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Review article

Nutrition, production, and processing of virgin omega-3 polyunsaturated fatty acids in dairy: An integrative review

Guoxin Huang [a,b,c,1], Ning Li [a,c,1], Xufang Wu [a,c], Nan Zheng [a,c], Shengguo Zhao [a,c], Yangdong Zhang [a,c,**], Jiaqi Wang [a,c,*]

[a] *Key Laboratory of Quality & Safety Control for Milk and Dairy Products of Ministry of Agriculture and Rural Affairs, Institute of Animal Sciences, Chinese Academy of Agricultural Sciences, Beijing, 100193, PR China*
[b] *College of Life Science, Nankai University, Tianjin, 300071, PR China*
[c] *State Key Laboratory of Animal Nutrition, Institute of Animal Sciences, Chinese Academy of Agricultural Sciences, No. 2 Yuanmingyuan West Road, Haidian District, Beijing, 100193, PR China*

A R T I C L E I N F O

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A B S T R A C T

With improving living standards, functional and healthy foods are accounting for an increased share in human food. The development of dairy products that are rich in virgin omega-3 polyunsaturated fatty acids (n-3 PUFAs) has become a topic of interest. Virgin n-3 PUFA milk can provide high-quality protein and calcium, as well as provide n-3 PUFAs to improve human health. This review aims to investigate the effect of virgin n-3 PUFAs in milk on human health and discuss the content of virgin n-3 PUFAs in milk regulated by dairy animal diet and the effect of food processing on the content of virgin n-3 PUFAs in dairy production. The interaction between n-3 PUFAs and proteins in milk is the key to improving the nutritional value of n-3 PUFAs in milk. n-3 PUFA supplementation in the diet of dairy animals is the key method to improve n-3 PUFAs in raw milk, as well as to adjust the types of virgin n-3 PUFAs. Compared with a common source, virgin n-3 PUFAs in milk show higher antioxidant activity, but elevated temperatures and long-term thermal processing should be avoided.

1. Introduction

Omega-3 polyunsaturated fatty acids (n-3 PUFAs) are essential fatty acids (mainly including α-linolenic acid: ALA, C18:3, *cis*-9,*cis*-12,*cis*-15-octadecatrienoic acid; C20:3, *cis*-11,*cis*-14,*cis*-17-eicosatrienoic acid, ETE; C20:5, *cis*-5,*cis*-8,*cis*-11,*cis*-14,*cis*-17-eicosapentaenoic acid, EPA; C22:5, *cis*-7,*cis*-10,*cis*-13,*cis*-16,*cis*-19-docosapentaenoic acid, DPA; and C22:6, *cis*-4,*cis*-7,*cis*-10,*cis*-13,*cis*-16,*cis*-19-docosahexaenoic acid, DHA) that play critical roles in most vital organs. The n-3 PUFAs are important substances for brain and muscle structure [1,2]. n-3 PUFAs are also beneficial for cardiovascular health and other conditions [3,4]. Some n-3 PUFA every day is good for health. Studies found that 1 g/day of ALA intake can reduce cardiovascular disease [3], and the optimal intake of DHA + EPA

* Corresponding author. Key Laboratory of Quality & Safety Control for Milk and Dairy Products of Ministry of Agriculture and Rural Affairs, Institute of Animal Sciences, Chinese Academy of Agricultural Sciences, Beijing, 100193, PR China.
** Corresponding author. Key Laboratory of Quality & Safety Control for Milk and Dairy Products of Ministry of Agriculture and Rural Affairs, Institute of Animal Sciences, Chinese Academy of Agricultural Sciences, Beijing, 100193, PR China.
E-mail addresses: zhangyangdong@caas.cn (Y. Zhang), jiaqiwang@vip.163.com (J. Wang).
[1] These authors have contributed equally to this work.

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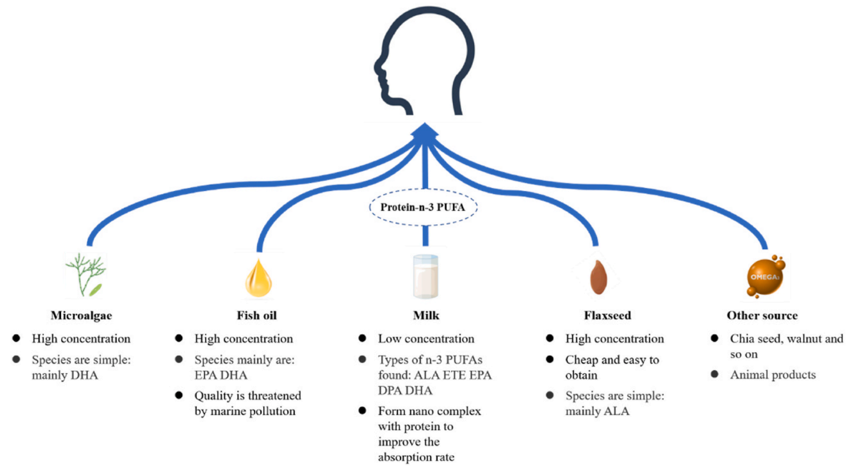

Fig. 1. Characteristics of n-3 PUFAs from various sources. n-3 PUFAs: omega-3 polyunsaturated fatty acids, ALA: α-linolenic acid, ETE: eicosatrienoic acid, EPA: eicosapentaenoic acid, DPA: docosapentaenoic acid, DHA: docosahexaenoic acid.

Table 1
Mean values of n-3 PUFAs in Holstein and Jersey cows, buffalo, yak, human, goat, donkey, camel [26], moose [27], and sheep [28] milk, and flaxseed oil [29], fish oil [10], and microalgae [30] (g/100 g fatty acid).

Fatty acid	Holstein	Jersey	Buffalo	Yak	Human	Goat	Donkey	Camel	Flaxseed oil	Fish oil	Microalgae oil
ALA	0.40	0.30	0.14	1.12	0.88	0.30	2.57	0.99	50.8	1.11	0.03
DPA	0.01	0.01	0.01	0.02	0.04	0.01	0.01	0.03	0.00	–	–
EPA	0.03	0.04	0.03	0.06	0.04	0.04	–	0.06	0.00	7.06	0.41
ETE	0.07	0.07	0.07	0.07	0.15	0.11	0.08	0.18	0.00	1.34	–
DHA	0.01	0.01	0.01	0.03	0.38	0.03	–	0.03	0.00	6.76	29.98
Σ n-3	0.52	0.44	0.25	1.43	1.49	0.49	2.75	1.28	50.8	17.62	30.50

"-": unreported, n-3 PUFAs: omega-3 polyunsaturated fatty acids, ALA: α-linolenic acid, ETE: eicosatrienoic acid, EPA: eicosapentaenoic acid, DPA: docosapentaenoic acid, DHA: docosahexaenoic acid. Σ n-3 = ALA + ETE + EPA + DPA + DHA.

is 0.25 g/day [5]. Even in the context of the Coronavirus disease 2019 (COVID-19) outbreak, n-3 PUFAs have been shown to reduce the risk of death [6].

The main n-3 PUFA foods for humans are fish, oil seeds (flax, chia, perilla, etc.), and microalgae [7–9] as shown in Fig. 1, and other n-3 PUFA products such as eggs that are specifically rich in n-3 PUFAs [10]. The n-3 PUFAs in microalgae are mainly DHA and in flaxseed are mainly ALA. Fish oil is a good source of n-3 PUFAs, but its quality is affected by marine pollutants [11]. Milk contains multiple virgin n-3 PUFAs (such as ALA, ETE, EPA, DPA, and DHA) which are potential dietary sources. In addition, n-3 PUFAs in milk play a special role, and studies have found that virgin n-3 PUFA milk could reduce the risk of asthma in children [12].

Milk is considered a complete food source because of its extraordinary nutritional value [13]. Milk fat is the most important constituent of milk and is easily digested and absorbed compared with other fats. Thus, unlike other n-3 PUFA sources, n-3 PUFAs in milk are easily absorbed by the human body. Similar to calcium, n-3 PUFAs can also combine with proteins to form nanocomplexes [14], and this nanocomplex shows many benefits for fatty acids: 1) increases fatty acid absorption, 2) protects fatty acids from oxidation or other stresses, and 3) changes the bioavailability of fatty acids [15]. In milk, there are numerous kinds of proteins, such as β-lactoglobulin (β-LG), α-lactalbumin (α-LA), and lactoferrin (LF). The n-3 PUFAs exert multiple functions by binding to different proteins. For example, compared with other complexes, only the LF–ALA complex showed a higher inhibitory effect on cancer cells. Therefore, increasing the n-3 PUFA content in dairy production is a good way to improve human health [16].

The concentration of virgin n-3 PUFAs in milk can be adjusted via the diet of the mammal [17,18]. Supplementation of flaxseed in the diet can increase the content of ALA, ETE, EPA, DHA, and total n-3 PUFAs in raw milk [19]. Fish oil and microalgae can increase the concentration of virgin n-3 PUFAs in milk, but the type varies [17]. The processing of dairy products, such as heat treatment, also affects the concentration of virgin n-3 PUFAs in milk [20].

To our knowledge, there is no detailed information about the nutritional characteristics, production, and processing of virgin n-3 PUFAs in dairy products. Therefore, this study aimed to highlight the nutritional characteristics and key factors affecting the concentration and type of virgin n-3 PUFAs in raw milk and dairy products.

2. Methodology

The scholarly articles used in this review were searched from the web using Google Scholar, Science Direct, PubMed, and subject-

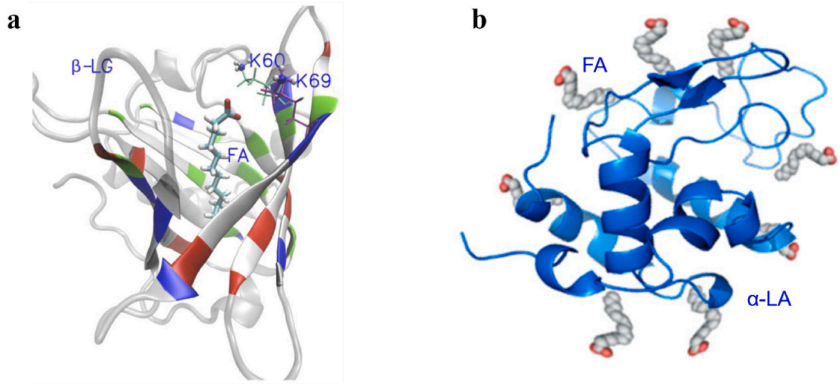

Fig. 2. Protein structure representation of bovine β-lactoglobulin [52] (a) and α-lactalbumin [53,54] (b) bound to fatty acids. β-LG: β-lactoglobulin, FA: fatty acid, α-LA: α-lactalbumin.

specific professional websites, and the data from 1999 to 2022. The keywords "omega-3," "α-linolenic acid," "eicosatrienoic acid," "docosapentaenoic acid," "docosahexaenoic acid," "microalgae," "fish oil," "flaxseed," "dairy," and "cheese" were used in the search. The articles chosen in this review should show the nutrition, production, or processing of virgin n-3 PUFAs in dairy.

2.1. Virgin n-3 PUFAs in milk

There are many kinds of n-3 PUFAs in milk, such as ALA, ETE, EPA, DPA, and DHA, but their contents are low, as shown in Table 1. There are three main forms of n-3 PUFAs in milk: phospholipids (PLs) [21,22], triacylglycerol (TAG) type [23], and free fatty acids [24]. Different n-3 PUFAs have different nutritional and functional roles in human health [25].

2.1.1. n-3 PUFAs in phospholipids

Lipids distributed in milk fat globules mainly exist in the form of PLs. PLs play an important role in the human body and infant development [31,32]. In general, PLs have a lower content of saturated fatty acids as well as short-chain fatty acids (C4–C10), but a higher content of unsaturated fatty acids in milk [33,34]. PLs containing PUFAs play an important role in the body, for example, DHA contained in PLs could improve the function of mitochondria [35]. Previous studies in animals and humans showed that n-3 PUFAs in the form of PL could have superior biological and nutritional functions [36]. Compared with the traditional n-3 PUFAs, the PL forms showed higher efficacy in the body [37], such as EPA-PLs and DHA-PLs. EPA-PLs and DHA-PLs can reduce neuroinflammation and anti-oxidation in the brain through changes in the brain cell structure and neurotransmitters, which are beneficial for brain function [38,39]. PLs can be classified into three types according to their molecular structure: glycerophospholipids (GPLs), sphingomyelins (SMs), and phospholipids (PLs) [40]. Recently, n-3 PUFAs connected with PLs, such as EPA-GPLs and DHA-GPLs, have received increasing attention. A previous study reported that DHA-GPLs could improve learning disabilities by altering brain lipid composition [41]. EPA-GPLs have many nutritional functions in humans, improving brain function, favoring visual and nervous system development, and regulating lipids in the blood [42].

2.1.2. n-3 PUFAs in triacylglycerols

The main form of milk fatty acids is TAGs, which account for more than 98 % of milk fat. n-3 PUFAs are located at three positions (sn-1, sn-2, and sn-3) in TAGs [20,43], and different positions in fatty acids play different roles in human health [44]. n-3 PUFAs in sn-1 and sn-3 are hydrolyzed by pancreatic lipase to form free n-3 PUFAs and sn-2 monoacylglycerols [45]. Free n-3 PUFAs can bind to β-LG because of their higher affinity for β-LG than for other blood components [14]. The n-3 PUFAs located at the sn-2 position showed higher absorption efficiency in the body compared with other positions [46,47]. Owing to their high absorption efficiency, sn-2 n-3 PUFA lipids play important roles in the body. A previous study reported that sn-2 DHA lipids are beneficial for brain functions, such as anxiety, cognitive decline, stress, and stroke [48]. Dietary supplementation with n-3 PUFAs in dairy animals can increase the concentration of n-3 PUFAs at the sn-2 position in milk [49]. Thus, regulating the dietary fatty acid composition can increase the content of virgin n-3 PUFAs in milk, which has many benefits for human health.

2.1.3. n-3 PUFAs in free fatty acids

The combination of fatty acids can alter the function of proteins [50]. The combination of β-LG and n-3 PUFAs can promote the absorption of n-3 PUFAs, and LF and n-3 PUFAs can enhance the inhibitory effect on cancer cell growth [50].

2.1.3.1. Functions of β-LG–n-3 PUFAs and α-LA–n-3 PUFAs complexes. β-LG and α-LA are milk-specific proteins synthesized by breast epithelial cells, accounting for about 50 % and 36 % of the total whey protein in milk [51]. As members of the lipid carrier protein family, β-LG and α-LA have multiple ligand binding sites, which can bind with fatty acids, such as oleic acid, linoleic acid, and conjugated linoleic acid (CLA) to form complexes as showed in Fig. 2a [52] and Fig. 2b [53,54]. These complexes can increase their

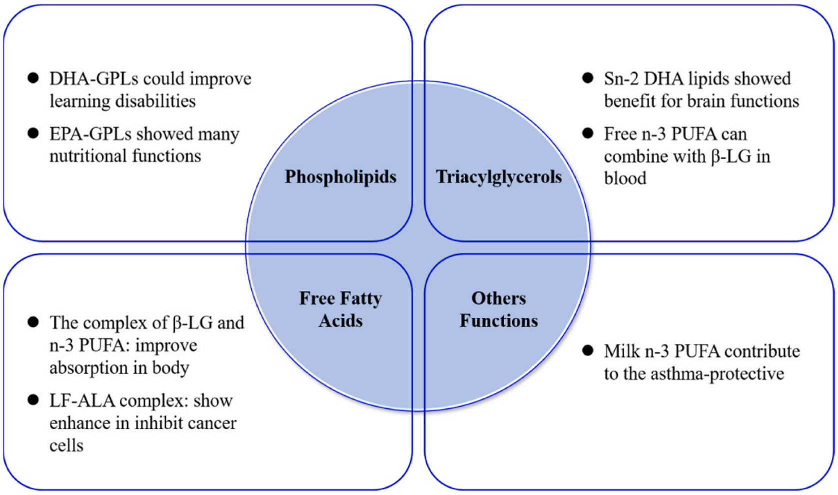

Fig. 3. Potential benefits of different kinds of n-3 PUFAs to human health. n-3 PUFAs: omega-3 polyunsaturated fatty acids, ALA: α-linolenic acid, ETE: eicosatrienoic acid, EPA: eicosapentaenoic acid, DHA: docosahexaenoic acid, β-LG: β-lactoglobulin, LF: lactoferrin, GPL: glycerophospholipids.

conformational stability to tryptic degradation [55], and can effectively embed, transfer, and protect bioactive components from oxidation and degradation [56]. β-LG and CLA can synthesize β-LG–CLA complexes. β-LG–CLA showed good stability in the gastrointestinal environment; thus, the complex can increase the absorption of CLA compared with CLA monomer (85.9 vs 45.8 μmol/L) [57]. Oleic acid (OA) and linoleic acid (LA) can bind to β-LG to form β-LG–OA and β-LG–LA, respectively. The two complexes, β-LG–OA and β-LG–LA, have cytotoxic activity on tumor cells and can induce cell decay [58]. In addition, β-LG–LA exhibited better thermostability than β-LG–OA [58]. β-LG and n-3 PUFAs can spontaneously combine to form nanoscale complexes [54], and these nanocomplexes have a good protective effect on n-3 PUFAs [14]. β-LG–n-3 PUFAs can delay the oxidative degradation of n-3 PUFAs during storage. β-LG can also effectively inhibit the degradation of n-3 PUFAs in the intestine and improve their absorption in the body. Most studies on α-LA have focused on the complexes of α-LA and OA. Although some studies have reported that α-LA and ALA can combine to form the complex α-LA–ALA [54], few studies have reported on the function of α-LA–n-3 PUFAs.

2.1.3.2. Functions of lactoferrin–n-3 PUFAs complex. LF is a natural, harmless, bioactive iron-binding glycoprotein with a molecular weight of approximately 80 kDa. LF is produced by mammalian glandular epithelial cells and neutrophils and is widely expressed in various body fluids [59], such as milk. Previous studies found that LF plays a positive role in the human body [60–62]. The combination of LF and n-3 PUFAs may be similar to the complex of LF and OA, and the LF–OA complex induces apoptosis in tumor cells [63]. LF combined with n-3 PUFAs can enhance the inhibitory effect on cancer cells, especially in combination with ALA [51]. Thus, LF and n-3 PUFAs may also synthesize the LF–n-3 PUFA complex (LF–ALA complex), which may play a role in the body. Nowadays, the Coronavirus disease 2019 (COVID-19), which is caused by the SARS-CoV-2 virus, is rapidly spreading globally. LF may play an important role in the prevention of SARS-CoV-2 virus infection [64], and it can prevent SARS-CoV-2 virus infection by blocking the virus's attachment to cellular heparin sulfate [65]. The LF–n-3 PUFA complex may have an inhibitory effect on SARS-CoV-2 infection.

Overall, as shown in Fig. 3, protein combined with n-3 PUFAs can increase the absorption of n-3 PUFAs and exert stronger physiological functions. β-LG–n-3 PUFAs may increase the absorption of n-3 PUFAs and avoid oxidation of n-3 PUFAs in milk. LF combined with n-3 PUFAs can enhance the inhibitory effect on cancer cells. Currently, there is limited research on the functionality of protein–n-3 PUFAs.

2.2. Regulation of virgin n-3 PUFAs in milk by feeding

Although n-3 PUFAs are similar in structure, different types of n-3 PUFAs play different functions in the body. ALA is an essential fatty acid that cannot be synthesized in the body and must be obtained from food [66]. Longer n-3 PUFAs can be synthesized using ALA. DHA has the highest concentration of n-3 PUFAs in the brain and plays an important role in maintaining normal brain development and function [67]. DHA is beneficial for cognitive behavior and can improve the health of children [68]. EPA mainly affects blood physiology and EPA intake can decrease serum and hepatic lipid levels; however, DHA is ineffective [69]. Therefore, the development of milk rich in different types of n-3 PUFAs may become a trend.

The kinds of n-3 PUFAs in milk, including free fatty acid, PLs and TAG, can be regulated by the diet of dairy animals [70]. The main n-3 PUFA feeds include flaxseed, fish oil, microalgae, and algae. These feeds can be used to produce milk that is rich in different types of n-3 PUFAs.

2.2.1. Regulation of virgin ALA in milk

Flaxseed has high ALA content [71], which can effectively increase the content of ALA in raw milk as dairy cow feed [72]. As shown

Table 2
Summary of the content of virgin n-3 PUFA in milk with dietary flaxseed supplementation.

Core material	Dosage	Breed	n-3 PUFA in milk (g/100 g fatty acid)					Results	Reference
			ALA	ETE	EPA	DPA	DHA		
Whole flaxseed	0.00 %	Holstein cows	0.52	–	0.01	0.01	–	–The concentration in milk	[78]
	5.00 %		0.66	–	0.01	0	–	Increased: ALA	
	10.00 %		0.82	–	0.02	0.21	–	No influence: EPA and DPA	
	15.00 %		0.96	–	0.01	0	–		
Extruded flaxseed	0.00 %	Holstein cows	0.44	0	0.03	0.008	0.003	–The concentration in milk	[74]
	5.00 %		0.8	0.001	0.05	0.009	0	Increased: ALA and EPA	
								No influence: DPA and DHA	
Flaxseed oil	0.00 %	Holsteins cows	0.31	<0.01	0.03	–	<0.01	–The concentration in milk	[79]
	2.50 %		0.99	<0.01	0.04	–	<0.01	Increased: ALA	
								No influence: ETE, EPA and DHA	
Flaxseed oil	0 mL	Holstein cows	0.21	0	0.01	0.05	–	–The concentration in milk	[28]
	110 mL		1.89	0	0.02	0.08	–	Increased: ALA and DPA	
	220 mL		3.3	0.01	0.02	0.08	–	No influence: ETE and EPA	
Whole flaxseed	0.00 %	Friesian cows	0.26	0.29	0.015	0.05	0.02	–The concentration in milk	[84]
	1.93 %		0.31	0.27	0.015	0.05	0.02	Increased: ALA	
								No influence: ETE, EPA, DPA and DHA	
	0.00 %	Jersey cows	0.22	0.23	0.011	0.03	0.02	–The concentration in milk	[84]
	1.93 %		0.28	0.23	0.013	0.04	0.02	Increased: ALA	
								No influence: ETE, EPA, DPA and DHA	
Whole flaxseed	0.00 %	Sarda goats	1.05	0.01	0.005	–	0.012	–The concentration in milk	[73]
	21.00 %		1.65	0.02	0.037	–	0.013	Increased: ALA and EPA	
								No influence: ETE and DHA	
Flaxseed oil	0 g/d	Malagueña goats	0.35	–	0.03	0.09	0.02	–The concentration in milk	[75]
	30 g/d		0.66	–	0.04	0.09	0.02	Increased: ALA and EPA	
								No influence: DPA and DHA	
Extruded flaxseed	0.00 %	Alpine goats	0.62	–	0.085	0.121	0.049	–The concentration in milk	[77]
	21.60 %		2.19	–	0.101	0.107	0.031	Increased: ALA	
								No influence: EPA, DPA and DHA	
Extruded flaxseed	0.00 %	ewes	0.36	0.012	0.02	0.06	0.03	–The concentration in milk	[85]
	6.00 %		1.27	0.01	0.04	0.08	0.03	Increased: ALA, EPA and DPA	
	12.00 %		1.91	0.01	0.04	0.08	0.03	No influence: DHA	
Flaxseed	0.00 kg	sheep	0.74	0.01	0.07	0.07	0.02	–The concentration in milk	[80]
	0.22 kg		1.87	0.02	0.07	0.08	0.02	Increased: ALA	
								No influence: ETE, EPA, DPA and DHA	
Whole flaxseed	0.00 %	Comisana ewes	0.57	0.02	0.07	0.08	0.05	–The concentration in milk	[81]
	9.06 %		1.53	0.03	0.08	0.09	0.05	Increased: ALA, ETE and EPA	
								No influence: DPA and DHA	
Flaxseed oil	0.00 %	Water buffaloes	0.383	–	0.024	–	0.016	–The concentration in milk	[82]
	2.50 %		0.768	–	0.021	–	0.069	Increased: ALA and DHA	
								No influence: EPA	

"-": means not detected, n-3 PUFAs: omega-3 polyunsaturated fatty acids, ALA: α-linolenic acid, ETE: eicosatrienoic acid, EPA: eicosapentaenoic acid, DPA: docosapentaenoic acid, DHA: docosahexaenoic acid.

Table 3
Summary of the content of n-3 PUFAs in fish oil and microalgae.

Core material	n-3 PUFAs g/100 g fatty acid					Reference
	ALA	ETE	EPA	DPA	DHA	
Fish oil	2.84	0.2	8.19	1.62	13.83	[86]
Fish oil	–	–	8.261	–	37.374	[87]
Fish oil	1.95	–	35.81	–	28.43	[88]
Microalgae	0.1	–	1.0	13.2	35.3	[89]
Microalgae oil	0	–	1.4	15.4	39.5	[89]
Microalgae	0.03	–	0.41	6.31	29.89	[30]

"-": means not detected, n-3 PUFAs: omega-3 polyunsaturated fatty acids, ALA: α-linolenic acid, ETE: eicosatrienoic acid, EPA: eicosapentaenoic acid, DPA: docosapentaenoic acid, DHA: docosahexaenoic acid.

in Table 2, there are many forms of flaxseed (including whole flaxseed, extruded flaxseed, and flaxseed oil) in the diet of different dairy animals (buffalo, goat, and sheep). All studies found that supplementation with flaxseed in the diet can increase the content of ALA in milk. However, different studies have reported different results for other longer-chain n-3 PUFAs. Studies have reported that flaxseed supplementation in the diet can cause an increase in virgin EPA [73–75] or DPA [28] in milk. However, some studies have shown no influence on the concentration of EPA [28,76–79] or DPA [80,81] in milk. Several studies have reported that flaxseed supplementation can increase the concentration of virgin DHA in milk [82]. A study on buffalo milk found that the DHA content in milk can be increased

Table 4
Summary of the content of virgin n-3 PUFAs in milk with fish oil supplement in the diet.

Fish oil Dosage	Breed	n-3 PUFAs in milk g/100 g fatty acid					Results	References
		ALA	ETE	EPA	DPA	DHA		
0 g/d	cow	0.41	0.013	0.06	0.09	0.03	–The concentration in milk	[93]
75 g/d		0.38	0.017	0.06	0.08	0.03	Increased: ETE, EPA, DPA, and DHA	
150 g/d		0.39	0.056	0.07	0.1	0.05	No influence: ALA	
300 g/d		0.48	0.323	0.17	0.18	0.10		
0 %	Holstein cows	0.51	–	0.23	–	0.59	–The concentration in milk	[88]
1.80 %		0.44	–	1.66	–	3.11	Increased: EPA and DHA No influence: ALA	
0 %	Holstein cows	0.75	0.001	0.003	–	0.001	–The concentration in milk	[77]
1.10 %		0.84	0.019	0.060	–	0.117	Increased: ALA, ETE, EPA, DPA, and DHA	
0	Holstein cows	0.4	0	0.03	0.06	0.02	–The concentration in milk	[92]
0.80 %		0.41	0.04	0.05	0.08	0.03	Increased: ETE, EPA, DPA, and DHA No influence: ALA	
0 %	Brown Swiss cows	1.04	–	0.14	0.2	0.06	–The concentration in milk	[90]
2.00 %		1.35	–	0.39	0.3	0.15	Increased: EPA, DPA, and DHA No influence: ALA	
0 %	Assaf ewes	0.33	0.02	0.03	0.06	0.02	–The concentration in milk	[94]
1 %		0.34	0.05	0.15	0.18	0.38	Increased: ETE, EPA, DPA, and DHA No influence: ALA	
0 %	Assaf ewes	0.56	–	0.06	0.09	0.16	–The concentration in milk	[96]
1.70 %		0.4	–	0.42	0.44	1.18	Increased: EPA, DPA, and DHA No influence: ALA	
0 %	Assaf ewes	0.58	–	0.07	0.1	0.03	–The concentration in milk	[95]
1.50 %		0.46	–	0.35	0.35	0.99	Increased: EPA, DPA, and DHA No influence: ALA	

n-3 PUFAs: omega-3 polyunsaturated fatty acids, ALA: α-linolenic acid, ETE: eicosatrienoic acid, EPA: eicosapentaenoic acid, DPA: docosapentaenoic acid, DHA: docosahexaenoic acid.

Table 5
Summary of the content of virgin n-3 polyunsaturated fatty acids (PUFAs) in milk with microalgae supplement in the diet.

Microalgae Dosage	Breed	n-3 PUFAs in milk g/100 g fatty acid					Results	Reference
		ALA	ETE	EPA	DPA	DHA		
0 g/d	Holstein cows	0.273	–	0.022	–	0.002	–The concentration in milk	[29]
100 g/d		0.318	–	0.028	–	0.242	Increased: ALA, EPA, and DHA	
0 g/d	Holstein cows	0.45	0.13	0.07	–	0.08	–The concentration in milk	[99]
50 g/d		0.46	0.14	0.07	–	0.15	Increased: ALA, ETE, and DHA	
100 g/d		0.49	0.14	0.06	–	0.25	No influence: EPA	
150 g/d		0.05	0.16	0.07	–	0.37		
0 g/d	Holstein cows	0.48	0.18	0.08	–	0.04	–The concentration in milk	[98]
100 g/d		0.47	0.17	0.09	–	0.22	Increased: DHA No influence: ALA, ETE, and EPA	
0 g/d	cows	0.66	0.018	0.072	0.11	0.074	–The concentration in milk	[101]
310 g/d		0.53	0.051	0.36	0.29	1.15	Increased: ETE, EPA. DPA, and DHA Decreased: ALA	
0 g/d	Alpine goats	1.18	–	0.09	0.22	0.04	–The concentration in milk	[103]
10 g/d		0.95	–	0.07	0.18	0.32	Increased: ETE, EPA. DPA, and DHA Decreased: ALA	
0 g/d	goats	0.62	0.018	0.052	0.1	0.078	–The concentration in milk	[102]
40 g/d		0.51	0.019	0.15	0.18	0.77	Increased: EPA. DPA, and DHA Decreased: ALA No influence: ETE	
0 g/d	ewes	3.33	0.18	0.00	0.00	0.00	–The concentration in milk	[100]
23.5 g/d		0.31	0.19	0.04	0.21	0.43	Increased: EPA. DPA, and DHA	
47 g/d		0.33	0.09	0.12	0.28	0.69	Decreased: ALA and ETE	
94 g/d		0.25	0.05	0.21	0.31	1.24		
0 g/d	Assaf sheep	0.49	–	0.04	0.10	0.05	–The concentration in milk	[102]
0.70 %		0.48	–	0.06	0.12	0.38	Increased: EPA. DPA, and DHA No influence: ALA	

n-3 PUFA: omega-3 polyunsaturated fatty acid, ALA: α-linolenic acid, ETE: eicosatrienoic acid, EPA: eicosapentaenoic acid, DPA: docosapentaenoic acid, DHA: docosahexaenoic acid.

Table 6
Summary of the content of virgin n-3 PUFAs in milk with heat treatments.

Milk	Heat treatments	n-3 PUFAs in milk g/100 g fatty acid				Reference
		ALA	EPA	DPA	DHA	
Cow	65 °C for 30 min	decrease 29.63 %	–	–	–	[111]
	Boiling for 1 min	decrease 52.85 %	–	–	–	
Buffalo	65 °C for 30 min	decrease 15.38 %	–	–	–	
	Boiling for 1 min	decrease 40.38 %	–	–	–	
Cow	85 °C for 15 s	no	no	–	–	[19]
	135 °C for 15 s	decrease 8.50 %	decrease 21.11 %	–	–	
Cow	72 °C for 15 s	no	no	–	–	[105]
	75 °C for 15 s	no	no	–	–	
	80 °C for 15 s	no	no	–	–	
	85 °C for 15 s	no	no	–	–	
	90 °C for 15 s	no	no	–	–	
	95 °C for 15 s	no	no	–	–	
	100 °C for 15 s	no	no	–	–	
	105 °C for 15 s	no	no	–	–	
	110 °C for 15 s	no	no	–	–	
	115 °C for 15 s	no	no	–	–	
	120 °C for 15 s	no	no	–	–	
Human	62.5 °C for 30 min	no	no	no	no	[106]
	62.5 °C for 30 min and pressurized for 5 min at 400 MPa	no	no	no	no	
	62.5 °C for 30 min and pressurized for 5 min at 500 MPa	no	no	no	no	
	62.5 °C for 30 min and pressurized for 5 min at 600 MPa	no	no	no	no	
Human	62.5 °C for 30 min	–	–	–	no	[107]

Decrease = (raw milk fatty acid – dairy products fatty acid) × 100/raw milk fatty acid, no: no influence.
n-3 PUFA: omega-3 polyunsaturated fatty acid, ALA: α-linolenic acid, EPA: eicosapentaenoic acid, DPA: docosapentaenoic acid, DHA: docosahexaenoic acid.

with flaxseed supplementation in the diet [81,82]. ALA can be converted to longer-chain n-3 PUFAs (ALA → ETE → EPA → DPA → DHA) via enzyme action *in vitro* [83]. In general, flaxseed is used to produce virgin ALA dairy products.

2.2.2. Regulation of virgin EPA and DHA in milk

Fish oil and microalgae contain high concentrations of n-3 PUFAs [17] (mainly EPA and DHA) and can be used as feed sources to increase the content of virgin milk EPA and DHA. However, as shown in Table 3, the EPA and DHA contents in fish oil and algae are different, and the EPA concentration in fish oil is higher than that in microalgae. The main n-3 PUFAs in microalgae are DPA and DHA.

The main n-3 PUFAs in fish oil are EPA and DHA [80], and dietary supplementation of dairy animals can increase the concentration of EPA and DHA in raw milk [88,91], as shown in Table 4. In addition, the addition of fish oil to the diet of dairy animals can also increase the levels of other kinds of n-3 PUFAs such as ETE and DPA [92–94]. Furthermore, fish oil supplementation in the diet of dairy animals does not influence the concentration of ALA in raw milk [91,95,96]. However, some research reported that fish oil addition to the diet can increase the concentration of ALA in raw milk. This may be due to the composition of n-3 PUFAs in fish oil being different. Some fish oils contain ALA [86], so some researchers found that the content of ALA in raw milk can be increased with ALA supplementation in the diet. However, the content of ALA in fish oil is very low [87]. Thus, fish oil can be used to produce virgin EPA and DHA dairy products.

2.2.3. Regulation of virgin DHA in milk

As high-quality DHA feed [97], microalgae can be used to produce virgin DHA dairy products (shown in Table 5) [98]. In addition to DHA, microalgae can also increase the content of ETE [99], EPA [29], and DPA [100] in raw milk. One study reported that microalgae supplementation can increase the concentration of ETE (0.018–0.051 g/100 g fatty acid; 283 times), EPA (0.072–0.360 g/100 g fatty acid; 500 times), DPA (0.110–0.290 g/100 g fatty acid; 264 times), and ETE (0.074–1.150 g/100 g fatty acid; 1554 times) [101]. In addition, some studies reported that microalgae supplementation did not affect the concentration of ETE [98] and EPA [99] in milk and may have even decreased the ETE concentration [102] in milk. Most studies have reported that microalgae supplementation does not influence or decrease the concentration of ALA in milk [29,101]. Thus, microalgae can be used to produce virgin DHA in dairy products, as a feed for cows.

2.3. Virgin n-3 PUFAs changes in various dairy products

Raw milk can be used to produce various dairy products. In particular, milk and cheese are the two main dairy foods in our daily

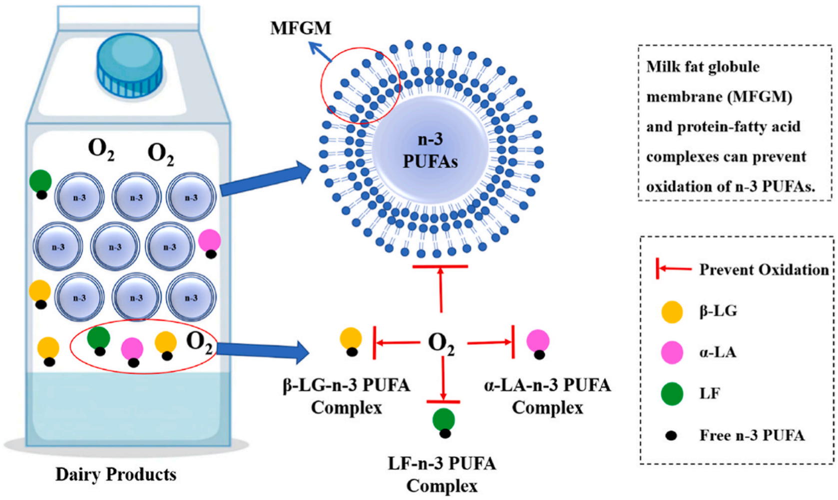

Fig. 4. Virgin n-3 PUFAs on lipid oxidation in dairy foods. BLG: β-lactoglobulin, α-LA: α-lactalbumin, LF: lactoferrin, n-3 PUFAs: omega-3 polyunsaturated fatty acids, MFGM: milk fat globule membrane.

lives.

2.3.1. Dairy products

2.3.1.1. Liquid milk. Sterilization is the main process for liquid milk, which is an important means of killing pathogens and destroying bacteria in raw milk. The sterilization methods include thermal technology (pasteurization, ultrahigh temperature processing and high-pressure processing) and nonthermal techniques (ultraviolet radiation, high-power ultrasound, and bactofugation).

Thermal technology is a commonly used sterilization method in commercial production. However, because of the high unsaturation, the n-3 PUFAs are easily oxidized by heat treatment [104]. The temperature and processing time of thermal technologies are the two main factors that influence the content of n-3 PUFAs in dairy products. As shown in Table 6, when the temperature was not higher than 120 °C, short-term (15 s) heat treatment did not affect the n-3 PUFA content in milk [105]. However, the concentration of n-3 PUFAs (ALA, EPA, and DHA) in milk decreases [19] after treatment at 135 °C for 15 s. In addition, milk heated at 62.5 °C for 30 min also showed no influence on the concentration of n-3 PUFAs in milk [106,107]. However, treatment at 65 °C for 30 min or boiling for 1 min decreased the ALA content in milk. In general, controlling the temperature and duration of heat treatment can provide healthy and safe dairy products for humans.

The main nonthermal technologies include ultraviolet radiation, high-power ultrasound, and bactofugation. Ultraviolet radiation, as one of the emerging food processing technologies [108], has a huge potential in milk processing. Ultraviolet radiation kills microorganisms in milk without producing heat. Thus, studies have found that ultraviolet radiation does not affect n-3 PUFAs in milk [109]. High-power ultrasound and bactofugation are two sterilization methods used in milk production. High-power ultrasound and bactofugation could reduce the loss of nutrients in milk while sterilizing [110]. Therefore, the development of nonthermal technologies is conducive to the production of n-3 PUFA-rich dairy products.

2.3.1.2. Cheese. Cheese is a nutritious and versatile food whose nutritional value is affected by the type of milk used [112]. Thus, increasing the concentration of virgin n-3 PUFAs in raw milk can increase the n-3 PUFA content in cheese [113,114]. Because the fat content in cheese is influenced by several factors, such as the method of manufacture, studies have reported that higher concentrations of n-3 PUFAs were observed in cheese than in raw milk (cheese vs raw milk: 4.05 vs 3.71) [115].

2.3.2. Oxidation of virgin n-3 PUFAs in dairy products

The n-3 PUFAs have high oxidation sensitivity [116], thus the concentration of n-3 PUFAs in milk decreases with storage time by direct incorporation of n-3 PUFA sources [117,118]. Fatty acid oxidation can cause off-flavor in milk [119]. However, virgin n-3 PUFAs are hardly oxidized during storage time [91], and compared with added n-3 PUFAs in milk there is no odor due to the oxidation of virgin n-3 PUFAs during storage [91,120]. A previous study found that the concentration of virgin n-3 PUFAs in cheese was not influenced by storage [115]. This may be due to approximately 99 % of fatty acid being compartmented in milk fat globules, and most n-3 PUFAs are surrounded by the milk fat globule membrane (MFGM). The MFGM can protect n-3 PUFAs against lipolysis and dispersion [121] and reduce the oxidation of virgin n-3 PUFAs in milk [112], as shown in Fig. 4. In addition, nanocomplexes of n-3 PUFA–β-LG could also protect n-3 PUFAs against lipolysis and dispersal.

In conclusion, the main factor influencing the concentration of virgin n-3 PUFAs in dairy products is heat treatment. Owing to the protection provided by the MFGM and milk protein, the content of virgin n-3 PUFAs remained constant during storage.

3. Conclusion

Dairy products with virgin n-3 PUFAs are potentially healthy functional foods. However, the development of virgin n-3 PUFA dairy products is still at the primary stage. To date, most studies only focused on how to obtain a stable content of virgin n-3 PUFA raw milk. However, studies on the nutrition of virgin n-3 PUFA dairy products are still insufficient, such as the relationship between the production and preservation of virgin n-3 PUFA dairy. Thus, further studies can focus on two aspects: 1) comprehensive functional evaluation of virgin n-3 PUFA milk and 2) the relationship between the concentration of virgin n-3 PUFAs in milk and heat treatment, and the development of emerging nonthermal technologies.

CRediT authorship contribution statement

Guoxin Huang: Writing – original draft, Formal analysis, Data curation, Conceptualization. **Ning Li:** Investigation. **Xufang Wu:** Software. **Nan Zheng:** Writing – review & editing. **Shengguo Zhao:** Validation. **Yangdong Zhang:** Supervision. **Jiaqi Wang:** Supervision, Formal analysis.

Data availability statement

No data was used for the research described in the article.

Declaration of competing interest

The authors declare that they have no known competing financial interests.

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