

Lactoferrin: Multifunctional Whey Peptide Super Food

Lactoferrin is a protein of very high iron binding affinity found in milk, and secreted in most mammalian external fluids as well as in tears and saliva. Lactoferrin, made up of a single peptide chain (MW: 77,000 D), is one of the major proteins in human colostrums. It is also found in the specific granules of neutrophil leucocytes. It is thought to act as a first line defense agent against infections by inhibiting the entry and growth of pathogenic bacteria/virus in the body owing to its wide presence in external fluids. Its highest natural food source is un-denatured (low temperature processed) whey proteins and colostrums.

Lactoferrin content in milk of different mammals

human > 2000 mg/mL
guinea pig, mouse, mare > 200-2000 mg/mL
cow, goat, sow > 20-200 mg/mL
rat, rabbit, dog < 50 mg/mL

Lactoferrin in the human the human body

Tears > 1500-2000 ug/mL
seminal fluid > 500-1000 ug/mL
cervical mucus > 500-1000 ug/mL
nasal secretions > 100 ug/mL
saliva > 5-10 ug/mL
urine > 1 ug/mL
blood > (normal) 1-2 ug/mL
blood > (inflammation) 4-200 ug/mL
neutrophils > 2-15 ug/10⁶ cells

Lactoferrin is a multifunctional protein

Research has shown Lactoferrin to have the following functions:

- Iron Uptake: As Lactoferrin binds very tightly to iron, Lactoferrin is thought to allow efficient up take of iron into the body. This is thought to be beneficial for anemia.
- Antibacterial: Killing many disease causing bacteria while protecting the body's natural flora.
- Anti fungal: Lactoferrin kills a range of fungi and yeast's, including the causative agent of the rash, Candida Albicans.
- Antiviral: Research has shown that Lactoferrin can prevent viruses, such as HIV, hepatitis and CMV, from binding to the body's cells and therefore prevent viral infection.
- Anti-tumor: Lactoferrin and related peptides have been shown to suppress tumor growth and prevent tumor formation in laboratory trials.
- Antioxidant: The strong binding of iron by Lactoferrin, prevents "free iron" from forming free- radicals. Free radicals have been implicated as a cause for many infectious diseases and cancers.

Anti-microbial actions of lactoferrin

- Bacteriostatic effects occur through ferro-privation (iron binding).
- High susceptibility micro-organisms to bovine lactoferrin:
 - Escherichia coli
 - Salmonella enteritidis
 - Klebsiella pneumoniae
 - Pseudomonas aeruginosa
 - Proteus vulgaris
 - Listeria monocytogenes
 - Staphylococcus aureus
 - Bacillus subtilis
 - Candida Albicans

Anti -viral actions of bovine lactoferrin

- Bovine lactoferrin was able to able to prevent viral replication. 1
- Clinical effectiveness of bovine lactoferrin on hepatitis C patients has been reported.
- Bovine lactoferrin showed considerable inhibitory activity against HIV-1. 2

Cancer prevention by bovine lactoferrin

- In experimental studies, bovine lactoferrin has been found to significantly inhibit colon, esophagus, lung, and bladder carcinogenesis in rats and bladder when administered orally.
- More extensive clinical trials are now underway in the National Cancer Center Hospital and other institutes to further explore the preventive potential against colon carcinogenesis. 3

Anti-inflammatory activities of bovine lactoferrin

- Lactoferrin is thought to exert a protective effect via modulation of the immune system and correction of cytokine imbalance. 4
- Lactoferrin caused significant induction of the anti-inflammatory cytokines IL-4 and IL-10, significant reductions in the pro-inflammatory cytokines TNF-a and IL-1b. 5

Anti-oxidant activities of lactoferrin

- A principal function of Lf is that of scavenging free iron in fluids and inflamed areas so as to suppress free radical-mediated damage and decrease the availability of the metal to invading microbial and neoplastic cells. 6

Lactoferrin and Exercise Recovery

- Intense exercise causes a dramatic rise in free radicals with a simultaneous reduction of antioxidant systems within the body to fight them
- Free radicals cause inflammation =
 - damage to muscle damage
 - fatigue
 - possibly immune system suppression
- Oxidative stress has been associated with decreased physical performance.

Safety and Toxicity

Bovine lactoferrin is safe. Oral toxicity (1 day, 4 week and 13 week dose) in rats revealed no lethal toxicity, at 2000 mg/kg/day.

Lactoferrin has been passed as safe by the US FDA. Oral supplementation with bovine sourced Lactoferrin in adults can prevent the onset of infectious diseases caused by proliferation of opportunistic pathogens through the enhancement of your body's host defense ability or improved immune system response.

Lactoferrin Dosage

Oral lactoferrin dosed at 40 mg daily has been used in a couple of clinical trials. Those who supplement with lactoferrin separately in pill form may take 300 mg or more daily! Bio available lactoferrin content in whey products varies greatly related to the type of processing used and the amount of heat exposure.

Overview of Recent Scientific Investigations

The Baylor School of Medicine received three patents in the 1990s covering the cloning of lactoferrin and lactoferrin peptides for therapeutic and nutritional applications. An array of lactoferrin-related patents (1983-1997) points to the ingredient's potential in a number of areas, from infant diarrhea and support for newborn growth (Nichols & McKee, 1988) to food and pharmaceutical applications (Dubois, 1988).

Lactoferrin is an iron-binding protein rich in bioactive functionality. For that reason, it has received much attention in the research field. Initially, interest focused on lactoferrin's capacity of acting in iron transport and as an antimicrobial agent, due to its iron-chelating ability. In terms of biological activities/benefits, lactoferrin is a highly significant whey protein. Lately (Shimazaki, 2000) the component's multiple potential health benefits are expanding into the following areas.

General benefits have been addressed in at least ten publications over the last three years (1999-2001). These include explorations of the extra benefits of lactoferrin (Potjewijd R, 1999) and investigations into the usefulness of bovine lactoferrin in animals and, importantly, in humans (Yamauchi K, Teraguchi S & Hayasawa H, 1999).

Anticancer support has been established for mice and rats (Iigo M et al., 1999; Noorby K et al., 2001 and others). A recent study on the role of dairy products in cancer prevention (Tsuda H et al., 2000) focused on lactoferrin's biological activities.

Antimicrobial studies have been extensive, beginning with Arnold et al. (1979) and continuing through research on the protective effects (Valenti P et al., 1999) and antibacterial effects (Venkitanarayanan KS et al., 1999) of lactoferrin. Kawasaki Y et al. (2000) reported on lactoferrin's inhibitory effect on the adherence of E. coli to host cells.

Synergistic effects from the combination of lactoferrin, lactoperoxidase and beta-lactoglobulin have been shown to eliminate certain microorganisms in mice and thus prevent death.

Antiviral benefits have been explored, demonstrating that lactoferrin is an effective protector against several viruses (Marchetti et al., 1996; Shimazu et al., 1996). Recent studies have

examined lactoferrin's effectiveness in inhibiting/fighting hepatitis C, hantavirus, HIV and other serious infections.

Antioxidant work has looked at lactoferrin's inclusion in infant formulas (Satue-Gracia MT et al., 2000).

Immunomodulation studies have focused on lactoferrin's effects on mice (Debbabi H et al., 1998), Atlantic salmon (Lygren B et al., 1999) and humans (Miyachi H et al., 1998).

Insulin-like growth factor (IGF) research is at the beginning of the curve (Baumrucker CR & Erondy NE, 2000).

Iron transport, the focus of initial lactoferrin research, is of continuing importance. The China Dairy Industry (Jiang DM, 1999) recently researched the effects of iron-saturated lactoferrin on iron absorption.

Peptide derivatives of lactoferrin (produced by the action of pepsin on lactoferrin) have been shown to promote enhanced antimicrobial action. One study (Konig et al., 1995) examined an immuno-stimulating, lactoferrin-derived peptide's ability to modulate release of inflammatory mediators from immune system cells.

1) *Anti-adenovirus activity of milk proteins: lactoferrin prevents viral infection.* Arnold et al, Antiviral Res, 2002, 53, 153-8-

2) *Characterization of the anti HIV effects of native lactoferrin and other derived milk proteinsd peptides.* Berkhout et al, Antiviral Res, 2002 341-55

3) *Cancer prevention by bovine lactoferrin and underlying mechanisms: a Cancer prevention by bovine lactoferrin and underlying mechanisms: a review of experimental and clinical studies.* Tsuda et al, Biochem Cell review of experimental and clinical studies. Biol, 2002, 80, 131-6 , from National Cancer Center Research Institute, Tokyo, Japan

4) *Lactoferrin reduces colitis in rats via modulation of the immune system and correction of cytokine imbalance.* Togawa et al, Am J Physiol Gastrointest Liver Physiol, 2002, 283, G 187-95 21

5) *Administration of exogenous human or bovine Lf to hosts with various infected or inflamed sites has resulted in prophylactic or therapeutic effects. – Human lactoferrin: a novel therapeutic with broad spectrum potential.* J Pharm Pharmacol, 2001, 53, 1303-10, Weinberg ED. Department of Biology and Program in Medical Sciences, Indiana University, Bloomington 47405, USA

6) Immune Modulation: an overview According to Brock J (1995) Immunology Today 16, 417-419

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