

Review

Membrane-Based Fractionation of Milk Proteins for the Production of High Value Dairy Ingredients—A Systematic Review

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Abstract

Membrane-based processes have emerged as efficient alternatives to conventional separation methods because they enable protein fractionation under mild processing conditions while preserving protein functionality and bioactivity. Furthermore, whey, traditionally regarded as a by-product of cheese manufacture, is now recognized as a valuable source of proteins and bioactive compounds that can be recovered and valorized through membrane processing. Despite this, the literature on protein fractionation processes based on membrane technologies remains limited across different membrane technologies and operational scales. This systematic review evaluates microfiltration (MF), ultrafiltration (UF), nanofiltration (NF), and reverse osmosis (RO) in the context of milk protein fractionation, with a focus on industrial relevance, process limitations, and the resulting high-value protein fractions. Unlike previous narrative reviews, the study integrates comparative performance metrics, including pressure, protein recovery, purity, process limitations, and resulting products. Following the PRISMA guidelines for the selection and assessment of eligibility for a systematic review, 55 studies were included in the final qualitative synthesis. The analysis shows that UF consistently achieves high protein recovery (>90%) and represents the dominant industrial technology for the production of whey protein concentrates and isolates, although its efficiency is limited by concentration polarization and flow rate drop at elevated volumetric concentration factors. Consequently, future research should prioritize integrated performance reporting, quantitative measurement, and integration of sustainability indicators to enable more robust industrial application of membrane-based dairy technologies. Moreover, more reporting bases on standardized industrial performance indicators and commercial case studies are needed to support the wider adoption and optimization of membrane technologies in dairy processing.

Keywords: milk proteins; membrane fractionation; microfiltration; ultrafiltration; whey proteins; food-by products; dairy ingredients; diafiltration; systematic review



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1. Introduction

Milk proteins are among the most valuable constituents of milk due to their high nutritional quality, balanced amino acid composition, and broad range of functional properties. In addition to serving as a source of essential amino acids, they contribute significantly to texture formation, emulsification, water-holding capacity, and overall product stability [1].

Consequently, milk-derived protein ingredients have become components of infant formulas, sports nutrition products, clinical nutrition formulations, and functional foods [2,3]. The applicability of membrane technologies extends beyond dairy proteins, as membrane concentration has also been successfully employed for the recovery and concentration of bioactive compounds from plant-derived streams while preserving their functional properties [4]. The increasing demand for protein-enriched foods has stimulated interest in technologies capable of selectively isolating and concentrating specific milk protein fractions while preserving their native structure and functionality. Among the available separation technologies, membrane-based processes have emerged as particularly attractive due to their ability to operate under relatively mild conditions, minimizing thermal damage and preserving the biological activity of sensitive proteins [5,6]. Pressure-driven membrane processes, including MF, UF, NF, RO and DF are widely applied in the dairy industry for protein concentration, fractionation, demineralization, and valorization of dairy side streams. These technologies enable the selective separation of casein micelles and whey proteins, production of whey protein concentrates (WPC) and whey protein isolates (WPI), as well as recovery of bioactive protein fractions with enhanced nutritional and technological value. Compared with conventional thermal processing methods, membrane technologies offer improved energy efficiency, greater process flexibility, and better preservation of protein functionality [6]. Despite their widespread industrial implementation, membrane processes face several challenges that limit separation efficiency and long-term operational performance [5,6]. Membrane fouling, concentration polarization, and complex interactions between process parameters and feed composition frequently result in lower performance than predicted by theoretical models. Consequently, optimization of membrane configuration and operating conditions remains a critical area of research [7]. Although numerous studies have investigated individual membrane technologies and specific dairy applications, a comprehensive evaluation of membrane-based fractionation strategies for the production of high-value dairy ingredients remains limited [5–7]. In particular, there is a need to critically assess the relationships between membrane process selection, separation efficiency, protein recovery, product purity, and process sustainability. Therefore, the aim of this systematic review is to evaluate current membrane-based approaches for milk protein fractionation, summarize the main factors influencing process performance, and assess their contribution to the production of high-value dairy ingredients and the sustainable valorization of dairy side streams.

2. Materials and Methods

The study selection process followed the PRISMA 2020 guidelines and consisted of four phases: identification, screening, eligibility assessment, and inclusion. A systematic search of the scientific literature was conducted in the *Scopus*, *Web of Science*, *Science Direct*, *Pub Med*, and *Google Scholar* databases. The search strategy focused on studies investigating membrane technologies for milk protein fractionation and the production of high-value dairy ingredients. The initial search identified a total of 762 records, distributed as follows (Figure 1). Following the eligibility assessment, 55 studies met all inclusion criteria and were included in the qualitative synthesis. These studies formed the basis for the analysis of milk protein composition and functionality, membrane separation technologies, microfiltration of casein micelles, ultrafiltration and diafiltration of whey proteins, selective isolation of α -lactalbumin and β -lactoglobulin, production of whey protein concentrates (WPC), production of whey protein isolates (WPI), generation of bioactive peptides, technological limitations and future developments of membrane-based dairy processing. Overall, the final dataset consisted of 55 peer-reviewed studies, which were systematically analyzed and synthesized within this review.

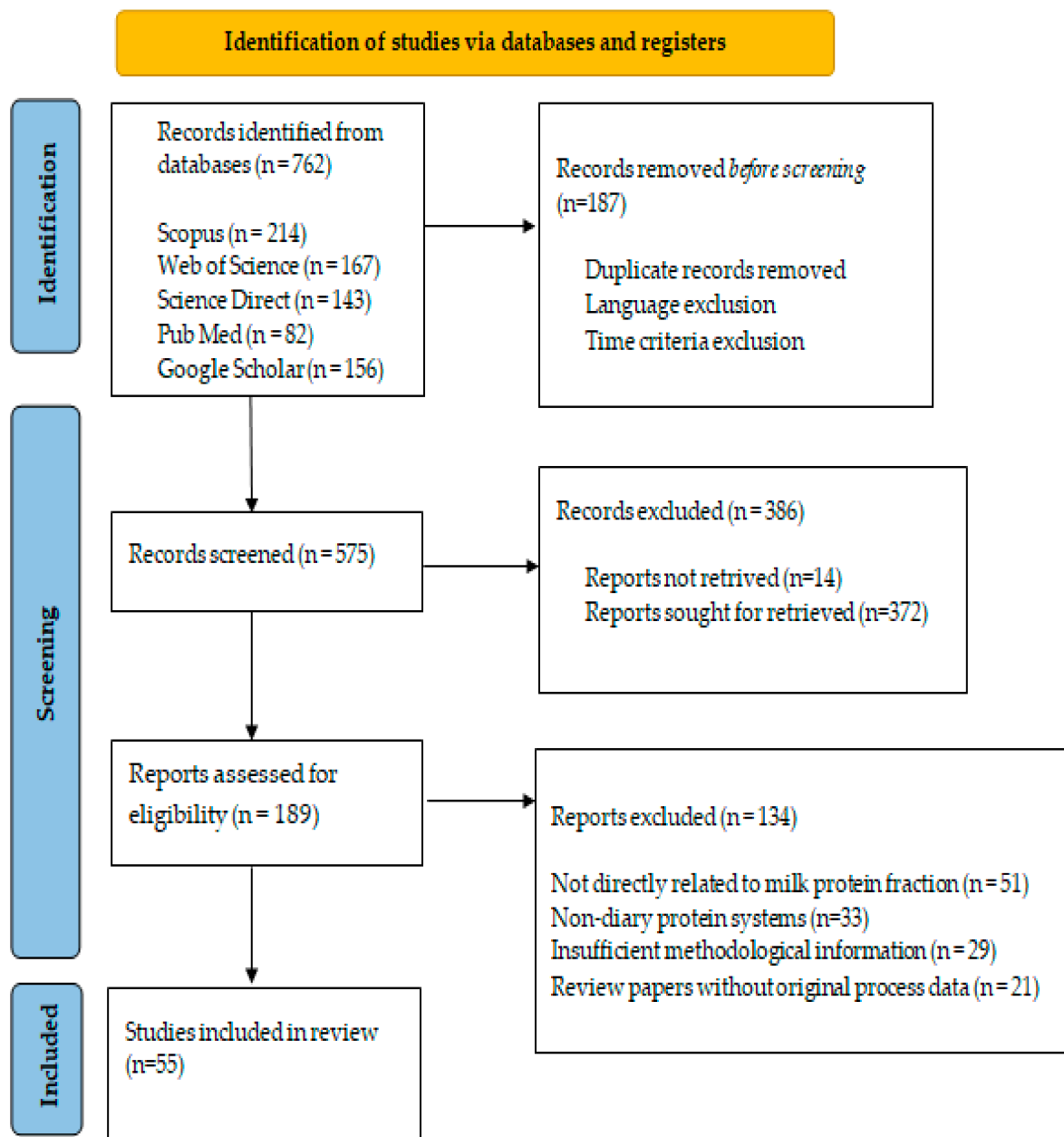


Figure 1. Utilization of the PRISMA flow diagram for conducting database searches and elucidating accessible articles for review.

2.1. Review Design

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The review aimed to identify, critically evaluate, and synthesize the available scientific evidence concerning membrane-based fractionation of milk proteins and its application in the production of high-value dairy ingredients. Particular emphasis was placed on the use of pressure-driven membrane technologies, including MF, UF, NF, RO and DF for the selective separation of casein micelles, whey proteins, and derived functional dairy ingredients. These technologies were selected because they provide efficient and selective fractionation of milk proteins while maintaining their functional and nutritional properties. Due to high heterogeneity in membrane configurations, operating conditions, feed composition, and reporting metrics, statistical pooling (meta-analysis) was not feasible.

2.2. Literature Search Strategy

A comprehensive literature search was performed using the *Scopus*, *Web of Science Core Collection*, *ScienceDirect*, *PubMed*, and *Google Scholar* databases. The search covered the period from 2000 to March 2026, thereby encompassing both foundational studies and recent technological developments in membrane-based dairy processing. The search strategy was designed to maximize sensitivity while maintaining relevance to the research objective. The following Boolean search expression was employed and adapted to the syntax requirements of individual databases: (“milk protein*” OR casein OR “whey protein*” OR “milk-derived protein*”) AND (“microfiltration” OR “ultrafiltration” OR “nanofiltration” OR “reverse osmosis” OR diafiltration OR membrane*) AND (fractionation OR separation OR concentration OR purification OR isolation). To minimize publication omission, manual searches of reference lists from relevant review articles and primary research papers were additionally conducted. Duplicate records were removed prior to the screening process.

2.3. Eligibility Criteria

Studies were considered eligible for inclusion if they fulfilled all of the following criteria: (i) investigated membrane-based processing of milk, whey, or dairy-derived streams; (ii) evaluated the fractionation, concentration, purification, or selective isolation of milk proteins; (iii) examined the performance of MF, UF, NF, RO, DF, or integrated membrane systems; (iv) reported experimental, pilot-scale, or industrial-scale data; (v) assessed process performance, protein recovery, fraction purity, membrane selectivity, or functional properties of the obtained ingredients; and (vi) were published as full-text articles in peer-reviewed scientific journals. Studies were excluded when they: (i) focused exclusively on non-dairy protein systems; (ii) investigated non-membrane separation technologies without integration of membrane processes; (iii) consisted solely of conference abstracts, editorials, patents, technical reports, or book chapters; (iv) lacked sufficient methodological detail to permit critical evaluation; or (v) were unavailable in full text.

2.4. Study Selection Process

Following database searching and duplicate removal, all records underwent screening procedure. Initially, a database of 762 scientific papers was collected. Before starting the search, articles outside the scope of this study, based on their year of publication and duplicate records ($n = 187$) were removed. From the remaining articles ($n = 575$) studies not relevant to the systematic review title ($n = 372$), inaccessible articles ($n = 14$), not directly related to milk fraction ($n = 51$), non-dairy protein systems ($n = 33$), insufficient methodological information ($n = 29$), review papers without main process data ($n = 21$) were excluded. Ultimately, 55 scientific papers were analyzed in this study. Discrepancies arising during the study selection process were resolved through repeated evaluation of each article’s objectives, methodology, and reported outcomes until a consensus was reached between the reviewers. The entire selection procedure is illustrated in the PRISMA flow diagram (Figure 1), which provides an overview of the identification, screening, eligibility assessment, and final inclusion of studies.

2.5. Data Extraction

A structured data extraction framework was developed to ensure consistency across studies. The following information was extracted from each eligible publication: author(s) and year of publication; dairy matrix investigated (milk, whey, skim milk, retentate, permeate); membrane technology applied; membrane material and pore size or molecular weight cut-off; operating conditions (temperature, transmembrane pressure, cross-flow velocity, pH); protein recovery and transmission rates; degree of protein purification; production

of specific dairy ingredients; reported technological limitations; major conclusions and industrial implications. Extracted information was synthesized qualitatively because of the considerable heterogeneity observed in experimental designs, membrane configurations, operating conditions, and reported performance indicators.

3. Results and Discussion

Table 1 summarizes the key studies included in the qualitative synthesis of this systematic review, selected according to the PRISMA 2020 methodology. The table provides an overview of the principal research themes, membrane technologies, feed streams, and processing objectives investigated across the literature. Specifically, it highlights the application of pressure-driven membrane processes, including MF, UF, DF, NF and RO, for the fractionation, concentration, and purification of milk proteins. The included studies encompass a wide range of dairy streams, primarily skim milk and cheese whey, and address the production of high-value dairy ingredients such as micellar casein concentrates (MCC), milk protein concentrates (MPC), WPC, WPI, and selectively enriched protein fractions. In addition to conventional membrane processing, the literature also covers topics related to membrane fouling, process optimization, membrane material development, sustainability, by-product valorization, and emerging technologies. This shift reflects the growing emphasis on obtaining specific milk proteins with high biological and commercial value rather than simply increasing the overall protein concentration. Recent advances in membrane technologies have enabled the selective separation of individual whey proteins, particularly β -lactoglobulin and α -lactalbumin, while preserving their native structure and functionality [6]. These proteins are increasingly sought after because of their distinct functional properties and applications in functional foods and pharmaceutical formulations. As a result, modern membrane processes are increasingly designed to recover targeted bioactive protein fractions with higher purity and added value instead of producing conventional protein concentrates alone. For clarity and conciseness, only the key studies most relevant to membrane-based milk protein fractionation are presented in Table 1. A complete overview of all 55 studies included in the systematic review, together with their characteristics and research focus, is provided in Supplementary Table S1.

Table 1. Key studies included in the qualitative synthesis.

Study	Year	Membrane Process	Feed Stream	Main Objective
Aguero et al. [7]	2017	UF/Membrane review	Whey	Whey protein separation and purification
Ahmadi et al. [8]	2024	ON	Milk	Casein micelle structure and stability
Anand et al. [9]	2014	MF/UF systems	Dairy streams	Membrane biofilm control
Arunkumar and Etzel [10]	2018	UF	Skim milk	Milk protein concentration
Bazinet and Doyen [11]	2017	Membrane processes	Food streams	Recovery of bioactive compounds
Bildyukevich et al. [12]	2020	UF	Skim milk	Membrane fouling mechanisms
Blais et al. [13]	2022	MF/UF/NF	Milk and whey	Multistage membrane fractionation
Brans et al. [14]	2004	MF/UF	Milk	Milk protein fractionation challenges
Caballero et al. [15]	2021	Integrated membrane systems	Whey	Whey valorization
Cunha et al. [16]	2022	Membrane processing	Dairy products	Theoretical membrane applications
Dobozi et al. [17]	2026	UF/DF	Whey	Separation efficiency monitoring

Table 1. Cont.

Study	Year	Membrane Process	Feed Stream	Main Objective
Du et al. [18]	2017	Pressure-driven membranes	Various feeds	Shear stress and fouling
Giles et al. [19]	2026	Membrane filtration	Whey	α -Lactalbumin recovery
Granger-Delacroix et al. [20]	2020	MF	Skim milk	Serum protein transfer
Karasu et al. [21]	2010	Ceramic vs. polymeric membranes	Milk	Casein concentrate production
Macedo et al. [22]	2021	Integrated membrane systems	Dairy by-products	Eco-efficiency improvement
Mardal et al. [23]	2024	MF + DF	Skim milk	Fouling and process performance
Puri et al. [24]	2020	UF	Skim milk	Temperature effects on membrane performance
Reig et al. [6]	2021	MF/UF/NF/RO	Milk and whey	Dairy membrane technologies overview
Toro-Sierra et al. [25]	2013	Membrane fractionation	Whey protein isolate	α -LA and β -LG separation
Wang et al. [26]	2024	Membrane purification	Whey	β -Lactoglobulin isolation
Wang, W.-Q. et al. [27]	2019	UF	Whey	Membrane processing and fouling mechanisms
Sukmana et al. [28]	2025	Various membrane techniques	Whey and buttermilk	Protein separation and valorization
Li et al. [29]	2020	Nanocomposite membranes	Various streams	Fouling-resistant membranes
Gavrilaş [30]	2025	Nanomembranes	Food systems	Advanced membrane materials
Zaidi et al. [31]	2025	AI-assisted systems	Food processing	Artificial intelligence applications

3.1. Milk Protein Fractions Relevant for Membrane Separation

Recent studies emphasize integrated membrane systems, advanced antifouling materials, and digital process monitoring to improve process efficiency while reducing water and energy consumption and maximizing the recovery of valuable dairy components [29–31]. The efficiency of membrane-based fractionation of milk proteins is primarily determined by the physicochemical differences between casein micelles and whey proteins. The functional properties of milk proteins, including water-binding, emulsifying, foaming, and gelling abilities, contribute significantly to their technological importance in food systems [32]. Variability in the physicochemical composition of milk can affect membrane processing performance, highlighting the importance of food characteristics in protein fractionation systems [33]. Variations in particle size, molecular structure, solubility, and electrical charge provide the basis for selective separation using pressurized membrane processes, but also determine which type of filtration to choose [8,34]. Caseins constitute approximately 80% of total milk proteins and are organized into colloidal micelles with diameters ranging from 20 to 300 nm [8,21]. Their relatively large particle size allows for efficient retention during MF, facilitating the production of micellar casein concentrates and casein-enriched dairy ingredients. The reviewed studies show that the structural stability of casein micelles is strongly influenced by calcium phosphate balance, pH, ionic strength and temperature, all of which directly affect membrane separation performance and product quality [8,35]. Whey proteins constitute approximately 20% of the total milk proteins and remain soluble under normal milk conditions. The dominant whey proteins, β -lactoglobulin and α -lactalbumin, together account for almost 70% of the whey protein fraction, but constitute an industrially valuable product [7]. Their significantly smaller molecular dimensions compared to casein micelles allow them to pass through microfiltration membranes and at the same time allow for efficient retention during the UF process [6]. This pronounced size

difference is the fundamental basis for membrane fractionation of milk proteins, as they are retained in the retentate during UF since their molecular weight is greater than the MWCO cutoff, while water, lactose, minerals and other low molecular weight components pass into the permeate. In addition to their nutritional value, whey proteins possess important functional and biological properties that have prompted the development of highly selective fractionation technologies. Several studies [7,36] included in this review highlight the growing industrial interest in obtaining purified α -lactalbumin and β -lactoglobulin fractions for their applications in infant formula, clinical nutrition, and specialized functional foods. In particular, advances in membrane-assisted fractionation have enabled the production of protein ingredients with improved purity while preserving their original functionality [25,36]. Taken together, the reviewed literature shows that successful fractionation of milk proteins depends not only on the characteristics of the membrane but also on the intrinsic physicochemical properties of the protein fractions being separated [8,25,36]. The significant differences between casein micelles and whey proteins provide a scientific basis for the widespread application of membrane technologies in the production of high-value dairy ingredients [6,34].

3.2. Comparative and Critical Performance Analysis of Membrane Technologies

The separation mechanisms governing MF, UF, NF and RO are based on differences in molecular size, charge and membrane selectivity, which constitute the fundamental principles of membrane technology described in [36]. Evaluation of membrane technologies shows that no single process is universally optimal for milk protein fractionation. Instead, each technology fulfills a specific functional role within an integrated processing framework [6,13,14,36]. Pressure-driven membrane processes form the technological basis of modern milk protein fractionation, and their separation efficiency is determined by differences in molecular size, charge, membrane selectivity, operating conditions and feed characteristics [36]. Membrane fouling is still an unavoidable obstacle in the application of pressure-driven membranes [18]. Although membrane classification is primarily based on pore size and MWCO, practical performance is strongly influenced by membrane configuration, process parameters, concentration polarization, membrane fouling and feed composition [6,14].

Among the available technologies, MF shows the highest selectivity for the separation of casein micelles from whey soluble proteins due to the significant size difference between these protein fractions [37]. Under optimized operating conditions, MF allows the production of micellar casein concentrate while preserving the original structure of whey proteins through minimal thermal exposure. Reported whey protein transmission generally ranges between 70% and 95%, with further improvements achieved by integrating DF into the process [6,14]. However, membrane fouling, protein aggregation and thermal pretreatment remain major factors limiting the separation efficiency [21], which is reflected in the increased costs, also limiting the use of MF/DF [14]. According to a study [37], MF has emerged as one of the most efficient technologies for the separation of casein micelles and whey proteins due to the significant difference in particle size between these fractions. By using membranes with a pore diameter of approximately 0.1 μm , casein micelles (50–500 nm) are retained in the retentate, while smaller whey proteins (3–6 nm), together with lactose and minerals, pass through the membrane [37]. This process allows the production of MCC and original whey protein fractions directly from milk. Reviewed studies show that the separation efficiency is strongly influenced by the operating conditions, in particular temperature, cross-flow rate and membrane configuration [6,14,37]. Higher temperatures and increased cross-flow rates generally improve the transfer of whey proteins and increase the purity of the casein-rich retentate [14]. Under optimized conditions, whey

protein transfer typically ranges from 70% to 80%, while integration with DF can increase the transfer efficiency to approximately 95% [20,23]. Despite the high selectivity, the performance of MF can be compromised by heat treatment and changes in the protein–mineral balance [23]. High pasteurization temperatures ($>78^{\circ}\text{C}$) promote denaturation of whey proteins and interactions between denatured whey proteins and casein mycelia, reducing membrane selectivity and casein purity. Conversely, processing at low temperatures can cause partial dissociation of β -casein from the micellar structure, changing the composition of the fraction and affecting the process performance [38]. The industrial application of MF provides several technological advantages, especially in cheese production, where increased casein concentration improves cheese yield, reduces rennet consumption, and improves process control [28]. In addition, MF permeate represents a valuable source of natural whey proteins with preserved functionality. However, challenges related to membrane fouling, process optimization, and handling of highly concentrated micellar casein systems remain important limitations for large-scale implementation [38,39]. The reviewed literature identifies MF as the preferred technology for casein and whey protein fractionation due to its superior selectivity and ability to preserve protein functionality, but also tends toward MF/DF integration. However, successful industrial application requires careful control of heat treatment and operating conditions to maximize protein recovery and product quality.

UF is the most widely used membrane process in the dairy industry and is the industry standard for whey protein concentration and purification [6]. Unlike MF, which primarily performs fractionation, UF selectively concentrates proteins while allowing lactose and minerals to pass through the membrane. Reviewed studies consistently report protein recoveries of greater than 85%, while UF combined with DF often achieves protein purities above 90%, allowing for the efficient production of whey protein concentrates and isolates [10,26]. However, increasing retentate viscosity and concentration polarization progressively reduce permeate flux at high concentration factors. Despite this, UF is the dominant membrane technology for whey protein concentration and fractionation in the dairy industry. UF systems account for the largest share of the membrane market (35%), followed by the MF process (33%) and the least represented integrated NF/RO system (30%) [6]. Compared to conventional thermal evaporation, UF offers the major advantage of avoiding extensive heat treatment, thus preserving the nutritional and functional properties of thermolabile whey proteins [40]. However, although UF remains the industry standard, its limited ability to achieve extremely high protein purity demonstrates the need for integration with additional purification techniques. The principle of UF is based on the selective permeability of membranes. Membranes with defined molecular weight cutoffs retain proteins in the retentate, while allowing lactose, minerals and water to pass through. Consequently, UF changes the composition of the whey streams and increases the protein concentration within the retentate fraction. UF systems can operate in recirculation or concentration mode. During concentration processing, the reduction in the volume of the feed mixture is quantified by the volumetric concentration factor (VCF), defined as the ratio between the initial volume of the feed mixture and the final volume of the retentate. Increasing the VCF increases the protein concentration, but at the same time reduces the permeate flux due to increased viscosity, osmotic pressure, concentration polarization and membrane fouling [41]. Experimental studies show a continuous accumulation of proteins in the retentate during UF, while lactose and minerals are progressively reduced due to membrane permeation [38]. However, UF alone cannot completely remove low molecular weight compounds, and residual lactose and minerals remain present in the final concentrate, which is a drawback of this type of filtration and requires an integrated approach [6]. Furthermore, long-term system operation enhances fouling phenomena,

reducing process efficiency and requiring continuous optimization of operating conditions. Despite these limitations, UF remains an essential technology for WPC production because it allows high protein utilization while maintaining biological functionality. Its selectivity, energy efficiency and operational flexibility make UF a standard technology in modern whey processing [40].

DF involves the addition of water or alternative washing media into the retentate stream to remove low-molecular-weight compounds such as lactose and mineral salts. This technique is essential for the production of WPI containing more than 90% protein. The reviewed literature indicates that DF significantly improves whey protein transmission and overall purification efficiency. Various DF media may be used, including water, dairy by-products, or ultrafiltration permeate (UFP). However, the composition of the diafiltration medium strongly influences membrane fouling and permeate flux behavior. Studies show that the use of UFP or calcium-containing media decreases permeate flux compared to mineral-free water, regardless of whether ceramic or polymeric membranes are applied. In contrast, water-based DF increases permeate flux because lower mineral concentrations enhance electrostatic repulsion between proteins and alter cake layer structure [23]. Integration of UF and DF improves removal of lactose and minerals while increasing protein concentration within the retentate [6]. Addition of solvent reduces viscosity and osmotic pressure, stabilizing process conditions and improving permeate flow. The largest increase in flux is generally observed during the initial stages of DF, while later stages depend strongly on membrane fouling characteristics and pore blockage behavior. MWCO defines the molecular size at which approximately 90% of molecules are retained by the membrane. Membranes with lower MWCO values provide higher protein retention but may reduce purification efficiency, whereas larger MWCO values facilitate lactose removal at the expense of increased protein losses before process stabilization. Therefore, optimization of MWCO is essential for balancing protein recovery, purity, and process efficiency [17]. Although DF substantially increases protein purity, it also increases water consumption and generates additional wastewater streams, raising important sustainability concerns regarding long-term industrial application. Table 2 summarizes representative studies published between 2018 and 2026 investigating membrane-based fractionation of milk proteins. The available evidence demonstrates that UF and DF consistently achieve protein recovery values above 90%, making these technologies the preferred industrial approaches for the production of whey protein concentrates and isolates [6]. MF exhibits superior selectivity for casein micelle separation and native whey protein recovery, whereas NF and RO primarily serve as complementary technologies for demineralization and concentration. The reviewed studies additionally highlight the strong influence of operating conditions on process performance. Recovery, purity, and permeate flux vary considerably depending on membrane material, molecular weight cut-off, transmembrane pressure, temperature, and feed composition. Consequently, optimization of membrane configuration and process parameters remains essential for maximizing separation efficiency [6,17].

NF and RO primarily serve complementary functions within integrated membrane systems rather than acting as primary protein fractionation techniques [6,13]. NF is mainly applied for lactose concentration and partial demineralization of whey streams through the selective removal of monovalent ions, thereby improving the quality of dairy ingredients intended for infant formula and specialized nutritional products. In contrast, RO is predominantly employed as a pre-concentration process, efficiently removing water while retaining proteins, lactose, and minerals, thereby substantially reducing the energy demand of downstream evaporation. Nevertheless, increasing osmotic pressure at elevated solids concentrations limits RO productivity [6].

Table 2. Representative studies on membrane-based milk protein fractionation published between 2018 and 2026.

Study	Membrane Process	Feed Stream	Main Product	Protein Recovery (%)	Protein Purity (%)	Permeate Flux (L m ^{−2} h ^{−1})
Arunkumar and Etzel (2018) [10]	UF + DF (100 kDa charged membrane)	Skim milk	MPC	>95	75–85	80–150
Wang et al. (2019) [26]	UF/DF Review	Cheese whey	WPC	85–95	35–80	20–120
Granger-Delacroix et al. (2020) [20]	0.1 µm MF	Skim milk	Native Whey Proteins	70–95 transmission	80–90	50–150
Puri et al. (2020) [24]	UF	Skim milk	Protein-rich Retentate	>90	70–85	15–90
Reig et al. (2021) [6]	MF, UF, NF, RO	Milk and Whey	Various Dairy Ingredients	80–95	60–95	20–200
Mardal et al. (2024) [23]	MF + DF	Skim milk	Micellar Casein Concentrate	85–95	80–95	40–120
Wang et al. (2024) [36]	Selective Membrane Fractionation	Whey Protein Isolate	β-Lactoglobulin Fraction	60–90	80–95	10–80
Ramanamane (2022) [42]	Integrated Membrane Systems	Whey and Buttermilk	High-Value Protein Fractions	80–95	75–95	20–150

MF—microfiltration; UF—ultrafiltration; DF—diafiltration; NF—nanofiltration; RO—reverse osmosis; MPC—milk protein concentrate; WPC—whey protein concentrate.

A consistent finding in the reviewed studies is that integrated membrane systems combining MF, UF, DF, NF, and RO show better results than single-stage membrane operation [6,13]. Process integration simultaneously improves protein recovery, enhances product purity, increases overall process efficiency, and enables more effective valorization of dairy side streams while mitigating the individual limitations of each membrane technology [23]. Consequently, current evidence suggests that future industrial development will increasingly focus on multistage membrane configurations rather than on further optimization of individual membrane processes alone. This trend is additionally supported by sustainability assessments demonstrating that integrated membrane systems can reduce energy and water consumption while improving the overall eco-efficiency of dairy processing [43]. Overall, the reviewed literature indicates that MF provides the greatest selectivity for casein–whey protein separation, UF coupled with DF delivers the highest protein recovery and purity, whereas NF and RO primarily enhance process economics through concentration and demineralization. Therefore, integrated membrane processing currently represents an effective technological strategy for producing high-value dairy protein ingredients while simultaneously improving process sustainability and resource utilization [6]. Table 3 summarizes benchmarking of different technologies reviewed and also highlights the principal membrane materials used in the fractionation of milk proteins.

Table 3. Overview of different membrane fraction technologies more often used in the dairy industry. Adapted from [5,6].

Technology	Pore Size/MWCO	Membrane Material	Operating Pressure	Primary Dairy Applications	Main Advantages and Performance Metrics
MF	0.1–10 µm/>100 kDa	Ceramic membrane, 1.4 µm Standard and gradient ceramic membranes (0.14–0.8 µm)	Low pressure (below 2 bar) driven membrane process 0.1–2.0 bar	Fat fractionation, bacteria and spore removal, casein recovery	High selectivity for large particles; operates at low pressure; preserves the native state of proteins [37].
UF	1–100 nm/1–800 kDa	UF membrane (50 kDa MWCO)	Medium pressure driven process to overcome the viscosity 2–10 bar	Protein concentration (WPC/WPI), standardization of milk, mineral modification	Largest market share (35%); high productivity; efficient for converting whey into refined proteins [28]

Table 3. *Cont.*

Technology	Pore Size/MWCO	Membrane Material	Operating Pressure	Primary Dairy Applications	Main Advantages and Performance Metrics
NF	0.5–2 nm/150–1000 Yes	Polyamide spiral-wound membrane (NTR-7450-S2F; FILMTEC NF270)	Medium to high pressure mass transfer phenomena by size exclusion and electrostatic interactions 5–40 bar	Partial demineralization, lactose recovery, concentration	Simultaneous demineralization and concentration; low rejection for monovalent salts (NaCl) [37]
RO	No pores	Thin-film composite (TFC) polyamide membrane (spiral-wound configuration)	High pressure 30–100 bar	Pre-concentration of milk/whey, water recovery	Maximum solute retention; essential for water reuse; can concentrate up to 27% dry matter [5]

3.3. Influence of Process Parameters and Membrane Materials

The reviewed literature identifies operating conditions as main determinants of membrane separation performance. Although membrane pore size and molecular weight cut-off define theoretical selectivity, actual process efficiency is primarily governed by interactions among transmembrane pressure, temperature, pH, ionic strength, feed composition, and hydrodynamic conditions [6,22]. Consequently, membrane performance frequently deviates from theoretical predictions due to concentration polarization and membrane fouling. Among the investigated parameters, temperature exerts a particularly important influence on both permeate flux and protein stability. Increasing temperature reduces feed viscosity and enhances mass transfer, resulting in higher permeate flux. However, excessive temperatures may induce whey protein denaturation, mineral precipitation, and irreversible changes in protein functionality. Several studies identified temperatures around 50 °C as the optimal compromise between process productivity and preservation of protein bioactivity [24,29]. The reviewed studies further demonstrate that pH and ionic strength strongly influence protein-membrane interactions [35]. Changes in pH alter the electrical charge of both proteins and membrane surfaces, directly affecting protein aggregation, membrane selectivity, and fouling behavior. As the pH approaches the isoelectric point of casein, protein aggregation increases significantly, promoting membrane deposition and reducing filtration efficiency [35,44]. Similarly, elevated salt concentrations may increase viscosity and modify electrostatic interactions, further affecting process performance. Hydrodynamic conditions, particularly cross-flow velocity, play a central role in controlling concentration polarization and fouling layer formation. Increased cross-flow velocity generates greater shear stress at the membrane surface, reducing protein accumulation and improving mass transfer. However, these benefits must be balanced against higher energy requirements associated with increased pumping capacity [18]. Although transmembrane pressure is the primary driving force of membrane filtration, the reviewed studies indicate that increasing pressure does not always result in proportional increases in permeate flux. Beyond a critical threshold, compression of the fouling layer and partial pore blockage may limit productivity and accelerate flux decline [19,27]. This observation highlights the importance of process optimization based on critical flux concepts rather than simply maximizing operating pressure [18,19,27]. The membrane material also plays an important role in process performance and long-term operational stability. Polymeric membranes remain the dominant industrial option due to lower cost and operational flexibility, while ceramic membranes offer superior thermal resistance, chemical stability, and cleaning tolerance [21]. Recent studies have further demonstrated the potential of nanocomposite and surface-modified membranes to reduce protein adsorption and improve fouling resistance [30,45]. Ceramic membranes, particularly those composed of alumina (Al₂O₃), are predominantly employed in microfiltration owing to their excellent thermal, chemical, and mechanical stability, making them suitable for the selective separation of casein micelles, bacterial removal, whey defatting, and immunoglobulin recovery [6]. In contrast,

ultrafiltration primarily relies on polymeric membranes with specific MWCO values for the concentration and purification of whey proteins, including WPC and WPI. Polyamide spiral-wound nanofiltration membranes are mainly applied for whey demineralization and purification, allowing the selective removal of minerals while retaining valuable proteins and lactose. According to literature studies, membrane material selection is determined by the targeted separation mechanism, desired product characteristics, and process requirements, highlighting the complementary roles of ceramic and polymeric membranes in modern dairy protein fractionation [6,18,27]. More details on Regulatory aspects of EFSA related to nanocomposite membranes are covered in Section 3.7. Finally, the reviewed evidence suggests that membrane performance is more strongly determined by fouling control and process optimization than membrane characteristics alone [6,18,19,27]. Consequently, successful fractionation of milk proteins requires integrated management of operating conditions, membrane properties, and feed composition, rather than optimizing individual parameters separately.

3.4. Fractionation of Caseins and Whey Proteins

The food industry tends more and more towards greater use of by-products. The purpose of fractionation of membrane processing of dairy products is the selective fractionation of casein and whey protein [6,7,28]. The growing interest in whey protein fractionation is also related to the generation of bioactive peptides, as enzymatic hydrolysis of whey protein concentrate has been shown to produce peptides with angiotensin-converting enzyme (ACE) inhibitory activity and potential health benefits [46]. The reviewed studies show that the successful separation of proteins depends not only on the selectivity of the membrane, but also on the preservation of protein functionality and the control of physicochemical interactions that occur during processing [6,47]. The growing demand for purified whey protein fractions has also prompted the development of analytical methods for accurate protein quantification. Ref. [48] reported a biosensor-based immunoassay capable of rapid determination of β -lactoglobulin content in bovine milk. MF has emerged as the preferred technology for separating casein micelles from soluble whey proteins due to the significant difference in particle size between these fractions. Under optimized operating conditions, it allows the production of micellar casein concentrates while simultaneously extracting the original whey proteins with minimal thermal damage. Several studies have reported whey protein transfer values ranging from 70% to 95%, especially in the MF/DF combination [20,23]. However, the selectivity of the process can be significantly reduced by protein denaturation resulting from intensive heat treatment or changes in the mineral balance that affect the stability of casein micelles [8]. UF remains the dominant technology for whey protein concentration and purification. The literature reviewed consistently shows that UF systems achieve high protein recovery while maintaining the biological and functional properties of whey proteins [10,26]. The market for UF milk is continuously growing due to the increasing demand for high-protein products [6]. However, increasing protein concentration inevitably induces concentration polarization, viscosity increase, and membrane fouling, resulting in a progressive decrease in flux during operation. In addition to food applications, whey-derived proteins can also serve as functional biomaterials. Ref. [49] demonstrated the potential of whey protein-based edible films and coatings as active packaging materials to improve food preservation and microbial stability. Consequently, protein recovery is strongly dependent on operating conditions and membrane configuration. DF is often integrated with UF to enhance lactose and mineral removal and increase final protein purity. Reviewed studies show that UF/DF combinations routinely achieve protein purities greater than 90%, making them the preferred industrial approach for the production of whey protein isolates [17,23]. However, the increased water demand associated with

DF raises important sustainability considerations and highlights the need for improved management strategies. An important trend observed in the reviewed literature is the growing interest in the selective extraction of individual whey protein fractions, especially α -lactalbumin and β -lactoglobulin [36,42]. These proteins possess different nutritional and functional properties and are increasingly used in infant nutrition, clinical nutrition and specialized food formulations [7,36]. Several studies have shown that combining selective heat treatment with membrane filtration can significantly improve separation efficiency and product purity, although process optimization remains challenging due to the sensitivity of protein structure to temperature, pH, and ionic conditions [19,25]. Collectively, the reviewed evidence indicates that integrated membrane strategies consistently outperform single-phase processes in terms of protein separation, purity, and process flexibility. While MF provides superior selectivity for casein and whey separation, UF and DF remain the mainstays for protein concentration and purification (Table 2) [10,24,26].

Future developments are therefore likely to focus on hybrid membrane systems capable of maximizing selectivity while minimizing fouling, resource consumption, and processing costs [10,36,42]. Figure 2 summarizes the principal membrane fractionation pathways used for the recovery, concentration, and purification of milk protein fractions and illustrates the relationship between membrane operations and the resulting dairy ingredients.

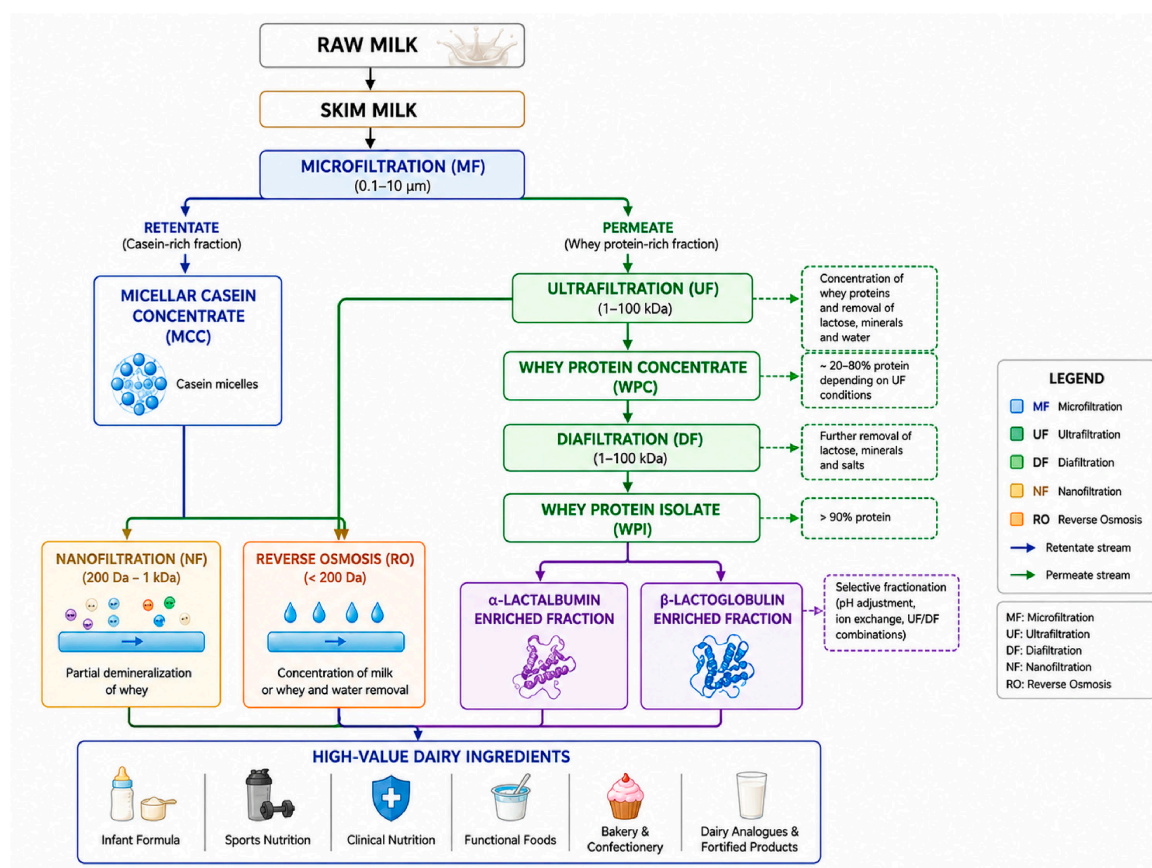


Figure 2. Integrated membrane processing scheme for milk protein fractionation and recovery of high-value dairy ingredients. Skim milk is first subjected to MF, producing MCC in the retentate and a whey protein-rich permeate. The permeate is subsequently processed by UF to obtain WPC, followed by DF to produce WPI. WPI can be further fractionated into α -lactalbumin- and β -lactoglobulin-enriched fractions. NF and RO are integrated for whey demineralization, concentration, and water removal, enabling the production of high-value dairy ingredients for applications in infant formula, sports nutrition, clinical nutrition, functional foods, bakery products, and dairy analogues. Adapted from Reig et al. (2021) [6].

3.5. Production of High-Value Dairy Ingredients

Selective isolation of α -lactalbumin and β -lactoglobulin has attracted increasing industrial and scientific interest because these proteins possess distinct nutritional and functional properties. Together, α -La and β -Lg account for approximately 70% of total whey proteins [50]. α -Lactalbumin is characterized by high tryptophan content and is associated with positive physiological effects related to serotonin synthesis, cognitive function, and psychological well-being. Due to the absence of free thiol groups, α -La exhibits relatively high thermal stability at neutral pH, making it suitable for applications where gel formation during heating is undesirable. In infant formula production, α -La is particularly valuable because it reduces allergenic potential and provides protein composition more similar to human milk [25]. In contrast, β -lactoglobulin possesses a free thiol group and pronounced amphiphilic properties that contribute to excellent emulsifying and foaming capacities. Partial denaturation further enhances its functionality, particularly regarding binding of flavor compounds and hydrophobic molecules [50]. Because of these differences, selective recovery of individual whey protein fractions represents a major technological objective. Although chromatographic methods provide high purity, their industrial applicability remains limited due to high costs and process complexity. Alternative industrial approaches rely on selective protein aggregation followed by centrifugation or membrane separation. One particularly effective strategy involves mild thermal treatment under acidic conditions (pH 3.0–4.6), where α -lactalbumin selectively precipitates while β -lactoglobulin remains soluble. Under these conditions, α -La transitions from its calcium-bound form to a calcium-free state, reducing stability and increasing aggregation tendency. Importantly, this process remains reversible because proteins may be resolubilized after cooling and pH readjustment. Current industrial development focuses on hybrid membrane systems combining MF, UF, and DF to achieve efficient separation and high-purity fractions. These integrated systems typically include selective thermal precipitation of α -La, aggregate growth, membrane separation of soluble β -Lg, purification stages, resolubilization of precipitated proteins, and final UF polishing steps. Optimization of transmembrane pressure and shear conditions is particularly important because these parameters strongly affect separation efficiency and the quality of final protein fractions [25]. WPC and WPI are among the most important high-value ingredients obtained through membrane fractionation of whey, a major by-product of cheese production. Significant advances in membrane processing technologies have enabled the development of protein ingredients with improved nutritional quality and tailored functional properties. WPC generally contains between 35% and 75% protein, whereas WPI contains more than 90% protein. Increasing protein concentration is accompanied by a reduction in lactose, mineral, and lipid content, making WPI a purer and more functionally specialized ingredient. The main whey proteins present in these products include β -lactoglobulin, α -lactalbumin, serum albumin, and immunoglobulins, whose relative proportions strongly influence the functional behavior of the final product [50]. Although whey proteins are widely recognized for their excellent nutritional and functional properties, their industrial application is often constrained by the balance between biological activity and technological stability. Processing conditions required for protein isolation, concentration, and purification may induce partial denaturation, aggregation, or conformational modifications, which can reduce bioactivity and alter functional performance. Consequently, current industrial processing strategies still face limitations in achieving highly specific functional ingredients while simultaneously preserving native protein structure and biological functionality.

3.5.1. Process-Dependent Variability of Composition and Functionality

The composition and functional characteristics of WPC and WPI products vary considerably depending on several technological factors, including the type of whey (sweet or acid whey), cheese-making conditions, pH, thermal treatment, enzymatic coagulation, whey pretreatment, membrane filtration parameters, and drying conditions. These variables directly affect protein composition, residual lactose and mineral content, lipid concentration, and the degree of protein denaturation [50]. Such variability significantly influences important techno-functional properties, including solubility, emulsifying capacity, foaming ability, gel formation, water-holding capacity, and thermal stability. Variations in protein structure and composition may therefore affect the applicability of whey protein ingredients in specialized food systems and medical or nutritional formulations. The literature suggests that insufficient process standardization remains one of the major limitations in the production of highly consistent whey protein ingredients with predictable functionality.

3.5.2. Bioactive Peptides Derived from Milk Proteins

Milk proteins represent important precursors of bioactive peptides generated through enzymatic hydrolysis or microbial fermentation. Depending on their amino acid composition and sequence, these peptides exhibit a wide range of biological activities, including antioxidant, antimicrobial, antihypertensive, immunomodulatory, and opioid effects [29]. Due to these properties, bioactive peptides have attracted increasing interest as functional ingredients and natural biopreservatives in food systems. Fermented milk products constitute a particularly important source of bioactive compounds. During fermentation, proteolytic activity of microorganisms leads to the release of peptides and other microbial metabolites into the soluble fraction of the product, while living microorganisms themselves may exert probiotic effects. Together, these components contribute to improved gastrointestinal health and enhanced nutritional value of fermented dairy products [51]. The integration of membrane technologies with enzymatic hydrolysis and fermentation processes therefore represents a promising approach for the production of next-generation functional dairy ingredients with potential applications in nutraceuticals, clinical nutrition, and health-oriented foods.

3.5.3. Application of Functional Dairy Proteins in the Food Industry

Functional dairy proteins obtained through membrane fractionation are widely applied in various sectors of the food industry due to their favorable nutritional, rheological, and techno-functional properties. Liquid whey protein concentrates (LWPC) can be directly incorporated into acidified gel systems such as yogurt and dairy desserts, eliminating the need for spray drying and reducing overall production costs. In meat products, WPC improves texture, water retention, and product stability, particularly in low-fat formulations such as sausages [52]. The functional performance of dairy protein systems is strongly influenced by gel microstructure and protein particle dimensions, which determine water-holding capacity, permeability, texture, and visual appearance [53]. These structural characteristics govern the retention of water and other components within the gel network and therefore directly affect product stability and quality. Rheological properties are particularly important because they influence processing behavior, storage stability, and sensory perception of dairy products. Parameters such as viscosity, syneresis, firmness, and color contribute significantly to consumer acceptance and perceived product quality. Consequently, understanding the rheological behavior of protein systems is essential for the development of dairy products with optimized texture, stability, and sensory characteristics [52]. Overall, the reviewed literature demonstrates that membrane-derived dairy proteins represent highly versatile functional ingredients with broad industrial applicability.

However, their optimal utilization continues to depend on precise control of processing conditions and improved standardization of membrane fractionation technologies.

3.6. Technological Challenges of Membrane-Based Milk Protein Fractionation

Despite the considerable technological progress achieved in membrane processing, several limitations continue to restrict the full industrial potential of milk protein fractionation. Membrane technology nevertheless represents one of the most promising approaches for the selective separation and concentration of milk components at an industrial scale. Certain membrane-based separation steps are already widely implemented in dairy processing, whereas others still require further technological and economic development. Increasing membrane process capacity and controlling membrane fouling remain crucial for achieving long-term process efficiency and industrial feasibility [14]. The literature consistently identifies membrane fouling and concentration polarization as the most significant challenges affecting process performance. Concentration polarization occurs when retained components accumulate near the membrane surface, creating a localized concentration gradient. This phenomenon reduces mass transfer rates and limits permeate flux even under increased TMP. Numerous studies indicate that concentration polarization frequently precedes membrane fouling and contributes to progressive declines in process efficiency [22]. Membrane fouling represents an even more significant obstacle in dairy membrane applications. The deposition of proteins, minerals, microbial cells, and colloidal particles on membrane surfaces increases hydraulic resistance and reduces membrane permeability. In dairy systems, protein fouling is particularly problematic due to the tendency of whey proteins to denature and aggregate under unfavorable processing conditions. Mineral fouling, primarily associated with calcium phosphate precipitation, further complicates long-term operation. Fouling should therefore not be regarded solely as an operational inconvenience, but rather as a fundamental limitation defining the performance boundaries of membrane systems [54]. The reviewed studies demonstrate that operating conditions strongly influence fouling intensity. Elevated temperatures improve permeate flux by reducing viscosity, but simultaneously increase the risk of protein denaturation and mineral precipitation. Similarly, excessive transmembrane pressures accelerate deposit formation and membrane pore blockage. Consequently, optimal process design requires balancing productivity, selectivity, and membrane stability. Operating parameters do not exhibit simple linear relationships, but rather complex synergistic and antagonistic interactions, making industrial optimization significantly more difficult [18,24]. Another challenge involves the limited selectivity of membrane systems under industrial conditions. Although theoretical separation is primarily determined by membrane pore size and MWCO values, actual performance is strongly influenced by physicochemical interactions among proteins, minerals, and membrane materials. As a result, the purity of isolated protein fractions often remains below theoretical expectations. In practice, selective fractionation is therefore determined not only by membrane characteristics, but also by feed composition, hydrodynamic conditions, temperature, ionic strength, and protein conformational stability during processing [17]. The economic impact of fouling is particularly significant in industrial dairy processing. Progressive flux decline reduces system productivity and prolongs processing time. For example, UF processes have shown approximately a 35% decrease in permeate flux during concentration, significantly extending processing time [55]. Additional operational costs arise from the need for higher TMP values and increased cross-flow velocity to maintain acceptable permeate fluxes, leading to greater energy consumption [6]. Furthermore, regular cleaning-in-place (CIP) procedures are necessary to restore membrane permeability, resulting in increased consumption of chemicals, water, and wastewater treatment resources. Time spent on cleaning and disinfection proce-

dures also represents non-productive operational downtime, reducing overall equipment utilization [22]. Irreversible fouling further shortens membrane lifespan and necessitates frequent membrane replacement, which constitutes a major maintenance expense. Fouling additionally affects membrane selectivity and may lead to the retention of undesirable compounds or loss of valuable proteins into the permeate stream, thereby reducing the purity and commercial value of products such as WPC and WPI [56,57]. Nevertheless, cost-benefit analyses indicate that membrane systems remain economically viable in small and medium-sized dairy plants despite fouling-related limitations, with estimated payback periods of approximately three years. However, process profitability remains highly sensitive to membrane fouling and process optimization. Inadequate pretreatment, insufficient fat removal or poorly optimized operational parameters may significantly compromise economic performance [6,58]. Another important limitation concerns DF processes. Although DF substantially improves protein purity by removing lactose and minerals, it simultaneously increases water consumption and generates additional process streams requiring treatment or valorization [59,60]. Consequently, sustainability concerns associated with water use and waste generation must be addressed in future industrial developments [23].

3.7. Regulatory and Safety Considerations for Nanocomposite Membranes

As mentioned earlier, development of nanocomposite and surface-modified membranes has expanded the potential of membrane technologies for dairy protein fractionation by improving permeability, selectivity, mechanical stability, fouling resistance, and antimicrobial properties [6]. However, the incorporation of nanomaterials into membranes intended for food processing requires rigorous safety assessment and compliance with international food-contact regulations before their commercial application. Within the European Union, all materials and articles intended to come into contact with food are regulated by Regulation (EC) No. 1935/2004, which establishes the general safety requirements for food-contact materials. According to this regulation, membrane materials must not transfer their constituents into food in quantities that could endanger human health, cause unacceptable changes in food composition, or adversely affect the organoleptic properties of food. These general requirements provide the regulatory framework for all membrane materials used in dairy processing [61]. For polymeric membranes, including those containing nanomaterials, Commission Regulation (EU) No. 10/2011 specifies that substances in nanoform require explicit authorization before they may be used in plastic food-contact materials. This regulation recognizes that nanomaterials may exhibit physicochemical properties that differ from those of their conventional counterparts and therefore require an independent safety evaluation [62]. To support regulatory decision-making, the European Food Safety Authority (EFSA) published the Guidance on Risk Assessment of Nanomaterials to be Applied in the Food and Feed Chain (2021). According to these guidelines, the safety assessment of nanomaterials should include comprehensive physicochemical characterization, including particle size distribution, morphology, surface chemistry, solubility, and dissolution behavior. In addition, EFSA recommends evaluating potential migration into food, consumer exposure, toxicokinetics, genotoxicity, repeated-dose toxicity, and other relevant toxicological endpoints [63]. Because the behavior of nanomaterials depends on both their chemical composition and nanoscale characteristics, each material should be assessed on a case-by-case basis rather than assuming equivalent safety to its conventional form. Similarly, the U.S. Food and Drug Administration (FDA) regulates food-contact substances through the Food Contact Substances Program, which requires manufacturers to demonstrate that the incorporation of nanotechnology does not alter the safety or regulatory status of materials intended for food-contact applications. The FDA also recommends that manufacturers evaluate whether nanoscale modifications influence

material properties, migration behavior, or consumer exposure. One of the principal safety concerns associated with nanocomposite membranes is the potential migration of engineered nanoparticles from the membrane matrix into food products during processing. Although currently available studies generally indicate minimal nanoparticle migration under normal operating conditions, the available evidence remains limited for long-term industrial operation and repeated cleaning and sanitation cycles.

3.8. Research Gaps and Future Research Priorities

Although membrane technologies have achieved widespread industrial implementation, several important scientific and technological challenges remain unresolved. First, the majority of published studies have been conducted on a laboratory or pilot scale. Relatively few investigations have evaluated long-term industrial operation under commercial processing conditions. Consequently, there is limited knowledge regarding membrane performance, fouling behavior, and economic feasibility over extended operating periods. Second, current membrane systems still exhibit limited selectivity for the isolation of individual whey protein fractions. The separation of α -lactalbumin, β -lactoglobulin, lactoferrin, and immunoglobulins frequently requires integration of membrane filtration with thermal treatment, pH adjustment, or chromatographic techniques. Development of highly selective membranes remains a major research priority [64,65]. Third, membrane fouling continues to represent the most significant obstacle to process efficiency. Future research should focus on advanced antifouling membrane materials, surface modifications, dynamic filtration systems, and real-time monitoring technologies capable of predicting fouling development before substantial performance losses occur. Fourth, the application of artificial intelligence, machine learning, and digital twins in membrane process optimization remains largely unexplored. Data-driven models could significantly improve process control, optimize operational parameters, reduce energy consumption, and increase membrane lifespan. Finally, sustainability challenges associated with water consumption during DF and wastewater generation require additional investigation. Overall, future progress in membrane-based milk protein fractionation will depend on the successful integration of advanced membrane materials, hybrid processing systems, digital process control technologies, and sustainable manufacturing concepts.

4. Conclusions

Membrane-based fractionation has become a novel technology in modern dairy processing, enabling the selective separation, concentration, and purification of milk proteins while preserving their nutritional and functional properties. The reviewed literature demonstrates that microfiltration (MF), ultrafiltration (UF), nanofiltration (NF), reverse osmosis (RO), and diafiltration (DF) are effective tools for producing high-value dairy ingredients, including micellar casein concentrates, whey protein concentrates, whey protein isolates, and bioactive protein fractions. Among these technologies, UF and DF remain the most widely applied for protein concentration and purification, while MF is particularly suitable for the recovery of native whey proteins and micellar casein. Despite these advantages, membrane fouling, concentration polarization, and flux decline continue to limit process efficiency, emphasizing the need for optimized operating conditions, appropriate feed pretreatment, and improved membrane materials. Although membrane technologies are well established in industrial dairy processing, publicly available data on long-term membrane performance, operating costs, and membrane lifespan remain limited. In addition, the development of novel membrane materials should be accompanied by appropriate safety assessment and compliance with food-contact regulations. Further research should focus on industrial-scale validation, techno-economic feasibility, and environmental sustainability

to facilitate broader commercial implementation. Overall, membrane-based fractionation represents a versatile and sustainable platform for the production of next-generation dairy ingredients and is expected to play an increasingly important role in meeting the growing demand for high-quality protein products.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/pr14142335/s1>, Table S1: Detailed overview of the 55 studies included in the qualitative synthesis, including research focus, principal findings, and their contribution to the review.

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Abbreviations

The following abbreviations are used in this manuscript:

ACE	Angiotensin-Converting Enzyme
AI	Artificial Intelligence
CC BY	Creative Commons Attribution
CHIP	Cleaning-In-Place
DF	Diafiltration
LWPC	Liquid Whey Protein Concentrate
MCC	Micellar Casein Concentrate
MF	Microfiltration
MPC	Milk Protein Concentrate
MWCO	Molecular Weight Cut-Off
ON	Not Available/Not Applicable
NF	Nanofiltration
PRISM	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RO	Reverse Osmosis
TMP	Transmembrane Pressure
UF	Ultrafiltration
UFP	Ultrafiltration Permeate
VCF	Volumetric Concentration Factor
WPC	Whey Protein Concentrate
WPI	Whey Protein Isolate
α -La	Alpha-Lactalbumin
β -Lg	Beta-Lactoglobulin

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