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Bioactive peptides in fermented milk products and their functionality

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Abstract
Milk and milk products are the rich source of several health driven bioactive peptides. The presence of these bioactive peptides in fermented dairy products viz. cheese, yoghurt and sour milk helps in preventing oxidative stress mediated diseases. Several types of bioactive peptides in fermented dairy products have been characterized. These are the specific protein fragment that exhibits their functionality only after release from the parent protein. Depending upon the specific functionality of peptides, bioactive peptides can be categorize as antioxidative, antihypertensive, immunomodulatory, antimicrobial, antithrombotic and mineral binding peptides. These are released during the product manufacturing process either by spontaneous endogenous enzymatic degradation of milk proteins, or with the use of commercial peptidases under controlled hydrolytic conditions. Bioactive peptides can also liberated during gastrointestinal digestion. The generation of peptides involved the endogenous endo and exo peptidases and adequate processing conditions for the enzymes involved to be in active state. On the other hand, bioactive peptides can also be released by the combined proteolytic activity of endogenous and microbial peptidases. Proteolytic microflora linked with the starter and non starter bacteria also contribute to the release of peptides. So far the functionality of the bioactive peptides is still inadequately characterized so have to carry out further study to confirm the functionality.

Keywords: Bioactive peptides, fermented dairy products, functionality, enzymes

Introduction
Milk is a diverse assortment of mammalian group which exhibits a broad range of physico-chemical and functional properties. Milk protein components are mainly responsible for the different compositional and functional properties. The variability in composition and functionality can be observed in protein also. Milk proteins comprises of serum and glandular derived compounds that are different in molecular size, concentration and functionality (Regester *et al*., 1997) [25]. Milk is considered to be essential growth supplement for neonate of mammalian species, children and also for adult human beings (Park, 2009b) [23]. Milk protein provide protection for enteropathogens as well as essential for manufacture and characteristic dairy products (Korhonen and Pihlanto-leppala, 2004) [16].
Recent studies showed that milk exhibited a broad range of bioactive components which protect neonates and adults from pathogens and illness like immunoglobulin, antibacterial peptides, antimicrobial proteins, lipids apart from the minor components (Park, 2009b) [23]. apart from the nutritional value milk also contained biologically active components i. e casein, whey proteins and other minor constituents that have important biochemical and physiological activities which has impact on human metabolism and health (Schanbacher *et al*., 1998) [27]. Milk components bioactivity is classifies in four major areas like gastrointestinal development, activity and function (2) immunological function and development (3) infant development (4) antibiotic and probiotic activity (Gobbetti *et al*., 2007) [6]. Identification and separation of bioactive milk ingredient is an emerging and new lucrative sector for dairy industries.
The dairy industry has a major key role in the development of functional foods and also has commercialized these products. The functional dairy products have enhanced bioactive properties reduction in elevated blood pressure, control over the body weight and prevention of osteoporosis (FitzGerald *et al*., 2004; Hartmann and meisel, 2007; Korhonen and Marnila, 2006) [4, 8, 14]. The aim of this paper is to review the recent advances on bioactive peptides derived from milk of major species concerning various forms of naturally occurring bioactive compounds, their physiological, biochemical and nutritional functionalities in human health, and (2) elucidate some recent studies on potential applications and development of functional foods using bioactive peptides and components in bovine milk as well as in other species milk.

Bioactive peptides in milk and dairy products and their functionality

Several studies have been conducted on functional properties of bioactive components in milk and dairy products particularly in human and bovine milk, even though more people drink the milk of goats than that of any other single species worldwide (Park, 1990, 2006) [20, 21]. Further, the characterization of bioactive components in milks is difficult, because of the low concentrations of certain very potent agents in milks, their biochemical complexities, require to develop precise methods to quantify certain factors due to their particular forms in milks, the compartmentalization of some of the agents, and the dynamic effects of lactation length and other maternal factors on concentrations or functions of the components of the systems (Goldman and Goldblum, 1995) [7].

Among the milk bioactive components, bioactive peptides are the widely studied components. These are the specific protein fragment which has positive impact on body functions like metabolic as well as physiological functions (Kitts and Weiler, 2003) [13]. Bioactive peptides can be delivered to conventional foods, dietary supplements, Functional foods and also in medical foods.

These bioactive peptides possess an important biological properties such as antioxidant, antimicrobial, immunomodulatory, opoid and mineral binding properties. Bioactive peptides derived from dietary protein have been studied by many researchers (Li *et al*., 2004) [17]. These are released in three different ways: by enzymatic hydrolysis, by proteolytic hydrolysis and through the activity of proteolytic enzymes derived from microorganisms (Kohonen and Pihlanto 2007b) [15]. The various functionality of bioactive peptides are as follow:

ACE inhibitory Peptides

Angiotensin is the powerful vasoconstrictor that acts in the body by controlling arterial blood pressure via contraction of smooth muscles of the blood vessels (Park, 2009a) [22]. Angiotensin converting enzyme (ACE) inhibit the conversion of angiotensin I to angiotensin II. The ACE elevates the blood pressure by conversion of angotensin I to potent vasoconstrictor, angiotensin II and by degradation of bradykinin which is a vasodilator and also by degradation of enkephalins (Petrillo and Ondetti, 1982) [24]. ACE derived peptides from milk proteins like casein named as casokinins (Meisel and Schlimme, 1994) [19] or whey proteins like lactokinins (FitzGerald and Meisel, 2000) [3].

Antioxidant Peptides

Casein derived peptides have antioxidant activity and also inhibits the enzymatic and non enzymatic lipid peroxidation (Rival *et al*., 2001; Suetsuna *et al*., 2000) [26, 29]. Proteolytic enzymes also released antioxidative peptides from milk proteins. The specific dipeptides (Glutamylcysteine) present in whey protein promote the synthesis of glutathione.

Antimicrobial Peptides

The bioactive peptides have membrane lytic activities which disrupt the membrane permeability. The antibacterial activity of milk is the contribution of immunoglobulin and non immunoglobulin such as lactoferrin, lactoferricins, lactoperoxidase, lysozyme, lactenin, casecudubs, etc. (Gobbetti *et al*., 2007; Park, 2009a) [6, 22].

Among antimicrobial peptides, lactoferricin derived from bovine and human lactoferrin have been studied in detail (Kitts and Weiler 2003; Wakabayashi *et al*., 2003) [13, 32]. It has antimicrobial activity against various Gram-positive and -negative bacteria, yeasts and filamentous fungi (Korhonen and Pihlanto, 2007b) [15]. Lactoferricin is an amphipathic, cationic peptide with anti-microbial (Wakabayashi *et al*., 2003) [32] and anti-cancer (Eliassen *et al*., 2002) [1] properties. it can also be generated from pepsin mediated digestion of lactoferrin. Lactenin is the first antibacterial factor present in milk, released from rennet hydrolysis of milk (Jones and Simms, 1930) [12]. Casecidins are the high molecular weight, glycosylated polypeptides that posseses bactericidal activity against lactobacilli and several other pathogenic bacteria such as Staphylococcus aureus. Isracidin is another antibacterial peptide derived from αs1-CN, which is hydrolyzed with chymosin (Hill *et al*., 1974) [9].

Immunomodulatory Peptides

Bioactive peptides derived from caseins and major whey proteins exhibits immunomodulatory activity such as lymphocyte proliferation, antibody synthesis and cytokine regulation (Gill *et al*., 2000) [5]. These peptides have become special interest to food researchers and food processing industry due to their immune cell functions. These immunomodulatory peptides have been shown to modulate the proliferation of human lymphocytes, to stimulate the phagocytic activities of macrophages, and to down-regulate the production of certain cytokines (Matar *et al*., 2003) [18].

Antithrombotic Peptides

These bioactive peptides inhibit the formation of blood clots. Caseinomacropeptides (CMP) released from k-casein by rennin action. These have activity to inhibit the aggregation of blood platelets and binding of the human fibrinogen γ-chain to platelet surface fibrinogen receptors (Fiat *et al*., 1993) [2]. Casoplatelin, peptide released from κ-CN exhibited influence on platelet function and inhibited the aggregation of ADP-activated platelets and the binding of human fibrinogen γ-chain to its receptor region on the platelets surface (Jolles *et al*., 1986) [11].

Mineral binding peptides

Caseinophosphopeptides have the ability to bind to different minerals via formation of soluble organophosphate salts particularly, calcium ion**.** The αs1-, αs2- and β-CN of cow milk contain phosphorylated regions which can be degraded by digestive enzymes. Specific CPPs can form soluble organophosphate salt and enhances the Ca absorption by limiting Ca precipitation in the ileum (Korhonen and Pihlanto, 2007b) [15]. Most CPPs contain a common motif, such as a sequence of three phosphoseryl followed by two glutamic acid residues (Gobbetti *et al*., 2007) [6]. The negatively charged side chains, particularly the phosphate groups, of these amino acids of CPPs are the specific binding sites for minerals (Gobbetti *et al*., 2007) [6]. Chemical phosphorylation of αs1- and β-CN increased the binding capacity and the stability of these proteins in the presence of Ca2+ (Yoshikawa *et al*., 1981) [33].

Whey Proteins derived bioactive peptides

Several whey proteins based bioactive peptides have been identified. Some of these peptides are α-lactorphin, β-lactorphin, βlactotensin, serorphin, albutensin A and lactoferricin. Some of the whey protein derived bioactive peptides are known to possess weak opoid activity. Other bioactives are peptides lactoferroxin from lactoferrin and

lactotensin from β-lactoglobulin (Shah, 2000; Tani *et al*., 1994) [28, 30]. It was found that minor whey proteins such as lactoferrin, lysozyme, lactoperoxidase and immunoglobulins are believed to be antimicrobial proteins. These whey proteins generate bioactive peptides. Lactoferrin is a dominant whey protein in human milk and plays an important role in iron uptake in the intestine (Hutchens *et al*., 1994; Vilgoen, 1995) [10, 31]. Bovine lactoferrin is homologous to human lactoferrin. Lactoferricin is a simple peptide consisting of 25 amino acid residues. A similar active peptide consisting of 47 amino acid residues has been obtained from human lactoferrin. The lactoferrin molecule is folded into two globular units, where each one is capable of binding one ferric (Fe+3) ion (Shah, 2000) [28].

Conclusions

Bovine milk and colostrums are the important source of bioactive components which are beneficial for the human nutrition and health. Bioactive peptides are liberated during gastrointestinal digestion and fermentation of food materials by lactic acid bacteria. Research have proven that these peptides exhibit a wide variety of physiological functionalities, including antimicrobial, antihypertensive, antithrombotic, antioxidative, opioid, anti-appetizing, immunomodulatory, mineral-binding and growth promoting activities. The myriad of innate bioactive peptides and biologically and physiologically active milk compounds from casein, whey proteins and other components in milk have been discovered. They present an excellent source of natural ingredients for different applications in functional foods. Industrial or semi-industrial scale processing techniques are available for fractionation and isolation of major proteins from colostrum and milk. In the near future, several break-through products based on these ingredients will be launched on worldwide markets. These bioactive peptides and milk components could be targeted to the development of functional food products for infants, elderly and immune-compromised people as well as to improve performance and prevent diet-related chronic diseases.

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