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Chapter 3

REGULATION OF THE INTAKE OF ARACHIDONIC ACID BY MODIFYING ANIMAL PRODUCTS AND ITS EFFECT ON INFLAMMATORY PROCESSES IN THE HUMAN BODY

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ABSTRACT

In this study we focused on the problem of arachidonic acid metabolism, belonging to the group of *n-6*. In recent years, there has been a marked increase in human consumption of polyunsaturated fatty acids *n-6*, with a simultaneous reduction of *n-3* intake. Arachidonic acid, a component of the lipid bilayer, is a precursor of many biologically important compounds include eicosanoids (prostaglandins, leukotrienes) involved in the stimulation of inflammatory processes. To prevent this, our diet should contain foods rich in *n-3*, which compete with *n-6* for the same metabolic pathways, thereby reducing the level of arachidonic acid

in cells and extinguish the inflammation. This can be achieved by changing diet and modifying the composition of products of animal origin, such as eggs, milk and meat. Studies on the properties of *n-3* and *n-6* have been widely carried out in terms of their pharmacological use in the treatment of diseases with acute and chronic inflammation.

Keywords: Arachidonic acid, inflammatory process, omega acids, eicosanoids, metabolism of arachidonic acid

ABBREVIATION

AA – arachidonic acid;
ALA – α-linolenic fatty acid;
CLA – conjugated linoleic acid;
COX – cyclooxygenase;
DGLA - dihomo-γ-linolenic acid;
DHA – docosahexaenoic acid;
DPA – docosapentaenoic acid;
EFAs – essential fatty acids;
EPA – eicozopentaenoic acid;
FFAs – unesterified fatty acids;
GLA – γ-linolenic acid;
LA – linoleic acid;
LCFAs – long chain fatty acids;
LCPUFAs – long chain polyunsaturated fatty acids;
LOX – lipoxygenase;
LT – leukotrienes;
NSAIDs – nonsteroidal anti-inflammatory drugs;
PG – prostaglandin;
PGI – prostacyclin;
PGHS – prostaglandin synthase;
PUFAs – polyunsaturated fatty acids;
TX – thromboxanes;
5-HETE – 5-Hydroxyeicosatetraenoic acid;
5-HPETE – 5-hydroperoxyeicosatetraenoic acid,
VEGF – vascular endothelial growth factor

1. INTRODUCTION

Long-chain polyunsaturated fatty acids (PUFAs) contain 18–20 carbons or more and can be grouped into two main families - *n-6* and *n-3*, depending on the position of the first double bond from the methyl end of the fatty acid (Venegas-Calerón et al., 2010). Arachidonic acid (AA) is a fatty acid with 20 carbon chain belonging to group *n-6*, what means its first double bond is located at the sixth carbon from the omega end.

AA next to docosahexaenoic acid (C22:6 DHA) is the major component of cell membranes. It is esterified in the membrane phospholipids at the sn-2 position and it occurs in abundant quantities in several tissues. The content of AA in plasma phospholipids and triglycerides is 8% and 1.64% respectively, when DHA content accounts for only 2.4% and 0.35% (Spector, 2000). In addition to the acids mentioned above also the linoleic acid (LA) from the *n-6* group (a precursor of arachidonic acid) constitutes a high lipid fraction (21%-23% of total fatty acids).

A large amount of PUFAs, especially AA, are presented in brain as well as in kidneys, heart, erythrocytes, neutrophils, monocytes and liver cells (Simopoulos, 2001; Wainwright, 2002; Palmquist, 2009). These fatty acids regulate several processes within the brain, such as neurotransmission, cell survival, neuroinflammation, mood and cognition. Overproduction or imbalance of the AA, DHA and their metabolites as well as their signaling pathways are impaired in various neurological disorders, including Alzheimer's disease and major depression (Kiso, 2011). AA is also a main fatty acid presented in placenta (Khan et al., 2008; Kremmyda et al., 2011). AA derived prostaglandins participate in the maintenance of pregnancy and initiation of labor.

Arachidonic acid plays an important role in inflammatory process and inflammation related diseases. While moderate inflammation may have positive effects on human and animal health, the chronic form contributes to a number of disorders. Increased consumption of AA leads to enhanced production of pro-inflammatory factors, thus intensifying the inflammation. Recent studies have demonstrated that AA might be also involved in pathogenesis of diseases correlated with central nervous system, cardiovascular system, diabetes and cancer (Maekawa et al., 2009; Russo, 2009; Vainio et al., 2011). More than 25% of today available for sale drugs were developed to target signaling pathways involving AA (Li et al., 2011).

2. BIOSYNTHESIS OF ARACHIDONIC FATTY ACID

The linoleic fatty acid (C18:2 LA) from the *n-6* group as well as α-linolenic fatty acid (C18:3 ALA) from the *n-3* group are termed as „essential fatty acids" (EFAs) because they are necessary for proper growth, development and function but cannot be synthesized by mammalian cells (Le et al., 2009). This disability results from the lack of adequate enzymes Δ12- and Δ15-desaturase and therefore these acids must be obtained directly from the diet (Simopoulos, 2009). The term "essential" was first proposed by Burr and Burr during their studies on essential fatty acids deficiency in rats (Burr and Burr, 1930). It was noticed only LA and ALA among many other fatty acids provided with diet could reverse the symptoms of the disease. LA and ALA are precursors for the rest of fatty acids including highly important metabolites like arachidonic acid (AA) from the *n-6* group as well as docosahexaenoic acid (C22:6 DHA) and eicosapentaenoic acid (C20:5 EPA) from the *n-3* group which can be provided directly in the diet or synthesized in the body (Wall et al., 2010). The amount of arachidonic acid in organism varies depending on the type and amount of fatty acids provided in the diet and their ratios. It is worth noting that conversion of EFAs occurs more efficiently and more intensively in animal tissues compared to human (Palmquist, 2009). Because production of AA, EPA and DHA might be limited in some conditions like prematurity and growth periods, what requires exogenous supplementation, they can be considered as conditional EFAs (Le et al., 2009).

Enzyme Δ-6 desaturase converts linoleic acid (C18:2 *n-6*) to γ-linolenic acid (GLA C18:3 *n-6*) by inserting a double bond between the sixth and seventh carbon (Figure 1). The same enzyme is involved in the metabolism of α-linolenic acid (C18:3 *n-3*) into octadecatetraenoic acid (C18:4). Then, GLA is converted to dihomo-γ-linolenic acid (DGLA C20:3 *n-6*) by the action of elongase which elongates carbon chain. As a result of Δ-5 desaturase activity DGLA is next transformed to the arachidonic acid (C20:4 *n-6*) by addition of a double bond between the fifth and sixth carbons. Elongase and Δ-5 desaturase synthesize also eicosapentaenoic acid (EPA C20:5 *n-3*) from octadecatetraenoic acid. Arachidonic acid can be then converted to tetraeicosapentaenoic fatty acid (C24:5 *n-6*) and eicosapentaenoic acid is changed into tetradocosaheksaenoic fatty acid (C24:6 *n-3*). The end products of fatty acids biosynthesis are docosapentaenoic (DPA C22:5 *n-6*) and docosahexaenoic acids (DHA C22:6 *n-3*) respectively.

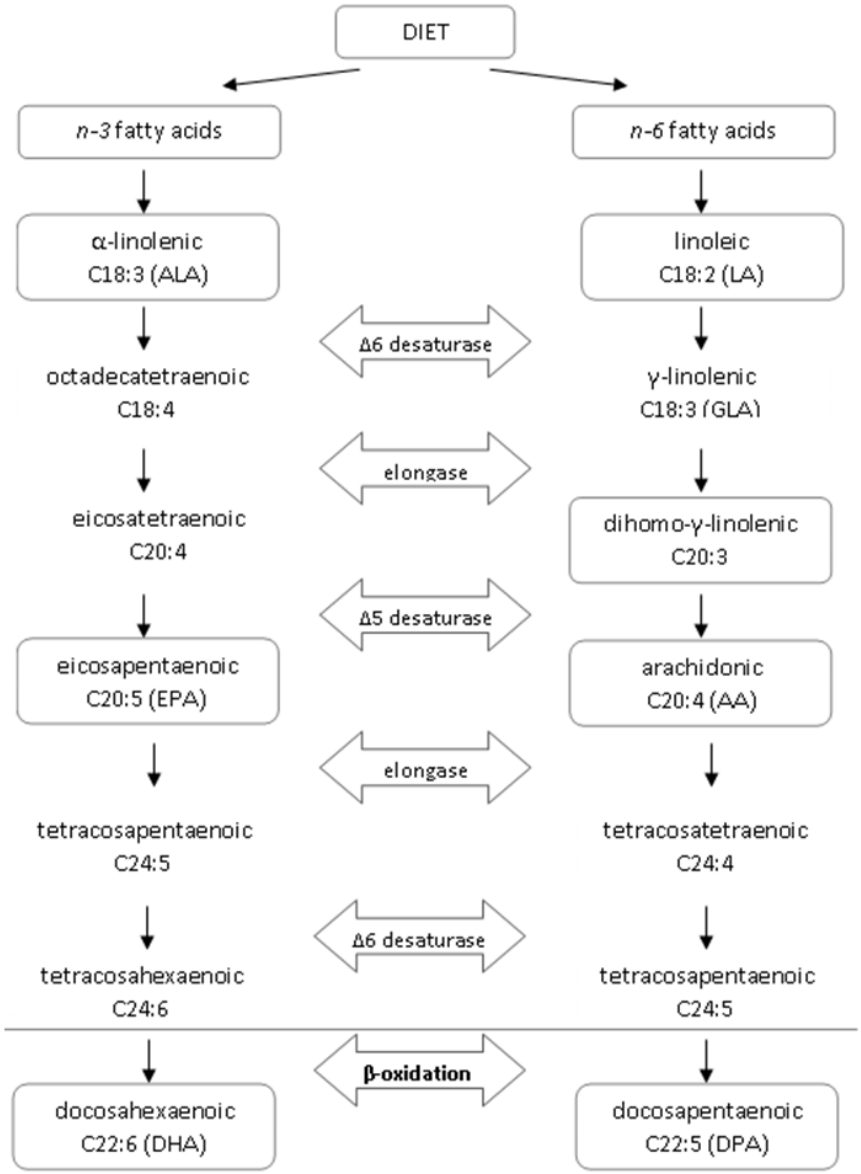

Figure 1. Biosynthesis of long chain polyunsaturated fatty acids from group *n-3* and *n-6*.

Desaturase and elongase are microsomal lipid layer associated enzymes which require the presence of zinc atoms for proper function (Nakamura et al., 2004). Transformation of ALA and LA depends mainly on the amount of desaturases, which activities decrease in the presence of saturated fats, cholesterol, trans-fatty acids, alcohol, adrenaline, insulin, glucocorticoids, diabetics and hypertensives (Das, 2008).

On the other hand factors such pyridoxine, zinc, nicotinic acid, and magnesium are co-factors for normal desaturase activity. The conversion efficiency of ALA-EPA-DHA varies also according to the sex. In adult men it is equal to 8% for reaction ALA-EPA and less than 0.1% for transformation of EPA to DHA, while the conversion efficiency to DHA in women is more than 9% (Abedi and Sahari, 2014). DHA concentration increase additionally during pregnancy and lactation due to estrogen action on Δ6-desaturase.

3. THE N-6/N-3 BALANCE

The amount of provided PUFAs it is not the only crucial factor for organism homeostasis and health. As it turned out, the ratio of *n-6*/*n-3* is even more significant as it is the key indicator of eicosanoids synthesis in the body. It follows from the fact that fatty acids from group *n-3* and *n-6* compete with each other for the same metabolic pathways. Thereby, long chain *n-3* PUFAs consumption extinguishes the inflammation by reducing the level of AA with simultaneous increase in EPA and DHA in cells due to reduced competition for Δ6-desaturase.

Unfortunately, enhanced marketing of cooking oils and margarines contributed to the increased intake of linoleic acid in Western countries over the last few years (Blasbalg et al., 2011). This changed pattern of consumption has caused a significant increase in the ratio of *n-6* to *n-3* PUFAs in the diet (Liu et al., 2015). This ratio should be approximately equal to 1, while nowadays in most Western populations it can be equal almost 20 (Burdge and Calder, 2006). The lowest ratio is observed among populations leaving in Coastal states, which consume a large quantity of fishes and seafoods rich in *n-3* fatty acids (Abedi and Sahari, 2014). A very good example are Japanese who take an ideal ratio of 1/2-4 (Aleksandra et al., 2009). The opposite site is represented by United States, where consumption of *n-6* is 10–30 times more than *n-3* (Abedi and Sahari, 2014). Not only a diet can influence the balance between *n-3* and *n-6* fatty acids. Some physiologic states such as aging, infant

prematurity, hypertension and diabetes also can regulate long-chain *n-3* PUFAs production (Liu et al., 2015).

Clinical studies provide evidence that decreased *n*−6/*n*−3 ratio acts protective against degenerative disorders and cancer, as well as contributes to increased number of leukocytes, platelets and vascular endothelial growth factor (VEGF) (Russo, 2009). Moreover, diet changing in order to achieve a 4:1 ratio by replacing corn oil (high in LA) with olive and canola oil (low in LA) results in 70% decreasing in total mortality (de Lorgeril et al., 1994). Elevated ratio of AA to *n-3* fatty acid was also showed to be associated with depression (Lotricha et al., 2013).

4. ARACHIDONIC ACID BIOLOGY AND METABOLISM

Supplied with food AA, LA together with other polyunsaturated fatty acids are esterified in the liver and then released into the bloodstream, bounded to lipoproteins and distributed to all cells (Nowak, 2009). A small amounts of released AA, as well as other fatty acids are returned to the bloodstream where they bind to albumin (Figure 2). Over 90% of the fatty acids circulate in the blood bound to plasma proteins. The concentration of free fatty acids (FFAs) is relatively low but they are the most metabolically active lipid fractions. Plasma FFAs might be also a source of PUFA delivered to brain (Spector, 2000). Studies using radiolabeled PUFAs showed that they are entering brain readily when injected into the plasma with almost all AA cleared within 2 minutes (Rapoport et al., 2001; Liu et al., 2015).

FFAs participate not only in initiation of inflammatory pathways in a variety of cell types, but also produce numerous bioactive metabolites, function as secondary messengers and regulate platelet aggregation and vascular tone (Baker et al., 2011; Le et al., 2009). Moreover, they can directly affect the expression of genes which modulate fatty acids oxidation as well as fatty acids, lipids and lipoproteins synthesis (Kremmyda et al., 2011). Free fatty acids can stimulate the activity of different receptors and thus affect the secretion of insulin or neuropeptide Y (Doege and Stahl, 2006). The majority of FFAs is transported into the cell by diffusion but the part of them is moved by protein-mediated transport (McArthur et al., 1999). This includes transport of long chain fatty acids (LCFA) into the cells of muscle, liver, heart, adipose and intestines, where the metabolism and storage of LCFA occurre intensively (Doege and Stahl, 2006).

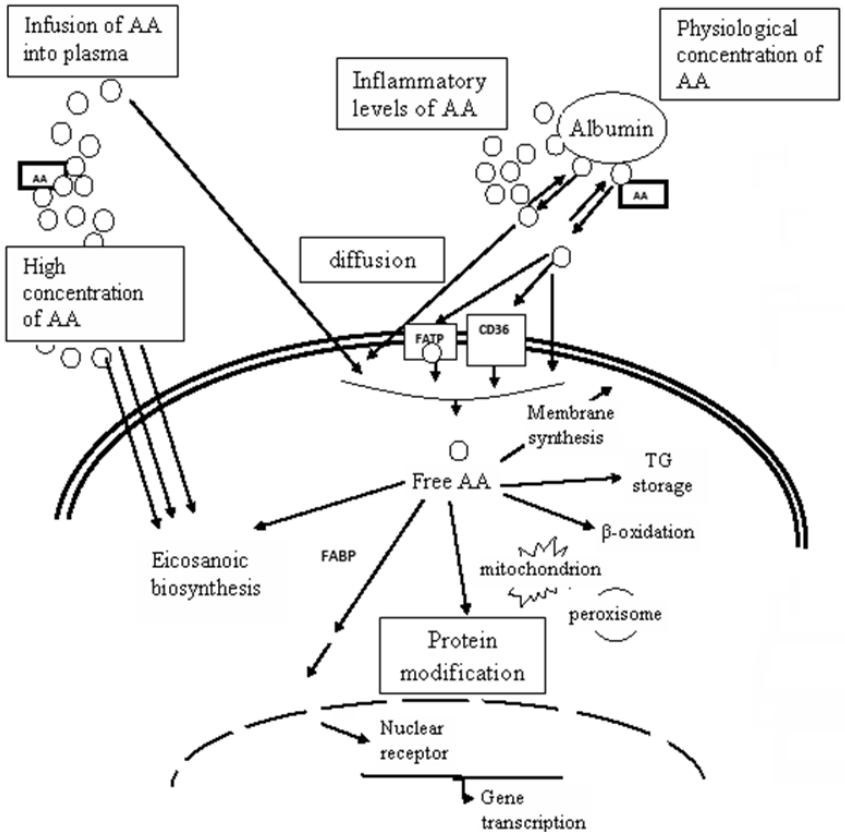

Figure 2. Metabolism of arachidonic fatty acid in the cells (adopted from Bederska-Łojewska et al., 2013).

Arachidonic acid may constitute a source of energy for cells trough β-oxidation process occurring in mitochondria as well as can be stored in form of energy reservoir in adipose tissue (Spector, 2000; Gao et al., 2009). When AA is released from membrane phospholipids it can either undergo resynthesis or be converted to eicosanoids (Doege and Stahl, 2006). Membrane proteins together with intracellular and extracellular receptors based on AA concentration decide which pathway will be processed. The concentration of AA in resting cell is kept at low level of 5 μM but the release of 1% of esterified AA from cell membranes may increase this level up to 50 μM (Brash, 2001). Introduction of high concentration of free AA is efficiently absorbed by the cells through diffusion and it is directly transformed to eicosanoids.

5. ARACHIDONIC ACID CASCADE AND INFLAMMATION

Among the many mediators of inflammation process being derivatives of polyunsaturated *n-3* and *n-6* acids (i.e. EPA - eicosapentaenoic acid, DHA - docosahexaenoic acid, DGLA - dihomo-γ-linolenic acid) those produced from arachidonic acid have the strongest biological activity (Harizi et al., 2008; James, 2010; Nowak, 2010). Inflammation is an important physiological phenomenon, without which it would be impossible to remove the pathological factor and repair the damages. Vasodilation of the blood vessels and their increased permeability enable the relevant proteins to migrate to damaged areas. The duration and severity of the inflammatory process depend on many factors such as location, size of the damage, personal profile of defensive reaction and the type of pathogen. Eicosanoids which include prostaglandins (PG), prostacyclin (PGI), thromboxanes (TX) and leukotrienes (LT) play a key role in the inflammatory process having an huge impact on the intensity and duration (Calder, 2006).

Typical inflammatory process last up to the moment when the pathological factor is removed and all damages are recovered in the body. However, in some cases, escalation of the immune response may appear which can be changed in the chronic form (Calder, 2006). Examples of diseases characterized by chronic inflammation are rheumatoid arthritis, inflammatory bowel disease (e.g. Crohn's disease), Type II diabetes, atherosclerosis, Alzheimer's disease, retinopathy, psoriasis, multiple sclerosis, chronic obstructive pulmonary disease, allergy and asthma (Calder, 2006; 2009; Nowak, 2010).

Eicosanoids are produced from arachidonic acid not directly but it requires a few reactions (Figure 3). In the first stage after the stimulation which may be: adrenaline, histamine, bradykinin, angiotensin II and thrombin, arachidonic acid is released from lipid bilayer by an enzyme phospholipase A_2. Then, with the involvement of cyclooxygenase (COX-1, COX-2), the molecules are converted to the cyclic eicosanoids: prostaglandins, prostacyclins and thromboxanes. Prostaglandin synthases: COX-1, COX-2 and PGHS exhibit their activities in the endoplasmic reticulum and lead to the transformation of arachidonic acid to PGG_2, reduced in the next step to PGH_2, which is a substrate for further synthesis of mentioned above eicosanoids.

Leukotrienes are also formed through multistep synthesis. As a result of an oxygen molecule insertion to the free arachidonic acid by 5-lipoxygenase, 5-hydroperoxyeicosatetraenoic acid (5-HPETE) is created. Then 5-HPETE can be reduced to two compounds: 5-hydroxyeicosatetraenoic acid (5-HETE,

involving the glutathione peroxidase) or leukotriene A_4 (LTA_4, by further action of 5-lipoxygenase). LTA_4 is the precursor for the synthesis of other leukotrienes (Smith, 1989, Harizi et al., 2008). Furthermore, EPA can be also a substrate for lipoxygenase and COX, what gives a rise to eicosanoids with a slightly different structure to those formed from AA (Calder, 2009).

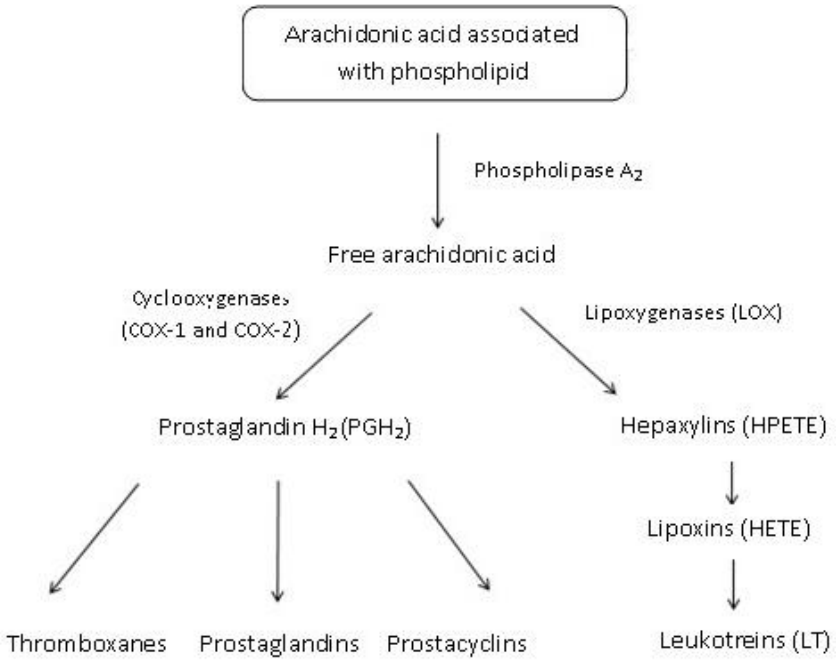

Figure 3. Scheme of the eicosanoids formation.

Eicosanoids exhibit a broad spectrum of action during the inflammatory response frequently performing contrary functions. The key for the proper conduction of the inflammatory process and for its extinction after deleting of all damages is correct interaction of these paracrine hormones. But sometimes, from different reasons, there is a need to mute the immune response. The inhibition of arachidonic acid cascade is a major mechanism of action of non-steroidal anti-inflammatory drugs.

5.1. Anti-Inflammatory Drugs

Non-steroidal and steroidal anti-inflammatory drugs have revolutionized the treatment of inflammatory diseases. The mechanism of action of the first one consists mainly on blocking eicosanoids synthesis via inhibition of cyclooxygenases (COX-1, COX-2). The first group of anti-inflammatory drugs (NSAIDs) include e.g. aspirin. At the heart of its action is inhibition of cyclooxygenases. By acetylation of serine 530 in the active site of enzymes the irreversible inhibition of both COX-1 and COX-2 occurs, which forbid the synthesis of eicosanoids. Aspirin demonstrates a much greater affinity for cyclooxygenase-1, what may contribute to the development of ulcers in the stomach or duodenum. Inhibition of prostaglandin synthesis in the gastrointestinal tract mainly through the inhibition of constitutive (permanently present in many cell types) COX-1 leads to a loss of protective effect of PG on gastric mucosa (Vane and Botting, 1998; Czyż and Watała, 2005). The mechanism of action of most non-steroidal anti-inflammatory, analgesic and antipyretic drugs i.e., indomethacin (acetic acid derivative), flubiprofen (ibufen derivative), naproxen (propionic acid derivative) or even ibufen rely on the inhibition of both cyclooxygenase-1 and cyclooxygenase-2 (Funk, 2001). However, in the case of ibufen there is no blocking of the active center, but competing with arachidonic acid for the substrate binding site of COX-1 and COX-2. The action of this drug is reversible and disappears when its decay (Thuresson et al., 2000). Improving the safety of anti-inflammatory compounds usage leads to the use of drugs selectively acting on COX-2 not constitutively secreted as COX-1 but only in response to inflammatory stimuli. Considered as very safe, but with a relatively weak action - paracetamol inhibits activity of the cyclooxygenase 3 (being a variant COX-1) present in the central nervous system – thereby there is observed decreased production of prostaglandins which results in a reduced sensitivity of the organism to the pain mediators (kinins, serotonin). However, due to the central action, there is no reduction in mucus secretion in the stomach and reduced barrier against hydrochloric acid. Importantly, paracetamol is characterized by ceiling effect, what means that the strength of its performance, above a certain dose, does not increase (Chandrasekharan et al., 2002).

In serious cases in the medicine there are used the narcotic drugs with analgesic action (morphine, codeine) and steroidal anti-inflammatory drugs. However, their main mechanism of action is not inhibition of arachidonic acid cascade. Narcotic drugs (opioids) act on specific receptors in the brain and spinal cord, which bind natural pain relief substances synthesized in the body

(endorphins, encephalins) (Galligan et al., 1984; Schlaepfer et al., 1998). Steroidal anti-inflammatory drugs inhibit or stimulate expression of genes which protein products are involved in inflammatory processes. However, their use raises serious concerns, even though efficacy in the treatment of several autoimmune diseases, asthma or the use as immunosuppressive agents after transplantation is extremely high. Their long term administration carries a high risk of occurrence of adrenal insufficiency, increased susceptibility to bacterial, fungal and viral infections, diabetes, myopathy, glaucoma and osteoporosis (Świerczewska et al., 2013).

Each drug treatment is associated with a potential risk of side effects. A well-balanced diet can help the healing process. Regulation of intake of fats which are precursors of the inflammatory mediators can come to the rescue to people struggling with the disorder characterized by an excessive immune response.

6. ARACHIDONIC ACID AND BRAIN DEVELOPMENT

For decades, it is known that *n-3* fatty acids (eg. DHA) and *n-6* (eg. arachidonic acid) are extremely important in the normal development of the human brain in both prenatal and postnatal life. At the beginning, the growing fetus receives them, with other nutrients from the mother through the placenta, and in the postnatal period with natural milk or formula. At this time it is very important that the food contains a high concentration of polyunsaturated fatty acids. Proper supply of these acids in the diet is particularly important in humans starting from the fetal period up to the second year of life as at this time there is a rapid accumulation in the brain and its intensive development (Martinez, 1992). How important are the polyunsaturated fatty acids for the nervous system shows the fact that AA and DHA constitute 16% of the dry matter of the brain with their highest contents in gray matter (Pawełczyk et al., 2008).

The brain during development demonstrates the great need for arachidonic acid. AA in the body plays a very important role – it is the building block of cell membrane phospholipids in retinal photoreceptors and neurons in the brain (Karłowicz-Bodalska and Bodalski, 2007; Kolanowski, 2007). The proper functioning of neuronal membrane is a necessary condition for the undisturbed conduction of nerve impulses. At resting potential, the unequal distribution of cations on both sides of the cell membrane makes the interior of

the cell more negative in comparison with the outer surface of the cell membrane.

Under the influence of stimulus, action potential appears and come to the rapid *influx* of sodium *ions* resulting in cell membrane depolarization. A moving depolarization wave along the cell membrane is a nerve impulse. When the signal reaches the end of the axon, the wave of depolarization goes to electrical or chemical synapse, where the signal is transmitted to the next cell. The cell which ended conductivity for some time remains in the lower excitability fase so-called hyperpolarisation, this prevent the wave of depolarization from going back. Potential changes in the lipid bilayer built from arachidonic acid are responsible for nerve cell activity (Michajlik and Ramotowski, 2003).

During the development of the nervous system arachidonic acid allows to create new neurons and later their maturation, the formation of synapse and correct brain plasticity. Numerous studies show that normal dietary intake of both AA and DHA promotes the maturation of brain structures important in cognitive processes such as the dorsolateral prefrontal cortex, supraorbital bark and associative parietal area (Willatts et al., 1998a; 1998b). Polyunsaturated fatty acids are largely responsible for specific structural and physicochemical properties of neuronal membranes. Their deficiency leads to disruption of neurotransmission through changes around fluidity of cell membranes, the tertiary structure of the membrane receptor and transport protein and the ligand-receptor interaction.

7. PRODUCTS OF ANIMAL ORIGIN AS A SOURCE OF ARACHIDONIC ACID AND ITS PRECURSORS

The type and amount of fat as well as proportion of fatty acids contained in the current diet have undergone major changes. Over the last 100 years there has been noticed a dramatic decrease in the consumption of polyunsaturated fatty acids from *n-3* group even up to 80%, and significantly increase of PUFAs from *n-6* group (Schwalfenberg, 2006; Russo, 2009). Such high intake of PUFAs *n-6* in the diet is caused by high consumption of vegetable oils (soybean oil, sunflower oil), due to their cholesterol-lowering properties in the serum (Simopolous, 2002; 2009). Excess of linoleic acid in the diet can cause adverse health effects (Margioris, 2009). The linoleic acid is metabolized to arachidonic acid which higher levels may contribute to

prostaglandin and thromboxane overproduction (Margioris, 2009). Nowadays, the animal products such as meat and eggs are also a source of linoleic acid from PUFAs *n-6* (Russo, 2009), which means that it also comprises higher level of arachidonic acid and an increased load of AA for the consumer (Shin et al., 2012). In the human diet, the main source of AA are meat and eggs with smaller amounts coming from milk and fish (Huag et al., 2010). The content of LA and AA commonly found in different types of meat from animal housing under standard production system are summarized in Table 1.

Table 1. Content of fat, arachidonic acid and linoleic acid in the lean meat of different species of livestock (Li et. al., 1998)

Type of meat	Fatty acids		
	Total FAT [g/100g]	Arachidonic acid [mg/100g]	Linoleic acid [% of acids sum]
Beef	1.4±0.2	28±5	5.6±1.1
Lamb	4.2±1.0	39±13	4.9±1.3
Pork	2.0±0.3	54±5	14.4±3.4
Chicken	2.3±0.5	43±10	14.4±1.7
Duck	1.7±0.3	99±38	18.2±3.4
Turkey	1.0±0.1	74±29	18.6±4.4

The fat content of lean meat ranges from 1g/100g in turkey meat to 4.2g/100g in lamb meat. Whereas the level of AA in beef and lamb meat is 1.5-2.5 times lower, compared to its content in meat of chicken, duck, turkey and pork respectively (Tab.1). Similar relationships refer to linoleic acid which is the precursor of AA, where there were 3 times lower levels of this acid in beef and lamb meat in comparison to chicken meat and pork. This is the result of different metabolism in ruminants: LA is degraded into monounsaturated and saturated fatty acids in the rumen by microbial biohydrogenation (70–95% and 85-100%, respectively) and only a small proportion, about 10% of dietary consumption, is available for incorporation into tissue lipids. Whereas, in monogastric animals the LA from diet is incorporated in unchanged form into tissue.

The content of fat as well as LA and AA is different in raw and cooked meat: beef, chicken, turkey, pork and also in eggs (Taber et al., 1998). It was also found that cooked meat and boiled eggs have shown higher content of AA and LA, up to 50-67% in comparison to the raw products. The average content of LA and AA in eggs is respectively: 1148mg/100g and 142mg/100g (Taber

et al., 1998) but in milk the range is 2.0-7.0% and 0.03-0.09% (Chilliard et al., 2008).

8. POSSIBILITIES TO REDUCE THE CONTENT OF ARACHIDONIC ACID ON THE NUTRITIONAL WAY IN ANIMAL PRODUCTS

Increasing level of LA *n-6* is due to the production of compound feed, which the dominant components are grains (corn, barley, wheat and triticale), vegetable oils (sunflower, corn, soybean) and oilseeds characterized by a high content of *n-6* LA (Shin et al., 2012). The consequence of this situation is the increasing level of LA and AA *n-6* in meat lipids and the decreasing level of ALA *n-3*. The ratio of PUFAs *n-6*/*n-3* is particularly high in meat and depends largely on the composition of the ration used in the animals compound feed. It is estimated that this ratio can reached even 23:1, which is unfavorable from the point of view of consumer health. From the standpoint of human dietetics is preferable to limit the LA and AA in meat and meat products by enrichment animal product with PUFAs *n-3*.

The results of studies conducted in recent years have shown that the composition of fatty acids contained in the meat can be relatively easily modified by the diet (Barowicz and Pieszka, 2001; Kouba et al., 2003; Pietras and Orczewska-Dudek, 2013). It was found that PUFAs contained in the compound feed for monogastric animals are absorbed and incorporated in the unchanged form into tissue lipids which influences the fatty acid composition of the muscle (Flachowsky et al. 1997; Barowicz et al., 2002). A rich source of polyunsaturated fatty acids used in animal diet are oil seeds and oils from oilseeds. Numerous studies have demonstrated the beneficial effect of plant oil supplements on the fatty acid profile of lipids in meat and eggs (López-Ferrer et al., 1999, López-Ferrer et al., 2001; Barowicz and Pieszka, 2001; López-Bote et al., 2002; Kouba et al., 2003; Daza et al., 2005; Smink et al., 2010, Skiba et al., 2011; Pietras and Orczewska-Dudek, 2013) (Table 2). Similar modifications in fatty acid composition can be accomplished in the milk and eggs (Rego et al., 2005; Oliveira et al., 2010).

Recent studies of Haug et al. (2012) indicate that poultry meat as a potential source of *n-3* PUFAs in the diet of modern societies can contribute to reduce the risk of cardiovascular disease. The authors enriched the chicken meat with PUFAs *n-3*, using a mixture of linseed oil and rapeseed oil as a

source of ALA in broiler chicken diet. The authors showed that enriched broiler chicken meat as a element of the human diet can increase the intake of EPA, DPA and DHA from ordinary food, but also decrease the intake of AA that is now too high. The similar results were obtained by Shin et al. (2012) when introducing flaxseed oil and long chain PUFAs (LCPUFAs) into chicken broiler diet. Also Coates et al. (2009) indicate that regular consumption of PUFAs *n-3* enriched pork can decrease the content of serum triglycerides and have beneficial effect on other biomarkers of cardiovascular health. They have also noticed that the AA levels in red blood cells in healthy subjects were diminished.

Table 2. Effect of fodder or feed additives on reducing the level of linoleic and arachidonic acids in animal products

Fodder or feed additives	Animal specie/effect	Author/source
Linseed	Dairy cattle/↓C18:2; ↓C20:4 Broiler chicken /↓C18:2; ↓C20:4	Chilliard et al., 2008 Azcona et al., 2008
Rape seed	Broiler chicken /↓C18:2; ↓C20:4	Azcona et al., 2008
Rape oil	Broiler chicken /↓C18:2; ↓C20:4	Nobar et al., 2007
Fish oil	Pigs/↓C18:2 Laying hens /↓C18:2; ↓C20:4	Skiba et al., 2011 Carvalho et al., 2009
Linseed oil	Laying hens/↓C18:2; ↓C20:4 Broiler chicken/↓C18:2; ↓C20:4 Broiler chicken/↓C18:2; ↓C20:4	Oliveria et al., 2010 Nobar et al., 2007 Shin et al., 2012
Camelina oil	Broiler chicken /↓C18:2; ↓C20:4 Laying hens /↓C18:2; ↓C20:4	Pietras and Orczewska-Dudek, 2013 Cherian et al., 2009
CLA	Pigs /↓C18:2 Broiler chicken /↓C18:2	Pieszka et al., 2006 Shin et al., 2011
Pasture (grass)	Beef cattle /↓C18:2 Lambs /↓C18:2	Noci et al., 2005 Nuernberg et al., 2006
Lard	Pigs/↓C18:2	Skiba et al., 2011

The ruminant meat, especially lamb and the young cattle meat nourished on the basis of grazing system with a limited amount of compound feed characterized by favourable profile of PUFAs (Noci et al., 2005; Nuernberg et al., 2006). In beef cattle according to high biohydrogenation of unsaturated fatty acids, the use of fish oil is the most effective way of decreasing the AA level in meat together with increasing the level of *n-3* acids (Scollan et al., 2001). There were also trials on the protection of fatty acids from fish oil in

feeding by microencapsulation conducted on dairy cattle what caused the significant increase of *n-3* acids level in milk (Lacasse et al., 2002). The easiest and cheapest method to protect the fatty acids in the rumen before biohydrogenation process and thus improving the utilization of the polyunsaturated fatty acids by ruminants, is introduced into the ration of whole oilseeds (Woods et al., 2008).

Feeding flax, camelina and marine oils has been also used to increase the *n-3* fatty acids content in poultry-based food products (Gonzales and Lesson, 2001; Pita et. al., 2010; Pietras and Orczewska-Dudek, 2013). Eggs from laying hens fed a diet containing graded levels of microencapsulated fish oil were characterized by lower content of AA and LA and grater content of EPA and DHA (Lawlor et al., 2010). Furthermore, the level of these LCPUFAs increased linearly with increasing level of microencapsulated fish oil in the hens diet.

Another way of lowering the levels of arachidonic and linoleic acids in the diet is the use of conjugated linoleic acid (CLA) isomers additives, which stimulate the activity of Δ9-, Δ5- and Δ6-desaturase (Eder et al., 2002, Smith et al., 2002, Shin et al., 2012). The use of CLA in compound feeds for pigs and broiler chickens increased levels of fatty acids of *n-3* group and decreased levels of *n-6* acids (Pieszka et al., 2006, Shin et al., 2011). Scientists also tried to change the fatty acid profile using minerals such as copper and chromium - addition of copper to feed of growing pigs resulted in an increase of content of saturated acids together with reduced level of unsaturated fatty acid in blood (Dove and Haydon, 1992), but an oversupply of these elements creates toxicological concerns and that is why there is no practical application in nutrition.

CONCLUSION

The modern human diet is characterized by intake of very high levels of *n-6* fatty acids, what causes adverse for health increased ratio of acids *n-6*/*n-3* group (Asif, 2011). Recent studies show that excess of *n-6* fatty acids inhibit the metabolism of fatty acids *n-3*, what contributes to impaired physiological balance of synthesized from them biologically active compounds (Pike and Barlow, 2000; Marciniak-Łukasiak, 2011). Excessive intake of arachidonic acid and linoleic acid can be a cause of abnormal cell membrane permeability, blood coagulation and the overactive immune system, increase inflammation and may contribute to the development of neurodegenerative diseases (Asif,

2011). The proper ratio of both PUFAs groups is essential for maintaining homeostasis and may be extremely important in the treatment of diseases characterized by intensive inflammation. Overproduction of pro-inflammatory factors may be limited by consumption food containing large amount of *n-3* fatty acids. A properly balanced diet can help to obtain possibly the best profile of fatty acids contained in animal products and thus improve our health.

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