The negative effects of hydrogenated trans fats and what to do about them

Fred A. Kummerow*

Department of Bioscience, College of Veterinary Medicine, The Burnsides Research Laboratory, University of Illinois, Urbana, IL 61801, United States

A R T I C L E   I N F O

Article history:
Received 14 July 2008
Received in revised form 23 February 2009
Accepted 7 March 2009
Available online 19 March 2009

Keywords:
Coronary heart disease
Atherosclerosis
Trans fatty acids
Endothelial cells
Coronary arteries
Diet
Unsaturated
Artificial isomers

A B S T R A C T

Partially hydrogenated vegetable oils have been in the American diet since 1900. More than 50 years ago they were found to contain trans fatty acids that were different from natural fatty acids in plant oils and in animal fat. There was growing evidence that the consumption of trans fats have negative health effects, including increasing plasma lipid levels. In 2003, the Food and Drug Administration (FDA) ruled that the amount of trans fat in a food item must be stated on the label after January 1, 2006; food items could be labeled 0% trans if they contain less than 0.5 g/serving.

Since the initial ruling, it is now known that the fatty acids in partially hydrogenated vegetable oil are 14 cis and trans isomers of octadecenoic and octadecadienoic acids that are formed during hydrogenation. They cause inflammation and calcification of arterial cells: known risk factors for coronary heart disease (CHD). They inhibit cyclooxygenase, an enzyme required for the conversion of arachidonic acid to prostacyclin, necessary for the regulation of blood flow.

There have been several reformulations of hydrogenated fat containing varying amounts of trans fatty acids and linoleic acid, an essential fatty acid that is converted to arachidonic acid. Epidemiological data suggest that when trans fat percentages go up and linoleic acid percentages go down, death rates rise; when trans goes down, death rates go down. In spite of the harmful effects of trans fats, the FDA allows it in the food supply as long as the amount in a food item is declared on the label. Trans fat should be banned from the food supply.

© 2009 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

This paper will review the history of hydrogenated trans fat including the identification of their chemical composition and properties leading to its use. It will compare natural trans fat found in ruminant fats, e.g. butter, to those from hydrogenated fat. Studies showing the negative effects of hydrogenated trans fats will be reviewed and epidemiological data presented to further illustrate a concern with the continued usage of these fats. New research on the composition of cis and trans fatty acids and their effect on blood fluidity is included. The Food and Drug Administration (FDA) ruling on trans fat will be explained, and data presented on the limitations of the current ruling. Courses of action such as banning hydrogenated trans fats in its current form and reformulating its composition are suggested.

2. Fats and oils background

Geography first determined which fats and oils were included in the diet: butter, lard and beef tallow in Northern Europe and North and South America, and olive, sesame, sunflower seed and soybean oils in Southern Europe and the rest of the world [1]. No matter the geography or the form, all fats and oils are composed of triglycerides, which is glycerol attached to three fatty acids. If these fatty acids are largely saturated fatty acids, such as stearic acid, they are a solid fat (like butter) at room temperature [2]. If they are attached to an unsaturated fatty acid, such as linoleic or linolenic acid, known as polyunsaturated fatty acids (PUFA), they are an oil (like soybean oil) at room temperature [3]. In the late 1800s, a French chemist [4] discovered that an unsaturated fatty acid can be converted to a saturated fatty acid by bubbling hydrogen through a heated vegetable oil in a closed vessel. If completely hydrogenated, they become stearic acid [5].

The exact fatty acid composition of the hydrogenated oil was essentially unknown until the development of gas chromatography (GC) by James and Martin in 1952 [6]. The FDA, using the AOCS method [7], labeled the isomers in partially hydrogenated fat as only one peak (elaidic acid) [8]. It is only with a GC equipped with a 200 m column that it is possible to further separate the fatty acid isomers of partially hydrogenated fat into at least 14 separate isomeric fatty acids [9].
Using soybean oil as an example, differences between the natural oil and the result of the hydrogenation process is explained below. Soybean oil in its natural form [9] contains 52.5% linoleic (18:2 $\Delta^{9,12}$) acid, which is also known as 18:2n6 or omega-6. It contains 7.5% linolenic (18:3 $\Delta^{9,12,15}$) acid also known as 18:3n3 or omega-3. The designation 18:2 $\Delta^{9,12}$, and 18:3 $\Delta^{9,12,15}$ means that these two fatty acids have double bonds at position 9 and 12 or 9,12 and 15 at which hydrogen can be added. During hydrogenation the double bond at any of these 9,12 or 9, 12, 15 positions can be shifted to form new cis and trans unsaturated fatty acid isomers not present in vegetable oil. The double bond of the cis-natural linoleic and linolenic fatty acids can also change the configuration from cis to trans, creating a geometric isomer like trans $\Delta^{11}$-18:1 vaccenic acid (Fig. 1). Oleic acid, the largest percentage of the natural fatty acid in the human body, is cis $\Delta^{9}$-18:1 (the number after delta indicates the position of the double bond at the carbon atom counting from the carboxyl group). Oleic acid goes through geometrical isomerisation during hydrogenation to trans $\Delta^{9}$-18:1: acid known as elaidic acid; thus the “natural” oleic acid is turned into elaidic acid during the hydrogenation process, and becomes an “unnatural” fatty acid (Fig. 1). It twists into a new form and can be both a cis and/or a trans fatty acid. In addition to geometrical isomerisation, the double bond of either cis or trans fatty acids can theoretically migrate along the 18 carbon chain of oleic, linoleic, and linolenic acid changing their position from $\Delta^{9}$ or $\Delta^{9,12}$ $\Delta^{9,12,15}$ creating 5 monoene cis positional isomers, 6 trans monoene isomers and 3 trans diene positional isomers (9). Thus hydrogenated soybean oil contains 24.1% trans monoens, 6.2% trans dienes and 9.4% cis monoene isomers or a total of 39.7% isomeric fatty acids. They were identified as cis and trans octadecenoic and octadecadienoic isomers on a GC equipped with a 200 m column by their mixed melting points [10] with authentic octadecenoic and octadeca-dienoic acids purchased from Sigma–Aldrich, St. Louis, MO. None of these fatty acids are present in natural soybean oil. For simplicity, the isomers will be referred to as trans fat in this paper whenever possible.

3. The need for essential fatty acids (EFA) in the diet

It was unknown until 1930 that linoleic (18:2n6) and linolenic (18:2n3) acids were EFA [11], and like the nine essential amino acids and the vitamins [12], cannot be synthesized in the human body; they must come from a diet that includes natural fats and oils. The 14 isomers in hydrogenated fat can be used as a source of energy but they cannot substitute for EFA because they do not have the required double bond structure.

EFA are required to synthesize the eicosanoids that are needed to regulate blood flow in the arteries and veins [13]. Linoleic acid (n–6) is synthesized into arachidonic acid and linolenic acid (n–3) is synthesized into eicosapentaenoic acid (Fig. 2). Both in turn are made into prostacyclin or thromboxane. Prostacyclin and thromboxane have to be continually made from the EFA because they last only about 10 s in the blood and thus must be constantly replaced [14]. Prostacyclins are synthesized in the endothelial cells that line the blood vessel wall. Thromboxanes are synthesized in the platelets in the blood [15]. Fish have already converted the linolenic acid they get from seaweed into eicosapentaenoic acid. Hence fish oil is often recommended as a dietary supplement, although as (Fig. 2) indicates, prostacyclin and thromboxane can be made from linoleic acid as well. The least expensive source of omega-3 and omega-6 is soybean oil, which is sold as vegetable oil.

The balance between prostacyclin for flow and thromboxane for clotting is a very delicate one and can be changed by different diets [14] and different drug prescriptions. For example, Coumadin (Warfarin) may be prescribed for those who have heart disease in order to keep their blood from clotting. However, Coumadin plus the natural production of prostacyclin may cause too much bleeding [16]. This can lead to macular degeneration, an eye disease in which the optic nerve is affected, or excessive nose bleeding or internal bleeding. Vitamin K may be recommended when the blood is too fluid, although it is often in the diet, especially in greens. Vitamin K in excess has the opposite effect, creating too much clotting that could lead to heart attacks caused by coronary artery blockages or strokes caused by cerebral (brain) artery blockages [17]. Vioxx, a medication to alleviate the pain of arthritis, was recently withdrawn from the market because of its effect on heart attacks and strokes; it led to too little production of prostacyclin [18].

EFA are also needed for reproduction. Since the 1930s, it was known that reproduction always failed on fat-free diets [19]. In studies on rats, reproduction continued under low fat conditions because the rats had enough linoleic acid stored in their bodies. They synthesized arachidonic acid from the linoleic acid in their own fat, so they could reproduce healthy young even after a fat-free
diet. If the rats did not have enough linoleic acid stored in their bodies (such as rats born to mothers on fat-free diets), they could not make enough of the arachidonic acid needed for healthy reproduction, and their young died. Women need the EFA for reproduction, and the easiest way to supply them is from plant oils [9]. EFA are also necessary for growth and development [20] in other body functions, such as brain activity and vision [21]. Brain cells contain 70% fat including 24% omega-3 and 28% omega-6 fatty acids [22]. Veins and arteries also contain these fatty acids, with the veins of adults containing 5% omega-3 and 6% omega-6 fatty acids [23].

3. Differences between natural and hydrogenated trans fats and their metabolism

Butterfat from dairy cows contains 2–4% trans fatty acid, known as trans vaccenic acid (t\(\Delta 11\)-18:1). It is produced from the linolenic (18:3\(\Delta 6\)) and linoleic (18:2\(\Delta 6\)) acids in the grass fat by the microorganisms' enzymes in the stomach of dairy cows. Natural trans fats are metabolized differently from hydrogenated trans fats.

For example, a study with piglets [24] from mothers fed hydrogenated soybean oil showed that their arteries contained less linoleic acid converted to arachidonic acid than the arteries of piglets from mothers fed butterfat or corn oil. This indicated that the trans fat in hydrogenated soybean oil inhibited the metabolic conversion of linoleic to arachidonic acid. Furthermore, an analysis of the fat embedded in the arteries of the piglets from mothers fed partially hydrogenated soybean oil showed that they contained 3% trans fat incorporated into their phospholipids by 48 days of age. The arteries of piglets from mothers fed butter or corn oil contained only traces of trans fat. The hydrogenated fat used in this study contained 30.3% of trans fat [25]. The butterfat contained only 2–4% of trans present as vaccenic acid (t\(\Delta 11\)-18:1) which was metabolized into conjugated linoleic acid [26]. Vaccenic acid did not inhibit the metabolic conversion of linoleic to arachidonic acid. Epidemiological studies of intake of ruminant trans fat and risk of coronary heart disease (CHD) indicated that the intake of ruminant trans fatty acid was innocuous or even protective against coronary heart disease [27].

Pilgeram has discussed in two reviews the use of fat in the human body [28,29]. The mitochondria in heart smooth muscle cells use fatty acids as a source of energy through oxidative phosphorylation, a process that involves many steps before the mitochondria can use that energy [30]. The trans fatty acid (elaidic acid) in hydrogenated fat metabolized more slowly than the cis oleic acid in unhydrogenated vegetable oil [31,32]. During a heart attack, it is likely that more energy is needed quickly than is provided by the slower metabolizing elaidic acid.

4. Health effects of trans fatty acids in hydrogenated fat

This section discusses several types of studies regarding the health effects of hydrogenated trans fats.

4.1. The negative effect on plasma lipids

There are thousands of papers documenting the effects of trans fat on plasma lipid levels in the blood. The best known are the clinical studies by Katan and others [33–42] in the 1990s that indicated trans fat increased low-density lipoprotein (LDL) levels and lowered high-density lipoprotein (HDL) plasma levels. They focused on the level of LDL and HDL plasma levels in healthy subjects and found that the replacement of 10% of energy from saturated fatty acids by trans fat decreased plasma HDL by 21% and impaired flow mediated vasodilatation as an endpoint in dietary intervention. An increase in LDL plasma concentrations was believed to be a risk factor for CHD.

Studies on CHD during the 1950s and 1960s typically did not consider the percentage of trans fat and the percentage of linoleic acid in the diet as factors in plasma cholesterol levels. One of the most comprehensive studies on the possible role of hydrogenated fat (The National Diet-Heart Study) [43] in heart disease was carried out in 1968. In this study, persons consuming margarine C (with 12% trans fat and 62% linoleic acid) had plasma cholesterol levels 20 mg/lower than those consuming margarine D (with 38% trans fat and only 12% linoleic acid). At the time, this study was interpreted to mean that certain formulations of margarine were healthy since LDL cholesterol levels were lower; however in retrospect, it appears that it was the presence of the linoleic acid that led to these lower cholesterol levels.

4.2. Effect on increasing systematic inflammation

The inflammatory process in the arteries is presently believed to be a risk factor in heart disease, and studies show that hydrogenated trans fats increase the inflammation in the arteries. According to Sun et al. [44], higher levels of trans fat of red blood cells are associated with systematic inflammation and an increased risk of CHD in women. Basu et al. [45] studied dietary factors and their role in inflammation; they found that trans fat promoted low grade inflammation. Lopez-Garcia et al. [46] also believed that consumption of trans fat is related to plasma biomarkers of inflammation and endothelial dysfunction. Their study suggested that the higher intake of trans fat could adversely affect endothelial function.

Several researchers have studied the effects of other dietary factors and inflammation, often through the presence of C-reactive proteins (CRP), which are associated with inflammation. For example, Massaro et al. [47] believed that atherosclerosis was a dynamic process with inflammatory changes in the endothelium of conduit arteries. Furthermore they showed that the presence of omega-3 fatty acids decreased the amount of inflammation. Giugliano et al. [48] researched several dietary strategies included adequate omega-3 fatty acids intake, reduction of saturated and trans fats, and consumption of a diet high in fruits, vegetables, nuts, and whole grains and low in refined grains. Each of these strategies was associated with lower generation of inflammation. Most of the studies using fish oil or pure omega-3 fatty acids supplementation failed to show any effect on CRP levels unless the fish oil supplement was given at a high dose (14 g/day).

Harvey et al. [49] concluded that the presence of inflammation was an independent risk factor for atherosclerosis; sudden death from cardiac causes like diabetes and heart failure may result. They further stated that effects of trans fats may account in part for inflammatory effects on cardiovascular health. Increased levels of the inflammatory biomarker, high-sensitivity CRP, predicted cardiovascular events. Since statins lower levels of high-sensitivity CRP as well as cholesterol, Ridker et al. [50] hypothesized that people with elevated high-sensitivity CRP levels but without hyperlipidemia (high cholesterol levels) might benefit from statin treatment. This randomized trial of apparently healthy men and women who did not have hyperlipidemia but did have elevated levels of high-sensitivity CRP, indicated that the rates of a first major cardiovascular event and death from any cause was apparently reduced among the participants who received rosuvastatin as compared with those who received a placebo [51]. These studies looked at inflammation from a variety of perspectives and provided a link between consumption of trans fats and inflammatory effects.
4.3. Effect on Cyclooxygenase-2 (COX-2) expression

COX-2 is the enzyme that is necessary to make prostacyclin to keep the blood flowing, thus lowering the potential for a heart attack. Mozaffarian et al. [52] calculated the potential effect of reducing the intake of industrially produced trans fatty acids on the incidence of CHD in the United States. They predicted on the basis of changes in total and HDL cholesterol levels alone, a meaningful proportion of CHD events (3–6%) would be averted. However, they believed that this reduction was underestimated, since trans fats may also influence the risk of CHD through other mechanisms, such as inflammatory or endothelial effects. It has also been shown that trans fat inhibited the conversion of linoleic acid to arachidonic acid and inhibited the secretion of prostacyclin [9]. Vane et al. [53] have shown that COX, an enzyme that converts arachidonic acid to prostaglandin H2, is further metabolized to prostanooids. Vane et al. [54] stated two isoforms of COX existed, a constitutive (COX-1) and an inducible (COX-2) enzyme. COX-2 may be the enzyme that recognizes the isomers produced during hydrogenation as a foreign substrate and reacts to them by causing inflammation and inhibition of prostacyclin. COX-2 is the inducible isof orm of COX. COX-1 is present constitutively while COX-2 is expressed primarily after the inflammatory insult. The activity of COX-1 and -2 results in the production of a variety of potent biological mediators (the prostaglandins) that regulate homeostatic and disease processes [55].

4.4. Negative impact on prostacyclin synthesis

The biochemical studies of Holman et al. [56–58] indicated that trans fat inhibited the conversion of linoleic to arachidonic acid. Both the cis and trans fatty acid isomers in hydrogenated fat competitively inhibited the synthesis of arachidonic acid from linoleic acid and eicosapentaenoic acid from linolenic acid. Thus, it may not be only the trans fatty acid isomers, but the cis fatty acid isomers as well that inhibit this synthesis. Holman and co-workers [59] showed how the liver microsomes desaturated the unsaturated 18 carbon fatty acid isomers in hydrogenated fat [59,60]. To desaturate [61] means adding a double bond like the conversion of linoleic acid (18:2n6) to arachidonic acid (20:4n6).

Kummerow et al. [9] carried this a step further with endothelial cells, those cells which are the first layer in the arteries. They cultured endothelial cells in a medium that contained 100 μM of the fatty acids of hydrogenated soybean oil. The cells contained trans fat in their membrane phospholipid and secreted significantly less prostacyclin than endothelial cells that had been cultured with 100 μM of the fatty acids from unhydrogenated soybean oil. These data showed that the incorporation of trans fat from hydrogenated soybean oil into endothelial cell membrane phospholipid inhibited the synthesis of linoleic acid to arachidonic acid and depressed the secretion of prostacyclin (Table 1). They also showed that incorporation of trans fat into the phospholipids fractions of the endothelial cells that line human coronary arteries may depress the secretion of prostacyclin that keep the blood from clotting. Cheng et al. [62] have shown that prostacyclin had a role in the cardiovascular response to thromboxane. The addition of an excess amount of linoleic acid to this hydrogenated soybean oil fatty acids did not increase the secretion of prostacyclin in endothelial cells. The concentration of trans fatty acid rather than the concentration of linoleic acid was therefore responsible for regulating the synthesis and secretion of prostacyclin in endothelial cells. The trans fat in hydrogenated fat not only inhibited the synthesis of prostacyclin that regulated the clotting of blood but also, could not serve as precursors for prostacyclin synthesis. The trans fat “incorporated” into the membrane lipids of blood vessels and muscle tissues and displaced the essential linoleic, linolenic and arachidonic acids [24].

<table>
<thead>
<tr>
<th>Table 1 Prostacyclin synthesis from endogenous arachidonic acid by endothelial cells which had incorporated fatty acids in soybean oil or hydrogenated soybean oil.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatty acid fraction</td>
</tr>
<tr>
<td>Basal</td>
</tr>
<tr>
<td>Total fatty acid of soybean oil</td>
</tr>
<tr>
<td>Monoene fraction of soybean</td>
</tr>
<tr>
<td>oil + 18:2 (3:1)</td>
</tr>
<tr>
<td>38.9 ± 3.1</td>
</tr>
<tr>
<td>2.4 ± 0.5</td>
</tr>
<tr>
<td>14.6 ± 2.0</td>
</tr>
<tr>
<td>9.4 ± 0.4</td>
</tr>
</tbody>
</table>

Results are given as means ± standard deviation of three experiments.

4.5. The association of trans fat with CHD

CHD is due to either atherosclerosis severe enough to block blood flow or to a blood clot due to a lack of prostacyclin secretion in the endothelial cells that line the coronary arteries. Both result in a lack of nutrients to the muscle cells in the heart and they stop functioning. Consumption of trans fat is considered a risk in CHD [33,52]. There is a belief, however, that the negative effects of consuming trans fats can be overcome with consumption of polyunsaturated fats. Oh et al. [63] found an inverse association between polyunsaturated fat intake and CHD risk, and it was strongest among overweight women. In addition, trans fat intake was associated with increased risk of CHD, particularly for younger women [64]. In patients who died from primary cardiac arrest, Lemaître et al. [65] showed an increase of trans fat in their red cell membrane was also accompanied by a decrease of total n-3 fatty acids.

Several researchers have documented the effects of foods without trans fat and their positive effects on lowering CHD. Mozaffarian et al. [66] showed that n–3 PUFAs from both seafood and plant sources may reduce CHD risk, with little apparent influence from background n–6 PUFAs intake. They found lower death rates among those with high seafood and plant-based diets. Plant-based n–3 PUFAs may particularly reduce CHD risk when seafood-based n–3 PUFAs intake was low, which has implications for populations with low consumption or availability of fatty fish [66]. Kris-Etherton et al. [67] found that nuts and peanuts routinely incorporated in a healthy diet with a composite of numerous cardioprotective nutrients reduced the risk of CHD. They also suggested that higher intake of trans fat could adversely affect endothelial function, which might partially explain why the positive relationship between trans fat and cardiovascular risk is greater than one would predict based solely on its adverse effects on plasma lipids.

4.6. Suggested mechanisms that are involved in CHD

Two mechanisms may be involved in CHD: (1) the oxidation of the fatty acids and oxidation of the cholesterol in the LDL; (2) the deposition of trans fat in the cardiovascular system of the veins and arteries. These two mechanisms are outlined in Fig. 3.

When sufficient biological antioxidants are not present [68–76] in the plasma, the LDL is oxidized to oxLDL and cholesterol is oxidized to oxysterol [23,71,72]. Oxysterols incorporated into the endothelial layer of the arteries and veins can change the phospholipid cell membrane composition so that more sphingomyelin...
incorporates into the membrane which becomes “leaky” to calcium infiltration [73]. Oxysterols were present at higher concentrations in the plasma of patients who had coronary artery bypass grafting (CABG) surgery [74]. These patients had 40 times more calcium in their bypassed veins than normal veins in the same patient [75]. When oxysterol purchased from Sigma–Aldrich were added to plasma from patients who did not need CABG surgery, endothelial cells cultured in their blood and tested with radioactive calcium the incorporation of radioactive calcium did not differ from that of plasma from CABG patients [76]. This indicates that oxysterols stimulated calcification. When endothelial cells were cultured with oxysterols in a standard culture media, the cells became calcified in a similar way to those of the CABG patient [23]. The oxidation of cholesterol and deposition of calcium is the primary cause for the development of atherosclerosis in the arteries and veins [71–76].

The second mechanism that may be involved in CHD is trans fat. Trans fat calcifies both the arteries and veins and causes blood clots. As discussed earlier [9,51–54], trans fat inhibits COX-2, an enzyme which converts arachidonic acid to prostacyclin that is needed to prevent blood clots in the coronary arteries [9,51–54,76,77]. A blood clot in any of the coronary arteries can result in sudden death [77,78]. The American Heart Association has stated that 42% of victims of a sudden heart attack do not reach a hospital still alive [79].

To demonstrate the process of calcification, endothelial cells cultured under two conditions showed that trans fatty acid calcify arterial cells. One with a trans fatty acid added as the “unnatural” elaidic acid (18:1n9) and the other with a cis fatty acid added as the “natural” oleic acid (cis 18:1n7) and testing with radioactive calcium. More radioactive calcium infiltration occurred into the endothelial cells cultured with elaidic acid than with oleic acid [77]. An autopsy of 24 human specimens showed that human subjects that had died of heart disease contained up to 12.2% trans fat in their adipose tissue, 14.4% in liver, 9.3% in heart tissue, and 8.8% in aortic tissue and in atheroma [78].

5. Epidemiological data collected by the Center for Disease Control (CDC)

Epidemiological data collected by the CDC further illustrate the potential harmful effects of trans fat [79]. These data showed that, death from CHD in the USA increased from 265.4/100,000 in 1900 to 581/100,000 population by 1950. During this time period, both margarine and shortening had a high percentage of trans fat ranging from 39 to 50% and a low percentage of linoleic acid (ranging from 6 to 11%) according to the technical director of the Institute of Shortening and Edible Oils [80]. In 1968, the President of the Institute persuaded its members to lower the trans fat and increase the linoleic acid content of margarine and shortening. The composition of margarine and shortening was changed in 1968 with trans fats ranging from 20 to 27% and the linoleic acid ranging 24–25%. The death rate from heart disease dropped substantially during the next decades even though the consumption of hydrogenated fat kept increasing and animal fat was decreasing [81] as shown in Fig. 4. Lower trans fat and increased linoleic acid are possible explanations for this change. The death rate from CHD declined [70] after 1968 from 588.8/100,000 to 217/100,000 in 2004. CHD deaths in the USA, according to American Heart Association data [82], were 451,300 in 2004. Heart disease is still the number one cause of death in the USA. In a population of approximately three hundred million, total deaths would have been 1,840,000 in 2008, had the 1950 rate of deaths from CHD continued [83]. Unfortunately, this downward trend may have ended. According to a recent autopsy study of young men [84], the CHD rate has been increasing since 2004. The recent reformulation of partially hydrogenated fat raises the trans fatty acid levels from 20% to almost 40%. Whether the increase in the CHD rate is due to the increase in trans fat in partially hydrogenated fat needs further epidemiology study.

6. The FDA response to trans fat in the diet

6.1. The FDA trans fat labeling ruling did not consider other potential mechanisms leading to heart disease

On July 23, 2003, the FDA issued a directive that required labeling by January 1, 2006 of foods that contain trans fat [85,86]. The FDA based this directive on peer-reviewed articles [33–42]. The FDA’s major concern was the role of trans fat in increasing the plasma cholesterol concentration of LDL. These findings were reviewed earlier in the paper in the plasma lipid level section. The FDA did not consider other factors involved in the development of heart disease and the impact of trans fat in that development. As we previously discussed, these include the effect on prostacyclin, Cox-2, CRP, inflammation and changes in cell structure.

6.2. Failure to differentiate between effects of hydrogenated and naturally occurring trans fats

In 2003, the metabolism of the trans fat in hydrogenated oil was assumed [85,86] to follow the same pathway as the natural ruminant trans fat in butterfat. The FDA has stated [84] that the main reason for the trans fat in partially hydrogenated oil to remain in the diet in the USA rested on the generally held belief that trans fat is metabolized the same way as the natural trans fat in butterfat. A study described earlier comparing the metabolic uses of butterfat versus hydrogenated trans fat showed this not to be true [24]. The FDA allowed the isomeric fatty acids in hydrogenated vegetable oils to remain in food products, because they assumed that some of that
trans may be from the natural vaccenic acid that had no harmful effects. Their figures suggested that approximately 2.6% of the total daily fat intake is from trans fat and that 50% of the trans may be from vaccenic acid (18:1\(^\text{n11}\)). Trans fats were seen as a health concern to the point that the FDA mandated its labeling in food items; items with less than 0.5 g/serving are exempt [86]. There was a failure to differentiate between the compositions of hydrogenated and naturally occurring trans fat.

6.3. Use of an assay that underestimates the trans fat content of food

Under the current mandate in the USA [85], food items with any amount of isomeric fatty acids were still allowed as long as they were labeled. Products containing less than 0.5 g/serving can be labeled as trans free. There was also no limit on how much hydrogenated fat a food product can contain. In 2003, the daily intake of trans fat for men was estimated by the FDA to be nearly 7 g/day and for women almost 5 g/day [85]. The FDA admitted the presence of hydrogenated fat in the diet would cause the deaths from heart disease of 500–1000 Americans/year at a cost of 1 billion dollars in medical costs [86].

To further illustrate the point consider that two cookies represent a serving. If two cookies contain less than 0.5 g trans fat/serving the cookies could be listed as trans free or 0% trans fat. However, two servings (4 cookies) could provide more than 0.5 g trans fat. On the other hand, as long as the amount per serving was listed, a two-cookies serving could contain 2 g or more of serving of trans fat. On the basis of weight/person, two cookies with 2 g of trans fat eaten by a 30-pound toddler, compared to a 180-pound man eating those same cookies, would be equivalent to eating 12 g of trans fat for the child.

6.4. Criteria to classify food as trans fat and its potential effects

The USA FDA defines trans fat chemically as “all unsaturated fatty acids that contain one or more isolated (i.e., unconjugated) double bonds in a trans configuration” [85]. To check the labeling process, common food products labeled to contain hydrogenated fat were analyzed [9]. Fatty acid analysis, on a GC 200 m column of the fat in those food products, is shown in Table 2. A summary of the fatty acids in the unhydrogenated soybean oil is listed in Table 2 for comparison purposes alongside the partially hydrogenated soybean oil. The cis and trans 18:1 and 18:2 fatty acid isomers were present in the partially hydrogenated soybean oil and also were present in every food product, even though labeled as trans free. All contained both the cis and trans 18:1 fatty acid isomers with one double bond (the cis and trans monoene) and the trans 18:2 with two double bonds (c,c, t,t or t:c: 18:2). Three of these products, the biscuits, one of the margarines and the vegetable shortening, were labeled to contain less than 0.5 g/serving or zero or no trans fat, suggesting they contained no trans fat as allowed by the FDA. This labeling, thus, is misleading. One of the four margarines was labeled to contain no trans fat, yet it contained trans fat.

If a mother was breast-feeding her child and was also eating foods containing trans fat, she would have a substantial amount of trans fat in her milk supply and pass those to her infant [87]. The piglet study described earlier [24] showed that the plasma of the lactating mothers contained 11.3% trans fat at the birth of their piglets and decreased during lactation to 4% in 21 days. The plasma of the piglets increased from 5% trans fat 3 days after birth to 15.3% at 6 weeks of age. Transferring this result to humans, a human mother would also transfer the trans fat in her milk supply to her infant. The infant would incorporate the trans fat into its arterial cells and inhibit arachidonic acid synthesis and prostacyclin secretion. Furthermore calcium deposition into the endothelial cells could be enhanced. To date, the FDA has not considered the daily intake of trans fat relevant to the health of small children since they do not exhibit overt heart disease. This can be shortsighted thinking. In cases where children have died of unknown causes and had been autopsied, 99% of them showed the beginning stages of hardening (calcifications) of the arteries, which ultimately can lead to heart disease [88,89].

7. Reasons for the industry to still use trans fat

The fat industry uses hydrogenated fats for several reasons. It provides some special features to margarines, which unlike butter, allowed margarine to be taken out of the refrigerator and immediately spread on a slice of bread. Adding 5–10% mono- and diglycerides to hydrogenated fat provided superior baking properties compared to lard. Another reason to use partially hydrogenated fat is its “mouth feel.” It melts in the mouth and leaves no waxy after taste due to the melting points of 13–44 °C of the cis and trans octadecenoic and octadecadienoic isomers [10].

Three types of hydrogenated fat have been produced since 1900. The first was a solid fat, similar to lard or beef tallow that was used as a frying and baking fat. This fat was used until 2004. It contained 45% “trans” fatty acids and 0% essential fatty acids (linoleic and linolenic acid) according to its producer [25]. A second type of hydrogenated fat [81] was used from 1968 to 2004. It contained 20–27% trans fatty acid with approximately 24% linoleic acid [81]. The third type of hydrogenated fat now being used extensively contains 39.7% isomeric cis and trans fat, 16.6% linoleic acid and 0.7% linolenic acid [9]. A recent conference on hydrogenated fat indicated 16 billion pounds of soybean oil were produced in the USA in 2006 of which 8 billion pounds were hydrogenated [90]. According to the president of the Institute of Shortening and Edible Oils there are 33 plants making hydrogenated fat in the United States [91]. According to the director of research of the largest company in the world that was hydrogenating plant oils, they could have provided a trans fat free product 40 years ago, but at a higher cost, and the

### Table 2

Summary of percentage fatty acid composition in soybean oil, hydrogenated soybean oil and in seven food products purchased from a grocery store.

| Fatty acid | Soybean oil | Hydrogenated Soybean oil | Cookies | Biscuits* | Margarines | Shortening*
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Linoleic, (\text{cis}) (18:2)</td>
<td>52.5</td>
<td>16.6</td>
<td>8.4</td>
<td>24.6</td>
<td>27.2</td>
<td>38.4</td>
</tr>
<tr>
<td>Linolenic, (\text{cis}) (18:3)</td>
<td>7.5</td>
<td>0.7</td>
<td>0.4</td>
<td>2.0</td>
<td>4.4</td>
<td>5.8</td>
</tr>
<tr>
<td>Total trans Monoene (18:1)</td>
<td>0.0</td>
<td>24.1</td>
<td>28.0</td>
<td>22.0</td>
<td>21.3</td>
<td>15.6</td>
</tr>
<tr>
<td>Total cis (18:1)</td>
<td>1.3</td>
<td>9.4</td>
<td>12.1</td>
<td>7.4</td>
<td>7.5</td>
<td>4.9</td>
</tr>
<tr>
<td>Total trans diene (18:2)</td>
<td>0.0</td>
<td>6.2</td>
<td>2.2</td>
<td>1.7</td>
<td>1.1</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Trans 18:1 represents a sum of isomers with double bonds at the tran 8, 9, 10, 11, 12 or 13 positions; 18:1 cis isomers represent a sum of isomers with double bonds at cis 9, 10, 11, 12, 13 or 14 positions; total diene represents a sum of trans, tran; trans, cis; and cis, trans 18:2 isomers, margarine 4 represents a margarine that claimed to have no trans fat, but in fact did.

* Products labeled as containing no trans fat.

b Cis isomers other than oleic acid.
company would not have been able to remain competitive. At least one company is already doing so.

8. Conclusion

It is evident that partially hydrogenated fats have excellent culinary properties but have detrimental health effects. Partially hydrogenated fats change plasma lipid levels in negative ways. They calcify cells and cause inflammation of the arteries, which are known risk factors in heart disease. They are not metabolized the same way as the trans vaccenic acid in ruminant fat and are not harmless. Trans fats inhibit cyclooxygenase (COX-2) an enzyme which converts arachidonic acid to an eicosanoid that is necessary to prevent blood clots in the arteries and veins. A blood clot in the coronary arteries can result in sudden death. These inhibitions cannot be completely prevented by adding more linoleic acid to the partially hydrogenated fat. The FDA practice of assigning a label of 0% tran fat when it is below 0.5 g/serving is misleading. The only course to protect the health of consumers is to eliminate the production of partially hydrogenated trans fats.

Acknowledgments

I would like to acknowledge the helpful suggestions of Dr. M. Mahfouz, Dr. Q. Zhou and Dr. Jean Kummerow and the financial support of the University of Illinois Foundation and the Hildebrand Foundation.

References


[92] Personal communication: President of the Institute of Shortening and Edible Oils.