REVIEW ARTICLE

FACTS ABOUT TRANS FATTY ACIDS

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Introduction

Fatty acids constitute the main class of lipids in the human diet, being found in nature mainly as glycerol esters that originate triacylglycerols. In the vegetal and animal kingdoms, fatty acids generally have *cis* unsaturations. In this form, the hydrogens bound to the double bond carbons are on the same side. In another possible configuration, called *trans*, the hydrogens are bound to un saturations, carbons on opposing sides. Fatty acids with one or more un saturations in the *trans* configuration are called *trans* fatty acids (TFAs).[1-4]

There are two major sources of TFA, those that come from ruminant animals and those that are industrially produced.

The majority of TFAs are found in partially hydrogenated vegetable oils, which contain 10–40% as TFA.[5] Hydrogenation is based on the reaction of unsaturated fatty acids of either vegetable or marine oil in the presence of a catalyst, in general nickel. The objective is to increase the oxidative stability of oils by reduction of the concentration of more unsaturated fatty acids and changing their physical properties, thus extending their application. Hydrogenation depends mainly on oil temperature, hydrogen pressure, stirring speed, reaction time, and the catalyst type and concentration. According to the process conditions, hydrogenation is classified as either partial or total and either selective or nonselective.[6] It has been estimated that dietary TFAs from partially hydrogenated oils may be responsible for between 30,000 and 100,000 premature coronary deaths per year in the United States.[7]

The concentration of TFA in meat and milk from ruminants (i.e., cattle, sheep, goats, etc.) contain 3 to 8% of total fat.[5] It is hypothesized that ruminant TFAs, or certain TFA isomers from ruminant sources, may confer some health benefits; however, since TFA from animal sources accompany saturated fatty acids (SFA), an increase in a single ruminant TFA in the diet is not appropriate because it will increase SFAs.[8] In addition, processes such as edible oil refining, meat irradiation, food frying, also contribute to increase the daily intake of TFA.[9,10]

Intake of TFAs has been consistently shown in multiple and rigorous randomized trials to have adverse effects on blood lipids, most notably on the LDL: HDL cholesterol ratio, which is a strong cardiovascular risk factor.[11-13] When a mixture of TFA isomers, obtained by partial hydrogenation of vegetable oils, is used to replace oleic acid, there is a dose-dependent increase in the LDL: HDL ratio. The relationship between amount of TFA as the percent of energy and the increase in the LDL: HDL ratio appears to be approximately linear (figure 1),[12] with no evidence of a threshold at low levels of intake, and with slope twice as steep as that observed by replacing oleic with saturated fats. The average impact of TFA induces changes in the LDL: HDL ratio corresponds to tens of thousands premature deaths in the US alone. Although dramatic, this effect is substantially smaller than the increase in cardiovascular mortality associated with TFA intake in epidemiological studies, suggesting that other mechanisms are likely to be contributing in the toxicity of TFA.[11]

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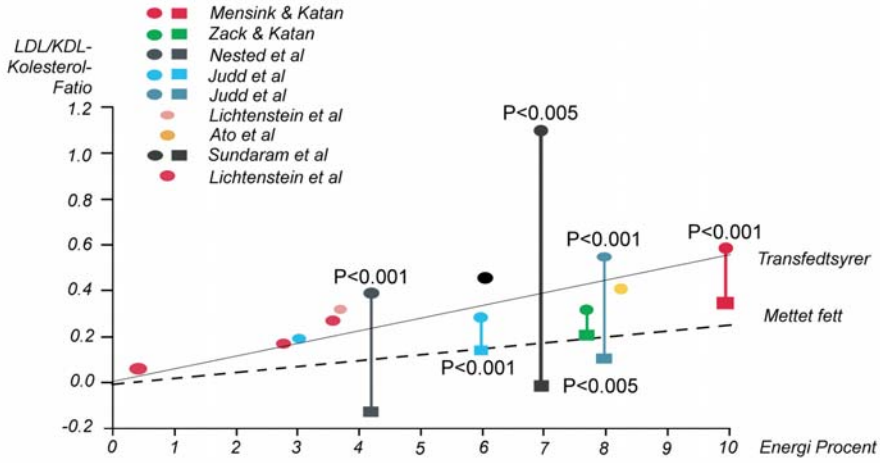

Figure 1: Results of randomized studies of the influence of industrially produced trans fatty acids (circles) and saturated fat (squares) on the LDL: HDL cholesterol ratio (y-axis). A diet with isocaloric levels of unsaturated fatty acids was used as a comparative basis.[12] The x-axis indicates in per cent energy a replacement of unsaturated fat with either saturated fatty acids or industrially produced trans fatty acids.

Besides the increase of the LDL: HDL ratio, TFA increase lipo-protein (a) and triglycerides when substitute saturated fat.[13-16] Other reported effects of TFA on blood lipids include alterations in the LDL particle size profile and in the composition of postprandial lipoproteins. The mechanisms mediating the effects of trans fatty acid on blood lipids are still incompletely understood, but may involve opposite effects on ApoA-I and LDL ApoB-100 catabolism.[14] N.R. Matthan et al, Dietary hydrogenated fat increases high-density lipoprotein apoA-I catabolism and decreases low-density lipoprotein apoB-100 catabolism in hypercholesterolemic women.[17,18]

Consumption of TFA predicts higher risk of coronary heart disease, sudden death, cancer and possibly diabetes mellitus.[19-22] Additionally, the high consumption of TFA during pregnancy has been associated with effects on intrauterine development.[23] TFA may have adverse effects on growth and development by interfering with essential fatty acid metabolism, direct effects on membrane structures or metabolism, or secondary to reducing the intakes of the cis essential fatty acids in either mother or child. TFA are transported across the placenta and secreted in human milk in amounts that depend on the maternal dietary intake.[24-26] Inverse associations have been shown between TFA and the essential n − 6 and n − 3 fatty acids in newborn infants, human milk and preschool children. It supports the need to reduce industrially produced TFA and improve dietary fat quality, particularly by increasing intake of n − 3 fatty acids. The use of partially hydrogenated fats and oils by industry, particularly in baked and processed foods that are widely consumed by women and children result in exposure to TFA in amounts shown to have adverse health effects on blood lipids and inflammatory markers in adults. In addition, high exposure to TFA is consistently related to lower levels of Docosahexaenoic acid, a fatty acid that is crucial for normal neural development and function.[24,27-29]

It has also been observed a rise in allergic diseases upon the high ingestion of this fatty acid.[30] These associations are greater than would be predicted by effects of TFA on serum lipoproteins alone. Systemic inflammation and endothelial dysfunction may be involved in the pathogenesis of atherosclerosis, acute coronary syndromes, sudden death, insulin resistance, dyslipidemia, and heart failure. Fatty acids may also directly or indirectly modulate metabolic and inflammatory responses of the endoplasmic reticulum [31] (Figure 2). Evidence from both observational and experimental studies indicates that TFA are pro-inflammatory.

Inflammation is an independent risk factor for cardiovascular diseases (CVD). Epidemiologic studies have suggested that TFA may have an adverse effect on inflammatory markers. In the Nurses' Health Study, TFA intake, assessed by semi-quantitative food - frequency questionnaires, was positively associated with tumor necrosis factor receptor (TNFR) levels in healthy women (P for trend < 0.001), and was also associated with levels of C-reactive protein (CRP) and IL-6 in women with higher BMI (P < 0.05) [32-35]. Limited evidence suggests that pro-inflammatory effects may be stronger for trans isomers of linoleic acid (trans-C18:2) and oleic acid (trans-C18:1), rather than of palmitoleic acid (trans-C16:1), but further study of potential isomer-specific effects is needed. TFA also appear to induce endothelial dysfunction. The mechanisms underlying this effect is not well-established, but may involve TFA incorporation into endothelial cell, monocyte/macrophage, or adipocyte cell membranes (affecting membrane signaling pathway relating to inflammation) or ligand-dependent effects on peroxisome proliferator-activated receptor (PPAR) or retinoid X receptor (RXR) pathways.[36,37] Activation of inflammatory responses and endothelial dysfunction may represent important mediating pathways between TFA consumption and risk of coronary heart disease, sudden death, and diabetes.[16]

The possibility that TFAs decrease the threshold for cardiac arrhythmias has been supported by the results from a more recent case control study of the risk of sudden cardiac death. When levels of TFAs in red blood cells as a marker for trans fatty acid intake were compared in 179 cases of sudden cardiac death with 285 controls, it was found that dietary levels of TFAs were associated with a moderately increased risk and that levels of trans linoleic acids were associated with a markedly increased risk of sudden cardiac death.[38] The mechanism behind this finding can theoretically be related to changes in the fatty acid composition of muscle cell membranes[39-42] (Figure 2). This affects the function of the ion channels, which are important for the formation and propagation of the electrical impulses in the cells.

Numerous expert committees have made evidence-based statements that recommend limiting dietary TFA intake;

- Institute of Medicine, TFA consumption should be as low as possible.[43]
- Dietary Guidelines Advisory Committee (DGAC), TFA consumption by all population groups should be kept as low as possible, which is about 1% of energy intake or less.[44]
- Dietary Guidelines for Americans, keep TFA consumption as low as possible.[45]
- WHO/FAO report, Diet, Nutrition, and Chronic Disease, the population nutrient intake goal for TFA is less than 1% of energy from TFA.[46]
- International Society for the Study of Fatty Acids and Lipids (ISSFAL), the maximum level of TFA should be 1% of energy.[47]
- Nutrition and Diet for Healthy Lifestyles in Europe, EURODIET, a population goal of less than 2% energy from TFA.[48]
- UK Ministry of Agriculture, less than 2% of energy.[49]
- Netherlands Health Council, less than 1% of energy intake should be from TFA.[50]
- National Cholesterol Education Program, intakes of TFA should be kept low.[51]
- American Heart Association (AHA), less than 1% of energy as TFA.[52]
- American Diabetes Association, intake of TFA should be minimized.[53]

Thus, according to the American Heart Association, the best message for consumers presently is limitation of dietary TFA, SFA, and cholesterol by following a healthy overall dietary pattern that emphasizes fruits, vegetables, whole-grain foods, fat free and low fat dairy products, lean meats, poultry and fish twice a week. Following this dietary pattern will limit TFA and SFA intake and is consistent with current dietary recommendations made by many organizations worldwide.[8]

Elimination of hydrogenation of vegetable oils represents a cost-effective means of improving heath. It also avoids destruction of essential polyunsaturated fatty acids.[7]

Review articles have special structure that is not considered in this article. A review article begin with introduction that explain the aim of this review clearly, then it continues with the description of the subject using other articles, it is necessary to explain how did you extract other articles, which data banks you used for search and what

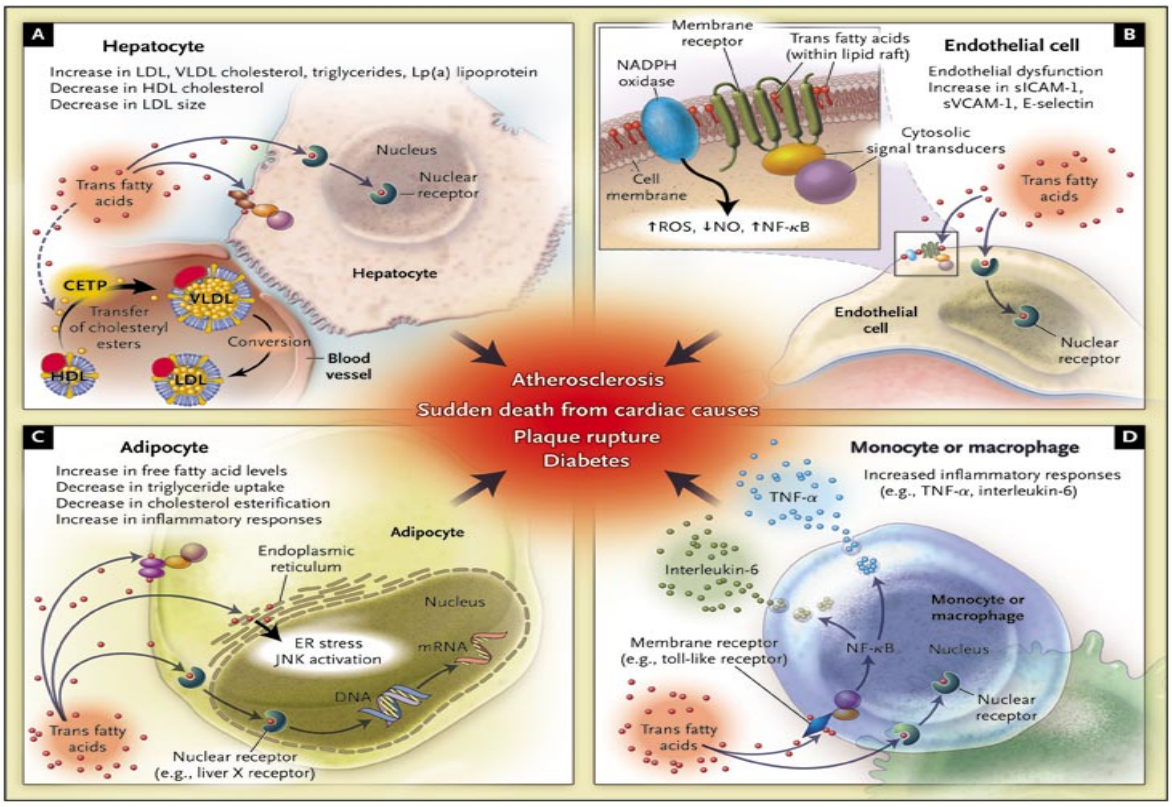

Figure 2. Potential Physiological Effects of Trans Fatty Acids.

was the inclusion and exclusion criteria of articles you used for your review. Finally you should have a clear conclusion that persuades the readers of your review. Usually review article is written by an expert person that is about that subject. Changes in hepatocyte production, secretion, and catabolism of lipoproteins, together with effects on plasma cholesteryl ester transfer protein (CETP), probably account for adverse effects of trans fatty acids on serum lipid levels (Panel A). The effect on CETP is probably not direct but mediated through effects on membrane or nuclear receptors (dashed line). Trans fatty acids also alter fatty acid metabolism and, possibly, inflammatory responses of adipocytes. In addition, nitric oxide–dependent endothelial dysfunction and increased levels of circulating adhesion molecules (soluble intercellular adhesion molecule 1 [sICAM-1] and soluble vascular-cell adhesion molecule 1 [sVCAM-1]) are seen with trans fat intake. Trans fatty acids also modulate monocyte and macrophage activity (Panel D), as manifested by increased production of inflammatory mediators. Each of these effects has been seen in controlled studies in humans and may, individually or in concert, increase the risk of atherosclerosis, plaque rupture, sudden death from cardiac causes, and diabetes. The subcellular mechanisms for these effects are not well established, but they may be mediated by effects on membrane receptors that localize with and are influenced by specific membrane phospholipids (Panel B), such as endothelial nitric oxide (NO) synthase or toll-like receptors; by direct binding of trans fatty acids to nuclear receptors regulating gene transcription, such as liver X receptor (Panel C); and by direct or indirect effects on endoplasmic reticulum (ER) responses, such as activation of Jun N-terminal kinase (JNK). Such hypothesized subcellular pathways — which have been shown to exist for other fatty acids — require further investigation. TNF-α denotes tumor necrosis factor α, ROS reactive oxygen species, NF-κB nuclear factor κB, and mRNA messenger RNA.

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