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Equidae milk promises substitutes for cow and human breast milk

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Abstract: Milk is the most nourishing natural biofluid. Milk bioactives contribute significantly to meeting nutrient requirements while minimizing the risks of cancers, traumas, and metabolic complexities. Some mothers may not be able to feed their infants breast milk for a prolonged period. Very young infants and the elderly may be intolerant to cow milk and its proteins and cholesterol. Thus, viable substitutes are needed to complement human breast milk in such cases. This review describes the most significant research findings to date and highlights the special nutritional and health properties of donkey and mare milks as promising substitutes for cow and human milks. Donkey and mare milks have similar biophysical and biochemical characteristics to human milk. Thus, their consumption can minimize allergies, hyperlipidemia, and related abnormalities occurring with cow milk consumption, particularly in infants, children, and the elderly. Despite the limited Equidae dairy production and research data, the emerging perspectives should fuel more research that will form the base for commercial investments in breeding dairy Equidae and manufacturing value-added Equidae dairy products. Effective education and renewed data dissemination are among the requirements for developing the unbiased science of cow, human, and Equidae milk. These are to ensure adequate public awareness of livestock milk's nutritional and functional values and its contribution to maintaining optimum human health.

Key words: Milk, human, breast, donkey, mare, health

Introduction

Depending on the nature of animal ecology, evolution, genetics, and feeding management, milk composition and nutritional properties differ vastly among species (Table). The highest per capita dairy consumption is in Western Europe, Scandinavia, Australia, and Canada (1), emphasizing the necessity of ongoing education and insight dissemination in these and other world regions of the human health implications of livestock milk. Cow milk contributes about 85% to the total world milk production (1,2). The average nutrient intakes in many regions are still well below minimum daily requirements of 70 g of protein and 800 mg of calcium (3). Insufficient palatability, protein related allergies, unfavorable immune responses, hyperlipidemia, and gut intolerances continue to limit cow milk preference for certain groups of people including infants, children, newly lactating mothers, and the elderly (4,5). Consequently, research has focused on the biochemical description and nutritional capacity of milk from other less-known species with the potential to substitute for cow milk and human breast milk (6-11). Thus, effective public education on the nutritional importance of noncow milks is an evolving necessity. Donkey and mare milks have been found to be the most similar to human milk, thus receiving increasing research and commercial

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Table. Average milk composition per kilogram of milk in different species

Component	Cow	Donkey	Mare	Human
Fat, g	40	11	13	40
Protein, g	34	17	21	19
Lactose, g	48	66	64	65
Minerals, g	7	4	4	2
Solids, nonfat, g	90	92	93	73
Total solids, g	133	102	105	121
Cholesterol, mg	140	22	45	200
Calcium, mg	1200	680	890	320
Phosphorus, mg	930	500	560	140
Saturated FA, g	24	4	4	18
Monounsaturated FA, g	11	2	3	16
Polyunsaturated FA, g	1	4	5	5

FA = fatty acids.

interests for infant and elderly nutrition (12). The primary objective of this review is to delineate research-based nutritional and health properties and assess the implications of Equidae milk as a potential substitute for cow and human milks for optimum human nutrition and health in different age groups.

Milk and humans: a science update

Milk is biosynthesized from volatile fatty acids, ammonia, peptides, and microbial mass resulting from reticulorumen fermentation of plant cell wall and solubles (13,14). Consequently, milk is made of numerous bioactives functioning beyond their nutritional importance (15,16). As such, milk is considered the most natural functional biofluid. The bioactives includes essential amino acids, specialized casein and peptides, lactalbumins, immunoglobulins, nucleosides, nucleotides, unsaturated and conjugated linoleic acids, sphingomyelins, and fat soluble vitamins and calcium (16,17). However, the rising concerns of infant allergies, adult cardiovascular issues, and aging complexities, at least in part due to improper cow milk nutrition, have contributed to a global demand for healthier substitutes (18). Very early neonatal cow milk intake has been related to insulin-dependent diabetes (19,20). Despite all the health and nutritional benefits of cow milk, viable substitutes are required for such specific circumstances. The following sections will focus on the science of Equidae milk, including mare and donkey milks.

Donkey milk as a substitute

Donkey milk biochemistry is similar to that of human milk (5). However, limited data exist on the biochemical and nutritional properties of donkey milk. Donkey milk is very similar to mare milk, with low total solids (8%-10%) and protein (1.5%-1.8%) contents and high lactose (6%-7%) content. Donkey milk fat ranges between 0.28% and 1.82% (6,21). Milk protein has 47.3% casein and 36.9% whey and has a reasonably high β-lactoglobulin content of about 30% (22). It is also rich in peptide-bound amino acids (AAs) and essential AAs. Compared with all other milks, donkey milk is the richest in valine and lysine. Its special peptides stimulate intestinal functional recovery and development via growth factors and protective agents (5). As such, donkey milk is considered a suitable alternative for cow milk-intolerant infants (5,23). Donkey milk favorably affects osteogenesis and atherosclerosis, coronary heart disease, and cholesterolemia (24).

However, because of limited donkey milk production, the quantities available for human consumption are, in realistic scales, still inadequate. China has the highest number of donkeys worldwide at 8,000,000 (12). China has recently improved donkey milk production via advanced breeding strategies to an annual milk yield of 40,000 t (12,25). Human milk protein contents, and its ratio of casein to total protein, are low and similar to those of donkey and mare milks (26). Donkey milk is considered the most similar natural milk to human milk. Pediatric research data support its use in infant nutrition (27).

Human milk must develop a soft curd for effective assimilation in the infant gut. Such a soft curd is partly due to lower soluble calcium. It is convincing that in many regions of the world infants have been safely fed donkey milk instead of cow milk (26,28). Cow and buffalo milks make harder curds more favorable for cheese-making. These should be diluted with water before feeding them to infants. A recent study on Jiangyue donkeys in northwestern China showed that the milk contained 9.5% total solids, 1.6% protein, 1.2% fat, 6.3% lactose, and 0.4% ash, similar to mare and human milks (12). Donkey milk is rich in β-lactoglobulin and lysozyme. The percentage of 8 essential AAs in donkey milk protein was about 38%, higher than that of mare and cow milks. Donkey milk protein has greater serine (6.2% vs. 4.8% and 5.1%), glutamic acid (22.8% vs. 23% and 17.8%), arginine (4.6% vs. 3.3% and 4%), and valine (6.5% vs. 4.8% and 6%) and lower cystine (0.4% vs. 0.6% and 1.7%) compared to cow and human milks, respectively (12). Donkey milk proteins primarily include αS1- and β-caseins, lysozyme, α-lactalbumin, and β-lactoglobulin (29). The average β-lactoglobulin and α-lactalbumin contents are 3.75 and 1.8 mg/mL, respectively, with a high lysozyme content (1.0 mg/mL) compared with other milks (29).

Donkey milk bioactives can enhance interleukin-2 (IL-2), interferon-γ (IFN-γ), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and interleukin-1β (IL-1β) secretion (9). Specialized proteins and lysozyme act to depress tumor proliferation and destroy tumors, through activating lymphocytes and macrophages (9). As such, donkey and goat milks are considered nutraceuticals in replacing human and cow milks at times of allergy, atopy, and inflammatory conditions. They also modulate immunity and nitric oxide (NO) and IL-8 release, or potent antiatherogenic vasodilators (30,31). Fermented donkey milk modulates immunity in the elderly with intestinal mucosal immune responses (31). Donkey milk and colostrum induce NO release and CD25 and CD69 expression on human peripheral blood mononuclear cells (11). In addition, donkey milk induces interleukins (IL-12, IL-1β, and IL-10) and TNF-α. These imply a potential in preventing atherosclerosis and reducing immune depression.

Recent studies suggest highly similar protein fractions of donkey and human milks (8,32), both being hypoallergenic and suitable for infant nutrition (33) and cosmetic materials (34,35). The high lactose content suits the making of fermented products and drinks (7), further highlighting donkey milk's potential role in human nutrition (10,36). Raw donkey milk has a low bacteria count (about 4 × 104 CFU/mL), which is related to its high lysozyme content, which stabilizes pH. Donkey milk has been a growth medium for probiotic *L. rhamnosus* strains (7). It thus may be used in manufacturing commercial probiotic supplements (7,37).

Mare milk as a substitute

Mare milk's protein content is higher than that of human milk and lower than cow milk. Its casein content is also medium, being between that of human and cow milks. However, mare milk's fat content is lower than both those of human and cow milks (38). Mare and human milks are similar in milk fat diglyceride and triglyceride distribution, with polyunsaturated fatty acids (PUFAs) being higher in mare and human milk fats than in cow milk fat. As such, mare milk is more suitable than cow milk for human and infant feeding (38). In 25 children in an age range of 19-72 months old with immunoglobulin-E-mediated cow milk allergy, all showed strong positive skin test responses to cow milk, whereas only 2 children did so to mare milk. Again, all the children showed a positive response to an oral food cow milk challenge, whereas only one child reacted to mare milk (4). Based on these findings, mare milk may be a suitable substitute for cow milk in young human nutrition.

Mare milk solids change across lactation. Milk total solids and fat contents were respectively 24.25%-

26.28% and 2.85%-2.93% on the first day, 12.15%-12.78% and 2.05%-2.17% on days 2-5 postpartum, and 10.37%-10.61% and 1.04%-1.32% on days 8-45 postpartum (39). Great differences exist in milk fatty acid composition between mare and cow milks. Mare-to-cow milk fat ratios of octanoic, decanoic, dodecanoic, linoleic, linolenic, stearic, myristic, and palmitic acids were 9.6, 3.1, 2.1, 4.4, 224, 0.2, 0.6, and 0.5, respectively. Mare colostrum contents of vitamins A, D_3, K_3, and C were respectively 0.88, 0.0054, 0.043, and 23.8 mg/kg, which were 1.4-2.6 times their levels in milk (i.e. 0.34, 0.0032, 0.029, and 17.2 mg/kg). Vitamin E content is similar between mare colostrum and milk (1.342 and 1.128 mg/kg, respectively), being similar to cow milk (39).

Total protein, whey protein, casein, and nonprotein nitrogen (NPN), respectively, were 16.41%, 13.46%, 2.95%, and 0.052% in colostrum; 4.13%, 2.11%, 2.02%, and 0.043% in milk at 2-5 days postpartum; and 2.31%, 1.11%, 1.20%, and 0.031% in milk at 8-45 days postpartum (40). Milk ratios of true and whey proteins to total protein decreased while casein and NPN increased from foaling to 45 days in milk. However, milk AAs decreased in the same period. Mare mammary secretions' biological value is the highest (132.3) immediately postpartum due to high threonine and lysine levels, decreasing to 119.7 at 5 days postpartum and 107.9 at 45 days postpartum (40), suggesting much higher biological values than cow milk. Calcium is lowest immediately after foaling (747.7 mg/kg) and highest at 5 days postpartum (953.7 mg/kg) (40).

Pregastric fermentation and fatty acid saturation dilute efforts that aim to increase cow milk PUFA levels (41,42). Mare milk contains higher α-linolenic acid (ALA) and linoleic acid (LA) (i.e., essential fatty acids, EFA) that are precursors of omega-3 and omega-6 PUFA, respectively (39). ALA ($C_{18:3n-3}$) and eicosapentaenoic acid (EPA; $C_{20:5n-3}$) give rise to prostaglandins such as prostacyclin (PGI) with vasodilatory effects, thromboxane (TXA) with vasoconstrictive effects, and docosahexaenoic acid (DHA; $C_{22:6n-3}$). Linoleic acid ($C_{18:2n-6}$) makes other groups of prostaglandins (PGI_2) and TXA (43,44). Mare milk has large EFA proportions, especially of linoleic acid, that cannot be produced by humans. The LA to ALA ratios of 1.3-2 make mare milk also suitable for infant nutrition. The liver transforms LA and ALA to EPA, DHA, and arachidonic acid. These PUFAs enhance endothelial NO synthesis, inhibit proinflammatory cytokine production, lower cholesterolemia, and lower risks of atherosclerosis and coronary heart diseases (45). Mare milk's saturated-to-unsaturated fatty acids ratio is about 1.2 (46), which suits human and infant nutrition.

Implications

Milk contains numerous bioactives that function beyond their nutritional significance. Such nutritional properties, especially for noncow milks, are to be continuously disseminated to advance the public awareness of an unbiased livestock milk science. Allergies, and immune and gut complexities, may arise by consuming cow milk, especially in certain groups including infants, patients, and the elderly. Thus, viable substitutes are required for cow and human milk for such groups that are highly reactive and sensitive to allergies and anaphylactics. Equidae milk is considered very similar to human milk. Although Equidae dairy production and research data are limited, the emerging knowledge and perspectives should fuel more research that will base commercial investments in breeding dairy Equidae and manufacturing value-added dairy products. Effective education and data dissemination is an ongoing priority for the promising nature of such substitutes to be optimally assimilated by the public into routine dietary practices to optimize human nutrition and health.

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References

1. Food and Agriculture Organization of the United Nations. FAOSTAT Data. FAO, Rome. c2012. Available at http://faostat.fao.org.
2. Food and Agriculture Organization of the United Nations. Production Year Book, Statistical Series, No. 117. FAO, Rome. 2004.
3. National Academy of Sciences. Dietary Reference Intakes. Recommended Intakes for Individuals, Food and Nutrition Board, Institute of Medicine, National Academies. National Academy of Sciences, Washington, D.C. 2007.
4. Businco, L., Giampietro, P.G., Lucenti, P., Lucaroni, F., Pini, C., Di Felice, D., Iacovacci, P., Curadi, C., Orlandi, M.: Allergenicity of mare's milk in children with cow's milk allergy. J. Allerg. Clin. Immunol., 2000; 105: 1031-1034.
5. Carroccio, A., Cavataio, F., Montaldo, G.D., Amico, D., Alabrese, L., Iacono, G.: Intolerance to hydrolyzed cow's milk protein in infants: clinical characteristics and dietary treatment. Clin. Exp. Allerg., 2000; 30: 1597-1603.
6. Chiavari, C., Coloretti, F., Nanni, M., Sorrentino, E., Grazia, L.: Use of donkey's milk for a fermented beverage with lactobacilli. Lait, 2005; 85: 481-490.
7. Coppola, R., Salimei, E., Succi, M., Sorrentino, M., Nanni, M., Ranieri, P., Belli, R., Blanes, J., Grazia, L.: Behaviour of *Lactobacillus rhamnosus* strains in ass's milk. Ann. Microbiology, 2002; 52: 55-60.
8. D'Auria, E., Agostoni, C., Giovannini, M., Riva, E., Zetterström, R., Fortin, R., Greppi, G.F., Bonizzi, L., Roncada, P.: Proteomic evaluation of milk from different mammalian species as a substitute for breast milk. Acta Paediat., 2005; 94: 1708-1713.
9. Mao, X., Gu, J., Sun, Y., Xu, S., Zhang, K., Yang, H., Ren, F.: Anti-proliferative and anti-tumour effect of active components in donkey milk on A549 human lung cancer cells. Int. Dairy J., 2009; 19: 703-708.
10. Monti, G., Bertino, E., Muratore, M.C., Coscia, M., Cresi, F., Silvestro, L., Fabris, C., Fortunato, D., Giuffrida, M.G., Conti, A.: Efficacy of donkey's milk in treating highly problematic cow's milk allergic children: an in vivo and in vitro study. Pediat. Allerg. Immunol., 2007; 18: 258-264.
11. Tafaro, A., Magrone, T., Jirillo, F., Martemucci, G., D'Alessandro, A.G., Amati, L., Jirillo, E.: Immunological properties of donkey's milk: its potential use in the prevention of atherosclerosis. Curr. Pharmaceut. Design, 2007; 13: 3711-3717.
12. Guo, H.Y., Pang, K., Zhang, X.Y., Zhao, L., Chen, S.W., Dong, M.L., Ren, F.Z.: Composition, physiochemical properties, nitrogen fraction distribution, and amino acid profile of donkey milk. J. Dairy Sci., 2007; 90: 1635-1643.
13. Nikkhah, A.: Ruminant milk and human wellbeing: a multi-species review. In: Rekik, B., Ed. Milk Production. NOVA Science Publishers, Inc., New York. 2012, 21-35.
14. Nikkhah, A.: Science and pseudo-science of milk intake and human health. In: Rekik, B., Ed. Milk Production. NOVA Science Publishers, Inc., New York. 2012, 15-20.
15. Nikkhah, A.: Science of camel and yak milks: human nutrition and health perspectives. Food Nutr. Sci., 2011; 2: 667-673.
16. Donnet-Hughes, A., Duc, N., Serrant, P., Vidal, K., Schiffrin, E.J.: Bioactive molecules in milk and their role in health and disease: the role of transforming growth factor-β. Immunol. Cell Biol., 2000; 78: 74-79.
17. Stelwagen, K., Carpenter, E., Haigh, N., Hodgkinson, A., Wheeler, T.T.: Immune components of bovine colostrum and milk. J. Anim. Sci., 2009; 87(13 Suppl.): 3-9.
18. Lanou, A.J.: Should dairy be recommended as part of a healthy vegetarian diet? Counterpoint. Am. J. Clin. Nutr., 2009; 89: 1638S-1642S.
19. Gerstein, H.C.: Cow's milk exposure and type I diabetes mellitus: a critical overview of the clinical literature. Diabetes Care, 1994; 17: 13-19.
20. Scott, F.W.: Cow milk and insulin-dependent diabetes mellitus: is there a relationship? Am. J. Clin. Nutr., 2005; 51: 489-491.
21. Oftedal, O.T., Jenness, R.: Interspecies variation in milk composition among horses, zebras and asses (Perissodactyla: Equidate). J. Dairy Res., 1988; 55: 57-66.
22. Salimei, E., Fantuz, F., Coppola, R., Chiofalo, B., Polidori, P., Varisco, G.: Composition and characteristics of ass's milk. Anim. Res., 2004; 53: 67-78.
23. Muraro, M.A., Giampietro, P.G., Galli, E.: Soy formulas and nonbovine milk. Ann. Allerg. Asth. Immunol., 2002; 89(Suppl. 1): 97-101.
24. Chiofalo, B., Salimei, E., Chiofalo, L.: Ass's milk: exploitation of an alimentary resource. Riv. Folium, 2001; 1(Suppl. 3): 235-241.
25. Yang, H.F., Ma, L., Zhao, X.G., Su, D.Q.: Studies on the development and exploitation of donkey milk. Clin. Food Nutr., 2006; 4: 22-24.
26. El-Agamy, E.I.: Immunological characterization of goat milk proteins with respect to human health and nutrition. Sm. Rum. Res., 2007; 68: 64-72.
27. Polidori, P., Beghelli, D., Mariani, P., Vincenzetti, S.: Donkey milk production: state of the art. Ital. J. Anim. Sci., 2009; 8: 677-683.
28. Zhao, X.X.: Milk production of Chinese Bactrian camel (*Camelus bactrianus*). In: Proceedings of the Workshop on Dromedaries and Camels as Milking Animals. Nouakchott, Mauritania, 1994: 101-105.
29. Vincenzetti, S., Polidori, P., Mariani, P., Cammertoni, N., Fantuz, F., Vita, A.: Donkey's milk protein fractions characterization. Food Chem., 2008; 106: 640-649.

30. Amati, L., Marzulli, G., Martulli, M., Tafaro, A., Jirillo, F., Pugliese, V., Martemucci, H., D'Alessandro, A.G., Jirillo, E.: Donkey and goat milk intake and modulation of the human aged immune response. Curr. Pharmaceut. Design, 2010; 16: 864-869.

31. Jirillo, F., Jirillo, E., Magrone, T.: Donkey's and goat's milk consumption and benefits to human health with special reference to the inflammatory status. Curr. Pharmaceut. Design, 2010; 16: 859-863.

32. Fantuz, F., Vincenzetti, S., Polidori, P., Vita, A., Polidori, F., Salimei, E.: Study on the protein fractions of donkey milk. Proc. of the ASPA Congress, Firenze, 2001: 635-637.

33. Iacono, G., Carroccio, A., Cavataio, F., Montalto, G., Soresi, M., Balsamo, V.: Use of ass's milk in multiple food allergy. J. Pediat. Gastroenterol. Nutr., 1992; 14: 177-181.

34. Doreau, M., Boulot, S., Martin-Rosset, W., Robelin, J.: Milking lactating mares using oxytocin milk volume and composition. Reprod. Nutr. Dev., 1986; 26: 1-11.

35. Ballestra, F.: Process for conservation of donkey milk and its application in the pharmaceutical and cosmetic industry. French Patent Application, 1995: FR 2 707 877 Al. 6.

36. Salimei, E., Cattaneo, M., Chiofalo, B., Dell'Orto, V.: Exploitation of mare's milk by polyunsaturated fatty acids enrichment, In: Enne, G. and Greppi, G.F., Eds. Food and Health: Role of Animal Products. Biofutur Elsevier, Paris. 1996, 223-227.

37. Zhang, X.Y., Zhao, L., Jiang, L., Dong, M.L., Ren, F.Z.: The antimicrobial activity of donkey milk and its microflora changes during storage. Food Cont., 2008; 19: 1191-1195.

38. Malacarne, M., Martuzzi, F., Summer, A., Mariani, P.: Protein and fat composition of mare's milk: some nutritional remarks with reference to human and cow's milk. Int. Dairy J. 2002; 12: 869-877.

39. Csapó, J., Stefler, J., Martin, T.G., Makray, S., Csapó-Kiss, Zs.: Composition of mares' colostrum and milk: fat content, fatty acid composition and vitamin content. Int. Dairy J., 1995; 5: 393-402.

40. Csapó-Kiss, Zs., Stefler, J., Martin, T.G., Makray, S., Csapó, J.: Composition of mares' colostrum and milk. Protein content, amino acid composition and contents of macro and micro-elements. Int. Dairy J., 1995; 5: 403-415.

41. Glavert, H.P.: Fatty Acids in Foods and Their Implications. M. Dekker, New York. 1992.

42. Kempster, A.J.: Reducing Fat in Meat Animals. Elsevier, Amsterdam. 1990.

43. Gibney, M.J.: Fish oils in human health. In Farrell, D.J. Ed. Recent Advances in Animal Nutrition in Australia. University of New England, Armidale, Australia. 1993: 2351.

44. Calder, P.C.: Effects of fatty acids on dietary lipids on cells of immune system. Proc. Nutr. Soc., 1996; 55: 127-150.

45. Das, U.N.: Essential fatty acids as possible mediators of the actions of statins. Prostaglandins Leukot. Essent. Fatty Acids, 2001; 65(1): 37-40.

46. Orlandi, M., Goracci, J., Curadi, M.C.: Essential fatty acids (EFA) in Haflinger and Thoroughbred mare's milk. Ann. Fac. Med. Vet. Pisa, 2002; LV: 319-325.