Crimson Publishers
Wings to the Research

Mini Review

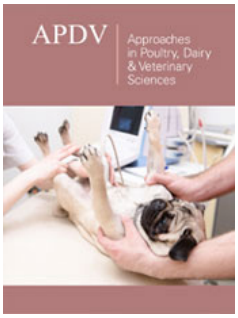
Lactoferrin- Extremely Important Whey Protein of Milk

Vorlová L[1]*, Navrátilová P[1], Bartáková K[1], Hanuš O[2], Nejeschlebová H[2] and Dluhošová S[1]

[1]University of Veterinary Sciences Brno, Faculty of Veterinary Hygiene and Ecology, Department of Hygiene and Technology of Food of Animal Origin and Gastronomy, Brno, Czech Republic

[2]Dairy Research Institute Ltd., Prague, Czech Republic

ISSN: 2576-9162



***Corresponding author:** Vorlova L, University of Veterinary Sciences Brno, Faculty of Veterinary Hygiene and Ecology, Department of Hygiene and Technology of Food of Animal Origin and Gastronomy, Brno, Czech Republic

Submission: September 16, 2022

Published: September 26, 2022

Volume 9 - Issue 2

How to cite this article: Vorlová L*, Navrátilová P, Bartáková K, Hanuš O, Nejeschlebová H and Dluhošová S. Lactoferrin- Extremely Important Whey Protein of Milk. Appro Poult Dairy & Vet Sci 9(2). APDV. 000708. 2022.
DOI: 10.31031/APDV.2022.09.000708

Abstract

Milk whey proteins are a nutritionally and commercially interesting commodity. The importance of individual representatives is the subject of several studies. One of the most interesting biomolecules is lactoferrin, which has a few biological functions, which include antibacterial, antifungal, antiviral, antiparasitic, anti-inflammatory, immunomodulatory, anticarcinogenic, bifidogenic and enzymatic. Isolated, especially bovine lactoferrin, finds wide application not only in preparations for the promotion and restoration of human health, but also in animal nutrition, food production and cosmetics. The review provides basic information about the biological properties of lactoferrin.

Keywords: Bovine lactoferrin; Biological functions; Antimicrobial activity

Introduction

Lactoferrin (LF) is synthesized by the secretory cells of the mammary gland, but it can also be synthesized by other exocrine glands [1]. LF is an integral part (together with lysozyme and lactoperoxidase system) of natural inhibitory substances of milk. Due to their remarkable interspecific similarity (homology between human and bovine milk LF is 77%), its antibacterial, antifungal, antiviral, antiparasitic, anti-inflammatory and immunomodulatory activities are very similar [2]. Lactoferrin is a glycoprotein transferrin with a high affinity for iron. It is also notable for its certain thermostability and proteolytic resistance [3,1]. The widespread and increasing use of isolated bovine LF in the promotion and restoration of health was influenced by the significant EU legislation, which by Regulation (EC) No 258/97 of the European Parliament and of the Council allowed the placing on the market of bovine LF as a novel food ingredient. One of the first applications led to the enrichment of infant milk formula. Supplementation of other foods is significant in many ways, whether it is an increase in the biological value of food, support of iron absorption, probiotic bifidogenic influence on the intestinal microbiome, or others. Another application is its use in food preservation. In the form of dietary supplements, it is mainly about targeting the improvement of the immune system, anti-inflammatory effects and more. LF is also widely used as part of pharmaceuticals designed for prophylactic and therapeutic use in several diseases [4].

Lactoferrin in milk

In addition to the mammalian species, the concentration of LF in milk is influenced by other factors: breed, individuality of the individual, order of lactation, stage of lactation, state of health [2,5,6]. For these reasons, LF concentrations may vary even in one mammalian species. The highest concentrations were found in human milk (1.7mg/mL), while in donkey milk the concentration was lowest (0.07mg/mL) Camel milk contains higher concentrations of LF (0.22mg/mL) than milk of other mammalian species except humans [7]. The concentration of LF in milk varies depending on the stage of lactation. The most significant changes were noted

in colostrum and in the time of dry standing. Abd El-Gawad et al. [6] analyzed colostrum and milk of buffaloes, sheep, cows, goats and camels. The results of the work show that in the colostrum of all studied species, the concentration of LF is higher, and subsequently its gradual decrease occurs daily until it reaches the physiological value of mature milk (15-30 day after birth). An important role is played by the LF in the mammary gland in the period of involution, where it is an important component of the non-specific defense system and protects the secretory tissue against bacterial infection. Welty et al [14]. monitored the LF content in the mammary gland during the dry standing period in cows of 2 breeds (Holstein and Jersey). The maximum concentration of LF (ca. 20mg/mL) in most dairy cows was reached at the beginning of week 4 of the dry standing period. The observed changes represented up to a 100-fold increase in LF concentration compared to mature milk. Maximum lactoferrin concentrations were variable and were influenced by the individuality of the dairy cow. Tsuji et al. [8] found that the order of lactation shows a significant effect on the concentration of lactoferrin in dairy breeds, when at higher lactations there is 2-3 times higher LF content than in first-time calves. An increase in lactoferrin concentration accompanies mastitis in dairy cows already at the preclinical stage. It is essential to find out that neither the structure nor the bacterial activity of LF is affected by the standard pasteurization regime (72 °C for 15s) nor spray drying of milk [9].

Antimicrobial activity

Lactoferrin affects the growth and proliferation of various infectious agents, including gram-positive and gram-negative bacteria, viruses, or fungi. The bactericidal function of LF (as well as the peptides resulting from it) consists in damaging the permeability of the outer membrane of Gram-negative bacteria by releasing lipopolysaccharides from the cell wall. This damage is exacerbated by the action of natural antibacterial agents (e.g., lysozyme) or pharmaceuticals (e.g., antibiotics) [10]. The bacteriostatic function of LF is related to its strong affinity for iron, which allows it to bind any available iron at the sites of infection, thereby making this essential nutrient for growth in microbes requiring iron inaccessible [11,3,10]. LF inhibits replication of a wide range of RNA and DNA viruses. The most widespread hypothesis of antiviral action of LF lies in binding to glycosaminoglycan virus receptors, blocking them, thereby inhibiting the first contact of the virus with the host cell and preventing the development of infection. The antiparasitic effect of LF occurs both through the presence or absence of iron (also used in the role of antifungal) or by binding to the membrane lipids of the parasite leading to its rupture and damage [10].

Additional functions of lactoferrin/selection from published studies

LF is an immune system modulator and inhibitor of the inflammatory cascade, it can prevent the development of inflammation and subsequent tissue damage caused by the release of pro-inflammatory cytokines and reactive oxygen forms. LF with its positive charge binds negatively charged molecules on the surface of various cells of the immune system and this is associated with the trigger mechanism of the cellular immune response, such as activation, differentiation and proliferation. Many cells of the immune system have receptors for LF [12]. Inhibition of the production of pro-inflammatory cytokines increases the chemotactic activity of neutrophils and thus ensures faster movement from the blood to the site of inflammation. Like inflammation, LF can modulate cytokine production in cancer and can induce apoptosis and arrest of tumor growth in vitro. LF can be internalized into the cell nucleus, the site of action of most anti-cancer drugs, and is used as a targeting ligand to achieve active delivery of anticancer drugs to tumor tissue. In clinical trials, oral consumption of 3g/day of bovine lactoferrin significantly affected the growth of adenomatous polyps in the colon. Human recombinant lactoferrin has been shown to increase survival by an average of 65% of patients with advanced stage non-small cell lung cancer [11,3,5,10,13,1,2,4].

Acknowledgments

This research was supported by the Ministry of Agriculture of the Czech Republic, grant no. NAZV QK21010326.

References

1. Giansanti F, Panella G, Leboffe L, Antonini G (2016) Lactoferrin from milk: nutraceutical and pharmacological properties. Pharmaceuticals 9(4): 61.
2. Wang B, Timilsena YP, Blanch E, Adhikari B (2017) Lactoferrin: structure, function, denaturation and digestion. Critical Reviews in Food Science and Nutrition 59(4): 580-596.
3. Farnaud S, Evans RW (2003) Lactoferrin-a multifunctional protein with antimicrobial properties. Molecular Immunology 40(7): 395-405.
4. Superti F (2020) Lactoferrin from bovine milk: a protective companion for life. Nutrients 12(9): 1-25.
5. Adlerová L, Bartošková A, Faldyna M (2008) Lactoferrin: a review. Veterinarni Medicina 53: 457-468.
6. Abd El-Gawad, El-Sayed EM, Mahfouz MB, Abd El-Salam A (1996) Changes of lactoferrin concentrations in colostrum and milk from different species. Egyptian Journal of Dairy Science 24: 297-308.
7. El-Agamy EI (2006) Camel milk. In: Park YW, Haenlein GFW (Eds.), Handbook of Milk of Non-bovine Mammals, Blackwell Publishing Professional, USA, pp. 297-344.
8. Tsuji S, Hirata Y, Mukai F, Ohtagaki S (1990) Comparison of lactoferrin content in colostrum between different cattle breeds. Journal of Dairy Science 73(1): 125-128.
9. Young W Park, George FW Haenlein (2013) Milk and dairy products in human nutrition. Wiley Blackwell, USA, pp. 700.
10. Gonzáles-CHáves SA, Arévalo-Gallegos S, Rascón-Cruz Q (2009) Lactoferrin: structure, function and applications. International Journal of Antimicrobial Agents 33(4): 301-308.
11. Ward PP, Uribe-Luna S, Connely OM (2002) Lactoferrin and host defense. Biochemistry and Cell Biology 80(1): 95-102.
12. Korhonen H, Marnila P (2003) Lactoferrin. In: Roginski H, Fuquay JW, Fox PF (Eds.), Encyclopedia of Dairy Science (1. vyd.), Amsterdam, Academic Press, USA, pp. 1881-1894.

13. Embleton ND, Berrington JE, McGuire W, Steward JC, Cummings S (2013) Lactoferrin: antimicrobial activity and therapeutic potential. Seminars in Fetal and Neonatal Medicine 18(3): 143-149.

14. Welty FK, Smith KL, Schanbacher FL (1976) Lactoferrin concentration during involution of the bovine mammary gland. J Dairy Sci 59(2): 224-231.