



Microfiltration retentate co-product from whey protein isolate production - Composition, processing, applications and potential for value addition

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ABSTRACT

Background: Microfiltration retentate (MFR), also called whey protein phospholipid concentrate, is a co-product of whey protein isolate (WPI) production derived through microfiltration (MF) of whey or whey protein concentrate. Microbiological quality and protein denaturation/aggregation in the MFR stream present challenges in valorizing the stream for utilization in specialized nutritional products. As a result, MFR is underutilized, with its current applications largely limited to commodity applications in the animal feed industry as a milk replacer and in confectionery, for example. On the other hand, the production of MFR is increasing year on year due to the increase in demand for WPI with its current production representing 14–18% of the total whey processed worldwide.

Scope and approach: In this review, we discuss MFR processing options, composition, current applications, future perspectives, and potential valorization strategies and challenges. Our approach includes a comprehensive literature review of recent studies and advancements in MFR processing. We systematically selected and analyzed peer-reviewed articles, industry websites, and reports to provide a holistic view of the current state and future directions of MFR technology.

Key findings and conclusions: The gross chemical composition of MFR is highly variable, with typical values of fat, protein, lactose, and ash ranging from 11 to 38%, 50–70%, 1–11%, and 2–4%, respectively. The protein constituents in MFR include β -lactoglobulin, α -lactalbumin, bovine serum albumin, lactoferrin, immunoglobulins, and caseino-macropptide. Additionally, MFR is enriched with milk fat globule membrane-associated proteins such as butyrophilin, mucin 1, xanthine oxidase, and phospholipids like sphingomyelin and phosphatidylcholine. Significant research gaps exist in understanding the microbiology, bioactivity, and bioavailability of MFR components, which are crucial for supporting its valorization. Despite these gaps, there is great potential for utilizing MFR in the food industry, neonatal nutrition, and pharmaceutical applications. This potential provides opportunities to develop targeted, novel value-added ingredients from the MFR stream.

1. Introduction

Traditionally, whey has been defined as a byproduct of cheese-making and was historically regarded by cheese producers as a waste product with little or no commercial value (Ghatawat et al., 2019; Walzem et al., 2002). Its accumulation posed a significant environmental challenge due to its high organic content and high biochemical oxygen demand (Julian, 2019; Ozturk et al., 2022). Consequently, the dairy processing sector was not permitted to dispose of whey through conventional means, necessitating additional treatment steps to reduce its pollution index, which in turn increased production costs (Pesta et al.,

2007). However, advances in scientific research and technology, coupled with environmental considerations and a growing demand for natural, sustainable products, have inspired researchers and the dairy sector to re-evaluate whey as a valuable resource. Today, whey is increasingly seen as a source of valuable ingredients with multifunctional benefits (Kaur et al., 2020).

The development and adoption of membrane separation technology have revolutionized the dairy industry, bringing a major breakthrough in whey processing and valorization. This technology enables the recovery of whey proteins, milk fat globule membrane (MFGM) fragments, and residual fat in the retentate (i.e., whey protein concentrate, WPC)

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through ultrafiltration (UF), while separating lactose and minerals in the permeate stream (Saxena et al., 2009). As consumer demand for higher protein purity and lower fat content increased, further manufacturing processes were developed to produce whey protein isolate (WPI), a product with a high protein and low fat content. Whey protein isolate contains over 90% protein and is produced from conventional WPC with a protein content of 35–80% (Julian, 2019). During the manufacturing of WPI, WPC undergoes microfiltration, which separates native whey proteins (permeate) from residual fat and other denatured and aggregated whey proteins (retentate). This microfiltration retentate is processed by manufacturers into whey protein phospholipid concentrate (WPPC) or high-fat whey protein concentrate (HFWPC) (ADPI, 2023). In this review, this retentate stream is referred to as microfiltration retentate (MFR).

The chemical composition of MFR is influenced by several factors, including the origin and composition of the whey, pretreatment methods, membrane material and configuration, pore size, processing temperature, concentration factor, and extent of fouling (Carter et al., 2021; France et al., 2021, 2024; Heino et al., 2010; Jørgensen et al., 2016). Consequently, the composition of liquid or dried powder produced from the MFR stream varies considerably between different manufacturers and batches (Levin et al., 2016a; Lucey, 2022; Mestawet et al., 2024; Ozturk et al., 2022; Swaminathan et al., 2023). Representative gross chemical compositions of MFR from product specifications of selected commercial suppliers and research papers are provided in Table 1. The data reveal significant variability in the composition of WPPC and related products, reflecting diverse raw materials and processing methods.

The variability in the composition of MFR poses significant challenges for its application in various industries. In the food industry, consistent composition is crucial for product formulation and quality control. Variations in protein content and bioactive compounds can affect the functional properties of food products, such as texture, flavor, and the nutritional value. Despite these challenges, there is limited research addressing the standardization of MFR production. Most available studies focus on specific aspects such as composition (Levin et al., 2016a; Ozturk et al., 2022), applications (Bund & Hartel, 2013; Levin et al., 2016b), partitioning mechanisms of components during MF (Mestawet et al., 2024), partial enrichment of phospholipids (PLs) in MFR (Swaminathan et al., 2023), and organic extraction of PLs (Price et al., 2018), without considering the broader implications of compositional variability. In addition, the methods used to analyze MFR are often inconsistent. For instance, fat determination through Röse Gottlieb versus Floch or PLs determination through nuclear magnetic resonance versus phosphorus assay or HPLC, makes it difficult to compare results across different studies.

With the current growing production of MFR, there is a need for standardized production process and analytical methods for valorizing MFR. Reports indicate that worldwide whey production has increased from 145 million tonnes in 2017 (Ganju & Gogate, 2017) to 190 million tonnes per year (Asunis et al., 2020) with an annual increase of 1–2% (Buchanan et al., 2023). In the same period, the global market has shown a 31% increase in WPI production (Persistent Market Research Pvt Ltd., 2023). The market is projected to exhibit growth of 5.2% annually, according to the Persistent Market Research Pvt Ltd. (2023). Microfiltration retentate represents 14–18% of the total whey processed worldwide, with an estimated 32 million tons produced in 2020 (Buggy et al., 2018; Mollea et al., 2013; Setiowati et al., 2020).

There is growing interest in the composition of MFR, driven by the increasing scientific studies on the techno-functional and bio-functional properties of specific components, such as MFGM-associated proteins and PLs (Abd El-Salam & El-Shibiny, 2020; Brink & Lönnerdal, 2020; Fontecha et al., 2020; Kuchta et al., 2012; Lee et al., 2018). For example, infants fed with formula enriched in bovine MFGM fragments and lactoferrin (from sources other than MFR) recorded significantly accelerated neurodevelopmental profile at day 365, improved language subcategories at day 545 and reduced occurrence of diarrhea and respiratory-associated adverse events, compared to infants fed on unsupplemented formula (Li, Ye, & Singh, 2019). Currently, MFR is provided to animals as a component of milk replacers (e.g., calf milk replacer), used in bakeries and confectioneries, used as soil fertilizer, or treated as waste (Badman et al., 2019; Huang et al., 2020a), with this proportion representing 42% of the total MFR produced (Ganju & Gogate, 2017). The unexploited and under-valorized MFR side-stream presents opportunities for several novel, promising and sustainable food and non-food applications (Ghatawat et al., 2019; Huang et al., 2020a; Ozturk et al., 2022). The increase in the quantity of MFR produced provides manufacturers with opportunities and challenges in valorizing this co-product and finding new novel applications (Swaminathan et al., 2021).

This comprehensive review includes the current state of research on MFR, its practical applications, and opportunities for innovation, while recognizing limitations in the existing scientific knowledge base. Specifically, the authors aim to provide a detailed analysis of MFR by discussing the processing methods used to generate it, and to examine its diverse chemical composition, focusing on macronutrients and key bioactive components such as PLs and MFGM proteins. In addition, challenges related to microbial quality and protein aggregation, which hinder the use of MFR in high-value applications, are reviewed, and possible solutions presented. In the later sections, current applications of MFR are reviewed, followed by an exploration of potential strategies for valorization of MFR. This work incorporates an analysis of the

Table 1

Typical composition of microfiltration retentate compiled from a number different authors and commercial supplier information.

Product name	Moisture (%)	Fat (%)	Protein (%)	Lactose (%)	Ash (%)	Phospholipids in total fat (%)	Reference
WPPC	≤6	≥12	≥50.0	NA	≤8	NA	ADPI (2023)
WPPC	2.9	12.5	69.2	5.1	4.1	NA	Levin et al. (2016)
WPPC	3.9	27.0	65.0	NA	7.9	29.1	Price et al. (2018)
WPPC	3.0	24.2	56.6	NA	2.6	1.8	(Huang et al., 2020a)
WPPC	3.6	18.7	64.8	NA	2.3	2.2	(Huang et al., 2020a)
WPPC	4.0	18.5	65.0	NA	2.3	2.2	(Huang et al., 2020a)
WPPC	4.5	13.7	70.0	2.9	2.1	NA	Levin et al. (2016)
WPPC	4.8	17.7	63.5	10.3	3.2	NA	Levin et al. (2016)
WPPC	3.6	15.6	54.7	3.5	3.5	NA	Levin et al. (2016)
WPPC	4.1	10.9	69.8	10.7	2.5	NA	Levin et al. (2016)
WPPC	4.3	15.5	50.3	4.0	2.6	NA	Levin et al. (2016)
WPPC	2.7	38.1	52.9	1.1	1.9	NA	Levin et al. (2016)
WPPC	1.9	32.4	54.4	1.0	2.1	NA	Levin et al. (2016)
Pro-cream	5.0	21.1	63.2	13.2	2.6	NA	Bund and Hartel (2013)
WPPC	NA	13.1–28.1	52.6–76.2	NA	NA	NA	Ozturk et al. (2022)
SureStart™ MFGM Lipid 70	NA	16.0	73.0	2.0	NA	5.0–7.0	Company web page
Bongards® PC - Protein	NA	10.9	50.0	NA	NA	NA	Company web page

NA: Not available, WPPC: whey protein phospholipid concentrate, ADPI: American Dairy Products Institute.

challenges in adding value to MFR, and identifies avenues for future research and development required to scientifically underpin the valorization of MFR.

2. Process options for generating microfiltration retentate from whey

The dairy industry continues to explore ways to extract greater value from whey co-products, and advancements in membrane filtration technologies play a crucial role in this effort (Carter et al., 2021; France et al., 2021; Saxena et al., 2009). Techniques such as MF and UF, with membrane pore sizes ranging from 0.1 to 1.0 μm and 0.01–0.10 μm respectively (Fig. 1), along with DF are key methods used to produce whey-based ingredients (France et al., 2021). These technologies are integral to valorizing the whey stream, including the production of MFR. A recent study by France et al. (2024) highlighted the impact of membrane pore size and processing temperature on retentate composition and functionality. Using a 1000 kDa molecular weight cut-off membrane, equivalent to a 0.1 μm pore size, at lower temperatures was found to enhance the permeation of bio-functional compounds such as β -casein, while also improving the heat stability of the retentate. This finding underscores the importance of selecting appropriate pore size and temperature conditions to maximize the quality and value of retentate.

Emerging techniques for whey protein fractionation, as reviewed by Chen et al. (2023), offer several advantages over traditional methods, including higher selectivity, improved efficiency, and the preservation of protein functionality. Notably, electromembrane separation uses electrical fields to achieve more precise separation based on charge, resulting in higher purity levels of isolated proteins. Membrane chromatography, which combines the selectivity of chromatography with the high throughput of membrane filtration, potentially allows for faster processing times and increased efficiency in protein recovery and

purification. These innovative approaches are crucial for optimizing yield and quality in dairy processing, highlighting the ongoing advancements in membrane technology. In considering these advancements, it is essential to optimize operational parameters such as temperature, transmembrane pressure, and membrane pore size, as emphasized by Heino et al. (2010). These parameters significantly impact the efficiency of component isolation and the extent of membrane fouling. By carefully controlling these factors, it is possible to enhance ingredient purity and yield while minimizing fouling, thus improving overall process efficiency.

Under the current methods for generating MFR, one of the process options involves centrifuging cheese whey to remove large fat globules and MFGM fragments, producing whey cream and whey. Following this centrifugation, the whey undergoes UF and DF, which separates lactose, minerals, and water (permeate) from proteins, residual fat, MFGM fragments, and smaller milkfat globules (retentate, i.e., WPC). To produce WPI and MFR, this WPC can be further processed. Typically, WPC is subjected to a tight pore MF (0.1–0.5 μm) step, which retains denatured and aggregated proteins, MFGM fragments, and fat globules, while unaggregated protein, lactose, and minerals pass through the membrane, yielding MFR as a co-product and WPI. In this method, the whey protein concentrate often undergoes different levels of heat treatment during various stages, contributing to the denaturation and aggregation of proteins (Mestawet et al., 2024). Alternatively, after the centrifugation of cheese whey, the whey can be directly subjected to tight pore MF, avoiding these different levels of heat treatment prior to MF. This approach reduces the extent of whey protein denaturation and aggregation, thereby enhancing protein permeation and reducing the retention of undesired components in the MFR. As a result, the efficiency and quality of the resulting WPI and MFR products are improved, providing a more streamlined and effective processing method (Fig. 2).

Traditionally, MFR was generated using ceramic MF plants with membrane pore sizes of 0.1–0.5 μm . However, the high capital and

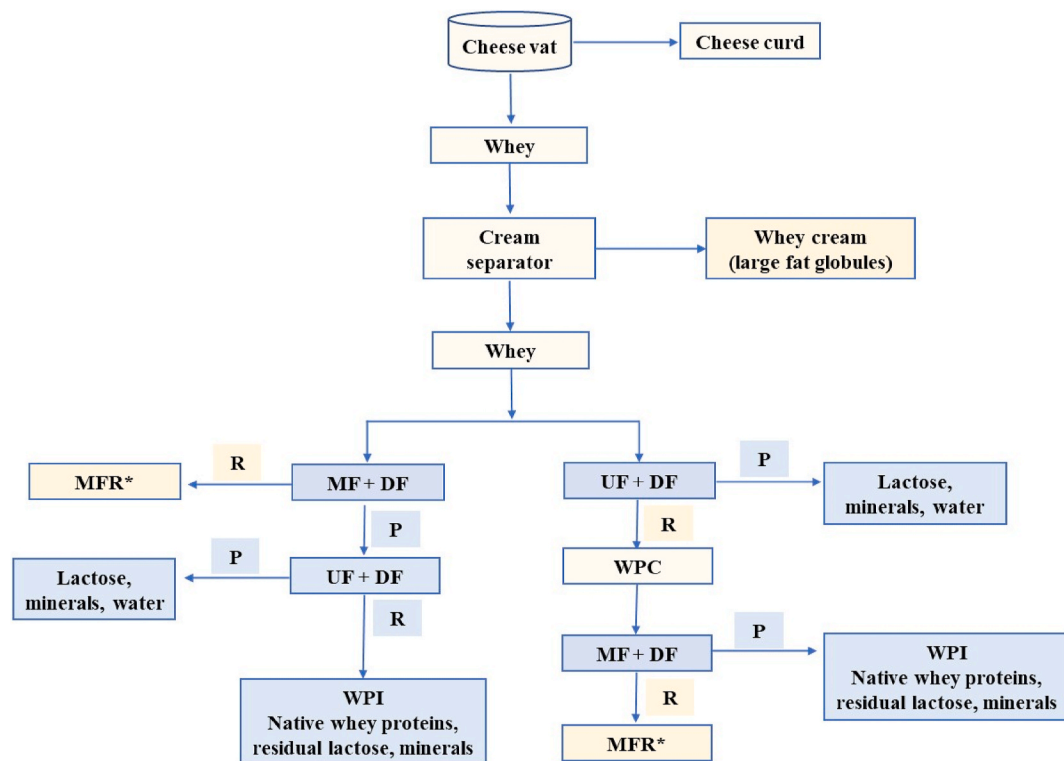


Fig. 1. Schematic representation of process required to produce microfiltration retentate (MFR). *Contents are fragments of milk fat globule membrane, denatured whey proteins, glycomacropeptides, lipids, residual native whey proteins, lactose, and minerals. UF: ultrafiltration, DF: diafiltration, MF: microfiltration, P: permeate, R: retentate, WPC: whey protein concentration, WPI: whey protein isolate.

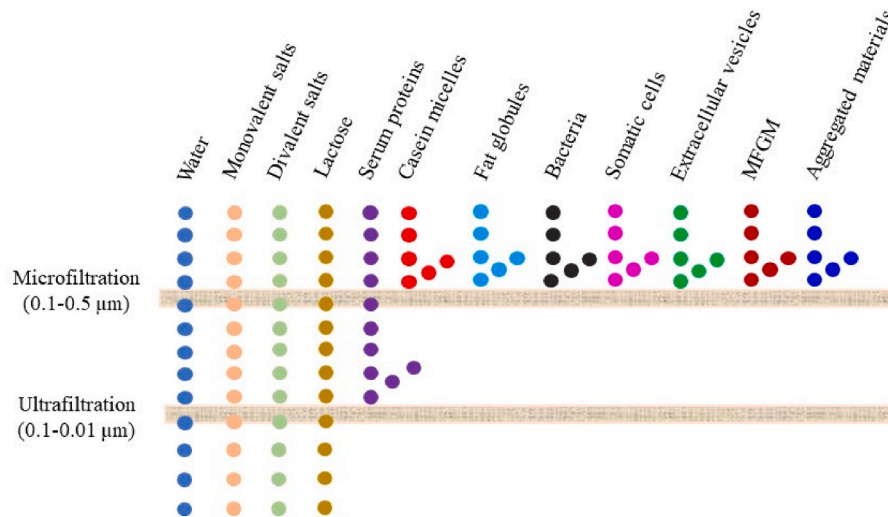


Fig. 2. Dairy components partition through different sized membrane. MFGM: milk fat globule membrane.

maintenance costs associated with ceramic MF plants have led to the adoption of more cost-effective alternatives, such as spiral-wound polymeric membranes (Julian, 2019). Microfiltration of WPC or cheese whey following centrifugation has typically been performed under warm conditions (45–50 °C), which offers the benefit of high initial permeate flux and high whey protein purity. However, this process is now commonly performed under cold conditions (4–20 °C), as it has been shown to reduce fouling, extend processing time, and decrease the levels of denatured whey proteins (Crowley et al., 2015; France et al., 2021; Heino et al., 2010; O'Mahony & Tuohy, 2013; Song et al., 2022).

The primary target of any dairy industry that produces WPI using MF is to maximize the permeation of whey proteins into the permeate stream while retaining as little whey protein as possible. Performing MF at low temperatures (i.e., ≤20 °C) helps reduce whey protein denaturation, microbial growth, and spore proliferation (Luo et al., 2015; McCarthy et al., 2017; Schiffer et al., 2021). Furthermore, MF at lower temperatures can reduce fouling (Heino et al., 2010), which enhances whey protein permeation and improves the yield of WPI. This process also enriches PLs and MFGM-associated proteins in the MFR. The implementation of cold MF proves to be an effective method for generating MFR enriched with specific bio-functional compounds.

3. Composition of microfiltration retentate from whey

Milk composition is influenced by various factors including animal feed and nutrition, seasonality, lactation stage, parity, and cow health (Li & Singh, 2019; Lopez et al., 2011; Mesilati-Stahy & Argov-Argaman, 2014). Beyond the quality of the initial milk, the cheese-making protocol, the composition of the resulting cheese whey, pre-MF processing steps such as heat treatment, and MF processing parameters (e.g., temperature and transmembrane pressure) also significantly affect the composition of the MFR stream (France et al., 2021; Levin et al., 2016a; Setiowati et al., 2020; Swaminathan et al., 2021). With increasing interest in MFR, the American Dairy Products Institute (2023) has established standards for MFR-derived products, which must contain a minimum of 50% protein, a minimum of 12% fat, a maximum of 8% ash in dry matter, a maximum of 6% moisture, and have a pH in the range of 5.7–7.5.

3.1. Macronutrients in microfiltration retentate of whey

The main macronutrients in MFR include lipids, proteins, lactose, and ash, regardless of the milk source or processing method (Lee et al.,

2018; Mestawet et al., 2024; Roy et al., 2020). Among these, whey proteins, MFGM-associated proteins, and lipids are the primary components (Fig. 3a, adopted with minor modification from Ozturk et al., 2022; Ferraris et al., 2020; Huang et al., 2020a; Levin et al., 2016a). The average composition of MFR from 8 different suppliers, as reported by Levin et al. (2016a), was 3.6% moisture, 19.5% fat, 60.9% protein, 4.8% lactose and 2.9% ash. Although there are few reports, one study by Mestawet et al. (2024) indicates the mineral content of MFR includes Ca, P, Mg, Na, and K at 38.0, 29.3, 17.7, 4.67, and 4.67 mg/100 g, respectively. These minerals, particularly cations, play a role in mediating protein aggregation during heat treatment, contributing to the complex composition of MFR.

The whey proteins in MFR include β -lactoglobulin (β -lg), α -lactalbumin (α -la), bovine serum albumin (BSA), lactoferrin (Lf) and immunoglobulins (Ig) (Levin et al., 2016a). These proteins exist in both unaggregated and aggregated states (Mestawet et al., 2024). Studies have shown that denatured and aggregated whey proteins consist of complexes of β -lg, α -la, BSA, lactoferrin, and Ig, which form during heat treatment at various production stages (Levin et al., 2016b; Ozturk et al., 2022; Xiong et al., 2021). In whey generated from cheese processing, casein-macropolymers (CMP) formed from enzymatic hydrolysis of kappa-casein (κ -CN) are also present in the MFR (Fox et al., 2016; Ozturk et al., 2022). Microfiltration retentate is naturally enriched with PLs, cerebrosides, free fatty acids, triglycerides, and other bioactive compounds such as lactoferrin and growth factors (Levin et al., 2016b; Ozturk et al., 2022; Walstra et al., 2006). Phospholipids present in the MFGM can exist either in free form or bound to protein aggregates in the MFR (Fig. 3b; adopted from Levin et al., 2016a). Fatty acids are the predominant lipids in MFR, with palmitic, oleic, stearic, and myristic acids being the most abundant, constituting 36.1%, 24.8%, 11.7%, and 10.8% of the total fatty acids, respectively (Mestawet et al., 2024; Ozturk et al., 2022).

3.2. Milk fat globule membrane components

The bovine MFGM is a complex glycosylated, protein-embedded, biophysical system that surrounds the MFG, typically measuring approximately 10–20 nm in cross-section (Fig. 4b). The composition of the MFGM is inherently complex and dynamic, influenced by various factors such as the developmental stage of the neonate, maternal genetics, and the animal's physical and biological environment (Dewettinck et al., 2008). The distribution of MFGM components across different dairy streams is significantly affected by processing methods, including cream washing and butter making. Recent studies, including

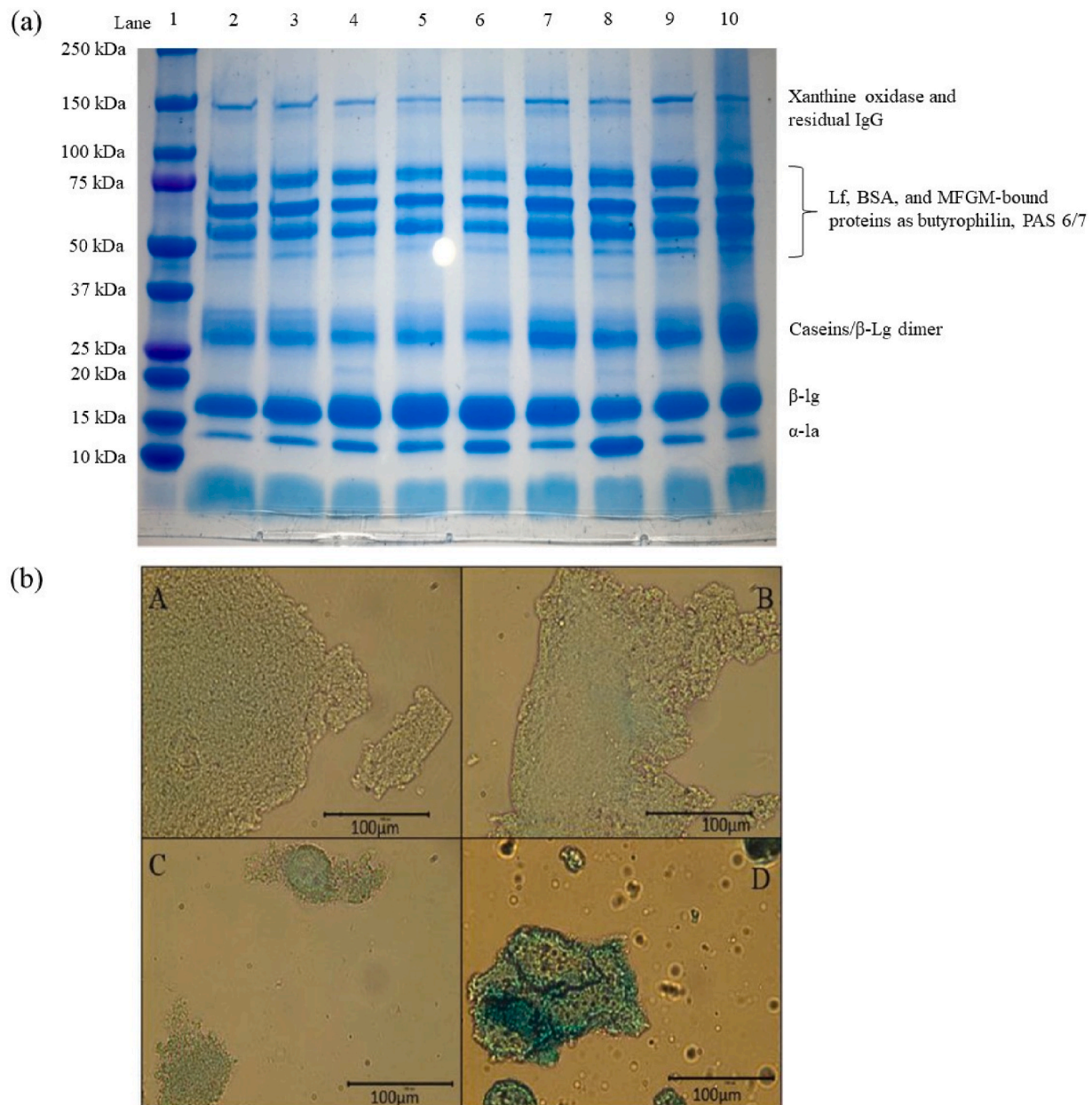


Fig. 3. (a) Sodium dodecyl sulphate polyacrylamide gel electrophoretogram showing protein profile and milk fat globule membrane associated protein in whey protein phospholipid concentrate (adopted with minor modification from [Ozturk et al., 2022](#)) and (b) light microscope image showing protein-phospholipid aggregation in whey protein phospholipid concentrate sample dyed with luxol fast blue. Blue section indicates PL bound to the protein aggregates (adapted from [Levin et al., 2016](#)). IgG: Immunoglobulin G, Lf: lactoferrin, BSA: bovine serum albumin, MFGM: milk fat globule membrane, PAS 6/7: periodic acid Schiff 6/7; β-Ig: β-lactoglobulin, α-la: α-lactalbumin. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

that by [Hokkanen et al. \(2021\)](#), have highlighted that the partitioning of MFGM components between streams is notably influenced by the thermal behavior and size of the fat globules. This partitioning is crucial for understanding the functional properties and nutritional value of dairy products, as it impacts the bioavailability and distribution of key MFGM components.

3.2.1. Milk fat globule membrane associated proteins

Milk fat globule membrane proteins play a crucial role in the structural integrity and functionality of the MFG, contributing to its emulsifying properties and stability ([Lopez et al., 2011](#); [Mesilati-Stahy & Argov-Argaman, 2014](#); [Ozturk et al., 2022](#)) (Fig. 4). The composition and concentration of MFGM proteins can vary significantly based on the processing methods used in dairy production, influencing their bioactive

properties and nutritional value. According to [Hokkanen et al. \(2021\)](#), the processing of cream, including washing and butter making, significantly affects the partitioning of MFGM components between different dairy streams such as buttermilk and butter serum. This differential distribution suggests that MFGM proteins and their associated health benefits may vary depending on the specific processing techniques employed.

Glycoproteins constitute approximately 50% of the dry weight of the MFGM ([Dewettinck et al., 2008](#)). To date, research has identified around 632 different proteins in bovine MFGMs, with the most abundant being glycosylated butyrophilin, mucins MUC1, xanthine oxidoreductase, lactadherin, cluster of differentiation proteins, non-glycosylated adipophilin, and fatty acid binding proteins. These proteins are consistently found across all mammalian species, indicating their crucial biological

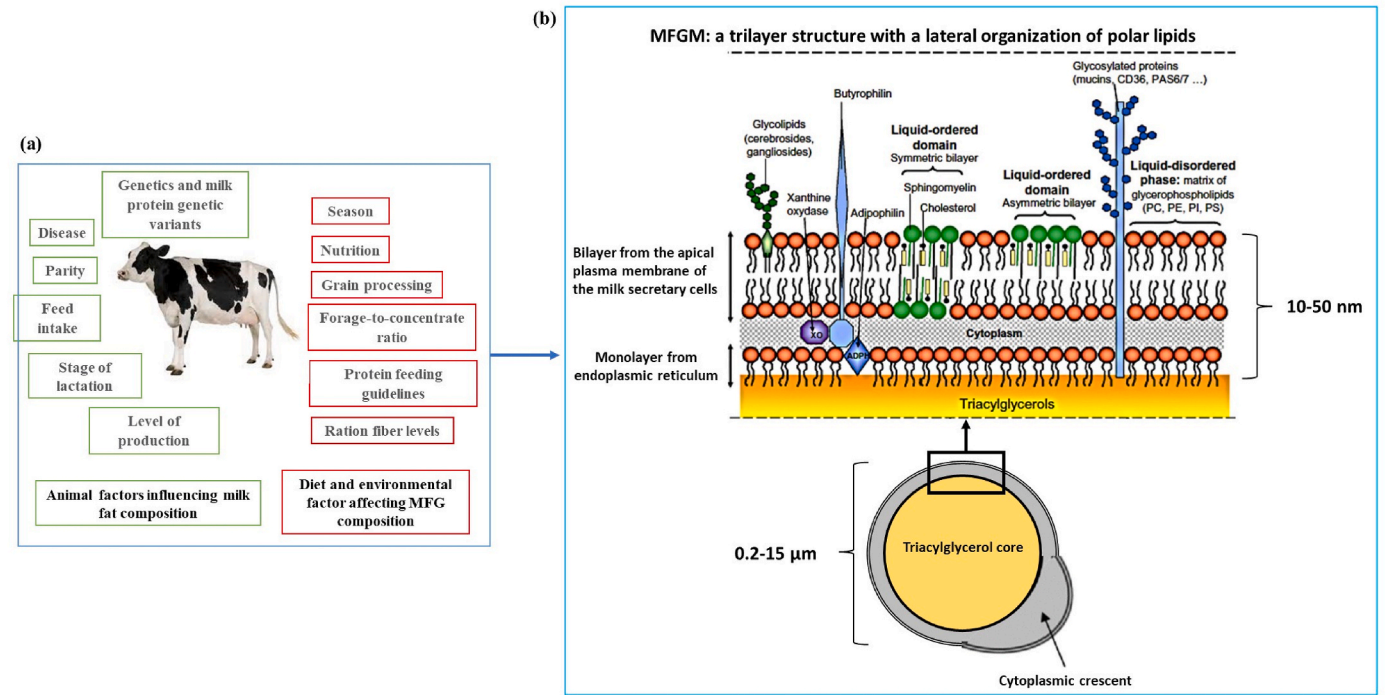


Fig. 4. (a) Factors influencing milk fat composition and (b) schematic representation of structural organization of milk fat globule and milk fat globule membrane. Fig. 4b is adapted with minor modification from Lopez et al. (2011).

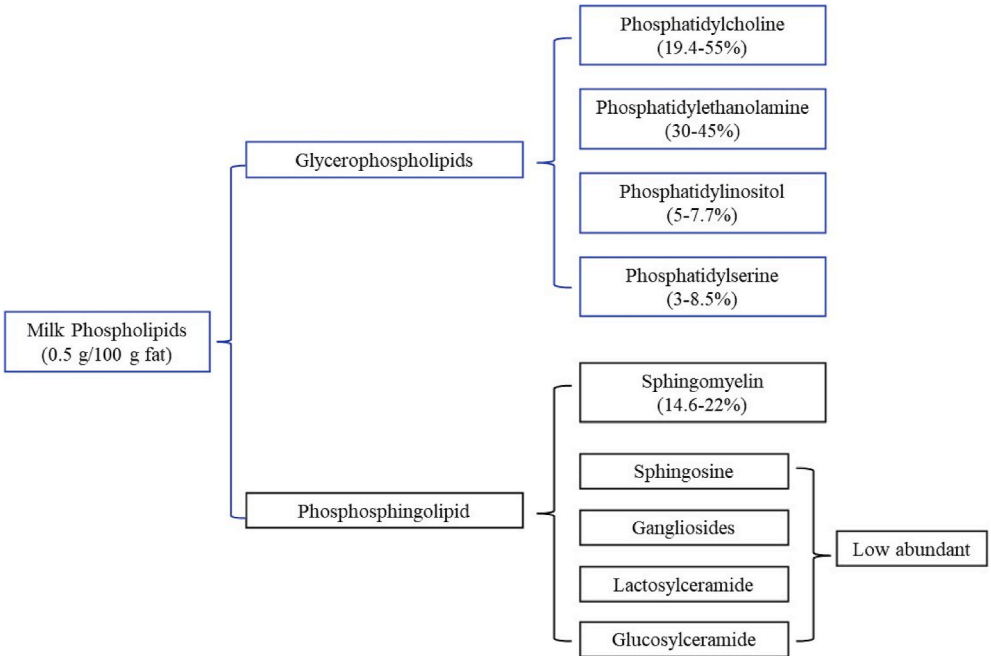


Fig. 5. Phospholipid classes and content as a percent of total phospholipids. (Adopted from Levin et al., 2016; Vanderghem et al., 2010).

roles (Reinhardt & Lippolis, 2006). Additional MFGM-associated protein families include glycoprotein B, redox enzymes, and the adhesive glycoprotein MFG-E8 (also known as lactadherin, p47, rAGS, PAS-6/7, and BA-46). Minor proteins within the MFGM include the polymeric Ig receptor, apolipoproteins E and A1, 71-kDa heat-shock cognate protein, clusterin, lactoperoxidase, Ig heavy chain, and peptidylprolyl isomerase A (Fong & Norris, 2009; Smoczyński et al., 2012). These components play significant roles in the structure and function of the MFGM, impacting both the nutritional and functional properties of dairy products.

Growing evidence suggests that MFGM proteins are associated with numerous health benefits, exhibit significant functional properties that influence milk processing, and serve as a versatile biophysical system for food applications (Dewettinck et al., 2008; Kliem & Shingfield, 2016; Le Huërou-Luron et al., 2019; Lee et al., 2018; Levin et al., 2016b; Smoczyński et al., 2012). Furthermore, MFGM proteins are being studied for their potential to improve cognitive development, immune function, and gut health. This growing body of research has led to increased interest in incorporating MFGM components into food products, particularly in areas such as infant nutrition, functional foods, and dietary supplements. The versatile nature of MFGM makes it a valuable ingredient for enhancing the nutritional profile and functional properties of various food products, thereby offering significant benefits to human health.

3.2.2. Milk fat globule membrane associated phospholipids

Globally, milk remains the primary source of polar lipids for humans, particularly infants (Venkat et al., 2022). Lipids are synthesized in the rough endoplasmic reticulum membrane of the mammary gland. These lipids accumulate as micro-lipid droplets within the cytoplasm of mammary epithelial cells in lactating animals (Walstra et al., 2006). These micro-droplets are encased by a diffuse interfacial layer of the endoplasmic reticulum, composed of proteins and polar lipids, forming the first inner layer of the MFGM. As they transit through the cytoplasm of secretory cells, the droplets merge and grow, leading to the formation of MFGs of varying sizes (Patel, 2015). Upon secretion into the lumen of the alveoli, these droplets are further encapsulated by a double-layered outer plasma membrane from the epithelial cells of the mammary gland. This structure, composed of proteins and polar lipids, gives the lipid fat droplet a tri-layered membrane structure known as the MFGM (Manoni et al., 2021). This membrane protects triglycerides from lipolytic enzymes and acts as an emulsifier, preventing fat droplets from coalescing and maintaining fat dispersion in milk plasma (Dewettinck et al., 2008).

Approximately 98% of the total lipids in milk are triacylglycerols, found in the core of the MFG and enveloped by the MFGM (Contarini & Povolito, 2013). The remaining lipid fraction comprises PLs and sterols, primarily cholesterol, along with smaller amounts of diacylglycerols, monoacylglycerols, and free fatty acids (Roy et al., 2020; Smoczyński et al., 2012). Phospholipids make up about 40% of the MFGM's dry weight, predominantly existing as polar lipids (Huang et al., 2020a; Roy et al., 2020). Hokkanen et al. (2021) highlighted that the composition of these lipids can vary significantly in dairy streams based on processing conditions, which in turn affects their functional properties and potential health benefits. Specifically, the partitioning of MFGM lipids during butter making is influenced by the physico-chemical properties of fat globules, such as their size and thermal behavior, which underscores the importance of understanding lipid dynamics in dairy processing for nutritional value enhancement.

Milk contains two main types of PLs: glycerophospholipids and sphingolipids (Fig. 5). Most PLs in milk are glycerophospholipids, consisting of a glycerol backbone with acyl chains at the sn-1 and sn-2 positions and a phosphate group at the sn-3 position, making the molecules amphipathic. Sphingomyelin (SM), characterized by a sphingosine backbone bound to a single acyl chain through an amide linkage and a phosphate group, is classified as both a sphingolipid and a phospholipid. The phosphate group in both glycerophospholipids and SM can bind to polar head groups such as choline, ethanolamine, serine, or

inositol, forming phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), and phosphatidylinositol (PI), respectively (Contarini & Povolito, 2013).

The principal polar lipids in MFGM include PC (35%), PE (30%), SM (25%), PI (5%), and PS (3%). Trace amounts of glucosylceramide (GluCer), lactosylceramide (LacCer), and gangliosides are also present. During dairy processes like cream churning for butter production or homogenization, the MFGM disintegrates, releasing its components, including PLs and proteins, into the serum phase. The availability and functional properties of PLs are influenced by factors such as the type of raw material (e.g., buttermilk or whey), heat treatment, and the methods used for component enrichment (Saffon et al., 2015; Zhu et al., 2020).

Phospholipids have been linked to various health benefits, including regulating inflammatory responses, chemopreventive and chemotherapeutic effects against certain cancers, and inhibiting cholesterol absorption (Hedrick et al., 2021; Le Huërou-Luron et al., 2019). They are also involved in cognitive development, metabolic health, and immune system development (Fontecha et al., 2020; Le Huërou-Luron et al., 2018). Beyond their nutritional contributions, PLs are excellent natural emulsifiers, widely used in the food industry for their amphipathic properties that enhance water-holding and foaming capabilities in confectionery applications (Wang et al., 2022). Since MFGM is concentrated in the MFR stream, it represents a promising starting material for concentrating PLs, thereby providing significant opportunities for the valorization of MFR.

3.3. Microbiology of microfiltration retentate from whey

Milk, with its rich nutrient content and high water activity (>85%), provides an ideal environment for the growth of microorganisms (Gebeyehu et al., 2022; Paludetti et al., 2019). The microbiological profile of MFR reflects the original milk microbiota and production management practices, resulting in variability similar to its chemical composition. The American Dairy Products Institute (2023) has established microbiological standards for MFR, including limits on standard plate count ($\leq 30,000$ cfu/g), yeast and mold (≤ 100 cfu/g), *Bacillus cereus* (≤ 100 cfu/g), clostridia (sulfite-reducing) (≤ 100 cfu/g), coliform (≤ 10 cfu/g), Enterobacteriaceae (≤ 10 cfu/g), and absence of *Salmonella* and coagulase-positive *Staphylococcus*.

Various bacteria, including thermophiles, aerobic or facultative anaerobic spore formers, obligate anaerobic spore formers, psychrotrophic, and pathogenic bacteria, have been detected in milk powders such as milk protein concentrate and skimmed milk powder (Buehner et al., 2015; McHugh et al., 2020; Ronimus et al., 2003; Sadiq et al., 2018). Although information on microbiological quality of MFR is lacking, it is speculated to be higher than in many other milk powders due to differences in processing methodology. This occurs because the pore sizes in the membrane are small enough to capture not only large particles but also microbial cells, which typically range from 0.4 to 2 μm in size (García et al., 2013). As a result, the MFR stream may have a higher microbial load compared to other milk powders. Consequently, the microbiological quality of MFR is potentially more variable and may require additional measures to ensure safety and consistency in the final product.

Conventional pasteurization (72 °C for 15 s) effectively targets pathogens and mesophilic microorganisms, but higher temperatures needed to eliminate thermophilic bacteria and spores can cause additional protein denaturation, reducing the biological value of MFR. Therefore, exploring alternative methods is essential. Recent advancements in thermal processing methods, such as microwave and radio frequency heating, offer promising alternatives. These methods can inactivate microorganisms with minimal impact on the structure and functionality of milk proteins, thus maintaining the nutritional quality of MFR. Hu et al. (2024) highlighted the broader impact of these methods on food safety, noting that radio frequency heating provides

uniform heating and deep penetration, which is particularly effective for controlling microorganisms in MFR processing without compromising functional properties.

Non-thermal technologies, which use physical and chemical means to inactivate microorganisms, also offer promising alternatives. These methods are effective against vegetative cells, and spore inactivation can be achieved through combined physical and chemical methods (Bevilacqua et al., 2019). In the dairy industry, innovative chemical methods such as ozonation are gaining attention for surface cleaning, soil removal, and ensuring microbiological safety (Feng et al., 2020a; Sert & Mercan, 2022). Ozone has been effective in inactivating microorganisms like *Staphylococcus* in fluid milk, *Cronobacter* in milk powder, improving the flow behavior and microbial properties of skim milk powder (Couto et al., 2016), inactivating *cronobacter* in skim and whole milk (Couto et al., 2016; Sert & Mercan, 2021; Torlak & Sert, 2013). Additionally, tea polyphenols, either alone or combined with ozonation, have shown significant effects on inactivating bacterial cells, spores, viruses, and fungi, as well as destroying botulinum toxin in milk and water (Feng et al., 2020a; Yin et al., 2015). High-pressure homogenization and ultrasound, which exert mechanical action on microorganisms through cavitation and micronization, also hold potential for enhancing the microbiological quality of MFR (Bevilacqua et al., 2019). These technologies collectively offer valuable alternatives to traditional methods, enhancing the microbiological quality and safety of MFR.

4. Applications of microfiltration retentate from whey

Microfiltration retentate has various applications in the food industry, animal feed, and non-food sectors. Predominantly processed in the USA, MFR is marketed as WPPC or HFWPC. Companies such as Diversified Ingredients, Leprino Foods, and MCT Dairies, Inc. play a significant role in its commercialization (ADPI, 2023). While some research has explored the application of MFR in the food industry (e.g.,

Bund & Hartel, 2013; Levin et al., 2016b) there is a notable scarcity of research on its application in animal feed. Only a few publications mention its use in animal feed (Levin et al., 2016a; Lucey, 2022; Swaminathan et al., 2021), and there is also limited research published on its application in infant formula, limited mainly to information available on company websites. Table 2 provides an overview of products derived from MFR, including Pro-cream™, Salibra® 700, NeoShield™, and others, which cater to diverse markets, including food, health, and animal nutrition. This section synthesizes available data on MFR applications and extrapolates findings from similar ingredients to highlight potential uses.

4.1. Current applications

4.1.1. Food industry

Microfiltration retentate is explored for its versatility in the food industry, serving as a baking improver, anti-staling agent, chocolate additive, wetting enhancer for instant products, and margarine stabilizer (Dewettinck et al., 2008; Levin et al., 2016b). Studies have shown its potential as a substitute for traditional dairy products, emulsifiers, and eggs in products like ice cream, soup, and confectionery. For instance, Bund and Hartel (2013) found that ice creams made with MFR-delactosed permeate blends had comparable sensory attributes and better physical properties than those made with non-fat dried milk. Similarly, Levin et al. (2016b) demonstrated MFR's efficacy as a natural emulsifier in ice cream, caramel, and cake, underscoring its functional versatility.

4.1.2. Animal feed

Although MFR's application in animal feed is primarily indicated on company websites (Table 2), and few mentions in research articles (Levin et al., 2016a; Lucey, 2022; Swaminathan et al., 2021, 2023), there is limited research detailing its use, target animal groups, or

Table 2
Commercially available products from microfiltration retentate and products available with similar composition, produced from alternative streams.

Product name	Content	Intended use/benefit	Company
MFR stream			
Pro-cream™	High fat and enriched with proteins	Stabilizing effect in whipped cream and other confectionaries	Sosa Redmond FINE Foods
Salibra® 700	Enriched with Ig, growth factors, lactoferrin and MFGM PLs	health benefit	Glanbia Nutritionals
NeoShield™	Enriched with Ig, growth factors, lactoferrin and MFGM PLs	Health benefit	Glanbia Nutritionals
Iso chill 3400 H F	Enriched with essential amino acids and branched chain amino acids and glutamine	Food application, medical nutrition confectioneries	Agropur
Bongards® PC - Protein	Lipids, MFGM, protein	Beverage, nutritional supplements, confectionery, animal feed, health benefit	Bongard Creameries
WPPC/HFWPC	High fat, PLs and protein	Food, bakeries, infant formula	Diversified Ingredients
WPPC/HFWPC	High fat, PLs and protein	Food, bakeries, infant formula	Leprino Foods
WPPC/HFWPC	High fat, PLs and protein	Food, bakeries, infant formula	MCT Dairies, Inc.
WPPC/HFWPC	High fat, PLs and protein	Food, bakeries, infant formula	Sachsenmilch Leppersdorf GmbH
WPPC/HFWPC	High fat, PLs and protein	Food, bakeries, infant formula	Tatua USA Ltd.
Non-MFR stream			
Lacprodan® MFGM-10	Rich in PL's and gangliosides along with lactoferrin, IgG and sialic acid	Health benefit	Arla Food Ingredients
Lacprodan® Premium ALPHA-10	Dry-blend variant of alpha-lactalbumin	Health benefit	Arla Food Ingredients
Smart Mama MFGM-packed	MFGM enriched	Cognitive development	Arla Food Ingredients
SureStart™ MFGM Lipid 70	Enriched with choline, phosphatidylserine, sialic acid containing gangliosides, and sphingomyelin	Brain and cognitive development	Fonterra
SureStart™ MFGM Lipid 100	Enriched with choline, phosphatidylserine, sialic acid containing gangliosides, and sphingomyelin	Brain and cognitive development	Fonterra
Vivinal® MFGM	Rich in proteins, lipids and bioactive compounds, immunoglobuline G (IgG) and lactoferrin	Health benefit, Brain and cognitive development	FrieslandCampina Ingredients

WPPC: whey protein phospholipid concentrate, HFWPC: high fat whey protein concentrate, MF: microfiltration, MFR: microfiltration retentate, MFGM: milk fat globule membrane; PLs: phospholipids; IgG immunoglobulin.

impact on production or reproduction traits. Nonetheless, animal feed replacers containing components similar to MFR have shown promise in improving calf performance, increasing weight gain, and enhancing feed conversion ratios, suggesting its potential as a valuable nutritional supplement for young animals (Badman et al., 2019; Huuskonen, 2017; Lammers et al., 1998; Tóthová et al., 2016).

4.2. Future applications and innovation opportunities

4.2.1. Nutritional applications

Microfiltration retentate holds promise in enhancing infant nutrition by supplementing infant formula (IF). Research has shown that infants fed with IF experience reduced neuro- and cognitive development, and are at a higher risk for atopic diseases, respiratory infections, necrotizing enterocolitis, and gastrointestinal complications compared to breastfed infants. This difference is largely attributed to the insufficient levels of important nutrients such as PLs and proteins in IF (Knudsen et al., 2021; Zhu et al., 2020). The primary ingredients in IF are derived from bovine milk, which significantly differs in composition from human milk (Barone et al., 2020; Knudsen et al., 2021). For instance, the PL SM is more abundant in human milk than in bovine milk, making human milk the only substantial source of SM for neonates (Cilla et al., 2016; Clau-marchirant et al., 2016). Significant efforts have been made over the years to closely replicate the dynamic features of breast milk in infant formula, aiming to enhance its composition, functionality, and health outcomes. Numerous research teams and IF manufacturers have explored incorporating ingredients rich in MFGM or complex lipids into formulas to enhance various growth and development outcomes (Hedrick et al., 2021; Li et al., 2019).

The potential of MFR in elderly nutrition is also significant, with research indicating that MFGM may support cognitive health and physical performance, particularly when combined with regular exercise (Abd El-Salam & El-Shibiny, 2020; Brink & Lönnnerdal, 2020; Her-nell et al., 2016). Older adults often aim to stay active, maintain energy levels, and preserve mental acuity. Milk fat globule membrane has been shown to benefit intestinal health, improve skin condition, and help manage conditions like hypercholesterolemia, obesity, and inflammation. In a recent study involving mice, a combination of MFGM supplementation and regular exercise effectively prevented age-related declines in muscle mass and strength (Sugita et al., 2021). Moreover, individuals with chronic inflammatory diseases of the gastrointestinal tract may benefit from dietary products that reduce autoimmune responses, thereby alleviating localized inflammation (Madureira et al., 2007).

In addition, MFR shows promise in the growing pet nutrition market, offering high-quality, balanced diets that promote pet health and vitality (Bontempo, 2005; Petersen et al., 2021). As pet owners increasingly seek functional foods that not only meet basic nutritional needs but also promote health and well-being, MFR stands out as a valuable ingredient in the formulation of premium pet foods. Its ability to enable the manufacturing of a balanced nutritional profile, while supporting various aspects of pet health aligns with the evolving consumer preferences in the pet nutrition market.

Another important component of milk, which can be enriched in the MFR stream, are the extracellular vesicles (EVs), also known as micro-vesicles, microparticles, ectosomes or exosomes. These EVs are secreted by all cell types including mammary stem cells (Jiang et al., 2021). Extracellular vesicles are cytosol fragments with spheroid morphology surrounded by double layered lipid membranes and hydrophilic proteins (Ong et al., 2021). The EVs are specialized vesicles that carry receptors, bioactive lipids, proteins, and nucleic acids, such as mRNA and micro-RNA. They are known to be a fundamental means of intercellular communication between the breastfeeding mother and her new-born as well as cross-species and involved in regulating the development of infant gut by promoting intestinal epithelial cell proliferation and survival (Sanwlani et al., 2020). The microRNA is involved in the expression of

numerous development-associated genes and signalling and is implicated in an immunomodulatory role in infants in adipogenesis, myogenesis and osteogenesis (Jiang et al., 2021; Yates et al., 2022). The EVs are in the size range of 30–1000 nm and, if present in the WPC feed, will be enriched in the MFR stream along with other larger components. This enrichment provides an additional component for use in various applications.

A promising avenue for MFR components is the development of functional foods designed to provide targeted health benefits, such as improved gut health, enhanced immune function, and cognitive support. Functional foods can address specific nutritional deficiencies and health conditions, leveraging the bioactive components of MFR for maximum benefit (Konstantinidi & Koutelidakis, 2019). Additionally, isolating specific bioactive compounds from MFR for use in nutraceutical products presents significant potential. Nutraceuticals, which combine the properties of nutrition and pharmaceuticals, can promote overall health and well-being. Microfiltration retentate-derived compounds have shown potential in reducing inflammation, enhancing immune responses, and supporting metabolic health, offering substantial opportunities for innovation in this field (Alali et al., 2021; Puri et al., 2022). These bioactive substances, present in common food sources, can provide significant health benefits in addition to their nutritional value, thus representing a promising area for further research and development in nutraceutical applications (Puri et al., 2022).

4.2.2. Non-food applications

Microfiltration retentate holds significant potential for applications, including drug delivery carrier systems, fat liquoring for leather softening, and as raw materials for ceramides and liposome production. The pharmaceutical industry, in particular, sees promise in MFR-derived components; for example, bioactive peptides and proteins extracted from MFR, such as lactoferrin, have shown antimicrobial and anti-inflammatory properties, making them suitable for therapeutic formulations targeting infections and inflammatory conditions (Chakrabarti et al., 2018; Patel, 2015). Future research may focus on producing bioactive peptides from MFR through enzymatic hydrolysis, which could offer health benefits like antihypertensive, antioxidant, and antimicrobial activities, thereby expanding the utilization of MFR.

Cosmetology represents a promising area where MFR can potentially find valuable applications. There is increasing interest in utilizing natural and bioactive ingredients in this field, which provides an avenue for components derived from MFR. Phospholipids and proteins extracted from MFR are valuable for their moisturizing, anti-aging, anti-wrinkle, and protective properties (Audic et al., 2003). These ingredients are particularly beneficial for enhancing the skin barrier function, providing hydration, and combating signs of aging. The use of MFR-derived components in skin and hair care products aligns with consumer preferences for effective and sustainable cosmetic solutions (Ahn et al., 2022). Incorporating these natural ingredients not only meets the demand for high-performance products but also supports the trend towards environmentally friendly and health-conscious beauty practices.

Moreover, MFR components have the potential to be utilized in manufacturing bio-based products, such as wood coatings, adhesives, and biological glues. This potential is attributed to their abundant functional groups, heat-induced interactions, and water solubility (Guo et al., 2019). Emerging applications in biotechnology also present promising opportunities, such as using MFR components to create biodegradable bioplastics and other eco-friendly materials. These sustainable packaging solutions contribute to circular economy principles, reducing environmental impact. For instance, bioplastics synthesized from plant sugars or engineered from microorganisms offer benefits over traditional plastics, including a smaller carbon footprint, enhanced biodegradability, and reduced reliance on fossil fuels (Rajvanshi et al., 2023). Additionally, bioplastics can decrease greenhouse gas emissions by partially or fully eliminating the use of fossil fuel derivatives (Rosenboom et al., 2022). By leveraging these opportunities, the dairy

industry can not only add value to the MFR stream but also contribute to the development of innovative products across various sectors. This multifaceted approach aligns with the global shift towards sustainability and the utilization of by-products, promoting a circular economy in the dairy sector.

5. Microfiltration retentate-derived products and future prospects

Several companies have developed and patented various products from MFR, such as Pro-cream, Salibra® 700, and NeoShield™. Products with similar compositions to MFR, like Smart Mama and Lacprodan®, are available commercially (Table 2). Most WPI manufacturers produce MFR as a co-product, though many do not explicitly present its applications. Notable companies like Sosa Redmond FINE Foods (Spain), Glanbia Nutritional's (Ireland), and Bongards Creameries (USA) are among those producing products from the MFR stream. The offerings from Arla Food Ingredients (Denmark), Fonterra (New Zealand), and FrieslandCampina Ingredients (The Netherlands) demonstrate the potential of utilizing the MFR stream, with products containing components similar to MFR showing positive health benefits, nutritional value, and techno-functional properties (Bhinder et al., 2017).

As awareness of MFR's benefits grows, more industry players are joining the effort to harness its potential. Recently, Diversified Ingredients, Leprino Foods, MCT Dairies Inc., Tatua USA Ltd in the USA, and Sachsenmilch Leppersdorf GmbH in Germany have started producing products derived from the MFR stream. This trend is expected to continue, with expanding opportunities in the isolation of MFGM materials, the enrichment and purification of extracellular vesicles, and the extraction of bioactive whey proteins. These advancements not only add value to the MFR stream but also align with the growing consumer demand for health-enhancing ingredients and sustainable practices in the food industry.

6. Opportunities for adding value to microfiltration retentate from whey: gaps and challenges

Microfiltration retentate offers considerable potential for enhancing various aspects of dairy and food product development, with its unique composition enabling innovative applications and market expansion. However, realizing these opportunities comes with challenges. This section explores potential avenues for adding value to MFR, identifies existing gaps in its current understanding and utilization, and outlines key challenges that must be addressed to fully capitalize on its benefits.

6.1. Opportunities for microfiltration retentate utilization

The potential for MFR in product development is significant, particularly in functional foods and nutritional supplements (Levin et al., 2016b). Microfiltration retentate can cater to the growing market of health-conscious consumers who are increasingly aware of the benefits of healthy nutrition. Its high protein content and bioactive components make MFR an excellent ingredient for nutritional supplements targeting various demographics, such as athletes, the elderly, and individuals with specific dietary needs (Lucey, 2022). In the dairy industry, MFR presents opportunities for innovation in cheese production, yogurt products, and infant formula (Walstra et al., 2006). For cheese production, MFR can enhance yield and improve the nutritional profile, contributing to enhanced texture and flavor. Similarly, incorporating MFR in yogurt and other fermented dairy products can increase their protein content, enhance consistency, and improve taste, making them more appealing to consumers who prioritize healthy eating (Tamime & Robinson, 2007).

From a production standpoint, MFR offers cost-effective benefits through resource optimization and sustainability (Baldasso et al., 2011). By utilizing MFR, dairy processors can maximize the use of whey, a

byproduct that might otherwise be underutilized, resulting in cost savings and increased profitability. Additionally, valorizing MFR helps companies reduce waste and improve the sustainability of their operations, aligning with the growing consumer demand for environmentally friendly products. There is significant potential for MFR in emerging markets, where the demand for high-quality, protein-rich dairy products is on the rise. This opens new revenue streams for dairy producers looking to expand globally. Furthermore, with the trend towards personalized nutrition, MFR can be used to develop products tailored to specific health conditions or dietary preferences, catering to niche markets.

Advancements in membrane technology present another significant opportunity for MFR. These advancements enable the fractionation and selective enrichment of milk/whey components and development of ingredients, thereby enhancing versatility and value of such dairy streams (France et al., 2024; Heino et al., 2010). Improved membrane technology can lead to more efficient and targeted processing, resulting in higher quality and more consistent products (Chen et al., 2023). Research and development will continue to drive innovation in MFR processing technologies, enhancing the quality and consistency of MFR and expanding its applications.

6.2. Current gaps in microfiltration retentate research and application

A significant research gap exists in understanding the microbiological profile of MFR. This gap persists due to the complex nature of MFR and the historical focus on other aspects of whey and side-stream processing (Julian, 2019). Understanding the microbiological profile is critical for ensuring the safety and quality of MFR-derived ingredients, especially for products with strict food safety standards. This is particularly important for applications in infant and clinical nutrition, where microbial contamination can pose serious health risks. Addressing this gap is crucial for both the scientific community and the dairy industry, providing foundational data to develop effective quality control measures and ensure product safety.

Recent studies have shown an unexpectedly high proportion of aggregated/denatured proteins in MFR, with aggregation partly mediated by cations and likely arising from heat treatment at different production stages (Mestawet et al., 2024). However, the nature and extent of this aggregation are not fully understood. Understanding protein aggregation is essential for improving component partitioning during MF, enhancing protein permeation, and enriching specific bioactive compounds. Detailed knowledge of aggregation can lead to better processing methods and product formulations, enabling the development of strategies to reverse or prevent aggregate formation. Research needs to elucidate the underlying mechanisms of aggregation to advance scientific knowledge and develop targeted solutions. Industry professionals require this knowledge to optimize processing conditions and improve product quality, ensuring that MFR-derived products meet high standards of functionality and stability.

There is very limited information available in the published literature on the functionality and bioavailability of components in MFR (Levin et al., 2016a; Ozturk et al., 2022). The presence of aggregated and denatured proteins complicates the understanding of these properties, because denaturation can alter how these components function, and consequently, their bioavailability. Additional research is needed to address this issue as understanding these aspects is crucial for developing high-value products with targeted health benefits, supporting innovations in food and nutritional products. Both the scientific community and the dairy industry stand to benefit from this research by gaining knowledge, creating new products, and enhancing existing ones.

6.3. Challenges in scaling and standardizing microfiltration retentate

Implementing the proposed valorization strategies for MFR presents several practical challenges that need to be addressed to make these

strategies viable. One of the primary challenges in valorizing MFR is the variability in its composition. This variability can affect the consistency and quality of MFR-based products, making it difficult to standardize and scale up production (Levin et al., 2016a; Swaminathan et al., 2023). Standardized methods for generating and selectively enriching target ingredients in MFR are lacking (Levin et al., 2016a; Mestawet et al., 2024; Ozturk et al., 2022). Promising results have been reported in recent studies involving the pretreatment of whey protein concentrate (unpublished data) and enzymatic hydrolysis of WPPC (Swaminathan et al., 2023), followed by membrane filtration. These studies have shown improvements in protein permeation and enrichment of PLs and MFGM-associated proteins in the MFR stream. However, achieving the desired purity level remains a challenge. Standardizing MFR composition through the development of consistent processing protocols and quality control measures is crucial for ensuring product reliability. Achieving this requires comprehensive research to understand the factors contributing to variability and designing protocols that can accommodate or eliminate these factors.

Emerging techniques for whey protein fractionation, such as electromembrane separation and membrane chromatography, face several challenges that hinder their widespread industrial adoption, as reviewed by Chen et al. (2023). These challenges include limited research and development, which has not yet provided sufficient evidence of their effectiveness and scalability for commercial use. Additionally, the high costs associated with specialized equipment and materials pose economic barriers, particularly when scaling up these techniques for industrial applications. Furthermore, while these methods aim to preserve protein functionality, there is a risk that the conditions used, such as pH and temperature, may negatively impact the bioactivity and functional properties of proteins. Addressing these challenges will require focused research, cost reduction strategies, and process optimization to ensure these technologies can be effectively commercialized.

One proposed process option for generating MFR is to introduce MF at an earlier stage in the filtration process, ideally before heat treatment (s), in contrast with current practices where MF is typically applied at a later stage. The rationale is that applying MF earlier would generate a stream enriched in PLs and MFGM by avoiding heat-induced aggregation with proteins and their retention (Mestawet et al., 2024). This approach is expected to increase protein permeation, which is the primary objective of microfiltering pretreated whey (Julian, 2019). Additional research is needed to address the effectiveness of this proposed process. Indeed, if demonstrated to be effective, scaling these techniques to industrial levels will still pose significant challenges, including substantial restructuring of existing processing plants.

The limitations of conventional pasteurization heat treatment necessitate the exploration of emerging thermal treatment methods such as microwave and radio frequency heating. As discussed by Hu et al. (2024), these methods offer the advantage of minimizing protein structural changes. However, they also come with challenges: microwave heating can cause uneven heat distribution, affecting food processing uniformity, while radio frequency heating requires careful control to prevent excessive heat that could degrade food quality. Therefore, further research is essential to optimize these methods and ensure consistent results. Additionally, investigating alternative non-thermal technologies (Bevilacqua et al., 2019; Mestawet et al., 2024; Munir et al., 2019) is important. Understanding how these methods impact microbiological quality, protein denaturation, aggregation, and overall protein retention in MFR will be crucial for improving the quality and functionality of dairy products.

7. Conclusion and outlook

There is growing evidence and awareness regarding the valuable components in MFR, prompting the dairy industry to diversify its production methods. This shift is driven by an increased focus on healthy nutrition, active lifestyles, and sustainable environmental practices. This

review has highlighted the composition of MFR, its increasing production, and its significant potential for applications across various fields. Microfiltration retentate is a rich source of MFGM components, including PLs and MFGM-associated proteins and whey proteins, all of which possess important bioactivities. The review also examines various process options, opportunities, gaps, and challenges associated with MFR. These include exploring innovative membrane technologies for selective enrichment and addressing the current lack of standardized methods for MFR production and analysis. Opportunities lie in the development of functional foods and nutraceuticals, while significant challenges remain in optimizing extraction methods and ensuring product safety and quality. Understanding the microbiological quality and the mineral and vitamin profiles of MFR are critical research areas that need to be addressed. Looking forward, the outlook for MFR is promising, with potential applications in extracting novel bioactive compounds and developing functional vehicles for delivering essential nutrients. To fully realize this potential, continued research and development are essential. This will ensure that MFR can be effectively utilized in both food and non-food applications. Collaborative efforts between industry and academia will be crucial in driving innovation, addressing existing challenges, and expanding the applications of MFR in new and diverse markets.

Data availability

Data will be made available on request.

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