



**International Journal of Biology, Pharmacy
and Allied Sciences (IJBPAS)**

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

EXPLORING THE DIVERSE BIOMEDICAL APPLICATIONS OF LACTOFERRIN

SRINIVASA RAO Y, SATYALAKSHMI S, SARANYA P*, KAMALA KUMARI PV

Department of Pharmaceutics, Vignan Institute of Pharmaceutical Technology, Near VSEZ,
Duvvada, Visakhapatnam-530049

*Corresponding Author: Saranya P: E Mail: lakshmisiragam48@gmail.com

Received 25th July 2024; Revised 8th Sept. 2024; Accepted 1st Oct. 2024; Available online 1st Oct. 2025

<https://doi.org/10.31032/IJBPAS/2025/14.10.9461>

ABSTRACT

Lactoferrin, a potential multifunctional glycoprotein that is widely found in milk from mammals and other mucosal secretions, has attracted a lot of interest in biomedical research. The goal of this review is to present a thorough summary of lactoferrin's biological uses, including its function in immunomodulation, antimicrobial activity, anti-inflammatory qualities, and potential future applications in cancer treatment. Studies upon lactoferrin potential in biomedicine were searched from PubMed, Google scholar databases between 2010-2023 and studied. A total of 30 articles emphasizing the chemical and biological properties of lactoferrin were examined. The anticancer effect of lactoferrin has also been studied in different cell lines. Because of its well-established immunomodulatory properties, it has strengthened both innate and adaptive immune responses, lactoferrin is a viable option for enhancing immune system performance and fending off infections. Furthermore, by controlling immune cell activation, reducing inflammatory signalling pathways, and modifying cytokine production, lactoferrin demonstrates anti-inflammatory qualities that point to its potential use as a treatment for inflammatory diseases such as sepsis, rheumatoid arthritis etc. Lactoferrin's anticancer potential has also been revealed by recent studies, which clarify how it might prevent the growth of cancer cells, trigger apoptosis, stifle angiogenesis, and improve the effectiveness of traditional cancer treatments. This research works done on various cell lines like Hs578T,

MDA-MB-231, T47D, MCF-10-2A etc, were searched and studied. Despite the enormous biological potential of lactoferrin, more investigation is required to clarify its modes of action, maximize its therapeutic uses, and confirm its clinical efficacy.

Keywords: Lactoferrin, Glycoprotein, Anti-cancer activity, Antimicrobial, Anti-inflammatory

INTRODUCTION

With a high degree of species homology, lactoferrin (Lf) is an 80 kDa glycoprotein that binds iron and has roughly 700 amino acids. It is categorized chemically as a protein that may bind iron ions and belongs to the transferrin family; in fact, it shares a great deal of similarities with serum transferrin. In 1939, LF was initially discovered in the milk of cows. In 1960, LF was extracted from human milk. As of right now, we know that the epithelial cells of a wide variety of mammalian species, including humans, cows, goats, horses, dogs, and several rodents, produce lactoferrins (Lfs) with a high degree of homology; in fact, the structural similarity between human and bovine Lfs is approximately 70%, while the structural similarity between chimpanzee and human Lfs is almost 97%. The number of amino acids in human and cow Lfs is about equal; that is, 691 amino acids in human Lf and 696 amino acids in cow Lf.

A variety of mammalian secretions, including colostrum, milk, tears, saliva, semen, nasal secretions, bronchial secretions, bile, gastrointestinal fluids,

pancreatic secretions, urine, vaginal fluids, and other mucosal secretions, are known to contain lactoferrin. These epithelial cells of various body organs also produce lactoferrin. With a projected value of USD 692.6 million in 2022, the global lactoferrin market is anticipated to grow at a compound annual growth rate (CAGR) of 9.98% to reach USD 1225.65 million by 2028 [1]. Like transferrin and serum iron transporter, lactoferrin is an iron-binding protein that serves multiple purposes within the transferrin family.

Structure

LF has a molecular weight of roughly 78 kDa and roughly 700 amino acid residues. Human lactoferrin contains 691 amino acids, whereas bovine lactoferrin (bLF) has 696. It has a reasonably high isoelectric point ($pI = 8.7$). The structure of LF is largely influenced by its iron saturation. The two N- and C-terminal lobes of each lactoferrin molecule are connected by a helix. Parts N1 and N2 or C1 and C2 make up each lobe. There are locations on both lobes where sugar residues can be attached and iron can be bound. These homologous

lobes can connect one iron atom to each other.

The quantity of bonded iron atoms determines the classification of the various kinds of LF. The type of LF known as holo-LF attaches iron at both lobes, while apo-LF has no iron at all. Additionally, there exist intermediate forms in which iron is connected to just one lobe. The amount of iron atoms that are linked to one another affects the cohesiveness of LF, making it more resistant to heat and proteolysis. The more iron atoms present in LF, the more

cohesive it is. The iron-binding site markings on holo- and apo-LF forms are displayed in **Figure 1**. There are many glycosylation isoforms of LF. The number of N-linked glycosylation sites varies depending on the species; in fact, human lactoferrin has three possible glycosylation sites, while bovine lactoferrin has five [2, 3]. Lactoferrin is known to be present in the milk of many species such as human, pig, horse, cow, buffalo, sheep, goat, camel, mouse and elephant. **Table 1** describes the sources of lactoferrin.

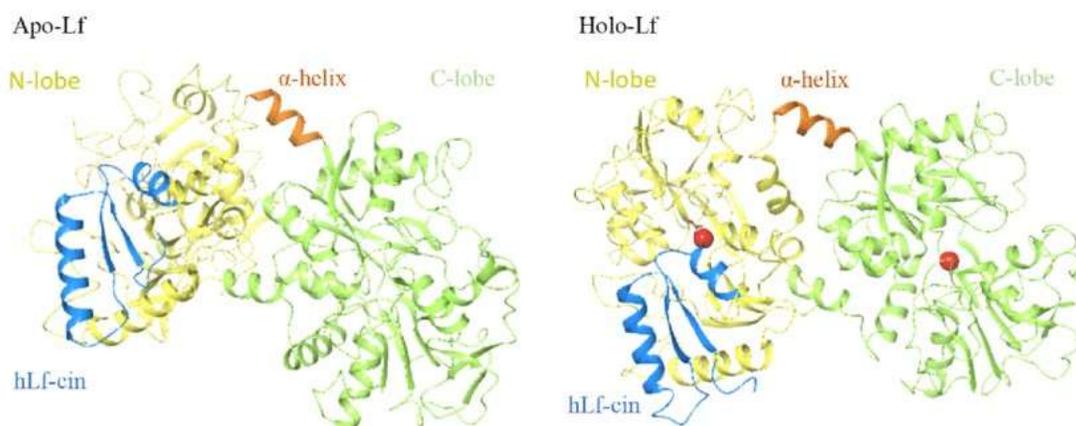


Figure 1: Lactoferrin structure

Table 1: Species from where lactoferrin is identified

Order	Species	Source of lactoferrin	References
Primates	Humans	Colostrum, milk, tears, saliva, bile/pancreatic secretions, urine, granules of neutrophils	[4,5,6,7,8]
	Rhesus monkey	Milk	[7]
	Patas monkey, macaque, baboon, orang-utan	granules of neutrophils	[6]
Carnivorous	Dog, bear, tiger, domestic cat, otter,	granules of neutrophils	[6,8]
Rodents	Rat, hamster, aguti.	granules of neutrophils	[6]
	Mouse, guinea pig	Milk, granules of neutrophils	[6]
Lagomorpha	Rabbit	granules of neutrophils	[6]
Artiodactyla	Sheep buffalo, camel	Milk	[9,10]
	Deer	granules of neutrophils	[4,6]

	Cow, goat, pig	Milk, granules of neutrophiles	[6]
Perissodactyla	Horse	Milk, granules of neutrophiles	[6]

Extraction of lactoferrin

Methods including salt extraction, chromatography, and membrane filtering can be used to separate bovine lactoferrin from raw milk, colostrum, or whey. Transgenic organisms can also be used to manufacture lactoferrin as a recombinant protein from a range of species, including humans [11].

Applications of lactoferrin

A multitude of beneficial qualities of LF are shown in humans, including anti-inflammatory, antibacterial, antiviral, immunomodulatory, antioxidant, and antitumor effects (**Figure 1**). Fresh pasteurized cow milk contains a protein complex called lactoperoxidase (LF), which can be used to defend human cells against COVID-19, according to research by the pharmaceutical company Quantec in New Zealand. Antibacterial, anti-inflammatory, and antioxidant properties are exhibited by the proprietary defence protein IDP [12]. Tissue engineering has also discovered uses for LF. LF also possesses anti-allergic properties [13]. When LF is administered, less allergic skin reactions, atopic keratoconjunctivitis, and hen's egg albumin-induced pleuritis occur. **Figure 2** describes the pharmacological applications of lactoferrin.

Anti-bacterial activity

Lactoferrin's antibacterial effectiveness against both Gram-positive and Gram-negative bacteria, particularly prevalent drug-resistant pathogens, has been extensively demonstrated both in vitro and in vivo. There are two primary pathways that lactoferrin uses to drive its antibacterial action. The first involves sequestering iron from infection sites, which has the bacteriostatic effect of depriving germs of this nutrition. The second process involves the direct interaction between the infectious bacteria and the lactoferrin molecule. Gram-negative bacteria's outer membrane is destroyed by the interaction between lactoferrin and lipopolysaccharide. Certain bacterial, viral, fungal, and parasitic surfaces may interact with positively charged amino acids in lactoferrin to produce anionic compounds that can lyse cells. Most significantly, lactoferrin is an element of the first immune defence system and a part of the human innate nonspecific immune system. It can also modulate innate immunity. The ability of lactoferrin's positive charge to bind to negatively charged molecules on the surface of different immune system cells has been identified through studies. Cellular reactions including activation, differentiation, and proliferation

are thought to be triggered by this combination of factors through signalling pathways. In addition to boosting skin immunity and reducing allergy symptoms, lactoferrin also induces systemic immunity [14-17].

Anti-fungal activity

Based on preliminary studies conducted on *Candida* species, Lf's antifungal characteristics originate from its ability to sequester iron, which has a fungistatic effect and stops the growth of both *Candida* and *Cryptococcus*. By adding iron, this effect can be mitigated. Lf's in vivo antifungal activity may involve iron sequestration, as demonstrated by the significance of apo-Lf's Fe^{3+} sequestration for host defence in *Aspergillus fumigatus*. More recent study suggests that the principal iron-independent antifungal mechanism of levofloxacin (Lf) is caused by direct interaction between Lf and the fungal cell surface, leading to membrane breakdown and leakage. Lf changes the permeability of the cell surface in *Candida albicans*, *Candida krusei*, and *Cryptococcus neoformans*, which results in cell death, according to supernatant protein tests and propidium iodide staining [18].

A major public health concern globally is the rising frequency of *Candida*-caused vulvovaginitis, given the rise in medical costs and the mortality rate among

immunocompromised individuals. By altering the cell wall and causing surface blebs that cause cell death, Lf, together with lactoferricin, lactoferrampin, and the N-terminal region, has shown effectiveness against numerous species of *Candida*. Similarly, Lf has been used in conjunction with multiple antifungal drugs to boost its efficacy in treating different yeasts, such as *Cryptococcus*, *Candida dubliniensis*, *Candida albicans*, and *Candida glabrata*. Likewise, enhanced expression of Lf against *Candida albicans* was seen in *Lactobacillus casei*, a component of the vaginal microbiome [19, 20]. Therefore, Lf has been observed to have well-defined antifungal capacities, which opens the opportunity for new lines of research in this field.

A synergistic antifungal effect has been shown when fluconazole is coupled with a variety of *Candida* species, including fluconazole-resistant strains of *Candida albicans*, *C. glabrata*, *C. krusei*, *C. parapsilosis*, and *C. tropicalis*. These yeasts were observed to be killed at sub-inhibitory concentrations when preincubated with hLf prior to introducing fluconazole, but not when fluconazole was introduced first. This suggests that hLf is in charge of starting candidacidal activity, while fluconazole acts in concert with it at a later stage [21].

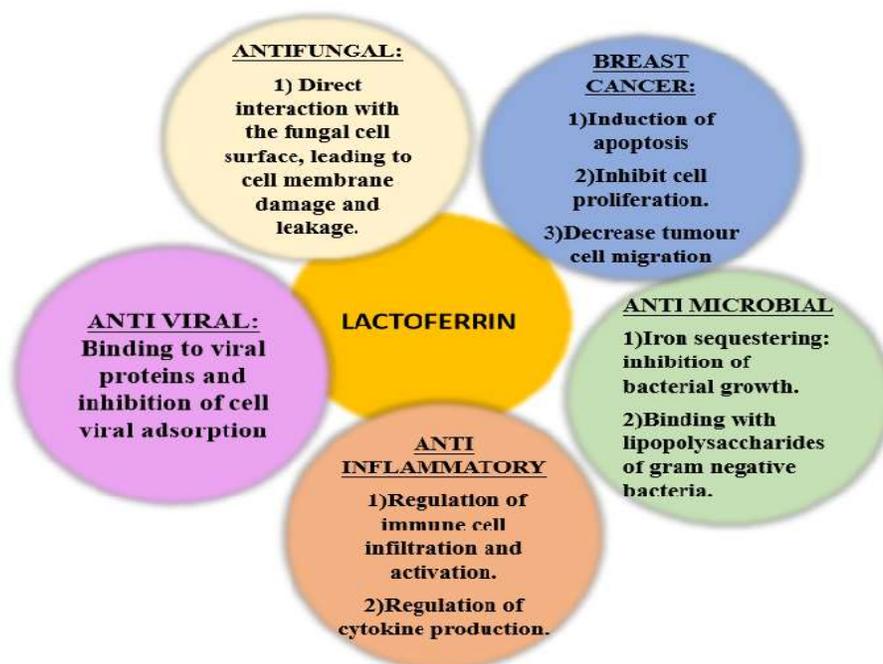


Figure 2: Pharmacological applications of lactoferrin

Anti-inflammatory activity

Lactoferrin's ability to interact with particular cell surface receptors on epithelial cells and immune system cells, as well as its ability to bind to pathogen-associated molecular patterns (PAMPs), which are primarily recognized by Toll-like receptors (TLRs), are related to its immunomodulatory and anti-inflammatory activity. Lipopolysaccharide (LPS) from Gram-negative bacteria has been shown to bind in this way. It has been noted that there is a contact between some TLRs and Lf, mediated by the molecule's glycans, allowing for an immunomodulatory impact. The processes of lactoferrin's interaction with different receptors are closely related to its glycan conformation. Additionally, Lf affects the antigen-presenting cells' (APCs)

differentiation, maturation, activation, migration, proliferation, and function. These cells include neutrophils, B cells, monocytes/macrophages, and dendritic cells. Macrophages and dendritic cells can bind leukemia factor (Lf) through interactions with surface receptors that cause the leukemia factor to mature and become functional. Additionally, the leukemia factor's effect on monocyte/macrophage activation and differentiation helps to lower the pro-inflammatory profile.^[22] However, Lf has the ability to lower the inflammatory response in a variety of diseases. By controlling the activity of Th1 and Th2 cells, it promotes the Th1 response in allergic rhinitis by producing IL-2 and IFN- γ and suppressing the Th2 response inflammatory

mediators IL-5 and IL-7, T-cell receptor cross linking so, inhibition of T-cells occur. Lf enhances reduction of TNF's and infiltration of CD4 cells [23].

Some skin care products like creams and serums contain lactoferrin due to its antimicrobial and anti-inflammatory property as these products may help reduce inflammation and protect from oxidative stress and promote overall skin health.

Anti-viral activity

Human norovirus, human papillomavirus, Zika, HIV, chikungunya, influenza virus (H1H1, H3N2), and human papillomavirus have all been shown to be susceptible to the antiviral activity of Lf. Due to its documented impact on SARS-CoV-1 internalization as well as its capacity to reduce the inflammatory response, Lf may also play a preventative role in SARSCoV-2 infection. Lactoferrin has the ability to prevent SARS pseudo virus infection, according to certain research. Lf appears to be a very promising preventive measure, but further research is required to confirm the behaviour of the novel coronavirus and its subsequent treatment. In this sense, it is thought that breast milk, which contains significant amounts of Lf, can confer important protection against the new coronavirus SARS-CoV-2 on the newborn. Because it interacts with viral hemagglutinin, which can enable Lf to

breach the viral envelope, it has antiviral effect against certain receptors, including heparan sulphate glycosaminoglycan cell receptors. Some reports suggested that changes in the molecule's glycosylation could affect the signalling intensity of different toll-like receptors, such as TLR-3 and TLR-8, which are involved in the recognition of viral particles. This could provide important insights into the nature of these interactions. To gain a better understanding of the glycoprotein antiviral activity, numerous questions have to be addressed [24]. To improve lactoferrin's stability, bioavailability, and targeted distribution to particular tissues or cells, researchers have created novel delivery vehicles, including hydrogels, liposomes, and nanoparticles. Lactoferrin-based medicines can be optimized for a range of biological uses with the help of these delivery systems.

Special focus of lactoferrin for its anticancer potential on diverse cell lines

According to the World Health Organization, cancer is one of the leading causes of morbidity and mortality in developed and underdeveloped countries and is the second leading cause of death globally [25]. The anticancer effects of Lf have been extensively studied, and it has been observed that in the presence of Lf, different cancer cells suffer significant

damage, such as cell cycle arrest, damage to the cytoskeleton, and induction of apoptosis, in addition to a decrease in cell migration. Even though this damage has been observed, the mechanism that underlies these effects remains to be elucidated.

a) Lactoferrin in breast cancer

A natural bridge between iron and estrogen is Lf. As thyroid steroid receptors modulate the expression of the Lf gene, this gene is sensitive to hormones, so Lf may be involved in hormone dependent cancers, such as breast cancer, where its expression seems to be progressively inhibited. On the other hand, in non-hormone dependent cancers like triple negative breast cancer, where hormone-targeted therapies are not available and the prognosis in general is not favourable. Lf could also be a potential alternative treatment as it has been shown to have an *in vitro* cytotoxic effect on human triple negative breast cancer cells. In this sense, we previously reported that recombinant human lactoferrin from *Pichia pastoris* has an apoptotic effect and causes cell cycle arrest in the S phase in non-metastatic and metastatic MDA-MB-231 cells. This seems to extend to Lf from other species; bovine lactoferrin (bLf), both in its free-iron form and in its iron-saturated form, has been used successfully in the induction of cytotoxicity and the reduction in cell proliferation of MDA-MB-231 and MCF-7

human breast cancer cells. In the same way, both forms of Lf can modulate some apoptotic molecules, including p53, and completely inhibit the expression of surviving, a multifunctional protein involved both in the apoptotic inhibition and in the regulation of the cell cycle, which promotes resistance to cancer cells in chemotherapy and radiotherapy. On the other hand, it has been reported that treatment with nanoparticles of calcium phosphate loaded with bovine saturated Lf is able to decrease the size of the tumours in murine models. Alternatively, specific bioactive peptides from Lf have also been used to test their antitumor effect, such as lobe C from hLf, which was used against breast cancer, promoting cellular apoptosis and generating significant growth arrest in MDA-MB-231 cells. These data indicate that both bovine and human Lf has high efficacy in the control of tumour proliferation in breast cancer [26].

A contrary study showed that treatment of human breast cancer cell lines with bovine Apo-lactoferrin increases apoptosis and decreases cell migration [27]. But bovine lactoferrin does not bind to the endothelin 1 promoter region. Hence, ET-1 is a lactoferrin-inducible gene and only the holo form of lactoferrin is responsible for the downregulation, as well as increased invasiveness, in breast cancer cells. It was

also found that the levels of lactoferrin and ET-1 were increased in TNBC specimens as compared to those in the control ER +/PR+ breast tumors [28].

Bovine Lf (bLf) preferentially induces apoptosis in the highly metastatic breast cancer cell lines Hs 578T and MDA-MB-231, which display a prominent localisation of V-H⁺-ATPase at the plasma membrane, but not in the lowly metastatic T-47D or in the non-tumorigenic MCF-10-2A cell lines. Also demonstrated that bLf decreases the extracellular acidification rate and causes intracellular acidification in metastatic breast cancer cells and, much like the well-known proton pump inhibitors concanamycin A and bafilomycin A1, inhibits V-H⁺-ATPase in sub-cellular fractions. These data further support that bLf targets V-H⁺-ATPase and explain the selectivity of bLf for cancer cells, especially for highly metastatic breast cancer cells [29].

The effects of bovine milk lactoferrin on human breast cancer HS578T and T47D cells were studied. The cells were either untreated or treated with lactoferrin concentrations ranging from 0.125 to 125 μ m. Lactoferrin decreased the cell viability of HS578T and T47D by 47 and 54%, respectively, and increased apoptosis about 2-fold for both cell lines. Proliferation rates decreased by 40.3 and 63.9% for HS578T

and T47D, respectively. For the T47D line, cell migration decreased in the presence of the protein. Although the mechanisms of action are not fully known, the results gathered in this work suggest that lactoferrin interferes with some of the most important steps involved in cancer development [30].

b) Lactoferrin in leukemia

Merely 1% of cancer patients globally are identified as having childhood cancer. There is little control over this illness in children. The malignancy that most commonly affects youngsters is leukaemia. The survival rate of children with leukemia is being improved by treatments for acute myeloid leukemia and acute lymphoid leukemia; nevertheless, long-term effects may include cardiovascular disorders, which raise the risk of death. Since Lf has been demonstrated to cause apoptosis in leukemia, it may serve as a substitute that reduces adverse effects in patients. Furthermore, it was shown that the hLf fragment PRF peptide possesses anticancer action as well. This peptide demonstrated necrotic action by inducing cell death in leukemia cells. Additionally, PRF peptide caused a G0/G1 cell cycle stop. Lactoferricin B, another peptide derived from bLf, has a strong cytotoxic effect on T-leukemia cells Jurkat and CCRF-CEM. Additionally, it can boost the expression of caspase-3 in the HL-60 leukemia cell line,

which will facilitate DNA fragmentation and the apoptotic pathway. Lastly, research has demonstrated that breastfeeding exclusively and for an extended period of time can lower an infant's chance of developing childhood leukemia since breast milk contains a variety of immunoprotective substances, such as lactoferrin [31, 32].

c) Cervical cancer

As the fourth most common cause of death for women globally, cervical cancer is also one of the most common cancer forms. Due to limited availability to preventive testing like pap screenings and vaccinations against the human papillomavirus (HPV), which is the cause of cervical cancer, it primarily affects women from developing nations and those with lower socioeconomic status. Radiation therapy, either alone or in conjunction with other techniques like surgery, is one of the most commonly utilized treatments for this kind of cancer; nevertheless, it has been noted that because radiation can lead to recurrence, its effects may be more detrimental than advantageous. In this situation, using possible therapeutic medicines like Lf can help patients experience less collateral risk [28]. Once more, prior research has demonstrated that Apo-Lf, but not Holo-Lf, triggered apoptosis in HeLa cells and altered the expression of proapoptotic genes, suggesting that Lf's effect on iron

metabolism may be related to its anti-cancer action. Proteins like BAX, whose expression rose in the presence of Lf as opposed to Bcl-2 and Mcl-2, which lowered it [30, 33].

The efficacy of hLF on the inhibition of U14 cervical cancer under *in vivo* conditions were investigated. Recombinant adenovirus carrying hLF (Ad-hLF) were constructed. Mice inoculated with U14 cells were randomly allocated to four treatments: i) Phosphate-buffered saline (negative control), ii) Ad-green fluorescent protein (negative control), iii) Ad-hLF (studied) or iv) cyclophosphamide (CTX; positive control). Tumor growth, as well as levels of natural killer (NK) cells, CD4⁺ and CD8⁺ peripheral blood T lymphocyte subpopulations, serum cytokines and vascular endothelial growth factor (VEGF) in tumor tissues were detected. Compared with the negative controls, tumor growth was inhibited by hLF and mice lifespans in the Ad-hLF-treated group were prolonged to reach the levels of the CTX-treated group. The activity of tumor-killing NK cells was upregulated by hLF. Moreover, the number of CD4⁺ and CD8⁺ peripheral blood T lymphocyte subpopulations increased following treatment with Ad-hLF. Treatment with Ad-hLF increased the levels of serum interferon- γ , serum interleukin-2 (IL-2) and tumor necrosis factor- α , and decreased the levels of serum IL-4 in tumor-bearing mice.

The expression of VEGF in tumor tissues was down regulated by hLF. In conclusion, hLF inhibits the growth of U14 solid tumors by modulating the immune response of tumor-bearing mice [33].

Recent ongoing trends in lactoferrin [34, 35]

• Nanotechnology and uses of lactoferrin

Lactoferrin–chondroitin sulfate nano complex (LFCSN) shown increased cytotoxicity and internalization into lung cancer cells (A549) via CD44 and TF receptors.

It was shown that LF-loaded gellan gum nanoparticles were a viable tool for enhancing LF's antibacterial properties and expanding its use as a food guardian. Furthermore, because of its many uses, LF is a prospective active ingredient that can be loaded or adsorbed onto NPs to generate stable, regulated surface NPs and increase the effectiveness of specific compounds.

• Microbiota modulation and gut health

Lactoferrin's impact on gut health and its relationship with the gut microbiota are subjects of increasing research. According to recent studies, lactoferrin may influence the composition of the gut microbiota, support a healthy intestinal environment, and treat gastrointestinal conditions like

irritable bowel syndrome and inflammatory bowel disease.

• Immunomodulation and immune support

Researchers are investigating the potential of lactoferrin's immunomodulatory qualities to boost immune responses and promote immunological health. Lactoferrin's impacts on immune cell activities, cytokine control, and host defence mechanisms are being studied by researchers. These effects may have consequences for vaccination techniques, autoimmune disorders, and infectious diseases.

• Personalized medicine and biomarker discovery

Developments in omics technologies, including proteomics, metabolomics, and genomes, are opening up new avenues for personalized medicine and lactoferrin research biomarker discovery. Lactoferrin is being studied for its potential as a biomarker for a number of illnesses as well as for use in targeted treatment interventions and diagnostics.

• Computational biology and bioinformatics: In lactoferrin research, advanced biological systems are modelled and massive datasets are analysed through the application of computational biology and bioinformatics techniques. Drug research and development procedures are

being sped up by the use of computational techniques to predict lactoferrin interactions, structure-function correlations, and therapeutic targets.

New directions in lactoferrin research are opening up intriguing possibilities for improving our knowledge of the biological actions and potential therapeutic uses of lactoferrin. They also demonstrate the dynamic nature of biomedical science. Further advancements in utilizing lactoferrin's potential to enhance human health and wellness will come from ongoing interdisciplinary collaborations and technical advancements.

CONCLUSION

As a result, lactoferrin is shown to be a flexible bioactive molecule with great promise for use in biomedicine, spanning from the treatment of infections and inflammation to the control of immunological responses and the inhibition of the growth of cancer. And also, some research works were searched and studied on cancer treatment from Pub Med, Google scholar etc. between 2010-2023 and their results were notified. To improve lactoferrin's stability, bioavailability, and targeted distribution to particular tissues or cells, lactoferrin-based formulations such liposomes and nanoparticles have also been produced. To fully use lactoferrin's therapeutic effects and turn them into

successful clinical therapies, more study and clinical studies are necessary.

ACKNOWLEDGEMENT

We express our sincere thanks to Dr. L. Rathaiah, Chairman, Vignan Group of Institutions for providing necessary facilities to carry out the above review.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

CCRF-CEM: Human T lymphoblasts isolated from the peripheral blood of a female; **Hs 578T:** An epithelial cell line isolated from breast tissue from a female breast cancer patient; **MCF-10-2A:** Non-tumorigenic cell line; **MDA-MB-231:** Isolated from a pleural effusion of a breast cancer patient; **SARS:** Severe acute respiratory syndrome; **SARS-CoV-2:** Severe-acute-respiratory-syndrome-related coronavirus; **T47D:** Pleural effusion of a ductal carcinoma of the breast

REFERENCES

- [1] Lactoferrin market size, share & trends analysis report by function (iron absorption, intestinal flora protection), By Application (Personal Care Products, Infant Formula), By Region (North America, APAC, Europe), And Segment Forecasts, 2021-2028. <https://www.grandviewresearch.co>

- [m/industry-analysis/lactoferrin-market](#)
- [2] Moore SA, Anderson BF, Groom CR, Haridas M, Baker EN. Three-dimensional structure of diferric bovine lactoferrin at 2.8 Å resolution. *J Mol Biol.* 1997; 274:222–236.
- [3] Gopinathan J, Hao TN, Cha E, Lee C, Das D, Noh I. 3D printable and injectable lactoferrin-loaded carboxymethyl cellulose-glycol chitosan hydrogels for tissue engineering applications. *Mater Sci Eng* 2020;113:111008.
- [4] Fujishima H, Okada N, Matsumoto K, Shimizu E, Fukuda S, Tomita M. Conjunctival injection reduction in patients with atopic keratoconjunctivitis due to synergic effect of bovine enteric-coated lactoferrin in 0.1% tacrolimus ophthalmic suspension. *J Clin Med.* 2020; 9:3093. doi: 10.3390/jcm9103093.
- [5] Masson PL, Heremans JF. Lactoferrin in milk from different species. *Comp Biochem Physiol B* 1971; 39B:119-129.
- [6] Barton JC, Parmley RT, Butler TW, Williamson S, Mackenzie S, Chandler DB, et al.. Neutrophil lactoferrin content: Variation among mammals. *Anat Rec.* 1988; 221: 567-575.
- [7] Davidson LA, Lönnerdal B. Isolation and characterization of Rhesus monkey milk lactoferrin. *Pediatr Res.* 1986; 20:197-201.
- [8] Berlov MN, Korableva ES, Andreeva YV, Ovchinnikova TV, Kokryakov VN. Lactoferrin from canine neutrophils: Isolation and physicochemical and antimicrobial properties. *Biochemistry.* 2007; 72:445-451.
- [9] Conesa C, Sanchez L, Rota C, Perez MD, Calvo M, Farnaud S, et al. Isolation of lactoferrin from milk of different species: Calorimetric and antimicrobial studies. *Comp Biochem Physiol B Biochem Mol Biol.* 2008;150:131-139.
- [10] Elagamy EI, Ruppen R, Ismail A, Champagne CP, Assaf R. Purification and characterization of lactoferrin; lactoperoxidase; lysozyme and immunoglobulins from Camel's Milk *Int Dairy J.* 1996; 6:129-145.
- [11] Cui S, Lv X, Sun G, Wu W, Xu H, Li Y, et al. Recent advances and prospects in purification and heterologous expression of lactoferrin. *Food Bioengineering.*

- 2022;1: 58-67.
doi:10.1002/fbe2.12003.
- [12] Poti F, Pozzoli C, Adami M, Poli E, Costa LG. Treatments for COVID-19: Emerging drugs against the coronavirus. *Acta Biomed.* 2020;91:118-136.
- [13] Zimecki M, Artym J, Kocieba M, Kruzel ML. Effects of lactoferrin on elicitation of the antigen-specific cellular and humoral cutaneous response in mice. *Postepy Hig Med Dosw.* 2012;66:16-22.
doi: 10.5604/17322693.975145.
- [14] Giansanti F, Panella G, Leboffe L, Antonini G. Lactoferrin from Milk: Nutraceutical and Pharmacological Properties. *Pharmaceuticals (Basel).* 2016;9(4):61. doi: 10.3390/ph9040061.
- [15] Brock J. Lactoferrin: A multifunctional immunoregulatory protein? *Immuno Today.* 1995;16:417-419.
- [16] Lonnerdal B, Iyer S. Lactoferrin: Molecular structure and biological function. *Annu Rev Nutr.* 1995; 15: 93-110.
- [17] Kirkpatrick CH, Green I, Rich RR, Schade AL. Inhibition of growth of *Candida albicans* by iron-unsaturated lactoferrin: relation to host-defence mechanisms in chronic mucocutaneous candidiasis. *J Infect Dis.* 1971;125:539-544.
10.1093/infdis/124.6.539
- [18] Ellepola ANB, Dassanayake RS, Khan Z. Impact of brief exposure to drugs with antifungal properties on the susceptibility of oral *Candida dubliniensis* isolates to lysozyme and lactoferrin. *Med Princ Pr.* 2018;27:523-530.
doi: 10.1159/000493391.
- [19] Fernandes KE, Carter DA. The antifungal activity of lactoferrin and its derived peptides: mechanisms of action and synergy with drugs against fungal pathogens. *Front Microbiol.* 2017;18;8:2. doi: 10.3389/fmicb.2017.00002.
- [20] Lupetti A, Paulusma-Annema A, Welling MM, Dogterom-Ballering H, Brouwer CP, Senesi S, et al. Synergistic activity of the N-terminal peptide of human lactoferrin and fluconazole against *Candida* species. *Antimicrob Agents Chemother.* 2003;47:262-267.
10.1128/AAC.47.1.262-267.2003
- [21] MacManus CF, Collins CB, Nguyen TT, Alfano RW, Jedlicka P,

- De Zoeten EF. VEN-120, a recombinant human lactoferrin, promotes a regulatory t cell [treg] phenotype and drives resolution of inflammation in distinct murine models of inflammatory bowel disease. *J Crohn's Coliti.* 2017;11:1101-1112.
- [22] Scala MC, Sala M, Pietrantonio A, Spensiero A, Di Micco S, Agamennone M, et al. Lactoferrin-derived peptides active towards influenza: identification of three potent tetrapeptide inhibitors. *Sci Rep.* 2017;7:1-11.
- [23] Carthagena L, Becquart P, Hocini H, Kazatchkine MD, Bouhlal H, Belec L. Modulation of HIV binding to epithelial cells and HIV transfer from immature dendritic cells to CD4 T lymphocytes by human lactoferrin and its major exposed LF-33 peptide. *Open Virol J.* 2011;5:27.
- [24] Mph KDM, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin.* 2016; 66:271-289. <https://pubmed.ncbi.nlm.nih.gov/38091520>
- [25] Onishi J, Roy MK, Juneja LR, Watanabe Y, Tamai Y. A lactoferrin-derived peptide with cationic residues concentrated in a region of its helical structure induces necrotic cell death in a leukemic cell line (HL-60). *J Pept Sci.* 2008; 14:1032-1038.
- [26] Richardson A, De Antueno R, Duncan R, Hoskin DW. Intracellular delivery of bovine lactoferrin's antimicrobial core (RRWQWR) kills T-leukemia cells. *Biochem Biophys Res Commun.* 2009;388:736-741.
- [27] Pereira CS, Guedes JP, Goncalves M, Loureiro L, Castro L, Geros H, et al. Lactoferrin selectively triggers apoptosis in highly metastatic breast cancer cells through inhibition of plasmalemmal V-H⁺-ATPase. *Oncotarget.* 2016;7(38):62144-62158. doi: 10.18632/oncotarget.11394.
- [28] Luzi C, Brisdelli F, Iorio R, Bozzi A, Carnicelli V, Di Giulio A, et al. Apoptotic effects of bovine apolactoferrin on HeLa tumor cells. *Cell Biochem Funct.* 2017;35: 33-41.
- [29] Shi H, Li W. Inhibitory effects of human lactoferrin on U14 cervical carcinoma through upregulation of the immune response. *Oncol Lett.*

- 2014;7(3):820-826. doi: 10.3892/ol.2013.1776.
- [30] Duarte DC, Nicolau A, Teixeira JARodrigues LR. The effect of bovine milk lactoferrin on human breast cancer cell lines. *J Dairy Sci.* 2011;94(1):1-12.
- [31] Bruni N, Capucchio MT, Biasibetti E, Pessione E, Cirrincione, S.; Giraud, L.; Antimicrobial activity of lactoferrin-related peptides and applications in human and veterinary medicine. *Molecules.* 2016;21:752.
- [32] Wisgrill L, Wessely I, Spittler A, Forster-Waldl E, Berger A, Sadeghi K. Human lactoferrin attenuates the proinflammatory response of neonatal monocyte-derived macrophages. *Clin Exp Immunol.* 2018; 192:315-324.
- [33] Ha NH, Nair VS, Reddy DN, Mudvari P, Ohshiro K, et al. Lactoferrin-endothelin-1 axis contributes to the development and invasiveness of triple-negative breast cancer phenotypes. *Cancer Research.* 2011; 71:7259-7269.
- [34] Tran TH, Tran PTT, Truong DH. Lactoferrin and Nanotechnology: The Potential for Cancer Treatment. *Pharmaceutics.* 2023;15(5):1362. doi: 10.3390/pharmaceutics15051362.
- [35] El-Fakharany EM, Abu-Serie MM, Ibrahim A. Anticancer activity of lactoferrin-coated biosynthesized selenium nanoparticles for combating different human cancer cells via mediating apoptotic effects. *Sci Rep.* 2023; 13:9579. <https://doi.org/10.1038/s41598-023-36492-8>