

## A REVIEW: DAIRY PHOSPHOLIPIDS IN HUMAN NUTRITION

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### Abstract

More than six billion people worldwide consume dairy products every day. Dairy products and their constituents contain hundreds of different components, but milk fat globule membrane (MFGM) polar lipids are still underestimated from a nutritional point of view. The unique composition of phospholipids (PLs) – the main MFGM component – provides high nutraceutical properties. Therefore, the research of bioactive dairy components and their impact has promising potential in human health by various mechanisms. The positive effects of MFGM PLs are mainly based on animal studies, but there are a small number of *in vivo* studies with volunteers. The present study aimed to review the research findings of dairy PLs in human nutrition and their functional properties. Dairy PLs effectively impact intestinal integrity and gut microbiota, lipid profile and risk lowering of cardiovascular diseases (CVDs), cognitive performance during stress, and neonatal brain development.

**Key words:** phospholipids, dairy products, MFGM.

### Introduction

The essential components of the milk fat globule membrane are – phospholipids (PLs) and sphingolipids (SLs). PLs and SLs are amphiphilic molecules consisting of a hydrophobic tail, given by fatty acids, and a hydrophilic head, given by a concrete polar group. Glycerophospholipids and phosphosphingolipids represent PLs, but sphingomyelin and ceramides – SLs (Anto *et al.*, 2020).

The essential part of a balanced and healthy diet is dairy products. The intake of dietary PLs from dairy products varies – approximately 2-8 g per day or 1-10% of the total daily fat intake (Cohn *et al.*, 2010). Primary dietary PLs sources are eggs, cereal grains, oilseeds, fish, beef, and dairy products. Dairy products represent a significant source of nutritional PLs in the human diet. Dairy products consumption in Europe corresponds to 9% of dietary energy supply (OECD/FAO, 2019).

Different dairy products provide different amounts of PLs: whole milk 0.2-0.3 g 100 g<sup>-1</sup> dry matter (DM), cream 0.2-0.4 g 100 g<sup>-1</sup> DM, butter 0.3 g 100 g<sup>-1</sup> DM, skimmed milk yogurt 0.2 g 100 g<sup>-1</sup> DM, buttermilk 1.1-2.0 g 100 g<sup>-1</sup> DM (Anto *et al.*, 2020). The production processes explain those differences. Additionally, the chemical composition of milk depends on environmental factors, feed composition, animal health status, lactation period, season, etc. (Pereira, 2014; Liu *et al.*, 2017; Timlin *et al.*, 2021; Conway *et al.*, 2013).

The research of bioactive dairy components has considerable potential in human health by various mechanisms. The number of studies of dairy PLs positive health effects on human health is still growing. Clinical researches suggest that dietary PLs effectively impact intestinal integrity and gut microbiota, inflammation, lipid profile and heart and circulatory system, brain development, and cognitive

improvements (Anderson *et al.*, 2011; Salcedo *et al.*, 2013; Lee *et al.*, 2014; Anderson *et al.*, 2018; Kosmerl *et al.*, 2021; Baumgartner *et al.*, 2013; Boyle *et al.*, 2019; Okuda, 2019; Hernell *et al.*, 2016).

The present study aimed to review the research findings of dairy PLs in human nutrition and their functional properties.

### Materials and Methods

Scientific databases Web of Science, Scopus, Wiley Online Journal (2000-2022) were studied to review the latest available data on dairy phospholipids in human nutrition and their functional properties. Full-text papers were included in this review. The monographic method was used in this study. The following keywords were used to select scientific literature: 'dairy phospholipids', 'milk fat globule membrane', 'buttermilk phospholipids', 'buttermilk', 'milk consumption', 'intake of phospholipids', 'dairy phospholipids'.

### Results and Discussion

The study titles and abstracts were screened (n = 3621), full-texts assessed (n=96). Twenty-three studies were included in a review. The main research areas were: the content of dietary PLs and SLs in different types of dairy products, PLs impact on lowering the CVDs risk and lipid profile changes, changes in gut microbiota and intestinal barrier functions, changes of cognitive performance during the stress, PLs effect on structural and functional development of the neonatal brain.

Everyday consumption of dairy products is high, especially in Western countries. Dairy products contain hundreds of components, but MFGM polar lipids are underestimated from a nutritional perspective. The structure of milk fat is specific, consisting of the fat and the membrane surrounding it, but the membrane

composition and bioactive role are insufficiently studied. The membrane contains polar lipids, sterols, proteins, nucleic acids, vitamins, and minerals. Polar lipids are richly present in the membrane and are therefore extracted from membranes for a wide use in food supplements and pharmaceutical purposes. A wide diversity of PLs provides complex metabolic pathways and thus influences different health conditions and organ systems. One of the most significant polar lipids is sphingomyelin (more than 25% of polar lipids), which is particularly important in preventing CVDs risks compared to polar lipids of other animal origins (less than 5% of polar lipids) or polar lipids of plant origin products (Bruno *et al.*, 2021).

#### *Intestinal integrity and gut microbiota*

The knowledge of intestinal permeability and barrier function regulating mechanisms has grown widely over the past years. Correct maturation of the intestinal barrier is significant for health during all life. Milk lipid fractions support the proper development and stability of the intestinal barrier by enhancing the integrity of intracellular tight junctions that control permeability. There are two leading roles of the human intestine – absorption of macro- and micronutrients and prevention of potentially harmful agents. The evolution and growth of the human intestinal immune system and microbial colonization development take approximately two years (Anderson *et al.*, 2011).

Dairy lipid fractions improved the integrity of the small intestinal epithelial barrier. Gangliosides represent glycosphingolipids in cellular membranes that can modulate membrane functions and the activity of membrane proteins. Gangliosides have two positive health-promoting mechanisms – the ability to decrease pathogenic bacteria adhesion and advance the growth of infant gut-associated bifidobacteria (Salcedo *et al.*, 2013; Lee *et al.*, 2014). In addition, the presence of gangliosides may cause the improvement in barrier integrity in response to dairy lipid fractions (Anderson *et al.*, 2018). However, more studies are required to understand further the relationship between phospholipids intake and the intestinal barrier and intestinal microbial integrity.

PLs directly interacts with bifidobacteria and lactic acid bacteria. This interaction with probiotic bacteria goes through interactions with bacterial surface proteins. Therefore, there are synergistic effects between MFGM and probiotics for positive human health outcomes at all ages. Furthermore, PLs enhance the efficiency of probiotics in the gut by promoting probiotic survival and boosting mucosal immune development (Kosmerl *et al.*, 2021). Unfortunately, the exact mechanism of the relationship between probiotics and PLs has yet to be thoroughly studied.

#### *Lipid profile and CVDs*

According to World Health Organisation data (WHO, 2021), CVDs – cerebrovascular disease, rheumatic heart disease, coronary heart disease – are the leading cause of death globally. CVDs are the most common cause of death in Latvia – 54.6% of all deaths in 2019 (Latvijas Universitātes Kardioloģijas un reģeneratīvās medicīnas zinātniskais institūts, 2020). In addition, a significant correlation is present between increases in triglyceride (TG), total cholesterol (TC) levels, and the risk of CVDs (Zhao *et al.*, 2021). The role of low-density lipoprotein cholesterol (LDL) in the pathogenesis of CVDs and the clinical benefit of lowering LDL cholesterol in high-risk patients has been demonstrated in many studies. Therefore, as part of the most important behavioral risk factors, diet plays a significant role in CVD risk lowering and prevention.

In plasma and cholesterol homeostasis, LDL concentration is supported by intestinal cholesterol absorption, endogenous cholesterol synthesis, and cholesterol withdrawal (Ros, 2000). The diet's impact on reducing intestinal cholesterol absorption has a remarkable effect on plasma cholesterol and LDL concentrations. *In vitro* studies have shown that buttermilk contains a high concentration of PLs, inhibiting cholesterol micellar solubility. Short-term consumption of buttermilk significantly reduced TC and TG concentrations in men and women. The reduction was even noticeable among individuals with higher LDL concentrations (Conway *et al.*, 2013).

Buttermilk is an excellent dietary source of sphingolipids and contains 17.9-34.5% of the total PLs (Conway *et al.*, 2014). Buttermilk sphingolipids and lactic acid bacteria influence the metabolism of cholesterol. At the same time, eggs are a concentrated source of dietary cholesterol and dietary PLs. Dietary cholesterol increases TC and LDL. 12-week egg consumption significantly raised TC and LDL concentrations in women, but the consumption of eggs with buttermilk increased TC and LDL moderately (non-significant). Buttermilk components influence the bioavailability of dietary egg cholesterol absorption and thus have beneficial effects on health (Baumgartner *et al.*, 2013).

Animal studies show that SLs lower cholesterol. Therefore, intake of dairy PLs may lower plasma cholesterol level by inhibiting the intestinal bioavailability of cholesterol (Conway *et al.*, 2013).

#### *Cognitive performance during stress*

Stress has become an integral part of everyday life, but in the case of high-stress levels or chronic states, it may cause different somatic and mental disorders. Stress reduces cognitive performance cognition and often underlies cognitive deficits (Nagy *et al.*, 2020). PLs have a lowering effect on the activity and reactivity of the hypothalamic-pituitary-adrenal axis (HPAA).

Supplementation with PLs has a positive lowering impact on the stress response and protects cognitive performance sensitive to stress initiation. Intake of milk PLs has shown the improvement of cognitive performance under conditions of psychosocial stress. A six-week daily intake of 2.7 g of PLs positively affects neuroendocrine and subjective stress reactions to an acute psychosocial stressor in individuals with a raised predisposition toward high-cortisol responsivity (Boyle *et al.*, 2019).

PLs most likely increase the availability of cortisol in chronically stressed men and may downgrade stress-induced memory analogs. PLs intake lowers morning salivary cortisol levels, which may conform to the prolonged availability of free cortisol. An increase of PLs on 0.5% provided a higher morning cortisol level. At the same time, no differences were noticed after a rise in PLs of 1%. Additionally, elderly participants with higher PLs intake showed better memory performance than the placebo and low PLs intake group (Schubert *et al.*, 2011).

#### Neonatal brain development

The first years after birth are a crucial period of structural and functional development of the brain and its complex underlying microstructural changes (Li *et al.*, 2019). Gangliosides play an essential role in neuronal growth and are involved in migration and maturation, neuritogenesis, synaptogenesis, and myelination during early life (McJarow *et al.*, 2009).

Atypical expression and metabolism of gangliosides can lead to neurologic diseases. Dairy gangliosides are not directly absorbed into tissues *in vivo*. Firstly, they are broken down in the intestinal tract and absorbed. Thus, it affects ganglioside expression in the tissues. An adequate level of ganglioside expression is necessary for maintaining overall membrane integrity. Therefore, the diet can indirectly control the expression of ganglioside metabolism-related genes (Okuda, 2019).

MFGM as a dietary source of PLs can supplement infant formulas to narrow the difference in performance between formula-fed and breastfed infants. In addition, such supplementation is safe from the first week of life in infants without serious side effects (Hernell *et al.*, 2016).

#### Conclusions

Dairy products are a valuable source of PLs and an essential part of a human healthy and balanced diet. The unique composition of PLs provides high nutraceutical properties. Intake of PLs positively impacts the number of health states – intestinal integrity and gut microbiota, lipid profile and heart and circulatory system, neonatal neurodevelopment, and cognitive performance during stress. The positive effects of MFGM PLs are mainly based on animal studies, but there are few *in vivo* studies with volunteers.

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