



The impact of different fatty acids and their thermal preparation method on atherosclerosis. A review

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Abstract. Atherosclerosis is a multifactorial disease where both oxidative and inflammatory processes play a key role in its development. Lipoproteins facilitate the entering of the lipids into the blood stream and carry them to their destination in the body. Because of the finite number of lipoprotein receptors, the excess amount of lipids enters into the circulatory system; they may become subject to oxidative processes. Fatty acids influence not only the lipoprotein secretion but even the cholesterol efflux and its homeostasis. Compared to the food production processes used in the food industry, domestic preparation methods of lipids do not significantly influence the properties of fatty acids, they do not contribute to the extra formation of trans-fatty acids, but they expose the fatty acids to oxidation. Characterizing the fatty acids according to their beneficial effect on health, it can be concluded that poly-unsaturated fatty acids have proven to be the most beneficial, followed by mono-unsaturated and saturated fatty acids, while the consumption of trans-fatty acids should be avoided as much as possible in order to eliminate a possible source of the development of atherosclerosis.

Keywords and phrases: atherosclerosis, lipoproteins, fatty acids, PUFA, trans-fatty acids.

1 Atherosclerosis

Atherosclerosis is considered to be the inflammation of the arteries. The inflammation is initiated by the entrance of lipids into the vascular system (*Toh et al.*, 2014).

The American Heart Association defines this disease as follows: fatty substances, cholesterol, cellular waste products, calcium and fibrin form an interior lining in the arteries. The accumulation of these substances is called arterial plaque (http://www.heart.org/HEARTORG/Conditions/Cholesterol/WhyCholesterolMatters/Atherosclerosis_UCM_305564_Article.jsp#).

The accumulation of lipids in the lesions of blood vessels eventually leads to the occlusion of these vessels. Both the oxidative and inflammatory processes play a role in the development of this multifactorial disease. Environmental factors, such as nutrition as well as genetic factors, play an important role in the modulation of inflammatory and oxidative state of the components that influence the development of the disease. Although some risk factors are already known to researchers, the molecular characteristics of the development and progression of this disease are still undiscovered (*Ortega et al.*, 2012). However, it is already known that lipids have an important role both in the development and in the progression of atherosclerosis.

2 Lipids

The term lipid is the generic name of a group of hydrophobic molecules, which includes fats, waxes, sterols (e.g. cholesterol), fat-soluble vitamins (such as vitamin A, D, E and K), mono-glycerides, di-glycerides, tri-glycerides or phospholipids. Lipids are not only a rich source of energy, but they also have an important role in intracellular signalling, regulating hormones, in the crossing of membranes and blood clotting (*Saba & Oridupa*, 2012).

From the point of view of atherosclerosis, the most important components to consider are the fats and the sterols.

2.1 Fats

As a subgroup of lipids, fats are not soluble in water. We distinguish between two types of fats, the liquid fats and the solid fats. Liquid fats are called oils, and the term fat remains the name of the solid fats. The difference between the physical state of these fats is due to the differences of the constituent components of the fat, the fatty acids. Each type of fatty acid has a different melting point.

2.2 Fatty Acids

Fatty acids are hydrocarbon structures, formed of at least three methyl groups attached to a carboxylic acid. Their physical and chemical properties (e.g. solubility in non-polar solvents, melting point) change according to the number of methyl groups (the number of carbon atoms) in the molecule. The greater the number of carbon atoms in the fatty acid chain, the higher the melting temperature will be. Depending on the number of carbon atoms, we further distinguish among short-chain fatty acids (from C4 to C10), medium-chain fatty acids (C12 to C14), long-chain fatty acids (C16 and C18), and very-long-chain fatty acids (C20 or more). Carbon atoms can be linked through a single bond; in this case, we are talking about saturated bond or double bonds, which are the unsaturated bonds. Fatty acids containing no double bonds are called saturated fatty acids, and those containing at least one double bond (and up to 6 double bonds) are called unsaturated fatty acids. Depending on the number of double bonds in the chain, we may talk about mono-unsaturated fatty acids (MUFA) containing a single double bond and poly-unsaturated fatty acids (PUFA) containing more than one double bond. The melting temperature is also influenced by the number of double bonds in the chain, and this way the unsaturated fatty acids have a lower melting point as saturated fatty acids, though containing the same number of carbon atoms. There are two essential fatty acids in the human body. These are the linoleic acid (C18:2 ω -6) and the α -linolenic acid (C18:3 ω -3). Another important fatty acid, the arachidonic acid (fulfilling important roles in cell signalling), becomes also essential in the absence of linoleic acid. Depending on the structure of unsaturated fatty acids, we distinguish between cis and trans isoforms. In the cis isoform, the hydrogen atoms linked by the carbon atoms involved in the double bond are positioned on the same side of the linkage, while in the case of the trans isomers, the hydrogen atoms are situated opposite one another. The main difference between these isomers is to be found in their melting temperatures. Thus, not only the biochemical behaviour of the fatty acid changes, but also its value as a nutrient (*Valenzuela & Valenzuela, 2012*).

3 Atherosclerosis and lipoproteins

The initial step in the development of atherosclerosis is the accumulation of lipoproteins containing apolipoprotein B in the endothelium. ApoB lipoproteins are composed from cholesterol esters and triglycerides (tri-acyl-glycerides), surrounded by a layer of phospholipids and proteins (*Ortega et al., 2012*).

Lipoproteins are formed to facilitate the circulation of lipids (in the form of triglycerides) in the blood (thus becoming soluble in aqueous solutions). The proteins that bind to the lipids carry them to their destination in the human body. Lipoproteins are characterized based on their density. There are high-density lipoproteins (HDL), low-density lipoproteins (LDL), intermediate-density lipoproteins (IDL), very-low-density lipoproteins (VLDL) and chylomicrons (CM). Each group has different functions, but only the high-density lipoproteins are beneficial from the point of view of preventing the development of atherosclerosis (*Saba & Oridupa, 2012*).

High LDL level decreases, while low HDL level raises the risk of the development of cardiovascular diseases. In addition to various factors, such as smoking, hypertension, high serum cholesterol level or diabetes, high LDL cholesterol and low HDL cholesterol have an important role in the development of atherosclerosis. Another function of lipoproteins is the transport of cholesterol. Cholesterol enters the cell via receptor-mediated endocytosis. This receptor recognizes the LDL molecule, which transports the cholesterol. The number of LDL receptors is a finite number. In the case of a deregulation of cholesterol synthesis in the body, the automatically increased formation of lipoproteins that will carry the formed cholesterol will cause an excess in circulating lipoproteins, which cannot be recognized by the already blocked LDL receptors. This excess LDL is prone to oxidization and will be recognized as waste by the macrophages, which will soon form the so-called foam cells, which remain blocked in the arteries, leading to inflammation (*Saba & Oridupa, 2012*).

4 Fatty acids regulate the lipoprotein secretion

The risk of developing atherosclerosis is highly influenced by the lipoproteins secreted by the body. Various factors influence the rate of secreted lipoproteins (e.g. disturbances in the production of cholesterol).

4.1 Poly-unsaturated fatty acids

Carluccio et al. demonstrated that the balanced rate of mono-unsaturated fatty acid and poly-unsaturated fatty acids may have a regulatory effect on lipoprotein secretion, increasing HDL cholesterol and lowering LDL cholesterol (*Carluccio et al., 2007*).

Another study effectuated by Machado et al. also demonstrated the role of poly-unsaturated fatty acids (PUFA) in preventing the development of

atherosclerosis. Mice, on which the study was carried out, had the genes responsible for the production of LDL receptors deleted. Because of the excess LDL cholesterol formed, they had to develop atherosclerosis. When feeding them a diet rich in PUFA (ω -6), the concentration of the total cholesterol in the aortic root and that of the total triglycerides was lower than when the mice were fed trans-fatty acids or saturated fatty acids. After measuring other factors involved in the development of atherosclerosis, the research team ultimately could conclude that a diet rich in PUFA prevented the development of atherosclerosis in the case of the mice analysed, even in pro-inflammatory conditions (*Machado et al.*, 2012).

4.2 Trans-fatty acids

Trans-fatty acids are the isomers of unsaturated fatty acids with cis geometry. The trans isomer form does rarely occur in nature, but it is formed under different conditions during the processing of food in the food industry. The only known natural source of trans-fatty acids are the conjugated acids. They are formed by bacteria in the rumen of the ruminants. The acids formed enter into the meat through the circulation, making it the only natural source of trans-unsaturated fatty acids.

The main industrial procedure by which trans-fatty acids are formed is the hydrogenation of unsaturated fatty acids. This procedure is used to produce saturated or partially saturated fatty acids from unsaturated fatty acids, thus obtaining a fat with a melting temperature higher than the initial one. In this way, spreadable fats, such as margarine or others made to replace butter, can be obtained from vegetable oils.

During the process of hydrogenation of unsaturated fatty acids, unsaturated trans-fatty acids are secondary – also referred to as contaminant – products brought into the product by the side reactions of the isomerization catalyst.

It is believed that elevated temperatures, such as temperatures reached while toasting or baking (200 °C), could also result in the formation of trans-fatty acids. But recent studies show that even temperatures reached during cooking in the kitchen, or even higher temperatures, do not lead to significant amount of isomerization of unsaturated fatty acids into trans-fatty acids. A more important problem to consider in this case would be the oxidation of unsaturated fatty acids (*Przybylski & Aladedunye*, 2012).

Epidemiological evidence associates trans-fatty acids (TFA) with heart disease. It is believed that the trans-fatty acids stimulate the development of atherosclerosis but have no additional effect when consuming high amounts of

dietary cholesterol, which is considered to be even more atherogenic (*Chantal, 2009*).

A recent study demonstrates similar detrimental effect of unsaturated trans-fatty acids on health as well, analysing it on the molecular level. In addition to the fact that unsaturated fatty acids (UFA) have the ability to prevent the harmful effects of diet consisting only of saturated fatty acids, which have as a result a reduced cholesterol efflux, it was demonstrated that unsaturated trans-fatty acids increase the level of cholesterol in macrophages, reducing the expression of the gene responsible for the production of the particular protein which regulates the cholesterol efflux and its homeostasis (ABCA1 gene protein CERP) (*Milessa da Silva et al., 2013*).

Kummerow et al. also showed that the consumption of unsaturated trans-fatty acids disturbed the metabolism of essential fatty acids of 30 pigs analysed, thereby leading to a change of aortic fatty acid composition, which is considered to be the most vulnerable tissue in terms of the development of atherosclerosis (*Kummerow et al., 2007*).

Mozaffarian et al. describe the unsaturated trans-fatty acids to be harmful because of the following facts: the consumption of only unsaturated trans-fatty acids in place of unsaturated fats, or even instead of saturated fats, increases the level of LDL cholesterol and decreases the level of HDL cholesterol, while it also increases the level of triglycerides in the blood, promotes inflammation (increasing the activity of the tumour necrosis factor system, TNF) and leads to endothelial dysfunction (*Mozaffarian et al., 2006*).

5 Conclusions

In addition to their role as an energy source, fats have an increased importance in the health of the human body. Depending on their physico-chemical structure, the components of fats, such as fatty acids, can have both beneficial and harmful effects. Categorizing fatty acids according to their harmful effects on health and their impact on atherosclerosis, it can be concluded that unsaturated trans-fatty acids is a category of fatty acids which needs to be avoided as much as possible. Being derived as by-products of industrial processes, the largest amount of consumed trans-fats is not part of a natural diet. On the other hand, we do not know exactly if even the naturally occurring conjugated fatty acids do have a beneficial effect on the body, although many studies try to answer this question. The second category indicated to be consumed in reduced quantities is the category of saturated fatty acids. Because

these fatty acids occur naturally in many of our foods too, they should not be avoided completely, but they should be consumed in moderate amounts to avoid the potential adverse consequences from the point of view of the development of atherosclerosis. On the other hand, poly-unsaturated fatty acids show interesting and beneficial effects in preventing atherosclerosis.

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