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Milk and Dairy Products as Functional Foods: A Review

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ABSTRACT

Role of food as an agent for improving health has proposed a new class of food, called functional food, with positive effects on host health and/or well-being beyond their nutritional value. Milk and dairy products have been associated with health benefits for many years containing bioactive peptides, probiotic bacteria, antioxidants, vitamins, specific proteins, oligosaccharides, organic acids, highly absorbable calcium, conjugated linoleic acid and other biologically active components with an array of bioactivities: modulating digestive and gastrointestinal functions, haemodynamics, controlling probiotic microbial growth and immunoregulation. Consumer's increasing interest for maintaining or improving their health by eating these specific food products has led to the development of many new functional dairy products. These dairy products contain many functional ingredients that decrease the absorption of cholesterol, can significantly reduce blood pressure, play role in the regulation of satiety, food intake and obesity-related metabolic disorders and may exert antimicrobial effects. This paper reviews and discusses some of the latest findings regarding the role of milk and dairy products as functional foods.

Key words: Functional foods, milk, dairy products, functional ingredients, health

INTRODUCTION

Scientific progress in understanding the relationship between nutrition and health has an increasingly profound impact on consumer's approach to nutrition which has resulted in the development of the concept of functional foods (Bhat and Bhat, 2010). Functional foods can be defined as foods containing significant levels of biologically active components that provide specific health benefits beyond the traditional nutrients they contain (Drozen and Harrison, 1998). A food marketed as functional contains added, technologically developed ingredients with a specific health benefit (Niva, 2007). Although defined several times (Roberfroid, 2002a), there is no unitary accepted definition for functional foods (Alzamora *et al.*, 2005). Furthermore, in most countries there is no legislative definition of the term and drawing a border line between conventional and functional foods is challenging even for nutrition and food experts (Mark-Herbert, 2004; Niva, 2007). Functional foods may improve the general conditions of the body (e.g., pre- and probiotics), decrease the risk of some diseases (e.g., cholesterol-lowering products) and could even be used for curing some illnesses. These are similar in appearance to conventional food and are intended to be

consumed as part of a normal diet but have been modified to subserve physiological roles beyond the provision of simple nutrient requirements (Bech-Larsen and Grunert, 2003). The unwillingness of the consumer to change dietary habits suggests that there is a great market potential for foods with altered nutritional characteristics but unchanged sensory attributes (Becker and Kyle, 1998). The term 'functional food' was introduced in Japan in mid 1980s for food products fortified with special constituents that possess advantageous physiological effects (Hardy, 2000; Kwak and Jukes, 2001; Stanton *et al.*, 2005). These types of foods are known in the Japanese market as Foods for Specified Health Use (FOSHU). The functional foods comprise conventional foods containing naturally occurring bioactive substances (e.g., dietary fiber) or foods enriched with bioactive substances (e.g., probiotics, antioxidants) or synthesized food ingredients introduced to traditional foods (e.g., prebiotics). Among the functional components, probiotics and prebiotics, soluble fiber, omega-3-polyunsaturated fatty acids, conjugated linoleic acid, plant antioxidants, vitamins and minerals, some proteins, peptides and amino acids, as well as phospholipids are frequently mentioned. It should be also stressed that functional foods are not pills or capsules but are consumed as part of a normal everyday diet.

Consumer demands in the field of food production have changed considerably in the last few decades. Consumers more and more believe that foods contribute directly to their health (Mollet and Rowland, 2002; Young, 2000; Elsanhoty *et al.*, 2009). Foods are not intended to only satisfy hunger and to provide necessary nutrients for humans now a day but also to prevent nutrition-related diseases and improve physical and mental well-being of the consumers (Menrad, 2003; Roberfroid, 2000b). There is an increasing demand of functional foods in developed countries that can be explained by certain factors like increasing cost of healthcare, the steady increase in life expectancy and the desire of older people for improved quality of their later years (Kotilainen *et al.*, 2006; Roberfroid, 2000a, 2002). This sizeable demand of functional foods provides important export opportunities for developing countries where demand for functional foods is small but growing. Although the functional foods market is increasing annually but it will only become significant in societies where food security is assured and basic foodstuffs are relatively cheap. However, increasing and varieties of the functional foods are a challenging perspective for promotion and formulation of healthy food and which can be useful for enhancements of human health (Abdel-Salam, 2010).

During last two decades, an increasing amount of attention has been focused on the emergence of a value added food category founded on the specific health and preventive properties provided by certain foods (Bhat and Bhat, 2010). Nutrition related diseases, such as cardiovascular disease and diabetes, associated with the over-consumption of animal fats is one of the serious consequences associated with the consumption of animal products (Bhat and Bhat, 2011) and is now responsible for a third of global mortality (WHO, 2001). In addition, in an older population, more people face the health challenge posed by aging. These trends create a receptive climate for the functional foods. Functional foods have been developed in virtually all food categories. These products have been mainly launched in the dairy, confectionery, soft-drinks, bakery and baby-food market (Kotilainen *et al.*, 2006; Menrad, 2003). Using food for health purposes rather than for nutrition opens up a whole new field for the food industry that can explore various possibilities, including the control of the composition of raw and processed materials by reformulation of fatty acid content or by inclusion of dietary fiber, antioxidants or probiotics, etc. (Jimenez-Colmenero *et al.*, 2001; Mendoza *et al.*, 2001; Scollan, 2007; Bhat and Bhat, 2010).

The health benefits of milk and dairy products are known to humanity since medieval times and may be attributed to the biologically active components that are present in milk and also, due to their suitably modulated activities produced through the action of probiotic bacteria, in the fermented milk products. Besides the modification of several milk components, probiotics may also act directly as preventive agents, or in therapy of some severe diseases (Ferencik and Ebringer, 2003; Gill and Guarner, 2004; Santosa *et al.*, 2006; Gursoy and Kinik, 2006; Abdel-Salam *et al.*, 2008). The functional role of fermented dairy products is either directly through interaction with consumed microorganisms (probiotic effect) or, indirectly, as a result of action of microbial metabolites like vitamins, proteins, peptides, oligosaccharides and organic acids, generated during the fermentation process (biogenic effect). The health-promoting mechanisms of probiotic action are mostly based on the positive effect they exert on the immune response (Isolauri *et al.*, 2001; Biancone *et al.*, 2002) due to stimulation of natural immunity (Newburg, 2005; Galdeano and Perdigon, 2006) and thereby modulating the production of cytokines and antimicrobial peptides (Trebichavsky and Splichal, 2006). Whey proteins possess antimicrobial, anticarcinogenic, immunostimulatory, health-promoting activities (Madureira *et al.*, 2007) and may reduce fat deposition and improve insulin sensitivity (Luhovyy *et al.*, 2007; Dunshea *et al.*, 2007).

Milk is a complex mixture of specific bioactive proteins, lipids and saccharides and contains numerous biologically active substances such as immunoglobulins, enzymes, antimicrobial peptides, oligosaccharides, hormones, cytokines and growth factors (Clare and Swaisgood, 2000; Donovan, 2006, Pouliot and Gauthier, 2006). Fresh milk contains a mixture of antimicrobial agents that exhibit bacteriostatic and even bactericidal activities. Mammalian milk contains more than 60 different enzymes (Fox, 2003) including digestion enzymes (proteinases, lipases, amylases, phosphatases) and enzymes with antioxidant and antimicrobial characteristics (like lysozyme, catalase, superoxide dismutase, lactoperoxidase, myeloperoxidase, xanthine oxidoreductase, ribonuclease, etc.) that are important in terms of milk stability and in terms of protection of mammals against pathogenic agents.

Lactose and other oligosaccharides comprise the third most abundant constituent of milk. Lactose is fermented to lactic acid that reduces pH and influences the physical properties of casein and thus promotes digestibility, improves the utilization of calcium and other minerals and inhibits the growth of potentially harmful bacteria. The individuals that are intolerant to lactose have insufficient activity of β -galactosidase that causes intolerance to the milk sugar. However, due of its lower lactose content, fermented milk can be tolerated by people with a reduced ability to digest lactose (Buttriss, 1997; McBean, 1999). Lactulose is a disaccharide that originates during heat processing of milk and has beneficial health effect mainly by selective stimulation of the growth and/or activity of probiotic bacteria including bifidobacteria and lactobacilli (Gibson, 2004). The sour milk products also contain some polysaccharides in addition to natural oligosaccharides produced by the probiotic bacteria, as well as their hydrolyzed products like kefiran, a basic bioactive component of kefir (Farnworth, 2005), that contribute to their stability and organoleptic properties. Kefir is used for its beneficial effects in a variety of conditions including metabolic disorders, atherosclerosis, allergic diseases, tuberculosis, cancer and gastrointestinal disorders (Ozlem and Ozlem, 2003).

Milk proteins include caseins, β -lactoglobulin, α -lactalbumin, immunoglobulins, lactoferrin and serum albumin that exert their biological activities either directly, or after degradation to different peptides that, through their action, affect not just the immune system, but also digestive, cardiovascular and nervous systems (Korhonen and Pihlanto, 2006). Milk proteins are currently

the main source of a range of biologically active peptides such as casomorphins, casokinins, immunopeptides, lactoferrin, lactoferricin and phosphopeptides. The main biological activities of these peptides are immunomodulation, anti-microbial activity, anti-thrombotic activity, blood pressure regulation and mineral or vitamin binding (Meisel, 1998; Schanbacher *et al.*, 1998; Tome and Ledoux, 1998). Fermented milks are also a rich source of whey proteins such as α -lactalbumin, β -lactoglobulin, lactoferrin, lactoperoxidase, immunoglobulins and variety of growth factors. These proteins have demonstrated a number of biological effects ranging from anti-carcinogenic activity to different effects on the digestive function (McIntosh *et al.*, 1998).

β -lactoglobulin acts as an effective emulgator and immunomodulator and its molecule contains a hydrophobic part which can bind vitamin A, vitamin D, calcium and FAs, simplifying their resorption (Brown, 1984; Cho *et al.*, 1994; Wang *et al.*, 1997; Beaulieu *et al.*, 2006). Besides it can exhibit physiological functions because of numerous bioactive peptides that are contained within the protein which are inactive within the sequence of the precursor protein but can be released by *in vivo* or *in vitro* enzymic proteolysis. Besides their antihypertensive, antithrombotic, opioid, antimicrobial, immunomodulant and hypocholesterolemic properties, all β -lactoglobulin-derived peptides also exhibit radical-scavenging activity (Hernandez-Ledesma *et al.*, 2007). β -Lactoglobulin is responsible for milk allergies and the peptides originating from it may cause oral tolerance and subsequently reduce the production of IgE which is specific for this protein (Pecquet *et al.*, 2000), an effect that can be used in the prevention of milk allergies. In contrast, α -lactalbumin has low immunogenicity and a low allergy inducing potential, which make it a good candidate to become a valuable nutrient for children. It can exert anticancer activity by inducing apoptosis of tumor and immature cells (Svensson *et al.*, 2000). Hydrolysis of α -lactalbumin produces peptides like tripeptide Gly-Leu-Phe with immunomodulatory effects which stimulates phagocytosis of macrophages through specific receptors as well as respiratory burst of neutrophils (Jaziri *et al.*, 1992) and as such considered to be a substance with an important antimicrobial activity (Pihlanto-Leppala *et al.*, 2000; Pellegrini, 2003). α -Lactalbumin may also exert antiulcerative properties and protects the rat stomach mucosa against ulcerative lesions caused by indomethacin (Mezzaroba *et al.*, 2006).

The main immunoglobulins present in milk are IgG1, IgM, IgA and IgG2 which are responsible for protection against microbial pathogens, activation of complement, stimulation of phagocytosis, preventing adhesion of microbes and neutralization of viruses and toxins. They also increase the intracellular levels of glutathione, which is the key cell antioxidant (Bounous and Gold, 1991) and their enhanced preventive activity against different microbial infections has been documented in several studies (Mehra *et al.*, 2006).

Besides immunoglobulins, many cytokines and chemokines have been discovered in human milk (Bottcher *et al.*, 2003; Ustundag *et al.*, 2005; Kverka *et al.*, 2007) including interleukins, interferon- γ , growth factors and chemokines (Garofalo and Goldman, 1998; Bottcher *et al.*, 2003; Kverka *et al.*, 2007) that operate in networks and produce various effects that contribute to the orchestration, development and functions of the immune system.

Lactoferrin, a multifunctional glycoprotein, is present in milk in smaller concentration and has many physiological roles which include regulation of iron homeostasis, host defense against a broad range of microbial infections, anti-inflammatory activity and cancer protection. It can act either as immunosuppressive, anti-inflammatory, or immunostimulatory agent. Lactoferricin is the main peptide that is produced in the course of lactoferrin degradation that is responsible for the majority of its immunomodulatory effects. Both lactoferrin and lactoferricin exhibit antiviral activity against hepatitis C (Isawa *et al.*, 2002), human papillomavirus (Mistry *et al.*, 2007), herpes simplex virus

(Jenssen, 2005) and in combination with interferon and ribavirin in patients with chronic hepatitis C (Kaito *et al.*, 2007). Preventive effects of lactoferrin and lactoferricin on chemically induced colon carcinogenesis in the rat and transplanted carcinoma cell metastasis in the mouse has been demonstrated. Recombinant human and bovine lactoferrin is now available for development into nutraceutical and pharmaceutical products (Weinberg, 2007).

Phosphopeptides, which are formed through proteolytic degradation of casein, are important from mineral nutrition viewpoint. They contain phosphate residues in the form of serine monoesters that create organophosphate salts which function as carriers of cations in the intestine. Phosphopeptides binds with calcium and inhibit the formation of caries lesions through recalcification of the tooth enamel (Reynolds, 1999; Aimutis, 2004) whereas the glycomacropeptide derived from κ -casein seems to contribute to the anticaries effect by inhibiting adhesion and growth of plaque-forming bacteria on oral mucosa (Brody, 2000; Malkoski *et al.*, 2001). They have been used for the treatment of rachitis (Kitts and Yuan, 1992) and their anticariogenic effect has been well documented (Meisel, 2001).

Kitts and Weiler (2003) defines bioactive peptides as specific protein fragments that have a positive impact on body functions or conditions and may ultimately influence health. Milk proteins are considered the most important source of bioactive peptides that are beneficial in reducing the risk of obesity and development of type two diabetes (Zimecki and Kruzal, 2007; Erdman *et al.*, 2008; Haque and Chand, 2008). Bioactive peptides, generated during milk fermentation with dairy starter cultures, have been found in a number of dairy products, such as various cheese varieties and fermented milks (Gobbetti *et al.*, 2002; Korhonen and Pihlanto, 2003; Matar *et al.*, 2003; Fitzgerald and Murray, 2006). Many biologically active peptides are formed during cheese ripening like calcium phosphopeptides (CPPs) have been identified in Comte' and Cheddar cheese (Roudot-Algaron *et al.*, 1994; Singh *et al.*, 1997) and recently in Herrgards cheese (Ardo *et al.*, 2007). Furthermore, secondary proteolysis during cheese ripening may lead to the formation of other bioactive peptides and the occurrence of bioactivity appears to be dependent on the ripening stage of the cheese. Meisel *et al.* (1997) detected higher ACE-inhibitory activities in middle aged Gouda cheese than in short-termed or long-termed ripened cheese. Ryhanen *et al.* (2001) observed that ACE-inhibitory peptides developed gradually during cheese ripening and their concentration was highest in a Gouda-type cheese at the age of 13 weeks, declining slowly thereafter. Saito *et al.* (2000) detected ACE-inhibitory activity in several cheese varieties and measured the highest activity in Gouda cheese aged two years. Manchego cheese showed some ACE-inhibitory activity in the cheese that was at least 15 days old (Gomez-Ruiz *et al.*, 2002). Gagnaire *et al.* (2001) identified a total of 91 peptides in Emmental cheese. Sabikhi and Mathur (2001) found small quantities of b-casomorphin-3 in Edam cheese during ripening. Butikofer *et al.*, (2007) investigated 44 hard, semi-hard and soft cheese samples of Swiss origin for occurrence of IPP and VPP and quantified these peptides. Ong *et al.* (2007) studied the release of ACE-inhibitory peptides in Cheddar cheese made with starter lactococci and probiotic strains *Lb. casei* 279 and *Lb. casei* LAFTI_L26 during ripening and isolated and identified such peptides. The occurrence of various bioactive peptides in fermented milks, e.g., yoghurt, sour milk and Dahi, has been reported in many studies. ACE-inhibitory, immunomodulatory and opioid peptides have been found in yoghurt and in milk fermented with a probiotic *Lb. casei* ssp. *Rhamnosus* strain (Rokka *et al.*, 1997). Also, ACE-inhibitory peptides have been detected in yoghurt made from ovine milk (Chobert *et al.*, 2005) and in kefir made from caprine milk (Quiros *et al.*, 2007).

Milk fat is known for its high proportion of saturated fatty acids and has been associated with an atherogenic blood profile and increased risk of coronary heart disease. However, only three (lauric, myristic and palmitic) of different saturated fatty acids in milk have the property of

raising blood cholesterol and that at least one-third of the fatty acids are unsaturated, with a cholesterol-lowering tendency (Gurr, 1992; German and Dillard, 2006). Furthermore, fermented milks contain components like calcium, linoleic acid, conjugated linoleic acid (CLA), antioxidants and lactic acid bacteria or probiotic bacteria with at least protective if not hypocholesterolemic effects (Rogelj, 2000). The various milk fat components, such as CLA, sphingomyelin, butyric acid, ether lipids, β -carotene and vitamins A and D, have anti-carcinogenic potential (Jahreis *et al.*, 1999; Parodi, 1999a; Akalin and Tokusoglu, 2003; Khanal and Olson, 2004). Many studies have confirmed the anti-carcinogenic activity of CLA, its role in preventing atherosclerosis and in modulating certain aspects of the immune system (Cook and Pariza, 1998; MacDonald, 2000). With dairy products being the primary source of uptake (Vesper *et al.*, 1999), sphingolipids and their metabolites are highly bioactive molecules with multiple beneficial effects on human health, e.g., cancer inhibition, antimicrobial and immunomodulatory activities, as well as inhibition of cholesterol adsorption (Vesper *et al.*, 1999; Possemiers *et al.*, 2005; Akalin *et al.*, 2006). Milk fat is not only a source of bioactive lipid components and also serves as an important delivery medium for nutrients, including the fat-soluble vitamins (Parodi, 1997). Butyric acid (C4:0) is found only in the fat of ruminants and it is believed to be an important anticarcinogen which, together with etheric lipids, vitamins A, D, E and the conjugated linoleic acid, forms a protective barrier mainly against different nontransmissible diseases (Parodi, 1999b, 2004; German, 1999). Caprylic and capric acid (C8:0 and C10:0) may have antiviral activities (Thormar *et al.*, 1994). Lauric acid (C12:0) may have antiviral and antibacterial functions (Sun *et al.*, 2002; Thormar and Hilmarsson, 2007) as well as anticaries and antiplaque activity (Schuster *et al.*, 1980).

CONCLUSIONS

Evidence of health benefits associated with the presence of specific components or bacteria in dairy products is progressively gaining established scientific credibility. The functional proteins, bioactive peptides, essential fatty acids, calcium, vitamin D and other milk components have favorable health effects on the immune and cardiovascular systems, as well as gastrointestinal tract and intestinal health. The functional milk components significantly contribute to the prevention of several diseases like hypertension, coronary vascular diseases, obesity, osteoporosis, cancer, diabetes and some transmissible diseases. There are several applications of these bioactive milk components like: phosphopeptides derived from casein are currently used as both dietary and pharmaceutical supplements (Reynolds, 1999; Aimutis, 2004). Several milk-derived growth factors are used in the treatment of skin disorders and gastrointestinal diseases (Pouliot and Gauthier, 2006). Health promoting effects observed in leg ulcers and psoriasis (Smithers, 2004; Paulin *et al.*, 2005), in gut health (Fell *et al.*, 2000) and in tissue bone regeneration-osteoporosis (Toba *et al.*, 2001). Dietary regulation of food intake by dairy products has the potential to contribute to the prevention and management of the obesity pandemic (Dunshea *et al.*, 2007; Luhovyy *et al.*, 2007) and the possibility of using health-promoting lipids as active ingredients in prophylactic and therapeutic dosage is considered (Haug *et al.*, 2007; Thormar and Hilmarsson, 2007). Milk and dairy products thus offer exciting opportunities in the area of functional foods and the functional food components in milk further serve to illustrate the value of dairy products in the human diet.

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