

Lactoferrin Update

by Will Brink

Readers of Life Extension magazine expect the latest research on natural non-toxic supplements that prevent disease and improve health. A lactoferrin update is therefore in order. Lactoferrin has captured the interest of many researchers as a natural compound with a wide variety of uses. What follows is a summary of previously published information on the research and effects of lactoferrin followed by some of the more up-to-date studies.

Lactoferrin appears to be a subfraction of whey with the best documented anti-viral, anti-microbial, anti-cancer and immune modulating/enhancing effects. When we talk about whey we are actually referring to a complex protein made up of many smaller protein subfractions (peptides). Many of these subfractions are only found in very minute amounts in cows' milk, normally at less than 1%. For example, lactoferrin makes up only 0.5% to 1% or less of whey protein derived from cows' milk. Mothers' milk, on the other hand, will contain up to 15% lactoferrin.

Conclusion

Science is examining lactoferrin in search for potential treatment and diagnostic tools in a wide range of human ailments. It is expected that further research will come to light regarding this bioactive peptide. Will Brink is a well known medical, fitness and health writer for a variety of publications. He is most noted for his articles and work with whey proteins and essential fatty acids in athletics and the treatment and prevention of various diseases.

Immunity

Lactoferrin is found throughout the human body and occurs in all secretions that bathe mucous membranes such as saliva, tears, bronchial and nasal secretions, hepatic bile, pancreatic fluids, and is an essential factor in the immune response. Lactoferrin is concentrated in oral cavities where it will come in direct contact with pathogens (i.e. viruses, bacteria, etc.) and kills or greatly suppresses these pathogens through a variety of different mechanisms. In fact, there are specific receptors for lactoferrin found on many key immune cells, such as lymphocytes, monocytes and macrophages, and is known to be directly involved in the upregulation of natural killer (NK) cell activity. One study with baby pigs found that only 17% of the pigs died when fed lactoferrin and injected with a toxin (escherichia coli) as opposed to 74% of the pigs that died without the lactoferrin!

Gastrointestinal function

Lactoferrin appears to be particularly important in the health and function of the intestinal tract. It has been found to greatly reduce systemic and intestinal inflammation in such conditions as inflammatory bowel disease, among others. Animals subjected to a variety of pathogens known to cause both systemic and intestinal inflammation and damage show much greater resistance and reduced inflammation when fed lactoferrin.

Antiviral effects

Lactoferrin has been found to both directly and indirectly inhibit several viruses that cause disease in humans. For example, in vitro (test tube) studies have found that lactoferrin strongly inhibits HIV (the virus thought to cause AIDS). The exact clinical relevance of this information has

yet to be elucidated, but lactoferrin may be an exceptionally effective, nontoxic compound in the fight against viruses that cause death and ill health in humans.

Anti-cancer effects

Perhaps one of the most promising uses for lactoferrin may be in its potential as a non-toxic, anti-cancer agent. Extensive in-vitro and in-vivo research with animals has shown lactoferrin to be a powerful anti-cancer agent. Multiple studies using both rats and mice exposed to a toxic chemical (azoxymethane) known to cause tumors throughout the gastro intestinal tract, administered concomitantly with lactoferrin, showed a large reduction in intestinal polyp development throughout the intestinal tract. One study found lactoferrin to be very effective at suppressing the growth of human pancreatic cancer cells. So much so the researchers concluded that lactoferrin "...might become one of the new drugs of choice for the adjuvant therapy against pancreatic cancer."

Antimicrobial effects

Probably lactoferrin's best known role is as an iron binding protein. It's referred to as hololactoferrin in its iron bound form and apolactoferrin in its iron depleted form. Studies have found that it is the apolactoferrin form that has the most powerful effects as an antimicrobial agent.

Lactoferrin is a powerful antimicrobial able to inhibit a wide range of pathogenic bacteria and other microbes. The mechanism appears to lie with lactoferrin's ability to bind iron, as it's known to have an extremely high affinity for this metal. Many pathogenic bacteria need a supply of free iron to multiply and in the presence of lactoferrin are strongly inhibited or killed. One study added lactoferrin to the drinking water of mice and subjected them to the toxic microbe called staphylococcal. The study found that the mice getting the lactoferrin as 2% of calories reduced kidney infections by 40% to 60%, and reduced bacterial counts 5-to-12 fold. They concluded, "The results suggest a potential for the use of lactoferrin as natural anti-bacterial proteins for preventing bacterial infections."

Lactoferrin as an antioxidant

Finally, lactoferrin is an antioxidant that scavenges free iron helping to prevent uncontrolled iron based free radical reactions, thus protecting certain cells from peroxidation. Though lactoferrin is both an iron scavenger and donor (depending on the cellular environment), it has been found to scavenge or donate iron at the appropriate times when the body is in need of the reaction. At normal physiological PH, lactoferrin binds iron tightly thus diminishing oxidative stress to tissues (from free radical production of iron). Apolactoferrin, but not hololactoferrin, has been shown to prevent lipid peroxidation. One study that examined the role of whey proteins, multi-fermented whey proteins and lactoferrin in oxidative stress made the bold statement, "We can conclude that whey protein, lactoferrin and multi-fermented whey are good candidates as dietary inhibitors of oxidative stress and should be considered as potential medicinal foods in various pathologies as HIV infection and cancer."

New research: antiviral, antibacterial, antifungal

Previous studies have found lactoferrin to be a powerful inhibitor of a wide range of viruses. Recently, lactoferrin was tested against the deadly hantavirus and was directly compared to the anti-viral drug ribavirin.¹ The study found that lactoferrin treated and pretreated cells greatly suppressed hantavirus. Perhaps even more intriguing, it was found that a powerful synergism

existed when lactoferrin was combined with ribavirin. The researchers concluded, "These results indicate that lactoferrin has anti-hantaviral activity in vitro and inhibition of virus adsorption to cells, which play an important role in revealing the anti-hantaviral activity of lactoferrin. This paper reports for the first time the anti-hantaviral effect of lactoferrin."

As mentioned above, lactoferrin has been found to be a powerful anti-microbial agent that suppresses bacteria. Scientists wanted to see if feeding animals either human derived lactoferrin, bovine derived lactoferrin or peptides derived from lactoferrin might be effective against urinary tract infections caused by the bacteria *Escherichia coli* (e coli).(2)

Urinary tract infections, or UTIs, are a common infection in humans, especially in women. Human lactoferrin, bovine lactoferrin and the peptides were given orally to female mice 30 minutes after the instillation of *Escherichia coli* bacteria into the urinary bladder. The study found that the amount of bacteria in the kidneys and bladder of mice was significantly reduced 24 hours later by the lactoferrin treatments, compared to the findings for the control group. Interestingly, only the human lactoferrin showed a strong anti-inflammatory effect, which contradicts other research. Previous studies have found that both BLF and HLF have strong anti-inflammatory properties, the BLF being the more powerful anti-bacterial agent. Lactoferrin may be effective as a combination therapy in the treatment of UTIs for women, but more research is warranted.

A clinical study was conducted to evaluate the effectiveness of lactoferrin in the treatment of tinea pedis.(3) Tinea pedis is a fungal infection often referred to as "athlete's foot" but can be found in other areas of the body. A dose of either 600 mg or 2000 mg of lactoferrin or a placebo was orally administered daily for eight weeks to 37 adults who were judged to have mild or moderate tinea pedis. A mycological cure was not seen in any of the subjects. However, there were statistically significant improvements found in dermatological symptoms (itching, redness, etc) in the active groups receiving lactoferrin, leading researchers to conclude, "The potential usefulness of lactoferrin as a functional food material for treating tinea pedis was seen for the first time in this study."

Additional studies of interest

- A study published in the Dec. 2000 issue of the *Journal of Cell Biochem* (15;79(4):583-593) found that lactoferrin is involved in the upregulation of CD4 lymphocytes, which are essential to the body's disease fighting abilities. It's well known that lactoferrin is directly connected to the host immune response, and this study may be another piece of the puzzle relating to the lactoferrin-immune-system connection.

- A recent study (*Early Hum Dev* 2000 Aug 1;59(2):95-105) called "Lactoferrin is responsible for the fungistatic effect of human milk" found that lactoferrin is the primary peptide in milk that suppresses the growth of dangerous fungi. Human milk has recognized anti-microbial effects and it has been repeatedly shown that breast-fed infants have fewer and less severe infections than formula-fed infants. While most studies have focused on anti-bacterial and anti-viral activities, few have focused on the anti-fungal effect of human milk. Dermal and other infections caused by fungi are common in infants with low bodyweight. In vitro, this study found milk to have a potent inhibitory effect on fungal growth. They concluded: "Most, if not all of this effect was caused by lactoferrin via its iron-binding capacity..." Interestingly, they state "...In contrast, other human milk proteins with known or suggested anti-microbial effects rather increased fungal growth."

- One study called "Lactoferrin and anti-lactoferrin antibodies: Effects of iron loading of lactoferrin on albumin extravasation in different tissues in rats" (Erga KS, Peen E, Tenstad O, Reed RK) found that iron depleted, but not iron saturated, lactoferrin may protect lung tissue during the release of reactive oxygen species. In vivo, only iron-free lactoferrin reduced inflammatory hyperpermeability in the lung tissue of mice and rats. Although interesting, additional research is

needed to confirm lactoferrin's protective role in lungs that have been damaged during hyper inflammatory periods.

- One interesting study used the level of lactoferrin in nasal secretions as a diagnostic tool for diagnosing the common cold from the more serious sinusitis (infection of the sinuses). As mentioned before, lactoferrin is found in all secretions that bathe mucus membranes and is a first line defense against viruses and other pathogens. It comes as no surprise that higher amounts of lactoferrin would be found in the nasal secretions of people with serious sinus infections. The study found nasal lactoferrin helps distinguish sinusitis from common colds. The study was called "Lactoferrin and eosinophilic cationic protein in nasal secretions of patients with experimental rhinovirus colds, natural colds, and presumed acute community-acquired bacterial sinusitis" (J Med Microbiol 2000 Aug;49(8): 719-23).

References

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