

Functional Foods Of Milk Origin

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Foods or food ingredients that provide a health benefit beyond nutritional effects through modulation of specific target functions are generally known as functional foods. All foods are functional to some extent as they provide taste, aroma, and nutrients required for normal metabolism, growth and maintenance. However, foods are now being examined intensively for added physiological, psychological and specific health benefits, which may reduce chronic disease risk and optimize health because of latest trend towards preventive health care. Milk provides complete nourishment for the infants for at least six months from birth contributing to development of various organ systems, immune system etc. There is age old perception that milk is a part of healthy diet as it contains a natural cluster of ingredients that protect health. Consumers are realizing the need for functional foods and functional food ingredients to cope up with the fast changing pace of modern life with risks of heart ailments, arthritis, diabetes, obesity etc. This scope is offering huge economic potential for manufacturing and marketing of functional foods through isolation and concentration of functional ingredients. Milk provides essential nutrients like essential amino acids, essential fatty acids, minerals and vitamins which are known to contribute to functional role. Significant bioactive components of milk with functional roles are indicated in the Figure 1 and table 1 and discussed here under. Table 1 further provides some of the commercial brand formulations of milk components being promoted or marketed as Health foods or health promoting products.

MILK PROTEINS

Proteins in raw milk form into two major groups viz. casein and whey proteins. Casein accounts for 80% of total protein in milk and the other 20% are whey proteins. They have significant bioactive properties, which influence a variety of regulatory activities through their primary sequences. Milk also contains numerous minor proteins found mostly in whey and milk fat globule membrane fraction like enzymes, metal binding proteins, enzyme inhibitors, vitamin binding proteins and numerous growth factors which are considered as bioactive ingredients.

Biological activities identified in general are

- i) Modulation of digestive and gastrointestinal functions,
- ii) Control of haemodynamics influencing hyper tension and gastric blood flow,
- iii) Anti carcinogenicity
- iv) Analgesic properties
- v) Growth factors
- vi) Immunoregulation and
- vii) Non immune disease defence

Most of the bioactivities are expressed by peptides derived from the amino acid sequences of native milk proteins. Proteolysis upon digestion liberates bioactive peptides which are beneficial to the hosts. A few commercial developments have been launched with health promoting anti-hypertensive, mineral binding and anti-carcinogenic functions as indicated in table 1. Bioactive peptides can be incorporated in the form of ingredients in functional and novel foods, dietary supplements and pharmaceuticals with the purpose of delivering specific health benefits. Such tailored dietary formulations are currently being developed at global level to optimize health through nutrition. Technological and regulatory aspects of these derivatives are being investigated world wide.

Glyco Macro Peptide (GMP) is a fraction of casein with positive implications for certain dietary restricted populations.

The GMP

- i) binds enterotoxins from *Vibrio cholerae* and *Escherichia coli* because of the mimicking ability of the carbohydrates attached to GMP to that of the entero toxin receptor sites.
- ii) inhibits acid gastric secretions and modifies the concentration of digestive peptides.
- iii) acts as a prebiotic.
- iv) Promotes the bifidobacterial growth

CaseinoPhosphopeptides (CPP) are phosphorylated casein derived fractions produced by proteolytic digestion of α and β caseins.

It improves the bio availability of minerals like calcium in intestinal absorption by keeping them soluble and by preventing precipitation. The serine phosphate cluster, glutamyl residues and glutamic acid residues in the CPP fraction of casein serve as mineral binding sites. The mineral chelating ability is highest with α -casein followed by β and κ caseins.

The insoluble acid casein is an important active ingredient in toothpaste, which is effective at reducing dental caries, Sodium Caseinate, CPP and GMP fraction of casein inhibit potential dental pathogens like *Streptococcus sobrinus* OMZ

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176 and *Streptococcus sangius* OMZ 9. Commercial potential exists in production of dairy derived bioactive peptides for use in products like gels and mouth rinses etc.

Whey is the liquid remaining after milk has been curdled and strained to remove the caseins and contains potentially rich sources of bioactive components. Whey proteins are sold as nutritional supplements and are particularly popular in the sport of body building, muscle growth, wound healing, acceleration in learning and reducing ageing. The major proteins of whey are β - lacto globulin, α -lactalbumin, glycomacropeptide, protease peptone 3, immunoglobulin and serum albumin.

β - lactoglobulin is the abundant whey protein which is an important source of essential amino acids. **β - lactorphin**, a peptide derived from β -lacto globulin has Angiotensin I Converting Enzyme (ACE) inhibitory activity and improves vascular relaxation. Proteolytic digestion in the GI tract leads to liberation of ACE Inhibitory Peptides from the milk peptides which can decrease the hyper tension.

β - lactotensin is an ileum contracting peptide from β - lactoglobulin which has anti stress effect and promotes abolition of fear memory, reduces sensitivity to painful stimuli and consolidates memory.

α -lactalbumin, another whey protein is an immunostimulator. It stimulates the production of IL-1 β stimulating peptide derived from bovine α - lactalbumin which binds to specific sites on human neutrophils and monocytes and stimulates super oxide anion production by neutrophils and human monocyte-macrophage adherence and phagocytosis of human senescent red blood cells. α -lactalbumin inhibits the growth of human colon adeno carcinoma cells by inducing apoptosis like death in human cells. It is also reported to inhibit the growth of skin papillomas in humans upon topical application. α -lactalbumin is a rich source of tryptophan, which can improve morning alertness and brain measures of attention upon evening intake of milk. α -lactalbumin can release serotonin and induce anxiolytic effects suggesting beneficial effects on mood. It can reduce oxidative stress as it chelates heavy metals.

Protease Peptone 3 (PP3) of whey is produced by fermentation of fat free bovine milk. It enhances mono clonal antibody production. Lactophorin, a synthetic amino acid residue fragment from PP3 can inhibit the growth of both Gram positive and Gram negative bacteria.

Immunoglobulins provide normally passive immunity for infants but they are potentially powerful agents which can be incorporated into diets to remove toxic dietary factors. Origo Biosciences have isolated a naturally occurring antibody in milk that binds cholesterol in the human digestive tract and prevents its absorption into the blood stream (<http://www.origobiosciences.com>). Whey proteins hold promise in adjunct therapies for the treatment and prevention of cancer and infection. Immunocal (<http://www.immunocal.com>) a whey protein concentrate from Immunotech Research is marketed as an adjunct in cancer treatments and for treatment of glutathione deficiency, high oxidative stress and immune deficiency. Lacto Pharma in a joint venture with Fonterra (<http://www.lactopharma.com>) is aiming to commercialize lactoferrin to augment cancer chemotherapy. Stolle Milk Biologics (www.smbimilk.com) markets Microlactin, a beverage to alleviate the symptoms and dysfunctions associated with osteoarthritis. DMV (www.campina.com) is marketing Praventin containing lactoferrin and active whey protein fractions which when ingested can reduce acne. Davisco Foods International Inc. markets Biozate 1, a hydrolysed whey protein for lowering blood pressure and cholesterol.

Deminerzalized whey has applications in infant formulations, baby foods, diets of patients with hyper tension or with degenerative liver or kidney failure. Technological developments have resulted in development and popularization of fruit flavored whey beverages, alcoholic whey beverages, carbonated whey beverages, enriched whey beverages, fermented whey beverages, chocolate whey beverages, whey milk beverages, whey based milk substitutes, infant food formulations and whey based lassi like beverages which can be fortified for cancer protection, immunomodulation, anti hyper tensive, thrombolytic and anti inflammatory effects.

Lactoferrin is an iron binding protein found in milk with numerous bioactive properties, which depend on the iron binding ability of the molecule. The bioactivities include

- i) Inhibition of proliferation of cancer cell lines
- ii) Antibacterial activity towards gram negative bacteria
- iii) Possible stimulation of the immune system

Lactoperoxidase is a porphyrin containing peroxidase found in the milk, which has antibacterial effects. It catalyzes the oxidation of thiocyanate to hypothiocyanate by using hydrogen peroxide produced by endogenous bacteria.

Milk Carbohydrates:

Lactose or milk sugar is the predominant carbohydrate in milk. When consumed as part of normal diet, lactose offers important nutritional benefits. The intestinal absorption of calcium and magnesium was enhanced in the presence of Lactose. Lactose is the fermentable base in milk probiotic cultures which are integral to all fermented milk products.

Probiotics are the health promoting factors produced by the microbes through intestinal microbial balance. The product contains viable defined micro organisms in sufficient numbers which when consumed alter the microbial balance of the gut through implantation or colonization and exert beneficial health effects.

Lactobacilli either as single species or in mixed cultures with other bacteria such as Bifidobacteria and /or Streptococci are the common probiotics in humans. These are widely used in the industrial manufacture of fermented milk products like yoghurt, acidophilus milk etc. Their function is

- i) To inhibit pathogenic enteric bacteria through decrease in luminal pH, secrete bactericidal proteins, colonization resistance and inhibitory to epithelial invasion.
- ii) Immuno regulation through transforming growth factor, stimulation of secretory immunoglobulins and decreasing tumor necrosis factor expression.

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- iii) They are known to contribute to consumer health through reduction of antibiotic and Rota viral induced diarrhoea, alleviation of lactose intolerance, reduction of cancer promoting enzymes and putrefactive bacterial metabolites in the gut, alleviation of allergies and atopic diseases in infants and hypo cholesterolemic effect, improvement of mouth flora and caries prevention, minimizing ischemic heart diseases and autoimmune diseases.

Prebiotics are the products which evade digestion by mammalian enzymes in the upper regions of the digestive tract, reach colon in an intact state and are metabolized by indigenous microbes through selective formulation resulting in inducing beneficial luminal and systemic effects. Fermented milk products containing inulin and starch fall under this category. Lactiol and Lactitol are other examples of prebiotics. Combination of probiotic dairy products with prebiotic products like oligosaccharides and starches labeled as synbiotics offer bright prospects in future.

Several lactic acid bacteria have been shown to produce the anti carcinogenic activity due to their antagonistic action on the organisms that convert procarcinogens into carcinogens during their growth. Sour milk with cultures of *Lactobacillus helveticus ss jugurti* and *Candida utilis* reduced the occurrence of tumors.

Fermented milk products like yoghurt are able to provide a benefit for lactose mal digesters as the starter culture bacteria contain the β - galactosidase which is the enzyme lacking in lactic mal digesters. Several fermented dairy products like bifidus and acidophilus bacteria containing yoghurt, milk beverages and kefir which contain several types of bacteria in symbiosis with yeasts were known for their cholesterol lowering ability. Consumption of fermented dairy products with large numbers of bacteria ($>1 \times 10^8$ CFU/g) will ensure passage of sufficient numbers into the intestines and alter the pH of stomach ensuring higher bacterial survival as they pass in large intestines. Once in the large intestines, these bacteria ferment indigestible carbohydrates and produce short chain fatty acids which decrease circulatory cholesterol concentrations either by inhibiting hepatic cholesterol synthesis or by re-distributing cholesterol from plasma to liver. Further, increased bacterial activity in the large intestines results in enhanced bile acid deconjugation. Deconjugated bile acids are not properly absorbed by the gut mucosa and are excreted. Consequently cholesterol being a precursor of bile acids is utilized to a greater extent for bile acid synthesis. These combined actions are presumed as contributing mechanisms to the association of fermented milk consumption with decreased cholesterol concentration thus diminishing the risk of cardiovascular diseases in the consuming population.

Lactulose is an isomer of lactose which is known to promote growth of bifidobacteria and has important implications in infant nutrition. **Lactobionic acid** is the glucose equivalent of gluconic acid and is useful in chelating iron, calcium and magnesium, ensuring their greater absorption.

Milk Fat:

Milk fat is secreted as lipid droplets encircled by special membrane composed of lipid bilayer and proteins known as milk fat globule membrane (MFGM). Both milk fat and MFGM are the bioactive components of milk fat. Milk products contain 3.1-6.1 mg of conjugated linoleic acid (CLA)/g of fat in comparison to 0.6-0.9 mg CLA /g of fat levels in chicken and pork. CLA may inhibit mammary carcinogenesis, inhibit atherosclerosis and can change body fat metabolism. Changes in body fat metabolism results in decreased body fat and increased muscle mass and bone growth. CLA may inhibit mammary carcinogenesis by targeting normal or initial epithelial cells with in the anatomical structures of the mammary epithelium including ducts, alveoli and terminal end buds or in transformed epithelial cells resulting in an inhibition of cell growth, or induction of cell death.

Milk fat globule membrane is known for its cholesterolemia lowering factor, inhibition of cancer cell growth, vitamin binders, inhibition of *helicobacterpilori*, and inhibition of beta glucuronidase of the intestinal *E.coli*.

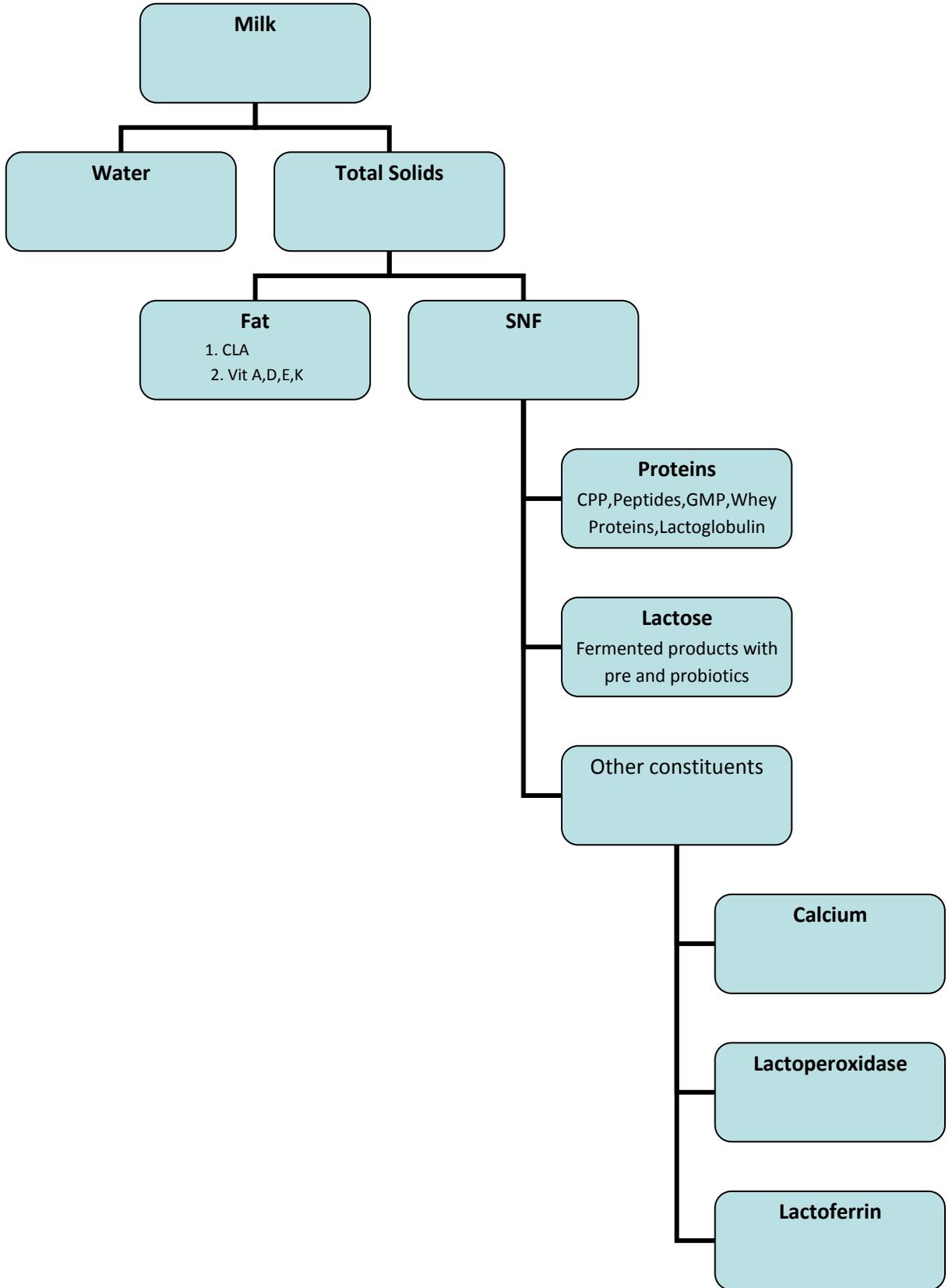
MINERALS AND VITAMINS:

Milk is the major source of calcium along with substantial amounts of potassium, phosphorous, riboflavin, vitamin B12, Zinc, magnesium, and vitamin A. Calcium is an essential nutrient for critical biological functions such as nerve conduction, muscle contraction, cell adhesiveness, mitosis, blood coagulation and structural support of the skeleton. Adequate intake of calcium is reported to reduce risk for chronic diseases such as osteoporosis, hypertension and possibly of colon cancer.

Milk and milk products are the major source of calcium. Dietary calcium requirements are difficult to be fulfilled without consumption of milk and milk products. Milk is a rich source of fat soluble vitamins A, D, E and K. Calcium and vitamin D in milk are reported to reduce risk of colon cancer.

Isolation and concentration of bioactive milk components as nutraceuticals and their incorporation into other foods as dietary supplements offers exciting prospects for dairy entrepreneurs of the country as India has already emerged as the leading producer of milk in the world with enough surpluses for value addition and product development. Though enough basis has been created on the scientific relevance of milk and its components in promoting human health as functional foods, research efforts need to be intensified to further substantiate and validate health claims and to instill greater confidence in consumers. While the needs of dairy industry for innovation in product development, marketing and promotion must be facilitated and supported for maximum exploitation of the phenomenal success of the India's dairy industry, an effective regulatory mechanism needs to be established to protect consumers from false and misleading claims.

Figure.1 Major bioactive components of milk



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Table 1: Bioactive Components of Milk With Their Brand Names And Functional Roles

Brand Name	Form	Bioactive component	Action	Manufacturer
Calpis	Sour milk	Val-Pro-Pro, Ile-Pro-Pro, derived from β -casein and κ -casein	Reduction of blood pressure	Calpis Co., Japan
Evolus	Calcium enriched fermented milk drink	Val-Pro-Pro, Ile-Pro-Pro, derived from β casein and κ -casein	Reduction of blood pressure	ValioOy, Finland
BioZate	Hydrolysed whey protein isolate	β -lacto globulin fragments	Reduction of blood pressure	Davisco, USA
BioPure- GMP	Whey protein isolate	κ -casein f(106-169) (Glycomacropeptide)	Prevention of dental caries, influence the clotting of blood, protection against viruses and bacteria	Davisco, USA
PRODIET F200/Lactium	Flavoured milk drink, confectionery capsules	α s1-casein f (91-100) (Tyr-Leu-Gly Tyr-Leu-Glu-Gln-Leu-Leu-Arg)	Reduction of stress effects	Ingredia, France
Festivo	Fermented low-fat hard cheese	α s1-casein f (1-9), α s1-casein f (1-7), α s1-casein f (1-6)	No health claim as yet	MTTagrifood Research Finland
Cysteine Peptide	Ingredient/hydrolysate	Milk protein derived peptide	Aids to raise energy level and sleep	DMV International, Netherlands
C12	Ingredient/hydrolysate	Casein derived peptide	Reduction of blood pressure	DMV International, Netherlands
Clarinol	Yoghurt	conjugatedlinoleicacid	Reducing body weight	Zero kilo

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