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EDITORIAL

Homo sapiens and milk: a valuable food in the past and in the future

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Abstract Milk is a food with a very high biological value, essential in the early stages of life, and has been used to produce ricotta and other cheeses in the Mediterranean area for at least for the last 6,000 years. From a nutritional point of view, in addition to a high water content, milk also contains glucids, proteins of a high biological quality, lipids, vitamins and minerals in highly absorbable forms. In terms of evolution, cholesterol also plays an important role in the activation and propagation of the hedgehog signaling cascade, which is responsible for the differentiation and development of the central nervous system. Finally, the authors analyze its potential as a vector of alimentary supplements, making this food fundamental for human nutrition and the future of Homo sapiens.

Keywords Milk · Homo sapiens · Evolution

Introduction

Milk is a food of high biological value: in the first period of life is the most natural and important nutrient, the only able to double the weight of the infant in the first 6 months of life and enable a strong cerebral development after birth. The suckle instinct, a mammals' characteristic, appeared with the development of the cerebral limbic system approximately 200 million years ago; however, this has grown considerably over the last 65 million years. In women, breasts develop independently of lactation and do not decrease in size until disappear after lactation, as in other mammals. Moreover, man is the only mammal to use milk from other species for nutrition, even after infancy. Archeologists at the Universities of Oxford and Cambridge and researchers from the local superintendency recently discovered one of the most ancient Mediterranean "farms", dating back to the copper age (approximately 6,000 years ago): the archeological site at Troina, in Sicily. Analyzing the findings, particularly vases, the researchers discovered not only that the ancient inhabitants of the site consumed large quantities of milk, but they also knew techniques of preservation of milk and were already able to produce two different types of cheese: ricotta and "tuma" a type of non-matured pecorino.

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Nutritional aspects

Milk, produced by secretion from the mammary gland, is a complex liquid that contains, besides water (87–88%), glucids (lactose 4.8%), which are utilized quickly and are useful to the nervous system, proteins (3.3%) of a high biological quality, lipids (3.5%), vitamins (particularly A, D, B_2) and minerals (calcium and phosphorus in highly absorbable forms).

Glucose and galactose originate from the lactose in milk: glucose is an important source of energy and galactose is indispensable for sphingolipid synthesis. Sphingolipides are cerebrosides components, essential for the development and functioning of the cerebral neurons, in the myelin sheaths of the axons.

Man has a natural ability to hydrolyze lactose in glucose and galactose, which is then lost on weaning. In populations with a long history of sheep farming, a mutant form of the lactase gene remains active throughout adult life. This genetic modification has been linked to mutations of single bases of DNA control regions, controlling the gene: these mutations differ according to the geographic regions [1]. Man's natural predisposition to hydrolyze lactose in glucose and galactose is reduced approximately in 40% of the general population, this seeming to be mainly associated with intestinal pathologies rather than a genetic deficiency of lactase [2, 3].

Protein content [4] comprises casein (80%) and lactalbumin, lactoglobulins, peptones and immunoglobulins (20%). The caseins, dispersed in a colloidal solution in the form of micelles, include the kappa, beta, alphaS1 and alphaS2 caseins; they do not coagulate except for acidification or curdling, thus giving rise to cheese formation. Lactoferrin has an antibacterial activity and carries out an important role in iron absorption. During casein digestion, several bioactive peptides are released. They have regulatory effects on several functions, such as nutrient absorption, minerals (calcium) transport in the gut (phosphopeptides); amino acids transport, intestinal fluids balance, gastrointestinal motility and hormones (insulin, somatostatin) secretion (beta-casomorphin); immunostimulation (fragments of alphaS1 and betacasein); anti-hypertensive effects (casokinine).

Milk's amino acid spectrum is of high quality, with an essential amino acids supply similar to that of beef and much better than that of wheat. In particular, milk is a good source of branched-chain amino acids (valine, leucine, isoleucine) (BCAA) (Table 1) [5]. One particular aspect of some amino acids metabolism is their capacity to modify neurotransmitter levels in the central nervous system. In fact, physical activity causes increased BCAA oxidation in muscle, reducing their plasma levels. An increase in free tryptophan blood levels also occurs; tryptophan is not linked to albumin, and, therefore, is able to cross biological barriers and to spread via a common "carrier". Finally, a significant increase in ammonia levels can be observed when substantial physical activity is performed. All those conditions increase tryptophan trespassing across hemato-encephalic barrier: tryptophan, as precursor to serotonin synthesis, induces a significative increase in brain's serotonin levels. Higher concentrations of serotonin result in mood disturbances, reduced concentration and drowsiness. This phenomenon is connected with the existence of a single competitive "carrier" (L-transport system, leucine-preferring) used to carry tryptophan and BCAA across hematoencephalic barrier: consequently, during exercise, the tryptophan molecule flow, which has a higher concentration, prevails over that of the BCAA, which are reduced. In addition, increased blood concentration of ammonia, which is also present in the cerebral liquor and structures, leads to an increase in glutamine, the mobile and non-toxic resource of ammonia radicals; glutamine transfers in the opposite direction, from liquor to blood, using a "carrier" similar to that used by BCAA; therefore circulating tryptophan finds higher levels of carriers available for inverse transport. In conclusion, an increased flow of tryptophan results in greater serotonin production, followed by early appearance of fatigue. On the other hand, a considerable BCAA supplementation would reduce the rise in plasma ammonia, hinder the passage of tryptophan and ultimately excessive serotonin production and would therefore reduce and delay the appearance of the sensation of fatigue, improving mental performance and preventing overfitness symptoms [4].

Milk's lipid phase [4] is made up of neutral lipids (glycerides) which represent 98% of the total, polar lipids (phospholipids), which represent approximately 1% of the total and various lipidic substances, including liposoluble vitamins. Saturated fatty acids (FA) represent approximately 2/3 of the total, with a significant presence of short-chain FAs, which pass into the liver direct through the portal vein without entering into systemic circulation, and stearic acid, which is desaturated in humans to oleic acid and for this reason may be included, from a functional viewpoint, among unsaturated fatty acids. The unsaturated FAs include oleic acid in particular. The FAs which are definitively considered arthrogenous are <60%. A considerable quantity of unsaturated fatty acids is constituted by oleic acid, whereas the linoleic and α-linolenic acids are present in much reduced concentrations (respectively approximately 80 and 50 mg per 100 g of whole milk). Among polyunsaturated acids, the CLAs (conjugated linolenic acid) isomers series have generated considerable interest. CLAs are formed from linoleic acid in ruminants' stomachs by specific microorganism's action. They are present mainly in milk, milk-based food and beef and their quantity depends on seasonality, farming conditions and the microbial flora in the rumen. The *cis*-9 *trans*-11 isomer carries out anticancer activity in different types of tumour [6], and a protective effect at the onset of atherosclerotic diseases [7] and obesity [8].

The cholesterol content is moderate (12.3 mg/100 g). The free form of cholesterol is the basis for the synthesis of biliary acids, vitamin D, steroid hormones and metabolic mediators, such as oxysterol; it takes part in cerebral neurons development and in the process of learning and memory. It is a constitutive part of cell membranes and influences the content of other lipids inside the membranes, especially sphingomyelin, making cholesterol a fundamental metabolic mediator for the activation and propagation of the hedgehog signaling cascade, responsible for central nervous system differentiation and development. In mammals, three hedgehog signaling cascades are activated by cholesterol: Sonic, Indian, and Desert. In fact, during initial embryonic development, the cells are not differentiated and most of the neural cells are multipotent; the

Table 1 Requirements of amino acids at different ages compared with the supply in cow's milk, beef and wheat

Essential amino acids	Amino acid requirements[a]				Amino acids supplied by different foods		
	Babies (1 year)	Infants (2–5 years)	Children (10–12 years)	Adult	Cow's milk	Beef	Wheat
Histidine	165	125	115	100	169	213	120
Isoleucine	290	190	180	80	294	301	232
Leucine	580	440	290	120	594	507	379
Lysine	415	390	290	100	488	556	159
Methionine + cystine	265	165	145	105	206	249	225
Phenylalanine + thyroxine	450	415	145	120	638	500	462
Threonine	270	225	180	55	275	287	192
Tryptophan	165	75	55	30	88	70	68
Valine	345	230	165	80	400	313	270
Total							
+Histidine	2,875	2,245	1,520	795	3,150	2,995	2,105
−Histidine	2,715	2,120	1,415	695	2,981	2,780	1,990

[a] FAO/OMS: calculated from values in mg/g of protein (Protein N × 6.25), rounded up to the nearest 5 mg

primary neuroectoderm divides into, giving rise to telencephalon, diencephalon, mesencephalon and rhombencephalon: DNA transcription and signal molecules (morphogenes), including cholesterol, are essential for providing information about neuronal differentiation and positioning. During pregnancy, adding to the endogenous fetal cholesterol production, placenta replenishes the fetus with a total amount of approximately 8 g. The lipid profile of the umbilical cord has an LDL-c level that is approximately one-third compared with that of an adult, and is rich in triglycerides and lacking in cholesterol, whereas the HDL-c level is approximately half, with many more HDL lipoproteins rich in ApoE, which is the dominant transporter towards the tissues of the fetus and of the rapidly growing newborn, especially at central nervous system level [9]. The hedgehog signaling cascades also play an important role in the brain after birth and in adult life [10]. Nerve impulses are transmitted along neuronal axons one hundred times faster when axons are sheathed in myelin and the myelin is deposited around the axons like insulating tape, wrapping itself around the axons up to 150 times between one node and the next. The myelin is produced like a laminar structure from two types of glial cells: the oligodendrocyte, shaped like an octopus, sheaths the central nervous system, whereas the myelin of each internode in the peripheral nervous system is formed by a single Schwann cell, in the shape of a sausage. The speed of conduction is greater in relation to the thickness of the insulation: the optimal ratio between unsheathed axon diameter and fiber total diameter (axon + myelin) is 0.6. The wrapping occurs at different ages: at birth, the myelin predominates only in some regions of the brain, it expands in bursts and in some regions it is not completely deposited until 25–30 years of age; during growth, myelinization generally proceeds in waves starting from the posterior cerebral cortex and proceeding towards the frontal part. Myelinization occurs last in the frontal lobes, which are responsible for planning and evaluation capacity. Myelinization is probably completed only at the start of adulthood. Glia can regulate myelinization in relation to the traffic of impulses transmitted along axons. The speed of transmission, secondary to myelinization, is different in relation to the distances between the cerebral centers: in the adult, 30% of axons are still without myelin. This variability means that it is possible to coordinate the speed of transmission, strengthening the connections in specific neuronal circuits and influencing cerebral functions [11]. A recent finding, made at Pinnacle Point in South Africa is particularly interesting, as it backdates the first appearance of esthetic consciousness to 164,000 years ago. Some fragments of red ochre, with clear signs of use, i.e. marks made by deliberate slashes suggesting body painting and a symbolic use of color, were found at the site, supporting the hypothesis of symbolic thought and articulated language expression by those ominides. Beside the ochre, there was a pile of the remains of meals based on molluscs and crustaceans proving that Homo sapiens moved to this marine region, probably to escape from a land environment made poor and hostile due to a glaciation lasting approximately 70,000 years (from 195,000 to 125,000 years ago) [12]. The scientific hypothesis is that the two phenomena are linked and that the diet based on crustaceans and molluscs, rich in cholesterol and polyunsaturated fatty acids, influenced brain evolution.

All these data support the importance of contemporary presence in milk of cholesterol, phospholipids and galactose, essential nutrients for the progressive myelinization of the neuron axons and for CNS development.

Minerals make up approximately 0.7–0.8% of milk and include several elements, such as potassium, sodium, magnesium, phosphorus, chlorides, sulfates and calcium and some trace elements, such as zinc, silicon, copper, iron, aluminum, manganese, cobalt, fluorine and iodine. The amount of phosphorus, potassium, magnesium and calcium is elevated; 1 l of milk contains approximately 1,200 mg of calcium, 910 mg of phosphorus and 120 mg of magnesium, with an optimum calcium/phosphorus ratio, required for the absorption of calcium and whole milk contains significant concentrations of vitamin D3 (Table 2) [5]. A high supply of calcium from milk and diary products in infancy and adolescence can ensure optimal bone mineralization and prevent osteoporosis, bearing in mind that one cup of milk provides approximately 30% of the calcium daily requirement, according to LARN [13].

Milk as a vector of alimentary supplements

Widespread consumption of diet supplements is the result of numerous epidemiological investigations that demonstrated significative relationships between nutritional mistakes and chronic-degenerative diseases, suggesting the need to increase the intake of some important trace nutrients (vitamins, minerals, antioxidants, etc.). A recent study presented at Cosmofarma 2008, sponsored by FederSalus (An Italian Federation which unites the companies producing health products) showed that almost one out of three Italians commonly uses nutritional supplements, in 6 out of 10 cases from more than 2 years. The list of regularly purchased products is long: vitamin and mineral supplements (52.5%) are at the top of the list, followed by prebiotics (36%) and sports energy supplements based on the vitamins, mineral salts, amino acids and proteins (14.4%), these being mostly appreciated by men (23 against 9.9% of women). Approximately, two-thirds of the consumers were women (mean 66%, increasing to 71.6% in the north-west), with a medium-high level of education (51.7%). Furthermore, 42.1% play sport and 39.1% habitually follow a healthy diet. However, a recent Cochrane metanalysis of clinical studies [14] does not show any significant effects of antioxidants supplementation on mortality, either in healthy or pathological subjects. In contrast, a significant increase in mortality following supplementation with beta-carotene, vitamin A and vitamin E, can be observed. The limits of this metanalysis are numerous: doses, times and procedures used are different and variable. In particular, authors took into consideration only the antioxidants taken as a supplement and not those added to food. Food is much more complex and bioavailability and efficacy of trace nutrients contained in it should have to be evaluated in a specific way.

Table 2 Mean content of calcium, phosphorus and vitamin D of milk (mg × 100 g of food)

	Whole milk	Skimmed milk
Calcium (mg)	120	123
Phosphorus (mg)	92	97
Calcium/phosphorus ratio (Ca/P)	1:0.76	1:0.78
Liposoluble vit. D (ng)	63	Trace

From this point of view, milk can play a very important role as a vector of supplements. In fact, complexity and nutritional stability of milk makes it an ideal vehicle for the supply of important trace nutrients to improve nutritional quality and to prevent the chronic-degenerative diseases widespread, typical of the industrialized world. Recent studies confirmed this perspective: for example, the addition of co-enzyme Q10 and omega-3 to milk significantly increases plasma antioxidant capacity [15] and can improve lipid balance assessment [16–18].

Conclusions

In conclusion, milk has almost unique characteristics, both for its nutrient content (notable quantities of good quality amino acids, especially BCAA, complete lipid spectrum, high content of lactose and thus of galactose, richness in trace nutrients, both minerals and vitamins, etc.), both for the ease of ingestion, the high degree of digestibility, the multiple uses (breakfast or meals or as a snack) and for the ability to act as a base for trace elements enrichment and supplementation. Therefore, it can be considered a food which played a fundamental role in the past and can still have a brilliant future in Homo sapiens nutrition.

Conflict of interest None.

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