OCCURRENCE, STRUCTURES AND ESTIMATION OF DAILY INTAKE OF TRANS FATTY ACIDS

Mirjana Milovanović

Abstract: The present review provides an outline of the current knowledge of trans fatty acids (TFA) including their structure and formation, occurrence in foods, especially in meat and meat products, and some estimation and evaluation of daily intake. Special emphasis is put on conjugated linoleic acids (CLA), related to unique beneficial physiological properties, such as on cancer inhibition via the immune system.

Key words: trans fatty acids, conjugated linoleic acids, review.

Introduction

The scope of the present review is to provide comprehensive information on trans fatty acids (TFA). It covers the structure and formation of TFA, estimations of the dietary intake as well as their occurrence in foods. Particular attention is paid to describe the conjugated linoleic acid (CLA) isomers, which possessed the great physiological effects, such as anti carcinogenic and anti atherosclerotic properties (Fritsche, J., Steinhart, H., 1998-a).

Structure and formation of trans fatty acids

In the diet of the most industrial nations, more than one quarter of total daily calories are provided by fatty acids, which contain at least one double bond. The usual configuration of these double bonds is in cis configuration, and the C=C double bonds are typically positioned at the 3rd, 6th 9th carbon atom from the terminal methyl group, e.g. oleic acid (18:1 cis9), or linoleic acid (18:2 cis9 cis12). However, some fatty acids have one or more double bonds in the trans configuration, the so-called trans fatty acids (TFA) (Figure 1).

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Both, TFA and CLA arise in the first stomach of ruminants as intermediates of the hydrogenation of dietary unsaturated fatty acids during bacterial fermentation. The first step in this bio-hydrogenation is the isomerization of the linoleic acid into mainly 18:2 cis9trans11 catalyzed by the anaerobic bacterium. In the next step, these intermediates are hydrogenated into the mixture of mainly trans vaccenic acid and elaidic acid (Figure 2).

Fig. 1. - Structure of oleic acid (18:1 cis9), elaidic acid (18:1 trans9), linoleic acid (18:2 cis9cis12), and the main CLA isomer (18:2 cis9trans11)

Fig. 2. - Formation of elaidic acid (18:1 trans9), trans vaccenic acid (18:1 trans11) and CLA
As the results of this reactions the fat in butter, cheese, milk and beef contains approximately 2-8% TFA by weight (Pfalzgraf, A., et al., 1994). TFAs are also formed in varying amounts during the industrial hydrogenation of vegetable or fish oils. The hydrogenation provides oxidative and thermal stability, in particular for the highly polyunsaturated oils, which contain linolenic acid (18:3, ω-3). In extreme case in the full hydrogenation the oil contains 0% of TFA. In practice, the TFA content is limited by the thermodynamics of the cis-trans equilibrium to approximately 75% of the total number of double bonds (Patterson, H.B.V., 1994).

In ruminants it is evidence that 18:1 trans-11 is the important precursor of the cis-9, trans-11 CLA, endogenously hydrogenated by Δ9-desaturase (Corl, B.A., et al., 2001). In addition, CLA can be also formed through the auto-oxidation of linoleic acid by free radicals, followed the deprotonation of the pentadienyl radical by proteins, as shown in Figure 2.

TFA and CLA contents in food

Edible oils and margarines

Edible oils such as refined or unrefined walnut, olive, sunflower, rapeseed, soybean or peanut oils or coconut fat have only disorderly amounts of TFAs and CLAs (Fritsche, J. and Steinhart, H., 1997 and Fritsche, J. and Steinhart, H., 1998-b). Refined oils contain significantly higher content of TFA in comparing with unrefined oils, as shown in Table 1. The all listed values are presented in minimum and maximum levels.

<table>
<thead>
<tr>
<th>Tab. 1. - Mean TFA and CLA contents in edible oils and margarines</th>
</tr>
</thead>
<tbody>
<tr>
<td>food</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>edible refined oils</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>edible unrefined oils</td>
</tr>
<tr>
<td>margarines</td>
</tr>
<tr>
<td>coconut, olive oils</td>
</tr>
<tr>
<td>margarines</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Legend: TFA- trans fatty acid, CLA-conjugated fatty acid, c-cis; t-trans
The TFA amounts in refined oils are influenced by duration and temperature of refining. Soybean oil can be partially hydrogenated for use in margarine to prevent flavor reversion (Frankel, E.N., 1987). Whereas Chin et al. (Chin, S. F. et al., 1992) found CLA in coconut and olive oil in an order of about 0.02g/100g fat.

The main TFAs in margarines are the 18:1 isomers, approximately 85% of total TFA content in vegetable margarine. The 18:1 trans, 18:2 cis/trans and 18:2 trans/cis, total CLA and TFA originating from different countries are also presented in Table 2. Distinct variations of TFA contents in margarine are observed. This wide variation can be explained by the different processing parameters, such as hydrogenation, or/and deodorization conditions. Another reason for reduce the TFA content is probably the changed blend oils in the margarine composition. Partially hydrogenated oils seem to have been replaced by palm, kernel or coconut oil to obtain acceptable consistency (Bayard, C.C. and R.L. Wolff, 1995). CLA does not arise in considerable amounts during regular processing conditions (Fritsche, J. and Steinhardt, H., 1998-b). Only a few reports, detectable CLA content, are observed in margarine. For instance, it was found that CLA content ranging from 0.31-2.04% in Turkish margarine (Kayahan, M. and Tekin, A., 1994).

Milk and dairy products

Milk fat generally is a fat of rich dietary source of TFA (see Table 2.). The major TFA isomers in dairy product is vaccenic acid (18:1 trans-11) and the other isomers have a lower amounts (Fritsche, J. and Steinhardt, H., 1997 and Fritsche, J. and Steinhardt, H., 1998-b). For instance, the contents of palmitelaidic acid (16:1 trans-9) varied between 0.04% (goat cheese) and 0.21% (light dammer) (Fritsche, J. and Steinhardt, H., 1997). Total TFA content

<table>
<thead>
<tr>
<th>food</th>
<th>origin</th>
<th>18:1 t (% of total fat)</th>
<th>18:2 c.t/c t (% of total fat)</th>
<th>Total TFA (% of total fat)</th>
<th>CLA (% of total fat)</th>
</tr>
</thead>
<tbody>
<tr>
<td>milk fat</td>
<td>Australia</td>
<td>/</td>
<td>/</td>
<td>6.01 (4.3-7.6)</td>
<td>0.9-1.2</td>
</tr>
<tr>
<td>cheese</td>
<td>Germany</td>
<td>3.13 (0.24)</td>
<td>0.48 (0.28)</td>
<td>5.12 (1.02)</td>
<td>1.16 (0.10)</td>
</tr>
<tr>
<td></td>
<td>USA</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.45 (0.06)</td>
</tr>
<tr>
<td></td>
<td>Germany</td>
<td>2.09 (0.89)</td>
<td>0.51 (0.14)</td>
<td>3.89 (1.92)</td>
<td>0.84 (0.38)</td>
</tr>
<tr>
<td>butter</td>
<td>USA</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.32 (0.89)</td>
</tr>
<tr>
<td>fluid milk</td>
<td>Germany</td>
<td>/</td>
<td>/</td>
<td>4.43 (1.99)</td>
<td>0.94 (0.48)</td>
</tr>
<tr>
<td>product</td>
<td>USA</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.40 (0.64)</td>
</tr>
<tr>
<td>processed cheese</td>
<td>USA</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.42 (0.52)</td>
</tr>
</tbody>
</table>

Legend: symbols are the same as listed in Table 1
ranged from 1.5% to 6.5% in raw milk. The variations of TFA contents in dairy products can be explained by varying TFA contents in milk fat. The milk fat content and composition are influenced by the season and also by the different processing parameters, such as heat treatment after pasteurization. An influence of fermentation on the TFA content in yogurt or cheese is also possible. Dairy products are also a major source of CLA, ranged from 0.24% to 1.77% (Table 2). The wide variability is caused by the range of CLA content in the raw material, which is probably influenced by different dairy cow breeds and feeding systems, as well as processing parameters (heat treatment, storage, composition of starter cultures and so on).

Meat, meat products and fish

The TFA contents in meat are presented in Table 3. They ranged from 0.2% in horse up to 10.6% in mutton. Meat from non ruminants such as pork or poultry shows distinctly lower TFA contents than the meat from the ruminants. The TFA content and isomer distribution in beef is similar to that in milk or dairy products (Pfalzgraf, A., Timm and M., Steinhart, H., 1994). The 18:1 trans isomers are the predominant isomers in the meat and with the amount about 80% of the total TFA. The TFA content in the meat product varied from 0.2% to 3.4% of the total fat. These values assume an intermediate position between meat from ruminants and non ruminants, depending of the raw starting material used. German products contain predominantly pork, and therefore reflect comparatively lower TFA amounts. Native fish oil negligible TFA content up to 1.1% compared with those of meat or dairy products. The major TFA isomers are also the octadecenoic acid isomers, average 60% of total TFA (Table 4). Carp has the highest TFA amount (1.1%), which might be caused by feeding TFA containing food to the fish in aquaculture (Fritsche, J. and Steinhart, H., 1997).

In addition the CLA content in the meat from ruminants from instance 1.2% of lamb, is higher than in the meat from non ruminants e.g. 0.12% in pork. In this case CLA may occur from dietary source such as feeding meat meal (Fritsche, J. and Steinhart, H., 1998-b). Another explanation may be the formation the CLA by the intestinal bacteria, as shown for rats (Chin, S.F., et al., 1994). The CLA content in meat products ranged from 0.27% to 0.44%. It seems that CLA content reflects their raw material and has been influenced neither by processing conditions nor by fermentation. The CLA levels in the fish ranged from 0.01% in pike to 0.09% in carp. Currently, a few data dealing with the CLA content in fish are available.
Tab. 3. - Mean TFA and CLA contents in meat and meat products

<table>
<thead>
<tr>
<th>food</th>
<th>origin</th>
<th>18:1 t (% of total fat)</th>
<th>18:2 c,t/t,c (% of total fat)</th>
<th>Total TFA (% of total fat)</th>
<th>CLA (% of total fat)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-meat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>round beef</td>
<td>USA, 1992</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.29 (0.01)</td>
</tr>
<tr>
<td>fresh ground beef</td>
<td>1992</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.43 (0.01)</td>
</tr>
<tr>
<td>lamb</td>
<td></td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.27 (0.02)</td>
</tr>
<tr>
<td>pork</td>
<td></td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.56 (0.03)</td>
</tr>
<tr>
<td>chicken</td>
<td></td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.06 (0.01)</td>
</tr>
<tr>
<td>fresh turkey</td>
<td>Germany, 1992</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.09 (0.002)</td>
</tr>
<tr>
<td>beef</td>
<td>Germany, 1992</td>
<td>1.4-2.4</td>
<td>0-0.3</td>
<td>1.9-3.2</td>
<td>/</td>
</tr>
<tr>
<td>lamb</td>
<td>1992</td>
<td>5.2-7.0</td>
<td>0.6-0.9</td>
<td>6.6-8.8</td>
<td>/</td>
</tr>
<tr>
<td>sheep</td>
<td></td>
<td>2.2</td>
<td>0.4</td>
<td>3.2</td>
<td>/</td>
</tr>
<tr>
<td>mutton</td>
<td></td>
<td>6-8.9</td>
<td>0.9-1.2</td>
<td>8.2-10.6</td>
<td>/</td>
</tr>
<tr>
<td>pork</td>
<td></td>
<td>0.2-0.4</td>
<td>trace</td>
<td>0.2-0.4</td>
<td>/</td>
</tr>
<tr>
<td>poultry</td>
<td></td>
<td>0.2-1.2</td>
<td>0-0.2</td>
<td>0.2-1.4</td>
<td>/</td>
</tr>
<tr>
<td>rabbit</td>
<td></td>
<td>0.3</td>
<td>trace</td>
<td>0.4</td>
<td>/</td>
</tr>
<tr>
<td>horse</td>
<td></td>
<td>0.2</td>
<td>trace</td>
<td>0.2</td>
<td>/</td>
</tr>
<tr>
<td>pork</td>
<td>Germany, 1997</td>
<td>0.22-0.42</td>
<td>0.02-0.03</td>
<td>0.46-0.68</td>
<td>0.12-0.15</td>
</tr>
<tr>
<td>lamb</td>
<td>1997</td>
<td>7.53</td>
<td>0.23</td>
<td>9.80</td>
<td>1.20</td>
</tr>
<tr>
<td>turkey</td>
<td></td>
<td>0.89</td>
<td>0.08</td>
<td>1.19</td>
<td>0.20</td>
</tr>
<tr>
<td>beef steak</td>
<td></td>
<td>2.29</td>
<td>0.19</td>
<td>3.57</td>
<td>0.65</td>
</tr>
<tr>
<td>beef liver</td>
<td></td>
<td>2.27</td>
<td>0.03</td>
<td>2.84</td>
<td>0.43</td>
</tr>
<tr>
<td>rabbit</td>
<td></td>
<td>0.16</td>
<td>0.03</td>
<td>0.37</td>
<td>0.11</td>
</tr>
<tr>
<td>chicken</td>
<td></td>
<td>0.52</td>
<td>0.10</td>
<td>0.88</td>
<td>0.15</td>
</tr>
<tr>
<td>-meat products</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>meat products</td>
<td>Germany, '93,</td>
<td>0.14-0.53</td>
<td>0.02-0.12</td>
<td>0.48-1.09</td>
<td>0.27-0.44</td>
</tr>
<tr>
<td>1997</td>
<td></td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.08-0.33</td>
</tr>
<tr>
<td>meat products</td>
<td>USA, 1992,</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td></td>
<td>/</td>
<td>/</td>
<td>/</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>/</td>
<td>/</td>
<td>/</td>
<td></td>
</tr>
</tbody>
</table>

Legend: symbols are the same as in Table 1

Tab. 4. - Mean TFA and CLA contents in fish

<table>
<thead>
<tr>
<th>fish</th>
<th>origin</th>
<th>18:1 t (% of total fat)</th>
<th>18:2 c,t/t,c (% of total fat)</th>
<th>Total TFA (% of total fat)</th>
<th>CLA (% of total fat)</th>
</tr>
</thead>
<tbody>
<tr>
<td>salmon</td>
<td>USA</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.03 (0.005)</td>
</tr>
<tr>
<td>sea scallops</td>
<td>1992</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.03 (0.005)</td>
</tr>
<tr>
<td>mussels</td>
<td></td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.04 (0.004)</td>
</tr>
<tr>
<td>shrimp</td>
<td></td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0.06 (0.01)</td>
</tr>
<tr>
<td>carp</td>
<td>Germany, '97</td>
<td>0.50</td>
<td>0.27</td>
<td>1.10</td>
<td>0.09</td>
</tr>
<tr>
<td>pike perch</td>
<td></td>
<td>0.56</td>
<td>0.02</td>
<td>0.91</td>
<td>0.01</td>
</tr>
<tr>
<td>ocean perch</td>
<td></td>
<td>0.54</td>
<td>0.04</td>
<td>0.88</td>
<td>0.06</td>
</tr>
<tr>
<td>salmon</td>
<td></td>
<td>0.33</td>
<td>0.05</td>
<td>0.71</td>
<td>0.07</td>
</tr>
<tr>
<td>wolf fish</td>
<td></td>
<td>0.36</td>
<td>0.07</td>
<td>0.58</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Legend: symbols are the same as in Table 1
Estimation and evaluation of daily TFA and CLA intake

The dietary TFA has been estimated from the dietary questionnaires or recall data, milk fat data or food content analysis data. Commonly, the basis of TFA intake calculation varies resulting in varying intake levels in the literature. The main dietary TFAs are the trans-octadecenoic acids, which contribute to approximately 80-90% of total TFA content in foods. One of the most recent TRANSFAIR studies (Van de Vijver et al., 2000) reported a very low intake of TFA amounting to 0.87% in man and 0.95% in woman, respectively (Table 5). It should be mentioned that the TFA intake in these study was observed with range 2.40±1.53g/day for man and 1.98±1.49g/day for women.

Table 5. - The fatty acids intake according to the TRANSFAIR study, presented as absolute amounts and in percentage energy*

<table>
<thead>
<tr>
<th></th>
<th>Men (n=327)</th>
<th>Women (n=299)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount (g/day)</td>
<td>En%</td>
<td>Amount (g/day)</td>
</tr>
<tr>
<td>Total fat content</td>
<td>93.25</td>
<td>46.6</td>
</tr>
<tr>
<td>SFA</td>
<td>33.6</td>
<td>12.1</td>
</tr>
<tr>
<td>MUFA</td>
<td>32.4</td>
<td>16.2</td>
</tr>
<tr>
<td>PUFA</td>
<td>13.3</td>
<td>6.6</td>
</tr>
<tr>
<td>TFA</td>
<td>2.4</td>
<td>0.87</td>
</tr>
</tbody>
</table>

*SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids;

Table 6 presents an overview of the daily intake TFA and CLA intake in different countries. It seems that that the individuals from the Mediterranean regions have a lower intake of TFA, around the 2g/day, compared with to individuals from other European countries (Wolff, R. L., 1994). The British Ministry of Agriculture published average TFA intake data from frying oils and foods cooked in frying oils. The intake was estimated in the region of 2.0-1.7 g/day for man and women, respectively (Ministry of Agriculture, 1997). It was reported (Pfalzgraf, A. and Steinhart, H., 1992) the daily intake of TFA in 1992 to be 4.1g/day for man and women in Germany. In a view of decreased of TFA content in German margarines since 1992 the estimation of the daily TFA intake was updated in 1997 to 2.3 g/day (Fritsche, J. and Steinhart, H., 1997). These results showed a decrease of daily TFA intake since 1992 approximately 40%.

The TFA intake in USA seems to be elevated compared with the intake in Europe, probably due to the higher total fat intake. Since 1984 the per capita availability of TFAs from household salad, cooking oils, margarines, and spread has decreased, however. This decreased is the case of household salad and cooking oils is probably due to the switch of the most manufactures unhydrogenated oil for this product. Per capita TFA consumption from meat and...
dairy products has remained relatively constant and was estimated to 1.34 g/day per person in 1989 (Hunter, J.E. and Applewhite, H.T., 1991).

Only a few data concerning the CLA intake are reported. The daily CLA intake in Germany has been estimated to be 0.36 g/day for women and 0.44 g/day for man (Fritsche, J. and Steinhardt, H., 1998-b). Compared with the estimated daily TFA intake, the CLA intake is approximately one fifth. Therefore, the human nutrition in Germany may provide about one fifth of the 0.1% beneficial level of CLA in the diet, based on the relatively contents of the main CLA isomer and total food intake (see Table 6).

Tab. 6. - Estimation of daily TFA and CLA intake in different countries (g/day)

<table>
<thead>
<tr>
<th>Country</th>
<th>years</th>
<th>gTFA/day</th>
<th>gCLA/day</th>
<th>basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>1986</td>
<td>7.6</td>
<td></td>
<td>-market size and share data combined with TFA product data</td>
</tr>
<tr>
<td></td>
<td>1989</td>
<td>8.1</td>
<td></td>
<td>-availability data</td>
</tr>
<tr>
<td></td>
<td>1990</td>
<td>12.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GB</td>
<td>1984</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1995</td>
<td>3.1</td>
<td></td>
<td>-analysis data from frying oils and fried foods</td>
</tr>
<tr>
<td></td>
<td>1997</td>
<td>1.7 (women)</td>
<td>2.0 (men)</td>
<td></td>
</tr>
<tr>
<td>Ireland</td>
<td>1995</td>
<td>2.6</td>
<td></td>
<td>- availability data from ruminant and margarine sources</td>
</tr>
<tr>
<td>France</td>
<td>1995</td>
<td>2.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>1995</td>
<td>1.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Portugal</td>
<td>1995</td>
<td>2.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>1995</td>
<td>1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greece</td>
<td>1995</td>
<td>2.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>1992</td>
<td>3.4 (women)</td>
<td>4.1 (man)</td>
<td>-German Nutrition Study and TFA survey data</td>
</tr>
<tr>
<td></td>
<td>1995</td>
<td>3.7</td>
<td></td>
<td>-dietary plans</td>
</tr>
<tr>
<td></td>
<td>1996</td>
<td>1.5-3.1 (kids)</td>
<td>0.31 (women)</td>
<td>-German Nutrition Study and TFA and CLA data</td>
</tr>
<tr>
<td></td>
<td>1997</td>
<td>1.9 (women)</td>
<td>0.35 (women)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1997</td>
<td>2.3 (man)</td>
<td>0.43 (man)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.5-1.5</td>
<td>-nutrition data and CLA content of milk fat and CLA content of ruminant fat</td>
</tr>
<tr>
<td>Australia</td>
<td>1994</td>
<td>0.31</td>
<td>0.43 (man)</td>
<td></td>
</tr>
</tbody>
</table>

Acknowledgement

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Occurrence, structures and estimation on daily intake of trans fatty acids

Conclusion

Partially hydrogenated vegetable oils, dietary products and meat from ruminants are the major sources of TFA in diet. During the past several years the TFA content in most European margarines has decreased significantly, therefore the total daily TFAs decreased in some manner. In numerous foods, particularly in dietary foods CLA have been observed. In contrast to the conventional TFAs, CLAs are linked with unique anti carcinogenic properties. So, the supplementation of CLAs in food should be considered.

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TRANS MASNE KISELINE: ZASTUPLJENOST, STRUKTURE, MIŠLJENJA I DNEVNI UNOSI

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Rezime

Ovaj pregledni rad daje prikaz poznatih i aktuelnih saznanja o trans masnim kiselinama (TFA), uključujući njihovu strukturu i nastajanje, zastupljenost u ishrani i namirnicama, posebno u mesu i proizvodima od mesa, i potrebe u dnevnim unosima. Posebno je istaknuta konjugovana linolna kiselina (CLA), koja poseduje značajne fiziološke osobine, jer inhibira nekoliko vrsta karcinoma.

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