

THE ROLE OF DIETARY FATS FOR PREVENTING CARDIOVASCULAR DISEASE. A REVIEW

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ABSTRACT

At the present, there is a pandemic of chronic non-communicable disease (NCD) affecting most countries of the world. The World Health Organisation (WHO) has identified the main contributing determinants to be cardiovascular disease (CVD), diabetes, malignant cancer and chronic disease of the respiratory system. Unhealthy nutrition, as well as other adverse lifestyle health behaviour are recognised to be part of the prime factors responsible. According to WHO guidelines, a healthy lifestyle should include substituting saturated fatty acids (SFAs) with polyunsaturated fatty acids (PUFAs) together with eliminating trans-fatty acids from the diet and limiting the intake of refined carbohydrates in conjunction with increasing the consumption of fruit, vegetables, nuts and wholegrain cereal products.

Recent studies on the relations between CVD prevention and dietary fats have been however unclear. The present study thus aims to provide a review of current evidence and opinion on the type of dietary fat most appropriate for preventing arteriosclerosis. The adoption of dated recommendations on the need to increase dietary PUFA in both Northern Europe and America has led to n-6 PUFAs being predominant in diets as compared to n-3 PUFAs. This disproportion may have caused mortality to rise, due to CVD, as a result of arteriosclerosis in these countries.

In contrast, a traditional Mediterranean diet yields a PUFA n-6/n-3 ratio of 2:1, which is much lower than for the aforementioned northern countries. Some authors however consider that assessing this ratio is irrelevant and that decreasing n-6 PUFA may be harmful. Such differences of opinion leads to confusion in adopting an effective approach for arteriosclerosis management regarding dietary n-6/n-3 ratios. Moreover, recent studies have added much controversy to the notion that the characteristics of SFAs are responsible for arteriosclerosis. These found that replacing dietary SFAs with carbohydrates did not reduce the risk of ishaemic heart disease (IHD). Furthermore, changing to monounsaturated fatty acids (MUFAs) gave equivocal findings, but only changing to PUFAs reduced the risk of IHD. This last statement however requires qualification in that dietary n-6 PUFAs increases the risk of IHD. It is only the n-3 PUFAs that are beneficial. Up till now these controversies remain unsolved. It is however noteworthy that adopting a Mediterranean diet reduces IHD mortality. This is explained by a low consumption of SFAs but high intake of unsaturated fatty acids including n-3 PUFAs, and is linked to choosing the right vegetable fats. Oils that contain α -linoleic acid (ALA) are to be preferred in the diets of northern countries.

Key words: saturated fatty acids, n-6 fatty acids, n-3 fatty acids, prevention of cardiovascular diseases

STRESZCZENIE

Pandemia przewlekłych chorób niezakaźnych, do których Światowa Organizacja Zdrowia (WHO) zalicza głównie choroby sercowo-naczyniowe (CVD), cukrzycę, nowotwory złośliwe i przewlekłe choroby układu oddechowego, obejmuje obecnie prawie wszystkie kraje świata. Niezdrowe żywienie, oprócz innych niezdrowych cech stylu życia, jest wżną przyczyną tych chorób.

Zgodnie z wytycznymi WHO zdrowy sposób żywienia powinien charakteryzować się między innymi zastępowaniem nasyconych kwasów tłuszczowych (SFA) kwasami wielonienasyconymi (PUFA), eliminacją kwasów

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tłuszczowych trans, ograniczaniem spożycia rafinowanych węglowodanów i soli, a zwiększaniem owoców, warzyw, orzechów i pełnoziarnistych produktów zbożowych.

W świetle badań przeprowadzonych w ostatnich latach dużo niejasności wiąże się z wyborem tłuszczu w diecie w prewencji CVD. Celem naszej pracy jest przegląd aktualnych poglądów i wyciągnięcie wniosku odnośnie wyboru tłuszczu właściwego w profilaktyce miażdżycy.

Przyjęty dawniej pogląd o potrzebie zwiększania udziału PUFA w diecie krajów Europy Północnej i Ameryki Północnej doprowadził do znacznej przewagi udziału PUFA n-6 w stosunku do PUFA n-3 w żywieniu. Ta dysproporcja może być jedną z przyczyn wysokiej umieralności na choroby sercowo-naczyniowe powodowane miażdżycą w krajach północnych. W tradycyjnej diecie śródziemnomorskiej stosunek PUFA n-6/n-3 wynosi jak 2:1. Jest to wartość znacznie niższa niż w krajach północnych. Część autorów uważa jednak, że obliczanie tego stosunku jest niecelowe, a obniżanie spożycia PUFA n-6 może być szkodliwe. Ta rozbieżność poglądów utrudnia zajęcie stanowiska w sprawie proporcji PUFA n-6/n-3 w diecie pożądanego w profilaktyce miażdżycy.

Także przyjęty dawniej pogląd o miażdżycotwórczych właściwościach SFA jest kontrowersyjny w świetle ostatnich badań. Wykazano bowiem, że zastępowanie w diecie SFA przez węglowodany nie zmniejsza ryzyka choroby niedokrwiennej serca (IHD). Zamiana na jednonienasycone kwasy tłuszczowe (MUFA) daje wyniki niepewne. Dopiero zamiana na PUFA zmniejsza ryzyko IHD. Ta ostatnia informacja wymaga jednak uściśleń w świetle poglądu, że PUFA n-6 zwiększają ryzyko IHD. Tylko PUFA n-3 są pod tym względem korzystne. Te kontrowersje pozostają dotychczas niewyjaśnione.

Pozytywną informacją w kontekście tych rozbieżności poglądów jest fakt, że dieta śródziemnomorska cechuje się niską umieralnością na IHD. Tłumaczone to jest małym spożyciem SFA a dużym nienasyconych kwasów tłuszczowych, w tym PUFA n-3. Dlatego za rozsądne przyjmuje się zalecenie zastępowania w diecie krajów północnych SFA przez PUFA, z dużym udziałem PUFA n-3. Wiąże się to z odpowiednim wyborem tłuszczów roślinnych. Oleje o dużym udziale kwasu *alfa*-linolenowego (ALA) zasługują na preferencję w diecie krajów północnych.

Słowa kluczowe: nasycone kwasy tłuszczowe, kwasy tłuszczowe n-6, kwasy tłuszczowe n-3, prewencja chorób sercowonaczyniowych

INTRODUCTION

The current pandemic of chronic non-communicable disease (NCD) has recently come to the attention of the United Nations (UN) who now recognise the need for adopting far reaching population measures designed for their prevention. In this regard, a resolution entitled 'A Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases' was passed during the 66th Session of the General Assembly on September 19th, 2011 [27]. This highlighted the importance of reducing risk factors for CVD, chronic respiratory disease, diabetes and cancer. Such risk factors included unhealthy diets, low physical activity, smoking and alcohol abuse. The resolution stressed the vital need for all governments to take responsibility for effective action in preventing and controlling NCD based on the World Health Organization (WHO) guidelines [6]. These state that an optimal diet for reducing the risk of CVD, some cancers and diabetes should include the following:

- maintaining an appropriate energy balance between dietary intake and physical activity to keep weight within the normal range;
- reducing total fat intake to less than 30% of calories, substituting unsaturated fatty acids for saturated fatty

acids and eliminating trans-fatty acid intake;

- reducing refined sugar intake;
- reducing the overall salt intake, with the proviso that domestic salt should anyway be iodised;
- increasing the intake of fruits, vegetables, whole grains and nuts.

Within these recommendations, the need for a further in-depth debate on dietary fat is recognised, as opinions vary and some issues still remain unclear. The aim of this review is to compile opinions concerning recommended intakes of various fatty acids and vegetable oils regarding their roles in the primary prevention of CVD.

KEY STUDIES BACKING CURRENT RECOMMENDATIONS FOR FATTY ACID INTAKES

The well-documented effect of nutrition on CVD incidence and mortality, constitute the knowledge base for the role that nutrition plays in preventing NCD. For many years now, the notion that SFAs increase serum cholesterol level and thus contribute to the risk of atherosclerotic disease has been generally accepted. This had been first observed in the 1950s, particularly as reported by Bronte-Steward [1, 2]. In a series of experiments on Bantu subjects, results showed that when fats containing large amounts of SFAs including butter, beef fat, lard, and eggs (with a high cholesterol content) are introduced into a mainly plant-based diet, then this resulted in an increase in serum cholesterol levels. In contrast, plant oils with a high content of unsaturated fatty acids (such as corn, sunflower, safflower, peanut and olive oil) were shown to reduce cholesterol levels. The addition of sunflower oil to beef fat or fried eggs was observed to neutralise the hyperlipaemic effect of the diet. It was also shown that hydrogenated plant oils did not exert a lipid-lowering effect. Of note, the calorific content of the diet remained unchanged, which suggested that carbohydrate intake was partially replaced with fat intake.

In a prospective epidemiological study on males from seven countries (i.e. Japan, Greece, Italy, Serbia, the Netherlands, USA and Finland) mortality due to IHD was shown to be positively correlated with mean cholesterol levels and average SFA consumption [9]. It was from these findings that the widely held view became established, that SFA intake is a strong determinant of serum cholesterol levels, and that the latter is a major determinant of mortality due to IHD. However, evaluating the possible relations between unsaturated fatty acid intake and mortality was not performed in this study. Along with others, these investigations formed the basis on which the recommendation was made to reduce SFA intake, but moderately increase mono- and polyunsaturated fatty acid intake in the treatment of hypercholesterolaemia. Reducing cholesterol intake was also recommended, and this approach was accepted in later European and American expert consensus statements and guidelines that mainly focused on treating hypercholesterolemia [15, 25].

CURRENT DISCREPANCIES IN OPINION ON THE ROLE OF FATTY ACID INTAKES FOR PREVENTING CVD

The 2003 Joint WHO/Food and Agriculture Organization (FAO) Expert Consultation on Diet, Nutrition and the Prevention of Chronic Diseases recommended that, for the general population, the average total fat intake should provide 15% to 30% of total calories, including less than 10% of total calories from SFA, 5-8% of total calories from n-6 PUFAs, 1-2% of total calories from n-3 PUFAs and less than 1% of total calories from trans-fatty acids (TFAs) [14]. Recommended intakes of MUFAs were not clearly defined, but it was thought that these should reflect the difference between total fat intake and the recommended intakes of SFAs, PUFAs and TFAs. Such recommendations were translated to a need for reducing SFA intakes but increasing PUFA intakes, mainly of n-3 PUFAs, and targeted to the most developed countries, particularly those of non-Mediterranean Europe and Northern America.

Recommendations regarding the intake proportion of dietary n-6 PUFAs, (mostly linoleic acid, LA), to n-3 PUFAs (mostly α -linolenic acid, ALA), spurred controversies on whether it would be appropriate to set any particular ratio of n-6 PUFA to n-3 PUFA. *Simopoulos* reported that the ratio of n-6 PUFA to n-3 PUFA ranged from 2:1 to 1:1 [16], in the traditional Mediterranean diet, compared to about 15:1 in the usual European diet and 16.74:1 in the Northern American diet.

Likewise a study by *Renaud* concluded that the metabolic balance of LA and ALA requires this ratio to be in the range of 3-5:1 [13]. Both LA and ALA compete for the same enzymes during their conversion into thromboxanes, leukotrienes, and prostacyclin. A high dietary intake of LA inhibits metabolism of ALA, resulting in the formation of thromboxanes and leukotrienes with potent prothrombotic and proinflammatory properties, which promote development of atherosclerosis and its arising complications.

These conclusions were nevertheless questioned by other authors. Effective reduction in the dietary ratio of n-6 PUFA to n-3 PUFA would require limiting the intake of n-6 PUFAs and increasing the intake of n-3 PUFAs. Experts from the American Heart Association believe that n-6 PUFA intake should provide 5% to 10% of total calories and any reduction in n-6 PUFA intake, compared to the current values, might increase rather than decrease IHD risk [7]. Such discordant views thereby indicate that this issue is still open for debate and requires further studies to resolve the matter.

The recommendation to limit SFA intake to less than 10% of total calories has also proved controversial. Current SFA intakes in non-Mediterranean European and Northern American countries are higher than this set level. Reducing SFA intake is recommended as a means to limit the epidemic of atherosclerotic cardiovascular disease, based on the notion of pro-atherogenic effects of SFA. Meta-analyses for studies published in recent years on cardiovascular disease incidence and mortality in relation to SFA intake, however cast some doubts on the usefulness of the advice for limiting consumption of SFA in the prevention of these diseases [8, 17, 18, 19, 20]. In particular, Siri-Tarino et al expressed the view that clear evidence of the relations between SFA intake and cardiovascular disease are lacking [19]. Nevertheless, they admitted that epidemiological studies and randomised clinical trials indicate that substituting saturated fats with unsaturated fats, in contrast to carbohydrates, is beneficial in the prevention of IHD [20].

CURRENT REFERENCE INTAKES FOR DIETARY FATTY ACIDS AND THE EMERGING NEED FOR A MORE ACCURATE DEFINITION

The studies of *Siri-Tarino* et al and their conclusions have been heavily criticised by *Stamler* who is one of the pioneers for researching the role of nutrition in preventing atherosclerosis [21]. He stated unequivocally that reduction of SFA intake to 6-7% of total calories in the context of a rationally balanced diet is merited.

A later report, from 2010, of the Joint FAO/WHO Expert Consultation on Fats and Fatty Acids in Human Nutrition attempted to clarify opinions regarding these controversial issues [5]. Here it clearly states that there is convincing evidence that dietary substitution of PUFAs for SFAs reduces the risk of IHD. It was also considered likely, that substituting SFAs with carbohydrates (mostly in the form of refined sugars) has no beneficial effect on IHD and may even increase its risk. In addition, such a dietary modification probably promotes the development of metabolic syndrome. Thus, no clear statement has been offered on the usefulness of limiting SFA intakes, although this is indirectly supported by the observed benefits of substituting PUFAs for SFAs. Of note, this report also reiterated the previous recommendation of FAO/WHO experts to reduce SFA intakes to 10% of total calories.

A tabularised version of the 2010 FAO/WHO report recommendations on fatty acid intakes is provided (Table 1), keeping in mind some of the contrary statements made regarding their levels. consumption were found to be identical with the FAO/ WHO recommendations. The lowest possible intakes of SFA and TFA were recommended but no specific recommendations were provided for overall MUFA and PUFA intakes. The adequate intake (AI) of LA was defined as being 4% of total calories and an AI of ALA as 0.5% of total calories. For the total intakes of eicosapentaenoic acid and docosahexaenoic acid (i.e. EPA+DHA), the AI was defined as being 250 mg/day. Nutritional guidelines provided for the Polish population, that were updated in 2012, were found to be consistent with these EFSA recommendations [11].

It is noteworthy that any need for calculating the dietary ratio of n-6 PUFAs to n-3 PUFAs has not been referred to in neither the FAO/WHO report nor the EFSA recommendations, despite this ratio being low in the Mediterranean diet which is considered by many authors to be an optimal nutritional approach in Europe. In light of some theoretical considerations, this ratio may reflect important beneficial health effects of the Mediterranean diet. Connected to this, a recent randomised controlled study of note by Ramsden et al [12] on patients after myocardial infarction, evaluated the effect of partial dietary substitution of SFA with LA on the mortality rates due to CVD. An increased total, cardiovascular, and IHD mortality was demonstrated in the intervention group compared to controls, during the 39 month median period of follow-up. This is the first literature report indicating an unfavourable effect of dietary substitution of LA for SFA, thus casting doubt whether it is prudent to replace SFA-rich fats with oils and margarines with high LA content. The authors suggested that previous reports of CVD risk reduction,

Fat/FA	AMDR	U-AMDR	L-AMDR	AI	EAR	UL
Total fat	20-35% E	35% E	15% E			
SFA		10% E				
PUFA-total	6-11% E	11% E	6% E	2.5-3.5% E		
PUFA n-6 (LA)	2.5-9% E			2-3% E	$2\pm0.5\%$ E	
PUFA n-3 (ALA)	0.5-2% E		> 0.5% E			
$(EPA + DHA)^{a}$	0.25-2 g/d					
MUFA	by difference ^b					
TFA ^c						< 1% E

Table 1. Recommended dietary intakes for adults (according to 2010 FAO/WHO report [4])

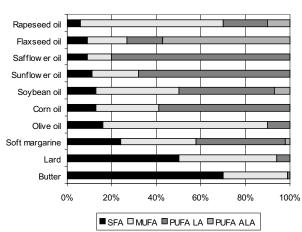
^a in secondary prevention;

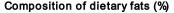
^b can be up to 20% E;

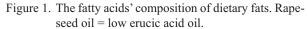
^c trans-fatty acids from ruminant and industrially produced sources;

Abbreviations: AMDR – acceptable macronutrients distribution range; U-AMDR- upper value of AMDR; L-AMDR- lower value of AMDR; AI – adequate intake; EAR – estimated average requirement; UL- tolerable upper intake level; % E – percent of energy; FA – fatty acids; SFA – saturated fatty acids; PUFA n-6 (LA) – n-6 polyunsaturated fatty acids, linoleic acid; PUFA n-3 (ALA) – n-3 polyunsaturated fatty acids, α -linoleic acid; EPA – eicosapentaenoic acid; DHA – docosahexaenoic acid; MUFA – monounsaturated fatty acids; TFA – trans-fatty acids.

Notwithstanding, somewhat different values were proposed by the European Food Safety Authority (EFSA) in 2010 [4]. Recommendations on total fat following substitution of SFA with PUFA, might have been related to the beneficial effects of n-3 PUFAs.







Abbreviations: SFA – saturated fatty acids; MUFA – monounsaturated fatty acids; PUFA LA – n-6 polyunsaturated fatty acids, linoleic acid; PUFA ALA – n-3 polyunsaturated fatty acids, α -linoleic acid.

(Data from: *H. Kunachowicz* et al: Food Composition Tables. PZWL, Warsaw 2005)

CHOICE OF DIETARY FATS IN THE PREVENTION OF CVD

The presented review of available evidence indicates that appropriate selection of dietary fat plays a vital role in preventing atherosclerotic CVD. Fats that have the lowest possible SFA content but large n-3 PUFA levels should be preferred. Figure 1 indicates that oils with these characteristics include rapeseed and flaxseed oil. The former contains the lowest amount of SFA and a relatively large amount of n-3 PUFA. One tablespoon of rapeseed oil contains enough ALA to provide the recommended daily intake (RDI). The ratio of n-6 PUFA to n-3 PUFA in this oil is 2:1, identical to that found in the Mediterranean diet. Rapeseed oil is relatively stable and may be consumed both cold and after a one-time heating during food processing.

Flaxseed oil has somewhat higher SFA levels and its ALA content is the highest of all edible oils, with a very low LA : ALA ratio. It is however, less stable than rapeseed oil. As reported by *Tańska* et al. the potential stability of flaxseed oil compared to rapeseed oil is threefold lower, with the actual stability in the thermal degradation test being twice lower, [24]. For this reason, rapeseed oil is considered more appropriate for shortterm heating during food processing; e.g. for frying. The benefits of a regular daily consumption of flaxseed oil in preventing atherosclerosis nonetheless remain yet to be established. Soybean oil contains significant amounts of ALA but also has high amounts of LA and a higher content of SFAs compared to rapeseed oil. Other oils contain only small amounts of ALA.

ROLE OF THE MEDITERRANEAN DIET IN PREVENTION OF CVD

As mentioned earlier, guidelines for an optimal diet to reduce the risk of CVD, some cancers, and diabetes were published by WHO. These recommendations not only include making appropriate choices of dietary fat but also limiting intake of refined sugars and sodium as well as increasing the intakes of fruit, vegetables, whole grains and nuts; such a diet essentially being the traditional Mediterranean diet. Low CVD mortality in Mediterranean countries has been widely recognised and evidence of its benefits in the secondary prevention of IHD was provided by the Lyon Diet Heart Study [10]. A recent prospective study in Spain [3] for evaluating the Mediterranean diet's efficacy in primary prevention, was undertaken on 7447 men and women aged 55-80 years; all with a high CVD risk and who were randomised into three nearly equal study groups. Subjects in the first group were assigned to a Mediterranean diet enriched with extra virgin olive oil, those in the second group were assigned to a Mediterranean diet enriched with nuts and the third group consumed a reduced-fat diet (i.e. a control group). Overall, during the 4.8 year median duration of follow-up, there were 288 myocardial infarctions, strokes and cardiovascular death. The hazard ratios for cardiovascular mortality and morbidity in the first and second groups were respectively 0.7 and 0.72 when compared to controls.

It should nonetheless be stressed, that the preventive efficacy of an enriched Mediterranean diet was demonstrated in a country where such diets are prevalent and customarily eaten. Adopting the Mediterranean diet in non-Mediterranean European and Northern American populations (given their distinct and different dietary habits) may prove to be even more beneficial. Popularising the diet in these countries however requires some adaptations to local dietary habits; in particular regarding the choice of dietary fat. Olive oil, which is a typical component of the Mediterranean diet is more expensive in these countries than other fats usually consumed. In contrast, the less expensive rapeseed oil has highly beneficial characteristics, with its large content of ALA and LA in the recommended proportion, small SFA content and significant MUFA content. It also contains large amounts of natural antioxidants that have an important role in preventing atherosclerosis.

In Poland, rapeseed oil is especially useful for adapting to a Mediterranean diet. The CVD mortality

trends in this country had been rising until 1991 after which large falls had been recorded up to the present [26]; applying equally to both women and men. Concomitant with this decrease, an improvement in the nutrition of the Polish population was seen [22, 28, 30]. During 1989-2002, the consumption of animal fats was markedly reduced whilst that for vegetable oils rose. Decreased consumption of red meat was also coupled with a rise in poultry consumption. In addition, the eating of fruit increased. It should be stressed that rapeseed oil accounts for 80% of all oil consumed in Poland and similar findings have been observed in many other countries of Eastern Europe. *Zatonski* et al has hypothesised that they may be dependent on the increased consumption of α -linoleic acid [29].

In Poland, the decreasing trend of animal fat consumption stopped in 1995, whilst in 2002 the end of the increase of vegetable oil consumption was noted. In similar fashion, the positive trends in meat and fruit intakes were also halted. It is significant that since 2005, the decreasing CVD mortality rates stopped in younger population groups, and that rates of decrease were reduced in persons aged 60 years and over [23]. The former observation can be attributed to stabilization of changes in model of nutrition. In the elderly population, reduced rates of mortality decrease result probably from popularization of statin treatment in individuals with increased risk of coronary heart disease, and also from improvement of cardiological treatment.

CONCLUSIONS

In order to prevent cardiovascular disease, vegetable oils with low amounts of saturated fatty acids but high contents of α -linoleic acid should be preferred in the diet of northern countries.

Conflict of interest

The authors declare no conflict of interest.

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