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An overview on lactoferrin as a natural antimicrobial in food industry

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Abstract

Milk proteins have equitable composition of amino acids assuring a fundamental functional product, and they also enhance the texture and sensory qualities of various dairy products. Among them is lactoferrin (LF), which is effective against a wide range of bacteria and has both bacteriostatic and bactericidal activity. The major iron-binding protein in milk is lactoferrin (LF), which considered as a multifunctional protein that exists in human as well as animal milk that helps adjusting the amount of free iron in body fluids; this makes LF bacteriostatic and healthy. Lactoferrin (LF) is a protein belonging to the transferrin family that is found in milk and colostrum, as well as body fluids such as saliva, tears, spleen, stomach mucosa, lymph nodes, skin, and even white blood cells. As lactoferrin binds iron, so it is depriving growth of microorganisms such as *Bacillus stearothermophilus, E. coli, Bacillus subtilis* and *Shigella* from its necessary building blocks, it also appears to serve as a protective factor against infections from bacteria, viruses, and fungi. In addition to prolonging shelf life and being used in infant formulas, it acts as a natural antimicrobial agent for the bio-preservation of dairy, seafood, meat, beverages and bakery goods, and protects against serious diseases such as hepatitis, cancer, foodborne illnesses, and respiratory infections, also helps to ensure safety and improve health. Briefly, the current review aimed to shed light on the safety and importance context of lactoferrin in food industry field as well as the benefits for human health.

Keywords: *Lactoferrin, food, preservation, shelf-life, health benefits.*

Introduction

Food antimicrobials are a variety of compounds that are employed as preservatives and reduce the microbial deterioration of food. They might impede the growth of microbes in food by disrupting its vital functions. Additionally, Antimicrobials are commonly used as preservatives in a wide range of food products. in order to improve food quality, prolong shelf life, and guarantee the final product is free of microbiological contamination **Bouarab *et al*., (2019)**. Consumers find it bothersome when chemical preservatives are used in processed meals, and their demand for natural foods is growing daily **Perez *et al.* (2012).** People are drawn to natural additives because they are conscious of their nutrition **Asghar *et al.* (2011).** Lactoferrin is considered as a promising when implemented as an antimicrobial for production of different food products medicines, biologically active additives, and cosmetic preparations. Lactoferrin acquires plentiful health benefits regarding antifungal, antibacterial, antiparasitic, antiviral, and antitumor effects, it affirms bone growth, safeguards the intestinal epithelium, and promotes recovery of

immune system functions in animals. Lactoferrin is incorporated in hepatitis- C treatment, and also enhance health condition of patients with Alzheimer's disease **Hao *et al.* (2019).** The average level of natural LF in cow's milk is around 0.2 g/L, but its maximum content can reach as high as 50 to 100 g/L in cow milk while, in human milk, it reach 2–4 g/L, and 6 to 8 g/L in human colostrum **Kai *et al.* (2002).** Moreover, LF plays a defensive function against infections of gastrointestinal system and participates to secretory immune function systems **Mayeur *et al.* (2016)**. Experimentally, it was proved that lactoferrin protects from gastritis caused by *Helicobacter pylori*, reduces virulence during infection with enterotoxigenic *E. coli*, and sustains the integrity of intestinal mucosa **Brodsky *et al.* (2013).** It was granted that LF has bacteriostatic characteristics toward gram-negative pathogens that needs extreme iron as coliforms, and it still behaves in opposition to microorganisms such as *Bacillus* species*, S. aureus,* and *L. monocytogenes* due to the interaction between LF and lipo-polysaccharides of microorganisms exposed sheet causing change in permeability **Niaz *et al.* (2019). Binyameen *et al.* (2021)** revealed that consuming LF fortified milk is linked to higher iron levels in the body with enhancing iron absorption through the intestines of breast-feeding infants. Furthermore, purified LF is applied in canned food, pharmaceutical preparations, sports nutrition, oral care products and cosmetics. The inclusion of products with LF offers numerous benefits, such as the preventing the infection development, enhancement of immune function, as well as anti-inflammatory and antioxidant effects. General uses of bovine LF in food production including fermented milk and milk products, dietary iron supplements, infant and cosmetics formulas, beverages, chewing gums, immune-enhancing nutraceuticals, feed and pet care supplements, and inhibits bacterial adhesion on abiotic surfaces. Lactoferrin plays a crucial role in safeguarding the mucosal barrier by preventing viral and microbial assaults. Moreover, it has been found that LF effectively combats the formation of biofilms, and when administered orally, it has successfully treated respiratory and oral infections. Lactoferrin has been certified as GRAS prestige by the **Niaz *et al.* (2019)**, it has been employed as health-promoting additives in commercially available food items, and it has also gained approval as a food ingredient in products by the European Food Safety Authority **Tomita *et al.* (2009).**

History of Lactoferrin:

In 1939, LF was firstly discovered by **Sorensen and Sorensen, (1940),** as a red protein in whey, it was extracted and refined from milk of human and bovine in 1960. Lactoferrin was related to serum transferrin structure, LF is categorized as a member of the Transferrin family as mentioned by **Lambert *et al.* (2005).**

Functional Properties of LF:

The particular structure of LF has been given a lot of nutritional and medical value, because it transfers iron and eliminates free radicals from body fluids; LF is essentially regarded as safe and efficient component for delivering iron to individuals who are iron deficient. **Gupta *et al.* (2016) and Lopez *et al.* (2016).**

Anti-microbial activity of LF:

The iron-free form of LF, or apo-LF, is thought to contribute in iron deficiency, which is necessary for the continuation of essential microbial processes and, ultimately, a slower rate of bacterial growth **Law and Reiter (1977).** Laterally, numerous investigations have shown that the growth of various bacterial strains were inhibited by holo-LF, the iron saturated form of lactoferrin **Ellison 3rd and Giehl (1991); Ochoa and Cleary (2009); Ostan *et al.* (2017).** Also, it has been observed that LF exhibits antiviral properties during the initial stages of infection, this can occur through the prevention of host cell infection or in the event that host cells have already been infected, by preventing the growth of specific viruses. **Superti *et al.* (1997); Marchetti *et al.* (1999); Ikeda *et al.* (2000); Beljaars *et al.* (2004).** Lactoferrin could target a wide range of fungal species, as it can effectively eliminating *Candida albicans* and *Candida kruseibdue* due to its potent iron (Fe3+) content **Al-Sheikh (2009).**

Food applications:

Bio- preservation:

In the dairy industry, it was convinced that lactoferrin improves the sensory characteristics of Kariesh cheese that has been experimentally contaminated with certain foodborne pathogens such as *E. coli* O157:H7*, S. aureus, B. cereus* and *L. monocytogenes*, in addition, to extending its shelf-life at refrigerated storage **Ombarak *et al.* (2019). Azhar *et al.* (2022)** achieved that LF exhibiting variable effects on the viability of *E. coli* compared to *S. aureus*, as well as *E. coli* count in Kariesh and Dominate cheese. In this regard, using of 2% of LF can inhibit *S. aureus* viability in Kariesh cheese significantly. **Da Silva *et al.* (2012)** concluded that LF prevent *S. aureus* population to increase in the processed cheese. **Al Habty and Ali (2022)** reported that LF favored a convenient food preservative in yoghurt due to powerful antibacterial activity against multidrug resistant (MDR) *S. aureus* and its perfect sensorial properties, as well as LF is considered as an assuring tool for controlling growth of *E.coli* and *S. aureus* in milk and Kariesh cheese and investigated that the LF application improved the overall sensory qualities and extended the shelf-life of Kariesh cheese dramatically. In a study obtained by **Shashikumar and Puranik (2011) and Yassin and Abd Elhady (2023)** they noticed that LF included into cheese at different levels (10, 15, and 20 ppm) resulted in fundamental reduction in bacterial growth, such reduction increased as the LF concentration increased, ultimately leading to a substantial extension of the cheese shelf-life when compared to the control samples. **Taha *et al.* (2019)** declared that LF could become a bright method to decline *E. coli* non-O:157 (*E. coli* O1 and O26) growth in pasteurized milk, decrease *E.coli* non-O:157 associated illness in humans consequently.

Regarding industry of meat products, LF has an efficient role in meat preservation. **Colak *et al.* (2008)** pronounced that total aerobic bacteria, total psychrophilic bacteria, *pseudomonas spp*., *coliform, E. coli*, yeast, and mold counts in meatballs were significantly reduced by LF treatment alone and when used in combined with nisin. The meatballs treated with this combination showed the largest reduction, extending the refrigerated shelf-life up to 10 days. Using LF at concentrations of 3% and 5% for treatment of meat samples that were contaminated with *E. coli* O157:H7 led to a reduction of 2 logs by the 9th day of storage at 10ºC **Soyer *et al.* (2020).** The impact of LF treatment was positively assessed the shelf-life of chilled chicken breast during storage at 4°C. Significance difference ($P<0.05$) was noticed between the scores of sensory traits regarding chilling times and different LF concentrations, but no significant difference ($P>0.05$) in taste scores. Supplementary, the concentration of 20 mg/g LF treated group had the best sensory scores and microbiological counts all over the refrigerating times until the 13th day of storage **Elsayed and Hussei (2022). Del Olmo *et al.* (2012)** demonstrated that contaminated chicken breast samples with bacterial cultures, followed by treatment with LF and its derivatives (0.5 and 5 mg/g) concentration, and exposed to high hydrostatic pressure processing (HHP) at 400 MPa for 10 min at 10°C resulted in great reduction in bacterial counts, and a good quality of sensorial aspects.

Food packaging:

It is expected that further expansion of research related to the field of packaging materials with antimicrobial properties will occur in the near future, as it will create a significant improvement in preserving food safety and quality for as long as feasible **Niaz *et al.* (2019).** The combination of natural antimicrobials and edible films may be a good way to address consumer concerns about food safety and act as a physical barrier and antimicrobial mediator **Montone *et al.* (2023).** Lactoferrin is known for its antioxidant properties, enhancing antioxidant activity and helping in reducing the oxidative stress (ROS) **Gould (1996).** Utilization of LF as nutritional supplement is Generally Recognized as Safe (GRAS) as mentioned by the USFDA and a narrative food component by EFSA. Additionally, LF exhibits remarkable heat resistance, making it highly effective in food preservation **Martinez – Hernandez *et al.* (2017); Mulder *et al.* (2008). Brown *et al.* (2008)** declared that LF can be applied in chitosan edible film altering *E. coli* and *L. monocytogenes* growth. Moreover, when combined with Lysozyme, LF and chitosan films considerably decline the growth of *E. Coli* O157:H7

and *L. monocytogenes* by about 3-log.

The application of an alginate-based coating activated with hydroxyapatite/lactoferrin/ quercetin complexes, has also demonstrated a high ability to inhibit the growth of spoilage microorganisms in fresh meat products. Additionally, after being stored for 15 days at 4 °C, it retards the generation of TVB-N and delays the changes in firmness and sensory attributes of both cooked and uncooked pork fillets **Montone *et al.* (2023). Rollini *et al.* (2016)** produced a film contained LF and lysozyme, proving to be highly efficient in combating hydrogen sulfide-producing bacteria found in salmon fillets. A plasma coating functionalized with lactoferricin B was found to be a good tool to control deterioration caused by microorganisms like *Pseudomonas* and extending the shelf -life of cheese **Quinteri *et al.* (2013). Barbiroli *et al.* (2012)** developed a cellulose-based active packaging material that included lysozyme and LF, a release of antimicrobials was observed due to the synergism between the two components in experiments conducted with prevalent food contaminants. An edible coating of whey protein fortified with LF was studied by **Muhammad *et al.* (2023),** and showed a great effect on the microbial growth in soft white cheese by eliminating or reducing of proteolytic, lipolytic bacteria, yeast and molds, as well as protect food from unfavorable storage conditions, which led to a prolongation of storage time as compared to other treatments coated or uncoated with any other additives. Many other applications of LF in was conducted in food and dairy industries as freeze-drying and ultrafiltration dairy industries, remarkably bioactive and pure LF, allowing LF incorporation in infant formula **Giansanti *et al.* (2016).**
Through conducting this study, it is expected to obtain a good effect of lactoferrin in preserving foods of animal origin, reducing microbial contamination, preserving product quality, and protecting consumer health from foodborne pathogens.

Conclusion

Lactoferrin application as biologically active protein is widely developed. Lactoferrin supplementation in food industry should be taken into consideration because it is believed to hold promise for the supply of food products with an iron-binding component, enhancing their antioxidant and immunomodulating properties, and expanding the shelf life of the products. Additionally, the use of LF in food products can change their quality by increasing their healthy properties and extending shelf-life. Other advantage of LF: as an iron-containing protein, it can be used to treat anemia, primarily in expectant mothers and their newborn children. Allow for higher milk production rates to meet the needs of residents in developing nations. Establish appropriate and affordable industrial and on-farm technology to extract high -value LF protein from milk and use it for biopreserving fresh, cut fruits, vegetables, meat, and milk products to extend shelf life, prevent disease, and improve public health.

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