

Industrial Trans-Fatty Acid Intake Associated with Coronary Heart Disease Risk: A Review

Firdaus MA, Mishra Sunita*

Department of Food & Nutrition, Babasaheb Bhimrao Ambedkar University, Lucknow, Uttar Pradesh, India

ABSTRACT

Background: Trans-fatty acids (TFAs) are unsaturated fatty acids with at least one non-conjugated double bond in the trans-configuration; categorized as natural or artificial, based on their sources. Industrially produced trans-fats (iTFA) are created artificially during the hydrogenation of vegetable oils, resulting in partially hydrogenated vegetable oils (PHVOs). Increasing epidemiologic and biochemical evidence suggests that iTFA adversely affect multiple cardiovascular risk factors, leading to a global rise in the risk of coronary heart disease (CHD).

Aims: To highlight the prevalence and risk factors due to dietary consumption of the industrial trans fatty acids, as iTFA increase the ratio of low density lipoproteins (LDL) cholesterol to high density lipoproteins (HDL) cholesterol along with many other health complications.

Methodology: For the writing of this article, we searched the major electronic database including Web of Science, Cochrane, PubMed, Embase and Scopus. The analyzed and selected articles were cohorts, national and multicenter studies, local and national registries, retrospective analysis, randomized trials, review articles etc.

Results and Conclusion: The WHO's 2018 'REPLACE' action package seeks to eliminate trans-fatty acids completely from the global food supply by 2023. Over the next 25 years, it is estimated that just eliminating iTFA would save 17 million lives. We therefore in this review, summarize the evidence from various human studies revealing the effects of industrial trans fatty acid intake on CHD, the current status of iTFA consumption globally, and some highly recommended replacement options for the trans-fat in food products.

Keywords: Unsaturated fatty acids; Industrial trans-fatty acids; Coronary heart disease; Partially hydrogenated vegetable oils

INTRODUCTION

Coronary heart disease (CHD) develops when the heart's arteries are unable to deliver enough oxygen rich blood to the heart [1]. Along with many other risk factors including infection, diabetes, smoking, physical activity, increased body mass index, and high triglyceride levels, the diet has also been identified as an important risk factor for CHD. Therefore, in recent years, the impact of trans-fatty acids (TFAs) on Coronary heart disease has become an area of great interest [2].

Trans-fatty acids are unsaturated fatty acids with at least one methylene group and carbon-carbon double bond in the trans-configuration rather than the typical cis-configuration. TFAs are

found naturally (ruminants trans-fatty acid) in meat and dairy products and artificially (industrial trans-fatty acid) in vegetable oils through partial hydrogenation [3-5]. Partially hydrogenated vegetable oils (PHVOs) are the primary source of industrially produced trans fatty acids (iTFA), which are also considered a major health concern when it comes to CHD risk [6,7]. TFAs were once called a healthier replacement for saturated fatty acids (SFAs) when the adverse effects of SFAs, including increased blood cholesterol and CVD risk became known. This fat has been used in the food industry since the 1960's due to its functional properties such as plasticity, emulsion stability, and low cost, which make them a key component in commercially produced processed food items such as margarine, vegetable shortenings, bakery products, and other snacks and fast food [8-10].

Correspondence to: Mishra Sunita, Department of Food & Nutrition, Babasaheb Bhimrao Ambedkar University, Lucknow, Uttar Pradesh, India, Tel: +919415228811; E-mail: sunitabbau@gmail.com

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However, evidence has become clear that TFAs provide no nutritional benefits and are even more harmful than SFAs in terms of raising the risk of cardiovascular disease, and the consumption of trans-fatty acids, found in partially hydrogenated oils, is associated with a significantly increased risk of coronary heart disease, which is the one leading cause of death worldwide [4,6,11,12]. This is most likely due to the effect on lipid levels, as trans-fat increases LDL ("bad") cholesterol levels while lowering HDL ("good") cholesterol levels, promotes inflammation, and causes dysfunction in the lining of the heart and blood vessels [3-6,13,14]. Consumption of 5 grams of TFAs per day has been shown to increase the risk of cardiovascular disease by 29% [8]. Similarly, a 2% rise in energy intake from trans-fat has been associated with a 23% increase in the risk of Coronary heart disease (CHD) [6,13].

As a result, globally, more than 500,000 deaths each year are due to the consumption of TFAs and are estimated to cause more than half a million deaths from CHD every year around the world [8,15,16]. The discovery of adverse effects on the blood cholesterol profile and the increased risk of coronary heart disease of industrial trans-fat have resulted in public health recommendations to reduce total trans-fat intake to below 1% of total energy intake (En%), primarily by the elimination of industrial trans-fatty acids [17].

Source of trans-fatty acids

There are two main sources of dietary trans-fatty acids; naturally occurring trans-fats are present in small amounts in the fatty parts of meat and dairy products as a result of anaerobic fermentation in the guts of ruminant animals and do not generally harm the human body due to its tiny amount in food products [4,6,10,13]. Industrially produced trans-fats, on the other hand, are formed through partial hydrogenation of vegetable oils or fish oils and cause negative health effects on humans [4]. In meat and dairy products, naturally occurring TFAs (ruminant TFAs) do not usually exceed 6% of total fatty acids, whereas partially hydrogenated oils (PHOs) account for up to 60% of total fatty acids [17].

The main source of industrially produced trans-fat is the partially hydrogenated vegetable oil (PHVO) and the processed food made from such fat [10]. This process is widely commercialized mainly for two purposes: converting liquid oils to solids and improving the oxidative stability of these fats [4,13]. Commercially produced TFAs occurred in the human diet after 1902 when Norman used hydrogenation for the first time.

The primary dietary TFAs are vaccenic acid and elaidic acid (Table 1). Vaccenic acid (18:1, trans-11) is the major ruminant TFA, while elaidic acid (18:1, trans-9) is the main TFA isomer in industrial hydrogenation, both share the characteristic of having at least one double bond in the "trans-" rather than "cis-" configuration [4,7,18]. The TFA content of partially hydrogenated vegetable oils (PHVOs) usually depends on variables of the hydrogenation

process i.e. time, catalyst, temperature, and hydrogen pressure; the types and proportions of oils and composition of monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA) [4].

Table 1: The major source of dietary trans-fatty acids [19].

Common name	Chemical name of common isomers	Major source
Elaidic acid	C18:1 t9	Partially hydrogenated oils
Vaccenic acid	C18:1 t11	Ruminant meat and milk
Linolelaidic acid	C18:2 t9t12	Partially hydrogenated oils
Conjugated linoleic acid (CLA)	C18:2 t10c12	Ruminant meat and milk

Trans-fatty acid in food products

The majority of trans-fat found in foods is artificial. It is prepared by adding hydrogen to vegetable oil, which transforms this fat into solid fat (at room temperature) [16]. Partially hydrogenated foods were first introduced into the food supply in the late 19th and early 20th centuries as a replacement for fats such as butter and lard as these have functional properties such as extended shelf life, low cost, ability to tolerate repeated heating, and better plasticity which give them an edge over butter and other fats, and as such their use in bakery products, fried foods, and snacks has become extensive.

Nowadays PHVO is an ingredient in various foods, including margarine, vegetable shortening, and vanaspati ghee; fried foods and doughnuts; baked goods like crackers, biscuits, and pies; and pre-mixed products such as pancake and hot chocolate mix. Baked and fried street and restaurant foods often contain industrially produced trans-fat too. While sources of industrially produced TFAs vary by country, some common sources are shown in Table 2 [8,19,20].

Table 2: Common dietary sources of Industrial trans-fatty acids worldwide.

1	Margarine, vanaspati ghee, vegetable shortening
2	Baked goods such as biscuits, pies, crackers, buns, cakes, pastries, sweet rolls
3	Fried foods such as french fries, chicken nuggets, doughnuts
4	Restaurant and street foods whether baked or fried

CHD RISKS OF INDUSTRIAL TRANS-FATTY ACIDS (ITFAS)

A growing body of epidemiological and biochemical evidence suggests that there is a relationship between the consumption of industrial trans-fatty acids and raising the level of LDL cholesterol

(Low Density Lipoprotein) in the blood while reducing the level of HDL cholesterol (High Density Lipoprotein), resulting in cardiovascular diseases, particularly coronary heart disease (Figure 1) [3-4]. Such changes in the lipoprotein profile contribute to the deposition of fat in the arteries, favoring the formation of the atheroma plaque as well as its inflammatory process, obstructing the blood flow, or even causing total blockage of the arteries [7].

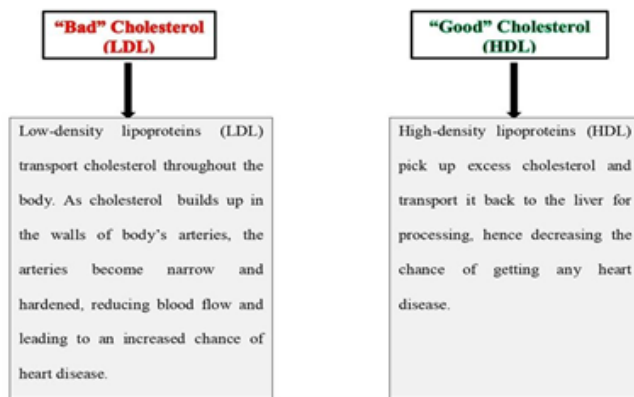


Figure 1: The important role of LDL and HDL in body [21].

Observation/intervention studies on trans-fatty acid

TFA was thought to be a safe alternative when the negative effects of eating saturated fatty acids became known. However, In 1990 Mensink et al., and in 1994 Harvard University researchers Willet et al. reported that TFA increases the total and low density lipoprotein cholesterol (LDL-C) and decreases the high density lipoprotein cholesterol (HDL-C) [5,21,22]. LDL cholesterol increased as PHVO intake increased from 2% to 6% energy, while HDL cholesterol dropped throughout this range or at least as TFA intake rose to >3% energy [21-23].

According to a comprehensive evaluation of a large number of TFA-related research published in 2006, trans-fats tend to increase the risk of CHD more than any other micronutrient. In a meta-analysis of prospective studies on TFAs and risk of coronary heart disease, Mozaffarian et al. reported that TFA intake was shown to be positively associated with the ratio of LDL to HDL cholesterol in the participants. A 2% increase in trans-fatty acid energy consumption was linked to a 23% increase in the risk of coronary heart disease (pooled relative risk 1.23; 95% confidence interval 1.11 to 1.37). They noted that trans fatty acids had negative effects even when intake was very low, at only 3% of total daily energy intake (20-60 calories), or around 2-7 g for a person eating 2000 calories (8.37 mJ) per day [4,5,12,24].

The association was stronger in the Nurses' Health Study where the multivariable relative risk of CHD was 1.33 (95% CI, 1.04 to 1.70) linked with 2% energy from trans-fat intake [18]. Another meta-analysis found that trans-unsaturated fatty acid consumption was linked to a 34% increase in all-cause mortality, a 28% increased risk in CHD mortality, and a 21% increase in CHD risk. Furthermore, these findings imply that industrially

produced trans-fats are associated with a 30% increase in the risk of CHD incidence and an 18% increase in the risk of CHD mortality. Ruminant trans-fat, on the other hand, showed no such associations [18]. In a meta-analysis, Oomen et al. found that reducing the amount of energy coming from TFAs by about 2%-4% results in a 23% decrease in mortality rate due to heart attack [19,25]. Similar outcomes were seen in the Health Professionals Follow up Study. After 14 years of follow up, the multivariate model discovered that, for every 2% increase in energy in TFA consumption, the Relative Risk of CHD events increased by 26% (RR, 1.26 (95% CI, 1.11-1.37)). In Zutphen Elderly Study (667 individuals) the RR for a 2% change in TFA intake was 1.28 (95% confidence interval: 1.01-1.61) [23].

In a nested case control study among US women over 6 year period, total trans-fatty acid content in erythrocytes was associated with dietary intake of trans-fat (correlation coefficient=0.44, $P < 0.01$) and was significantly correlated with increased plasma low density lipoprotein cholesterol (P for trend=0.06), decreased plasma high density lipoprotein cholesterol concentrations (P for trend<0.01), and increased plasma low density lipoprotein to high density lipoprotein ratio (P for trend<0.01) [26]. Brouwer et al, published a quantitative review comparing the effect of TFA from industrial (PHVO) and animal (ruminant) sources on plasma lipoproteins. CLA (conjugated linoleic acid) was also evaluated. The conclusion from this investigation was that all fatty acids with one or two double bonds in the trans configuration have similar effects on the LDL-C: HDL-C ratios. The results deny claims made for CLA for improving the lipoprotein profile. The findings also suggest that even if the effects of ruminant TFA appear linear according to linear regression analysis, the quantity that is likely to be consumed currently is doubtful to be detrimental [23].

In order to assess the effect of supplementation with 0.6% E or 1% E industrial TFAs, three intervention trials were carried out. In the first one, subjects consumed control and TFA cookies containing 0.04 g (0.02% E) and 1.13 g (0.6% E) of TFAs, respectively. It was found that there were no significant between group differences in the serum concentrations of total, LDL or HDL cholesterol. For the second intervention, 51 volunteers consumed one cookie every day for four weeks, containing 0.6% E (the TFA diet group) or 0.04% E (the control diet group). Between the control and TFA groups, again there were no significant variations in serum total, LDL, or HDL cholesterol levels. The findings of this study show that dietary supplementation with 0.6% E industrial TFAs (for a total TFA intake of about 1% E) had only a little influence on blood cholesterol levels in young and adult healthy participants. In the last one, 65 healthy young Japanese women, in addition to their regular meals, consumed one cookie each day containing either 1% E or 0.04% E (control) of TFA for four weeks. There were again no significant variations in blood LDL or HDL cholesterol levels between the two groups, according to the findings. Therefore, the results of these three intervention

trials support the soundness of 2003 WHO's recommendation of below 1% E of TFAs [26,27].

Based on several such studies, it was concluded that there were no nutritional benefits of TFA, and according to both controlled trials and observational studies, the consumption of TFA from partially hydrogenated oils adversely affects various cardiovascular risk factors and adds considerably to an elevated risk of CHD events [28-30]. These studies have demonstrated that Industrial TFA at dietary levels above 4%-6% E raises blood LDL cholesterol and lowers HDL cholesterol. These findings also suggest that industrial TFA is more likely to elevate the risk of CHD compared to dietary SFAs, which increase both LDL and HDL cholesterol [27].

CURRENT STATUS OF TFA POLICIES

TFA removal from the global food supply is a priority target of the World Health Organization's (WHO) current strategic plan (Thirteenth General Programme of Work; GPW13 2019-2023), highlighted as an effective and cost-effective policy measure to save lives that would help to achieve the WHO's worldwide goal of reducing premature deaths from Non communicable Diseases (NCDs) by one third by 2030 (compared to 2015) ensuring better health and well-being to one billion people [7,8,31]. Therefore, as a part of the Global Monitoring Framework for NCDs, World Health Organization (WHO) released the 'REPLACE' action package in May 2018, calling on governments to eliminate trans-fats from the global food chain by 2023 and replace with polyunsaturated fatty acids (PUFA) [7,32-34].

A national policy to eliminate industrially produced TFAs was first announced in Denmark, where banning the sale of food items with TFA has brought down the number of deaths from Coronary heart disease (CHD) by nearly 50% over a period of 20 years [30-31]. According to the apex global public health agency in a report, countries increasingly adopting best practice policies which include a compulsory limit for industrially produced trans fats to 2% of oils and fats in all foods and/or banning partially hydrogenated oils (PHO), the major source of industrially produced trans fats [35]. Table 3 depicts countries and territories that have imposed a TFA limit or PHO ban [8]. To date, 58 countries have enacted legislation to protect their populations from trans-fat, which will protect 3.2 billion people by the end of 2021 [35]. However, 100 have yet to act, and out of the 15 countries with the greatest number of deaths from coronary heart disease (Azerbaijan, Bangladesh, Bhutan, Canada, Ecuador, Egypt, India, Iran, Latvia, Mexico, Nepal, Pakistan, Republic of Korea, Slovenia, USA), only five have introduced regulations since 2017 (Canada, Latvia, Slovenia, USA and India) [34-36]. The most up to date estimates of total trans-fat consumption ranged from 0.3 to 4.2% of total energy intake (En%) across countries [17].

Table 3: Countries and territories with TFA limit or PHO ban [8].

Countries with a TFA limit of 2% for all foods- Austria, Belgium, Bulgaria, Chile, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of Cyprus, Romania, Slovakia, Slovenia, South Africa, Spain, Sweden, Uruguay, UK.

Countries with a TFA limit of 2% for fats/oils and 5% for all other food- Argentina, Colombia, Iran.

Countries with a TFA limit of 2% for fats/oils only- Armenia, Belarus, Ecuador, Georgia, Kazakhstan, Kyrgyzstan, Russia, Singapore, Switzerland.

Countries with a TFA limit of 3 per cent for fats/oils only- India.

Countries with a TFA limit of 4 per cent for foods with a total fat content of <20%, and a TFA limit of 10 per cent for foods with a fat content of <3% - Uzbekistan.

Countries and territories with a ban on PHOs- Canada, Chinese Taipei, Guam, Northern Mariana Islands, Peru, Saudi Arabia, Thailand, United States.

In high income countries, trans-fat regulation has been effective, and many products have been reformulated using trait-enhanced oils, interesterification, fractionation, and blending without significantly increasing saturated fatty acids (SFA) [32]. This has resulted in average energy intakes of 1%-2% in European countries and less than 1% in the United Kingdom, with a major proportion coming from dairy and meat. Trans-fatty acid intake from ruminant sources is around 0.5 E% in Europe and the United States [33]. Yang et al. investigated the relationship between plasma TFA and serum lipid levels before and after the USFDA enacted food labeling regulations in 2006, finding a 54% reduction in plasma TFAs in adult men and women in the United States from 1999-2000 to 2009-2010. Similarly, TFA consumption in several European and Asian countries is estimated to be no more than 2% Energy on average [27]. However, trans-fat remains prevalent in many developing countries where low cost partially hydrogenated oils have become staples not only for the food industry but also for home use. This shift away from traditional cooking oils toward partially hydrogenated oils is contributing to the global epidemic of cardiovascular diseases, particularly CHD [8].

Progress in Asia

Currently only two Asian countries have implemented best practice trans-fat policies so far: Thailand's Ministry of Public Health announced in January 2018 that partially hydrogenated oils and food products containing them would be banned by

January 2019. India In 2011, India passed regulations limiting TFA levels in oils and fats to 10%, which was later reduced to 5% in 2015 [37-39]. After that, FSSAI passed a policy in early 2021 to reduce the current permissible limit of trans fats in oils and fats in food products from 5% to 2% by 2022 [15]. To achieve the goal of a transfat free India, the Indian regulatory body has implemented several strategies, including lowering the trans-fat limit in oils and fats, requiring mandatory food labeling, and introducing a "Trans-fat free" claim and logo [10].

CONCLUSION AND RECOMMENDATIONS

The negative effects of industrial trans-fatty acids (iTFA) on heart health are undeniable, and it is widely accepted that lowering LDL cholesterol by any means reduces the risk of coronary heart disease. As advised by WHO, TFA intake as a percentage of total energy should not exceed 1%, and the total fat consumption as a percentage of energy should not be less than 15% and should not be more than 30%.

Nowadays, with public health concerns, there is considerable interest in zero and low trans-fat food products among food industries. The current use of such products is increasing in high income countries and the manufacturing units are switching to alternative processes to reduce or eliminate TFAs and produce healthier fat products. These technological options include: Modified hydrogenation process, structured oils (oleogelation and interesterification), fractionation, and specialty oils/genetically modified oils. Modified hydrogenation process gives health promoting hydrogenated vegetable oils containing high levels of conjugated linoleic acids that can be used in baking shortenings and spreads. By oleogelation and interesterification, structured oils are produced by structuring and reshuffling fatty acids to achieve desired physical and chemical properties. It gives vegetable oils a solid like quality. Fractionation enables to get desired functionality through a controlled crystallization process, resulting in crystals that give applicability to use in baked shortenings, margarine, etc. Specialty oils/Genetically modified oils are a new approach to plant breeding that aims to get rid of trans fatty acids and increase the content of oleic, linolenic, and stearic fatty acids while maintaining desired physical properties at the primary stage of crop improvement, allowing them to be used in a variety of food applications such as confectionery, bakery, and frying.

The mandatory addition of saturated fat and trans-fatty acid content on nutrition labels to raise consumer awareness has enabled consumers to select healthier food choices. It is well known that the consumption of unsaturated fatty acids (in cis form) is beneficial for health. WHO advised that partially hydrogenated oils be replaced with unhydrogenated oils, which would likely result in significant reductions in CHD incidence. Furthermore, a number of research indicated that higher intakes of whole grain carbohydrates and PUFA are linked to a lower CHD risk. Polyunsaturated fats, both n-6 and n-3, have been

shown to lower the incidence of CHD by improving blood lipids, insulin sensitivity, thrombosis inhibition, and the threshold for ventricular fibrillation. Monounsaturated fatty acids (MUFA) have been reported to lower LDL cholesterol while raising HDL cholesterol. In addition, most vegetable oils are high in vitamins and phenolic compounds, both of which are beneficial for health.

However, low and middle income countries bearing up to 90% of the global CVD burden alone, where people are still unaware of what fats they should or should not be consumed and many are likely consuming trans-fats above the maximum intake recommended by the WHO, four strategies are strictly needed to limit trans-fat 1. Consumer awareness is extremely important regarding the consequences of trans-fatty acids on the heart and overall health; 2. Government agencies should assist these efforts by enforcing legislation that would limit trans-fat use; 3. Health care providers should advise people about how to minimize the intake of trans fat in the diet, and how to recognize and avoid products containing trans-fats; 4. Restaurants and food manufacturers should use new technologies and alternative fats in food production and preparation to reduce trans fats. In addition, they should also be informed about the production of new TFA-free products to determine the health related effects, as it would be impractical to replace TFA with products that might be just as harmful, or even worse.

This way, these procedures should help reduce the consumption of trans fatty acids, resulting in significant health benefits in every part of the world.

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AUTHORS' CONTRIBUTION

First author performed the original writing and corresponding author finalized and approved the manuscript after editing of this work. Each author believes that the manuscript represents honest work.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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