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EFFECTS OF MILK BIOACTIVE COMPOUNDS ON HEALTH

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Milk provides a rich source of macro- and micro-nutrients, and other more original compounds, the value of which is significant from a nutritional as well as a physiological perspective. Milk proteins have an increased nutritional value that is widely recognised and in many countries dairy products contribute significantly to daily protein intake. The biodefensive properties of mammalian milk proteins as well as the unique biological activities associated with each of them have been widely acknowledged for many years. These aspects are important for the use of milk proteins and milk-protein-derived peptides in dietary and pharmaceutical applications, respectively. Moreover, proteins and peptides influence various health conditions and exert regulatory functions in the human organism. Immunoglobulins are a well-known example of bioactive milk proteins, as they offer an excellent natural defence system to the neonate against bacterial infections. Overall, a large range of bioactivities have been reported for the bioactive compounds contained in milk.

Our aim in this Special Issue is to explore in detail the bioactive compounds of milk and to identify their potential health effects.

The two first papers of this Issue provide information focused on proteins. Milk and colostrum contain peptides with potential therapeutic significance showing antiviral, antibacterial, antitumor, and/or immunoregulatory effects that have raised significant attention. A proline-rich polypeptide complex subsequently known as Colostrinin™ was found for the first time in bovine colostrum as a fraction accompanying colostral immunoglobulin G2. Subsequently, similar polypeptides were found in human, bovine and caprine colostrum. The proline-rich polypeptide possesses psychotropic as well as immunoregulatory properties including effects on humoral and cellular immune responses, shows regulatory activity in Th1 and Th2 cytokine induction, and has the ability to inhibit the overproduction of reactive oxygen species and nitric oxide. The paper by Janusz and Zablocka (7) investigates the characteristics of Colostrinin™ as well as its potential clinical use for neurodegenerative disorders given recent positive effects in Alzheimer's disease double-blind placebo-controlled trials. Milk and colostrum proteins have attracted a significant scientific and commercial interest as a source of biologically active molecules. In this light, the paper by Korhonen (9) discusses aspects related to the production and properties of health-promoting proteins and peptides from milk and bovine colostrum. The best-characterized colostrum-based bioactive proteins include alpha-lactalbumin, beta-lactoglobulin, immunoglobulins, lactoferrin, latoperoxidase, and growth factors. Currently, these proteins can be enriched and purified on an industrial scale from bovine colostral whey or cheese whey. The efficacy of specific peptides has been established in animal and human studies and the number of commercial products supplemented with specific mik peptides is envisaged to increase on global markets.

The third paper by Kiskini and Difilippo provides in depth information on the structure, health effects and isolation of the oligosaccharides in goat milk (8). Compared to other types of mammalian milk, human milk is the richest source of naturally derived oligosaccharides, which are compounds that have been widely recognized for their prebiotic and anti-infective properties. However, the structural complexity of oligosaccharides in human milk minimizes their use as a basis for functional foods. Goat milk constitutes an appealing alternative, since it contains the highest amount of oligosaccharides among domestic animals, while goat milk oligosaccharides show structural significant similarities to human milk oligosaccharides. Given that studies on goat milk oligosaccharides are scant, the information provided in this paper is valuable for biofunctional food development.

The paper by Fernandez and colleagues (5) investigates the modulation of maternal gut microbiota during pregnancy and lactation as well as its effects on infant health. Recent work has shown that human milk and colostrum, which had been traditionally considered sterile, provide a continuous supply of commensal and potential probiotic bacteria to the infant gut. The paper discusses the >200 different bacterial species (including staphylococci, lactic acid bacteria and bifidobacteria) that have been isolated from human milk samples so far as well as the cultivable bacterial diversity found in individual samples and the role of human milk on the bacterial colonization of the infant gut.

Cloetens et al. (4) overview the wide array of compounds contained in milk that have an established or putative pro- or anti-oxidant function, particularly the total antioxidant capacity. They also discuss the content of total antioxidant capacity and some related compounds in human and animal milks and infant formulas, and the effect of milk intake on antioxidant status in the body and on the activity of dietary flavonoids as studied in vitro and in vivo. Milk, whey, high-molecular-weight and low-molecular-weight fractions of whey have all been found to have antioxidant capacity. The major antioxidant in the low-molecular-weight fraction has been identified as urate. The authors also provide an extensive literature survey regarding data on the antioxidant capacity and related variables of milk obtained from different sources (i.e., human milk, infant formulas and animal milk) and subjected to different treatments.

The review by Tsakiris et al. (11) evaluates evidence published during the past 20 years regarding the concen-

tration of specific xenobiotics in human and dietary milk. This is an important topic since the presence of xenobiotics is one of the most important factors affecting the quality of milk in terms of product safety. Persistent organic pollutants (i.e. polychlorinated biphenyls, flame retardants), pesticides (i.e. organochlorine) and mycotoxins are some of the most commonly detected xenobiotics in both human and dietary milk. Due to globalization, milk products with xenobiotics may travel all around the word. Moreover, diet, smoking habits, and environmental problems may affect the quantity of specific xenobiotics in human breast milk. Therefore, the scientific community and the consumers ought to be alert and well informed of the risks and possible adverse health effects of the build-up of these xenobiotics in milk.

The production and the composition of milk and colostrum are influenced by a number of factors including species, breed, health status, feeding practices, as well as environmental conditions. The latter is important since productivity and reproduction efficiency of farm and wild animals are negatively affected by increased environmental temperatures. It is well known that colostrum and milk of various species differ widely in amounts and proportions of their principal constituents because of difference in physiology and digestion. However, the interspecies variations reflect largely the effects of environmental factors. Bernabucci and colleagues (2) provide a insightful discussion on the effects of heat stress on the composition of milk and colostrum in different species.

The paper by Carrillo and colleagues (3) reviews the available information regarding the effects of bovine colostrum supplementation on physical performance and heat tolerance, with a focus on gastrointestinal integrity and immune function. Many sport competitors have recently adopted bovine colostrum supplementation as a means of enhancing immune function as well as improving performance. Improvements in physical performance associated with bovine colostrum supplementation may stem from the ability of bovine colostrum to maintain gastrointestinal integrity by decreasing permeability. During exercise in the heat, blood flow to the gastrointestinal tract is reduced, which eventually leads to endotoxin leakage into circulation. Endotoxins, such as lipopolysaccharide, can trigger an inflammatory cascade leading to physiological strain that, in turn, increases heat storage and decreases time to exhaustion. Gastrointestinal permeability is attenuated during passive heat stress following bovine colostrum supplementation, but the influence of bovine colostrum supplementation on exercise heat stress remains to be determined. The implications of endotoxemia during exercise in the heat is a matter of growing importance and warrants further study given the global increase in ambient temperatures during sport competitions.

Recent evidence shows that poor nutrition in utero and in early life combined with over nutrition in later life may play a role in the programming of cardio-metabolic diseases. Human milk represents the best natural nutrition for all infants, for its unique nutritional properties (as far as the mother diet is optimal), and for the biological activities of several specific compounds that can favour infant good development and health of the future adult. Among them, some human milk hormones can provide a certain degree of protection against obesity. This point is reviewed by Savino et al. (10) who examine the evidence of association between breastfeeding and a decrease in risk of obesity later in life. They propose some mechanisms of action through the presence of leptin, adiponectin, resistin, ghrelin and obestatin in human milk, which can influence infants feeding behaviour and regulation of growth and appetite control later in life. Furthermore, other milk from mammalians that can provide biological active compounds at a same or even higher level than human milk, can be considered as food supplement comprising medicinal values. An informative illustration is given by Agrawal and colleagues (1) who examine the efficacy of camel milk consumption as an adjunct to routine diabetic management in type 1 diabetes. Research on the beneficial aspects of camel milk has been taking place in different corners of globe during the last three decades. Epidemiological studies showing low prevalence of diabetes in communities consuming camel milk suggest that it may have beneficial effects for treating hyperglycemia. The authors also review aspects related to camel milk production, composition, characteristics as well as its effects on blood glucose level, insulin dose, and beta cell function. In addition to providing nutrients for optimal development and the bioactive compounds for promoting future adult health, human milk represents the unique adequate early nutrition for the survival and subsequent quality of life in very premature neonates. Acting as the closure to the Special Issue, the review by Garcia et al. (6) provides a detailed overview of the bioactive compounds in human milk in relation to the maturity of the intestine in the very preterm newborn. A minimal enteral feeding with human milk is necessary during the first month of life to ensure normal development and functioning of the intestine, the organ that plays a key role in digestion/absorption of nutrients, for optimal growing, and in immunity for protection against pathogens leading to morbidity/mortality by necrotizing enterocolitis. The clinical benefits deriving from the use of human milk compared to formula seem to be associated to several compounds such as polyunsaturated fatty acids (especially DHA), phospholipids, cholesterol- all working together-, some specific proteins (enzymes, hormones and growth factors, sCD14, lactoferrin and immunoglobulins), prebiotics/probiotics, and possibly miRNAs.

Milk is a biological fluid of enormous interest in different domains. As such, further research is bound to highlight new bioactive compounds beneficial for human health in terms of prevention and nutri-therapeutical purposes.

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"To the memory of Professor Margit HAMOSH (August 13, 1933 - November 4, 2011) who initiated me to the beauty of the *Milky Way* "

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