Bioactive Components in Milk and Dairy Products

YOUNG W. PARK EDITOR

Although bioactive compounds in milk and dairy products have been extensively studied during the last few decades—especially in human and bovine milks and some dairy products—very few publications on this topic are available, especially in other dairy species’ milks and their processed dairy products. Also, little is available in the areas of bioactive and nutraceutical compounds in bovine and human milks, while books on other mammalian species are non-existent.

Bioactive Components in Milk and Dairy Products extensively covers the bioactive components in milk and dairy products of many dairy species, including cows, goats, buffalos, sheep, horse, camel, and other minor species. Park has assembled a group of internationally reputed scientists in the forefront of functional milk and dairy products, food science and technology as contributors to this unique book. Coverage for each of the various dairy species includes: bioactive proteins and peptides; bioactive lipid components; oligosaccharides; growth factors; and other minor bioactive compounds, such as minerals, vitamins, hormones and nucleotides, etc. Bioactive components are discussed for manufactured dairy products, such as caserins, casenates, and cheeses; yogurt products; koumiss and kefir; and whey products.

Aimed at food scientists, food technologists, dairy manufacturers, nutritionists, nutraceutical and functional foods specialists, allergy specialists, biotechnologists, medical and health professionals, and upper-level students and faculty in dairy and food sciences and nutrition, Bioactive Components in Milk and Dairy Products is an important resource for those who are seeking nutritional, health, and therapeutic values or product technology information on milk and dairy products from the dairy cow and species beyond.

Areas featured are:
• Unique coverage of bioactive compounds in milks of the dairy cow and minor species, including goat, sheep, buffalo, camel, and mare
• Identifies bioactive components and their analytical isolation methods in manufactured dairy products, such as caserins, casenates, and cheeses; yogurt products; koumiss and kefir; and whey products
• Essential for professionals as well as biotechnology researchers specializing in functional foods, nutraceuticals, probiotics, and prebiotics
• Contributed chapters from a team of world-renowned expert scientists

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Bioactive Components in Milk and Dairy Products
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Foreword

An old saying declares that “times are changing.” This book, *Bioactive Components in Milk and Dairy Products*, is a fine example of the truth in that old saying. For at least the last 100 years dairy science textbooks were about milk production from cows almost exclusively and about cow milk being the basic food for young and old. Now dairy science is joining the globalization of commerce worldwide and opening new focus on the long-neglected diversity of milk production from different mammals and on the complexity of milk composition as a source of a multitude of ingredients. These ingredients provide much more than basic nourishment to young and old; they also offer essential components with significant effects and benefits on body metabolism and body health.

This book provides an important contribution to the new globalized dairy science by detailing what is known of the milk of the other dairy animals whose milk contributes significantly to people’s nutrition and health in countries other than the developed West: buffaloes, goats, sheep, camels, and horses. The milk of yaks and reindeer is not covered in this book, but it will be in the future because of the importance of these animals in certain regions of the world.

*Bioactive Components in Milk and Dairy Products* also presents a comprehensive discussion of the many components in milk of all species; these components have a role beyond the basic nutrients of protein, fat, sugar, and minerals. Chapters detail the chemistry and function of a long list of widely unknown factors that have been proven to have properties and activities beneficial to body health: bioactive milk proteins; β-lactoglobulin; α-lactalbumin; lactoferrin; immunoglobulins; lysozyme; lactoperoxidase; peptides from αs1-, αs2-, and β-; κ-caseins; glycomacropeptides; phosphopeptides; oligosaccharides; conjugated linoleic acid; polar lipids; gangliosides; sphingolipids; medium-chain triglycerides; trans fatty acids; milk minerals; growth factors; and approximately 16 hormones in milk, vitamins, and nucleotides. These proven beneficial effects include being antimicrobial, biostatic, antihypertensive, ACE inhibitive, antiadhesion, antidiabetic, anticholesterol, anticarcinogenic, immunomodulatory, anticariogenic, antiobesity, probiotic, and prebiotic. These factors and effects are discussed for milk and dairy products. Furthermore, regulatory and technological aspects of purification, analyses, and fortification into functional foods are presented.

Renowned world authorities researching the different dairy species and the bioactive components in their milk are the contributors in this book, which makes it especially valuable as a new reference source, for which the editor deserves much credit, and for which a wide distribution of this book is greatly deserved and highly recommended.

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Bioactive Components in Milk and Dairy Products
INTRODUCTION

Milk has been known as nature’s most complete food. However, the traditional and contemporary view of the role of milk has been remarkably expanded beyond the horizon of nutritional subsistence of infants. Milk is more than a source of nutrients for any neonate of mammalian species, as well as for growth of children and nourishment of adult humans. Aside from nutritional values of milk, milkborne biologically active compounds such as casein and whey proteins have been found to be increasingly important for physiological and biochemical functions that have crucial impacts on human metabolism and health (Schanbacher et al. 1998; Korhonen and Pihlanto-Leppäla 2004; Gobbetti et al. 2007). Recent studies have shown that milk furnishes a broad range of biologically active compounds that guard neonates and adults against pathogens and illnesses, such as immunoglobulins, antibacterial peptides, antimicrobial proteins, oligosaccharides, and lipids, besides many other components at low concentrations (so-called “minor” components, but with considerable potential benefits). During the past decades, major progress has been made in the science, technology, and commercial applications of the multitude and complexity of bioactive components, particularly in bovine milk and colostrum. Cow milk has been the major source of milk and dairy products in developed countries, especially in the Western world, although more people drink the milk of goats than that of any other single species worldwide (Haenlein and Caccese 1984; Park 1990, 2006). Among the many valuable constituents in milk, the high levels of calcium play an important role in the development, strength, and density of bones in children and in the prevention of osteoporosis in elderly people. Calcium also has been shown to be beneficial in reducing cholesterol absorption, and in controlling body weight and blood pressure. Recent numerous research activities and advanced compositional identification of a large number of bioactive compounds in milk and dairy products have led to the discovery of specific biochemical, physiological, and nutritional functionalities and characteristics that have strong potential for beneficial effects on human health. Four major areas of bioactivity of milk components have been categorized: 1) gastrointestinal development, activity, and function; 2) infant development; 3) immunological development and function; and 4) microbial activity, including antibiotic and probiotic action (Gobbetti et al. 2007).

MILK AS A RICH SOURCE OF BIOACTIVE COMPONENTS

Milk contains a wide range of proteins that provide protection against enteropathogens or are essential for the manufacture and characteristic nature of certain dairy products (Korhonen and Pihlanto-Leppäla 2004). Milk has been shown to contain an array of bioactivities, which extend the range of influence of mother over young beyond nutrition (Gobbetti et al. 2007). Peptides are in a latent or inactive state within protein molecules but can be
Overview of Bioactive Components in Milk and Dairy Products

released during enzymatic digestion. Biologically active peptides released from caseins and whey proteins contain 3 to 20 amino acids per molecule (Korhonen and Pihlanto-Leppäälä 2004). Researchers for the last decade have demonstrated that these bioactive peptides possess very important biological functionalities, including antimicrobial, antihypertensive, antioxidative, anticytotoxic, immunomodulatory, opioid, and mineral-carrying activities. A simple schematic representation of major bioactive functional compounds derived from milk is presented in Figure 1.1.

Most of the bioactivities of milk proteins are latent, being absent or incomplete in the original native protein, but full activities are manifested upon proteolytic digestion to release and activate encrypted bioactive peptides from the original protein (Clare and Swaisgood 2000; Gobbetti et al. 2002). Bioactive peptides (BPs) have been identified within the amino acid sequences of native milk proteins. They may be released by proteolysis during gastrointestinal transit or during food processing. Enzymes such as digestive, naturally occurring in milk, coagulants and microbial enzymes, especially those from adventitious or lactic acid starter bacteria, usually generate these bioactive compounds. BPs are released from milk proteins during milk fermentation and cheese maturation, which enriches the dairy products (Gobbetti et al. 2002). The major biologically active milk components and functions in milk precursors and components are summarized in Table 1.1.

Several milk-derived peptides have shown multifunctional properties, and specific peptide sequences have two or more distinct physiological activities. Certain regions in the primary structure of casein contain overlapping peptide sequences that exert different activities, as shown in Table 1.2. These fragments have been considered as strategic zones that are partially protected from further proteolytic

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**Figure 1.1.** Schematic representation of major bioactive functional compounds derived from milk.
Table 1.1. Major biologically active milk components and their functions

<table>
<thead>
<tr>
<th>Milk Precursors or Components</th>
<th>Bioactive Compounds</th>
<th>Bioactivities Observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-, β-caseins</td>
<td>Casomorphins</td>
<td>Opioid agonist (Decrease gut mobility, gastric emptying rate; increase amino acids and electrolytes uptake)</td>
</tr>
<tr>
<td>α-, β-caseins</td>
<td>Casokinins</td>
<td>ACE inhibitory (Increase blood flow to intestinal epithelium)</td>
</tr>
<tr>
<td>α-, β-caseins</td>
<td>Phosphopeptides</td>
<td>Mineral binding (Ca binding; increase mineral absorption, i.e., Ca, P, Zn)</td>
</tr>
<tr>
<td>α-, β-caseins</td>
<td>Immunopeptides</td>
<td>Immunomodulatory (Increase immune response and phagocytic activity)</td>
</tr>
<tr>
<td>αs1-casein</td>
<td>Isracidin</td>
<td>Antimicrobial</td>
</tr>
<tr>
<td>αs2-casein</td>
<td>Casocidin</td>
<td>Antimicrobial</td>
</tr>
<tr>
<td>κ-casein</td>
<td>Casoxins</td>
<td>Opioid antagonist</td>
</tr>
<tr>
<td>κ-casein</td>
<td>Casoplatelins</td>
<td>Antithrombotic</td>
</tr>
<tr>
<td>κ-casein glyco-macropeptide</td>
<td></td>
<td>Probiotic (Growth of bifidobacteria in GI tract)</td>
</tr>
<tr>
<td>α-lactalbumin (α-La)</td>
<td>Lactorphins</td>
<td>Opioid agonist</td>
</tr>
<tr>
<td>β-lactoglobulin(β-La)</td>
<td>Serorphin</td>
<td>Opioid agonist</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>Lactokinins</td>
<td>ACE inhibitory</td>
</tr>
<tr>
<td>α-La, β-La and Serum albumin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunoglobulins</td>
<td>IgG, IgA</td>
<td>Immunomodulatory (Passive immunity)</td>
</tr>
<tr>
<td>Lactoferrin</td>
<td>Lactoferrin</td>
<td>Immunomodulatory (Increase natural killer cell activity, humoral immune response, thymocyte trafficking immunological development, and interleukins-6; decrease tumor necrosis factor-α)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antimicrobial (Increase bacteriostatic inhibition of Fe-dependent bacteria; decrease viral attachment to and infections of cells)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Probiotic activity (Increase growth of Bifidobacteria in GI tract)</td>
</tr>
<tr>
<td>Lactoferrin</td>
<td>Lactoferoxins</td>
<td>Opioid antagonist</td>
</tr>
<tr>
<td>Oligosaccharides</td>
<td>Oligosaccharides</td>
<td>Probiotic (Increase growth of bifidobacteria in GI tract)</td>
</tr>
<tr>
<td>Glycolipids</td>
<td>Glycolipids</td>
<td>Antimicrobial (Decrease bacterial and viral attachment to intestinal epithelial cells)</td>
</tr>
<tr>
<td>Oligosaccharides</td>
<td>Oligosaccharides</td>
<td>Immunomodulatory (Increase lymphocyte and thymocyte trafficking, and immune development)</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Prolactin</td>
<td></td>
</tr>
<tr>
<td>Cytokines</td>
<td>Interleukins-1,2,6, &amp; 10</td>
<td>Immunomodulatory (Lymphocyte trafficking, immune development)</td>
</tr>
<tr>
<td></td>
<td>Tumor necrosis factor-α</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Interferon-γ</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transforming growth Factors-α, β; leukotriene B₄</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prostaglandin E₂, F₅</td>
<td></td>
</tr>
<tr>
<td>Growth factors</td>
<td>IGF-1, TGF-α, EGF, TGF-β</td>
<td>Organ development and functions</td>
</tr>
<tr>
<td>Parathromone-P</td>
<td>PTHrP</td>
<td>Increase Ca²⁺ metabolism and uptake</td>
</tr>
</tbody>
</table>

Adapted from Schanbacher et al. (1998), Meisel (1998), and Clare and Swaisgood (2000).
### Table 1.2. Examples of physiologically active milk peptides derived from milk

<table>
<thead>
<tr>
<th>Peptide Sequence&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Name</th>
<th>AA&lt;sup&gt;3&lt;/sup&gt; Segment</th>
<th>Physiological Classification</th>
<th>Release Protease</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFVAP</td>
<td>α&lt;sub&gt;s1&lt;/sub&gt;-Casokinin-5</td>
<td>α&lt;sub&gt;s1&lt;/sub&gt;-CN (f23–27)</td>
<td>ACE inhibitor</td>
<td>Proline endopeptidase</td>
<td>Maruyama et al. (1985)</td>
</tr>
<tr>
<td>AVPYPQR</td>
<td>β-Casokinin-7</td>
<td>β-CN (f177–183)</td>
<td>ACE inhibitor</td>
<td>Trypsin</td>
<td>Maruyama et al. (1985)</td>
</tr>
<tr>
<td>YGLF</td>
<td>α-Lactorphin</td>
<td>α-LA (f50–53)</td>
<td>ACE inhibitor and opioid agonist</td>
<td>Synthetic peptide</td>
<td>Mullally et al. (1996)</td>
</tr>
<tr>
<td>ALPMHIR</td>
<td>β-Lactorphin</td>
<td>β-LG (f142–148)</td>
<td>ACE inhibitor</td>
<td>Trypsin</td>
<td>Mullally et al. (1997)</td>
</tr>
<tr>
<td>KVLVPVPQ</td>
<td>Antihypertensive Peptide</td>
<td>β-CN (f169–174)</td>
<td>Antihypertensive peptide</td>
<td>Lactobacillus CP790 protease, and synthetic peptide</td>
<td>Maeno et al. (1996)</td>
</tr>
<tr>
<td>MAIPKKKNQDK</td>
<td>Casoplatelin</td>
<td>κ-CN (f106–116)</td>
<td>Antithrombotic</td>
<td>Trypsin and synthetic peptide</td>
<td>Jollès et al. (1986)</td>
</tr>
<tr>
<td>KDQDK</td>
<td>Thrombin</td>
<td>κ-CN glycol-inhibitory peptide macropeptide (f112–116)</td>
<td>Antithrombotic</td>
<td>Trypsin</td>
<td>Qian et al. (1995b)</td>
</tr>
<tr>
<td>KRDS</td>
<td>Thrombin inhibitory peptide</td>
<td>Lactotransferrin (f39–42)</td>
<td>Antithrombotic</td>
<td>Pepsin</td>
<td>Qian et al. (1995a)</td>
</tr>
<tr>
<td>Peptide Sequence</td>
<td>Name</td>
<td>AA Segment</td>
<td>Physiological Classification</td>
<td>Release Protease</td>
<td>Reference</td>
</tr>
<tr>
<td>------------------</td>
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<td>------------------------------</td>
<td>------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>QMEAES<em>IS</em>S<em>S</em>EEIVPNS*VEQK</td>
<td>Caseinophosphopeptide</td>
<td>αs-CN (f59–79)</td>
<td>Calcium binding and transport</td>
<td>Trypsin</td>
<td>Schlimme and Meisel (1995)</td>
</tr>
<tr>
<td>LLY</td>
<td>Immunopeptide</td>
<td>β-CN (f191–193)</td>
<td>Immunostimulatory (+)</td>
<td>Synthetic</td>
<td>Migliore-Samour et al. (1989)</td>
</tr>
<tr>
<td>FKCRRWQWRMKKLGAPSITCVRAF</td>
<td>Lactoferrin B</td>
<td>Lactoferrin (f17–41)</td>
<td>Immunomodulatory (+) and antimicrobial</td>
<td>Pepsin</td>
<td>Bellamy et al. (1992) &amp; Miyauuchi et al. (1998)</td>
</tr>
<tr>
<td>YQQPVLPVR</td>
<td>β-Casokinin-10</td>
<td>β-CN (f193–202)</td>
<td>Immunomodulatory (+/-) and ACE inhibitor</td>
<td>Synthetic</td>
<td>Meisel and Schlimme (1994)</td>
</tr>
<tr>
<td>RYLGYLE</td>
<td>α-Casein exorphin</td>
<td>αs-CN (f90–96)</td>
<td>Opioid agonist</td>
<td>Pepsin</td>
<td>Loukas et al. (1983)</td>
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<tr>
<td>YGFAQNA</td>
<td>Serorphin</td>
<td>BSA (f399–404)</td>
<td>Opioid agonist</td>
<td>Pepsin</td>
<td>Tani et al. (1994)</td>
</tr>
<tr>
<td>YLLF.NH₂</td>
<td>β-Lactophorin amide</td>
<td>β-LG (f102–105)</td>
<td>Opioid agonist = ACE inhibitor</td>
<td>Synthetic or trypsin</td>
<td>Mullally et al. (1996)</td>
</tr>
<tr>
<td>YIPIQYVLSR</td>
<td>Casoxin C</td>
<td>κ-CN (f25–34)</td>
<td>Opioid antagonist</td>
<td>Trypsin</td>
<td>Chiba et al. (1989)</td>
</tr>
<tr>
<td>[YVPF PPF]</td>
<td>Casoxin D</td>
<td>αs-CN (f158–164)</td>
<td>Opioid antagonist</td>
<td>Pepsin-chymotrypsin</td>
<td>Yoshikawa et al. (1994)</td>
</tr>
<tr>
<td>YLGSGY-OCH₃</td>
<td>Lactoferroxin A</td>
<td>Lactoferrin (f318–323)</td>
<td>Opioid antagonist</td>
<td>Pepsin</td>
<td>Yamamoto et al. (1994)</td>
</tr>
</tbody>
</table>

1 Adapted from Clare and Swaisgood (2000).
2 The one-letter amino acid codes were used; S* = Phosphoserine.
3 Amino acid.
breakdown (Fiat et al. 1993). Various peptide fragments have different physiological activities. Peptides containing different amino acid sequences can exhibit the same or different bioactive functionalities. The specific bioreactions associated with each physiological class have been characterized, and recent research data have been classified according to their physiological functionality. Some examples of BPs are compiled as shown in Table 1.2 (Clare and Swaisgood 2000).

**BIOACTIVE COMPOUNDS IN FOODS AND FUNCTIONAL FOODS**

In recent years, functional foods and bioactive components in foods have drawn a lot of attention and interest of food scientists, nutritionists, health professionals, and general consumers. A functional food may be similar in appearance to a conventional food, is consumed as a part of normal diet but has various physiological benefits, and can reduce the risk of chronic diseases beyond basic nutritional functions. The volume of market sales for functional foods has grown steadily. The global functional foods market continues to be a dynamic and growing segment of the food industry (Marketresearch.com 2008). Rapid growth is predicted to continue for the next year, but taper off by 2010, when functional foods are expected to represent 5% of the total global food market. The current global functional foods market is estimated to be US$763 billion, depending on sources and definitions (Marketresearch.com 2008), and is expected to grow to US$167 billion by 2010. The global growth rate for functional foods will likely achieve an average of 14% annually through 2010. After 2010, the functional foods market size is expected to comprise approximately 5% of total food expenditures in the developed world (Marketresearch.com 2008). Mintel International Group Ltd. (2008) reported that U.S. sales in the dairy segment of functional (bioactive) foods increased by more than 33% over the review period of 2005–07, and its share of the total market grew from 71–74% with a value of nearly US$2 billion, to nearly 75% of the total market (Table 1.3). In the bars and snacks segment, sales of functional foods more than doubled from 2005 to 2007 to a value of US$197 million. However, the segment still remains quite small, accounting for just 7% of the market in 2007. Functional cereal sales gains were modest as 6% from 2005 to 2007 with a value of US$434 million, making up 16% of market share. Bakery’s share of the functional food sales stood at just 2%, which was a 29% decrease for the same period, suggesting that functional foods for the bakery segment may be the one that represents the most untapped potential (Table 1.3).

The consumption volumes of functional foods, especially for those manufactured using dairy bioactive compounds, are likely to increase in the developed countries. The U.S. sales of functional foods were forecasted to increase by 46% from 2007 to 2012 at current prices and by 28% at inflation-adjusted prices, following strong performance from 2002 to 2007 (Table 1.4). The number of new functional products drastically increased between 2002 and 2007. Product proliferation is a boon to this market because it promotes familiarity with the functional concept. However, the Mintel reports (2008) predicted that proliferation would lead to market saturation and that future growth in the spe-

**Table 1.3. Sale volumes of functional foods in the U.S. during 2005 and 2007**

<table>
<thead>
<tr>
<th></th>
<th>2005</th>
<th></th>
<th>2007</th>
<th></th>
<th>Change 2005–07</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$ million</td>
<td>%</td>
<td>$ million</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Dairy and margarine</td>
<td>1,459</td>
<td>71</td>
<td>1,959</td>
<td>74</td>
<td>34</td>
</tr>
<tr>
<td>Cereal</td>
<td>410</td>
<td>20</td>
<td>434</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>Bars and snacks</td>
<td>92</td>
<td>5</td>
<td>197</td>
<td>7</td>
<td>113</td>
</tr>
<tr>
<td>Bakery</td>
<td>79</td>
<td>4</td>
<td>56</td>
<td>2</td>
<td>–29</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2,041</strong></td>
<td><strong>100</strong></td>
<td><strong>2,646</strong></td>
<td><strong>100</strong></td>
<td><strong>30</strong></td>
</tr>
</tbody>
</table>

Data may not equal totals due to rounding.
*Source: Mintel/based on Information Resources, Inc. InfoScan® Reviews Information.*
specifically defined market may slow down as manufacturers and marketers favor more general promotional methods (Table 1.4).

Globally, digestive health claims are leading functional claims for foods. A recent report also showed that functional foods and beverages providing digestive health benefits are growing, both in the traditional categories where the claim emerged for "yogurt and dairy-based beverages" and in unique and new categories, such as prepared meals and snack mixes (Prepared Foods 2008). In coming years, functional foods and beverages are expected to grow continuously. This trend stems from an ever-growing number of products capitalizing on natural ingredients that provide digestive health benefits. When it comes to digestive health, the key to business successes for manufacturers is to identify creative positioning strategies and launch new product introductions that would make a clear difference (Prepared Foods 2008). Table 1.5 shows the top 10 U.S. digestive health subcategories by number of new product introductions up to May 2008.

The term bioactive components refers to compounds either naturally existing in food or ones formed and/or formulated during food processing that may have physiological and biochemical functions when consumed by humans. Food scientists have been exploiting bioactive components of milk and dairy products for application in functional foods and for potential pharmaceutical use. Milk is often considered as a functional food since it contains varieties of different bioactive components. Because of its chemical composition and structural properties, milk is also a good vehicle to formulate

### Table 1.4. Total U.S. sales and forecast of functional foods at current prices, 2002–2012

<table>
<thead>
<tr>
<th>Year</th>
<th>Million</th>
<th>% Change</th>
<th>Index (2002 = 100)</th>
<th>Index (2007 = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>1,620</td>
<td>—</td>
<td>100</td>
<td>61</td>
</tr>
<tr>
<td>2003</td>
<td>1,666</td>
<td>2.8</td>
<td>103</td>
<td>63</td>
</tr>
<tr>
<td>2004</td>
<td>1,776</td>
<td>6.6</td>
<td>110</td>
<td>67</td>
</tr>
<tr>
<td>2005</td>
<td>2,041</td>
<td>14.9</td>
<td>126</td>
<td>77</td>
</tr>
<tr>
<td>2006</td>
<td>2,385</td>
<td>16.9</td>
<td>147</td>
<td>90</td>
</tr>
<tr>
<td>2007</td>
<td>2,646</td>
<td>10.9</td>
<td>163</td>
<td>100</td>
</tr>
<tr>
<td>2008 (fore)</td>
<td>2,879</td>
<td>8.8</td>
<td>178</td>
<td>109</td>
</tr>
<tr>
<td>2009 (fore)</td>
<td>3,117</td>
<td>8.3</td>
<td>192</td>
<td>118</td>
</tr>
<tr>
<td>2010 (fore)</td>
<td>3,359</td>
<td>7.8</td>
<td>207</td>
<td>127</td>
</tr>
<tr>
<td>2011 (fore)</td>
<td>3,611</td>
<td>7.5</td>
<td>223</td>
<td>136</td>
</tr>
<tr>
<td>2012 (fore)</td>
<td>3,874</td>
<td>7.3</td>
<td>239</td>
<td>146</td>
</tr>
</tbody>
</table>

Source: Mintel/based on Information Resources, Inc. InfoScan® Reviews Information; Mintel forecasts inflation-adjusted growth of 28% during 2007–12.

### Table 1.5. Top U.S. digestive health subcategories (by number of new product introductions)

<table>
<thead>
<tr>
<th>Category</th>
<th>2008*</th>
<th>2007</th>
<th>2006</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spoonable yogurt</td>
<td>42</td>
<td>28</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>Cheese</td>
<td>7</td>
<td>15</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Dairys-based frozen products</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Snack/Cereal/ Energy bars</td>
<td>5</td>
<td>9</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Soy yogurt</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Juice</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Prepared meals</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hot cereals</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Drinking yogurts/ liquid cultured milk</td>
<td>2</td>
<td>6</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cold cereals</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Snack mixes</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

functional foods. Although bioactive compounds in milk and dairy products have been extensively studied during the last couple of decades, especially in human and bovine milk and some dairy products, there are very few publications on this topic available for other dairy animal species that provide valuable nourishment, especially in developing countries in Asia and Africa.

WHY IS THIS BOOK UNIQUE?

So far only a limited number of publications have been available about the biochemistry and technology of bioactive and nutraceutical compounds in bovine and human milk, and the milk of other mammalian species has not received much research attention in this regard. This book is therefore unique in also covering extensively bioactive components in milk and dairy products of goats, sheep, buffalo, camels, and horses by internationally renowned scientists who are in the forefront of research in functional components of milk and dairy products and their chemistry and technology. The bovine milk chapter starts the discussion in order to present the updated reference scientific information and research data in the field of bioactive components and functional food ingredients with respect to those in other dairy species. This book benefits readers around the world, including students, scientists, and health-conscious consumers who are looking for scientific information on bioactive compounds and functional food ingredients with respect to those in other dairy species. This book presents the best available current knowledge and reports on the up-to-date information written and forwarded by world authorities and experts in bioactive and nutraceutical components in milk and processed milk products of different dairy species.

This volume is uniquely different from other published works because it not only contains rich compilations of a variety of research data and literature on milk of different mammalian species, but because it also extensively delineates bioactive compounds in the various important manufactured dairy products. Other integral aspects of functionality of bioactive compounds are also included in this book, such as potential for improving human health with these components in milk and dairy products. The introductory section describes the overview of bioactive components in milk and dairy products and the general concept of bioactive compounds and functional foods derived from milk and dairy products. Section I covers the bioactive components in milk of the different major dairy species, which makes this book a special reference source of detailed information not otherwise available. This work therefore would be valuable to readers who seek special scientific information and data for their unique locations, environments, traditions, and availabilities of their own dairy species. Considering this rapidly emerging and fascinating scientific area in human health and nutrition, this work is a special reference source because of its unique and significant contributions to the field. Section II looks closely at the bioactive components in manufactured dairy products, such as caseins, caseinates, cheeses, yogurt products, koumiss and kefir, whey products, probiotics, and prebiotics. Section III touches on other related issues in bioactive compounds in dairy products, such as regulatory issues and functional health claims on bioactive compounds, new technologies for isolation, and analysis of bioactive compounds. This section also delineates several aspects of potential for improving human health, including immunomodulation by dairy ingredients, calcium bioavailability of milk and dairy products, and iron fortification of dairy products.

ACKNOWLEDGMENT

The reviews of this and other chapters rendered by Dr. George F. W. Haenlein are greatly appreciated, and his editorial advice to this book is herewith gratefully acknowledged.

REFERENCES


Chapter 1: Overview of Bioactive Components in Milk and Dairy Products


Section I
Bioactive Components in Milk
INTRODUCTION

Functional foods have emerged as a new approach to improve human nutrition and health in an environment where lifestyle diseases and aging populations are considered a threat to the well-being of the society. The advent of this new food category has been facilitated by increasing scientific knowledge about the metabolic and genomic effects of diet and specific dietary components on human health. Accordingly, opportunities have arisen to formulate food products that deliver specific health benefits, in addition to their basic nutritional value.

Bovine milk and colostrum are considered the most important sources of natural bioactive components. Over the last 2 decades major advances have taken place with regard to the science, technology, and commercial applications of bioactive components present naturally in bovine milk and colostrum.

Bioactive components comprise specific proteins, peptides, lipids, and carbohydrates. Chromatographic and membrane separation techniques have been developed to fractionate and purify many of these components on an industrial scale from colostrum, milk, and cheese whey (Smithers et al. 1996; McIntosh et al. 1998; Korhonen 2002; Kulozik et al. 2003; Pouliot et al. 2006; Korhonen and Pihlanto 2007a). Fractionation and marketing of bioactive milk ingredients has emerged as a new lucrative sector for dairy industries and specialized bioindustries. At present many of these components are being exploited for both dairy and nondairy food formulations and even pharmaceuticals (Korhonen et al. 1998; Shah 2000; German et al. 2002; Playne et al. 2003; Rowan et al. 2005; Krissansen 2007). The dairy industry has achieved a leading role in the development of functional foods and has already commercialized products that boost, for example, the immune system; reduce elevated blood pressure; combat gastrointestinal infections; help control body weight; and prevent osteoporosis (FitzGerald et al. 2004; Zemel 2004; Cashman 2006; Korhonen and Marnila 2006; Hartmann and Meisel 2007). There also is increasing evidence that many milk-derived components are effective in reducing the risk of metabolic syndrome, which may lead to various chronic diseases, such as cardiovascular disease and diabetes (Mensink 2006; Pfeuffer and Schrezenmeir 2006a; Scholz-Ahrens and Schrezenmeir 2006). Beyond essential nutrients milk seems thus capable of delivering many health benefits to humans of all ages by provision of specific bioactive components. Figure 2.1 gives an overview of these components and their potential applications for promotion of human health.

This chapter reviews the current knowledge about technological and biological properties of milk- and colostrum-derived major bioactive components and their exploitation for human health. A particular emphasis has been given to bioactive proteins, peptides, and lipids, which have been the subjects of intensive research in recent years.

BIOACTIVE PROTEINS AND PEPTIDES

The high nutritional value of milk proteins is widely recognized, and in many countries dairy products
Figure 2.1. Bioactive milk components and their potential applications for health promotion.
contribute significantly to daily protein intake. The multiple functional properties of major milk proteins are now largely characterized (Mulvihill and Ennis 2003). Increasing scientific and commercial interest has been focused on the biological properties of milk proteins. Intact protein molecules of both major milk protein groups, caseins and whey proteins, exert distinct physiological functions in vivo (Shah 2000; Steijns 2001; Walzem et al. 2002; Clare et al. 2003; Floris et al. 2003; Pihlanto and Korhonen 2003; Madureira et al. 2007; Zimecki and Kruzel 2007). Table 2.1 lists the major bioactive proteins found in bovine colostrum and milk and their concentrations, molecular weights, and suggested biological functions. Many of the bioactive whey proteins, notably immunoglobulins, lactoferrin and growth factors, occur in colostrum in much greater concentrations than in milk, thus reflecting their importance to the health of the newborn calf (Korhonen 1977; Pakkanen and Aalto 1997; Scammel 2001). Furthermore, milk proteins possess additional physiological functions due to the numerous bioactive peptides that are encrypted within intact proteins. Their functions are discussed in the section “Production and Functionality of Bioactive Peptides” later in this chapter.

**Fractionation and Isolation of Bioactive Milk Proteins**

Increasing knowledge of the biological properties of individual milk-derived proteins and their fractions has prompted the need to develop technologies for obtaining these components in a purified or enriched form. Normal bovine milk contains about 3.5% of protein, of which casein constitutes about 80% and whey proteins 20%. Bovine casein is further divided into α-, β- and κ-casein. Various chromatographic and membrane separation techniques have been developed for fractionation of β-casein in view of its potential use, e.g., in infant formulas (Korhonen and Pihlanto 2007a). However, industrial manufacture of casein fractions for dietary purposes has not progressed to any significant extent, so far. Whole casein is known to have a good nutritive value owing to valuable amino acids, calcium, phosphate and several trace elements. Individual casein fractions have been proven to be biologically active and also a good source of different bioactive peptides (see review by Silva and Malcata 2005).

The whey fraction of milk contains a great variety of proteins that differ from each other in their chemical structure, functional properties and biological functions. These characteristics have been used to separate individual proteins, but the purity has proven a critical factor when evaluating the biological activity of a purified component. Membrane separation processes, such as ultrafiltration (UF), reverse osmosis (RO) and diafiltration (DF), are now industrially applied in the manufacture of ordinary whey powder and whey protein concentrates (WPCs) with a protein content of 30–80%. Gel filtration and ion-exchange chromatography techniques can be employed in the manufacture of whey protein isolates (WPI) with a protein content of 90–95% (Kelly and McDonagh 2000; Etzel 2004). The chemical composition and functionality of whey protein preparations are largely affected by the method used in the process. Their biological properties are also affected and are difficult to standardize due to the complex nature of the bioactivities exerted by different proteins (Korhonen 2002; Foegeding et al. 2002). Therefore there is growing interest in developing specific techniques for isolation of pure whey protein components. Industrial or semi-industrial scale processing techniques are already available for fractionation and isolation of major native milk proteins, e.g., alpha-lactalbumin (α-La), beta-lactoglobulin (β-Lg), immunoglobulins (Ig), lactoferrin (LF) and glycomacropeptide (GMP). Current and potential technologies have been reviewed in recent articles (Korhonen 2002; Kulozik et al. 2003; Chatterton et al. 2006; Korhonen and Pihlanto 2007a). Recently Konrad and Kleinschmidt (2008) described a novel method for isolation of native α-La from sweet whey using membrane filtration and treatment of the permeate with trypsin. After a second UF and diafiltration of the hydrolysate, the calculated overall recoveries were up to 15% of α-La with a purity of 90–95%. In another recent method β-Lg was isolated from bovine whey using differential precipitation with ammonium sulphate followed by cation-exchange chromatography (Lozano et al. 2008). The overall yield of purified β-Lg was 14.3% and the purity was higher than 95%. The progress of proteomics has facilitated the use of proteomic techniques, for example, two-dimensional gel electrophoresis, in characterization of whey proteins (O’Donnell et al. 2004; Lindmark-Måsson et al. 2005). Using this technique, Fong et al. (2008)