TRANS FATTY ACIDS AND THEIR ROLE IN INFLAMMATION AND CARDIOVASCULAR DISEASE

Streszczenie

Kwasy tłuszczowe trans (TFA) nie są syntetyzowane w organizmie człowieka, ale są obecne w wielu produktach żywnościowych. Badania wykazały, że wysokie spożycie TFA nie jest związane z ryzykiem chorób metabolicznych. Opisano dodatnią korelację między zwiększonym spożyciem TFA a ryzykiem choroby niedokrwiennej serca, jak również inicjacją i rozwojem miażdżyca.

W pracy przedstawiono źródła w diecie i wpływ TFA na proces miażdżycowy.


Summary

Trans fatty acids (TFAs) are not synthesized in the human body but are found in many food products. Several reports have shown that high consumption of TFA is unrelated to the risk of metabolic diseases. Increased consumption of TFAs was reported to be positively correlated with risk of ischemic heart disease, as well as with initiation and progression of atherosclerosis.

This work focuses on dietary sources and effects of TFA on the atherosclerotic process.

Intake and dietary sources of trans fatty acids

Trans fatty acids (TFAs) are found in many food products, some of them consumed by man since thousands of years. It was only in the last century that their share in human nutrition increased dramatically [1] following the introduction of hardened vegetable oils (margarines) into the diet. When experimental, epidemiological, and clinical studies began to uncover the adverse effects of TFAs on the human body, action was undertaken to restrict their content in food products. During 2 years (2005–2007), TFA levels in some food products sold in Canada decreased from 26 ± 13% to 2 ± 4% (mean ± SD) and 72% of a total of 221 products was reformulated to decrease the content of trans and saturated fatty acids (TFA + SFA) and increase cis unsaturated fat [2]. The food industry in the USA also made progress in reducing TFA levels in food products such as margarines and butters, cookies and snack cakes, and savory snacks. Unfortunately, some food products with decreased TFA + SFA content turned out to be more expensive and thus rejected by the price-conscious consumer [3]. It is known today that the intake of industrially hydrogenated TFAs in
many countries is declining as a result of reduced content of man-made trans fatty acids in foods and changes in consumer choices [2, 4, 5].

Current sources of information indicate that the greatest consumption of TFAs occurs in Iran (12.3 g/day) and North America (3–4 g/person as estimated from food frequency questionnaires or more than 10 g/person as estimated by extrapolation of human milk data). In Europe, intake of TFAs ranges from 1.4–2.1 g/day in Italy, Portugal, Greece, and Spain to 2.1–5.4 g/day in Germany, Finland, Denmark, Sweden, France, United Kingdom, Belgium, Norway, The Netherlands, and Iceland. Differences in European countries reflect dietary habits. Mediterranean countries, where olive oil is widely used, are notable for increased cis instead of trans and saturated fatty acid content [5, 6]. All in all, there are three main dietary sources of trans isomers: milk products, beef fat (hydrogenation of unsaturated fatty acids in the stomachs of ruminants by enzymes of the bacterial flora), and hardened vegetable fats (chemical hardening during industrial processes).

The quantity of TFAs accumulating in the adipose tissue of animals is relatively small, reaching 6% of all fatty acids. Sixteen- and eighteen-carbon positional trans isomers with a double bond at C10–C14 predominate. The main trans isomer in animal fat is monounsaturated octadecenoic acid (vaccenic acid: trans-11 C18:1) constituting almost 70% of all trans monounsaturated acid isomers in milk fat [1, 4, 7, 8] (tab. 1). Besides trans isomers of octadecenoic acid, small amounts of trans palmitoleic acid (trans-C16:1) and trans isomers of linoleic acid (cis, trans-C18:2, trans, cis-C18:2) are found in cow’s milk. Negligible amounts of trans isomers of C14:1, C15:1 and C17:1 have also been identified [9, 10, 11]. The content of trans isomers in milk and milk products is nevertheless small, not exceeding 2.5–8% according to various sources.

<table>
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<tr>
<th>Table 1. Trans fatty acids content in common foods</th>
<th>Tabela 1. Zawartość izomerów trans kwasów tłuszczowych w żywności</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product</strong></td>
<td><strong>Main isomer</strong></td>
</tr>
<tr>
<td>Milk products Nabiał</td>
<td>trans-11 C18:1 (vaccenic acid kwas wakcenowy)</td>
</tr>
<tr>
<td>Beef meat Wołowina</td>
<td>trans-11 C18:1</td>
</tr>
<tr>
<td>Light margarine Margaryna niskotłuszczowa</td>
<td>trans-9 C18:1 (elaidic acid / kwas elaidynowy)</td>
</tr>
<tr>
<td>Hard margarine Margaryna wysokotłuszczowa</td>
<td>trans-9 C18:1</td>
</tr>
<tr>
<td>Soups, sauces Zupy, sosy</td>
<td>trans-9 C18:1</td>
</tr>
<tr>
<td>Sweets / Slodycze</td>
<td>trans-9 C18:1</td>
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</table>

Fluctuations in TFA content in milk and milk products are associated with the type of fodder.

Today, like in the past, the main dietary source of TFAs are margarines which may contain up to 50% TFAs. The use of new oil hardening techniques resulted in a significant elimination of TFAs from food products [1, 4, 12]. Apart from margarines, other chief dietary sources of TFAs include bakery products, deep-fried foods, and confectionery fats which contain trans fatty acids in amounts reaching 40–50% of all fatty acids. The contribution of milk, dairy products, and meats to the dietary intake of TFAs is estimated at 10–30% [4, 9].

The main representatives of TFAs in margarines are trans-9 elaidic acid (trans-9 C18:1, trans bond at carbon 9) and trans-11 vaccenic acid (trans-11 C18:1, trans bond at carbon 11). Trans isomers of di- and triunsaturated fatty acids are found in trace quantities, being mainly limited to isomers of linoleic acid (mostly trans-9, trans-12 linoleaidic acid C18:2) [13, 14]. The content of trans isomers in margarines is quite variable and depends on the hardening conditions of the oil. The majority of light margarines (used as bread spreads) contain no more than 10% trans isomers. However, hard margarines (used for frying) reveal a much higher TFA content which may even reach 50% of the fatty acid pool [4].

**Absorption of trans fatty acids**

Glycerol esters containing trans isomers are hydrolyzed by pancreatic lipase and are incorporated into chylomicrons after resynthesis of triacylglycerols. Together with chylomicrons, TFAs are transported into the circulatory system where they become substrates of vascular lipase. In humans, absorption of trans isomers of fatty acids is as rapid and efficient as absorption of cis isomers (this correlation applies to mono-, poly-, and di-unsaturated fatty acids). For example, it was found that elaidic acid (trans-9 C18:1) passed into lymph as rapidly as oleic acid (cis-9 C18:1) [15, 16]. Once fatty acids are released and taken up by the cell, trans isomers of fatty acids may be used as an energy source (in the process of β-oxidation) or as a substrate for esterification of glycerol and cholesterol and formation of phospholipids.

The intake of fat containing trans isomers was shown to cause changes in the composition of fatty acids of lipids in all tissues. Trans fatty acids are incorporated into cellular lipids proportionally to their food content. Long-term effects of TFAs after their incorporation into tissue lipids are unknown, but the fact that they occupy the position of cis isomers may raise concern. In animals fed partially hardened vegetable oils, the content of elaidic acid (trans-9 C18:1) in phospholipids isolated from myocardial mitochondria increased by 20% with a concomitant reduction in cis fatty acid content. Incorporation of TFAs into cellular membrane phospholipids changes some of their...
properties, like liquidity, permeability, and number and activity of receptors [17]. This phenomenon is attributed to properties of cis and trans fatty acids: cis isomers confer liquidity to biological membranes, while trans isomers with a linear structure resembling that of saturated fatty acids add rigidity to the membrane structure. Trans fatty acids also change molecular dynamics, thermotropic phase behavior, “fluidity”, lateral mobility, and permeability of membranes [18].

Like other fatty acids, TFAs may be stored in human adipose tissue (subcutaneous and perivisceral) after incorporation into triacylglycerols. Because TFAs are not synthesized in the human body, their concentration in fatty acids reflects personal dietary habits. Concentrations of the most common dietary monounsaturated TFAs (with 18 carbon atoms) in the adipose tissue of healthy persons is 0.5–2.5%. It should be of interest that the content of TFAs in human tissues has changed during the last two decades. Pioneering studies have shown that the content of TFAs stored in adipose tissue and in atherosclerotic arterial walls today may reach 12% and 8% of the content of all fatty acids, respectively [15]. This clearly contrasts with 4% in the adipose tissue and 3% in the aorta noted at the end of the 1980s.

An interesting conclusion was made from data on the distribution of TFAs in foods and human tissues: trans isomers contained in human tissues have originated from hardened vegetable fats and only to a minimal extent from butter and other animal fats [16, 19, 20, 21]. However, it must be remembered that non-nutritional factors, such as absorption, metabolism, genetic determinants, and lifestyle have their share in modifying the accumulation of fatty acids in tissues [22, 23]. Long-term effects of the diet on TFA composition of the body can conveniently be studied by monitoring TFA concentrations in erythrocytes which have a long half-life (120 days) compared to plasma lipoproteins [23, 24]. Nevertheless, the effects of long-term intake of TFA by humans are difficult to evaluate. In the case of coronary heart disease, there are several factors which may play a significant role and thus require particular attention.

Trans isomers of fatty acids may cause deficiencies in essential fatty acids of the body

It was observed that animals on a diet containing hardened vegetable fats had symptoms characteristic for essential fatty acids (EFA) deficiency [17]. Essential unsaturated fatty acids (linoleic acid and α-linolenic acid) are used for further metabolic reactions (e.g. syntheses of eicosanoids) exclusively as cis EFA isomers. Essential fatty acids trans isomers are solely used as a source of energy for the cell and are devoid of all other properties of EFA. In the human body, EFA undergo further transformations like chain elongation and introduction of additional double bonds (desaturation) [25].

Linoleic acid (cis-9 cis-12 C18:2) is converted to its respective metabolites through a series of alternating desaturations and elongations (to C22:5 – not shown) – figure 1. Trans fatty acids may disrupt these pathways at points denoted by asterisks. Dietary linoleic acid and arachidonic acid are incorporated into membrane phospholipids. Arachidonic acid is predominantly released from phospholipids by phospholipase A2. Free arachidonic acid (C20:4) is rapidly converted to endoperoxides: 15-hydroperoxy-9α, 11α-peroxido-5-cis-13-trans prostadienoic acid (PGG3) and 15-hydroxy-9α, 11α-peroxido-5-cis-13-trans prostadienoic acid (PGH3). Arachidonic acid is converted to thromboxane A2 (TXA2) in platelets. In endothelial cells, PGH3 is converted to a potent antiaggregatory and vasodilator compound – prostacyclin I1 (PGL1). Free arachidonic acid is metabolized by tissue lipoygenase to hydroperoxyeicosatetraenoic acid (HPETE) which is rapidly converted to hydroxyeicosatetraenoic acid (HETE) – figure 2.

Trans fatty acids act as inhibitors of Δ5-desaturase and Δ6-desaturase which are necessary for the initiation of transformation of polyunsaturated fatty acids of the n-3 and n-6 families into eicosanoids (physiologically active prostaglandins, thromboxanes, and leukotrienes) [26, 27]. Inhibition of desaturase activity (particularly Δ5-desaturase) increases the body’s requirements for EFAs and contributes to an increase in blood cholesterol level raising the risk of atherosclerosis and ischemic heart disease [28, 29]. Studies in rats have demonstrated that EFA deficiency resulting from a diet rich in TFAs can effectively be prevented by increasing the share of EFAs in everyday nutrition. It was estimated that an increase in the dietary content of linoleic acid to 2% of the total quantity of fatty acids is enough to prevent EFA deficiency. In situations when the consumption of trans isomers is very high, the content of linoleic acid in the diet should be proportionally increased up to as much as 5% of the total quantity of fatty acids [30].

Trans isomers of fatty acids as substrates undergoing desaturation and elongation may replace cis isomers in metabolic pathways. It is known that TFAs administered to animals with fodder lower the content of arachidonic acid in cellular membrane lipids. Concern has been raised that TFAs may affect the activity of enzymes synthesizing eicosanoids. For example, linolelaidic acid (trans-9, trans-12 C18:2) inhibits the elongation of linoleic acid to arachidonic acid through inhibition of Δ6-desaturase activity. In this manner, linolelaidic acid reduces the quantity of arachidonic acid in the cell which leads to lower availability of this acid for further transformations, e.g. to prostanoids and thromboxanes.

The entry of trans isomers into desaturase pathways results in the formation of atypical compounds which are different from those acting as natural precursors of eicosanoids. One such compound, arachidonic acid containing trans bonds, was found in the tissues of rats given trans isomers of fatty acids (cis-9 and trans-12 C18:2 and trans-9, cis-12 C18:2) with their chow [17, 31].
Dietary linoleic acid cis-9 cis-12 C18:2
Kwas linolowy cis-9 cis-12 C18:2 w pokarmie

Acylase/deacyla
Acylaza/deacyla

6 desaturase*
6 desaturaza*

Gamma-linolenic acid C18:3
Kwas gamma-linolenowy C18:3

Membrane phospholipids*
Fosfolipidy bonowe*

Elongase*
Elongaza*

5 desaturase
5 desaturaza

PGE₁, PGF₁
Dihomo-gamma-linolenic C20:3
Kwas di-homo-gamma-linolenowy C2:3

Lipoxygenase*
Lipoksigenaza*

PGE₂, PGF₂
Arachidonic acid C20:4
Kwas arachidonowy C20:4

Cyclooxygenase*
Cykloksigenaza*

PGG₂-PGH₂
HPETE

HETE

PG₂, PGF₂
TXA₂
PGI₂

6 keto PGF₁

TXB₂
Heptadecatrienoic acid & MDA
Kwas heptadekatrienowy i MDA

MDA – malondialdehyde / aldehyd dimalonowy

Fig. 1. Metabolic pathway of linoleic acid (n-6) – modified from Kinsella et al. [17]

Ryc. 1. Szlak metaboliczny kwasu linolowego – modyfikowany przez Kinsella i wsp. [17]

Fig. 2. Trans fatty acids affect the activity of eicosanoid synthesizing enzymes in platelets

Ryc. 2. Izomery trans kwasów tłuszczowych zaburzają aktywność enzymów syntetyzujących ekozanoiidy w płytkach
Studies in animal models have revealed that reduced synthesis of eicosanoids will not be observed in animals consuming TFAs [12, 17]. Even relatively large amounts of TFAs in the diet of rats did not have any negative effects on the activities of enzymes synthesizing eicosanoids (lipoxygenases and cyclooxygenases) in liver microsomes and blood platelets. It should be emphasized that this correlation was observed in animals with sufficient amounts of linoleic acid in their diet. On the other hand, it is not known what the effect of TFAs would be on the synthesis of eicosanoids if the animals were on a diet containing an insufficient amount of linoleic acid [17].

In vitro studies conducted in human platelets have disclosed that TFAs inhibit the activity of 12-P lipoxigenase and cyclooxygenase, two platelet enzymes involved in the synthesis of eicosanoids. In this manner, TFAs directly contribute to reduced synthesis of thromboxane B<sub>2</sub> (TXB<sub>2</sub>) and 12-S-hydroxyeicosatetraenoic acid (12-S HETE) [17]. Based on these results it may be concluded that TFAs (through changes in the amounts of hydroxyacids) may contribute to a change in the activity of nuclear peroxisome proliferator-activated receptors (PPARs) [32]. Three mammalian PPARs, α, δ, and γ, have been isolated from human cells. Peroxisome proliferator-activated receptors are members of the nuclear hormone receptor superfamily that heterodimerizes with the retinoid receptor X (RXR) and functions as a transcriptional regulator of genes implicated in lipid metabolism and energy balance [31, 32].

**Trans fatty acids reduce cholesterol esterification and enhance cholesterol transport to tissues**

Another aspect of the induction of hypercholesterolemia may be the effect of TFAs on the activity of lecithin cholesterol acyltransferase (LCAT) and on the cholesterol ester transfer protein (CETP) [33]. As demonstrated in studies on acyltransferase conducted in animals, a 9-month diet supplemented with TFAs leads to a significant reduction in LCAT activity in plasma. Lecithin cholesterol acyltransferase activity correlated negatively with serum levels of free cholesterol [34]. Cholesterol ester transfer protein is a glycoprotein participating in the transfer of cholesterol esters from high-density lipoproteins (HDL) to lipoproteins rich in triacylglycerols (residual chylomicrons, VLDL and low-density lipoprotein – LDL). Abnormal transfer of cholesterol esters may contribute to atherosclerosis. It was observed that non-esterified fatty acids can modulate the CETP-mediated transfer of cholesterol esters from HDL to LDL; medium- and long-chain saturated fatty acids significantly increase CETP-mediated transfer from HDL to LDL in a concentration-dependent manner. In a study by Lagrost, oleic acid (cis-9 C18:1) and elaidic acid (trans-9 C18:1) had different effects on CETP-mediated redistribution of cholesteryl esters and on net mass transfer of cholesterol from HDL to LDL. Elaidic acid added to plasma increased CETP activity and reduced HDL-cholesterol levels [33].

**Trans fatty acids increase plasma lipid levels**

An important role in the generation of atherosclerotic lesions is played by LDL molecules [35]. Low-density lipoproteins undergo oxidation reactions in plasma to ox-LDL which are next taken up by scavenging receptors of macrophages and accumulate in these cells transforming them to foam cells, the main component of atherosclerotic plaques. The effect of TFA on plasma lipoprotein content and on the progression of atherosclerosis became the subject of numerous clinical and epidemiological studies. It was suggested that trans isomers administered in food may accelerate the development of atherosclerosis. Many studies have shown that patients with coronary atherosclerosis have an increased share of TFAs in their pool of plasma fatty acids. Pioneering studies conducted by Mensink and Katan revealed the direct effect of dietary TFAs on lipoprotein content in humans [36]. Patients with normal baseline lipid parameters placed for 3 weeks on a diet containing trans isomers (10% of the daily energy intake) demonstrated an increase in LDL-cholesterol and triacylglycerol levels and a decrease in HDL-cholesterol levels in plasma [36]. Even when the content of trans isomers in food was reduced to 8% of the daily energy intake, a significant increase in LDL levels and a reduction in HDL levels in plasma was noted [37, 38]. The same results were obtained by Sundram et al. with fat providing 3.2% of the energy from TFAs [39].

American studies in 1994 [40] proved that a 6-week diet with a moderate TFA content (6.6%) resulted in increased plasma cholesterol levels. A reduction in the TFA content to 3.8% did not lead to the expected reduction in cholesterol levels. These results indicate that a diet containing TFAs contributes to an increase in plasma LDL-cholesterol levels and to a concomitant reduction in HDL-cholesterol levels. It is interesting that when the effects of dietary TFAs and saturated fatty acids were compared, the latter produced elevated plasma levels of LDL-cholesterol but did not contribute to a reduction in plasma levels of HDL-cholesterol [37]. Changes in LDL- and HDL-cholesterol levels were proportional to the intake of trans isomers in food; when TFAs delivered 5% of the total energy, reductions in HDL-cholesterol levels oscillated around 2.5 mg/dL. The study of Matthan et al. found that the mechanism for the adverse lipoprotein profile observed with hydrogenated fat intake is dependent in part on increased apoA-I and decreased LDL apoB-100 catabolism [41]. In this study, plasma apoA-I levels and pool size were lower, whereas the apoA-I fractional catabolic rate (FCR) was higher on hydrogenated fat compared to the saturated fat diet. Low-density lipoprotein apoB-100 levels and PS were significantly higher and LDL apoB-100 FCR was lower.
in the case of saturated and hydrogenated fat diets compared to the unsaturated diet [35]. In addition, TFAs may damage LDL-receptors, leading to hypercholesterolemia and atherosclerosis.

Different effects were observed with ruminant trans fatty acids. Interesting findings were obtained in 2 studies which compared the influence of TFA intake from both ruminant and industrial hardened fat on plasma lipoproteins. Consumption of 11–12 g/day (5% of total energy) rTFA lead to a significant increase in HDL-cholesterol and LDL-cholesterol in women but not in men. Blood apoB and apoA-I levels were in line with changes in the concentrations of HDL and LDL. However, no significant alteration in lipoprotein subclasses after intake of TFA in hardened fat was noted. Trans fat from natural or industrial sources may exert different effects on CVD risk [42]. A study conducted in men showed significantly higher LDL-cholesterol concentrations in plasma using diets with a high content of rTFA (10.2 g/day/2500 kcal) and iTFA (10.2 g/day/2500 kcal) as opposed to diets with a moderate rTFA content (4.2 g/day/2500 kcal) or low in TFA (2.2 g/day/2500 kcal). High-density lipoproteins-cholesterol levels decreased in patients placed on a diet rich in rTFA compared with a diet with a moderate rTFA content [43]. Tricon et al. concluded that dairy products containing cis-9, trans-11 CLA and trans-11 18:1 do not appear to have a significant effect on the blood lipid profile [44].

Trans fatty acids contribute to an increased plasma content of lipoprotein(a)

Lipoprotein(a) – Lp(a) is considered to be an independent risk factor of atherosclerosis. Lipoprotein(a) levels are believed to largely be controlled by genetic factors. Some reports, however, have indicated that the type of fat consumed can alter Lp(a) levels [45, 46, 47, 48]. As documented by Clevidence et al., fatty acids (monounsaturated and saturated) consumed in quantities typical for Western diets (16.7% monounsaturated acids and 16.2% saturated acids) have only a weak effect on Lp(a) levels in plasma [45]. On the other hand, TFAs ingested in relatively moderate quantities (6.6% of all fatty acids in the diet) caused a 5% increase in Lp(a) levels in plasma. The fact that this tendency was observed in a group of patients with initially high levels of Lp(a) is of particular concern [49].

Trans fatty acids may contribute to aggravation of inflammatory reactions

Trans fatty acids are strongly associated with systemic inflammation in patients with heart disease, suggesting that the amount of TFA intake may be important for secondary prevention efforts. In healthy subjects exposed to TFAs in the diet and in patients with established heart failure, TFA levels were positively associated with C-reactive protein (CRP), interleukin (IL) 1 beta, IL-1 receptor antagonist, IL-6, IL-10, tumor necrosis factor (TNF) alpha, TNF receptor 1, TNF receptor 2, monocyte chemoattractant protein 1 (MCP-1), E-selectin, soluble cell adhesion molecules (sICAM-1 and sVCAM-1), and brain natriuretic peptide levels [50, 51, 52, 53, 54]. It is worth noting that inflammation leads to increased production of 3 radicals which may target lipids esterified to cellular membrane phospholipids and generate toxic oxidized lipids leading to alterations in biochemical processes. Lipid peroxidation induced by nitrogen dioxide radical (*NO2) or its precursors (peroxynitrite, nitrous acid, nitrogen trioxide) is known to involve arachidonic acid cis double bonds producing four trans isomers of arachidonic acid (nitrooicosanoids). Products formed from peroxidation of arachidonic acid are structurally similar to enzymatically derived prostaglandins and leukotrienes (isoeicosanoids). Inflammation is associated with NO formation and increased TAA levels in cells, tissues, and systemic circulation. Clinical consequences of this diet coinciding with endogenous biosynthesis of trans fatty acids are unknown [54, 55].

Trans fatty acids, atherosclerosis, and risk of coronary heart disease

It is estimated that more people die annually from CVDs than from any other cause. In 2005, 17.5 million people died from CVDs (30% of all global deaths) including 7.6 million who died because of coronary heart disease and 5.7 million who suffered stroke. Unhealthy diets, physical inactivity, and tobacco use are the main causes of heart disease and stroke [56].

Atherosclerosis is a chronic pathologic process. It is generally accepted that lipids together with coagulation and inflammatory factors play an important role in plaque formation. It seems that increased intake of margarines rich in TFAs is associated with increased risk of myocardial infarction [50]. Studies comparing TFA content in the myocardium and the aortal wall failed to reveal any accumulation of these isomers in persons who died as a result of cardiovascular disorders [19]. In addition, TFA content in the adipose tissue of patients with clinical symptoms of coronary atherosclerosis and post-myocardial infarction did not significantly differ from TFA content in the adipose tissue of persons without symptoms of atherosclerosis [20, 21, 22, 57]. Nevertheless, metabolic studies in Australia have clearly shown that trans fatty acids lead to atherosclerosis. In one study conducted between 1995 and 1997, links between adipose tissue levels, dietary intake of TFA, and first myocardial infarction were examined. During the study, TFAs were eliminated from margarines sold in Australia [22]. Cases biopsied before mid-1996 had greater levels of trans-9 elaidic acid (32%) and trans-11 vaccenic acid (23%) than controls biopsied before mid-1996. After June 1996, there were no differences between cases and controls in any adipose tissue TFA measured. The authors found that trans...
Vaccenic acid was an independent predictor of the first MI. Additionally, TFAs in adipose tissue were associated with an increased risk of coronary artery disease. When TFAs were excluded from margarines, they rapidly disappeared from adipose tissue [50, 58, 59]. As evidenced by recent studies, TFAs may accumulate to a level of 0.1% in atherosclerotic plaques. Monounsaturated elaidic acid (trans-9 C18:1) is the main trans isomer in plaques. Small amounts of acids with two double bonds, i.e. linoleic acid (trans-9, trans-12 C18:1) and isomers of conjugated dienes of linoleic acid are also present [60]. Coronary heart disease (CHD) may be caused by arteriosclerosis-related hypertension, diabetes, tobacco smoking, elevated homocysteine concentrations, elevated concentrations of LDL and Lp(a), and reduced concentrations of HDL [37, 38, 45, 46, 47]. The effect of dietarycis and trans fatty acids on serum Lp(a) in primary hypertriglyceridemia has been reported [36, 46, 49]. Fatty acids and cholesterol in food are known to modify concentrations of lipoproteins in blood, increasing the risk of CHD. Research shows that a diet rich in elaidic acid (trans-9 C18:1) adversely affects the lipid profile, increasing LDL and Lp(a) and decreasing HDL concentrations [36, 45, 47, 48]. In the Nurses’ Health Study, daily intake of trans fatty acids (approx. 5.7 g) increased the risk of CHD by 50% compared to the group consuming approximately 2.4 g/day [61]. The positive correlation between TFA consumption and incidence of CHD was also revealed by Pietinen et al. [62] and other authors [63, 64]. However, no such correlation was found in Native Americans in spite of their average daily intake of 4.9 g TFA [65]. Pedersen et al. observed higher concentrations of trans fatty acids, α-linolenic acid, and linoleic acid, and lower concentrations of long-chain n-3 fatty acids in the subcutaneous adipose tissue of patients after a myocardial infarction compared with the control group [65]. It appears that C18:2t have a greater influence on the risk of CHD than C18:1t [23, 24, 66, 67].

According to Canadian studies, an additional 1 g/d intake of trans fat (estimated with a quantitative food-frequency questionnaire) was associated with a 0.03 mm increase of coronary artery disease. When TFAs were excluded from margarine, they rapidly disappeared from adipose tissue [50, 58, 59]. As evidenced by recent studies, TFAs may accumulate to a level of 0.1% in atherosclerotic plaques. Monounsaturated elaidic acid (trans-9 C18:1) is the main trans isomer in plaques. Small amounts of acids with two double bonds, i.e. linoleic acid (trans-9, trans-12 C18:1) and isomers of conjugated dienes of linoleic acid are also present [60]. Coronary heart disease (CHD) may be caused by arteriosclerosis-related hypertension, diabetes, tobacco smoking, elevated homocysteine concentrations, elevated concentrations of LDL and Lp(a), and reduced concentrations of HDL [37, 38, 45, 46, 47]. The effect of dietary cis and trans fatty acids on serum Lp(a) in primary hypertriglyceridemia has been reported [36, 46, 49]. Fatty acids and cholesterol in food are known to modify concentrations of lipoproteins in blood, increasing the risk of CHD. Research shows that a diet rich in elaidic acid (trans-9 C18:1) adversely affects the lipid profile, increasing LDL and Lp(a) and decreasing HDL concentrations [36, 45, 47, 48]. In the Nurses’ Health Study, daily intake of trans fatty acids (approx. 5.7 g) increased the risk of CHD by 50% compared to the group consuming approximately 2.4 g/day [61]. The positive correlation between TFA consumption and incidence of CHD was also revealed by Pietinen et al. [62] and other authors [63, 64]. However, no such correlation was found in Native Americans in spite of their average daily intake of 4.9 g TFA [65]. Pedersen et al. observed higher concentrations of trans fatty acids, α-linolenic acid, and linoleic acid, and lower concentrations of long-chain n-3 fatty acids in the subcutaneous adipose tissue of patients after a myocardial infarction compared with the control group [65]. It appears that C18:2t have a greater influence on the risk of CHD than C18:1t [23, 24, 66, 67].

According to Canadian studies, an additional 1 g/d intake of trans fat (estimated with a quantitative food-frequency questionnaire) was associated with a 0.03 mm higher IMT (carotid artery intimal medial thickness). This finding proves that greater intake of saturated and trans fatty acids is positively correlated to subclinical atherosclerosis [68, 69]. According to Ghaemremanpour et al., the total TFA content in the adipose tissue of patients with angiographically proven coronary stenosis is higher than in healthy subjects with no history of heart disease. These findings suggest that dietary intake of TFA is associated with increased risk of coronary artery disease [59].

Trans fatty acids increase the instability of atherosclerotic plaques

The study of Naruszewicz et al. has shown that trans fatty acids cause a significant increase in the secretion of metalloproteinase-9, reactive oxygen species, interleukin-6, and tumor necrosis factor. It was concluded that trans fatty acids may contribute to the destruction of endothelial integrity and to increased risk of plaque rupture [69].

References


