ES Food and Agroforestry
DOI: https://dx.doi.org/10.30919/faf1854

Equine Milk Lactoferrin: Current Evidence and Future Prospects in Medicine and Nutraceuticals

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Abstract

The rising demand for functional foods has increased interest in milk-derived bioactive proteins, particularly whey proteins and their peptides, which contribute to nutrition, immunity, and disease prevention. Lactoferrin (LF), an iron-binding glycoprotein, is one of the most studied milk proteins due to its antimicrobial, antiviral, antioxidant, and immunomodulatory functions. While bovine and human lactoferrin have been extensively investigated and applied in pharmaceuticals and nutraceuticals, equine milk lactoferrin (eLF) remains underexplored despite its distinctive advantages. Equine milk, which closely resembles human breast milk, is rich in whey proteins and contains higher concentrations of lactoferrin, offering enhanced digestibility and hypoallergenicity. Recent studies suggest that enzymatic hydrolysis of eLF generates bioactive peptides with antibacterial, antiviral, antihypertensive, and anti-inflammatory activities, making it a promising source of functional ingredients. Nevertheless, research on eLF is limited by insufficient characterization of its molecular mechanisms, lack of comparative studies with bovine and human LF, and poor understanding of its peptide-derived activities. Moreover, clinical evidence on safety, bioavailability, and long-term efficacy is scarce, restricting its broader application in therapeutic and nutritional products. This review synthesizes current knowledge on the structure, biological activities, and mechanisms of equine lactoferrin while highlighting its potential in antimicrobial defense, oxidative stress regulation, and functional nutrition. By identifying existing knowledge gaps and proposing future research priorities, this work positions eLF as a promising bioactive protein for next-generation pharmaceuticals, nutraceuticals, and functional foods.

Keywords: Equine milk; Lactoferrin; Biologically active peptides; Functional foods.
Received: 21 September 2025; Revised: 30 October 2025; Accepted: 03 November 2025
Article type: Review article.

1. Introduction

The development of functional foods enriched with bioactive ingredients has become one of the most dynamic and promising directions in the modern food and health industries. Rising concerns over antibiotic residues in food products and their associated public health risks have intensified interest in natural alternatives.[1] In this context, milk and its protein fractions have gained particular attention as versatile raw materials for functional food design. Milk, long valued as a fundamental nutritional resource, represents a particularly rich source of biofunctional molecules. Within its complex matrix, whey proteins such as α-lactalbumin, lactoferrin, lysozyme, and immunoglobulins have been identified as powerful agents capable of exerting antimicrobial, immunomodulatory, antiviral, and antioxidant activities, inspiring their incorporation into pharmaceuticals, nutraceuticals, a nd functional food products.[2,3]

Among these proteins, lactoferrin has attracted special attention as a multifunctional cationic glycoprotein belonging to the transferrin family. Structurally, it is an 80-kDa iron-binding protein composed of two homologous lobes, each capable of binding a ferric ion, a feature that underlies its ability to regulate iron homeostasis and to inhibit microbial growth through sequestration of essential nutrients. Beyond this, lactoferrin demonstrates direct bactericidal activity by interacting with microbial membranes, modulates immune responses through cytokine regulation, and provides protection against oxidative stress.[4-7] Its pleiotropic functionality has secured its place in infant formulas, therapeutic formulations, and dietary supplements. While bovine lactoferrin has been the primary subject of research and commercial development, there is growing recognition that lactoferrin derived from other species may offer unique and

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complementary benefits.[8,9]

Equine milk lactoferrin is a particularly compelling candidate in this regard. Equine milk, unlike bovine milk, is classified as albumin-type milk and shares greater compositional similarity with human breast milk.[10] This resemblance arises from its lower casein content and higher proportion of whey proteins, with whey constituting approximately 45% of total protein compared to only 20–22% in bovine and ovine milk.[11] Within this whey fraction, lactoferrin is present at concentrations ranging from 0.2 to 2 g/kg, levels up to ten times higher than those found in cow's milk.[12,13] Such elevated concentrations suggest that equine milk may be a uniquely rich reservoir of bioactive proteins capable of conferring health benefits distinct from or superior to those of ruminant milks. Moreover, the high lactose content and relatively low-fat composition of equine milk contributes to its digestibility and favourable metabolic profile, features that further enhance its suitability as a functional food matrix.[14]

Traditional knowledge has long recognized the nutritional and therapeutic qualities of equine milk. In Central Asia, particularly in Kazakhstan, Mongolia, Kyrgyzstan, and Uzbekistan, equine milk is consumed fresh or in fermented forms such as *kumis*, where it is valued for its restorative and immunostimulatory properties.[15,16] Ethnopharmacological observations attribute benefits in digestion, detoxification, and immune support to its consumption, though such claims remain largely anecdotal in the absence of rigorous scientific validation. Contemporary biochemical analyses confirm that equine milk is rich in bioactive whey proteins, including lactoferrin, lysozyme, and immunoglobulins, all of which contribute to its antimicrobial and immunoprotected effects.[17] Yet, compared to the extensive body of work on bovine lactoferrin, systematic investigations into equine milk lactoferrin remain sparse and fragmented.

The limited state of knowledge presents both a challenge and an opportunity. While the pharmacological and nutritional roles of equine lactoferrin are not yet fully characterized, its high concentration in milk, structural similarities to human lactoferrin, and potential for therapeutic applications suggest considerable untapped promise. Its antimicrobial activity may prove valuable in an era of rising antimicrobial resistance, its immunomodulatory properties may support emerging strategies in preventive healthcare, and its antioxidant effects may contribute to the management of oxidative stress-related chronic conditions.[18-20] The possibility of incorporating equine lactoferrin into functional foods, nutraceutical formulations, and even targeted pharmaceuticals raises compelling prospects for both scientific research and industrial development.

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In recent years, global interest in natural bioactive proteins has intensified, driven by the dual imperatives of health promotion and sustainability. Equine milk lactoferrin, situated at the intersection of food science, medicine, and biotechnology, has the potential to emerge as a next-generation ingredient with significant impact on public health. Nevertheless, robust biochemical characterization, mechanistic studies, preclinical and clinical validation, and scalable purification techniques are required before this potential can be fully realized.[21,22] At present, the pharmacological efficacy of equine lactoferrin remains underexplored, its industrial applications are not standardized, and its clinical value has not been sufficiently established through controlled trials.

This review integrates existing scientific knowledge on equine milk lactoferrin, situating it within the broader context of milk bioactives while highlighting its unique compositional and functional attributes. By examining its biological activities, exploring its potential roles in medicine and nutraceuticals, and identifying the gaps that constrain its wider adoption, this work underscores the importance of elevating equine lactoferrin research to the same level of scientific scrutiny already applied to its bovine counterpart. In doing so, it aims to establish a foundation for advancing equine lactoferrin from a relatively obscure protein to a recognized contributor in the growing field of functional foods and therapeutic nutrition.[23]

2. Equine milk lactoferrin (eLF)

Lactoferrin (LF), an ~80 kDa glycoprotein belonging to the transferrin family, is secreted by exocrine glands and neutrophils and plays a central role in iron metabolism and host defense (Table 1). First identified in bovine milk, it has since been detected in human breast milk and a variety of other biological fluids, including tears, saliva, and mucosal secretions. Its concentration varies considerably across species and according to the stage of lactation. For instance, in human breast milk, LF concentrations Lactoferrin (LF), an ~80 kDa glycoprotein belonging to the transferrin family, is secreted by exocrine glands and neutrophils and plays a central role in iron metabolism and host defense average around 5 g/L in colostrum and decline to approximately 2 g/L in mature milk. Structurally, LF is highly conserved across mammals, typically comprising 690–710 amino acid residues depending on the species. Human lactoferrin (hLF) contains 711 amino acids, bovine lactoferrin (bLF) 689 residues, and equine lactoferrin (eLF) approximately 695 residues, as confirmed in our prior work using MALDI-TOF MS analysis. LF adopts a bilobed three-dimensional structure, consisting of two homologous lobes (the N-lobe, residues 1–333, and the C-lobe, residues 345–692) connected by a short α-helix. Each lobe possesses a highly conserved binding site capable of chelating one ferric ion (Fe^{3+}) in cooperation with a synergistic carbonate anion, enabling a single LF molecule to bind two Fe^{3+} ions.[24,25]

Table 1: Biological properties of milk lactoferrin.

Biological Function	Mechanism of Action	References
Fe^{3+} binding ability	Depriving microorganisms of free iron, essential for their growth.	[13]
Antipathogenic property	Inhibition of biofilm formation Increase bacterial membrane permeability Lysis of pathogens through competition iron binding	[26]
Cell – secreted immunomodulatory effect	Activates immune and adaptive immunity Inhibition pro-inflammatory (IL-1, IL-2, TNF-α) cytokine production Enhance cytotoxic function of monocytes, NK cells	[27,28]
Antioxidant activity	Preventing formation of free radicals	[29]
Antiviral activity	Inhibition of infections by interacting with viral receptors and surface proteins of cells	[30]
Antimicrobial activity (peptide lactoferricin)	LF peptides interacts with specific binding sites bacteria and disrupts cellular membrane	[31]
Anti-parasitic activity	Membrane damage, iron sequestration, increased oxidative stress, and immune modulation leading to parasite death	[15,32]

Equine lactoferrin exists in two conformational state apolactoferrin (iron-free) and hololactoferrin (iron-saturated). Apolactoferrin is characterized by an open conformation in the N-lobe and a closed conformation in the C-lobe, whereas hololactoferrin adopts a closed conformation in both lobes (Fig. 1). This structural shift enhances protein stability and resistance to proteolytic degradation. LF is typically present as a monomer, although tetrameric forms have been reported; notably, only the monomeric form is capable of binding DNA. Its iron-sequestering ability deprives microorganisms of this essential nutrient, thereby exerting a bacteriostatic effect and contributing to innate immunity.

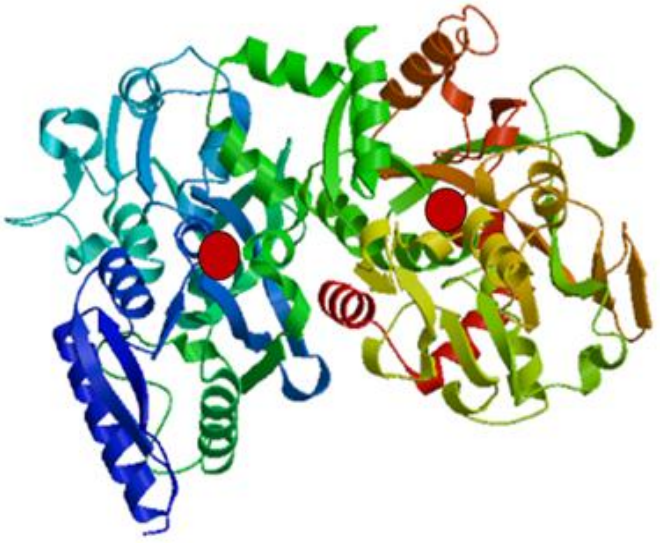

Fig. 1: The structure of Kazakhstani equine lactoferrin (eLF) consists of two lobes: the blue represents the N-lobe, the green indicates the C-lobe, and the red spheres represent iron molecules. The three-dimensional structure of eLF was predicted using Phyre2.2.

Isolation and purification of lactoferrin from milk is influenced by both species and protein composition. Goat and bovine milk, which contain a higher proportion of high-molecular-weight whey proteins, are typically processed using Sephadex G-200 gel filtration for LF purification.[33,34] By contrast, equine milk is enriched with smaller whey proteins such as lysozyme and serum albumin, which complicates the isolation of lactoferrin due to overlapping physicochemical properties. Studies have demonstrated that Sephadex G-100 gel filtration is more effective for the purification of equine LF.[35]

Our own analyses confirmed that Kazakhstani equine milk lactoferrin is composed of a single polypeptide chain of 695 amino acids, consistent with reports describing LF as a single-chain glycoprotein of 690–710 residues in other mammalian species.[36,37] Enzymatic digestion of eLF with trypsin further revealed a complex peptide profile comprising 56 distinct fragments, ranging from short oligopeptides to longer chains, highlighting the structural complexity and potential bioactivity of this protein.[38]

3. Antioxidant and metal chelating activity of eLF

Human lactoferrin (hLF) has long been regarded as the benchmark or "gold standard" among milk-derived lactoferrins, largely due to its potent biological activities and exceptional antioxidant potential. Its high degree of glycosylation enhances structural stability and protects the protein from proteolytic degradation, thereby prolonging its functional activity under physiological conditions.[39,40] Bovine lactoferrin (bLF), while widely exploited in the food and nutraceutical industries, generally exhibits lower antioxidant activity compared to equine lactoferrin (eLF), particularly in assays that measure radical scavenging and metal chelation efficiency. A distinguishing feature of eLF is its enhanced ability to bind divalent metal ions, especially Fe^{2+}, thereby preventing the generation of highly reactive hydroxyl radicals through the Fenton reaction. This superior chelation capacity underpins its effectiveness in protecting cellular membranes and biomolecules from oxidative damage. Comparative studies indicate that eLF not only demonstrates stronger inhibition of lipid peroxidation but also stimulates the

expression of endogenous antioxidant enzymes, including superoxide dismutase (SOD) and catalase (CAT), highlighting its potential as a functional bioactive ingredient in oxidative stress management. Furthermore, because of its structural similarity to hLF, equine lactoferrin is of particular interest for applications in infant nutrition, such as the development of breast milk substitutes and specialized formulations for vulnerable populations, where oxidative balance is crucial for growth and immunity. Equine lactoferrin exhibits strong radical-scavenging and metal-chelating activity, positioning it as a promising natural antioxidant for functional foods. Comparable antioxidant and antimicrobial effects have also been reported from plant-derived phytochemicals such as those identified in Phlomis tuberosa L., highlighting the growing importance of diverse bioactive sources in human nutrition and disease prevention.[41,42]

Our investigations provided the first comprehensive demonstration of the antioxidant potential of eLF by integrating classical radical scavenging assays (DPPH, ABTS, and FRAP) with divalent metal chelation analyses. Results confirmed that eLF efficiently neutralizes reactive oxygen species, donates reducing equivalents, and effectively disrupts free-radical propagation. Complementary switchSENSE® nanobiosensor analyses revealed that eLF can chelate a range of pro-oxidant divalent metals, including Zn^{2+}, Ca^{2+}, Cu^{2+}, and Fe^{2+}, at physiologically relevant micromolar concentrations. This multifunctional metal-binding capacity likely contributes not only to its antioxidant role but also to broader regulatory functions in mineral metabolism.[9]

In contrast, hLF and bLF are best characterized as Fe^{3+}-binding proteins, with strong affinity for ferric ions that supports their established roles in iron homeostasis, microbial growth inhibition, and suppression of iron-driven reactive oxygen species (ROS) generation[43,44] While this classical Fe^{3+} sequestration mechanism is fundamental to the antimicrobial and antioxidant functions of hLF and bLF, equine lactoferrin exhibits a broader and more versatile antioxidant profile. Its dual ability to scavenge free radicals and chelate multiple redox-active metal ions positions eLF as a more multifunctional antioxidant defense system compared to its bovine counterpart.

Collectively, these findings highlight equine lactoferrin as a promising natural antioxidant uniquely abundant in equine milk. Its dual radical-scavenging and metal-chelating functions expand its potential applications beyond conventional dairy bioactives. Prospective areas of application include nutraceuticals targeting oxidative stress, functional foods designed for preventive health, and adjunctive therapies for stress-related disorders, metabolic diseases, and conditions characterized by oxidative imbalance (Fig. 2; Table 2). By integrating both classical antioxidant mechanisms and multifunctional metal interactions, eLF emerges as a bioactive protein of significant therapeutic promise within the growing field of food-derived antioxidants.

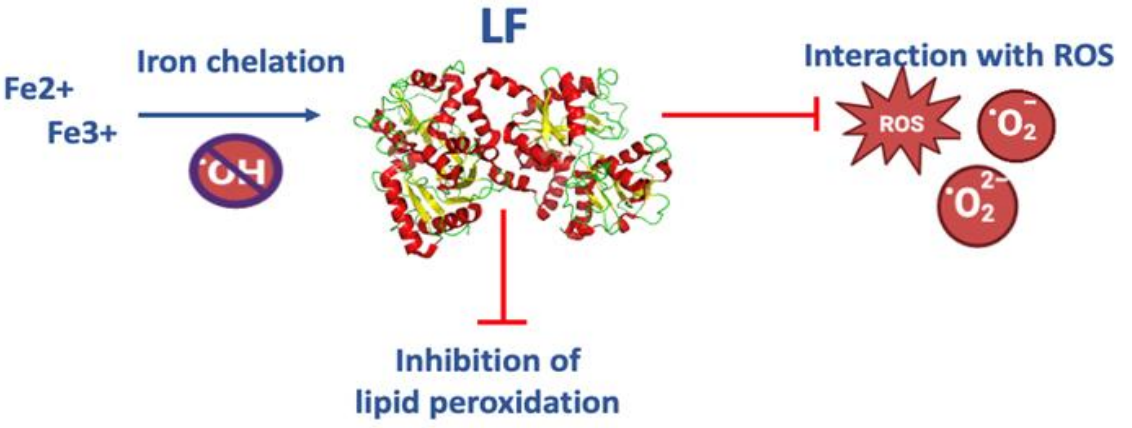

Fig. 2: Antioxidant and metal chelating activity of lactoferrin.

Table 2: Antioxidant and metal chelating activity of LF.

Feature / Property	Equine LF (eLF)	Bovine LF (bLF)	Human LF (hLF)
Length	~695 aa	~700 aa	~700 aa
Main Fe-binding	Fe^{2+}, Fe^{3+} (moderate µM Kd)	Fe^{3+} (high affinity Kd, ~10^{-20}–10^{-22} M)	Fe^{3+} (high affinity Kd ~10^{-20}–10^{-22} M)
Other metals	Zn^{2+}, Ca^{2+}, Cu^{2+}	Zn^{2+}, Cu^{2+}, Ca^{2+}, Mn^{3+}	Zn^{2+}, Cu^{2+}, Mn^{3+}
Antioxidant activity	Strong via radical scavenging and metal chelation	Prevents ROS through Fe sequestration, stabilizes emulsions	Prevents ROS via Fe sequestration, modulates antioxidant enzymes

4. Equine milk lactoferrin-derived biologically active peptides

Milk proteins and their enzymatic hydrolysates are increasingly recognized as rich reservoirs of bioactive peptides with diverse physiological functions. Among these, lactoferrin-derived peptides have attracted particular attention due to their pronounced antimicrobial and immunomodulatory activities. Proteolytic cleavage of lactoferrin by enzymes such as pepsin or trypsin generates peptide fragments that often display stronger antibacterial and antiviral effects than the intact protein. Importantly, the peptide profiles generated are species-specific, as the same protein substrate can yield peptides of different lengths, amino acid compositions, and bioactivities depending on the source.

For example, Wang *et al*. (2020) compared peptides produced by trypsin hydrolysis of camel (CaW) and cow (CoW) whey proteins and evaluated their antibacterial activity against both Gram-positive bacteria (Streptococcus mutans, Staphylococcus aureus) and Gram-negative bacteria (Escherichia coli, Salmonella typhimurium). They demonstrated that camel milk yielded smaller peptides (<3 kDa) with significantly greater antimicrobial potency than peptides derived from cow milk.[45] The mode of action of such milk protein–derived antimicrobial peptides typically involves electrostatic binding to negatively charged lipopolysaccharides and lipoproteins in bacterial cell walls, leading to membrane disruption, leakage of cellular contents, and eventual cell death.[46,47]

Lactoferrin itself, whether of natural or recombinant origin, is widely documented to possess both bacteriostatic and bactericidal activity. In its bacteriostatic role, LF sequesters ferric iron (Fe^{3+}), thereby restricting microbial access to this essential nutrient; bacterial growth can often be restored by supplementing excess iron. In its bactericidal role, LF acts independently of iron availability by directly binding to microbial surface components such as lipopolysaccharides (LPS), disrupting membrane integrity and causing depolarization and lysis.[14] Short LF-derived peptides often retain or even amplify these activities. Japelj *et al*. (2005), for instance, reported the strong antimicrobial and endotoxin-neutralizing effects of LF11, an 11-amino-acid peptide derived from human lactoferrin.[48] Similarly, Sinha *et al*. (2013) characterized naturally occurring lactoferrin-derived peptides generated by pepsin digestion, including lactoferricin (Lfcin), lactoferrampin (Lfampin), and the hLF1–11 peptide, all of which exhibited potent antimicrobial properties.[49] Building on this foundation, our recent work provided novel insights into peptides derived from equine milk lactoferrin (eLF). Using enzymatic digestion with trypsin followed by HPLC–MS analysis, we successfully isolated and identified 56 distinct peptides, ranging from short oligopeptides to longer chains. These were classified by charge distribution into 13 cationic, 23 anionic, and 20 neutral peptides. Notably, cationic and neutral peptides, particularly those enriched with aromatic residues such as phenylalanine, demonstrated the greatest potential for bioactivity, consistent with the general principle that cationic peptides interact strongly with negatively charged bacterial membranes. Several short peptides derived from eLF hydrolysates were identified as particularly promising candidates for therapeutic development. For example, FCLFK (5 amino acids), RCSSSPLLEACAFLR (15 amino acids), CSSSPLLEACAFLR (14 amino acids), and CACSSQEPYFGYSGAFK (17 amino acids) displayed predicted antimicrobial, antihypertensive, and anti-inflammatory activities.[38] These findings highlight the multifunctional potential of eLF-derived peptides, extending their relevance beyond antimicrobial defense to broader health-promoting roles.

Nevertheless, the biological activity of in silico–predicted eLF peptides requires confirmation through rigorous in vitro, in vivo, and eventually clinical studies. Complicating this task is the fact that enzymatic digestion with different proteases produces distinct peptide profiles; for instance, pepsin and trypsin cleave lactoferrin at different sites, generating non-overlapping sets of bioactive fragments. This variability underscores the challenge of standardizing the isolation and evaluation of eLF-derived peptides but also reflects the structural versatility and rich bioactive potential of this protein.

5. Prospects for the application of LF in medicine

As previously discussed, equine milk bears close compositional resemblance to human breast milk, particularly in its high digestibility and its enrichment in bioactive proteins such as lactoferrin (LF) and lysozyme. This compositional advantage positions equine milk as a potential therapeutic alternative for individuals with cow's milk allergy, infants with sensitive digestive systems, and patients with gastrointestinal disorders or iron-deficiency conditions. Beyond its nutritional role, LF has attracted significant attention in clinical medicine owing to its iron-binding, antioxidant, immunomodulatory, and antimicrobial properties. Recent in silico modeling and peptide-profiling studies have also identified equine lactoferrin-derived bioactive peptides with predicted antihypertensive, anti-inflammatory, and antimicrobial activities, underscoring its potential as a multifunctional therapeutic agent.[50]

Emerging research has revealed diverse applications of LF across several disease areas. Salaris *et al*. (2021) demonstrated the in vitro antiviral potential of LF against SARS-CoV-2 infection in CaCo-2 intestinal epithelial cells.[51] The study showed that LF not only inhibited viral entry and replication but also enhanced the expression of host antiviral genes, indicating its dual role as a direct antiviral agent and as an immune modulator. These findings suggest that LF could be employed as a safe adjunctive therapy in COVID-19 management, particularly for gastrointestinal manifestations of the disease.

One of the most clinically validated applications of LF lies

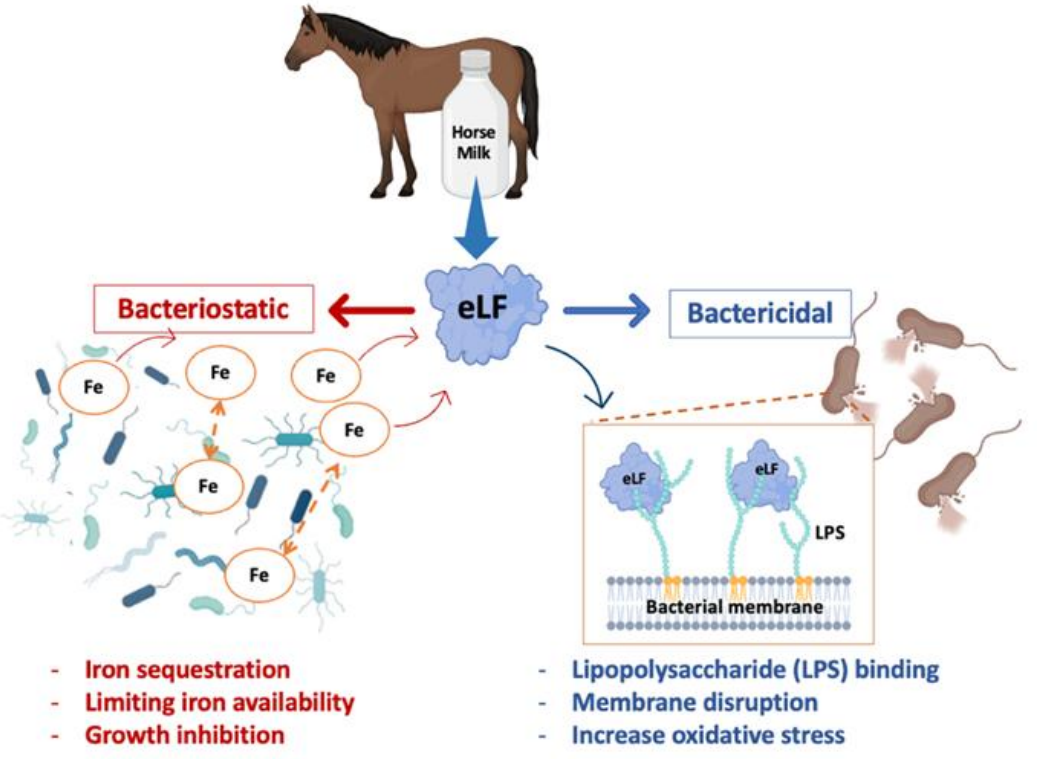

Fig. 3: Antimicrobial mechanism of action of equine milk lactoferrin (eLF). Bioactive peptides derived from eLF inhibit microbial growth through two distinct mechanisms: bacteriostatic and bactericidal.

in the treatment of iron deficiency anemia (IDA). Because of its high bioavailability and capacity to facilitate iron absorption, LF supplementation has been investigated as a non-invasive alternative to injectable iron therapies. Hegazi *et al*. (2025) recently evaluated the use of oral LF supplementation in children with chronic kidney disease suffering from anemia and found that LF not only improved hemoglobin levels but also reduced inflammatory markers, indicating benefits beyond iron delivery.[52] Similar studies in pregnant women with IDA have shown that LF supplementation is more effective and better tolerated than conventional ferrous sulfate treatments, reducing gastrointestinal side effects while improving maternal and neonatal outcomes.

Recent advances also point to LF's potential role in neurodegenerative disease management. Xu *et al*. (2019) reported that LF protects dopaminergic neurons in Parkinson's disease by modulating iron metabolism, preventing excessive iron accumulation, and reducing oxidative stress in neuronal tissues.[53] In Alzheimer's disease, LF has been detected in amyloid plaques, suggesting a protective role in amyloid clearance and neuroinflammation modulation. Experimental models further indicate that LF can cross the blood–brain barrier via receptor-mediated transport, strengthening the rationale for its therapeutic use in neurodegenerative conditions.

Beyond neurological disorders, LF supplementation has shown promise in metabolic disease management. Clinical and animal studies suggest that LF regulates glucose homeostasis, enhances lipid oxidation, and prevents lipid accumulation, thereby contributing to the prevention and management of obesity and metabolic syndrome.[53,54] By improving insulin sensitivity and reducing systemic inflammation, LF may serve as a supportive therapy for type 2 diabetes and obesity-related complications. Additionally, LF has demonstrated anti-cancer potential, with studies showing its ability to inhibit tumour growth, suppress angiogenesis, and enhance host immune surveillance. Clinical investigations of bLF in colorectal cancer prevention, for example, have demonstrated reduced polyp formation in at-risk populations.

Despite this growing body of evidence, the vast majority of clinical investigations have focused on bovine and human lactoferrin, with equine lactoferrin (eLF) remaining comparatively understudied. Given that eLF exhibits structural and functional similarities to human LF and has been shown to possess superior antioxidant and multifunctional metal-binding properties compared to bovine LF, its therapeutic potential may extend to a broad spectrum of clinical applications. However, systematic preclinical and clinical studies are urgently required to validate these hypotheses.

Taken together, lactoferrin represents a highly versatile natural glycoprotein with promising applications across infectious diseases, metabolic disorders, neurodegenerative conditions, and oncology. The challenge moving forward is to expand current research beyond bovine and human LF to

equine lactoferrin, which, due to its unique bioactivity and abundance in equine milk, may represent an underutilized but highly valuable resource for next-generation nutraceuticals and therapeutic formulations.

6. Potential in functional foods

Lactoferrin's multifunctional bioactivities, including antimicrobial, antioxidant, immunomodulatory, and iron-binding properties, make it an attractive candidate for incorporation into functional foods and nutraceuticals. In the food industry, lactoferrin has gained recognition not only as a nutritional supplement but also as a bio-preservative and functional ingredient that enhances food safety and quality. Natural bioactives such as lactoferrin are increasingly investigated as safe food preservatives, capable of suppressing microbial growth while maintaining nutritional quality. Similar approaches have been reported with other biopolymers such as carboxymethyl chitosan, which was shown to enhance biofilm formation of Cryptococcus laurentii and improve biocontrol efficacy against Penicillium expansum in grapefruit.[55] A nutrition study by Konstanti *et al*. (2022) demonstrated that bovine lactoferrin, either used alone or in combination with complementary compounds such as carbohydrates and vitamin D, promoted beneficial gut microbiota in elderly women. This finding underscores its role as a safe nutraceutical that supports intestinal and metabolic health in vulnerable populations.[56]

One of the most widely investigated applications of lactoferrin in functional nutrition relates to iron metabolism. Lactoferrin supplementation effectively prevents and treats iron deficiency anemia, particularly in groups with elevated iron requirements such as infants, pregnant women, and endurance athletes. For instance, studies on long-distance female runners show that LF supplementation mitigates sport-related anemia by improving iron absorption and reducing inflammation.[57] These results highlight lactoferrin's potential as a natural alternative to synthetic iron supplements, offering better tolerance and fewer gastrointestinal side effects.

The technological stability of lactoferrin also contributes to its application in food processing. Owing to its thermostability and resistance to proteolysis, lactoferrin and its derived peptides can function as natural preservatives in a variety of food systems. Their ability to inhibit microbial growth extends shelf life and improves safety in products such as yogurt, cheese, meat, fermented milk, and infant formula.[58] This dual role, serving as both a nutritional enhancer and a bio-preservative, makes lactoferrin highly versatile for modern food applications.

In infant nutrition, lactoferrin has already been incorporated into formula products as a functional additive to better mimic the protective and developmental properties of human breast milk.[59] Studies have shown that infant formulas fortified with LF improve gut health, support immune system development, and reduce the incidence of gastrointestinal infections.[59] Similarly, equine milk, due to its compositional similarity to human milk and its naturally high lactoferrin content, has strong potential for use in hypoallergenic infant formulas and therapeutic nutrition for children with cow's milk intolerance.[6]

In addition to pediatric nutrition, LF shows promise in sports nutrition. By enhancing iron absorption, promoting recovery from exercise-induced oxidative stress, and improving immune function, lactoferrin-based supplements could provide athletes with a natural strategy to prevent fatigue, maintain performance, and reduce susceptibility to infections during intense training.[60,61]

Another emerging application of lactoferrin is in synbiotic and probiotic formulations. Lactoferrin has been shown to selectively modulate gut microbiota by supporting the growth of beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*, while simultaneously inhibiting pathogenic strains like *E. coli* and *Salmonella*.[62] This makes lactoferrin a potential adjunct to probiotics and prebiotics in functional food formulations aimed at maintaining gut homeostasis.

From an industrial standpoint, lactoferrin is increasingly regarded as a value-added protein with market potential in multiple sectors.[63] It is now used in dairy-based beverages, fortified cereals, oral supplements, and clinical nutrition formulations. The rising consumer demand for natural, multifunctional bioactive ingredients further strengthens its position as a high-value component of the functional food market. As noted earlier, the unique protein composition of equine milk offers additional advantages. Its high proportion of bioactive whey proteins, particularly lactoferrin, positions it as a superior raw material for next-generation functional foods. Equine lactoferrin (eLF), with its superior antioxidant and multifunctional metal-chelating capacity compared to bovine LF, could be strategically developed into therapeutic food products tailored for children, elderly individuals, and athletes.[9] Moreover, the combination of traditional consumption of fermented equine milk (*kumis*) with modern food technology provides a culturally rooted yet scientifically validated platform for functional food innovation.[9] Taken together, these findings emphasize that lactoferrin and its peptides represent a highly promising class of food bioactives. Their incorporation into infant formula, sports supplements, probiotic blends, dairy products, and clinical nutrition formulations not only enhances product value but also contributes to public health by addressing iron deficiency, oxidative stress, and immune dysfunction. Future research should focus on optimizing delivery systems, scaling up equine LF extraction, and conducting large-scale clinical trials to confirm efficacy across diverse populations.

7. Conclusion and future directions

Equine milk lactoferrin (eLF) represents an effective, bioavailable, and easily digestible form of a multifunctional natural immunomodulator. Its hypoallergenic profile, superior antimicrobial and antioxidant properties, and close structural similarity to human milk lactoferrin make it particularly

promising for use in sensitive populations such as infants, the elderly, and individuals with compromised immunity. Despite these advantages, eLF remains significantly underexplored compared to its bovine and human counterparts. Current gaps in knowledge regarding its molecular structure, glycosylation patterns, mechanisms of action, and peptide bioactivity continue to limit its translation into pharmaceuticals, nutraceuticals, and functional food formulations. Future research should adopt a multi-pronged strategy to unlock the therapeutic and nutritional potential of eLF. At the molecular level, comprehensive sequencing and glycoproteomic studies across different horse breeds are needed to identify potential variations in amino acid composition and glycosylation that may influence stability and bioactivity. Structural biology approaches, including X-ray crystallography and cryo-electron microscopy, could provide deeper insight into conformational dynamics of apo- and holo-eLF, enabling correlations between structural features and functional properties.

At the bioactivity level, rigorous in vitro and in vivo studies are essential to evaluate the antimicrobial, antiviral, anti-inflammatory, and immunomodulatory properties of eLF. In particular, functional studies should investigate how eLF interacts with host immune cells, modulates cytokine production, and influences gut microbiota composition. Parallel work should explore the role of eLF-derived peptides, such as lactoferricin and lactoferrampin, as potential next-generation antimicrobial and antihypertensive agents. Standardized enzymatic digestion protocols and peptide libraries will be crucial to systematically map the bioactive potential of eLF hydrolysates.

At the technological and industrial level, innovation in isolation and purification techniques is required to ensure scalable production of eLF while maintaining its native structure and activity. Traditional methods such as cation-exchange chromatography and gel filtration must be optimized or combined with advanced membrane separation and affinity purification technologies for higher efficiency. Furthermore, encapsulation strategies (*e.g.*, liposomes, protein-based nanoparticles) should be developed to enhance stability, bioavailability, and targeted delivery of eLF in functional food and pharmaceutical applications.

From a clinical perspective, safety and efficacy trials are urgently needed to validate eLF as a therapeutic agent. Clinical studies should assess its role in preventing iron deficiency anemia, modulating immune responses during viral infections, improving metabolic health in obesity and diabetes, and providing neuroprotection in conditions such as Parkinson's and Alzheimer's diseases. Given its strong resemblance to human milk lactoferrin, eLF is also a particularly promising candidate for incorporation into hypoallergenic infant formula, pediatric supplements, and maternal nutrition products.

Finally, the application spectrum of eLF extends beyond human health into broader areas such as veterinary medicine, probiotics, prebiotics, and food preservation. Its thermostability and antimicrobial properties make it suitable for dairy fortification, functional beverages, fermented foods, and sports nutrition supplements. As consumer demand grows for natural, biologically active proteins, equine lactoferrin is poised to become a high-value ingredient in the global nutraceutical and biopharmaceutical markets.

In conclusion, equine milk lactoferrin stands at the crossroads of nutrition and medicine. Unlocking its full potential will require coordinated efforts in molecular characterization, mechanistic biology, food science innovation, and translational clinical research. With strategic investment and interdisciplinary collaboration, eLF could emerge as a next-generation bioactive protein with transformative applications in health promotion, disease prevention, and therapeutic intervention.

Acknowledgments

This research was funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan (Grant No. AP19676645).

Conflict of Interest

There is no conflict of interest.

Supporting Information

Not applicable.

CRediT Statement

Meiramkul Narmuratova and **Saltanat Orazova:** Conceptualization. **Zhanar Narmuratova** and **Shattykgul Kanayat:** Validation. **Meiramkul Narmuratova** and **Assiya Serikbayeva:** Resources. **Meiramkul Narmuratova:** Writing original draft. **Meiramkul Narmuratova**, **Saltanat Orazova** and **Assiya Serikbayeva:** Writing - Review & editing. **Meiramkul Narmuratova**, **Shattykgul Kanayat** and **Saltanat Orazova:** Visualization. **Meiramkul Narmuratova:** Supervision. **Meiramkul Narmuratova:** Project administration, Funding acquisition. All authors have read and agreed to the published version of the manuscript.

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