands available in Europe.[37] The researchers found that PBMAs typically contained similar SFA and total protein but much lower cholesterol than the meat-based burgers. Only the plant-based products that incorporated some animal-based ingredients (eg, dairy) contained cholesterol. The reason for the similar SFA content was that many of the PBMAs used coconut oil as a fat source. The PBMAs also tended to have less monounsaturated fatty acid (MUFA) but more PUFA, largely driven by a higher linoleic acid content, which has been associated with a lower risk of total and CVD mortality.[38-40] Animal-based burgers tended to contain slightly more trans fat, although the absolute amounts were low in both types of burgers. The PBMAs also tended to have more favourable mineral profiles, but with sodium content similar to the meat products. Zinc was the only mineral that was significantly less abundant in the PBMAs. Additional analyses that evaluated a broader range of products in Sweden and Spain generally reported similar findings, although they did note a lower SFA content in the PBMAs, and the latest analysis in Spain found that plant-based burgers, sausages, and meatballs contained less salt, on average, than their meat-based counterparts, which is contrary to findings from some analyses conducted in other markets.[41-43] This may be due to the addition of salt as a preservative in the meat products.

Katidi et al. compared plant-based cold cuts, sausages, red meat products, and poultry imitations available in Greece vs their meat alternatives and found differences between

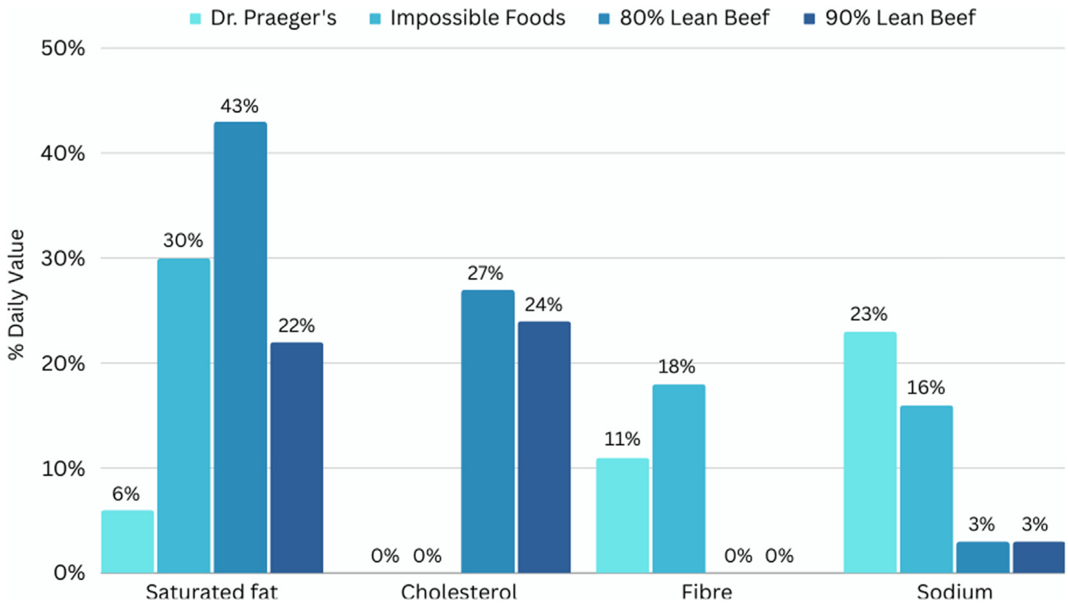

Figure 2. Percentage daily value for saturated fat, cholesterol, fibre, and sodium provided by a 113 g serving of Dr Praeger's Perfect Burger, Impossible Foods Plant-Based Burger Patty, 80% lean beef, and 90% lean beef. Nutritional data for Dr Praeger's and Impossible Foods were retrieved from their respective Nutrition Facts labels, and data for 80% lean beef (raw) and 90% lean beef (raw) were retrieved from the USDA's FoodData Central.

categories.[44] Plant-based cold cuts tended to have more sugar than animal-based cold cuts, with no significant differences in other macronutrients, whereas plant-based sausages had more protein, less total and saturated fat, and less sodium than meat sausages. The higher protein content appears to be specific to the plant-based sausages made with vital wheat gluten. There were no significant differences in any macronutrients or sodium content between red meat or poultry and their respective alternatives. In addition, Melville et al. evaluated 132 PBMAs and 658 meat products in Australia and found that PBMAs tended to have less SFA and sodium but more fibre and slightly higher sugar content than the meat products.[45] They also had higher Health Star ratings, which score the foods based on several characteristics related to long-term health, with the most striking difference in scores being the comparison between plant-based and animal-based bacon.

Finally, a recent analysis of 91 PBMAs in the Canadian food supply found that they usually provide less calories, fat, SFA, cholesterol, protein, and sodium while providing more calcium, total carbohydrates, fibre, and sugar than their animal-based counterparts, although the absolute fibre and sugar contents were low, at an average of 2.7 g and 1.7 g, respectively.[46] Using the Australia–New Zealand Nutrient Profiling Scoring Criterion, PBMAs were rated as being of greater overall nutritional quality than meat products on average, and level of processing showed no significant associations with nutritional quality.

Although PBMAs tend to be higher in fibre and lower in SFA and cholesterol content compared with animal-based products, there is a concern that the high sodium content of some products and the potential rise in blood pressure may negate the benefits of a healthier fatty acid profile. A modelling study of the diets of French adults suggests that ideally formulated plant-based meat alternatives can improve diet quality when substituted in place of meat; however, given the heterogeneity of the available products, it raises important questions about how different types of products affect cardiovascular risk compared with their animal-based counterparts.[47] There is some research evaluating the impact of replacing meat with PBMAs on CVD risk factors, but the literature overall is too limited to support definitive conclusions.

Trials Evaluating PBMAs and CVD Risk Factors

A systematic review and meta-analysis of 12 controlled trials suggested that PBMAs could reduce total cholesterol (TC) by 0.50 mmol/L, low-density lipoprotein cholesterol (LDL-C) by 0.39 mmol/L, and triglycerides (TG) by 0.15 mmol/L, with no statistically significant effects on fasting blood glucose, blood pressure, high-density lipoprotein cholesterol (HDL-C), or body weight.[48] But there are notable limitations to this dataset. First, the trial with the second largest effect size for TC and largest effect size for blood glucose was not randomised and did not report apolipoprotein B (ApoB) values, a more accurate predictor of CVD risk than TC or LDL-C.[21] Second, control diets varied between studies and were sometimes the participants' habitual diets. Finally, the dietary interventions in some trials were not isolated to PBMAs or implemented a variety of PBMAs that may differentially affect CVD risk factors.

Some of the dietary trials in the meta-analysis, as well as some that were published afterward, had specifically replaced meat products with PBMAs and took steps to control for other dietary variables. The characteristics and main findings of the discussed trials are summarised in Table 1 and Supplemental Table S1. Turnbull et al. conducted one of the earliest trials on PBMAs and CVD risk factors, comparing

Table 1. Summary of study characteristics and findings from randomized controlled trials investigating the impact of plant- or mycoprotein-based dietary interventions on cardiovascular disease risk factors

Study author, year	Study design	Plant-based intervention	Control	Main findings: TC	LDL-C	HDL-C	TG	ApoB	ApoA1	FBG	SBP	DBP	Weight	WC	TMAO
Turnbull, 1990[49]	Parallel RCT. Total n = 17 (5 M, 12 F); intervention n = 9; control n = 8. Duration 3 wk	Mycoprotein-containing PBMAs and homemade products	Equicaloric meat-containing foods	↓	↓	↑	NS	NS	NS	NS	NS	NS	NS	–	–
Azadbkht, 2007[60]	RCrT. n = 120 F. Duration 8 wk per phase. 3 diet phases. Eucaloric dietary intervention	DASH diet + 30 g TSP	DASH diet + 1 serving of lean red meat	↓	↓	NS	NS	↓	NS	NS	NS	NS	NS	NS	–
		DASH diet + 30 g soy nuts		↓	↓	NS	NS	↓	NS	NS	NS	NS	NS	NS	–
Bergeron, 2019[57]	RCrt. High SFA arm (∼14% kcal) n = 62 (27 M, 35 F); low SFA arm (∼7% kcal) n = 51 (17 M, 34 F). Duration 4 wk per phase. 3 phases. Eucaloric dietary intervention	Nonmeat protein: isoflavone-free soy products, legumes, nuts, grains, various PBMAs	Red meat	↓	↓	↓	NS	↓	↓	NS	NS	NS	NS	–	–
			White meat	↓	↓	↓	NS	↓	↓	NS	NS	NS	NS	–	–
Crimarco, 2020[51,54]	RCrT. n = 36 (12 M, 24 F). Duration 8 wk per phase. 2 phases	≥ 2 servings of Beyond Meat PBMAs per day	≥ 2 servings of organic meat products per day	–	↓	NS	NS	–	–	NS	NS	NS	↓	–	↓
Bianchi, 2022[59]	Parallel RCT. Total n = 155; intervention n = 58; control n = 57. Duration 8 wk	Mycoprotein-, legume-, and vegetable-based PBMAs	No intervention	NS	NS	NS	NS	–	–	–	NS	NS	↓	–	–
Farsi, 2023[50]	RCrT. n = 20 M. Duration: 2 wk per phase. 2 phases	Mycoprotein- based PBMAs	Red and processed meat	↓	↓	NS	NS	–	–	NS	NS	NS	NS	↓	NS

–, not reported; ↑, significant increase with intervention compared with control; ↓, significant reduction with intervention compared with control; ApoA1, apolipoprotein A-1; ApoB, apolipoprotein B-100; DBP, diastolic blood pressure; F, female; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, male; NS, not significant; RCrT, randomized crossover trial; RCT, randomized controlled trial; SBP, systolic blood pressure; SFA, saturated fatty acids; TC, total cholesterol; TSP, textured soy protein; TMAO, trimethylamine N-oxide; WC, waist circumference.

products made from mycoprotein vs meat.[49] Seventeen participants with TC concentrations from 5.2 mmol/L to 6.2 mmol/L were randomised to either the mycoprotein or the control group. Participants in both groups consumed closely matched meals in a metabolic unit for 3 weeks, while permitted to consume the provided snacks outside the unit. The diets were closely matched for total energy, SFA, PUFA, and protein content, whereas the mycoprotein diet provided 11.2 g more fibre, which is inherent to mycoprotein-based PBMAs, and 51 mg less cholesterol per day because mycoprotein contains none. The researchers did not report the sodium content of either diet but there was no statistically significant difference in systolic or diastolic blood pressure between groups. The mycoprotein group achieved a 13% reduction in TC, a 9% reduction in LDL-C, a 53% reduction in TG, a 14.8% reduction in ApoB, an 8% reduction in apolipoprotein A-1 (ApoA-1), and a 11% rise in HDL-C. The control diet resulted in a 12% increase in LDL-C, an 11% reduction in HDL-C, and a 53% reduction in TG, with no significant changes in other lipid markers. The results for TC, LDL-C, and HDL-C were significantly different between the diets. These results were largely supported by a more recent randomised crossover trial including healthy adult men, which evaluated the replacement of 240 g of red and processed meat daily with mycoprotein-based PBMAs in the context of their habitual diets.[50] Consumption of the PBMAs resulted in reductions in TC, LDL-C, and waist circumference, with little to no effect on other cardiometabolic biomarkers. The results of these trials may have been driven by the higher fibre and lower dietary cholesterol content of the mycoprotein-rich diet, suggesting that replacing meat with mycoprotein-based PBMAs could improve CVD risk factors even when closely matched for fatty acid content.

The **S**tudy **W**ith **A**ppetizing **P**lantfood—**M**eat **E**ating **A**lternative **T**rial (SWAP-MEAT) was a 16-week randomised crossover trial that compared the impact of Beyond Meat's pea protein−based PBMAs vs similar organic grass−fed meat products.[51] Participants were randomised to eat 2 or more servings of the PBMAs or meat products per day for 8 weeks before crossing over to the opposite product. Consuming PBMAs for 8 weeks resulted in 2.0 μmol/L lower trimethylamine-N-oxide (TMAO) levels than the organic meat, although the relevance of TMAO as a CVD risk factor is questionable.[52,53] Consumption of PBMAs also led to further reductions of 1.0 kg lower body weight and 0.28 mmol/L (10.8 mg/dL) LDL-C compared with meat, with no significant differences in blood pressure or inflammatory biomarkers.[51,54] Interestingly, there were no significant differences in overall fibre, SFA, protein, or sodium intake despite the PBMAs used in this trial being high in sodium, accounting for 939 mg of their total daily intake. Some of the meat products also contained added salt, and participants may have been salting their meat for flavour, resulting in similar sodium intake and blood pressure measurements between the 2 interventions. Another interesting finding is the reduction in LDL-C despite similar daily fibre and SFA intake. This may be partly explained by differences in dietary cholesterol intake, which has a smaller effect on LDL-C levels than SFA does.[20,55,56] The PBMAs used in this trial did not contain any dietary cholesterol, and participants tended to consume less overall during the PBMA phase.

Results from Bergeron et al.'s RCT comparing the effects of red meat, white meat, and plant protein concur with SWAP-MEAT.[57] This trial randomly assigned participants to high and low SFA arms where SFA provided 13%-14% and 7%-8% of the energy in the respective diets. Within each treatment arm, participants consumed diets that differed in the primary protein source, being red meat, white meat, or plant sources, including legumes, nuts, grains, isoflavone-free soy products, and PBMAs, in random order for 4 weeks each. The diets were otherwise closely matched for fibre, total carbohydrates, SFA, MUFA, and PUFA, with the plant protein diet resulting in lower cholesterol intake than the other two diets. Those in the high SFA arm had higher TC, LDL-C, non-HDL-C, and ApoB than participants in the low SFA arm. Within each treatment arm, red and white meat consumption resulted in higher TC, LDL-C, non-HDL-C, and ApoB than higher plant protein consumption, which may partly be driven by the differences in dietary cholesterol intake. While this trial did not solely use PBMAs as a replacement for meat, it further demonstrates that swapping meat for plant protein sources may improve blood lipid concentrations independently from SFA intake, as seen with the SWAP-MEAT trial.[51] However, the red and white meat led to slightly higher HDL-C and apoA-1 concentrations, particularly in the high SFA arm, although these changes may lack clinical significance.[57,58]

A subsequent RCT investigated the replacement of meat with a variety of mycoprotein, vegetable, and legume-based PBMAs over 8 weeks, although little information was given on the specific products that were used, and found that those consuming the PBMAs lost 0.6kg compared to those eating meat.[59] However, there were no significant differences in blood lipids unlike other trials. The lack of significant findings may be explained by the differences in meat and saturated fat intake between the intervention and control groups being 39 g and 4.2 g, respectively, while there was no significant difference in fibre intake by the final week of the trial. These contrasts in intake may be insufficient to yield significant differences in lipid concentrations.

Finally, Azadbakht et al. compared the impact of lean red meat, textured soy protein, and soy nuts in the context of a Dietary Approaches to Stop Hypertension (DASH) diet on cardiometabolic risk factors in postmenopausal women with metabolic syndrome.[60] In this trial, 120 women were randomised to 1 of the 3 DASH diet interventions, which differed only by the inclusion of 1 serving of red meat, 30 g textured soy protein, or 30 g soy nuts per day. The 3 diets otherwise provided similar nutrient profiles, with the most notable differences being the higher fibre and isoflavone content of the soy protein and soy nut diets, and the higher PUFA content of the soy nuts. Participants consumed each diet for 8 weeks in random order. The soy protein improved TC, LDL-C, ApoB, fasting insulin, and homeostasis-model assessment insulin resistance compared with red meat, and soy nuts further improved several markers, suggesting that textured soy protein, which is traditionally used as a meat alternative, may improve certain cardiometabolic risk factors compared with red meat, but not compared with whole soy.

Taken together, these data suggest that PBMAs may improve certain cardiovascular risk factors even when fatty acid and fibre content are closely matched. However, many modern PBMAs contain significantly less SFA and more PUFA than the PBMAs used in most of the aforementioned trials, which highlights the potential for an additive health benefit. In addition, different plant protein sources can contain unique beneficial compounds, such as isoflavones, the effect of which could not be directly measured in the available trials.[61]

While long-term research on PBMAs and CVD events is lacking, multiple meta-analyses of observational studies have suggested that higher plant protein consumption is associated with improvements in CVD risk whereas animal protein often has a neutral or detrimental impact on risk.[62-64] Red and processed meat consumption, in particular, are most consistently associated with an increased CVD risk.[65] Results from substitution analyses have suggested that replacing modest amounts of animal protein with plant-based protein sources may significantly reduce the risk of CVD outcomes, particularly when the animal protein is sourced from red and processed meat.[66,67] Risk reductions are also reported independently from changes in SFA and fibre intake when substituting as little as 3% of one's calories from animal protein with plant protein.[67] However, it would be inappropriate to extrapolate the results of these substitution analyses to popular PBMAs. The primary plant protein sources in most of these analyses tend to be grains and nuts, because legume consumption is generally low in Western populations and the more heavily processed PBMAs were not as accessible as they are today.[68] This further emphasises the need for long-term prospective studies on PBMA consumption investigating whether and to what degree the improvements in CVD risk factors translate to improvements in CVD outcomes.

Commonly Incorporated Protein Sources

Soy protein is one of the most commonly used proteins for PBMAs, and observational data consistently supports associations between soy consumption and a lower risk of CVD and other noncommunicable diseases.[69,70] A scoping review published in 2022 suggested that soy consumption may reduce risk of CVD, coronary heart disease (CHD), and stroke by 16%, 17%, and 18%, respectively, while also reducing risk of several cancers, including breast cancer.[69] These results may be driven partly by the benefits of the fibre and PUFA content of many soy products, as well as the replacement of foods associated with higher disease risk, such as red and processed meat.[24,25,38-40,65-67] In addition, soy isoflavones may have cardioprotective effects. A meta-analysis of 11 RCTs found that soy protein enriched with isoflavones reduced TC and LDL-C more than isoflavone-depleted soy protein, suggesting that isoflavones themselves may improve lipid profiles.[71] Soy isoflavone supplementation has also been shown to reduce blood pressure compared with placebo in individuals with hypertension.[72] Furthermore, dietary soy isoflavone intake has been associated with a lower risk of cardiovascular outcomes.[73] The versatility, nutritional profile, and cardiovascular benefits of soy consumption make it a valuable protein source for PBMAs.

Despite the benefits of soy protein, many PBMAs use nonsoy legume-based protein as the primary protein source; one of the most common types is pea protein. The most recent meta-analysis of observational studies of legume intake and CVD suggested that high legume intake is associated with 6% and 10% lower risks of CVD and coronary heart disease (CHD), respectively.[74] The dose-response analysis suggested that, compared to 0 g/wk of legumes, consuming 100 g/wk may lower the risk of CHD by 9%, with the largest reduction in risk occurring at 400 g/wk. Another recent meta-analysis of prospective cohorts evaluating legume intake and mortality found that, compared with participants with the lowest intake, those with the highest consumption had 6% and 9% reductions in risk of all-cause and stroke mortality, respectively, with each 50 g/d increment associated with a 6% reduction in risk of all-cause mortality.[75] However, these results cannot be directly extrapolated to protein that is isolated from whole food sources (eg, pea protein isolate), because much of the fibre and phytochemical content may be removed. Although preclinical studies suggest that it is possible that protein isolated from nonsoy legumes can improve CVD risk factors, including blood lipids and blood pressure, more research on human subjects is needed.[76] As one indication, the results from the SWAP-MEAT trial suggest that PBMAs containing pea protein can improve CVD risk factors compared with meat.[51,54] These protein sources may be good options for individuals who have allergies, intolerances, or health conditions that preclude them from consuming other commonly used protein sources such as soy or vital wheat gluten.

Vital wheat gluten, the primary ingredient in seitan, is another common protein source used to improve the texture of PBMA. Individuals with a soy allergy may seek products with vital wheat gluten as a suitable alternative. There is currently very little research on wheat gluten and CVD risk factors or outcomes. One randomised crossover trial replaced 11% of total dietary energy from starch in bread with wheat gluten in hyperlipidemic patients, otherwise matching diets for total energy and fat content.[77] Higher wheat gluten intake resulted in lower uric acid, oxidised LDL, and TG levels, which may translate to lower CVD risk. The effect, however, could be due to the reduction in refined carbohydrate intake rather than inherent properties of gluten—an important distinction considering that PBMAs would typically replace animal protein sources, not bread. Another RCT compared postprandial glucose and insulin responses in healthy individuals after consuming white bread or a cereal-based bread containing dried fruits and enriched with additional fibre and wheat gluten.[78] The gluten-enriched bread resulted in lower glucose and insulin responses, but the effects cannot be attributed to the gluten itself, because there were several nutritional differences between the breads. Also, postprandial glycemic responses are not necessarily pathologic.[79-81] Stronger evidence that gluten itself may have protective properties is long-term prospective cohort data suggesting that lower intakes of gluten are associated with a higher risk of developing type 2 diabetes than high consumption, with a weaker, yet still statistically significant, association after adjustment for cereal fibre.[82] Similar data on gluten consumption and CHD did not find a statistically significant impact on risk before adjustment for refined carbohydrate intake, but a 15% lower risk with higher gluten consumption after adjustment.[83,84] In this case, gluten may function as a proxy for whole grain intake, so it is less clear if gluten itself is protective against CHD.

A final commonly incorporated protein source in PBMAs is mycoprotein. This fungi-derived protein has been consumed in the UK for decades but has gained more traction in recent years, particularly in fitness communities. In sports nutrition research, mycoprotein has been shown to stimulate muscle protein synthesis to a similar or greater degree as animal protein sources, and a recent trial found that a plant-based diet rich in mycoprotein can promote muscle mass and strength improvements similarly to an omnivorous diet rich in animal protein.[85-87] Similar results have also been demonstrated with a vegan diet rich in soy protein compared to an omnivorous diet with whey protein.[88] As noted previously, 2 RCTs have shown that mycoprotein-based meat alternatives improve blood lipids compared with meat.[49,50] Three additional RCTs also evaluated the impact of mycoprotein on CVD risk factors, and a recent meta-analysis of the 4 earliest RCTs suggested that mycoprotein may lower TC and LDL-C levels, although the latter result was not statistically significant.[89-92] However, the studies used a variety of control foods, including meat, fish, soy, and wheat-based products, some of which may themselves improve lipid profiles, so the results of the meta-analysis do not reflect the specific replacement of meat with mycoprotein-based PBMAs.[93,94] Further research is needed to confirm the findings of the 2 trials that did specifically compare PBMAs to meat and to identify if there are any unique cardioprotective properties of mycoprotein. Some research also suggests that mycoprotein-based products may promote satiety relative to meat, possibly favouring weight loss, although this requires further investigation as well.[95]

Commonly Incorporated Fat Sources

The type of dietary fats consumed in the diet has been strongly associated with the risk of CVD. A Cochrane review of RCTs published in 2020 suggested that replacing SFA with PUFA can reduce the risk of CVD events by 22% and CHD events by 21%.[96] These results are supported by a meta-analysis included in the American Heart Association's Presidential Advisory on dietary fats and CVD.[97] One trial included for analysis in both of these papers that warrants further discussion is the LA Veterans Administration Hospital Study, which was an 8-year double-blind RCT.[38] The researchers in this study randomised 846 participants to 1 of 2 cafeterias that served similar meals, but for the intervention group much of the saturated animal fat in the foods was isocalorically replaced with vegetable oils rich in the omega-6 fatty acid linoleic acid, including corn, soybean, safflower, and cottonseed oil. Participants in the control group consumed 11 g/d linoleic acid and those in the intervention group 41 g/d. Overall, there were 60 deaths due to atherosclerotic events in the control group vs 39 in the intervention group, with the greatest reduction in events found in participants who were younger or had higher TC levels at baseline. This finding suggests that replacing SFA with PUFA at a younger age can be an effective intervention for lowering CVD risk, especially in those with suboptimal cholesterol concentrations.

Compared with animal fats, plant fats are generally lower in SFA content and higher in unsaturated fat. Therefore, the greatest potential for PBMAs to improve CVD risk may be by shifting toward a more cardioprotective fatty acid profile, including relatively less SFA per gram of dietary fat as seen with products such as Field Roast's Smoked Apple and Sage sausages, providing 0.5 g SFA and 8 g total fat per serving, and Yves' The Good Veggie Burger, providing 0 g SFA and 3.5 g of total fat per serving, according to their nutrition labels.[98,99]

PBMAs can achieve a low SFA content by using nontropical vegetable oils that are low in SFA and higher in unsaturated fats, including PUFA and MUFA, which aligns with public health recommendations for cardiovascular health.[100] Based on currently available evidence, arguably the most cardioprotective type of plant oil compared with SFA-rich oils is canola oil. A 2020 meta-analysis found that, overall, canola oil significantly reduced TC, LDL-C, and ApoB compared with other oils.[101] The researchers further evaluated specific substitutions, which suggested that canola oil can reduce TC, LDL-C, ApoB, and TG by 0.59 mmol/L, 0.49 mmol/L, 0.09 g/L, and 0.08 mmol/L, respectively, compared with SFA-rich options, as well as reduce TG compared with olive oil and LDL-C compared with both olive oil and sunflower oil, albeit to a lesser degree compared with SFA-rich sources. These data are supported by the National Institutes of Health—American Association of Retired Persons Diet and Health Study, which prospectively followed 521,120 Americans age 50-71 years, and found that substituting 1 tablespoon of butter with either canola oil, olive oil, or corn oil was associated with a lower risk of total, cardiometabolic, and CVD mortality, although the result for corn oil and CVD mortality was not statistically significant.[102] Similar results were obtained when substituting margarine for the aforementioned oils; however, the margarines may have contained harmful trans fats during the early years of this cohort.[103,104] Interestingly, in the Nurses' Health Study and Health Professionals Follow-Up Study, olive oil appeared to be noninferior to other vegetable oils containing more PUFA and less MUFA and SFA with regard to a number of health outcomes, including total and CVD mortality.[105] The results also suggested that substituting olive oil in place of butter, dairy fat, mayonnaise, or margarine may reduce the risk of total and CVD mortality. One reason that olive oil may be as protective as other vegetable oils against CVD despite a seemingly inferior fatty acid profile is its high polyphenol content, especially in extra-virgin olive oil; polyphenols are a class of plant compounds that can reduce inflammation, improve endothelial function, and help reduce blood pressure.[106-110]

Trials directly comparing PBMAs and meat have, however, often used PBMAs with an SFA content relatively close to their meat counterparts, or modified the background diet of intervention and control groups to closely match fatty acid profiles.[49,51] Although improvements in lipid profiles have been observed in most trials, the differences could be more substantial if the PBMA used was more representative of commercially available PBMAs with a higher PUFA and lower SFA content than their meat counterpart. For example, the primary fat source used in many of the PBMAs in the SWAP-MEAT trial was coconut oil, which is over 90% SFA.[51,111] Evidence still suggests this type of plant fat can lower LDL-C compared with butter, but it has been shown to significantly raise LDL-C levels relative to nontropical vegetable oils found in many other PBMAs.[111,112] Therefore, PBMAs that derive most of their fat content from nontropical vegetable oils would be expected to further reduce LDL-C and improve CVD risk.

Directions for Future Research

It is clear there are gaps in our current understanding of PBMAs and their long-term effects on CVD risk. The heterogeneous nutritional profiles of currently available PBMAs limits the generalisability of the relevant trials which have been published. More rigorous and prospective studies are needed to clarify what types of PBMAs could potentially improve health outcomes, in what amounts, and in replacing what types of food products (including whole-plant foods). It would also be informative if future trials evaluated any unique cardioprotective properties of various protein sources contained in certain PMBAs, such as vital wheat gluten and pea protein isolate.

Based on our summary of trials to date, future RCTs should investigate the impact of PBMAs with a more cardioprotective fatty acid profile (ie, containing a greater proportion of unsaturated fats) on primary CVD risk factors. Although we did not identify any blood pressure—raising properties of the PBMAs containing a high sodium content, further RCTs are warranted to test the reproducibility of these findings in populations with hypertension; such data could stimulate the formulation of new PBMAs with a lower sodium content to help reduce blood pressure compared with meat.

Finally, the effect of the processing of PBMAs in relation to CVD risk remains largely unknown, although we did not identify any potentially negative effects in studies that replaced meat with PBMAs. This further underscores the need for long-term prospective studies examining the impact of PBMA consumption on CVD events.

Conclusion

Commercially available PBMAs are nutritionally diverse but generally have a cardioprotective nutritional profile relative to meat, including less SFA and more fibre per serving. The available RCTs evaluating PBMAs are promising and suggest that replacing meat with PBMAs can improve CVD risk factors, including a reduction in LDL-C. PBMAs do not seem to negatively affecting other CVD risk factors such as blood pressure, despite their classification as UPFs and the high sodium content of many products. These improvements in CVD risk factors may result in a lower risk of developing CVD; however, there is a need for high-quality long-term studies evaluating CVD outcomes.

Ethics Statement

The research reported has adhered to the relevant ethical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article; this is a narrative review.

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Disclosures

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2023.11.005.