Peer-reviewed | Manuscript received: April 09, 2018 | Revision accepted: : July 09, 2018

Trans fatty acids

Origin, metabolism, health risks

Maria Pfeuffer, Gerhard Jahreis

Abstract

Trans fatty acids (TFA) are generated both during partial industrial hydrogenation of oils and by incomplete microbial hydrogenation of polyunsaturated fatty acids in the rumen. Elaidic acid (t9-18:1), the trans isomer of oleic acid, is the major isomer in industrial sources of TFA. Some trans isomers of linoleic acid and of α-linolenic acid may also arise, depending on the vegetable oil used for hydrogenation and processing conditions. Vaccenic acid (t11-18:1) is the major trans isomer in ruminant fats. Elaidic acid and vaccenic acid differ in various biochemical activities. TFA show adverse effects on blood lipids, inflammation parameters and endothelial function. Epidemiological studies observed an increased risk of coronary heart diseases and total mortality with increasing intake of industrially generated TFA. Particularly fats for baking, roasting and deep-frying have or had a high content of TFA. Originally, margarine was an important source. Due to mandatory regulations and voluntary measures the TFA content of foods and thus TFA intake decreased markedly in many countries. This probably decreased health risks.

Keywords: elaidic acid, vaccenic acid, metabolism, health risks, intake, (governmental) regulations

Citation:
Pfeuffer M, Jahreis G (2018) Trans fatty acids. Origin, metabolism, health risks. Ernahrungs Umschau 65(12): 196–203

This article is available online:
DOI: 10.4455/eu.2018.047

Origin and nomenclature of trans fatty acids

Unsaturated fatty acids have double bonds mostly in cis-configuration, leading to a kink in the hydrocarbon chain. Trans fatty acids (TFA) on the contrary are unsaturated carboxylic acids with at least one double bond in trans configuration. In contrast to the cis isomer the hydrocarbon chain of a monounsaturated trans fatty acid is almost straight (♦ Figure 1). Structure, melting point and other physical properties shift TFA in the direction of saturated fatty acids. For one TFA are generated during partial industrial hydrogenation of vegetable oils and, to a small extent, during oil refining [1]. This process turns liquid oils into semi-solid spreadable fats. Since the 1960s partially hydrogenated fats were a preferred alternative for saturated fats in the food industry. A high TFA content improves the functionality of a fat, i.e. texture and structure, thermal and oxidation stability and extends shelf life. There are also natural sources of TFA in fat from ruminants, i.e. milk fat and meat and products made from them, as enzymes of the rumen bacteria incompletely hydrogenate polyunsaturated fatty acids of the feed. Depending on the feeding regimen fat in cow's milk contains 2–8% TFA [1, 2].

Vaccenic acid (trans11-18:1), occasionally also called trans vaccenic acid, predominates in the ruminant TFA (R-TFA, rumen-derived), accounting for up to 70% of R-TFA, with the trans double bond in position n-7 (shorthand notation t11-18:1, t-18:1n-7 or (old delta-notation) C18:1 Δ11t). A minor fatty acid is trans palmitoleic acid (shorthand notation t9-16:1, t-16:1n-7 or t-16:1n7) [1, 2]. Monounsaturated TFA generated through partial industrial hydrogenation (I-TFA, industrially produced) with a chain length of 18 carbon atoms (C18) have trans double bonds in position C4 to C16. The most important ones are t9-18:1 and t10-18:1. Their percentage of total t-18:1 amounts to about 28% and 23% respectively [3]. Elaidic acid (shorthand notation t9-18:1, t-18:1n-9 or C18:1 Δ9t) is the trans isomer of oleic acid. But also t11-18:1 is found in I-TFA, with approximately 1% of total t-18:1 [3]. Thus I-TFA and R-TFA contain basically the same trans isomers, but in very different proportions. The t9 to t11 ratio (so-called t9/t11 index)

gives an indication of the origin of TFA in foods. For R-TFA it is usually < 1.0 [2].

TFA are largely monounsaturated (t-18:1). Depending on the vegetable oil used for hydrogenation and processing conditions also polyunsaturated TFA (t-18:2, t-18:3 and others) may arise, normally in low concentrations, in particular trans isomers of linolenic acid (e.g. c9,t12-18:2) and of α-linolenic acid (e.g. c9,c12,t15-18:3). If TFA have two or more double bonds a distinction needs to be made between those with isolated and conjugated double bonds, both for physiological and legal reasons. According to the Food and Drug Administration (FDA) and the Codex Alimentarius Commission only fatty acids with non-conjugated trans double bonds are defined as TFA, whereby at least one of these double bonds must be in trans configuration. According to this definition conjugated linoleic acid (CLA) c9,t11-CLA is not a TFA.

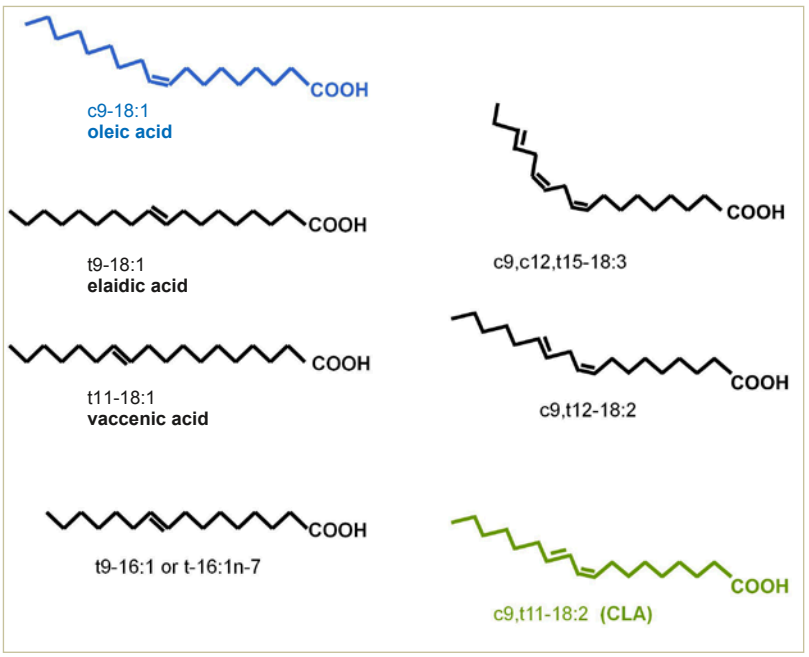

Fig. 1: **Structure of oleic acid, various trans fatty acids (TFA), and of conjugated linoleic acid (CLA)**
The position of the double bonds is usually indicated by the carbon atom counting from the carboxylic end of the carbon chain (delta-notation), different from the cis unsaturated fatty acids. One exception, for example, is t9-16:1, also called t-16:1n-7.

Metabolism

Incorporation into lipids of various tissues

Among men with an average TFA intake of 2.6 g/d (range 0.7–8.6 g/d), equal to 1.5 energy percent (En%) and 5.5% of total fat intake, the mean concentration of TFA in adipose tissue (upper buttock subcutaneous fat) was 4.9% (1.7–7.7%) [4]. TFA intake and concentration in adipose tissue were somewhat lower among women. Subjects consuming a diet high in soft margarine from partially hydrogenated soybean oil and providing 4.15 En% TFA had increased plasma TFA concentrations, 3.8% in phospholipids, 7.1% in triglycerides and 4.4% in cholesterol esters. The t-18:2 isomers (CLA not included) accounted for 26, 37 and 57% of total TFA [5]. Ten different TFA isomers were identified in plasma phospholipids in an US cohort (samples taken in 1992). Total TFAs represented on average 2.52% of plasma phospholipids including an average of 0.25% t-16:1, 2.01% t-18:1, and 0.27% t-18:2 isomers [6].

TFA were found in triglycerides, phospholipids and cholesterol esters of various tissues [5, 7]. Their incorporation relative to total lipid differed depending both on the tissue and trans isomer [8]. TFA incorporation decreases the fluidity of membranes. Therefore, incorporation into phospholipids, membrane lipids as well as functional lipids, is of special importance. This incorporation was isomer-dependent, too. Isomers of t-18:1 were mainly esterified at the sn1-position of glycerol in glycerophospholipids [9]. Among t-18:2 isomers c9,t12-18:2 was preferred for incorporation, predominantly at the sn2-position [10]. Among t-18:3 isomers c9,c12,t15-18:3 was the major one, also at the sn2-position [11]. Enzymes of the elongation-desaturation system may convert t-18:3 isomers to trans isomers of eicosapentaenoic acid [11] and docosahexaenoic acid [12]. Trans docosahexaenoic acid was detected in brain [12], but not t9-18:1 [8]. High intake of α-linolenic acid as compared to linoleic acid decreased the incorporation of TFA into rat liver and adipose tissue [7].

Fatty acid metabolic pathways

Concerning absorption, transport, and oxidation TFA undergo a fate similar to that of the corresponding cis isomers. TFA can inhibit Δ6-desaturase, the first step enzyme of the elongation-desaturation system. Trans isomers differ in their inhibitory effect, with t,t-18:2 being a more potent inhibitor than t9-18:1 [9]. Thus TFA can impair the synthesis of the long-chain fatty acids arachidonic acid (20:4n-6), eicosapentaenoic acid (20:5n-3) and docosahexaenoic acid (22:6n-3) and their

through ... from...	additional double bond (Δ9-desaturase)	chain shortening (partial ß-oxidation)
t9-18:1 also t-18:1n-9 (elaidic acid)	no	t7-16:1 also t-16:1n-9, t-16:1n9
t10-18:1	no	not known
t11-18:1 also t-18:1n-7 (vaccenic acid)	c9,t11-CLA	t9-16:1 also t-16:1n-7, t-16:1n7

Tab. 1: **Possible metabolites of major t-18:1 isomers** [15, 17]

incorporation into tissues. Higher content of trans eicosapentaenoic acid [11] and trans docosahexaenoic acid [12] in phospholipids of various rat tissues was accompanied by a decreased content of their cis analogues [11, 12]. But no major changes were observed in brain phospholipids [12]. In adults, a sufficient supply of essential fatty acids prevents detrimental health effects of TFA [9]. TFA pass the placental barrier and appear in breast milk. Their metabolic effects can thus affect fetus and infant. The concentration of t-18:1 and t,t-18:2 in breast milk, but not t9-16:1, was indeed inversely correlated with that of arachidonic acid and docosahexaenoic acid [13].

It is a special feature of TFA that Δ9-desaturase (stearoyl-CoA-desaturase), found in all human cells, can insert an additional double bond in some t-18:1 positional isomers (♦ Table 1). Thus t11-18:1 can be converted to c9,t11-CLA [8, 14, 15]. In mice the degree of conversion depended on the tissue examined [8]. The isomers t12-18:1 to t15-18:1, which occur in R-TFA but only in low concentrations in I-TFA, are also Δ9-desaturated [15]. Isomers predominating in I-TFA, t9-18:1 and t10-18:1, are not Δ9-desaturated [15]. Conjugated linolenic acids (e.g. c6,c9,t11-18:3) and conjugated eicosatrienoic acids (e.g. c8,c11,t13-20:3) can be synthesized from the precursor c9,t11-CLA by insertion of additional double bonds and chain elongation [16]. While t-18:1 isomers were mainly incorporated into triglycerides, the Δ9-desaturation products were selectively incorporated into phospholipids [15]. The t-18:1 isomers can also be shortened to t-16:1 isomers via partial peroxisomal ß-oxidation, namely t11-18:1 to t9-16:1 [17] and, in analogy, t9-18:1 to t7-16:1 (♦ Table 1). The conversion rate for t11-18:1 was on average 17% in humans [17].

The content of t9-16:1 in plasma phospholipids, originating from milk fat or endogenously synthesized from the precursor t11-18:1, was in cohort studies associated with lower concentrations of several risk markers, among others triglycerides, the inflammatory marker C-reactive protein and the ratio total/HDL cholesterol [18]. No theory has been put forward for a protective mechanism yet. The CLA-isomer c9,t11-CLA, which occurs in ruminant fat and is also endogenously synthesized from t11-18:1, reduced the synthesis of adhesion molecules on the surface of endothelial cells and the adhesion of macrophages. It improved insulin sensitivity in ob/ob mice [14]. A number of findings demonstrate that t11-18:1 (R-TFA) and t9-18:1 (I-TFA) are metabolized differently. Only t9-18:1 inhibited Δ5-desaturase activity in vitro [9]. Only t9-18:1 and t9,t12-18:2 disturbed insulin signal transduction in endothelial cells. Only t9-18:1, but not t11-18:1, impaired cholesterol efflux from macrophages [14]. In cell culture experiments, t11-18:1 possessed anti-inflammatory properties, though less pronounced than c9,t11-CLA [19]. In a human study supplementation with t11-18:1 changed neither immune cell function nor plasma biomarkers of immune function and inflammation [20]. Different from t11-18:1 neither t9-18:1 nor t10-18:1 are Δ9-desaturated (♦ Table 1). This may be an explanation for their more unfavorable pathobiochemical effect. They were more cytotoxic to liver cells and increased, different to t11-18:1, the expression of lipogenic genes (fatty acid synthase, Δ9-desaturase) and transcriptional regulators [15]. Both were incorporated in triglycerides and phospholipids to a greater extent than t11-18:1 [15].

Health aspects

Blood lipids

A high cholesterol concentration, particularly LDL cholesterol, is an important risk factor for the development of cardiovascular diseases (CVD) [21]. CVD include coronary heart disease (CHD), circulatory disorders, and stroke. The ratio total/HDL cholesterol is a particularly valuable predictive marker [21, 22].

According to a meta-analysis of intervention studies, TFA (mainly I-TFA) increased plasma LDL cholesterol, triglycerides, and the ratio total/HDL cholesterol more than saturated fatty acids, with a linear dose-response relationship [22] (♦ Figure 2). Another meta-analysis found a nonlinear S-shaped relationship between TFA intake and plasma LDL cholesterol. An intake below 1.4 En% did not increase LDL cholesterol, and an intake above 3 En% did not increase LDL cholesterol further [23].

The question if I-TFA and R-TFA have the same effect on lipids is not conclusively clarified. One review concluded that I-TFA increase the ratio LDL/HDL cholesterol not significantly more than R-TFA [24]. In an individual study, comparing I-TFA (predominantly t-18:1) with R-TFA

(TFA intake 2 En% each), only R-TFA increased total and LDL cholesterol modestly [25]. According to a meta-analysis higher intake of R-TFA in milk fat did not increase total/HDL cholesterol or LDL/HDL cholesterol ratios in intervention studies [26]. This was confirmed for R-TFA/c9,t11-CLA rich cheese in an individual short-term study [16]. A higher concentration of t9-16:1 in plasma phospholipids was in a US cohort associated with higher HDL cholesterol concentrations and a lower ratio total/HDL cholesterol [18].

Disease risks

At the very latest since the first publication of the Nurses' Health Study 1993 [27] it was no more questioned that TFA increase the risk for CHD. This increased risk of CHD is likely attributable to various mechanisms, such as the elevation of LDL cholesterol and lipoprotein(a) and the reduction in HDL cholesterol concentrations, an increase of triglycerides and of apolipoprotein B, proinflammatory effects, and impaired vascular elasticity [14, 28] as well as an increase of small, dense, and thus atherogenic LDL particles [28]. The risk of insulin resistance and of type 2 diabetes mellitus is probably also increased [28]. Their negative impact on health is more pronounced than could be expected from the effect on cholesterol concentration alone [22]. A new meta-analysis of cohort studies found that higher intake of I-TFA and total TFA significantly increased the risk of death due to CHD and the risk of CHD-associated events and illnesses combined. However, higher intake of R-TFA alone did not affect the risk [29]. Higher intake of R-TFA, calculated on the basis of the biomarker t9-16:1 in plasma, was associated with a lower risk of type 2 diabetes mellitus, whereas higher total TFA intake, i.e. largely I-TFA, tended to increase the risk [29] (♦ Table 2). t-18:2 isomers may carry a greater health risk than t-18:1 isomers [28].

In a large prospective cohort, in which plasma phospholipid t9-16:1 concentration was independently associated with lower risk of type 2 diabetes mellitus [18], the concentration of t9-16:1 was associated with intake of (particularly full fat) milk products [6]. It remains open if there is a causal link between t9-16:1 concentration and reduced diabetes risk, or if t9-

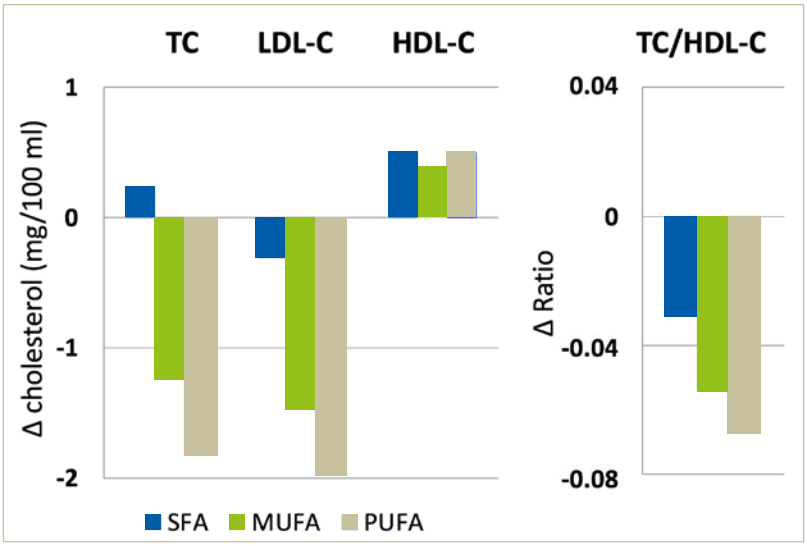

Fig. 2: **Changes in blood lipids, namely total cholesterol, LDL cholesterol, HDL cholesterol and the ratio TC/HDL-C, if dietary TFA are replaced by saturated, monounsaturated or polyunsaturated fatty acids (isocaloric replacement of 1 En% each)** (according to Mozaffarian & Clarke 2009 [22]; meta-analysis of 13 randomized controlled dietary trials including 41 different test diets)
HDL-C = HDL-cholesterol; LDL-C = LDL-cholesterol; MUFA = monounsaturated fatty acids; PUFA = polyunsaturated acids; SFA = saturated fatty acids; TC = total cholesterol; TFA = trans fatty acids

		n	RR	95%-CI
total TFA	all cause mortality	2/2	1.34***	(1.16–1.56)
	CHD total[a]	6/7	1.21***	(1.10–1.33)
	ischemic stroke	3/4	1.07	(0.88–1.28)
	diabetes mellitus type 2	6/6	1.10	(0.95–1.27)
I-TFA	all cause mortality	1/2	0.98	(0.92–1.04)
	CHD total[a]	2/2	1.42*	(1.05–1.92)
	ischemic stroke	0	-	-
	diabetes mellitus type 2	0	-	-
R-TFA	all cause mortality	1/2	1.04	(0.92–1.18)
	CHD total[a]	3/4	0.93	(0.73–1.18)
	ischemic stroke	0	-	-
	diabetes mellitus type 2	5/5	0.58***	(0.46–0.74)

Tab. 2: **Intake of total TFA (up to 80% I-TFA), I-TFA, and R-TFA and all cause mortality and disease risks** (according to de Souza et al. 2015 [29], meta-analysis)
[a] coronary heart disease, cases including deaths
I-TFA = industrially produced trans fatty acids; 95% CI = 95% confidence interval; n = number of studies/comparisons; RR = relative risk; R-TFA = rumen-derived trans fatty acids; TFA = trans fatty acids
* $p \leq 0.05$, *** $p \leq 0.001$

16:1 is simply a good biomarker for milk fat intake. In another population the concentration of t9-16:1 was also positively correlated with intake of margarine and sweet baked goods [30]. This seems plausible as t9-16:1 may also be derived from t11-18:1 occurring in I-TFA. The concentration of t7-16:1 and of various t-18:1 isomers (including t11-18:1) was equally positively correlated with intake of margarine and sweet baked goods [6]. Therefore, it would be useful to analyze tissue concentrations of t9-16:1 and t7-16:1 in parallel. As outlined before, both, supply with food and endogenous metabolism influence the concentration of trans isomers.

Many studies examined the association between trans isomers in plasma, plasma phospholipids or erythrocytes with disease risks. They found that only concentrations of t7-16:1 and t-18:1 were associated with higher risk of type 2 diabetes mellitus [31], while t9-16:1 was inversely associated [18, 30]. Furthermore t9-16:1 was not associated with increased CVD risk [32]. Only t9,t12-18:2 was associated with higher risk of all-cause and CVD mortality, but no other t-18:2 isomers, t7-16:1 or total t-18:1 [33]. And only t9-18:1, but not t11-18:1, t9,t12-18:2, and t9-16:1, was in a cohort representative of the general US population (National Health and Nutrition Examination Survey, NHANES) associated with increased CVD mortality [34]. A TFA index, calculated as the sum of isomers mainly derived from I-TFA divided by the sum of isomers mainly derived from R-TFA, showed (only) in erythrocytes a strong positive association with CHD risk [35]. The importance of individual isomers for the physiological effect of TFA overall and their utility as biomarkers for the dietary intake remain unresolved. This applies in particular to the various t-18:1 isomers, as they are highly intercorrelated [6, 33, 34]. Significant reductions in I-TFA intake in the US population (NHANES) from 1999–2000 to 2009–2010 resulted in significantly lower plasma TFA concentrations, on average by 54%. All trans isomers decreased, t9-18:1 only moderately more than the other ones (t9-16:1, t11-18:1 and t9,t12-18:2) [36].

Even though it has not been finally clarified if R-TFA and I-TFA should be rated equally critically, it is widely accepted that at the habitual intake levels R-TFA do not increase disease risk [14, 28, 29]. Intake of R-TFA cannot be separated from the consumption of milk and dairy products or milk fat. R-TFA assessment must always include that of these foods. Higher intake of R-TFA means also higher intake of saturated fatty acids, which are regarded as risk factor for CVD as well. However, recent studies which assessed saturated fatty acids in milk fat as components of complex foods (milk, dairy), came to a more differentiated assessment (references in [37]).

	Germany		United States	
time period	**2005–2006**		**1999–2002**	
intake	men 14–80 years	women 14–80 years	men > 20 years	women > 20 years
TFA (g/d)	1.9	1.4	6.8	5.2
TFA (En%)	0.7	0.7	2.3	2.5
TFA (% of fat[a])	2.1	2.2	7.1	7.6

Tab. 3: **TFA intake in Germany (NVS II) [43] and in the United States [44]** (means)
[a]total fat consumed
En% = energy percent ; NVS II = National Food Consumption Study II *(Nationale Verzehrstudie II)* ; TFA = trans fatty acids

Legal requirements

Inclusion of the TFA content on food labels became recently mandatory, for ≥ 0.5 g TFA per serving in the United States since 2006 and for ≥ 0.2 g TFA per serving in Canada since September 14, 2005. In 2015 FDA revoked the GRAS status (GRAS: generally regarded as safe) for I-TFA in the food supply, with a transition period of three years. New York City banned use of fats containing I-TFA in restaurants in 2007.

Denmark was the first European country that restricted the content of I-TFA to 2 g per 100 g fat or oil in 2003. After a short transition period this restriction also applied to fats in processed foods. R-TFA were excluded from the regulation. The implementation was successful, demonstrating that the removal of TFA is both feasible and achievable. In the meantime similar regulations went into effect in Switzerland, Austria, Iceland, Hungary and Norway. Sweden is preparing such a measure. Besides mandatory regulations also voluntary regulations helped to reduce I-TFA in foods, yet mandatory regulations were more effective [38]. In Germany, the TFA concentration in infant formulae and follow-on formulae must not exceed 3% of total fat according to the respective dietary regulation *(Diätverordnung)* [39]. There are currently no further quantitative limits.

Replacement options for TFA fats

For health reasons reduction in TFA intake should not lead to an increased intake of saturated fatty acids. Depending on the intended purpose replacement products with similar characteristics may e.g. be

manufactured by chemical or enzymatical interesterification of fats or by blending solid fats (in part fully hydrogenated vegetable oils) with fluid oils. In Denmark I-TFA were mostly replaced by saturated fatty acids (including coconut oil) and to a smaller extent by monounsaturated and polyunsaturated fatty acids [40]. In the United States TFA were only to a small extent replaced by saturated fatty acids, the content of TFA as well as the sum of TFA and saturated fatty acids decreased in supermarket foods and restaurant products [41].

Change in TFA consumption and consequences

Due to a wide range of TFA contents within given food groups, product reformulations and an inherent imprecision in measuring food intake, it was and remains difficult to accurately determine TFA intake. In the 1990s, total average TFA intake in Europe ranged from 1.4–5.4 g/d (0.5–2.0 En%). Intake in Germany was 2.1 g/d (0.9 En%) [42]. Based on the German National Food Consumption Study II *(Nationale Verzehrstudie II* (NVS II)) average TFA intake in Germany is at present 1.7 g/d (0.7 En%) [43]. Around the year 2000 men in the United States consumed on average 6.8 g and women 5.2 g TFA per day [44] (♦ Table 3). For persons > 2 years the intake was on average 5.8 g/d (2.6 En%) [45]. R-TFA made up approximately 20% of total TFA intake in the United States [45], while in Europe it made up between < 30% (The Netherlands, Norway) and ≥ 64% (Spain, France, Germany, and others) [42]. The most recent assessment found that in Germany R-TFA contribute 60–80% [43].

Originally margarine was a major source of TFA [1, 27]. From around the 1990s first the TFA content in margarines was considerably reduced through reformulation [1], later on other foodstuffs followed. In the meanwhile (largely sweet) baked goods, deep-fried products, snacks, and fast food became the main sources of I-TFA [44]. The FDA calculated that in the United States intake of I-TFA decreased from on average 4.6 g/d (2.0 En%) in 2003 to 1.3 g/d (0.6 En%) in 2010 and 1.0 g/d (0.5 En%) in 2012 [46]. In Europe mean TFA intake around the 2010s was 0.9–1.8 g/d (0.4–0.8 En%) [42]. Decreasing intake of I-TFA increased the percentage contribution of R-TFA to total TFA intake [42].

Reformulation of food products led to a lower intake of I-TFA and thus to decreased plasma TFA concentrations in the US population (NHANES), by 54% from 1999–2000 to 2009–2010 [36]. Nevertheless, TFA concentrations remained significantly associated with plasma cholesterol concentrations in 2009–2010 [36].

Decreased TFA intake decreased the TFA concentration in breast milk in Canada from on average 7.2% of fat in 1992 to 1.9% in 2011 [47]. Due to reformulations both TFA intake and TFA concentration in adipose tissue decreased in persons in Costa Rica. With decreased TFA concentration the positive association between the concentration of t-18:2 in adipose tissue and CHD risk was no longer significant [48]. Already the first report of the Nurses' Health Study [27] showed that those women had a higher CHD risk who had not reduced their I-TFA intake during the past ten years. The latest analyses (follow-up 30 and 32 years, up to 2010 and 2012) found in this cohort no significantly increased risk of a sudden cardiac death [49] and of total mortality [50] with higher TFA intake. The phenomenon may be explained by the overall lower TFA intake in later years, but also the older age of the participating women [51]. However, for women and men combined (Nurses' Health Study und Health Professionals Follow-up Study), there remained a significantly higher risk of total mortality and CVD mortality, by 16% in case of an intake of 2 En% TFA in place of saturated fatty acids [50].

The World Health Organization (WHO) recommends that TFA intake should be as low as possible, i.e. < 1% of total energy intake [40]. This recommendation is generally accepted. The German Federal Institute for Risk Assessment *(Bundesinstitut für Risikobewertung*, BfR) concluded that the current average TFA intake in Germany does not pose a health risk [43].

Conflict of Interest
The authors declare no conflict of interest.

Dr. Maria Pfeuffer[1]
Prof. Dr. Gerhard Jahreis[2]
[1] Kiel; m-pfeuffer@web.de
[2] Institut für Ernährungswissenschaften
Friedrich-Schiller-Universität, Jena
b6jage@uni-jena.de

References

1. *Ptok S, Heseker H (2010) trans-Fettsäuren. Ernährungs Umschau 57: 472–480*
2. *Kuhnt K, Degen C, Jahreis G (2016) Evaluation of the impact of ruminant trans fatty acids on human health: Important aspects to consider. Crit Rev Food Sci Nutr 56: 1964–1980*
3. *Wolff RL, Combe NA, Destaillats F et al. (2000) Follow-up of the delta4 to delta16 trans-18:1 isomer profile and content in French processed foods containing partially hydrogenated vegetable oils during the period 1995–1999. Analytical and nutritional implications. Lipids 35: 815–825*
4. *Lemaitre RN, King IB, Patterson RE et al. (1998) Assessment of trans-fatty acid intake with a food frequency questionnaire and validation with adipose tissue levels of trans-fatty acids. Am J Epidemiol 148: 1085–1093*

5. Vega-Lopez S, Ausman LM, Jalbert SM et al. (2006) Palm and partially hydrogenated soybean oils adversely alter lipoprotein profiles compared with soybean and canola oils in moderately hyperlipidemic subjects. Am J Clin Nutr 84: 54–62
6. Micha R, King IB, Lemaitre RN et al. (2010) Food sources of individual plasma phospholipid trans fatty acid isomers: the Cardiovascular Health Study. Am J Clin Nutr 91: 883–893
7. Koga T, Nonaka M, Gu JY et al. (1997) Linoleic and alpha-linolenic acids differently modify the effects of elaidic acid on polyunsaturated fatty acid metabolism and some immune indices in rats. Br J Nutr 77: 645–656
8. Beppu F, Asanuma M, Kawamura Y et al. (2015) Trans-octadecenoic acid positional isomers have different accumulation and catabolism properties in mice. J Oleo Sci 64: 1159–1167
9. Sugano M, Ikeda I (1996) Metabolic interactions between essential and trans-fatty acids. Curr Opin Lipidol 7: 38–42
10. Privett OS, Nutter LJ, Lightly FS (1966) Metabolism of trans acids in the rat: influence of the geometric isomers of linoleic acid on the structure of liver triglycerides and lecithins. J Nutr 89: 257–264
11. Loi C, Chardigny JM, Almanza S et al. (2000) Incorporation and metabolism of dietary trans isomers of linolenic acid alter the fatty acid profile of rat tissues. J Nutr 130: 2550–2555
12. Acar N, Bonhomme B, Joffre C et al. (2006) The retina is more susceptible than the brain and the liver to the incorporation of trans isomers of DHA in rats consuming trans isomers of alpha-linolenic acid. Reprod Nutr Dev 46: 515–525
13. Decsi T, Boehm G (2013) trans Isomeric fatty acids are inversely related to the availability of long-chain PUFAs in the perinatal period. Am J Clin Nutr 98: 543s–548s
14. Wang Y, Proctor SD (2013) Current issues surrounding the definition of trans-fatty acids: implications for health, industry and food labels. Br J Nutr 110: 1369–1383
15. Vahmani P, Meadus WJ, da Silva MLP et al. (2016) A trans10-18:1 enriched fraction from beef fed a barley grain-based diet induces lipogenic gene expression and reduces viability of HepG2 cells. Biochem Biophys Rep 7: 84–90
16. Pintus S, Murru E, Carta G et al. (2013) Sheep cheese naturally enriched in alpha-linolenic, conjugated linoleic and vaccenic acids improves the lipid profile and reduces anandamide in the plasma of hypercholesterolaemic subjects. Br J Nutr 109: 1453–1462
17. Jaudszus A, Kramer R, Pfeuffer M et al. (2014) Trans palmitoleic acid arises endogenously from dietary vaccenic acid. Am J Clin Nutr 99: 431–435
18. Mozaffarian D, Cao H, King IB et al. (2010) Trans-palmitoleic acid, metabolic risk factors, and new-onset diabetes in U.S. adults: a cohort study. Ann Intern Med 153: 790–799
19. Jaudszus A, Jahreis G, Schlormann W et al. (2012) Vaccenic acid-mediated reduction in cytokine production is independent of c9,t11-CLA in human peripheral blood mononuclear cells. Biochim Biophys Acta 1821: 1316–1322
20. Kuhnt K, Kraft J, Vogelsang H et al. (2007) Dietary supplementation with trans-11- and trans-12-18 : 1 increases cis-9, trans-11-conjugated linoleic acid in human immune cells, but without effects on biomarkers of immune function and inflammation. Br J Nutr 97: 1196–1205
21. Lewington S, Whitlock G, Clarke R et al. (2007) Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. Lancet 370: 1829–1839
22. Mozaffarian D, Clarke R (2009) Quantitative effects on cardiovascular risk factors and coronary heart disease risk of replacing partially hydrogenated vegetable oils with other fats and oils. Eur J Clin Nutr 63 Suppl 2: S22–S33
23. Allen BC, Vincent MJ, Liska D et al. (2016) Meta-regression analysis of the effect of trans fatty acids on low-density lipoprotein cholesterol. Food Chem Toxicol 98: 295–307
24. Brouwer IA, Wanders AJ, Katan MB (2010) Effect of animal and industrial trans fatty acids on HDL and LDL cholesterol levels in humans--a quantitative review. PLoS One 5: e9434
25. Radtke T, Schmid A, Trepp A et al. (2017) Short-term effects of trans fatty acids from ruminant and industrial sources on surrogate markers of cardiovascular risk in healthy men and women: a randomized, controlled, double-blind trial. Eur J Prev Cardiol 24: 534–543
26. Gayet-Boyer C, Tenenhaus-Aziza F, Prunet C et al. (2014) Is there a linear relationship between the dose of ruminant trans-fatty acids and cardiovascular risk markers in healthy subjects: results from a systematic review and meta-regression of randomised clinical trials. Br J Nutr 112: 1914–1922
27. Willett WC, Stampfer MJ, Manson JE et al. (1993) Intake of trans fatty acids and risk of coronary heart disease among women. Lancet 341: 581–585
28. Mozaffarian D, Aro A, Willett WC (2009) Health effects of trans-fatty acids: experimental and observational evidence. Eur J Clin Nutr 63 Suppl 2: S5–S21
29. de Souza RJ, Mente A, Maroleanu A et al. (2015) Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. Bmj 351: h3978
30. Mozaffarian D, de Oliveira Otto MC, Lemaitre RN et al. (2013) Trans-palmitoleic acid, other dairy fat biomarkers, and incident diabetes: the Multi-Ethnic Study of Atherosclerosis (MESA). Am J Clin Nutr 97: 854–861
31. Wang Q, Imamura F, Ma W et al. (2015) Circulating and dietary trans fatty acids and incident type 2 diabetes in older adults: the Cardiovascular Health Study. Diabetes Care 38: 1099–1107
32. de Oliveira Otto MC, Nettleton JA, Lemaitre RN et al. (2013) Biomarkers of dairy fatty acids and risk of cardiovascular disease in the Multi-ethnic Study of Atherosclerosis. J Am Heart Assoc 2: e000092
33. Wang Q, Imamura F, Lemaitre RN et al. (2014) Plasma phospholipid trans-fatty acids levels, cardiovascular diseases, and total mortality: the cardiovascular health study. J Am Heart Assoc 3: e000914
34. Li H, Zhang Q, Song J et al. (2017) Plasma trans-fatty acids levels and mortality: a cohort study based on 1999–2000 National Health and Nutrition Examination Survey (NHANES). Lipids Health Dis 16: 176
35. Liu XR, Deng ZY, Hu JN et al. (2013) Erythrocyte membrane trans-fatty acid index is positively associated with a 10-year CHD risk probability. Br J Nutr 109: 1695–1703

36. *Yang Q, Zhang Z, Loustalot F et al. (2017) Plasma trans-fatty acid concentrations continue to be associated with serum lipid and lipoprotein concentrations among US adults after reductions in trans-fatty acid intake. J Nutr 147: 896–907*
37. *Pfeuffer M, Watzl B (2018) Nutrition and health aspects of milk and dairy products and their ingredients. Ernahrungs Umschau 65(2): 22–33*
38. *Downs SM, Thow AM, Leeder SR (2013) The effectiveness of policies for reducing dietary trans fat: a systematic review of the evidence. Bull World Health Organ 91: 262–269H*
39. *Bundesministerium der Justiz und für Verbraucherschutz (2017) Verordnung über diätetische Lebensmittel (Diätverordnung). URL: www.gesetze-im-internet.de/di_tv/BJNR004150963.html Zugriff 15.06.18*
40. *WHO/Europe (2015) Eliminating trans fats in Europe – a policy brief. Copenhagen, Denmark: World Health Organization. URL: www.euro.who.int/__…/Eliminating-trans-fats-in-Europe-A-policy-brief.pdf. Zugriff 10.02.18*
41. *Mozaffarian D, Jacobson MF, Greenstein JS (2010) Food reformulations to reduce trans fatty acids. N Engl J Med 362: 2037–2039*
42. *Wanders AJ, Zock PL, Brouwer IA (2017) Trans fat intake and its dietary sources in general populations worldwide: A systematic review. Nutrients 9: 840*
43. *Bundesinstitut für Risikobewertung (BfR) (2013) Höhe der derzeitigen trans-Fettsäureaufnahme in Deutschland ist gesundheitlich unbedenklich. Stellungnahme 028/2013. URL: www.bfr.bund.de/de/a-z_index/trans_fettsaeuren-7572.html Zugriff 10.02.18*
44. *Kris-Etherton PM, Lefevre M, Mensink RP et al. (2012) Trans fatty acid intakes and food sources in the U.S. population: NHANES 1999–2002. Lipids 47: 931–940*
45. *US Food and Drug Administration (2003) Food labeling: Trans fatty acids in nutrition labeling, nutrient content claims, and health claims. Fed Regist 68: 41433–41506*
46. *US Food and Drug Administration (2015) Final determination regarding partially hydrogenated oils. Fed Regist 80: 34650–34670*
47. *Ratnayake WN, Swist E, Zoka R et al. (2014) Mandatory trans fat labeling regulations and nationwide product reformulations to reduce trans fatty acid content in foods contributed to lowered concentrations of trans fat in Canadian women's breast milk samples collected in 2009–2011. Am J Clin Nutr 100: 1036–1040*
48. *Colon-Ramos U, Baylin A, Campos H (2006) The relation between trans fatty acid levels and increased risk of myocardial infarction does not hold at lower levels of trans fatty acids in the Costa Rican food supply. J Nutr 136: 2887–2892*
49. *Chiuve SE, Rimm EB, Sandhu RK et al. (2012) Dietary fat quality and risk of sudden cardiac death in women. Am J Clin Nutr 96: 498–507*
50. *Wang DD, Li Y, Chiuve SE et al. (2016) Association of specific dietary fats with total and cause-specific mortality. JAMA Intern Med 176: 1134–1145*
51. *Wang Q, Afshin A, Yakoob MY et al. (2016) Impact of nonoptimal intakes of saturated, polyunsaturated, and trans fat on global burdens of coronary heart disease. J Am Heart Assoc 5: e002891*

DOI: 10.4455/eu.2018.047