

1 Review Article

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3 **Milk, milk products and disease free health: an updated**
4 **overview**

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22 **ABSTRACT**

23 The cow and its milk have been held sacred in India since the dawn of human
24 civilization. Indian ancient Vedic texts also describe the virtues of milk and dairy
25 products, as is authenticated by modern scientific principles and proofs. Therefore, milk
26 has been considered as one of the most natural and highly nutritive part of a daily
27 balanced diet. Currently, the integration of advanced scientific knowledge with
28 traditional information is gaining incredible momentum towards developing concept of
29 potential therapeutic foods. Furthermore, new advances towards understanding the
30 therapeutic roles of milk and milk products has also given a new impetus for unraveling
31 the old- age secrets of milk. At present, the best-known examples of therapeutic foods
32 are fermented milk products containing health promoting probiotic bacteria. In present
33 article, we have tried to review the various aspects of the therapeutic nature of milk and
34 fermented dairy products in a highly up-dated manner, and offer an in-depth insight
35 into the development of targeted therapeutic future foods; as per the admirable
36 requirements of consumers.

37 **Key words:** Milk, dairy products, synbiotics, functional foods, therapeutic foods.

38 INTRODUCTION

39 Milk, our very first food, is surrounded with emotional, cultural and religious
40 importance. We are habituated since childhood to think of milk as “nature’s most
41 perfect food”. Milk and dairy products have long been acknowledged as an important
42 constituent of a balanced diet. In addition, evidence of health benefits of milk products
43 allied with the presence of specific components or bacteria are progressively gaining
44 established scientific credibility. It is, therefore, logical that among the best-known
45 examples of functional foods are fermented milks and yogurts containing probiotic
46 bacteria (Weaver, 2003; Kurien et al, 2005). These days, the boundary line between
47 food and medicine is also becoming diffused with the enhanced understanding of food
48 science and technology. Among the various food products, milk has primarily been
49 identified to have a high potential for health improvements for human beings. It is an
50 optimally rich source of vital nutrients such as proteins, fat, lactose, vitamins, minerals,
51 enzymes, hormones, immunoglobulins and cells. Dairy products are consumed not only
52 for meeting the nutritional requirements of the consumers, but also for their role in
53 preventing various disorders such as obesity, osteoporosis, dental caries, poor
54 gastrointestinal health, cardiovascular diseases, hypertension, colorectal cancer, bone
55 ailments, eye diseases, ageing etc. (Sharma and Rajput, 2006). Hence, we have made an
56 attempt to highlight the various therapeutic aspects of milk and milk-based foods with
57 special reference to their role in combating several life-style diseases and disorders,
58 aside from some of the basic knowledge pertaining to this category of foods.

59 HISTORICAL PERSPECTIVE

60 Ancient Indian literature (Upnishads, Purans and Vedas) is full of evidences of the
61 beneficial and therapeutic properties of milk and milk products. The Rigveda describes
62 a cow as Amrutasya nabhih and compares ghee to nectar. Sadhays and Vasus, who
63 tasted cow milk, became immortal, as is said in the Atharva Veda. The milk of Surabhi,
64 which is considered the celestial cow and supreme among all bovines, is useful to
65 humans, as mentioned in the Mahabharata. Milk, according to Bhava Prakasha, is a
66 remedy for the patients of chronic diseases such as epilepsy, jaundice, heart ailments,
67 suppression of stool and urine, spleen enlargement and piles. Bhava Prakasha states that
68 Dadhi acts as an appetizer, tones up a weak person, and also work as an anti-tode
69 against chronic diseases of kidney. Ayurveda emphasizes on the ability of milk to
70 revitalize the energy system of the body. Buttermilk warmed with curry and/ or

71 coriander leaves, turmeric, ginger and salt is relished in Kerala (India), which, as per
72 the ancient science, is the reason for least cases of obesity and indigestion being
73 reported in that state (Sabikhi and Mathur, 2004). Milk, according to Ayurveda, is a
74 laxative whereas dahi has the opposite effect of curing diarrhea.

75 Cow's milk was first used as human food in the Middle East. Goats and sheep were also
76 domesticated in the Middle East between 9000 and 8000 BC. Around 7000 BC, cattle
77 were being herded in parts of Turkey. There is evidence of milk consumption in the
78 British Isles during the Neolithic period, and the use of cheese and butter spread in
79 Europe, and parts of Asia and Africa. Domestic cows, which previously existed
80 throughout much of Eurasia, were then introduced to the colonies of Europe during the
81 'Age of Exploration'. Russian Scientist Elie Metchnikoff was the first person to notice
82 the beneficial effect of fermented milk products as probiotics (Greek; pro = for, bios =
83 life) or therapeutics in his publication on 'Prolongation of Life, 1908'. He found that
84 the colon housed the friendly bacteria similar those good bugs found naturally in
85 fermented milk such as curd, yogurt, acidophilus milk, cultured buttermilk etc. called
86 *Lactobacillus*.

87 **MILK AND WELL BEING**

88 The three most important factors that primarily contribute to health are diet, exercise
89 and genetic factors. Milk is not only nature's food for a new born infant, but also a
90 source for a whole range of dairy products consumed by mankind. Milk contains about
91 87% water and 13% solids. The fat portion of the milk contains fat-soluble vitamins.
92 The solids (other than fat) include proteins, carbohydrate, water-soluble vitamins, and
93 minerals. Milk products contain high quality proteins. The whey proteins constitute
94 about 18% of the protein content of the milk. Casein, a protein found only in milk,
95 contains all of the essential amino acids and accounts for 82 % of the total proteins in
96 milk. Milk also contains calcium, phosphorus, magnesium, and potassium. The calcium
97 found in milk is readily absorbed by the body; Vitamin D plays a role in promoting the
98 calcium absorption and its utilization. Milk is also a significant source of riboflavin
99 (vitamin B2), which helps promote healthy skin and eyes (Dairy Facts, 2003). Dairy
100 products such as yogurts, cheeses and ice creams contain nutrients such as proteins,
101 vitamins and minerals. Consumption of dairy products has been associated with
102 decreased risk of osteoporosis, hypertension, colon cancer, obesity and insulin

103 resistance syndrome. The main dietary source of calcium and vitamin D are dairy
104 products (Weaver, 2003).

105 Milk can be converted into a number of dairy products, and most of these products have
106 already achieved a reputed health-oriented image in consumer's mind, and have proved
107 to be an excellent solution for formulating superior nutrition (Table 1). Overall, dairy
108 foods can be divided into three groups:

- 109 • Basic products i.e. milk, fermented milks, cheeses, ice-cream, etc.
- 110 • Value-added products, in which the milk composition has been changed, e.g. low-
111 lactose or lactose-free products, hypoallergenic formulae with hydrolyzed protein
112 for milk-hypersensitive infants, milk products enriched with Ca, vitamins, etc.
- 113 • Functional/ therapeutic dairy products, primarily those containing probiotic
114 bacteria, and quite frequently enriched with prebiotic carbohydrates.

115 Since, many chronic diseases such as cancer, osteoporosis, coronary heart disease and
116 hypertension are connected to an unbalanced diet; consumers have now started
117 accepting that diet has a great influence on health and well-being. As a result of this,
118 the food industry has taken benefit of new avenues for producing health oriented milk
119 products. Food processing and biotechnology has enabled the food industry to make
120 food with special characteristics. In addition to disease prevention, the role of food as
121 an agent for improving health has been projected. Probiotics, prebiotics, synbiotics and
122 functional foods have been created to describe food products with special
123 characteristics. Developing functional value in dairy-based products simply means
124 enriching the healthy nature of the original base. Functional foods are generally
125 described as foods that promote health beyond providing basic nutrition. A food can be
126 regarded as 'functional' if it satisfactorily demonstrates to affect beneficially one or
127 more target functions in the body, beyond adequate nutritional effects in a way that is
128 relevant to improved health or reduced risk of disease. These foods are eye-catching to
129 modern men and women who wish to reach old age in a healthy form. The best known
130 examples of functional food are fermented milks and yogurts containing probiotic
131 bacteria (Nagpal *et al.*, 2007a).

132 Milk, our very first food, is surrounded with emotional and cultural importance. We
133 have been habituated since childhood to think of milk as "nature's most perfect food.
134 Now, we (almost all of us, infants, the young, adolescents, adults and even the aged)

135 are a nation of milk drinkers. We drink several hundred gallons of milk a year and add
136 to that many pounds of dairy products such as cheese, butter and yogurt. Milk and dairy
137 products have long been acknowledged as an important constituent of a balanced diet.
138 These products provide a wide range of important nutrients. In addition, evidence of
139 health benefits of milk allied with the presence of specific components or bacteria is
140 progressively gaining established scientific credibility. It is therefore logical that among
141 the best known examples of functional foods are fermented milks and yogurts
142 containing probiotic bacteria. Milk itself is much more than the sum of its nutrients. It
143 is a natural source of a jumble of beneficial nutrients and biologically-active
144 compounds with a potential impact on human health. Further, probiotic microorganisms
145 present in milk or fermented milk products, such as dahi, cheese etc., beneficially affect
146 the host improving the properties of intestinal microbial balance. These probiotic
147 effects include alleviation of intestinal disorders such as lactose intolerance, acute
148 gastroenteritis due to enteric pathogens, constipation, inflammatory bowel disease, and
149 food allergy. Three most important factors contributing to health are diet, exercise and
150 genetic factors. There are only a few people who are familiar with terms like probiotics
151 and functional food. The determinants of healthful effects of dairy product are multi-
152 factorial, for example, live bacteria and other components of fermented milk such as
153 highly absorbable calcium, conjugated products of linoleic acid (CLA) and bioactive
154 peptides (Nagpal *et al.*, 2007b).

155 Coronary heart disease, the most common and severe form of cardiovascular disease, is
156 the foremost cause of death in developed countries. Milk and dairy products contain
157 components with at least a protective, if not hypocholesterolemic, effect such as
158 calcium, linoleic acid, conjugated linoleic acid, antioxidants and lactic acid bacteria or
159 probiotic bacteria. Calcium plays an important role in mediating vascular contraction
160 and vasodilatation, muscle contraction, nerve transmission and glandular secretion.
161 Linoleic acid is also favorable in reducing coronary heart disease risks in human
162 subjects. Probiotics, in the form of fermented milk products, have the reputation of
163 cholesterol-lowering properties in humans (Yadav *et al.*, 2006a, b; 2007a, b,c).

164 Hypertension is another modern day problem and again both genetic and environmental
165 factors influence blood pressure. People with high blood pressure are at increased risk
166 of coronary heart disease, stroke, and kidney failure. It is not only an excess of one
167 electrolyte (sodium) in our diets but rather inadequate levels of several others that

168 produce hypertension. An adequate intake of calcium, potassium, and magnesium has
169 now been documented to reduce blood pressure. It has already been proved that effect
170 of milk on blood pressure is greater and more rapid than that of calcium alone. Milk
171 and dairy products are meaningful sources of all three nutrients along with certain
172 bioactive peptides with a potential to reduce blood pressure due to their ability to
173 inhibit the formation of some potent vasoconstrictors (Ashar and Chand, 2004a).

174 Colorectal cancer is one of the leading causes of cancer morbidity and mortality in the
175 Western countries and it is thought to be caused by an interaction between dietary
176 factors and genetic predisposition. The components in dairy foods which may protect
177 against colon cancer are above all calcium, vitamin D, probiotic lactic acid bacteria, a
178 class of fatty acids known as conjugated derivatives of linoleic acid (LCA) and
179 bioactive peptides derived from milk proteins. The high amounts of colloidal calcium
180 phosphate in milk products cause intestinal formation of insoluble, amorphous calcium
181 phosphate, which precipitates bile acids, fatty acids, and other unknown cytotoxic
182 factors and thus inhibits colonic epithelial proliferation. The human colon is intensively
183 colonized with bacteria and as such an extremely complex microbial ecosystem. The
184 majority of these residents is in fact benign and may even offer some health-promoting
185 effect. The lactic acid bacteria termed probiotics are the most prominent representatives
186 of health promoting colon-residents. Oral administration of certain probiotic bacteria is
187 associated with a number of anti-carcinogenic actions, including reduction of colonic
188 pH, immuno-stimulation, anti-mutagenicity and reduction in the activity of enzymes
189 responsible for the conversion of procarcinogens to carcinogens. Fermented milk
190 products, specially those containing probiotic bacteria, may help reduce the risk of
191 cancer at a number of sites. Milk proteins are most likely another milk component with
192 anti-carcinogenic properties, and may therefore retard the development of colon tumors
193 and tumor precursors. Besides, milk whey also contains different high-affinity binding
194 proteins that bind iron, folic acid, vitamin B12, riboflavin, retinol and vitamin D. Their
195 bioactivity is very important for keeping an organism in a healthy condition.
196 Lactoferrin binds iron which is potentially pro-carcinogen and thus prevents intestinal
197 damage, whereas the vitamin binding proteins protect vitamins from intestinal
198 microflora (Daniel et al., 1990; Rokka et al., 1997).

199 Moreover, with an already healthy image, dairy is an excellent solution for formulating
200 flavorful and nutritious functional beverages such as sport drinks, energy drinks and

201 smoothies. Dairy-based beverages provide superior nutrition, as dairy is a source of
202 high quality proteins, calcium, potassium and other nutrients. Such protein-rich
203 beverages provide not only with a source of high-quality protein, but also may add a
204 variety of health benefits that make dairy proteins ideal for a variety of functional
205 beverages. The fat in milk can also be a natural source of conjugated linoleic acid,
206 which may offer health benefits. Dairy also provides an excellent vehicle for delivering
207 probiotics, which play an important role in intestinal health, immunity and other health
208 issues. In addition, ultra-filtered (UF) milk provides the opportunity to create unique
209 dairy-based beverages, such as low-carb/ high-protein drinks. Dairy proteins, such as
210 casein and whey, offer all of the essential amino acids the body requires. Higher daily
211 intake of proteins and their components, especially the high amount of leucine found in
212 dairy proteins, may help people lose fat while preserving lean muscle.

213 Dairy proteins contain several components that may help the human body protect itself
214 against toxins, bacteria and viruses. For example, lactoferrin, an iron-binding whey
215 protein, may increase iron absorption and transport, enhance immunity and stimulate
216 growth of beneficial bacteria in the intestinal tract. Probiotics are a perfect fit for these
217 dairy-based beverages, as dairy is an excellent vehicle to deliver beneficial bacteria
218 such as *Bifidobacterium* and *Lactobacillus* species. Consumption of probiotics with
219 dairy foods such as milk, yogurt and cheese buffers the stomach acid and increases the
220 chance that the bacteria will survive into the intestine. The healthful properties of
221 probiotics also work well with the healthful properties of dairy beverages. Probiotic
222 cultures have been shown in a variety of test systems to stimulate certain cellular and
223 antibody functions of the immune system. Lactic acid bacteria also enhance the levels
224 of certain immuno-reactive cells (e.g. macrophages and lymphocytes) or factors
225 (cytokines, immunoglobulins and interferon). Exposure to probiotics early in life may
226 decrease the risk of allergy. Dairy products are the major natural sources of CLA which
227 is naturally present in cow's milk, holds anti-cancer properties, and have a positive
228 impact on cardiovascular health (Nagpal *et al.*, 2007b). Calcium is not only essential
229 for bone health; it has also been linked to the maintenance of healthy blood pressure
230 and reduction of dental cavities. The resulting ultra-filtered (UF) milk, in both fluid and
231 powdered forms, offers opportunities for lower-carb beverages. From proteins and
232 probiotics to nine essential vitamins and minerals, dairy-based beverages have much to
233 offer today's health-conscious consumer.

234 **HEALTH PROMOTING MILK FOODS**

235 There is a growing trend of health awareness all over the world, wherein consumers
236 and health professionals alike are increasingly adopting a preventive approach rather
237 than a curative one to diseases. While antibiotic therapy is currently the most
238 commonly used approach to treat bacterial infections, it is essentially curative and is
239 associated with unpleasant side effects. Probiotics, on the other hand, score over
240 antibiotics by being preventive, non-invasive and free from any undesirable effects.

241 Consequently, the awareness and popularity of probiotics among the global population
242 is increasing rapidly (Sanders, 1998). Several health benefits have been attributed to the
243 ingestion of probiotic bacteria such as *Lactobacillus* spp and *Bifidobacterium* spp.
244 These bacteria enhance the population of beneficial bacteria in the human gut, suppress
245 pathogens and build up resistance against intestinal diseases. Ingestion of these bacteria
246 is considered to be very effective in preventing diarrhea in children and in alleviating
247 symptoms of lactose intolerance in adults (Salminen *et al.*, 1999; Goyal and Gandhi,
248 2006). Probiotic food products have also been called nutraceuticals, pharma-foods,
249 designer foods, nutritional foods, medical foods or super foods (Childs and Poryzees,
250 1998).

251 **Functional milk foods: foods with therapeutic values**

252 Probiotic bacteria are live microbial strains that, when applied in adequate doses,
253 beneficially affect the host by improving its intestinal microbial balance. Probiotic
254 foods are products that contain a living ingredient in sufficient concentration, so that
255 after their ingestion, the postulated effect is obtained (deVrese and Schrezenmeir,
256 2001). A good probiotic microorganism should meet the following criterion:

- 257 • Be easily produced at lab or home.
- 258 • Non-toxic and non-pathogenic to the host.
- 259 • Better adherence to the host intestine for positive and lasting results.
- 260 • Withstand at high acid in host's stomach.
- 261 • Remain viable for a longer period of time.

262 Common probiotics include 1) lactobacilli such as *L. acidophilus*, *L. johnsonii*, *L. casei*,
263 *L. delbrueckii ssp. bulgaricus*, *L. reuteri*, *L. brevis*, *L. cellobiosus*, *L. curvatus*, *L.*
264 *fermentum*, *L. plantarum*; 2) gram positive cocci such as *Lactococcus lactis ssp.*

265 *cremoris*, *Streptococcus salivarius* ssp. *thermophilus*, *Enterococcus faecium*, *S.*
266 *diacetylactis*, *S. intermedius*; and 3) bifidobacteria such as *B. bifidum*, *B. adolescentis*,
267 *B. animalis*, *B. infantis*, *B. longum* (Mercenier et al., 2002). Also other microbial
268 species, besides lactic acid bacteria (LAB) like *Bacillus subtilis*, *Propionibacterium*
269 spp. and yeasts (*Saccharomyces boulardii*) have been accepted and used as probiotics
270 (Jan et al., 2001).

271 The second generation of probiotics is genetically modified microorganisms (GMO)
272 providing the host with some necessary components e.g. production of immuno-
273 modulators (e.g. interleukins). Probiotic products may be conventional foods (yogurt,
274 cheese, milk) consumed for nutritional purposes, but also for the probiotic effect; food
275 supplement/ fermented milks or medicinal foods; dietary supplements: capsules,
276 tablets, liquids, powder (Ross, 2000; Temmerman et al., 2002). Probiotic preparations
277 used as food supplement can consists of one single strain (e.g. yakult, Japan – *L. casei*
278 Sirota) or there are mixed cultures of two (e.g. Bacilac, Belgium – *L. acidophilus* plus
279 *L. rhamnosus*) or even more (e.g. food supplement VSL-3, Italy, contains 8 LAB
280 species) strains.

281 Historically, humans were exposed to probiotics through fermented foods. The modern
282 diet however contains dramatically decreased numbers of fermented foods. Moreover,
283 the increased hygiene measures in food manufacturing plants and restaurants have
284 resulted in human beings exposed to as few as one millionth of the probiotic organisms
285 to which their ancestors were exposed (Markowitz and Bengmark, 2002). Ageing,
286 increased stress and a hectic lifestyle have further contributed to the declining
287 populations of probiotic organisms in the human gut (Lourens-Hattingh and Viljoen,
288 2001).

289 In the current situation, it becomes critical to supplement human diet with adequate
290 doses of probiotic microorganisms to re-establish the intestinal microflora balance and
291 help maintain good health. Consequently, in recent times, probiotics have been
292 marketed as dietary supplements in the form of tablets, capsules and freeze-dried
293 preparations (Shah, 2000). Probiotic cultures can be more effective, when ingested in a
294 food medium. An empty stomach has a low pH that destroys most bacteria. When food
295 is ingested, the pH in the stomach quickly rises and probiotic bacteria can easily pass
296 unharmed to the small intestine where they are most effective (German et al., 1999).

297 In addition to directly introducing live probiotics to the colon through dietary
298 supplementation, another approach to increase the numbers of beneficial bacteria in the
299 intestine is using prebiotics (Kurien et al, 2005; Mandal et al, 2006). Prebiotics are
300 defined as non-digestible food ingredients that beneficially affect the host by
301 selectively stimulating the growth of beneficial bacteria in the colon, and thus improve
302 host health (Gibson and Roberfroid, 1995). The prebiotics identified are non-digestible
303 carbohydrates that supply a source of fermentable sugar for beneficial bacteria only in
304 the colon (Crittenden, 1999).

305 An approach that combines both probiotics and prebiotics is called *synbiotics* (Ligi et
306 al, 2006). Synbiotics is defined as a mixture of probiotics and prebiotics that
307 beneficially affects the host by improving the survival and implantation of live
308 microbial dietary supplements in the gastrointestinal tract, by selectively stimulating
309 the growth of a limited number of health-promoting bacteria, and thus improving host
310 welfare (Gibson and Roberfroid, 1995). In contrast to probiotics, which introduce
311 exogenous bacteria into the human intestine, prebiotics stimulate the preferential
312 growth of a limited number of bacteria already existing in a healthy, indigenous
313 microbiota. The main dairy products enriched with prebiotics are yoghurts and yoghurt
314 drinks, but spreads, fresh cheeses and milks are also on the market.

315 Conventionally, food healthiness has been associated with nutritional factors such as
316 fat, fibre, salt and vitamin content. In addition to this traditional healthiness, food may
317 contain single components that may have a positive impact on our well-being. Products
318 that are claimed to have special beneficial physiological effects in the body have been
319 called nutraceuticals, pharma foods, designer foods, nutritional foods, medical foods,
320 therapeutic foods or super foods (Childs and Poryzees, 1998). More usually they are
321 termed *functional foods*. The first functional food products were launched in Japan
322 where a food category called FOSHU (Foods for Specific Health Use) was established
323 in 1991 to reduce the increasing health-care costs. The first functional probiotic
324 fermented milk drink 'Yakult' has been available in Japan already since 1935 (Karimi
325 and Pena, 2003).

326 According to a concerted action project FUFUSE (Functional Food Science in Europe)
327 coordinated by ILSI (International Life Sciences Institute), "a food can be regarded as
328 functional if it has been satisfactorily demonstrated to affect beneficially one or more
329 target functions in the body beyond adequate nutritional effects in a way that is relevant

330 to either an improved state of health and well-being and/or a reduction of risk of
331 disease” (ILSI Europe, 2002). Besides providing scientifically proven health effects,
332 functional foods have to maintain a food-like nature and they have to be easily
333 incorporated into the daily diet. A functional food must remain food and it must
334 demonstrate its effects in amounts that can normally be expected to be consumed in the
335 diet: it is not a pill or a capsule, but it is a part of the normal food pattern” (Diplock et
336 al., 1999).

337 It is now well established that there is a clear relation between diet and health. More
338 recent discoveries support the hypothesis that, beyond nutrition, diet may modulate
339 various functions in the body. Functional foods are gaining more widespread popularity
340 and acceptance throughout the developed world and are already well accepted in
341 countries like Japan and the United States. Functional foods can include probiotics,
342 prebiotics and synbiotics (DiRienzo, 2000). The concept of probiotics evolved from a
343 theory first proposed by Nobel Prize winning Russian scientist, Elie Metchnikoff who
344 suggested that the long life of Bulgarian peasants resulted from their consumption of
345 fermented milk products. Probiotic bacteria can be found worldwide in a variety of
346 products, including conventional food products, dietary supplements and medical
347 foods. The main outlets for probiotic bacteria are dairy foods and dietary supplements
348 and medical foods. Dairy foods containing probiotic bacteria include most major brands
349 of yogurt, culture containing fluid milks, such as sweet acidophilus milk and a few
350 brands of cottage cheese. Dairy foods seem to fit naturally with probiotics because of
351 the traditional association of beneficial fermentation bacteria and fermented dairy
352 product. Consumers naturally associate fermented dairy products with live cultures and
353 perceive a benefit in the presence of these cultures (Sanders, 2000).

354 The concept of functional foods seems to be attractive and consumers have accepted
355 such health-tailored food products. For instance, in 1998, Childs and Poryzees (1998)
356 reported that 42% of Americans were interested in regularly buying foods that could
357 help prevent disease. Functional food is intended for a population generally in normal
358 health and must demonstrate beneficial effects in amounts that are usually consumed in
359 the diet. Functional food is a natural food, to which a component has been added/
360 removed or a food in which the bioavailability of the components has been modified by
361 technological or biotechnological means (Korhonen, 2002). Functional foods can be
362 classified into different groups according to their effects: probiotics, prebiotics and

363 dietary fibers, antioxidants, vitamins, polyphenols, plant sterols, poly-unsaturated fatty
364 acids and minerals. The most promising targets for functional foods are the GI
365 functions and particularly control of nutrient bioavailability (Roberfroid, 2000).
366 However, functional foods can affect different systems in the body, e.g. balanced
367 colonic microflora, control of transit time and mucosal motility, bowel habits;
368 modulation of epithelial cell proliferation, balance of redox and antioxidant systems,
369 metabolism of macronutrients, esp. amino acids, carbohydrates and fatty acids.

370 **Functional symbiotic foods**

371 Historically, humans were exposed to probiotics through fermented foods. The modern
372 diet however contains dramatically decreased numbers of fermented foods. Moreover
373 the increased hygiene measures in food manufacturing plants and restaurants have
374 resulted in humans being exposed to as few as one millionth of the probiotic organisms
375 to which their ancestors were exposed (Markowitz and Bengmark, 2002). Ageing,
376 increased stress and a hectic lifestyle have further contributed to the declining
377 populations of probiotic organisms such as lactobacilli and bifidobacteria in the human
378 gut (Lourens-Hattingh and Viljoen, 2001). In the current situation, it becomes critical to
379 supplement human diet with adequate doses of probiotic microorganisms to re-establish
380 the intestinal microflora balance and help maintain good health. Consequently, in
381 recent times, probiotics have been marketed as dietary supplements in the form of
382 tablets, capsules and freeze-dried preparations (Shah, 2000). Some of the commercial
383 probiotic products available in the market are shown in Table 1.

384 Probiotic cultures can be more effective however, when ingested in a food medium. An
385 empty stomach has a low pH that destroys most bacteria, except those lactic acid
386 bacteria that adhere to the stomach mucosa. When food is ingested, the pH in the
387 stomach quickly rises and probiotic bacteria can easily pass mostly unharmed to the
388 small intestine where they are most effective. Such foods incorporated with probiotic
389 cultures fall under the category of functional foods which are broadly defined as ‘foods
390 similar in appearance to conventional foods that are consumed as part of a normal diet
391 and have demonstrated physiological benefits and/or reduce the risk of chronic disease
392 beyond basic nutritional functions’ (German et al., 1999). In addition to directly
393 introducing live bacteria to the colon through dietary supplementation, another
394 approach to increase the numbers of beneficial bacteria such as bifidobacteria in the
395 intestinal microbiota is using prebiotics, in the form of synbiotic foods.

396 MAJOR THERAPEUTIC ATTRIBUTES OF MILK FOODS

397 In this section, we have described various health benefiting roles of functional dairy
398 foods:

399 **Lactose intolerance**

400 Lactose, a type of sugar that naturally occurs in milk is hydrolyzed by lactase enzyme
401 developed in the small intestine. Some people are not able to produce enough lactase so
402 undigested lactose is broken up by the bacteria in the large intestine causing gas,
403 bloating, pain and diarrhea. This condition is called 'lactose intolerance' and is quite
404 common in most parts of the world. One can be born lactose intolerant or develop it
405 later in life (Heyman, 2006).

406 There is convincing evidence from several studies that symptoms of lactose-intolerance
407 are reduced with the consumption of probiotic dairy products (Fonden et al, 2000;
408 Salminen and Gueimonde, 2004). The mechanism of action of probiotic bacteria and
409 fermented products includes lowering of lactose concentration in the product that could
410 result in high lactase activity and thereby increasing the active lactase enzyme entering
411 the small intestine. The bacterial enzyme, beta-galactosidase found in the ileum after
412 consumption of fermented milk products with viable probiotic bacteria is the major
413 factor that improves digestibility by lactose hydrolysis (de Vrese et al., 2001; Saltzman
414 et al., 1999; Vesa et al., 2000; Vinderola and Reinheimer, 2003). This is true for all
415 fermented dairy products, especially yoghurt/ dahi, owing to the enzyme activity of the
416 culture and the higher consistency of fermented milks compared with ordinary milk.
417 Milk and milk products are highly nutritious, so people who suffer from lactose
418 intolerance should not give them up entirely. One can still consume milk in moderate
419 quantities i.e. half a cup of milk, three quarters of a cup of ice-cream or yoghurt etc.
420 Milk foods that contain lactose are better tolerated, if eaten with other foods containing
421 probiotic bacteria or spread out over the day, rather than being eaten in large amounts at
422 once (Talhok et al, 1996; Salminen et al, 1999).

423 **Hypertension**

424 According to the Vedic literature, milk also helps in relieving mental tension. Milk also
425 suppresses pain during abortion, childbirth and at times of extreme fatigue.
426 Hypertension, a modern day's problem is influenced by genetic and environmental
427 factors. People with high blood pressure are at increased risk of cardiovascular disease

428 and stroke. It is not only an excess of one electrolyte (sodium) in our diets but also
429 rather inadequate levels of several others that produce hypertension. An adequate intake
430 of calcium, potassium, and magnesium has now been documented to reduce blood
431 pressure. It has already been proved that effect of milk on blood pressure is greater and
432 more rapid than that of calcium alone. Milk and dairy products are meaningful sources
433 of all three nutrients along with certain bioactive peptides with a potential to reduce
434 blood pressure. Main components of milk products with anti-hypertensive activity
435 include: calcium, peptides derived from whey proteins, casein phosphopeptides,
436 fermented dairy products (Patel and Renz-Schanen, 1998; Marshall, 2004; Ashar and
437 Chand, 2004a, b).

438 **Heart diseases**

439 According to the Puran, consumption of milk with Nagara roots, Suvarcala salt and
440 Sivagharta was a remedy for all heart ailments. It was also reported that milk cooked
441 with dried pippali and consumed with honey, sugar and ghee cured cough and chronic
442 heart diseases. Milk and dairy products contain components with at least a protective, if
443 not hypocholesterolemic, effect such as calcium, conjugated linoleic acid, antioxidants
444 and probiotic bacteria. Linoleic acid is also favorable in reducing coronary heart
445 disease risks in humans. Probiotics, in the form of fermented milk products, have the
446 reputation of cholesterol-lowering properties in humans. Some bacteria harbor enzymes
447 that are capable of utilizing cholesterol (Gilliland et al., 1984; James et al., 1999; Xiao
448 et al., 2003).

449 **Overweight**

450 Due to lack of knowledge, a lot of people, who are trying to lose weight, avoid milk
451 and other dairy foods. However, it is well known that dairy foods in a low-calorie diet
452 may actually help with managing the body weight. A number of studies have shown
453 that a low-calorie diet, rich in dairy nutrients, may actually change the way fat cells
454 work, reducing the amount of body fat stored, particularly from around the abdominal
455 (waist) region. Weight loss from around the abdomen is beneficial for reducing the risk
456 of heart disease and type-2 diabetes. Maintaining a healthy body weight means burning
457 off at least as many calories as you eat. If you need to watch your weight, then choose
458 reduced fat and low fat dairy products for fewer calories (Zemel, 2005).

459

460 **Dentist milk foods**

461 Teeth and bones are very alike. So the calcium, phosphorus and protein found naturally
462 in dairy foods are just as important for building and maintaining strong healthy, teeth as
463 they are for your bones (Patel and Renz-Schanen, 1998; Bowen, 2002; Johansson,
464 2002). Dairy foods are beneficial for your teeth in a number of ways:

- 465 • Calcium, phosphorus and protein can help build and maintain strong, healthy teeth.
- 466 • Milk is a tooth friendly drink, safe for in between meals, as it does not promote
467 dental caries.
- 468 • The nutrients in milk and dairy can reduce the build up of acid on your teeth which
469 occurs after eating sugary foods
- 470 • The combination of casein, phosphorus and calcium in cheese may actually help
471 remineralize teeth and help reduce your risk of tooth caries.
- 472 • Stimulated saliva flow that is beneficial in a number of ways
- 473 • The dentists' recommends eating a small amount of cheese after meals as it may
474 reduce your risk of dental caries.

475 **Diabetes management**

476 People, who have a high low-fat milk food intake, have a lower risk of type-2 diabetes
477 mellitus; hence, diet and lifestyle modifications can substantially reduce the risk of
478 type-2 diabetes. While a strong inverse association has been reported between milk
479 food consumption and the insulin resistance syndrome among young obese adults, the
480 relation between milk food intake and type-2 diabetes is yet to be completely
481 understood. Dairy products i.e. dahi may produce an anorexic or insulintropic effect
482 and hence, reduces the risk of diabetes (Hyon et al, 2005; Yadav et al, 2006b).

483 **Disease resistance**

484 Some of the probiotic dairy products have been shown to enhance immune functions
485 and thus to reduce the risk of infection in consumers. Milk and colostrums contains
486 some natural immunoglobulins which reduce the risk of many infections in the host by
487 preventing the occurrence of infections by microbes (Haque and Chand, 2006).

488

489

490 **Sleeping sickness**

491 Melatonin is a hormone that controls the body's day and night rhythm. The secretion of
492 melatonin is high in early childhood and decreases rapidly with ageing. Stress
493 conditions and age causes lowering of the level of melatonin. It is secreted at nights in
494 both humans and bovines. The concentration of melatonin in cows' milk at night is
495 about four times higher than in milk collected during the day. The level of melatonin in
496 the milk complements that of the human body, and hence, the drink helps in having a
497 relaxed sleep if taken at night or late in the evening, without causing any drowsiness the
498 following morning (Irina et al, 1999; Valtonen et al, 2005).

499 **Against bad bugs**

500 Acute diarrhea is a serious cause of infant death. Bhava Prakash commends the
501 antimicrobial properties of milk and its usefulness in controlling gastrointestinal
502 disorders such as diarrhea and dysentery. The factors responsible for antimicrobial
503 properties of milk are:

- 504 • Immunoglobulins: are present in high levels in colostrums. These can detoxify
505 toxins, fight viruses, inhibit entero-pathogenic adherence to intestinal wall, prevent
506 the absorption of food antigens, suppresses the growth of pathogens and aid in
507 phagocytosis (Walzem, 2001).
- 508 • Lactoferrin: a whey protein present in bovine milk, strongly bind to iron, making it
509 unavailable to entero-phathogenic bacteria (Reiter, 1985; Marshall, 2004)
- 510 • Lysozyme: present in bovine milk, degrades the bacterial cell wall of invading
511 pathogens.
- 512 • Lactoperoxidase: interact with hydrogen peroxide produced by microbial growth,
513 producing certain intermediary compounds that eventually lyse the pathogenic
514 bacterial cell wall (Ballongue, 1998).

515 **Cancer**

516 Epidemiological studies indicate that humans who consume milk are less likely to
517 develop cancer of the colon and the rectum. Conjugated linoleic acid is a natural
518 component in milk fat and it may reduce the risk of certain diseases, such as breast
519 cancer. The amount of conjugated linoleic acid in milk is higher in whole milk than in
520 reduced or low fat milk. Yogurt consumption has been associated with a reduced
521 incidence of colon cancer in some population groups, which was associated with
522 peptides formed during fermentation (Ganjam et al, 1997).

523 Colorectal cancer is one of the leading causes of cancer morbidity and mortality and it
524 is thought to be caused by an interaction between dietary factors and genetic
525 predisposition. The components in dairy foods, which may protect against colon cancer,
526 are above all calcium, vitamin D, probiotic lactic acid bacteria, a class of fatty acids
527 known as conjugated derivatives of linoleic acid and bioactive peptides derived from
528 milk proteins (Marshall, 2004; Rehmeyer, 2006).

529 **Bone ailments**

530 Calcium is widely recognized as very important ingredient for proper bone health. The
531 consumption of milk and dairy products has been recommended since ancient times for
532 strong bones. In addition to being a rich source of calcium, whey protein contains an
533 active fraction that stimulates the proliferation of bone forming cells (Patel and Renz-
534 Schanen, 1998; Whiting and Lemke 1999; Heaney, 2000). Dairy foods, which are rich
535 in biologically available calcium, have long been shown to retard and minimize
536 osteoporosis. We need calcium everyday because bones are continually being repaired
537 and renewed (that's how broken bones mend!).

538 **Youthful foods**

539 Vasistha the ancient saint, retained perpetual youth for over thousand years by
540 consuming milk and milk products obtained from divine cow Nandini, as mentioned in
541 the Mahabharata. Milk products contain adequate amounts of essential nutrients that
542 help in maintaining normalcy in health and general well being. Halawa prepared from
543 whole- wheat flour and ghee is fed postpartum to ladies to overcome weight loss, to
544 prepare the body for the additional requirement of feeding the child and tone-up the
545 internal organs affected by pregnancy and childbirth (Grover and Dalal, 1993).

546 **Eye-ailments**

547 Milk incorporated with small amount of triphala paste acts as an excellent cure for
548 several eye diseases if applied regularly into the eyes. Bhava Prakash states that freshly
549 churned Makkhan is an excellent lubricant for eyes. Regular application of a few drops
550 of fresh cow ghee in eyes is useful in preventing eye ailments according to the
551 Ayurveda and also for exercising the eye muscles, as is practiced in traditional dance
552 form Kathakali. Bovine milk particularly colostrums has high levels of vitamin A
553 activity that initiates vision from light energy, and is essential for growth and in
554 maintaining the epithelial tissue of eye. Cataract is a major cause of blindness in the

555 elderly. Recent epidemiological evidences suggest that eating of yogurt leads to dose-
556 related protective effects against cataract (Salmon, 1994).

557 **Suppress appetite**

558 The soluble fraction remaining in whey after rennet coagulation of milk can suppress
559 appetite by stimulation of the pancreatic hormones, which stimulates the gall bladder
560 contraction and bowel mobility and regulates gastric emptying optimally (Walzem,
561 2001). Hence, this can avoid excessive and frequent dietary intake that ultimately leads
562 to several complicated disorders.

563 **Delaying of AIDS**

564 During the past several years there have been several reports that whey proteins can be
565 beneficial to patients with HIV infections. Supplementation with whey proteins
566 increases plasma glutathione in advanced HIV infections that lead to better tolerance of
567 the treatment. During a two weeks trial, the commercial source of protein did influence
568 the extent of increase in plasma glutathione levels (Micke et al., 2001, 2002). Whey
569 protein also has been shown to improve muscle strength in women with HIV (Agin, et
570 al., 2001). Lactoferrin has also been shown to be inhibitory to HIV virus (Berkhout, et
571 al., 2003). Ng et al. (2001) evaluated a number of bovine milk proteins for activity
572 against HIV-1 enzymes which are considered to be important for the life cycles of the
573 HIV virus.

574 **Rotavirus diarrhea**

575 Several studies have shown selected probiotics such as *L. reuteri*, *L. casei* Shirota, *B.*
576 *lactis* Bb12 and *L. delbrueckii* ssp. *bulgaricus* can shorten the duration of rotavirus
577 diarrhea by approximately one day (Boudra et al., 2001; Chandra, 2002; Kaila et al.,
578 1992; Saavedra et al., 1994; Shornikovacasas et al., 1997; Sugita and Togawa, 1994).
579 Shortening of the duration of rotavirus diarrhea using the probiotic strain *L. rhamnosus*
580 GG is perhaps the best documented probiotic effect. It has been well documented in
581 several studies around the world and in a recent multicenter study in Europe
582 (Guandalini et al., 2000). *L. acidophilus*, has also been documented to shorten the
583 duration of rotavirus diarrhea (Simakachorn et al., 2000). The mechanism behind this
584 favourable outcome is associated with enhancement of IgA to rotavirus and serum IgA
585 antibody level at convalescence. It is therefore suggested that certain strains of
586 probiotic bacteria promote systematic and local immune response to rotavirus, which

587 may be of importance for protective immunity against re-infections (DeRoos and
588 Katan, 2000; Fonden et al., 2000; McFarland, 2000).

589 **Antibiotic-associated diarrhea**

590 *L. rhamnosus* GG, *L. acidophilus*, *B. longum* and *B. animalis* have been reported to
591 prevent antibiotic-associated diarrhea when consumed either in yogurt form or as a
592 freeze-dried product (Arvola et al., 1999; Colombel et al., 1987; McFarland, 1998,
593 2000; Siitonen et al., 1990; Thomas et al., 2001; Vanderhoof et al., 1999; Witsell et al.,
594 1995). These effects are mainly documented in infants; however, in case of adults, the
595 data is not yet clear (Salminen and Gueimonde, 2004).

596 **Allergy prevention and alleviation**

597 The prevalence of allergic diseases has been on rise in the past few decades and is
598 likely to continue to do so. It has been found that differences in intestinal microbiota
599 composition precede the development of some allergic diseases (Bjorksten et al., 2001;
600 Kalliomaki et al., 2001). This therefore indicates potential application of probiotic
601 bacteria in this area. Administration of *L. rhamnosus* GG and *B. lactis* Bb12 prenatally
602 to mother and during the first few months to infants with high risk of atopic disease
603 reduced the prevalence of atopic eczema (HelinHaatela et al., 2002; Kalliomaki et al.,
604 2003; Majama and Isolauri, 1997). Additionally, supplementation of extensively
605 hydrolyzed whey with *L. rhamnosus* GG or *B. lactis* Bb12, has been found to be more
606 effective than unsupplemented formula on eczema alleviation in infants with atopic
607 eczema (Isolauri et al., 2000).

608 **BIOACTIVE PEPTIDES FROM MILK**

609 Milk is well known to contain an array of bioactivities, which extends the range of
610 influence of mother over young beyond nutrition alone. Most of the bioactivities of
611 milk are attributable to the proteins and peptides secreted into milk by mammary gland.
612 Many milk borne bioactivities are latent and require proteolytic release of bioactive
613 peptides from inactive native milk proteins. However, some are natural and do not
614 require digestion which otherwise destroy their bioactivities. Bioactive peptides have
615 been identified as decomposition products of several food proteins (Brantl et al., 1979;
616 Zioudrou et al., 1979; Loukas et al., 1983). Milk proteins are the most important
617 sources of bioactive peptides. These have been shown to have various activities
618 including opiate, antithrombotic or antihypertensive activity, immunomodulating or

619 mineral utilization properties. Some of them have been known to influence in insulin
620 secretion or the motility and secretion of the intestine (Daniel et al., 1990). Bioactive
621 peptides may be generated from milk protein *in-vivo* through gastrointestinal processes.
622 Often, this liberation serves to influence numerous physiological responses as a result
623 of their hormone like properties. These peptides encoded within the sequences of native
624 protein precursors may also be generated *in-vitro* by enzymatic hydrolysis, such
625 peptides from protein hydrolysates could be purified by various separation techniques.
626 The physiologically active peptides have been chemically synthesized to confirm the
627 biological properties associated with a specific amino acid sequence. There is
628 considerable evidence that many bioactive peptides serve in multifunctional capacities
629 and influence numerous biological processes evoking behavioral, gastro intestinal,
630 hormonal, immunological, neurological and nutritional responses. The specific bio-
631 reactions associated with each physiological class have been well characterized.

632 The major bioactivities of milk are summarized into four categories (based on their
633 biological roles) as shown below:

634 a) Having gastrointestinal developmental activity and function:

- 635 i) Break down product of casein – casomorphins, casokinnins (ACE-I)
- 636 ii) Lactoferrin
- 637 iii) Growth factors IGE₁, TGF, EGF etc.

638 b) Having role in infant development:

- 639 i) Milk peptides
- 640 ii) Prolactin
- 641 iii) Growth factors
- 642 iv) Prosuposin

643 c) Having immunological functions:

- 644 i) Immunoglobulin IgG and IgA
- 645 ii) Cytokinins
- 646 iii) Prolactin
- 647 iv) Lactoferrin

- 648 v) Caseins – casomorphs and casokinins
- 649 d) Having microbiotic activity:
- 650 i) Antibiotic: Immunoglobulins, Lactoferrin, Glycolipids and
- 651 Oligosaccharides
- 652 ii) Probiotic: Lactoferrin, k-casein glycomacropeptide and oligosaccharides

653 Depending upon their physiological functions, the bioactive peptides have been

654 categorized as below:

- 655 • Antihypertensive
- 656 • Antimicrobial
- 657 • Antithrombic
- 658 • Mineral Binding
- 659 • Opioid

660

661 Although bioactive peptides do exist in a number of processed and fermented foods,

662 their true physiological functions in humans are unknown. In healthy individuals

663 eating a varied diet, the presence of bioactive peptides may help in keeping the

664 nervous, immune and digestive systems in a well-maintained state. The future

665 potential value of bioactive peptides in the diet may be their ability to affect certain

666 pathological conditions, although this has yet to be proven. Casein derived peptides

667 have already found interesting applications as dietary supplements (phosphopeptides)

668 and as pharmaceutical preparations (phosphopeptides, casomorphins) (Brule et al.,

669 1982, Reynolds, 1994). The efficacy and safe conditions of use of these peptides in

670 animals and in humans remain to be proven. At present, ACE-inhibitory peptides

671 and phosphopeptides are an important area in which bioactive peptides may be found

672 to be useful ingredients for dietary applications. Peptides have also been shown to

673 exert beneficial physiological effects (Table 2). These milk peptides may be

674 considered as food additives and perhaps as starting components for development of

675 some drugs. Casein derived peptides have already found interesting applications as

676 dietary supplements and pharmaceutical preparations. Today, some of the biologically

677 active peptides are known to be released during the *in-vivo* digestion, however, their

678 physiological function are not clearly understood, and hence, more research is needed
679 to fully understand the functional significance of these substances.

680 **FUTURE PROSPECTS AND CONCLUSIONS**

681 The three most important factors contributing to health are diet, exercise and genetic
682 factors. People conventionally think that food is food and medicine is medicine with no
683 overlap between the two. At the end of the 1980s and particularly during the 1990s,
684 interest in the area of relation between milk, milk products and health was generated
685 and has increased significantly. Nowadays, such products are termed functional, i.e.
686 foods that have an effect on health beyond their nutritional value. Their development
687 has aroused immense interest and today, there are hundreds of foods in the market that,
688 in addition to nutrition, also have health-maintaining or even therapeutic effects. The
689 efficacy of the active ingredient used in a functional food or of a product that contains it
690 has to be demonstrated in humans. There has to be a sufficient quantity of the active
691 ingredient in the food. However, only a small fragment of global population is familiar
692 with terms like probiotics and functional food. Probiotics are perfect fit for these dairy-
693 based beverages, as dairy is an excellent vehicle to deliver beneficial bacteria such as
694 *Bifidobacterium* and *Lactobacillus* species. Consumption of probiotics with dairy foods
695 such as milk, yogurt and cheese buffers the stomach acid and increases the chance that
696 the bacteria will survive into the intestine. The healthful properties of probiotics also
697 work well with the healthful properties of dairy beverages. Probiotic cultures have been
698 shown in a variety of test systems to stimulate certain cellular and antibody functions of
699 the immune system. Exposure to probiotics early in life may decrease the risk of
700 allergy. However, more rigorous research is required before such claims gain improved
701 scientific credibility.

702 Milk is a rich source of nutritive compounds that can be enriched and/or further
703 modified to give the best benefit to the consumers. However, in developing therapeutic
704 dairy products, various groups of medical experts, nutritionists and microbiologists are
705 considered important for their association. Food technologists are looked-for product
706 development technologists and biotechnologists for processing the compounds,
707 chemists to analyze these and, finally, the experts for marketing the products. It is
708 important to remember that therapeutic dairy products are mainly for supplying
709 nutritive foods for everyday consumption. Hence, nutria-marketing is also preferred to

710 explain research results to healthcare professionals and consumers so as to convince
711 them of the benefits of therapeutic milk foods.

712

713 REFERENCES

714 Addeo, F., Chianese, L., Salzano, A., Sacchi, F., Cappuccio, U., Ferranti, P., and
715 Malorni, A. (1992). Characterization of the 12% trichloroacetic acid-insoluble
716 oligopeptides of Parmigiano-Reggiano cheese. *J Dairy Res.* **59**: 401-411.

717 Agin, D., Gallagher, D., Wang, J., Heymsfield, S.B., Pierson, R.N, and Kottler, D.P.
718 (2001). Effect of whey protein and resistant exercise of body cell mass, muscle
719 strength and quality of life in women with HIV. *AIDS* **15**: 2431-2440.

720 Ashar, M.N, and Chand, R. (2004a). Fermented milk containing ACE-inhibitory
721 peptides reduces blood pressure in middle aged hypertensive subjects.
722 *Milchwissenschaft* **59**: 363–366.

723 Ashar, M.N, and Chand, R. (2004b). Antihypertensive peptides purified from milks
724 fermented with *Lactobacillus delbrueckii* ssp. *bulgaricus*. *Milchwissenschaft*
725 **59**: 14-17.

726 Ballongue, J. (1998). Bifidobacteria and probiotic action. In: Lactic acid bacteria.
727 Salminen S and von Wright A (Eds) Marcel Dekker Inc. NY, Hong Kong. pp 519-
728 87.

729 Berkhout, B., vanWamel, J., Beljaars, L.B., Leoni, M., Dirk, K.F., Visser, S, and Floris,
730 R. (2003). Characterization of the anti-HIV effects of native lactoferrin and other
731 milk proteins and protein-derived peptides. *Antiviral Res.* **55**: 341-355.

732 Bowen, W.H. (2002). Effects of dairy products on oral health. *Scan J Nutr.* **46**:178-179.

733 Brantl, V., Teschemacher, H., Henschen, A, and Lottspeich, F. (1979). Novel opioid
734 peptides derived from casein (α -casomorphins) I. Isolation from bovine casein
735 peptone. *Physiol Chem.* **360**: 1211-1216.

736 Brulé, G., Roger, L., Fauquant, J, and Piot, M. (1982). Phosphopeptides from casein
737 derived material. *US Patent* 4: 358, 465.

738 Childs, N.M, and Poryzees, G.H. (1998). Foods that help prevent disease: consumer
739 attitudes and public policy implications. *Brit Food J.* **9**: 419.426.

- 740 Crittenden, R.G. (1999). Probiotics: A critical review. In: Tannoch GW (Ed.),
741 Wymondham, UK, Horizon Scientific Press, pp. 141-156.
- 742 Dairy Facts. (2003) Edition. Nutrition Information, 13. International Dairy Foods
743 Association. Washington, DC. pp 12.
- 744 Daniel, H., Vohwinkel, M. and Rehner, G. (1990). Effect of casein and α -casomorphins
745 on gastrointestinal motility in rats. *J Nutr.* **120**: 252-257.
- 746 DeVrese, M, and Schrezenmeir, J. (2001). Pro and prebiotics. *Innov Food Technol.*
747 May, 49-55.
- 748 Dionysius, D.A., Marschke, R.J., Wood, A.J., Milne, J., Beattie, T.R., Jiang, H.,
749 Treloar, T., Alewood, P.F, and Grieve, P.A. (2000). Identification of
750 physiologically functional peptides in dairy products. *Aust J Dairy Technol*, **55**:
751 103.
- 752 Diplock, A.T., Aggett, P.J., Ashwell, M., Bornet, F., Fern, E.B, and Roberfroid, M.B.
753 (1999). Scientific concepts of functional foods in Europe: consensus document. *Brit*
754 *J Nutr* **81**, 11-27.
- 755 DiRienzo, D.B. (2000). Symposium: Probiotic Bacteria: Implications for Human
756 Health. *J Nutr.* **130**: 382S-383S.
- 757 Ganjam, L.S., Thornton, W.H., Marshall, R.T., MacDonald, R.S. (1997).
758 Antiproliferative effects of yogurt fractions obtained by membrane dialysis on
759 cultured mammalian intestinal cells. *J Dairy Sci.* **80**: 2325-2329.
- 760 German. B., Schiffrin, E.J., Reniero, R., Mollet, B., Pfeifer, A, and Neeser, J.R. (1999).
761 The development of functional foods: lessons from gut. *Trends Biotech.* **17**: 492-
762 499.
- 763 Gibson, G.R, and Roberfroid, M.B. (1995). Dietary modulation of the human colonic
764 microbiota: Introducing the concept of prebiotics. *J Nutr.* **125**: 1401-1412.
- 765 Gilliland, S.E., Staley, T.E, and Busl, L.J. (1984). Importance of bile tolerance of
766 *Lactobacillus acidophilus* used as dietary adjunct. *J Dairy Sci* **67**: 3045-3051.
- 767 Goyal, N, and Gandhi, D.N. (2006). Combinational approach of *Lactobacillus* spp and
768 oral rehydration solution for rapid control of diarrhea. *Indian J Microbiol* **46**: 253-
769 258.

770 Grover, I, and Dalal, V. (1993). Traditional food practices during postpartum period.
771 National Seminar on Indigenous Technologies for Sustainable Agriculture, New
772 Delhi. March 23-25. Abstract, pp 69.

773 Haque, E, and Chand, R. (2006). Milk protein derived bioactive peptides. [On-line]
774 UK: Available: <http://www.dairyscience.info/bio-peptides.htm>.

775 Heaney, R.P. (2000). Calcium, dairy products and osteoporosis. *J Am Coll Nutr.* **19**:
776 83S-99S.

777 Heyman, M.B. (2006). Lactose intolerance in infants, children, and adolescents.
778 *Pediatrics* **118**: 1279-1286.

779 Hyon, K.C., Walter, C.W., Meir, J.S., Eric, R, and Frank, B.H. (2005). Dairy
780 Consumption and risk of type 2 diabetes mellitus in men. *Arch Intern Med.* **165**:
781 997-1003.

782 ILSI Europe. (2002) Scientific concepts of functional foods in Europe: consensus
783 document. *Brit J Nutr.* **81**, 1S-27S.

784 Irina, V., Richard, Z., Wurtman, I, and Wagstaft, J. (1999). Effects of a low dose of
785 melatonin on sleep in children with angelman syndrome. *J Pediat Endocrin Met.*
786 **12**: 57-67.

787 James, W., Anderson, M.D, and Gilliland, S.E. (1999). Effect of fermented milk
788 (yogurt) containing *Lactobacillus acidophilus* 11 on serum cholesterol in
789 hypercholesterolemic humans. *J Am College Nutr.* **18**: 43-50.

790 Jan, G., Leverrier, P., Pichereau, V, and Boyaval, P. (2001). Changes in protein
791 synthesis and morphology during acid adaptation of *Propionibacterium*
792 *freudenreichii*. *Appl Environ Microbiol* **67**: 2029-2036.

793 Johansson, I. (2002). Milk and dairy products: possible effects on dental health. *Scan J*
794 *Nutr.* **46**: 119-122.

795 Kahala, M., Pahkala, E, and Pilhlanto-Leppala, A. (1993). Peptides in fermented
796 Finnish milk products. *Agric Sci.* **2**: 379-386.

797 Karimi, O, and Pena, A.S. (2003). Probiotics: isolated bacterial strains or mixtures of
798 different strains? *Drugs Today.* **39**: 565-597.

- 799 Korhonen, H. (2002). Technology options for new nutritional concepts. *Int J Dairy*
800 *Technol.* **55**: 79-88.
- 801 Kurien, A., Puniya, A.K, and Singh, K. (2005). Selection of prebiotic and *Lactobacillus*
802 *acidophilus* for synbiotic yoghurt preparation. *Indian J Microbiol.* **45**: 45-50.
- 803 Ligi, J., Mandal, S., Puniya, A.K., Krauss-Etschmann, S, and Singh, K. (2006). Human
804 gut: A target organ for the development of functional synbiotics. *Bev Food World.*
805 (In press).
- 806 Loukas, S., Varoucha, D., Zioudrou, C., Streaty, R, and Klee, W.A. (1983). Opioid
807 activities and structures of α -casein derived exorphins. *Biochem* **22**: 4567-4573.
- 808 Lourens-Hattingh, A, and Viljoen, B.C. (2001). Yoghurt as probiotic carrier food. *Int*
809 *Dairy J.* **11**: 1–17.
- 810 Mandal, S., Puniya, A.K, and Singh, K. (2006). Effect of alginate concentrations on
811 survival of microencapsulated *Lactobacillus casei* NCDC-298. *Int Dairy J.* **16**:
812 1190-1195.
- 813 Markowitz, J.E, and Bengmark, S. (2002). Probiotics in health and disease in the
814 pediatric patient. *J Pediatric Gastroent Nutr.* **49**: 127–141.
- 815 Marshall, K. (2004). Therapeutic Applications of whey protein. *Alt Med Rev.* **9**: 136-
816 156.
- 817 Matar, C., Amiot, J., Savoie, L, and Goulet, J. (1996). The effect of milk fermentation
818 by *Lactobacillus helveticus* on the release of peptides during *in vitro* digestion. *J*
819 *Dairy Sci.* **79**: 971-979.
- 820 Matar, C., LeBlanc, J.G., Martin, L, and Perdigón, G. (2003). Biologically active
821 peptides released in fermented milk: Role and functions. In: Farnworth ER (Ed)
822 Handbook of fermented functional foods. Functional foods and nutraceuticals
823 series. CRC Press, Florida, USA, pp 177–201.
- 824 Meisel, H., Goepfert, A, and Gunther, S. (1997). ACE-inhibitory activities in milk
825 products. *Milchwissenschaft,* **52**: 307-311.
- 826 Mercenier, A., Pavan, S, and Pot, B. (2002). Probiotics as bio-therapeutic agents:
827 present knowledge and future prospects. *Curr Pharmaceutical Design* **8**: 9-110.

828 Miche, P., Beeh, K.M., Schlaak, J.F, and Buhl, R. (2001). Oral supplementation with
829 whey proteins increases plasma glutathione levels of HIV infected patients. *Eur J*
830 *Clinical Invest.* **31**: 171-178.

831 Micke, P., Beeh, K.M. and Buhl, R. (2002). Effect of long term supplementation with
832 whey proteins on plasma glutathione levels of HIV infected patients. *Eur J Nutr.*
833 **41**: 12-18.

834 Nagpal, R., Yadav, H., Puniya, A.K., Singh, K., Jain, S. and Marotta, F. (2007a).
835 Potential of probiotics and prebiotics for synbiotic functional dairy foods: an
836 overview. *Int J Probiotics Prebiotics.* **2**: 75-84.

837 Nagpal, R., Yadav, H., Puniya, A.K., Singh, K., Jain, S, and Marrota, F. (2007b).
838 Conjugated linoleic acid: sources, synthesis and potential health benefits: an
839 overview. *Curr Topics Nutraceutical Res* **5**: 55-66.

840 Nakamura, Y., Yamamoto, N., Sakai, K. and Takano, T. (1995). Antihypertensive
841 effect of sour milk and peptides isolated from it that are inhibitors to angiotensin I-
842 converting enzyme. *J Dairy Sci.* **78**: 1253–1257.

843 Ng, T.B., Lam, T.L., Au, T.K., Ye, X.Y., Wan, C.C. (2001). Inhibition of human
844 immunodeficiency virus type 1 reverse transcriptase, protease and integrase by
845 bovine milk proteins. *Life Sci.* **69**: 2217-2223.

846 Patel, R.S, and Renz-Schanen, A. (1998). Dietary calcium and its role in disease
847 prevention. *Indian Dairyman.* **50**: 49-51.

848 Rehmeier, J.J. (2006). Milk Therapy: Breast-milk compounds could be a tonic for adult
849 ill. *Sci News* (Univ. of Phoenix; Online). 170: P 376.

850 Reiter, B. (1985). The biological significance of the non-immunoglobulin protective
851 proteins in milk: lysozyme, lactoferrin and lactoperoxidase. In: *Developments in*
852 *dairy chemistry – 3.* Fox PF (Eds) Elsevier Applied Science Publishers, NY.

853 Reynolds, E.C. (1994). Antigariogenic casein phosphopeptide. 24th International Dairy
854 Congress. Melbourne, Australia. 18-22 September.

855 Roberfroid, M.B. (2000). Prebiotics and probiotics: are they functional foods? *Am J*
856 *Clin Nutr.* **71**: 1682-1687.

- 857 Rokka, T., Syvaoja, E.L., Tuominen, J, and Korhonen, H. (1997). Release of bioactive
858 peptides by enzymatic proteolysis of *Lactobacillus* GG fermented UHT milk.
859 *Milchwissenschaft*. **52**: 675-678.
- 860 Ross, S. (2000). Functional foods: food and drug administration prospective. *Am J Clin*
861 *Nutr.* **71**: 1735S-1738S.
- 862 Ryhänen, E.L., Pihlanto-Leppälä, A. and Pahkala, E. (2001). A new type of ripened;
863 low-fat cheese with bioactive properties. *Int Dairy J.* **11**: 441–447.
- 864 Sabikhi, L, and Mathur, B.N. (2004). Dairy products in human health: traditional
865 beliefs vs established evidence. *Indian Dairyman*. **56**: 61-66.
- 866 Salminen, S., Ouwehand, A.C., Benno, Y, and Lee, Y.K. (1999). Probiotics: How
867 should they be defined? *Trends Food Sci Technol.* **10**: 107-110.
- 868 Salmon, M. (1994). The Cultural Significance of breastfeeding and infant care in early
869 modern England and America. *J Social History.* **28**: 22-29.
- 870 Sanders, M.E. (1998). Overview of functional foods: Emphasis on probiotic bacteria.
871 *Int Dairy J.* **8**: 341-347.
- 872 Sanders, M.E. (2000). Symposium: Probiotic Bacteria: Implications for Human Health:
873 Considerations for Use of Probiotic bacteria to Modulate Human Health. *J Nutr.*
874 **130**: 384S-390S.
- 875 Shah, N.P. (2000). Probiotic bacteria: selective enumeration and survival in dairy
876 foods. *J Dairy Sci.* **83**: 894–907.
- 877 Sharma, R, and Rajput, Y.S. (2006). Therapeutic potential of milk and milk products.
878 *Indian Dairyman*. **58**: 70-80.
- 879 Singh, T.K., Fox, P.F. and Healy, A. (1997). Isolation and identification of further
880 peptides in the diafiltration retentate of the water-soluble fraction of Cheddar
881 cheese. *J Dairy Res.* **64**: 433–443.
- 882 Smacchi, E. and Gobbetti, M. (1998). Peptides from several Italian cheeses inhibitory
883 to proteolytic enzymes of lactic acid bacteria, *Pseudomonas fluorescens* ATCC 948
884 and to the angiotensin I-converting enzyme. *Enz Microbial Technol.* **22**: 687–694.
- 885 Talhouk, R.S., Abdo, R.A., Saad, A. (1996). Lactose intolerance. Diagnosis and dietary
886 treatment with milk substitutes. *J Med Liban.* **44**: 36-40.

- 887 Temmerman, R., Pot, B., Huys, G. and Swings, J. (2002). Identification and antibiotic
888 susceptibility of bacterial isolates from probiotic products. *Int J Food Microbiol.*
889 **81**: 1-10.
- 890 Valtonen, M., Niskanen, L., Kangas, A.P., Koskinen, T. (2005). Effect of melatonin-
891 rich night-time milk on sleep and activity in elderly institutionalized subjects.
892 *Nordic J Psychiatry.* **59**: 217-221.
- 893 Walzem, R.L. (2001). Health enhancing properties of whey proteins and whey
894 fractions. Applications monograph – nutritional and beverages. *US Dairy Export*
895 *Council.*
- 896 Weaver, C.M. (2003). Dairy nutrition beyond infancy. *Austr J Dairy Technol.* **58**: 58-
897 60.
- 898 Whiting, S.J. and Lemke, B. (1999). Excess retinol intake may explain the high
899 incidence of osteoporosis in Northern Europe. *Nutr Rev.* **57**: 192-198.
- 900 Xiao, J.Z., Kondo, S., Takahashi, N., Miyaji, K., Oshida, K., Hiramatsu, A., Iwatsuki,
901 K., Kokubo, S. and Hosono, A. (2003). Effects of milk products fermented by
902 *bifidobacterium longum* on blood lipids in rats and healthy adult male volunteers. *J*
903 *Dairy Sci.* **86**: 2452-2461.
- 904 Yadav, H., Jain, S. and Sinha, P.R. (2006a). Effect of Dahi containing *Lactococcus*
905 *lactis* on the progression of diabetes induced by a high-fructose diet in rats.
906 *Biosci Biotechnol Biochem.* **70**: 1255-58.
- 907 Yadav, H., Jain, S. and Sinha, P.R. (2006b). Effect of skim milk and dahi (yogurt) on
908 blood glucose, insulin, and lipid profile in rats fed with high fructose diet. *J Med*
909 *Food.* **9**: 328-35.
- 910 Yadav, H., Jain, S, and Sinha, P.R. (2007a). Antidiabetic effect of probiotic dahi
911 containing *Lactobacillus acidophilus* and *Lactobacillus casei* in high fructose fed
912 rats. *Nutrition* **23**: 62-68.
- 913 Yadav, H., Jain, S. and Sinha, P.R. (2007b). Formation of oligosaccharides in skim
914 milk fermented with mixed dahi cultures, *Lactococcus lactis* ssp. *diacetylactis* and
915 probiotic strains of lactobacilli. *J Dairy Res.* **12**: 1-6.
- 916 Yadav, H., Jain, S., Sinha, P.R. and Marrota, F. (2007c). Diabetes and probiotics: A
917 possible therapeutic link. *Int J Probiotics Prebiotics.* **2**: 15-20.

- 918 Zemel, M.B. (2005). Dairy augmentation of total and central fat loss in obese subjects.
919 *Int J Obesity* **29**: 391-7.
- 920 Zioudrou, C., Streaty, R.A. and Klee, W.A. (1979). Opioid peptides derived from food
921 proteins. *J Biol Chem.* **254**: 2446-2449.
- 922

923 **Table 1. Some commercial health-promoting probiotic products (Nagpal et al.,**
 924 **2007a)**

Product	Probiotic
Muller Vitality Probiotic Yoghurt, UK.	<i>L. acidophilus</i> and <i>Bifidobacterium</i> sp.
Crunch n Yogurt™, General Mills, USA	<i>L. acidophilus</i> , <i>L. bulgaricus</i> and <i>Streptococcus thermophilus</i>
Classic flavor, France	<i>L. acidophilus</i>
Lactinex powder, Hyson, Westcott and Dunning	<i>L. acidophilus</i> and <i>L. bulgaricus</i>
LGG capsules, Japan	<i>L. rhamnosus</i> GG
LGG Milk, Japan	<i>L. rhamnosus</i> GG
LGG+, Iceland and Greenland	<i>L. rhamnosus</i> GG
Dukat BioAktiv Dairy Product, Slovenia	<i>L. rhamnosus</i> GG
Tnuva LGG1, Israel	<i>L. rhamnosus</i> GG
Beautiful Day LGG, Taiwan	<i>L. rhamnosus</i> GG
Culturelle capsules, USA	<i>L. rhamnosus</i> GG
Yakult, Japan	<i>L. casei</i>
Bacilac, Belgium	<i>L. acidophilus</i> plus <i>L. rhamnosus</i>
VSL-3, Italy	8 LAB species
Vitacel® prolac, Rosenberg	<i>Lactobacillus reuteri</i>
Amul Prolife probiotic ice-cream, India	<i>L. cremoris</i> , <i>L. lactis</i> , <i>L. bulgaricus</i> and <i>L. acidophilus</i>
Probiotic Dahi (yoghurt), NDRI, Karnal, India	<i>L. acidophilus</i> and <i>L. casei</i>
Symbalance yogurt, Switzerland	<i>L. reuterii</i> , <i>L. acidophilus</i> and <i>L. casei</i>

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927 **Table 2. Bioactive peptides identified in various fermented milk products.**

Product	Bioactivity	Reference
<i>Fermented milks</i>		
Sour milk	Phosphopeptides	Kahala et al., 1993
Sour milk	ACE-inhibitory	Nakamura et al., 1995
Sour milk	β -casomorphin-4	Matar et al., 1996; 2003
Fermented milk (Treated with pepsin and trypsin)	ACE-inhibitory Immunomodulatory Opioid	Rokka et al., 1997
Yoghurt	ACE-inhibitory (weak), Immunomodulatory, Antihypertensive, Antiamnesic, Microbicidal, Antithrombotic	Meisel et al., 1997
<i>Cheeses</i>		
Parmesan and Reggiano	β -casomorphin precursors	Addeo et al., 1992
Cheddar	Phosphopeptides	Singh et al., 1997
Edam, Emmental, Gouda	ACE-inhibitory	Meisel et al., 1997
Mozzerella, Italico, Crescenza	ACE-inhibitory	Smacchi and Gobbetti, 1998
Edam, Emmental, Turunmaa	ACE-inhibitory	Ryhanen et al, 2001
Cheddar, Edam, Swiss, Feta	Antihypertensive Anti amnesic Opioid	Dionysius et al., 2000

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