Chapter

Medicinal Potential of Camel Milk Lactoferrin

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Abstract

Camel milk is a rich source of protein with well-recognized medicinal properties to treat various diseases. The objective of this work is to understand the role of camel milk lactoferrin in immunomodulation and in disease treatment. It has been found that camel milk lactoferrin is a very suitable nutraceutical agent by virtue of its bioactivity, immuno-compatibility, and safety. It can be used for the treatment of infectious, metabolic, and neurodegenerative diseases, besides cancer. It is a cost-effective biomolecule that also has high relative abundance and bioavailability.

Keywords: camel milk, lactoferrin, medicinal potential, commercial significance, immunomodulatory, anti-microbial, anti-cancer

1. Introduction

The medicinal properties of camel milk have long been recognized, especially in middle eastern countries. Camel Milk is a rich source of active proteins, especially enzymes that have several biological activities including antibacterial, antiviral, immunological, and antioxidant properties. Camel milk has been used to treat many diseases such as Hepatitis, Allergy, Liver, and kidney function, Diarrhea, and Diabetes. Moreover, camel milk has no allergenic properties and can be consumed by lactase-deficient people. Like human milk, camel milk has a high content of lactoferrin and α-lactalbumin but lacks β-lactoglobulin [1]. It differs from cow milk as it has lower fat, cholesterol, and lactose levels, besides this, there is an absence of beta-lactoglobulin and beta-casein. Beta casein is the allergenic component that is present in cow milk but absent in camel milk. Also, it has very low levels of lactose making it consumable by lactase deficient people [2]. It has been noted that despite the lack of refrigeration, camel's milk remains unspoiled for several days. This may be due to the antibacterial activity of certain proteins contained in camel's milk [3]. Furthermore, camel milk proteins are generally pH hydrolysis resistant and thermostable. Lactoferrin is well recognized as an adjunct to anti-cancer standard therapy by virtue of its immunomodulatory activity. It also exhibits immuno-compatibility, bioavailability, safety, relative abundance, and low-cost effectiveness. Moreover, the oral route of administration makes it very easy to be given to patients and it is usually well-tolerated [4]. Numerous studies on camel lactoferrin reported that it has anti-bacterial, anti-fungal, anti-viral, anti-inflammatory, antioxidant, and anti-tumor properties. Camel milk lactoferrin is a molecule that not only boosts the immune system but also acts against cancer. The

objective of this work is to understand the role of camel milk lactoferrin in immunomodulation and in disease treatment [5].

2. Camel milk

Camel milk has been found to be a healthier option for people with diabetes and those with food allergies. Several studies on camel milk have found its positive impact on autism, diabetes, liver disease, jaundice, and even cancer. Camel milk is high in vitamin C, many minerals, and immunoglobulins, which boost the immune system. It is not only a very nutritious dairy beverage but it also innately includes probiotics. Camel milk helps enhance gastrointestinal health besides improving systemic immunity. The drink has a low-fat content (only 2 to 3%, compared to cow milk) and thus is likely to attract more attention of health-aware consumers. In various Middle East countries and an Africa, it is used as a suitable supplement to feed undernourished children because it's similarity with human breast milk [6].

2.1 Medicinal properties of camel milk

Naturally occurring bioactive compounds have contributed effectively to cancer therapeutics, paving a way for better disease management. Camel milk is one such dietary food with immense nutritional and medicinal value. Like human and bovine milk, camel milk also contains numerous proteins such as immunoglobulins, alpha-lactalbumin, lactoperoxidase, casein, lysozyme, lactoferrin, amylase, etc. The major proteins present in camel milk along with their clinical significance have been depicted in **Table 1**. It forms a high nutritional source with low cholesterol, low sugar, high minerals (sodium, potassium, iron, copper, zinc, and magnesium), high vitamins (vitamin C, B2, A, and E), and high concentrations of insulin compared to the ruminant milk [20–22]. Moreover, very recently camel milk casein-derived nanoparticles have been used as carriers for the delivery of sorafenib in hepatocarcinoma cells [23].

2.2 Commercial value of camel Milk

Latest reports suggest that the global camel dairy market reached 2.3 billion US$ in 2020. A total of 2.9 million tons of camel milk production has been recorded annually worldwide [24]. Camel dairy market is expected to reach USD 10.07 billion by 2027 growing at a growth rate of 8.0% in the forecast period 2020 to 2027.

Camel milk is traditionally consumed in either a raw form or in a fermented form. But to cater with preferences of urban populations now manufacturers have stated the production of novel camel milk based food products such as flavored beverages, sweets, chocolates and Ice creams. These products are becoming increasingly popular in nations such as UAE, Saudi Arabia,, Kazakhstan, Algeria, Australia, Morocco, Egypt and India. Its increasing demand has resulted in a wide opportunity for product innovation and generation of new markets. Camel milk products are relatively more expensive than other cattle dairy food items due to its high production costs. In spite of being low in fat, camel milk has a relatively high content of unsaturated fatty acids, which are beneficial for us. It's suitable for lactose-intolerant people. Camel milk is actually considered a super food because of its high mineral and vitamin content. Moreover, its benefits for joint pain and diabetes has also been well documented. It's no wonder then that it's for long been consumed by the

S. No	Clinical condition	Therapeutic molecules in camel milk	Reference
1	Diabetes	Insulin-like molecule	[7]
2	Allergy	Low levels of β-Casein & lack of β-lactoglobulin	[8]
3	Liver and kidney function	Alanine aminotransferase and aspartate aminotransferase	[9]
4	Slimming properties	Low protein content and reasonable cholesterol content	[10]
5	Antitumor activity	Lactoferrin, Lysozyme, Lactoperoxidase	[11, 12]
6	Nutritional supplements	Unsaturated fatty acids	[13]
7	Easy assimilation in Lactase deficient patients	L-lactate	[14]
8	Bone formation	High level of calcium	[15]
9	Diarrhea	High levels of sodium and potassium	[16]
10	Immuno enhancer and antimicrobial activity	Peptidoglycan recognition protein (PRP)	[17]
11	Antibacterial and antiviral activity	N-acetyl-glucosaminidase (NAGase)	[18]
12	Confers special passive immunity	Heavy chain antibodies (HCAb) or variable heavy antibodies (VHH) or nanobodies	[19]

Table 1.
Application of camel milk molecules in treatment of various diseases.

Bedouins (nomadic Arab people) and many other desert communities of the world to face their harsh living conditions.

The dairy market in India reached a value of 13,174 billion INR in 2021. In the coming times, International market analysis research and consulting (IMARC) group expects the market to reach 30,840 billion INR by 2027. This would amount to a compound annual growth rate (CAGR) of 14.98% during the time interval 2022–2027. Actually, despite its availability, India has been late in entering the market scenario. Only in the end of 2016 did the Food Safety and Standard Authority of India (FSSAI) decide the standards for commercialization of camel milk. Notably, while government dairy cooperatives have been slow to respond, some entrepreneurs, interestingly, even from the Raika community of Rajasthan, have taken multiple dynamic initiatives. India's first camel milk brand Aadvik Foods is set to disrupt the dairy and organic milk products market. This New Delhi-based company started its journey in 2016 with just one liter of camel milk. Today, it is procuring around 10,000 liters a month, having sold over 2 lakhs liters over the last three-and-half years.

3. Clinical relevance of lactoferrin

Lactoferrin is a versatile molecule that has been molded by natural selection to be amongst the first line of defense in mammals [25]. As the second most abundant protein

in colostrum, it is responsible for conferring immunity on newborns within the first few weeks of life [26]. Lactoferrin is involved in various physiological functions such as regulating homeostasis and cell proliferation, besides being a very potent antimicrobial agent. It has antibacterial, antifungal, antiviral, antioxidant, immunomodulatory, and anticancer activities [25, 27–29]. During infection and inflammation processes, the lactoferrin concentration increases through the recruitment of neutrophils. The important properties of lactoferrin have been depicted in the flow diagram in **Figure 1**.

Lactoferrin, the natural protein, is proving to be a highly promising bio-drug as an antimicrobial, immunomodulatory, and anticancer agent. According to Cragg *et al.,* over 50% of the drugs in clinical trials for anticancer activity are isolated from natural sources or their ingredients. Several drugs currently used in chemotherapy are isolated from plant species and food sources [30, 31] Lactoferrin is a multi-functional protein with many beneficial properties. It is now recognized as a functional food for several products with commercial and clinical applications [32]. It is widely distributed in all biological fluids and is also expressed by immune cells, which release it under stimulation by pathogens.

The primary function of lactoferrin has been recognized to be in the modulation of the immune responses, besides iron transport, storage, and chelation. Lactoferrin activates immune cells and enhances their proliferation and differentiation. Its potential to perform multiple activities is often attributed to its capacity to bind iron and interact with diverse molecular and cellular components of hosts and pathogens. The multiple functions ascribed to lactoferrin can either be dependent or independent of lactoferrin's iron-binding ability [33]. Furthermore, it is noteworthy that lactoferrin concentrations are locally elevated in inflammatory disorders such as neurodegenerative diseases, autoimmune diseases (e.g., arthritis), and allergic inflammation.

3.1 Lactoferrin as an Immuno-modulator

Lactoferrin is a cell-secreted mediator that bridges innate and adaptive immune responses. For immune-modulatory functions, it interacts with specific receptors of the target cells (either epithelial cells or cells of the immune system) It also can bind to bacterial cell wall LPS. Lactoferrin modulates the activation, proliferation, maturation, differentiation, and migration of immune cells. The functional modulations take place in the T and B cells, neutrophils, monocytes/macrophages, and dendritic cells belonging to the antigen-presenting class of cells. It acts via two mechanisms of intracellular signal transduction, *i.e.,* nuclear factor kappa B and MAP kinase [34–36]. Furthermore, it affects the mechanisms of the innate response, by influencing the activation of the complement system, increasing the NK cell activity, increasing the phagocytic ability of monocytes, and by enhancing their cytotoxicity [37]. There are lactoferrin receptors on many immune cells, so lactoferrin directly affects how these cells function. Its action increases levels of cytokines such as tumor necrosis factor (TNF-alpha), interleukin 8 (IL-8), and Nitric Oxide production besides limiting pathogenic growth [37, 38].

Lactoferrin modulates innate and adaptive immune response because of its ability to bind LPS and CD-14. It also interferes with the formation of the CD14–LPS complex. This results in the attenuation of the LPS/CD-14/TLR-4, a signaling pathway involved in the pathogenesis of sepsis. Lactoferrin may stimulate the immune system by binding to CD-14 and then activating the TLR-4-mediated pathway while preventing overexpression of LPS-induced inflammation [39]. Lactoferrin, which functions as a natural iron scavenger and a modulator of signaling pathways, leads to the negative feedback of the inflammatory response. This is also shown by a decrease in the production of reactive oxygen species and various pro-inflammatory cytokines [40].

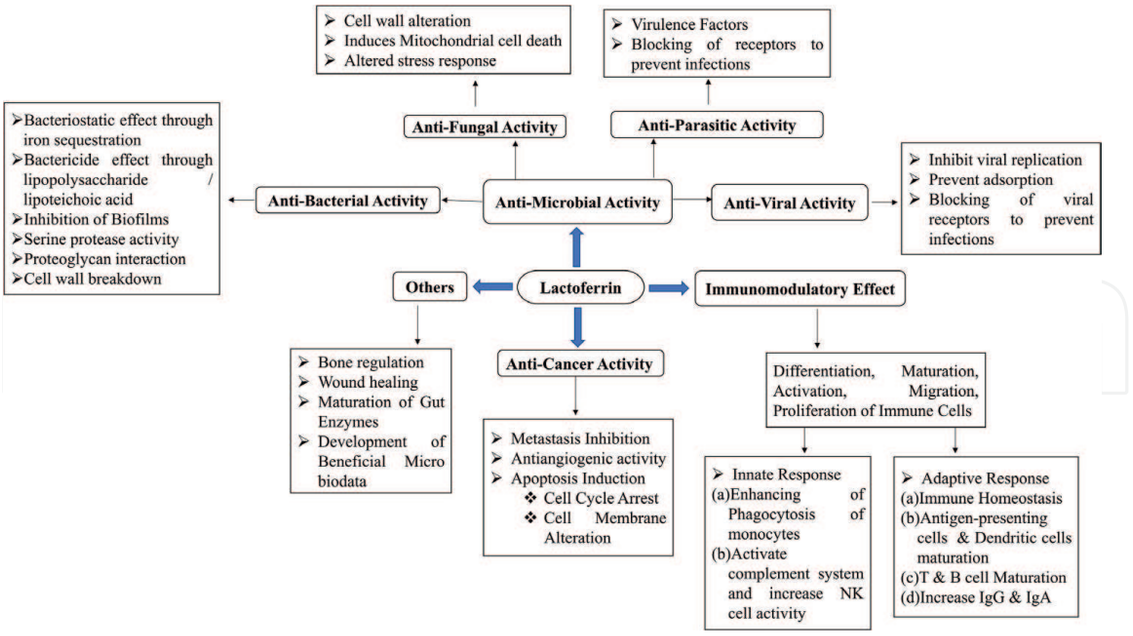

Figure 1.
Bioactivity of lactoferrin.

In addition to this, researchers have shown that in a murine model of diethyl nitrosamine-induced hepatocarcinogenesis, bovine milk lactoferrin significantly down-regulated the activity of liver antioxidant enzymes such as glutathione peroxidase, superoxide dismutase and catalase. It also increased the concentration of hepatic glutathione. Furthermore, bovine lactoferrin promoted the decrease of serum inflammatory markers and ameliorated in hepatic histological structures in a significant manner [41]. Furthermore, the applications of lactoferrin have been highlighted in **Table 2**.

Other than the direct modulation of the immune response, lactoferrin strategically acts as a potent anti-inflammatory agent by scavenging ROS. Pro-oxidant agents can both promote DNA damage and induce as well as sustain inflammatory disorders. Inflammation itself drastically contributes to cancer development. Lactoferrin can maintain the physiological balance of ROS levels by direct binding of free iron, one of the principal actors involved in ROS production. It can also act as a regulator of key antioxidant enzymes, thus protecting the host from ROS-mediated cell and tissue damage in an overall manner [51].

The protective character of lactoferrin against cancer has been demonstrated, on numerous occasions, including its impact on chemically induced tumors, in laboratory rodents. Lactoferrin has even been reported to inhibit the development of experimental metastases in mice [52–54]. Lactoferrin-mediated inhibition of tumor growth might be related to apoptosis of these cells, induced by the activation of the Fas signaling pathway. Nevertheless, the exact mechanism of this function has not been discovered so far [55].

3.2 Camel milk lactoferrin as an antimicrobial, anticancer, and immunomodulatory agent

Lactoferrin is a highly conserved molecule. It possesses high degree of sequence homology and exerts multiple identical functions across mammalian species. Its

S. No	Applications	Additional Information	References
1	Antihypertensive activity	Obtained from lactoferrin-derived peptides	[42]
2	Protection from anemia	Serves as an iron-containing protein useful for treatment	[43]
3	Bone regeneration	Beneficial effect	[44, 45]
4	Prevention of metabolic diseases	Eg. Obesity and diabetes	[46]
5	Acts as drug nanocarriers	Emphasis on tumor-targeted drug delivery.	[47]
6	Protection from Neurodegenerative diseases	Markedly increased expression upregulation in brain cells	[48]
7	Anti-inflammatory effect	By inhibition of the formation of hydroxyl free radicals.	[49]
8	DNA damage prevention	Prevention of tumor formation in the central nervous system	[50]
9	Activates the p53 tumor suppressor gene (TSG)	Suppression of tumor formation	[50]
10	Natural substitute for Antibiotics	Antimicrobial activity: Also, a promising candidate to help break the vicious cycle of antibiotic resistance	[49]
11	Natural food preservative	Antimicrobial activity	[49]

Table 2.
Applications of lactoferrin.

ability to act as an antibacterial, antifungal, antiviral and antiparasitic, anti-inflammatory and immunomodulatory agent is shared amongst most mammalian species and has already been discussed [56–58]. More specifically, it inhibits growth of *Escherichia coli, Klebsiella pneumonia, Clostridium, Helicobacter pylori, Staphylococcus aureus, Candida albican*s, etc.

According to studies, the most therapeutic effects of camel milk are due to lactoferrin and immunoglobulins. Redwan & Tabll, 2007 reported that lactoferrin of camel milk has anti-viral activity and inhibits the virus entry into the cells. The camel milk lactoferrin stops HCV entry and replication in infected HepG2 cells two times higher than lactoferrin in human, bovine, and sheep milk. Generally, camel milk lactoferrin may directly interact with viral molecules or receptors (heparan sulfate) on the cell surface and prevent the virus's attachment to the host cells and thus hinder infection. The virucidal mechanism of camel milk lactoferrin depends on its alpha-helical structure and cationic nature [59]. The antiviral effects of lactoferrin from camel milk have been demonstrated against many viruses. The mode of action behind this activity is the neutralization of virus particles and inhibition of their replication. Camel milk lactoferrin also has anti-pathogenic activity against human immunodeficiency virus, hepatitis B and C, cytomegalovirus as well as herpes simplex virus-1 infection. Not only this, but camel lactoferrin's immunomodulatory role is exemplified by the fact that it modulates the activation and maturation of various immune cells such as neutrophils, macrophages, and lymphocytes [60].

An earlier study on camel milk lactoferrin has demonstrated the ability to inhibit the growth of colon cancer cells line HCT-116. Camel milk lactoferrin exerted antioxidant activity through scavenging NO and the DPPH free radical. It has shown the capability to furnish reducing power as evident by total antioxidant assays. Camel milk lactoferrin also inhibited DNA damage most likely through binding catalytic iron [5].

Camel milk lactoferrin exhibits an anti-inflammatory activity against IL-1β induced activation of osteoarthritis associated chondrocytes in humans by blocking the NF-kappa B mediated signaling. Furthermore it inhibited cyclooxygenase-2 expression and PGE2 production in stimulated osteoarthritis chondrocytes. N. Rasheed et al., 2016 have reported that camel lactoferrin has cartilage protective and anti-arthritic activity. This novel mode of action of camel milk lactoferrin is very important in understanding the mechanisms behind its anti-inflammatory or anti-arthritic effects [61]. The above studies on lactoferrin derived from camel milk highlight the clinical relevance.

3.3 Anticancer potential of lactoferrin from other mammalian species

Human and Bovine lactoferrin has been suggested to be able to act in tumor prevention and treatment [62, 63]. The lactoferrin preventive effect has been demonstrated in several animal models bearing different types of malignancies, including lung, tongue, esophagus, liver, and colorectal tumors [64–67]. Whereas lactoferrin treatment, was found to be effective in inhibiting growth, metastasis, and tumor-associated angiogenesis [63, 68, 69].

Bovine lactoferrin prevents development of chemically induced tumors. This effect has been confirmed in studies conducted on laboratory rodents. Based on in vivo studies, oral administration of lactoferrin to rodents significantly decreased the chemically induced carcinogenesis in various organs such as breast, esophagus, tongue, lung, liver, colon, and bladder. It also hindered angiogenesis and decreased the incidence of metastases in experimental mice [67].

Furthermore, the combined administration of Lactoferrin and temozolomide enhances the effect of chemotherapy both in vitro and in vivo [55] Similarly, humans suffering from lung cancer undergoing chemotherapy had increased immune system response after taking human lactoferrin post-treatment [70].

Lactoferrin from a bovine source is a promising candidate as an anticancer agent [71] Although bovine milk contains lactoferrin, the human form has been found to be far more potent. Animal studies with mice or rats have shown beneficial effects of bovine lactoferrin ingestion as it can inhibit carcinogen–induced tumors in the colon, esophagus, lung, tongue, bladder, and liver [72].

The anticancer effect of lactoferrin has been extensively studied, and it has been observed that in the presence of Lactoferrin, cancer cells suffer significant damage. It is known to cause cell cycle arrest, damage to the cytoskeleton, and induction of apoptosis, in addition to decreasing cell migration[63, 73]. It decreased the viability and growth of breast cancer cell lines (HS578T and T47D). It also stopped cancer cell growth during the cell cycle and disrupted the cancer cell membrane [74]. Bovine lactoferrin efficiently inhibited the growth of breast cancer cells, suggesting that it has a potential to act as an anti-cancer agent against breast cancer [63, 75].

Lactoferrin helps to prevent the growth of cancer cells and shrinks the cancer cells. It is also known for its inhibitory action on cancer cell proliferation and its anti-inflammatory as well as antioxidant abilities against them [75]. Lactoferrin

expression levels are decreased in colorectal cancer as compared with normal tissue. Lactoferrin knockout mice demonstrated a great susceptibility to inflammation-induced colorectal dysplasia. Treatment of knockout mice with lactoferrin post-chemotherapy accelerated the reconstitution of the immune system, reducing the chances for infection, following chemotherapy treatment. Additionally, lactoferrin is significantly downregulated in specimens of nasopharyngeal carcinoma (NPC) and is negatively associated with tumor progression, metastasis, and prognosis of patients with NPC [76].

Lactoferrin was shown to have preventive effects against gastrointestinal cancers, such as cancer of the colon, stomach, liver, and pancreas, and against metastasis of such neoplasms [77, 78]. Xu *et al*. (2010) demonstrated that bovine lactoferrin induces apoptosis in stomach cancer, thereby suppressing it [79]. Oral administration of lactoferrin decreased the occurrence of colon cancer by 83%. The number of adeno-carcinoma cells in the gut of rats was reduced after the ingestion of lactoferrin.

Lactoferrin-mediated inhibition of tumor growth might be related to apoptosis of these cells, induced by the activation of the Fas signaling pathway [55]. It has been suggested that the treatment of lactoferrin knockout mice with lactoferrin (post-chemotherapy) accelerated the reconstitution of the immune system. This also reduced the chances of infection following chemotherapy treatment [76]. Lactoferrin can scavenge free iron in fluids and inflamed and infected sites, suppressing free radical-mediated damage and decreasing the availability of the metal to pathogens and cancer cells. Also, lactoferrin hinders migration in a model of human glioblastoma by reverting an epithelial-to-mesenchymal transition-like process [4, 32].

3.4 Lactoferrin in COVID-19 treatment

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection has recently become a primary global health concern, leading to the urgent development of therapeutic agents for its prevention and treatment. Iron overload is understood to have an important role in the pathogenesis of COVID-19. Actually some features (such as inflammation hyperferritinemia, hypercoagulation, and immune dysfunction) manifested a in COVID-19, are linked to iron overload. The presence of free iron, resulting from iron overload and dysregulation, is very highly reactive and toxic due to its reactive oxygen species (ROS) generation potential. The ROS produced react with very important cellular biomolecules and induce their subsequent damage. Nucleic acids, proteins as well as membranous and cellular lipids are effected by the highly activate inflammatory processes which may be either acute or chronic. The linkage of inflammation with multiple clinical conditions, such as cancer is well understood [80]. Lactoferrin has exhibited unique immunomodulatory, anti-inflammatory, and broad-spectrum antiviral activity indicating its potential for the cure of COVID-19 cases and prevention of its devastating effects on multiple target organs [81, 82]. Lactoferrin could counteract the coronavirus infection and inflammation, acting either as a natural barrier of respiratory and intestinal mucosa or reverting the iron disorders related to the viral colonization. Iron-catalyzed lipid damage is understood to exerts a direct effect on ferroptosis, the newly discovered cell death mechanism. Unlike programmed cell death (PCD), ferroptosis not only leads to amplified cell death but is also associated with inflammation. Iron chelators are generally recognized as safe and have been shown to protect patients in diseases characterized by iron overload. Research work also suggests that iron chelators exhibit antimicrobial activities. It is suggested that the naturally occurring iron chelators, such as lactoferrin, exert anti-inflammatory

as well as immunomodulatory effects. It binds to some of the same receptors used by coronaviruses and hence blocks its entry into host cells. Iron chelators may actually be of a very high therapeutic value during the present scenario of the ongoing COVID-19 pandemic [80]. Therefore, the use of lactoferrin may be of value in the prevention and management of COVID-19. The use of lactoferrin appears to be a promising approach to treating COVID-19, but further investigations are required to verify its antiviral activity *in vitro* and *in vivo* [83–85].

3.5 Lactoferrin assimilation *in vivo*

Lactoferrin shows high bioavailability after oral administration, high selectivity toward cancer cells, and a wide range of molecular targets controlling tumor proliferation, survival, migration, invasion, and metastasis. Notably, lactoferrin may either promote or inhibit cell proliferation and migration depending on whether its target cell is normal or cancerous. Significantly, its administration is well tolerated and does not exhibit any significant side effects. Furthermore, lactoferrin may prevent cancer development and growth by enhancing the adaptive immune response. Oral administration of lactoferrin has also led to promising improvement in the immune responses of antiretroviral therapy in naıve children suffering from HIV [86]. Oral administration of lactoferrin decreased the occurrence of colon cancer by 83%, while the quantity of adenocarcinoma cells was reduced in the gut of rats after ingestion of Lactoferrin, ameliorating tongue cancer.

Of particular interest is the notion that even its oral administration may be effective. This is different from many other therapeutic proteins, which typically require other invasive routes of administration [87]. Oral administration of bovine lactoferrin prevents carcinogenesis in the colon and other organs in rats. It also inhibits lung metastasis in mice. It might be mediating its anti-carcinogenesis effects is by increasing expression of relevant cytokines and inducing subsequent activation of immune cells [67]. It interacts with a wide range of molecular targets controlling tumor proliferation, survival, migration, invasion, and metastasis. It may be noted that lactoferrin can promote or inhibit cell proliferation and migration depending on whether it acts upon normal or cancerous cells, respectively. Moreover, lactoferrin can prevent the development or inhibit cancer growth by boosting adaptive immune response. Most importantly, lactoferrin administration is highly tolerated and does not present significant adverse effects.

Oral administration of lactoferrin is the most widely adopted method of its delivery into the human body. This still possesses some challenges that must be addressed before reaping the highest benefit from its intake. Since the functional domains of lactoferrin are highly dependent on its unique 3D structural conformation, the gastrointestinal breakdown of lactoferrin may cause undesirable loss of some of its functional properties. The important receptors of lactoferrin are located at the intestinal mucosa and lymphatic tissue cells in the gut [88–91]. Hence, the delivery of lactoferrin through oral administration requires that it is protected so that it passes through the stomach and is delivered to the absorption sites in a functionally active form. But the most important thing is to note that the digestive tract in infants and newborns is not mature enough (e.g., the intragastric pH and the gastric emptying rate are higher than in adults), and lactoferrin would not be completely digested under these conditions. This hypothesis has been confirmed by measuring the unhydrolyzed lactoferrin in fecal extracts of babies [92, 93]. Nevertheless, the degradation of lactoferrin during the gastrointestinal tract could also be beneficial. It has been reported that

strong antibacterial peptides such as lactoferricin and lactoferrampin are produced by its pepsin hydrolysis [94, 95]. This further benefits the utilization of lactoferrin in high value food products such as infant formula, nutritional supplements, and other formulations that aim at delivering lactoferrin through oral administration.

A commonly accepted method to protect lactoferrin during digestion is microencapsulation. In this method, a protective matrix is created around the lactoferrin core. Food grade proteins (e.g., bovine serum albumin, β- lactoglobulin) and polysaccharides (e.g., pectin, carrageenan, sodium alginate, gum Arabic) are commonly used as the shell materials. This core-shell structure excellently protects lactoferrin from the harsh environment prevailing in the human digestive system. The microencapsulation also helps achieve targeted and controlled release of lactoferrin by simply using shell materials with suitable properties.

Based on in vivo studies, oral administration of lactoferrin to rodents significantly decreased the chemically induced carcinogenesis in various organs such as the breast, esophagus, tongue, lung, liver, colon, bladder, and hindered angiogenesis [78]. During the past two decades, many animal and human studies have proved that orally administered Lactoferrin exerts many beneficial effects on the health of animals and humans [75].

3.6 Lactoferrin industries in the world

Human and bovine lactoferrin is generally recognized as a safe substance (GRAS) by the Food and Drug Administration (FDA, USA). Some pharmaceutical industries (*e.g.*, Morinaga Milk Industry Co LTD Venture LLC, Ventria Bioscience, AusBioMed, Biopharming, Max Biocare, etc.) are into commercialization of human and bovine Lactoferrin related products such as nutraceuticals and vitamin supplements for pediatric use. Also are being produced baby foods, beverages, and a cell growth promoting adjuncts for better child development.

According to Global Market Insights Inc. report, the global lactoferrin powder revenue size was US$195 million (€164 m) in 2020, which is set to surpass US$315 million (€364.1 m) by 2027 and is expected to register over 7.7% CAGR between 2021 and 2027. Owing to the anti-inflammatory attribute of lactoferrin its market is likely to surpass 70 Million USD by 2027. Its antiviral efficacy is being increasingly recognized during the COVID-19 pandemic. Furthermore, its immunomodulatory and anti-inflammatory capability is expected to raise product demand in an unprecedented manner from the pharmaceutical sector. It is estimated that the lactoferrin industry from the pharmaceutical application would actually exceed 53.78 Million USD by 2027. The global Lactoferrin Market is anticipated to attain substantial growth by the end of the forecast period (2021–2025).

Lactoferrin has also been used in different products, such as probiotics, supplemental tablets, cosmetics, and as a natural solubilizer of iron in food. It is also used in the treatment of diverse carcinomas, severe sepsis, and diabetic foot ulcers. Numerous attributes of lactoferrin, such as its iron absorption ability, antibacterial, anti-inflammatory, antioxidant, and immunity-boosting capabilities, are likely to provide promising opportunities for the lactoferrin industry. The ability of lactoferrin to prevent biofilm formation helps inhibiting the growth of bacteria. This can lead to an enhanced product demand owing to its therapeutic applications. The higher susceptibility of infections in infants and newborns due to an underdeveloped immune system can be supplemented by the lactoferrin industry. Growing demand for lactoferrin from physical fitness and sports nutrition application is likely to drive the growth of

lactoferrin capsules during the forecast period. Increasing instances of digestive and gastric disorders should boost the demand for lactoferrin as an anti-inflammatory ingredient.

4. Conclusion

Lactoferrin, a multifunctional ingredient amply found in camel milk. It has numerous applications as a natural antimicrobial food additive and pharmaceutical agent. Camel milk lactoferrin has unique antimicrobial, antioxidant, anti-infective and anti-cancer activity. It can be used as a natural alternative to chemical antibiotics. Camel milk also been suggested for weight management. Lactoferrin from the milk of different indigenous species is being increasingly used as a specialty ingredient in the dairy industry. Lactoferrin can be used for biopreservation of foods such as milk, meat, fresh-cut fruits and vegetables, and their products to increase shelf life, control diseases and enhance public health. Indeed, our feeling is that camel milk lactoferrin can be used in synergy with both, conventional therapies and recent advancements allowing many therapeutic agents with potential side effect to be administered at lower, more sustainable doses.

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Conflict of interest

The authors declare no conflict of interest.

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