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REVIEW ARTICLE

Nutritional and health beneficial application of lactoferrin in some animal species: an updated review

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Abstract

Throughout history, from ancient times to the present day in our contemporary and industrialized period, ensuring the availability of safe and hygienic food has been a significant challenge for the human population. With the global population steadily increasing, there is a growing need for animal-based food items. Consequently, the livestock sectors face mounting pressure to enhance productivity and sustainability. Hence, the farmer, manufacturer, producers, and researchers are seeking nutritional supplements that might improve the production and performance of animals. Lactoferrin (Lf) a miracle molecule is a newly discovered multifunction protein found in milk and other exocrine secretions. LF has demonstrated a wide range of biological activities, including antimicrobial, anti-inflammatory, anti-oxidant, immunomodulatory, hepatoprotective, anti-osteoporotic and allied pathophysiological conditions. These properties make lactoferrin a promising candidate for improving the health and productivity of livestock. LF is used as a dietary supplement in livestock and food animals to enhance growth, productivity, and overall health. Additionally, it improves the digestibility and absorption of nutrients in the intestine. Furthermore, LF also reduces the dependency on antibiotics and alleviates the environmental consequences caused by cattle husbandry. Although existing data indicates that lactoferrin may be a beneficial element in sustainable livestock production, further research is required to comprehensively comprehend its molecular processes, appropriate doses, and possible negative effects when used as a dietary supplement. This review aims to provide a comprehensive understanding of the applications and research surrounding lactoferrin as a dietary supplement in the livestock industry.

Keywords Lactoferrin · Functional feed additive · Livestock · Health benefits · Productive performance

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Introduction

The global demand for livestock products continues to rise, driven by population growth and increasing affluence, particularly in developing countries. However, the traditional reliance on antibiotics to promote growth and prevent disease in livestock production has led to growing concerns about antimicrobial resistance, which poses a significant threat to both animal and human health (Ahmed et al. 2024). As a result, there is an urgent need to explore alternative strategies that can maintain or even improve livestock productivity while reducing the use of antibiotics (Nabi et al. 2020a; Pirzado et al. 2021; Saeed et al. 2021). One promising alternative is the use of LF, an iron-binding glycoprotein present in milk and other bodily fluids. LF, has been shown to possess a wide range of antimicrobial, anti-inflammatory, and immunomodulatory properties, making it a potentially valuable tool in addressing the challenges faced by livestock producers (Arain et al. 2024; Ashraf et al. 2024).

The content of Lf is greater in colostrum, but it decreases in mature milk (Duan et al. 2024). It may be used in a powdered or liquid state. The supplementation of Lf in livestock is crucial for clean meat production from food animals. It enhances animal development, feed intake, feed conversion ratio, meat quality, carcass stability, and overall growth of the animals (Tanga and Ekesi 2024). Moreover, dietary addition of LF, improved the physiological functions of the intestinal leading to enhance the absorption and productivity of animals (Dong et al. 2024). The most important aspect of Lf is to decrease the growth of pathogenic bacteria and viruses (Ashraf et al. 2024). It was reported that addition of 0.1–1 g/L of bovine LF showed anti-inflammatory effect by increasing the extracellular signal regulated kinase (ERK) and down regulating IL-8 expression (Hong et al. 2024). Another study suggested that LF supplement in pregnancy and lactation increased the milk production (Fischer-Tlustos et al. 2024), and improved the level serum IgA, which improved the piglet's health and growth performance (Jahan et al. 2017). Moreover, bovine LF has been found to improve the growth performance of weaning piglets and reduce diarrhea. In addition to that Lf protect animals from various kinds of pathogenic bacteria, viruses, parasites and fungi by activating various underlying mechanisms including, bacteriostatic action by chelating free iron and stop the bacterial growth and proliferation; secondly, hydrolysis the peptides that are required by microbes for their growth; thirdly, increase the permeability of membrane of the pathogenic microbes and cause direct microbial death (Martinez-Castillo et al 2024). It was demonstrated that oral administration of colostrum in addition to the LF to pregnant goats and sheep improves the immune functions, increases the IgA concentration in postpartum milk and maintains the health and productivity (Dunière et al. 2022; Isobe et al. 2020).

Besides the above mentioned properties LF is a remarkable protein found in various mammalian secretions, including milk, saliva, and tears. This versatile molecule has garnered significant attention for its diverse range of beneficial health activities, including anti-inflammatory, anti-carcinogenic, anti-mutagenic, anti-oxidative, anti-microbial, and hypolipidemic effects (Marnila and Korhonen 2009). Furthermore, numerous studies have demonstrated that the oral administration of bovine lactoferrin (bLF) can enhance host protection against infections through its antimicrobial action and immunomodulatory effects (Tomita et al. 2009). Lactoferrin has also been shown to play a critical role in the development and maintenance of the intestinal epithelium. Preclinical studies have provided evidence that lactoferrin supplementation can improve intestinal mucosal structure, increase villus height, and stimulate crypt proliferation in both mice and piglets (Lönnerdal et al. 2011).

Similarly, another study found the effect of LF on the growth and diversification of intestinal microbiota, strengthen intestinal permeability, support microbial antagonism that discourages the colonization and proliferation of enteric pathogens, and enhance the growth and maturation of cell-monolayer components (Vega-Bautista et al. 2019). Moreover, LF triggers both innate and adaptive immune response and modulates acute and chronic inflammation. Meanwhile, the expression and secretion of LF on mucosal surfaces and on inflammatory sites have established its role as an agent that may be helpful in mitigating the pathological conditions.

Current study provides an updated overview of the health beneficial application of LF as a functional feed additive in livestock animals to enhance productive efficiency and explore possible health benefits in various livestock animals, such as cattle, goats, sheep, fish, and other experimental animals. The biological activities of LF, including its antibacterial, antioxidant, anti-inflammatory, anti-parasitic, and immunomodulatory methods were also included to provide the insight for future research.

Lactoferrin's history and sources

LF, is a multifunctional glycoprotein found in various bodily fluids, has a rich and diverse history that spans centuries and has been the subject of extensive research. This protein has close originating with the transferrin family of proteins, LF was first isolated and characterized in 1939 from bovine milk and later identified in human milk in 1960 (Tomita et al. 2009). Since then, researchers have delved into the intricate details of this remarkable biomolecule, uncovering its numerous bioactivities and potential applications. The early pioneering work on lactoferrin, conducted in the 1960s and 1970s, laid the foundation for our current understanding of this versatile protein. This novel dairy fractions, including LF, have been isolated from various source including human milk, exocrine secretions, camel milk and colostrum, plants and bacteria are the key source and commercially made available (Lönnerdal et al. 2011).

Therapeutic potential of lactoferrin

Lactoferrin, has garnered significant attention in the scientific community due to its diverse therapeutic potential. Numerous studies have been reported that LF has the potential to induce therapeutic effects against diverse pathophysiological conditions. It is well known that LF is a multifunctional protein and possess antimicrobial, anti-inflammatory, and immunomodulatory properties (Tomita et al. 2002; Wakabayashi et al. 2006). Experimental and clinical research has demonstrated its efficacy in combating bacterial, viral, and fungal infections, as well as its potential to regulate immune function and mitigate inflammation (Marnila and Korhonen 2009). The salient therapeutic effects of LF along with underlying mechanisms of action are shown in Fig. 1.

Anti-inflammatory potential

Inflammation is a complex biological response of the body's immune system against various stimuli, such as pathogens, damaged cells, or irritants, and it plays a crucial role in the body's defense mechanism (Aboamer et al. 2024; Saeed et al. 2024). Chronic inflammation, however, can have detrimental effects and has been linked to various health conditions, including cardiovascular disease, diabetes, and cancer. Dietary supplementation with specific compounds that possess anti-inflammatory properties has emerged as a potential strategy to mitigate the adverse effects of chronic inflammation (Arain et al. 2018; Nabi et al. 2020b; Hassan et al. 2023). LF has been shown to exhibit a range of biological activities, including antimicrobial, antiviral, and immunomodulatory effects, which may contribute to its potential anti-inflammatory properties (Arshad et al. 2018; Lönnerdal et al. 2011).

Recent studies have investigated the impact of LF supplementation on inflammation. A growing body of evidence suggests that LF may possess the ability to modulate inflammatory responses by regulating the production of pro-inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha (Wakabayashi et al. 2006). Furthermore, LF has been observed to enhance the activity of anti-inflammatory cells, such as regulatory T cells, and inhibit the proliferation of pro-inflammatory cells, such as effector T cells (Kanzato et al. 2008). These findings indicate that dietary supplementation of LF may be a promising approach to reduce inflammation and mitigate the associated health risks. However, further research is needed to elucidate the exact mechanisms behind anti-inflammatory effects of LF and to assess its efficacy in various clinical settings.

Antioxidant potential

Oxidative stress, a condition characterized by an imbalance between the production of reactive oxygen species (ROS), and the body's ability to counteract their harmful effects, has

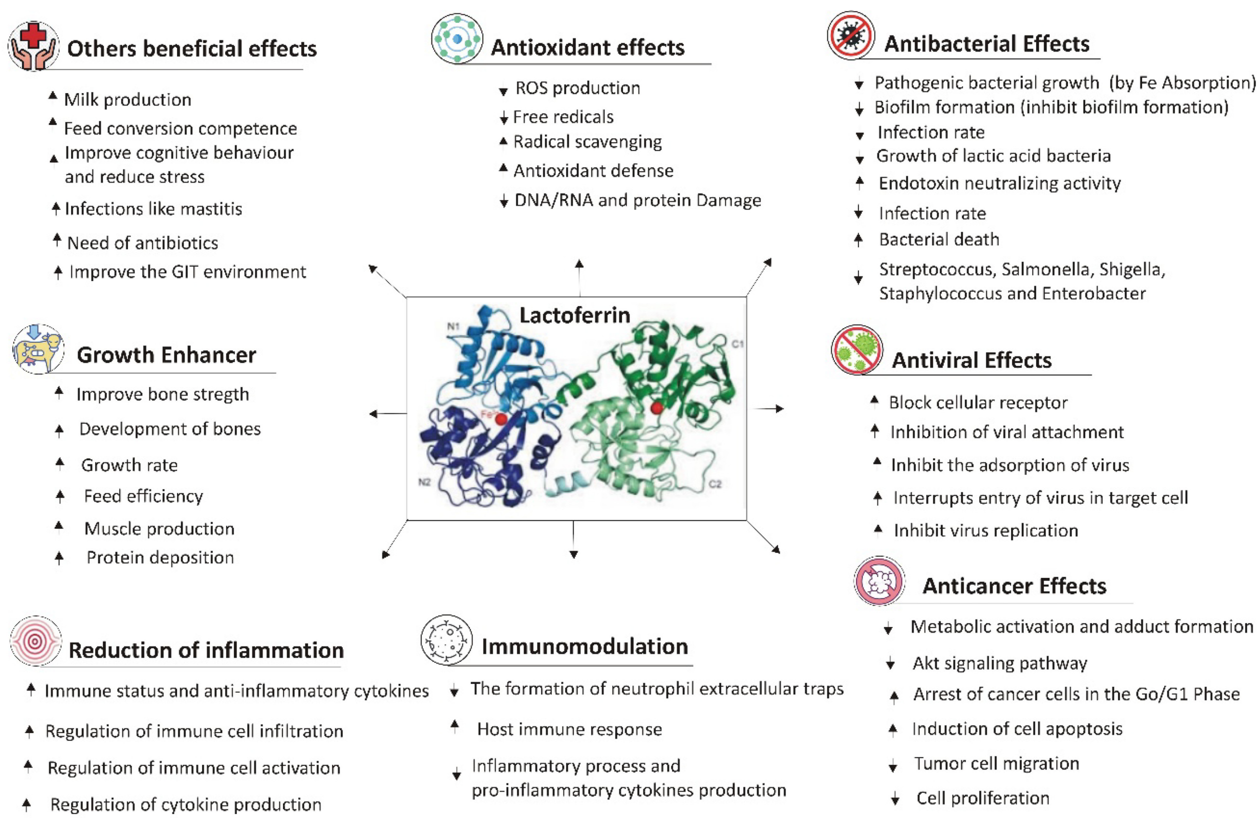

Fig. 1 Represents the various exceptional nutraceutical and biological activities of lactoferrin

been implicated in a wide range of health concerns, including diabetic complications, neurodegenerative diseases, and cardiovascular disorders (Harrison et al. 2003; Ozawa and Sasaki 2014). The underlying mechanisms of these disease pathogenesis are complex, numerous studies suggested that oxidative stress plays a crucial role in their development and progression (Ozawa and Sasaki 2014). The potential strategy to mitigate the impact of oxidative stress using the antioxidant supplements, such as LF, a multifunctional protein abundantly found in milk and other exocrine secretions (Elahi et al. 2009; Millar et al. 2017). It has been shown that LF possess potent antioxidant properties, which may help to counteract the deleterious effects of reactive oxygen species and potentially slow the progression of age-related diseases (Shwe et al. 2018).

Several studies have investigated the influence of LF supplementation on oxidative stress, with promising results. For instance, researchers have found that LF can protect cultured cortical neurons from oxidative damage, potentially through the inhibition of specific pathways involved in the generation of ROS. Furthermore, the antioxidant properties of LF may also contribute to its neuroprotective effects, as observed in studies examining the role of lutein, a plant-derived carotenoid, in retinal and cognitive function (Ozawa and Sasaki 2014; Stringham and Stringham 2015). The precise mechanisms by which LF exerts its antioxidant effects are not yet fully understood, the available evidence suggests that it may be a valuable intervention for mitigating the impact of oxidative stress on various aspects of health.

Immunomodulatory potential

Immunomodulation, is the strategic manipulation of the immune system, has emerged as a promising approach in the field of biomedical research. Recent advancements have highlighted the potential of immunomodulatory strategies in combating various diseases, including cancer and infectious disorders (Nijnik 2013; Yan and Jiang 2020). LF has gained significant attention in the realm of dietary supplementation due to its potential to modulate the immune system (Alagawany et al. 2020; Arain et al. 2023). Numerous studies have explored the biological activities of lactoferrin, revealing its antimicrobial, antiviral, and immunostimulatory properties. It has been demonstrated that oral administration of bLF can augment host protection against infections through its antimicrobial action and immunomodulatory effects (Tomita et al. 2009). In addition to its antimicrobial properties, LF has been shown to possess various other bioactivities, including regulation of immune function, stimulation of intestinal proliferation and differentiation, and facilitation of iron absorption (Lönnerdal et al. 2011).

Anti-bacterial potential

Lactoferrin, has gained significant attention for its potent antibacterial properties. It is a key component of the innate immune system, contributing to the body's first line of defense against microbial infections. The antibacterial activity of LF is multifaceted, involving both direct and indirect mechanisms that inhibit bacterial growth and proliferation (Liu and Chen 2023). One of the primary mechanisms by which LF exerts its antibacterial effect by sequestering iron, an essential nutrient for bacterial growth. By binding to free iron in the environment, LF effectively deprives bacteria of this critical resource, inhibiting their metabolic functions and subsequent growth (Zarzosa-Moreno et al. 2020). This iron-chelating property is particularly effective against iron-dependent pathogens such as *Escherichia coli* and *Staphylococcus aureus* (Kanwar et al. 2015; Zarzosa-Moreno et al. 2020). In addition to iron sequestration, lactoferrin exhibits direct bactericidal activity. It can bind to bacterial cell walls, destabilizing the membrane and increasing its permeability, leading to cell lysis and death. This mechanism is especially effective against Gram-negative bacteria, where LF targets lipopolysaccharides (LPS) in the outer membrane. Moreover, lactoferrin-derived peptides, such as lactoferricin, have shown enhanced antibacterial properties, further disrupting bacterial membranes and exhibiting broad-spectrum activity (Zarzosa-Moreno et al. 2020).

Lactoferrin also plays an indirect role in modulating the immune response to bacterial infections. It can enhance the activity of immune cells such as neutrophils and macrophages, promoting phagocytosis and the production of reactive oxygen species (ROS) that kill bacteria (Hong et al. 2024). Additionally, LF can inhibit the formation of biofilms, complex communities of bacteria that are resistant to antibiotics and the immune system. By preventing biofilm formation, LF enhances the effectiveness of antibacterial treatments and helps in eradicating persistent infections. Furthermore, LF antibacterial effect extends to its ability to bind and neutralize bacterial endotoxins, reducing inflammation and tissue damage associated with infections. This anti-inflammatory property is crucial in mitigating the harmful effects of bacterial infections and promoting recovery (Gori et al. 2024). In conclusion, lactoferrin is a versatile and powerful antibacterial agent with a range of mechanisms that inhibit bacterial growth and enhance the immune response. Its ability to sequester iron, disrupt bacterial membranes, modulate immune functions, prevent biofilm formation, and neutralize endotoxins underscores its potential as a therapeutic agent in combating bacterial infections.

Beneficial application of lactoferrin in different animals

Dietary supplements are important for farm animals at all stages of their life cycle as they can help to improve the performance and wellbeing of animals. They play a vital role in the maintenance of growth, structural development, boost immune functions, mitigate stress, reduce inflammation leading to improved productive and reproductive performance. The salient benefits of Lf in various animals are presented in Fig. 2.

Beneficial impact in goats

Lactoferrin, a multifunctional glycoprotein found in various bodily fluids, has garnered significant attention in the realm of goat health and productivity. Intrigued by its potential benefits, researchers have explored the impact of dietary LF supplementation on goats, particularly in areas such as nutrient intake, digestibility, ruminal fermentation, and growth performance (Buranakarl et al 2020). Bovine lactoferricin is a bioactive peptide derived from the iron-binding glycoprotein LF, which has garnered attention for its potential benefits in animal nutrition (Tomita et al. 2009)as depicted in Table 1. Recent research suggests that the supplementation of bovine lactoferricin in dairy goat diets can have a positive impact on oxidative stress and ruminal microflora (Lönnerdal et al. 2011; Tomita et al. 2009). Additionally, studies have shown that the oral administration of colostrum containing lactoferrin to pregnant goats can increase the IgA concentration in their postpartum milk, potentially enhancing the immune status of the offspring (Mehra et al. 2021). The antimicrobial and immunomodulatory properties of lactoferrin have been well-documented (Tomita et al. 2009). Its ability to scavenge free radicals and inhibit the growth of pathogenic microorganisms may contribute to the observed reduction in oxidative stress and the alteration of ruminal microflora in dairy goats (Lönnerdal et al. 2011; Tomita et al. 2009). Specifically, another study, found that the supplementation of bovine lactoferricin at a dose of 100 mg/kg/day was more effective in decreasing oxidative stress and modulating the ruminal microbiome compared to a higher dose of 200 mg/kg/day (Tomita et al. 2009).

It has been suggested that LF positively enhanced the growth performance, productive and reproductive

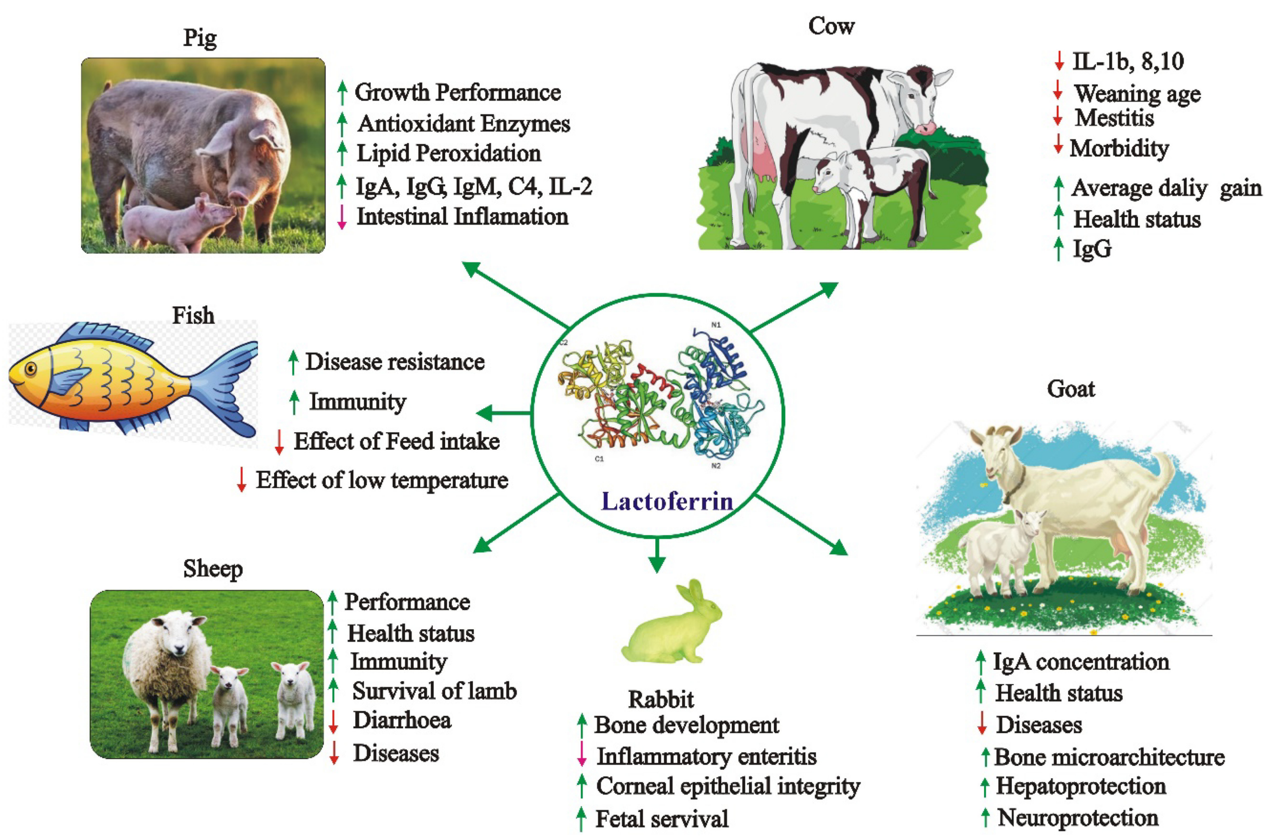

Fig. 2 Schematic representation of various biological properties of lactoferrin in food producing animals

Table 1 Summary of the various nutritional and therapeutic application of lactoferrin in various animal species

Lf Type	Species	Dose	Overall performance	References
LF	Friesian calves	1–2 mg/calve	↑ Body weight gain ↑ Total protein, Globulin, Glucose levels ↑ IgG and IgA ↓ Serum total lipids, Cholesterol, ↓ ALT, AST, Creatinine, Blood urea nitrogen	Omar et al. (2022)
bLF	Pre-weaned calves	30 mL of distilled water with 3 g of lactoferrin for 10 days	↓ Diarrhea ↓ Mortality	Habing et al. (2017)
LF	Holstein–Friesian calves	0.54 g powder mixed with 10 g of dry milk replacer	↑ IgG ↓ Diarrhea ↑ Weight gains	Prenner et al. (2007)
LF	Preweaning calve	1 g/d	↓ Bacterial diarrhea ↓ Intestinal inflammation ↑ Growth performance	Ma et al. (2024)
bLF	Dairy Cattle	1.5 g/day	↑ Feed efficiency and weight gain ↑ Immune response ↓ Mastitis incidence ↓ Somatic cell count ↑ Improved udder health	Khan et al. (2024)
LF	Dairy Cow	1.8–3.6 g	↑ Antimicrobial and antiviral properties ↑ Improve intestinal health ↑ Intestinal proliferation & differentiation ↑ Absorption of essential minerals	Lönnerdal et al. (2011)
LF	Dairy herd	10 g/d	↓ Mortality and morbidity ↑ Growth, feed intake, milk production	Ashraf et al. (2023), El-Sharawy et al. (2024) and Saeed et al. (2023)
LF	High milk-producing cattle	0.67, 1.67 and 2.67 mg/ml	↓ Mastitis ↓ Antibiotics load	Gomes and Henriques (2016)
bLFc	Lactating dairy goats	100 mg/kg/day	↓ Mastitis ↓ Oxidative stress ↓ Milk somatic cell count ↑ IgA	Muhammad et al. (2024) and Shao et al. (2021)
Bovine lactoferricin BLFc	Lactating dairy goats	100 mg/kg/day (LF-1) or 200 mg/kg/day (LF-2) 60 ± 10 days	↑ Serum Fe ↑ Total antioxidant (T-AOC) ↑ Immunoglobulin A (IgA) ↓ Malondialdehyde (MDA) ↓ Ruminal fluid pH	Shao et al. (2021)
LF	Dairy goats	100–200 mg per day	↑ Nutrient intake, digestibility, ↑ Ruminal fermentation, & growth performance	Buranakarl et al. (2020)

Table 1 (continued)

Lf Type	Species	Dose	Overall performance	References
bLF	dairy goat	200 mg/kg/day	↓ Oxidative stress ↑ Improve ruminal microflora ↑ Immune status	Lönnerdal et al. (2011) and Tomita et al. (2009)
LF	Egyptian Baladi goats	200 mg per day/goat	↑ Daily weight gain (DWG) ↑ Hemoglobin concentration, ↑ Total leukocyte count & various white blood cell	El-Sharawy et al. (2024)
		50 mg per day/goat	↑ Total protein, albumin, and creatinine levels	
bLF	Weaning piglets	Basic diet + 3 g/kg bLF for a day 7 and 14	↑ Immunity ↑ Ratio of villus height/crypt depth at the small intestinal mucosa ↑ Growth performance	Ma et al. (2023)
bLF	Pig	2 ml per piglet/day then on the 7 th day	↑ Growth performance ↑ Antioxidant activity ↑ Gut health	Lönnerdal et al. (2011) and Mehra et al. (2021)
bLF	Pig	100 mg/kg	↓ Intensity of diarrhea ↑ Immunity ↑ Intestinal morphology ↑ Barrier function ↓ Lipid peroxidation	Wang et al. (2007) and Chen et al. (2023)
rhLF	Pig	20 mg/g	↓ Intestinal inflammation ↑ Growth of lymphocytes ↑ Immunoglobulins (IgG, IgA, IgM) ↑ Interleukin-2 (IL-2)	Cooper et al. (2014)
LF	Gilts and lactating piglets	1g LF /day (treatment group)	↑ Milk production ↑ Levels of serum IgA	Jahan et al. (2017)
LF	Sheep	1.5 g per 12 h for 30 days	↑ Antibody response ↓ E. coli O157:H7 ↓ Bacterial colonization	Yekta et al. (2011)
Bovine lactoferrin (bLF)	Ossimi lambs	0.5 g /head orally twice daily for 30 consecutive days	↑ Serum catalase, Nitric oxide, GSH ↓ MDA level ↑ Tollip, TLR4, IL-5 and IL-6 gene expression	El-Ashker et al. (2018)
bLF	Ghezel lamb breed	0.25 and 0.50 g/day/head 56 days of experiment	↓ *Escherichia coli* ↑ Plasma iron concentration	Mallaki et al. (2021a)
LF	Karadi male lamb	1500 mg LF per week	↑ RBC, Hb, WBC and GOT	Abd and Kamal (2020)
LF	Young lambs	50–80 mg/kg/day	↑ Immune response ↑ Improved gastrointestinal health ↑ Growth and development ↑ Performance and health	Mukasa-Mugerwa and Lahlou-Kassi (1995) and Mallaki et al. (2021b)

Table 1 (continued)

Lf Type	Species	Dose	Overall performance	References
LF	Rabbit neurosphere culture	166 mg/kg bw/day for 14 days	↑ Neurite length ↓ IUGR-induced alterations on neuronal development	Kühne et al. (2023)
hLF	Rabbits	0.125 mM	↓ Infection of *Shigella flexneri* ↓ Inflammatory intestinal disease	Gomez et al. (2002)
rh-LF	Timed pregnant New Zealand White Rabbits	5mg/body	↑ Survival rate ↓ Fetal death ↓ Stillbirth and neonatal death ↓ Cervical infection	Kolesnikov et al. (2024)
LF	Farmed fish	600 mg/kg diet for 30 days	↑ Health and productivity ↓ Diseases	Chakraborty et al. (2014)
bLF	Aquatic animals	1200 mg/kg diet	↑ Host protection against infections ↑ Productive performance	Wakabayashi et al. (2006)
LF	Fish	800 mg/kg	↑ Innate immune response ↑ Fight against pathogens ↑ Promote overall health	Lönnerdal et al. (2011) and Harikrishnan et al. (2011)

performance and significantly reduced the embryo mortality in pregnant goats (Abdou et al. 2014). The goat kids were fed Lf as a supplement for a period of two weeks, which resulted in enhanced health and performance (Abdou et al. 2014). Moreover, (Isobe et al. 2020) reported similar findings, and suggested that dietary LF significantly reduced the mortality and morbidity in young kids, in addition to improved body weight, average daily gain, and food intake.

Beneficial impact on sheep

Emerging evidence suggests that the incorporation of LF into the diet of sheep can yield profound benefits, ranging from enhanced immune response to improved gastrointestinal health. Weaning is a critical period in the life of young lambs, as it can impact their subsequent growth and development (Mukasa-Mugerwa and Lahlou-Kassi 1995). The supplementation of bovine LF and probiotics has been shown to have a positive effect on the performance and health of young lambs (Mallaki et al. 2021b).

Lamb diet incorporated with LF, significantly reduced the infection rate by stimulating the passive immune functions to enhance the IgG level (Gokce et al. 2014). Similarly, another study demonstrated that LF fed to pre weaned lambs effectively reduced the morbidity, mortality and culling rate (Dunière et al. 2022). LF also reduces the severity of infection and accelerates recovery, particularly in animals experiencing diarrhea, which is prevalent among lambs (Dunière et al. 2022). Furthermore, the inclusion of Lf is a beneficial dietary choice for reducing iron deficiency in lambs (Carnicelli et al. 2021). It was reported that the dietary addition of folic acid in sheep feed resulted in elevated the production of LF in their milk, and induced positive impact on the growth and development of lamb by improving the immune response against bacteria and viruses, leading to increased survival rate (Wang et al. 2020).

Beneficial impact on dairy animals

Dairy animals are an essential part of the agricultural industry, providing a valuable source of milk and other dairy products. Among the various bioactive components found in dairy products, LF and lactoferricin have garnered significant attention due to their potential health benefits (Lönnerdal et al. 2011; Masood et al. 2011; Wakabayashi et al. 2006). Lactoferricin, a peptide derived from the cleavage of LF, has also been studied for its biological activities (Lönnerdal et al. 2011). The beneficial effects of lactoferrin and lactoferricin in dairy animals have been extensively explored in dairy animals and presented in Table 1. These compounds have been shown to possess antimicrobial and antiviral properties, helping to protect dairy animals from various infectious diseases (Lönnerdal et al. 2011). Additionally, LF have been associated with improved intestinal health in dairy animals. These compounds have been found to regulate intestinal proliferation and differentiation, as well as enhance the absorption of essential minerals, such as iron (Lönnerdal et al. 2011).

Earlier studies, reported that the addition of LF to the diet of dairy cattle enhances growth, feed intake, milk production, and considerably reduces mortality and morbidity in the dairy herd (Ashraf et al. 2024; Hussain et al. 2024). Mastitis is a most important problem faced by the dairy industry, particularly in high milk-producing breeds. Antibiotics are often used to treat mastitis, but their presence in milk is undesirable. Numerous studies indicate that LF is an effective therapeutic option to control the mastitis (Shimazaki and Kawai 2017a, b). Similarly, another study reported the synergistic effect when using LF in combination with antibiotics and effectively treat the mastitis in dairy cattle (Gomes and Henriques 2016).

Calves are more susceptible to infection compared to dairy cattle. It is imperative to provide a balance diet, along with appropriate feed supplements to ensure the proper growth and development particularly in weaning period. LF could be an ideal choice used to stimulate the growth of young calves during entire period of weaning. Previously it was reported that the addition of LF in the diet of young calves, significantly improved the average daily gain (ADG), increased dry matter intake, decrease in the weaning age and improves health status (Joslin et al. 2002). Similarly, another study found that dietary LF (1 g/d) combined with milk replacer improve FCR, increased average daily gains, better fecal scores, and reduced morbidity in pre-weaned calves (Robblee et al. 2003a, b; Cowles et al. 2006). In addition, dietary administration of LF, effectively increased the leukocytes population in peripheral blood and elevate the expression level of mRNA of numerous interleukins (IL), including IL-1β, IL-8, IL-10, and interferon gamma (IFNγ), in calves (Prgomet et al. 2007). Furthermore, oral supplementation of LF, stimulated the immune function by elevating the serum IgG level and increase size of Peyer's patches in the ileum to support digestion and absorption of nutrients (Mehra et al. 2022). In conclusion, the existing research suggests that LF and lactoferricin showed significant positive impact on the health and well-being of dairy animals. The antimicrobial, immunomodulatory, and intestinal-enhancing properties of these compounds make them potential targets for further investigation and potential applications in dairy animal production and health management (Arshad et al. 2018; Lönnerdal et al. 2011).

Beneficial impact on piggery

The pig industry, like other food-producing animals, is highly sensitive to dietary factors, making supplementation essential for optimizing the production. Bovine lactoferrin (bLF) has been found to be a promising supplement in the pig industry, with numerous studies demonstrating its beneficial effects on growth performance, antioxidant activity, and gut health (Lönnerdal et al. 2011; Mehra et al. 2021). Wang et al. (2007), reported that bLF supplementation improved growth performance and enhanced antioxidant enzyme activity and mRNA levels, while also reducing lipid peroxidation in pigs. Similarly, another study found that bLF, supplementation in weaning piglets improved growth performance, reduced the intensity of diarrhea, enhanced immunity, intestinal morphology, barrier function, and intestinal microbiota balance (Chen et al. 2023). The biological activities of bLF, are diverse and well-documented. LF has been shown to have antibacterial and antiviral effects, regulate immune function, stimulate intestinal proliferation and differentiation, and facilitate iron absorption (Mehra et al. 2021). Additionally, bLF has been found to have anti-inflammatory, anti-carcinogenic, and antioxidant properties (Mehra et al. 2021).

Previously, it was demonstrated that pig fed diet containing recombinant human lactoferrin (rhLF) or human lysozyme (hLZ), diminished intestinal inflammation. (Cooper et al. 2014). Similarly, the LF supplementation improves the growth of lymphocytes in the peripheral blood and spleen, upregulated the levels of immunoglobulins (IgG, IgA, IgM), interleukin-2 (IL-2), and serum iron, and stimulate the immunological activities in young piglets in weaning stage (Shan et al. 2018). Additionally, dietary LF fed during pregnancy and lactation in gilts had a substantial positive effect on milk production and elevated the levels of serum IgA in both the gilts and lactating piglets (Jahan et al. 2017). Conclusively it was suggested that LF supplementation had positive effect on the pig health and performance.

Beneficial impact of aquaculture

The aquaculture sector is now facing difficulties in controlling diseases and achieving sustainable output. However, the use of bioactive substances such as LF shows potential in enhancing the health and productivity of farmed fish (Chakraborty et al. 2014). LF, a multifunctional glycoprotein found in milk, has garnered significant attention in the field of aquaculture due to its potential to improve the health and productivity of farmed fish (Wakabayashi et al. 2006). Furthermore, studies have demonstrated that oral administration of bLF significantly enhanced host protection against infections and promoted productive performance of a wide range of aquatic animals. The use of LF in aquaculture has the potential to offer numerous benefits, particularly in the context of disease management and enhancing the overall health and well-being of farmed fish. The antimicrobial activity of LF, further promoted to use as an effective substitute to traditional antibiotics, potentially reducing the risk of antibiotic resistance in aquaculture environments (Lönnerdal et al. 2011). Additionally, its immunomodulatory effects may strengthen the fish's innate immune response, improving their ability to fight against pathogens and promote overall health (Lönnerdal et al. 2011). However, the efficacy of LF supplementation in fish and aquaculture remains an active area of research, with the need for further elucidation of the underlying mechanisms and optimal dosage regimens (Tomita et al. 2002). The potential use of LF and other phytochemicals as feed additives has been considered as a practical method to regulate the innate and adaptive immune systems of farmed finfish and shellfish (Harikrishnan et al. 2011). Furthermore, the advancement of LF-based treatments and the investigation of their modes of operation might have significant consequences for the future of environmentally-friendly fish farming.

Conclusion and future prospects

Lactoferrin showed the promising potential to enhance the nutritional and health profiles of food-producing animal. These benefits translate into improved animal health, reduced reliance on antibiotics, and enhanced food safety, addressing critical concerns in modern animal husbandry. Incorporating LF into animal diets not only promotes growth and productivity but also contributes to the overall well-being of livestock. The use of LF as a natural bioactive component aligns with consumer demand for more sustainable and health-conscious food production practices. This approach supports the development of functional foods and nutraceuticals, offering a strategic avenue to fortify animal-derived products with additional health benefits for humans. Despite the promising results, further research is necessary to optimize LF application methods, dosages, and delivery systems to maximize its benefits. Investigating species-specific responses and long-term effects will be crucial in solidifying LF's role in animal nutrition and health. Ultimately, LF stands as a valuable addition for improving the sustainability and safety of food producing animals.

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Data availability Since no new data were created by the authors, data sharing is not applicable regarding their own research results. Raw data on search criteria used for building the review, as well as the excluded material, will be available upon reasonable request to the corresponding author.

Declarations

Conflict of interest The authors declare no conflict of interest.

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