Milk Bioactives

More to milk than calcium

Bovine milk, a rich source of nutrients in the human diet, makes it invaluable to human health. Exciting new research into the activity of minor milk components shows milk can benefit our health even more than previously thought.

Milk contains bioactive elements beyond proteins, minerals and vitamins. These minor elements include immunoglobulins, hormones, growth factors, cytokines, nucleotides, polyamines, enzymes and bioactive peptides.

Many bioactive peptides are embedded within milk proteins and remain inactive until released and activated by gastrointestinal digestion or during food processing. Bioactive peptides are naturally found in milk, fermented milk and cheese.

Successful commercialization of milk bioactives is dependent upon developing new technologies for their production, producing innovative food and health ingredients, studying the mechanisms of actions, and conducting clinical studies to verify health effects.
Cardiovascular Effects
Milk peptides with blood pressure lowering effect are receiving special attention due to the prevalence and importance of hypertension (high blood pressure) in the Western population. Hypertension is a risk factor for cardiovascular diseases (CVD) such as myocardial infarction, stroke and heart failure. The angiotension-I-converting enzyme (ACE) is a key enzyme that modulates blood pressure. Its activity causes blood vessels to constrict, resulting in increased blood pressure. Inhibiting ACE activity lowers blood pressure.

Both casein and whey proteins are rich sources of bioactive peptides with ACE inhibitory activity. Their antihypertensive effect in humans has been shown in a number of clinical studies, thus providing alternatives to conventional ACE inhibitor drug treatments. Fermented milks and protein hydrolysates for blood pressure management are currently in the market.

Immunomodulating Peptides
Many peptide fractions in milk that affect immune function are hydrolysates of casein milk proteins. Whey proteins such as lactoferrin, β-lactoglobulin and α-lactalbumin also enhance immune cell function. The metabolic activity of probiotic lactic acid bacteria generates de novo immunoregulatory peptides from milk via enzymatic degradation of parent milk proteins. These peptides are involved in both the up- and down-regulation of the immune system.

Opioids refer to natural opiates (opium) and synthetic narcotics (i.e. morphine, heroin) that induce sleep and soothe the pain. The opioid agonists in milk peptides, derived from casein or whey protein, have shown morphine-like activity. For example, caseinomorphins prolong gastrointestinal transit time, prevent diarrhea, stimulate secretion of insulin and somatostatin and could play a role in appetite suppression.

Opioid antagonists such as casoxins and casoplatelins block the agonist effect of externally administered opioids and enkephalin (the endogenous neurotransmitter) thus affecting the release of pain-reducing endorphins.

Antimicrobial Activity
The major antimicrobial proteins of milk are lactoferrin, lactoperoxidase and the immunoglobulins. Lactoferrin is a multifunctional protein whose most important role appears to be as a defense mechanism against a broad range of microbial infections. Enzymatic hydrolysis of lactoferrin generates lactoferricin, a more potent antibacterial agent. Lactoferrin is also involved in regulating iron homeostasis, cellular growth and differentiation, has anti-inflammatory activity, and offers protection against cancer development and metastasis.

Canadian Suppliers
• Advitech Inc. Quebec, QC | www.advitech.com
• IRI Separation Technologies Vancouver, BC | www.iriseparation.com
• Ronald R. Chisolm Ltd. Optimal Ingredients Division Toronto, ON | www.rachisholm.com
• Saskatoon Colostrum Saskatoon, SK | www.saskcolostrum.com
• Technologie Biolactis Inc. Laval, QC | www.biolactis.com

Bovine Milk Peptides—Activity and Precursor

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<th>Bioactivity</th>
<th>Bioactive Peptide</th>
<th>Protein Precursor</th>
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<tr>
<td>Antihypertensive</td>
<td>Casokinins</td>
<td>α-, β-casein</td>
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<td></td>
<td>Lactokinins</td>
<td>α-, β-lactalbumin, serum albumin</td>
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<tr>
<td>Antimicrobial</td>
<td>Lactoferricin</td>
<td>Lactoferrin</td>
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<tr>
<td>Antithrombotic</td>
<td>Casoplatelins</td>
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<td>Immunomodulating</td>
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<td>Mineral carriers</td>
<td>Caseinophosphopeptides</td>
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<td>Opioid agonists</td>
<td>Caseinomorphins</td>
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<td>α-lactorphin</td>
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<td>β-lactorphin</td>
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<td>Lactoferroxins</td>
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<td>Casoplatelins</td>
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Lactoperoxidase is the most abundant milk enzyme. It has no antimicrobial activity itself. However, in the presence of hydrogen peroxide it catalyses the oxidation of thiocyanate. This reaction forms an intermediate product that plays a key role in protecting mucous membranes against bacterial invasion.

Colostrum has vital immunoglobulins and its use as a health product in treating gastrointestinal infections in humans and domestic animals is increasing. Bovine immunoglobulin concentrates derived from colostrum or whey proteins indicate they could be effective against diarrhea, oral pathogens (Streptococcus mutans, Candida albicans), Helicobacter pylori (the human gastric pathogen), rotavirus and enteropathogenic Eschericia coli infections in children.

**Bone Health and Anticariogenic Activity**

Caseinophosphopeptides (CPP) enhance the absorption of calcium and other minerals thereby contributing to bone health. CPP influences mineralization and demineralization of tooth enamel. When whey glycomacropeptides are included in a formulation with CPP, they prevent the adherence of oral bacteria and control acid formation in dental plaque. These compounds are used as active ingredients in toothpaste as protection against dental caries.

**Other Activities**

Conjugated linoleic acid (CLA) is another bioactive component in milk and dairy products. Whole fat dairy products provide the highest levels of the major CLA isomer, rumenic acid, and its precursor vaccenic acid. These trans fatty acids contribute to the anti-carcinogenic and anti-atherogenic effects in animal models of human disease. CLA may have other potential health benefits including changes in body fat metabolism, antidiabetic effects, and enhancement of bone growth.

A growing body of evidence supports the involvement of bioactive peptides such as casokinins or lactoferrin hydrolysates in cancer prevention.

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**Canadian Research Expertise**

**Agriculture and Agri-Food Canada**

Food Research and Development Centre
St. Hyacinthe, QC
- Antihypertensive activity of bioactive peptides from fermented whey (B. Lee)
- Whey and buttermilk fractionation to obtain functional ingredients (M. Britten)
- Gamma-amino butyric acid (GABA) from cheese fermentation (D. St-Gelais, C. Champagne)
- Isolation and characterization of caseinomacropeptide (G. Robitaille)

**Université Laval**

Institute of Nutraceuticals and Functional Foods (INAF) and STELA Research Centre
Quebec, QC
- Physico-chemical and biological properties of hydrolyzed β-lactoglobulins; antihypertensive peptides (ACE inhibitors) (S. Gauthier)
- Whey fractionation and separation by nanofiltration to derive new bioactive peptides (Y. Pouliot, S. Gauthier)
- Immune modulating peptides from whey hydrolysis (S. Gauthier, I. Fliss)

**University of Alberta**

Dairy Research and Technology Centre
Edmonton, AB
- Enhancing nutritional quality of milk and milk products for human health (J. Kennelly)

**Alberta Dairy Association Research Unit**

- Membrane processing, isolation, modification and functionality of milk proteins and protein hydrolysates (L. Ozimek)

**University of British Columbia**

Vancouver, BC
- Isolation and structure-function of bovine lactoferricin; antimicrobial activity of peptides from hydrolyzed lactoferrin (E. Li Chan)

**University of Guelph**

Guelph, ON
- Immunoprotective properties of bioactive peptides on intestinal mucosă (Y. Mine)

**Ontario Dairy Council/NSERC**

Research Chair in Dairy Technology
- Protein-protein and protein-polysaccharide interactions during processing (M. Corredig)

**University of Manitoba**

Winnipeg, MB
- Effects of CLA on insulin resistance, adipokines and adipose function (C. Taylor)
- Vascular response to injury; nutritional intervention in treatment of atherosclerosis (P. Zahradka)
- Processing effects on the level of CLA in dairy products (A. Hyamaka)
- Therapeutic potential of CLA for metabolic syndrome-associated cardiovascular disease (H. Anderson)

**University of Moncton**

Moncton, NB
- Probiotic fermentation of milk to develop bioactive peptides for immune system and tumours (C. Matar)
Applications

Milk bioactives have many opportunities for commercial applications. The antimicrobial activity of lactoferricin makes it ideal for inclusion in infant formulas, nutrition bars, and sports and performance products. The lactoperoxidase system is being used in acne preparations, shampoo, toothpaste, soft-serve ice cream and pastry cream. Caseinophosphopeptides are used as ingredients or fortifiers in some foods (i.e. chewing gum), beverages, toothpaste, gels or mouth rinses. Whey protein hydrolysates are also used in sport and nutrition beverages and food products.

In Canada, Advitech extracts growth factors and other bioactive peptides from milk and produces an oral natural health product used to treat mild to moderate psoriasis. Biolactis produces fermented whey products for food, nutraceutical, and pharmaceutical applications. Ronald Chisolm’s Optimal Ingredients Division markets a number of milk proteins and whey derivatives for functional and nutraceutical applications. Saskatoon Colostrum has a global human and animal health market for its colostrum products.

Looking towards future industry development in Canada, the Premium Milk Innovation Program (www.premiumlaitinnovation.ca) is fostering strategies for the development, production and processing of bioactive high value-added dairy ingredients.

References