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The Role of Polyunsaturated Fatty Acids in Dairy Products and Their Impact on Human Health: A Review

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Abstract: Dairy products are carriers of bioactive compounds such as polyunsaturated fatty acids (PUFA), including α-linolenic acid, linoleic acid, and Arachidonic acid, along with their metabolites. These compounds give dairy products their health-promoting and therapeutic properties for the treatment and prevention of life-threatening diseases, such as cardiovascular diseases, digestive disorders, inflammation reduction, improved immune biomarkers, and mitigating the impact of diabetes and cancer. Consequently, food and dairy industry trends are shifting towards developing functional foods from animal sources like milk, fortified with polyunsaturated fatty acids. This can be achieved by altering the diet of milk-producing animals or fermenting milk with lactic acid bacteria to enhance its health properties. This review provides an overview of the effects of PUFA and their metabolites on the body's biomarkers, highlighting their role in reducing plasma triglycerides without affecting body weight or levels of low-density lipoprotein (LDL).

Keywords: PUFA ، CLA ، α-linolenic acid ، LDL ، Prostaglandins.

INTRODUCTION

The rapid economic development in recent years has led to a significant change in human lifestyle, resulting in a substantial increase in the prevalence of chronic diseases such as cardiovascular diseases, diabetes, inflammation, and hypertension, which are major causes of death worldwide compared to other causes of mortality (Organizacion, 2020). The most significant risk factors contributing to chronic diseases include an unhealthy diet characterized by high blood pressure, elevated blood lipid levels, obesity, diabetes, osteoporosis, and cancer (Ministerio *et al*., 2016). Consequently, the cost of healthy food has increased, prompting some governments to promote and develop dietary systems that provide health benefits, leading to the emergence of functional foods that reduce the risks of these diseases (Durán & Valenzuela, 2010). Functional foods are defined as foods that serve three functions: providing essential nutrition for survival, sensory function based on taste, smell, and texture, and physiological function by positively affecting health (Yamada *et al*., 2008). One of the widely used functional foods is dairy products, as they contain secondary fermentation products resulting from the fermentation of milk by lactic acid bacteria. These products include organic acids, active compounds, and bioactive peptides that enhance health, as well as reducing lactose content, benefiting lactose-intolerant consumers. Additionally, they prolong shelf life and improve sensory and nutritional characteristics of food (Nyanzi *et al*., 2021). In general, consuming functional foods, including dairy products, helps reduce the risk of diseases. It has been observed that the consumption of dairy products leads to a decrease in saturated fatty acids, total cholesterol, triglycerides, and low-density lipoprotein (LDL) cholesterol, while increasing high-density lipoprotein (HDL) cholesterol and beneficial polyunsaturated fatty acids (PUFA), including docosahexaenoic acid, Arachidonic acid, and eicosapentaenoic acid, which have bioactive properties (Dawczynski *et al*., 2010). Furthermore, Al Musa and Al Garory (2022) noted that dairy products are known to prevent Hypothyroidism, reduce harmful LDL cholesterol, and increase beneficial HDL cholesterol, thereby reducing the risk of cardiovascular diseases.

Polyunsaturated fatty acids (PUFA) :

Polyunsaturated fatty acids (PUFA) are fat-soluble and beneficial for health due to their multiple unsaturated bonds. They are divided into α-linolenic acid and linoleic acid, as well as long-chain fatty acids such as docosahexaenoic acid, Arachidonic acid, and eicosapentaenoic acid (Islam *et al*., 2023). PUFA are essential fatty acids obtained from food, with a high presence of n-3 fatty acids in fish oil, seafood, flaxseed oil, walnuts, wheat germ, human milk, and an inability for the body to produce them. They improve immune biomarkers, act as anti-inflammatory agents, and reduce the risk of arteriosclerosis , obesity, metabolic disorders, diabetes, nervous disorders, heart disease, vascular diseases, and Alzheimer's due to their bioactive properties. On the other hand, n-6 fatty acids are found in corn oil, peanut oil, cottonseed oil, soybean oil, and many vegetable oils (Yashodhara *et al*., 2009). Linoleic acid (C18:2, LA) and α-linolenic acid are n-6 and n-3 isomers, respectively, which are not synthesized in the body. The n-3 acid is of greater physiological importance as it produces eicosapentaenoic acid and docosahexaenoic acid, while Arachidonic acid is created through n-6 acids. These isomers can be converted into metabolic products to remove saturation since their biosynthesis requires the same enzymes (Cartoni Mancinelli *et al*., 2022). γ-linolenic acid (GLA) has significant bioactive roles in human health despite its presence in a few oils. It reduces DNA damage caused by oxidation, thereby protecting body tissues and cells from cancer-causing agents (Rengachar *et al*., 2022). The health benefits of PUFA have drawn the attention of the scientific community to their vital roles, and subsequent studies have shown the preventive effects of dietary consumption of omega-3 fatty acids against chronic diseases and inflammation. The metabolic sources and products of essential fatty acids include Prostaglandins (PG), prostacyclin PGI, thromboxane TX, leukotriene LT (derived from the breakdown of docosahexaenoic acid, eicosapentaenoic acid, α-linolenic acid, and Arachidonic acid, respectively, and lipoxins (LX). Table (1) classifies the fatty acids related to metabolic pathways (Yashodhara *et al*., 2009). High cholesterol levels in the blood are a major risk factor for heart disease, vascular diseases, and stroke, with studies indicating that elevated cholesterol causes 4.5% of deaths, while a 1% reduction in cholesterol leads to a 2.3% decrease in coronary artery-related risks. Therefore, reducing LDL cholesterol is necessary to decrease heart disease-related deaths. Additionally, certain probiotic bacteria in dairy products improve gut health due to their acidic nature and their effect on fats and their ability to break them down (Pourrajab *et al*., 2020). Diabetes resulting from insulin deficiency and high blood glucose levels is closely associated with the risk of heart disease, vascular diseases, and non-alcoholic fatty liver disease. Insulin resistance and obesity contribute to all of these mentioned diseases. Probiotic bacteria in yogurt reduce glucose absorption as it is the main energy source. They also regulate inflammation pathways, inhibit and destroy cells that lower blood sugar levels in Langerhans islets, reduce fatty acid synthesis, regulate bile acid synthesis, and enhance fatty acid oxidation (Mirjalili *et al*., 2023).

Table (1) Classification of fatty acids related to the process of dietary metabolism (Yashodhara *et al*., 2009).

Fatty acid	Classified	Examples
Saturated	Non – essential	Butyric acid Palmitoleic acid Stearic acid
Unsaturated	Essential	Omega-3 α-linolenic acid Omega-6 Linoleic acid
	Non – essential	Omega-3 EPA,DHA Omega-6 GLA Omega-9 Oleic acid

* EPA: eicosapentaenoic, DHA: docosahexaenoic, GLA: γ -linolenic acid

α-Linolenic acid (ALA) :

Omega-3 is an essential fatty acid that cannot be produced by the body. It has a double bond at the carbon 3 atom and is obtained from foods such as walnuts, flaxseeds, green leafy vegetables. It plays vital roles in brain development, function, heart health, blood vessels, anti-inflammatory effects, and positive effects on the nervous system. However, excessive consumption can lead to digestive disorders (Stark *et al*., 2008). α-LA is synthesized in the mitochondria through the condensation reaction between glycine and succinyl-CoA. This reaction is facilitated by the enzyme ALA synthase and requires pyridoxal-5-phosphate as a coenzyme. After synthesis, α-LA is transported to the cytosol where a series of enzymatic reactions occur to complete the biosynthetic pathway of heme, which is the red pigment of hemeoglobin containing iron (Wachowska *et al*., 2011). α-LA is produced by desaturating Linoleic acid using the enzyme Δ15-desaturase, which is necessary for fatty acid synthesis and cannot be produced by the body. Therefore, it must be obtained through diet. ALA is an essential dietary precursor for the synthesis of eicosapentaenoic acid and docosahexaenoic acid (Punia *et al*., 2019). In recent years, the positive role of certain bioactive nutrients, including Omega-3, has attracted consumer interest. They are known as healthy fats due to their beneficial effects on maintaining normal levels of triglycerides, blood pressure, heart and blood vessel diseases, cancer, and their positive impact on the brain, retinal health, and the nervous system (Dal Bello *et al*., 2015). Numerous studies have demonstrated the protective concept provided by PUFA, especially Omega-3, in reducing the risks of irregular heartbeats, arteriosclerosis , platelet aggregation, and lowering HDL in plasma, which increases LDL and thus reduces blood pressure. Omega-3 also helps regulate blood sugar, digestive disorders, and reduce obesity (Yashodhara *et al*., 2009). Despite being poorer sources of Omega-3 compared to animal and marine sources, milk and dairy products are still major components in dietary regimes. Table (2) indicates the content of unsaturated polyunsaturated fatty acids in animal-based food sources, leading to the study of altering the fatty acid composition in milk through microbial biohydrogenation in the animal's rumen, converting saturated fats to unsaturated fats and increasing their concentration by introducing oilseeds into the animal's diet (Nguyen *et al*., 2019). Fermented dairy products can ensure a higher daily intake of nutrients, including Omega-3, and induce more positive changes than raw milk due to the presence of lactic acid bacteria that enhance health benefits (Matos *et al*., 2021).

Table (2) Content of polyunsaturated fatty acids in animal-based food sources

Item	Unit	EPA	DHA	DPA	n-3 PUFAs	Reference
Fish	mg/150g	-	-	-	350	Nichols *et al*.,2010
Beef	mg/100g	15	12	20	47	Garcia *et al*.,2008
Chicken breast	mg/100g	-	-	-	62.04	Konieczka *et al*.,2017
Sheep milk	mg/250ml	17.8	19.8	24.1	61.7	Nguyen *et al*.,2018
Sheep cheese	mg/40g	14.3	12.8	17.1	44.2	Nguyen *et al*.,2019
Cow milk	mg/100g	3.3	-	4.4	-	Benbrook *et al*.,2013

* EPA: eicosapentaenoic, DHA: docosahexaenoic, DPA: docosapentaenoic, n-3 PUFAs : Omega-3 polyunsaturated fatty acids.

Linoleic acid (LA):

Omega-6 is an essential unsaturated fatty acid that belongs to the essential fatty acids that must be consumed through food due to the body's inability to produce them (Whelan & Fritsche, 2013). It is found in various foods such as fish, nuts, seeds, and vegetable oils like wheat germ oil, sunflower oil, and corn oil (Taha, 2020). LA is beneficial for health as it plays a role in maintaining skin and hair health, helps improve heart and cardiovascular health, enhances the immune system, and lowers LDL levels in the body (Micha *et al*., 2014). Excessive intake beyond the body's needs can lead to inflammation and increased risk of certain chronic diseases (Simopoulos, 2016). Schuster *et al*., (2018) suggested the possibility of synthetically obtaining Linoleic acid through chemical processes involving the reaction of different carboxylic acids with specific chemicals, in addition to extracting it from plant oils. Milk contains unsaturated fatty acids including lauric, myristic, and palmitic acids, which have negative effects on human health. It also contains very low levels of beneficial monounsaturated and polyunsaturated fatty acids that help lower LDL levels and increase HDL levels, necessitating an increase in the content of these acids in milk and dairy products to improve their nutritional value by relying on feed processing strategies, animal diet, and milk fermentation to produce conjugated Linoleic acid (CLA), a polyunsaturated fatty acid of the positional isomer of Linoleic acid (cis9, cis12 C18:2). Milk fat and dairy products are the richest source of this isomer (Gutiérrez, 2016). The cis 9, trans 11-octadecadienoic acid (C18:2 cis 9, trans 11), known as rumenic acid, accounts for 90-75% of the total CLA, followed by the isomer (C18:2 trans 7, cis 9), which accounts for 10% of the total CLA. The remaining isomers appear in small proportions, and these isomers are classified as biologically active molecules due to their protective effects against various diseases, including obesity, arteriosclerosis , diabetes, and anticancer effects (Bauman *et al*., 2020). CLA content in fermented dairy products ranges from 3.4 to 8.8 mg/g of fat, while in commercial sour cream, it ranges from 4.5 to 8.2 mg/g of fat, and in kefir, it ranges from 7.6 to 22.6 mg/g of fat, indicating that the use of lactic acid bacteria for fermentation increases the concentration of CLA in dairy products compared to raw milk used in their production (Gutiérrez Álvarez *et al*., 2010). Hartigh, (2019) indicate that the effectiveness of CLA in reducing the risk of cancers such as breast and colon cancer by stimulating cancer cell death, its antioxidant activity , and inhibition of peroxide radicals, as well as its ability to contribute to weight loss by promoting fat breakdown through the 10,12 CLA isomer responsible for reducing obesity. There are variations in the opinions of researchers regarding the effect of different starters used in the production of fermented dairy products on CLA concentration, and Table (3) shows the concentration of CLA in mg/g fat in some fermented dairy products with different starters (Gutierrez, 2016).

Table (3): CLA concentration (mg/g fat) in fermented dairy products and the used starters (Gutierrez, 2016)

Product	Starter cultures	CLA
Yogurt	S. thermophilus + L. delbrueckii ssp. Bulgaricus	4.7-7.6
Fermented milk	Lc. lactis ssp lactis	5.1-5.5
Fermented milk	L. plantarum	4.9
Fermented milk	L. buchneri	4.3
Fermented milk	L. reuteri	4.8
Yogurt	S. thermophilus + L. delbrueckii ssp. bulgaricus B. bifidum	2.7-4.2
Yogurt	S. thermophilus + L. delbrueckii ssp. bulgaricus B. breve	2.3-4.4
Yogurt	S. thermophilus + L. delbrueckii ssp. bulgaricus L. acidophilus	3.3-5.6

Dahi	L. acidophilus + L. casei	10.5

Arachidonic acid (ARA):

Arachidonic acid (ARA) is a 20-carbon fatty acid with an uneven chain structure, consisting of four cis-type double bonds between atoms. The first double bond is located between carbon atoms 6 and 7, starting from the amino end of the molecule. ARA belongs to the polyunsaturated fatty acids (PUFA) of the Omega-6 family, and it plays important chemical and vital roles in the body, including the formation of biologically active compounds such as prostaglandins (Martin *et al*., 2016). ARA is naturally found in animal and plant tissues and is produced in the human body through several biological pathways involving various enzymes. It is also present in fatty-rich foods such as meats and fish, as well as in plant oils like corn oil, soybean oil, and sunflower oil. ARA is also added as a dietary supplement to some food products (Komprda *et al*., 2005). ARA contributes to reducing inflammation, improving immune biomarkers, participating in cell membrane formation, and acting as an intermediary in various biological processes in the body, including growth, development, and the functions of different organs (Hanna & Hafez, 2018). Tokuda *et al*., (2014) indicated that ARA is involved in the formation of a variety of bioactive compounds such as prostaglandins, which participate in several physiological processes in the body, including temperature regulation, blood circulation, thrombosis, body inflammation, and an increased intake of ARA with food poses a risk of heart diseases, artery diseases, and other conditions. ARA is naturally present in the body's cell membrane with structural phospholipids or stored in adipose tissues within immune cells (Weller, 2016). One of the most beneficial types of prostaglandins is 15-Deoxy-delta-12,14-PGJ2, which has the ability to reduce hydrogen peroxide, thereby reducing free radicals. Its levels increase after milk fermentation. Arachidonic acid is important for reducing inflammation, activating liver cell surface receptors, and enhancing the activity of the NADPH oxidase enzyme responsible for reducing non-alcoholic fatty liver disease (NAFLD) caused by high cholesterol levels in the blood (Chen *et al*., 2023). The metabolic byproducts of Arachidonic acid play various physiological roles in human health, contributing to cell proliferation, tissue regeneration, and disease diagnosis (Hanna & Hafez, 2018). Probiotics improve lipid metabolism disorders, as fermented milk with probiotics reduces body weight and blood fat levels by regulating the metabolic pathways of polyunsaturated fatty acids, including Arachidonic acid (Qu *et al*.,2022). Numerous studies have demonstrated the concept of protection provided by PUFA, especially Omega-3, in reducing the risks of irregular heartbeats, platelet aggregation, and lowering HDL levels in plasma, which increases LDL and, consequently, reduces blood pressure (Yashodhara *et al*., 2016)**.**

CONCLUSION

The current pattern of unhealthy fast-food consumption and the need for functional food containing healthy, biologically active polyunsaturated fatty acids (PUFA), along with the limited intake of oilseeds and seafood rich in these acids, have led to the search for animal sources and their enhancement to obtain these beneficial acids and their derived products. Since milk and dairy products are among the most consumed animal foods, despite the low concentrations of PUFA in milk due to its saturated fatty acid content, this review highlighted the possibility of developing dairy products with high concentrations of PUFA that have positive health effects, such as CLA, prostaglandins, leukotrienes, and others, through changes in the animal's diet by increasing PUFA in their feed or through the process of fermenting milk with lactic acid bacteria and probiotics. This review also highlighted the physiological roles of polyunsaturated fatty acids and their derived products in human health and disease prevention.

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