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VALORIZATION OF DONKEY MILK: ON CURRENT KNOWLEDGE, FUNCTION, THERAPEUTIC USES, AND FUTURE PROSPECT OF DONKEY MILK

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Abstract:

The whole milk is responsible for good source of all the nutrients and nowadays, donkey's milk consumption has been reevaluated for it's potential benefits to human health. For example, in infants with intolerance to cow's milk, donkey milk is a good alternative due to its chemical characteristics. The composition of donkey milk show resemblance to human breast milk for lactose, protein and ash when compared with goat, sheep, cow and camel milk. The microbiota present in donkey milk may be responsible for its beneficial effects. Microbiota contains high level of lactobacillus that reduce the growth of harmful microorganisms in milk, which can lead to milk spoilage and disease. Several scientific study has proven it's help potential benefits. Donkey milk also contains sufficient amount vitamin to permit regular the growth of the neonate. This review addresses various aspects of donkey milk and their role with special emphasis on milk yield, their function, composition, therapeutic uses and future prospective of donkey milk.

Keywords: Antimicrobial, Composition, Cosmetic, Donkey Milk, Therapeutic, Allergy, cow, donkey, elderly goat microbiota milk., human health, milk whey protein, milk fat, food allergies, immuno modulatory properties; cancer, intestinal microbiota oxidative stress, dyslipidemia, vitamins, human milk, vitamins deficiency, fortified foods

Introduction:

Donkey milk has a long history of use in both western and Eastern culture and it considered a therapeutic food. [1]. The health benefits of donkey milk was first described by Hippocrates (460-370BC) and pliny the elder(23-79AD). And beneficial properties of donkey milk are also reported in traditional Chinese Medicine manuals[2].

Donkey (Equus asinus) is belong to the equine family. Which has been used as a working animal mainly as pack since ancient time[3]. It also includes horses and zebras. The female donkey known as Jennies has been known for thousands of years for their milk[4]. The female donkey have very less quantity of milk as compared to other farming animals. One Jennies produced about 4cups(1liter) of milk per day. Thus the milk donkey is very difficult to find and considered a rare item[4, 5] It also available as freeze dried powdered form and an ingredient in in some European-imported chocolate bars. In Italy donkey milk used for infant and medical nutraceuticals[6].

Dr. Parrot's pioneering studies at l'Hospice des Infants Assists in 19th-century Paris marked an early scientific exploration of using donkey milk (DM) in infant feeding. His research involved feeding children affected by congenital syphilis directly from a donkey's udder. Dr. Parrot conducted some of the first controlled trials comparing DM with cow and goat milk, carefully recording milk intakes, children's weight gains, and analysing the chemical composition of DM. These ground-breaking studies eventually led to the establishment of a donkey farm dedicated to providing orphaned children with this unique source of nutrition[7].Recently found information about it's potential beneficial effects, Donkey milk is becoming popular in Europe, Croatia, France, Hungary, Italy the Netherlands and Serbia and in several Asian countries. Mostly china is a large donkey meat and milk producer and the donkey industry has become important in rural china.

Donkey milk is natural milk with the closest composition to human milk in terms of lactose content and protein and amino acid profile[8]. Indeed, scientific research focused on elucidating the composition of donkey milk and the presence of functional compounds has grown significantly in recent years. Studies have aimed to uncover various bioactive substances, including polyunsaturated and omega-3 fatty acids, functional proteins, vitamins, polar lipids, phytosterols, and have also explored the variability in milk composition. This expanding body of knowledge contributes to our understanding of the nutritional value and potential health benefits associated with donkey milk consumption[2].New knowledge has emerged leading to the development of studies focused on testing in vitro and in vivo the potential effects of Donkey milk in humans.

In the Western world, the duration of human breastfeeding has indeed seen a decline. Many mothers opt for infant formula due to various reasons and challenges associated with breastfeeding. Some of these reasons include the frequent night feedings, limited time available for breastfeeding due to work commitments, discomfort like nipple pain, and concerns about changes in breast appearance. It's a complex issue influenced by societal expectations, personal choices, and practical challenges[9].The formula of milk is not free of side effects such as anaphylaxis [10] and cow's milk allergy (CMA) is very common they cause tolerance in

young children and tolerance to milk starting by school age, and increasing through adolescence [11].The rates of allergy resolution for cow milk allergy (CMA) reported by Skripack and associates are as follows: 19% by 4 years, 42% by 8 years, 64% by 12 years, and 79% by 16 years. It's noteworthy that patients with persistent CMA exhibited higher levels of cow milk Immunoglobulin (Ig)E at all ages up to 16 years. These findings are different from a previous study that reported 75% of children with cow milk IgE-mediated allergy becoming tolerant by 3 years of age. In summary, these epidemiological data suggest that the natural history of CMA can vary, with some cases persisting until later ages [10].

IgE-mediated allergy is a common form of cow's milk-induced allergy, accounting for approximately 60% of cases even if a form of milk allergy without cow's milk specific IgE [12] so called non-IgE- mediated cow's milk protein intolerance (CMPI) and (CMPI) can indeed affect both the gastrointestinal system and the skin. Gastrointestinal symptoms like nausea, bloating, intestinal discomfort, and diarrhoea are common manifestations of CMPI. Additionally skin issues such as hives, eczema, or other allergic skin reactions can also be seen in individuals with CMPI [10].

In recent years, alternative milk sources like donkey's and goat's milk have gained attention for child feeding. These are often referred to as "niche" milks due to their limited production compared to cow's milk. Donkey's and goat's milk have shown unique biological properties and potential clinical applications. They are known for having a lower allergenic potential compared to cow's milk and also exhibit anti-inflammatory and immunomodulation activities, which can be valuable in various clinical scenarios.

Nutritional attributes of donkey milk

Donkey's and goat's milk consumption is indeed widespread in the Mediterranean area. These types of milk are often used to produce various dairy products like cheese and yogurt, and they are an integral part of the traditional Mediterranean diet[13].donkey milk composition is affected by the stage of lactation [14-18].

Furthermore, the composition of saturated fatty acids (SFAs) in donkey's and goat's milk is comparable to that of mare and human milk. This composition can have specific nutritional benefits, especially for infants and children. It's important for healthcare providers and caregivers to consider these factors when exploring alternative milk sources for child nutrition [19]. The fatty acid composition of donkey's milk is point indeed different from that of ruminant milk like cow's milk. While palmitic acid (C16:0) is the most abundant saturated fatty acid in donkey's milk, it is present in lower concentrations compared to cow's and human milk. Additionally, long-chain fatty acids such as stearic acid (C18:0) are found in modest amounts in donkey's milk, whereas they are detected at higher levels in cow's and human milk.

Interestingly, the saturated fatty acid (SFA) content in donkey's milk tends to decrease during lactation, which is different from the small changes observed in human milk and the increase in SFAs detected in cow's milk. Moreover, donkey's milk contains unsaturated fatty acids that are more similar to mare and human milk than ruminant milk, with a higher proportion (23-32%) of unsaturated fatty acids.

Donkey's and goat's milk, considered as "niche" milks due to limited production, have gained attention as alternative options for child feeding. They are less allergenic than cow's milk and have anti-inflammatory properties suitable for various clinical uses. While their saturated fatty acids are similar to human and mare

milk, they contain less palmitic acid (C16:0) than cow's and human milk. Long-chain fatty acids like stearic acid (C18:0) are in modest amounts, less than in cow's and human milk. Unlike cow's milk, SFA content in donkey's and goat's milk decreases during lactation. Donkey's milk has higher unsaturated fatty acids, making it more like human and mare milk than ruminant milk (cow). These differences have implications for nutrition and health [10].

The allergenicity1 of cow milk in children's nutrition can be attributed, in part, to the ratio between caseins and whey proteins. Donkey milk, which has a different ratio of these proteins compared to cow milk, is considered to have reduced allergenicity. This variation in protein composition is one of the factors that make donkey milk a potential alternative for individuals who may be allergic to cow [20]. Chemical composition determined among equine and human milk (Table 1) suggest the donkey milk can used as a dietary alternative for children with Ig E and non-IgE-mediated CMPA when breast milk is not available.

Jenny milk exceptionally having unique nutritional qualities that make it an interesting option for specific dietary needs. Its low fat content and high levels of certain nutrients, such as vitamins and minerals, can be beneficial for certain individuals, including newborns and those with heart or cholesterol issues. Donkey milk has been considered a potential alternative due to its nutritional profile. However, it's important to keep in mind that donkey milk production can be limited compared to more common sources like cow or goat milk. Farmers interested in this venture should carefully assess the market demand, the feasibility of production, and the ethical treatment of the animals involved. While it may be profitable and fulfill niche nutritional requirements, it's a unique endeavor that requires careful planning and consideration [21]Acquiring donkey milk can be important for addressing health issues like cow milk allergies, heart disease, and hypercholesterolemia due to its nutritional similarity to human breast milk, which is rich in vitamins, minerals, essential proteins, low in fat, and high in vitamin D, making it a potentially effective alternative.[3,22]Table 2 displays the nutritional information for 100 ml of donkey milk, vitamin D-fortified cow milk, and human breast milk.

Donkey milk is a complex liquid with a mix of different types of molecules. It includes proteins like casein and whey, proteins related to milk fat, enzymes (which are like tiny workers), and some other small proteins. This diverse collection of molecules gives donkey milk its unique nutritional composition, making it interesting for research and potential health benefits [23]The similarity between the molecules in donkey milk and human milk is quite interesting. Donkey milk's protein composition is notably different from cow milk, with lower total protein content, typically around 1.5-1.8 grams per 100 grams. This protein level is relatively similar to that of human and mare milk. Because of its lower protein content, donkey milk can be easier on the renal system, meaning it may place less strain on the kidneys compared to milk with higher protein content, like cow's milk. This aspect makes it potentially beneficial for individuals with certain dietary or health considerations [19]Donkey milk contains a relatively high amount of lactose (5.8-7.4%), which is similar to human milk and contributes to its pleasant taste. This lactose content also aids in the absorption of calcium, crucial for infant bone development.

In terms of proteins, donkey milk contains three main types: alpha-lactalbumin, beta-lactoglobulin, and lysozyme. Alpha-lactalbumin has been studied for its potential antiviral, antitumor, and antistress properties. Notably, beta-lactoglobulin, a common allergen in cow milk, is present in donkey milk but at a lower level, making it less likely to trigger allergic reactions, especially in children.

Donkey milk also contains two forms of casein, alpha S-1 and beta-caseins, but in smaller quantities compared to cow milk. Some research suggests that donkey milk has a lower percentage of allergenic proteins like beta-lactoglobulin and alpha S-1, making it potentially hypoallergenic. This quality makes it suitable for consumption by both infants and elderly individuals.

In summary, the composition of donkey milk, with its lower allergenic proteins and high lactose content, makes it an appealing option for those who may have allergies or digestive sensitivities, such as infants and the elderly [3]

Table 1- Main protein content in cow, donkey and human milk. (g/L)

Protein	Cow	Donkey	Human
Total protein	32.0	13-18	9-15
Total caseins	27.2	6.6	5-6
Total whey protein	4.5	6.5	8.0
Alpha s1- casein	10.0	n. d	0.8
Alpha s2- casein	3.7	n. d	n. d
Beta casein	10	n. d	4.0
k- casein	3.5	Trace	1.0
Alpha lactalbumin	1.2	1.80	1.9-2.6
Beta lactalbumin	3.3	3.7	n. d
Lysozyme	Trace	1.0	0.04-0.2
Lactoferrin	0.1	0.08	1.7-2.0
Immunoglobulins	1.0	n. d	1.6
Albumin	0.4	n. d	0.4

Table 2-.**Nutrient content of donkey milk with added Vitamin D versus human breast milk.**

Composition	Donkey	Mare	Human breast	Cow
pH	7.0-7.2	7.18	7.0-7.5	6.6-6.8
Protein g/100gm	1.5-1.8	1.5-2.8	0.9-1.7	3.1-3.8
Fat g/100gm	0.3-1.8	0.5-2.0	3.5-4.0	3.5-3.9
Calories g/100gm	49	51	70	61
Carbs g/100g	6	6	7	5
Lactose g/100gm	5.8-7.4	5.8-7.0	6.3-7.0	4.4-4.9
Total solids (TS) g/100g	8.8-11.7	9.3-11.6	11.7-12.9	12.5-13.0
Casein Nitrogen (CN) g/100g	0.64-1.03	0.94-1.2	0.32-0.42	2.46-2.80
Whey protein g/100g	0.49-0.80	0.74-0.91	0.68-0.83	0.55-0.70
NPN g/100g	0.18-0.41	0.17-0.35	0.26-0.32	0.1-0.19
Casein Nitrogen (CN) %	47.28	50	20.06	77.23
Whey protein %	36.96	38.79	53.52	17.54
NPN %	15.76	11.21	20.42	5.23
Vitamin D %	23	21	9	1
Calcium%	2	2	2	13
Cholesterol %	3	3	5	3
Riboflavin %	2	25	2	13

Composition of donkey milk

Milk is a natural and essential secretion produced by female mammals to nourish their offspring. It provides the necessary nutrients, energy, and antibodies required for the growth and development of the young animals, ensuring their overall well-being. Breast milk is indeed the best choice for infants, but when it's not possible, considerations like safety, allergies, availability, taste, nutrition, and cost become vital in selecting an alternative milk source. Donkey milk, due to its nutritional composition and lower allergenicity, can serve as a valuable alternative, not only for infants but also in addressing calcium deficiency issues in the elderly. It's

essential to make informed choices based on these factors to ensure the well-being of individuals at different life stages[24]. It's fascinating how donkey milk, because of its similarities to human breast milk, goes beyond being just food and is considered a nutraceutical. Nutraceuticals are products derived from food sources with health benefits beyond basic nutrition. Donkey milk's composition can indeed make it a valuable dietary supplement, not only for infants but also for elderly individuals. The active ingredient similarities of g/100g of donkey milk and human breast milk shown in Table 3.

Table 3-Percentage composition (g/100g) of donkey milk (evidence in bold) and comparison with donkey milk

Milk	Water	Dry matter	Fat	Protein	Lactose	Energy value (kJ/kg)
Human	87.57	12.43	3.38	1.64	6.69	2855.6
Donkey	90.39	9.61	1.21	1.74	6.23	1939.4

Milk's overall composition can vary due to genetic and environmental factors, such as animal breed, individual characteristics, lactation stage, milking frequency and efficiency, maternal age, health, and dietary choices. Donkey milk, in particular, contains less fat, with a 3.1% fat content, as opposed to the higher fat content in human and cow's milk, which stands at 3.7% [25].The pH level of donkey milk, as well as human milk, tends to be neutral or slightly alkaline, possibly attributed to its lower concentration of caseins and phosphates when compared to cow's milk [26].The size of fat globules in donkey milk could potentially impact milk digestibility. While there isn't conclusive data in the literature to explain this phenomenon, it appears that the diameter of milk fat globules may influence how fat is digested and metabolized [27]Certainly, some experts have suggested that smaller native milk fat globules might offer optimal digestive conditions because of the increased surface area they provide for lipase activity [28].

Donkey milk differs from the milk of other dairy species in various ways, including the number of milk fat globules per milliliter (mL) of milk. Donkey milk typically has a lower number of milk fat globules compared to cow, goat, and sheep milk. This difference in fat globule count can affect the texture and properties of the milk and dairy products made from it. Additionally, donkey milk is known for its unique composition, which includes lower fat and protein content but higher levels of certain nutrients like vitamins and minerals [29] .The fat globules in donkey milk have an average diameter of approximately 2 μm for about 70% of the total globules, which is similar to horse milk but smaller than both human (4 μm) and cow (2.8–4.6 μm) fat globules. Additionally, equine milk does not undergo creaming due to the absence of cryoglobulin, a protein that binds to fat globules as the temperature decreases, resulting in slow agglutination of fat globules The slow agglutination of fat globules in equine milk can have implications for processing and the properties of dairy products made from it. These unique characteristics contribute to the distinctiveness of donkey and horse milk compared to other types of milk [30].

Donkey milk contains several principal salts, including calcium, phosphorus, potassium, sodium, and magnesium. In comparison to human milk, donkey milk generally has higher concentrations of these elements, with the exception of potassium. However, when compared to species like cows, buffaloes, goats, or sheep, the concentrations of these salts in donkey milk are considerably lower. Specifically, the levels of calcium and phosphorus in donkey milk have been observed to be approximately 2–3 times higher than those found in human milk. These variations in mineral content can influence the nutritional properties [31] Indeed, casein micelles in milk serve as a vital source of amino acids, calcium phosphate, and bioactive peptides for neonates. While the precise mechanism explaining the tolerance of donkey's milk has not been fully elucidated, it's reasonable to hypothesize that the reduced allergenic properties of donkey's milk may be linked to structural differences in its protein components compared to cow's milk.

Donkey's milk contains a lower concentration of casein (about 50% of total protein) in contrast to bovine milk (which contains around 80% of total protein). Additionally, donkey's milk is rich in essential amino acids. These unique characteristics make donkey's milk a promising option as a dietetic food and a potential substitute for breast milk, especially for individuals who may have allergies or sensitivities to cow's milk. Further research in this area may provide valuable insights into the benefits of donkey's milk as a nutritional resource.( )According to this study, the percentages of the four caseins (αs1, αs2, β, and κ-CN) in decreasing order are as follows: β (54.28%) > αs1 (35.59%) > αs2 (7.19%) > κ-CN (2.79%). This assessment was carried out using Urea-PAGE analysis at pH 8.6, followed by immuno-detection with polyclonal antibodies and subsequent densitometric analysis. Understanding the specific composition of caseins in donkey milk can provide valuable insights into its nutritional properties and potential applications in the food industry or for individuals with dietary requirements or sensitivities [32].

Water soluble vitamin

It seems like the authors of a study investigated the vitamin content in milk from minor dairy species, and they found that mare and camel milk make a substantial contribution to the recommended daily requirements for vitamin B-complex and vitamin C for humans. This could have potential nutritional benefits for people who consume these types of milk In particular, vitamin B12 (Cobalamin) is naturally present exclusively in animal-derived foods. In fact, individuals with a diet low in animal-sourced foods often experience a deficiency in this vitamin. In Table3, the recommended nutrients intake for children younger than 3 years is listed for both water-soluble and fat-soluble vitamins [33].The vitamin C level found in donkey milk (57mg/L) is quite similar to the content reported in human milk (60mg/L), as indicated in Table 4. These eight B-complex water-soluble vitamins play crucial roles by acting as coenzymes in various cellular functions, participating in both catabolic and anabolic enzymatic reactions. Notably, the determination of vitamin B6 content in donkey milk is a recent development [34].In addition to vitamin B6, other B-complex vitamins like thiamine, riboflavin, and nicotinic acid are known for their lipid-lowering effects. Folic acid, another B-complex vitamin, plays a particularly crucial role in supporting the growth of children [35].

The thiamine concentration In donkey milk (0.66μM) is significantly higher than that found in human milk (0.12μM), and the riboflavin concentration in donkey milk (0.17μM) is also higher compared to human milk

(0.08µM). However, it's important to note that these riboflavin levels in donkey milk are relatively low when compared to cow and goat milk. Riboflavin is a precursor to two important cofactors flavin adenine mononucleotide FMN and flavin adenine dinucleotide FAD, which are involved in oxidation-reduction reactions. The high levels of both thiamine and riboflavin in donkey milk have been suggested as factors contributing to the health effects associated with the consumption of this milk in human nutrition[36].

According to Table 4, the nicotinic acid (Vitamin B3) content in donkey milk is notably higher at 18.75µM compared to human milk (4.64µM). Interestingly, it's similar to the content reported in goat milk. This variation in nicotinic acid levels among different types of milk can have implications for their nutritional value and potential health benefits [37]Indeed, nicotinic acid, also known as niacin, is a vitamin with the ability to exhibit lipid-lowering effects. It can help reduce both triglycerides and serum cholesterol levels, making it valuable for managing heart health and cholesterol-related issues [34].

The vitamin B6 (pyridoxine) content in donkey milk (5.38µM) is significantly higher than that in human milk (0.48µM), but it's relatively close to the value found in cow milk. Vitamin B6 plays vital roles in various biochemical pathways, including amino acid metabolism, lipid metabolism, and gluconeogenesis. It's worth noting that vitamin B6 deficiency is not uncommon, particularly among the elderly and fertile-aged women, and it can lead to reduced immune responses, underlining its importance in maintaining health health [38,39] .

Milk, especially for children under 1 year of age, is a significant source of folic acid (Vitamin B9). Donkey milk, as shown in Table 4, contains a higher amount of folic acid (0.83µM) compared to human milk (0.37µM). Folic acid is crucial for nucleic acid synthesis and plays a key role in the growth and development of the fetus in pregnant women. Insufficient vitamin B9 can lead to various health issues in different age groups, including neural tube defects in children, megaloblastic anemia and cardiovascular disease in adults, and even conditions like Alzheimer's disease in the elderly. Ensuring an adequate intake of folic acid is essential for overall health and well-being [36].

Vitamin B12 (cyanocobalamin) was not detected in donkey milk, which aligns with findings from the analysis of donkey milk collected from Indian small grey donkeys. Vitamin B12 is primarily found in foods of animal origin, and its absence in donkey milk underscores the importance of considering alternative dietary sources for this essential nutrient. The absence of vitamin B12 in equid milk compared to ruminant milk can indeed be attributed to the distinct digestive systems of these two herbivorous mammalian species. Vitamin B12 is synthesized by microorganisms within the digestive tract. Donkeys are hindgut fermenters, meaning most fermentation occurs in the hindgut, whereas in ruminants, such as cows, sheep, and goats, the majority of fermentation takes place in the rumen. These variations in digestive processes influence the availability of vitamin B12 in their respective milk [36].The similarity in vitamin C content between fresh donkey milk (57mg/L) and human milk (60mg/L), along with the significant difference compared to cow milk, suggests potential nutritional advantages in favour of donkey milk and human milk over cow milk in terms of vitamin C intake Vitamin C indeed plays important roles in various aspects of health. It aids in intestinal iron absorption, is essential for collagen formation, and can have a protective effect against atopic dermatitis in

high-risk children. These functions highlight the importance of maintaining an adequate intake of vitamin C in our diets for overall health and well-being [40].

Table 4-Water soluble vitamin content in human, cow and donkey milk.

Water soluble vitamin	Donkey milk	Cow milk	Human milk
Thiamine (Vitamin B1)	0.66	0.59	0.12
Riboflavin (Vitamin B2)	0.17	2.12	0.08
Niacin (Vitamin B3)	18.75	2.43	4.64
Pyridoxine (Vitamin B6)	5.38	5.5	0.48
Folic acid (Vitamin B9)	0.83	0.02	0.37
Cyanocobalamine (Vitamin B12)	n. d	3.3×10−3	n. d
Vitamin C	57 mg/L	27 mg/L	60mg/L

Fat soluble vitamin

Indeed, the diet of animals plays a significant role in the content of fat-soluble vitamins (A, D, E, and K) in their milk. Differences in fat-soluble vitamin content can be observed among different mammalian species, and even within a specific species, the animal's breed can influence the concentration of these vitamins in milk. For example, in dairy cows, breeds like Jersey and Guernsey, which produce milk with high-fat content, tend to have higher levels of fat-soluble vitamins compared to breeds like Friesian and Brown.

Furthermore, there's a direct correlation between the fat-soluble vitamins present in milk and the total milk fat content. These variations have implications for both the nutritional and sensory properties of milk, affecting its overall quality and potential health benefits for consumers [41].Vitamin A is a compound made up of active forms known as retinoids (found in animal sources) and precursor forms called carotenoids (found in plant-based foods). Both types are essential for functions like vision and overall health [42].

The conversion of carotenoids to retinol and the transfer of retinol to the mammary gland work in certain animals. The conversion rate can indeed vary based on an animal's digestive physiology, and retinol is important for various biological processes, including its secretion into milk fat globules for the benefit of offspring. This process highlights the importance of dietary sources of vitamin A, both from carotenoids in plants and retinoids in animal products, for maintaining health and nutrition [43].Vitamin A in milk is crucial for children's growth, immunity, and eye health. It also helps maintain the integrity of tissues like skin and mucous membranes. This vitamin is essential for overall child development and health [44].While human

milk is already a good source of vitamin A, with a slightly higher content compared to donkey milk, in Western countries where vitamin A deficiencies are rare, fortifying dairy products with vitamin A is a common practice. This fortification helps further improve nutritional status and provides an increased amount of vitamin A, especially for the benefit of children's nutrition and overall health [36].

Table 5-Fat soluble vitamin content in human, cow and donkey milk.

Fat-Soluble Vitamin	Human Milk	Cow milk	Donkey milk
Vitamin A	60µg/100m L	41µg/100m L	58µg/100mL
Vitamin D	0.06µg/100m L	0.08µg/100m L	2.23µg/100mL
Vitamin E	237µg/100m L	113µg/100m L	5.2µg/100mL
Vitamin K	0.2µg/100m L	1.1µg/100m L	n. d

Vitamin D comprises a group of compounds deeply involved in calcium and bone metabolism, thus contributing to its anti-rachitic effects in growing mammals while also serving as a hormone. In human milk, the vitamin D content is notably low at 0.06µg/100mL (as indicated in Table 4). Conversely, donkey milk boasts a higher total vitamin D level at 2.23µg/100mL compared to the amounts found in the milk of many other mammalian species, including humans.

Recently, various clinical trials have explored the potential anticarcinogenic, anti-celiac, and immunomodulatory properties of vitamin D, in addition to its well-established role in promoting bone mass formation and preventing osteoporosis. Vitamin E exists as a group of eight biologically active forms, encompassing four tocopherols and four tocotrienols, all of which possess antioxidant properties. In the case of donkey milk, both α-tocopherol and γ-tocopherol have been identified. In contrast, human milk stands out with a notably high vitamin E content at 237µg/100mL, a stark contrast to the lower levels found in donkey milk (5.2µg/100mL) and cow milk (as shown in Table 4).

Vitamin E is recognized as one of the primary natural antioxidants, demonstrating its protective effects on cell membranes by safeguarding them against oxidation or peroxidation processes. According to published data, vitamin K has not been found in donkey milk. In contrast, mare milk contains approximately three times more vitamin K than cow milk. Furthermore, human milk exhibits a very low level of vitamin K content. These variations in vitamin K levels among different types of milk highlight the diversity of nutrient compositions in various mammalian milks [36].

Role of donkey milk

Indeed, cow milk protein allergy (CMPA) is a prevalent food allergy among children under the age of 3, and it can lead to various adverse reactions. Donkey milk has gained attention as a natural hypoallergenic alternative due to its lower allergenicity. Many individuals who are allergic to cow's milk protein find that donkey milk is better tolerated, reducing the risk of adverse effects when consumed as a milk substitute.

However, it's essential to note that individual responses can still vary, and consulting a healthcare professional is advisable when considering such dietary changes for infants with allergies [45].

Donkey milk has been recognized for its lower allergenicity compared to cow's milk, making it a valuable option for infants and children with allergies or sensitivities. Its composition, including lactose, protein, and minerals, closely resembles that of human breast milk. Additionally, the presence of immune-active compounds like lysozyme and lactoferrin in donkey milk may contribute to boosting the immune system in infants. When supplemented with vegetable oil in specific proportions, donkey milk can mimic the nutritional profile of breast milk, which is essential for the healthy development of infants. These characteristics make donkey milk a noteworthy alternative for those seeking a hypoallergenic and nutritionally suitable milk source [46, 47].

Fermented donkey milk

Equid milk, derived from animals like donkeys and mares, has found extensive use as a suitable medium for producing probiotic beverages through fermentation with Lactobacillus bacteria. One of the well-known products resulting from this process is koumiss, a fermented equid milk beverage with a rich history. In Central Asia, koumiss has been enjoyed since ancient times, and it holds a special place as the national drink of Mongolia.

The Mongolian people even have a saying that "kumys cures 40 diseases," highlighting the traditional belief in the health benefits of this fermented milk beverage. This cultural tradition not only showcases the cultural significance of koumiss but also underscores its potential as a probiotic-rich and potentially therapeutic drink [48].

Cosmetic with donkey milk

In the modern cosmetic industry, there is a strong emphasis on using natural ingredients, and milk, being of natural origin, has become a key ingredient in many cosmetic products. Scientific studies have indeed demonstrated that cosmetic products containing donkey milk can offer exceptional benefits for the skin. This natural and nutrient-rich milk is valued for its potential to nourish and improve the skin's appearance, making it a sought-after ingredient in skincare formulations [49].

Donkey milk's richness in protein, minerals, essential fats, bioactive enzymes, and various growth factors, including riboflavin and vitamin D, indeed provides natural nourishment to the skin, helping to tone and improve its condition. Furthermore, the presence of antibacterial compounds such as lysozyme and lactoferrin in donkey milk plays a vital role in inhibiting the growth of pathogenic bacteria on the skin. This antibacterial action can be beneficial in reducing the risk of skin infections and maintaining skin health when donkey milk is used in cosmetic and skincare products [50,51].

Indeed, due to its beneficial properties, donkey milk, when formulated with appropriate compounds, can be utilized in the treatment of skin conditions such as acne, psoriasis, eczema, and other related skin infections. This natural milk's soothing and nourishing qualities make it a valuable ingredient in skincare

products designed to address these issues. In recent times, donkey milk has also gained popularity in the manufacturing of soaps and face creams, offering consumers an alternative and potentially beneficial choice for their skincare routines [52].

Does donkey milk maintain beauty and youthful qualities?

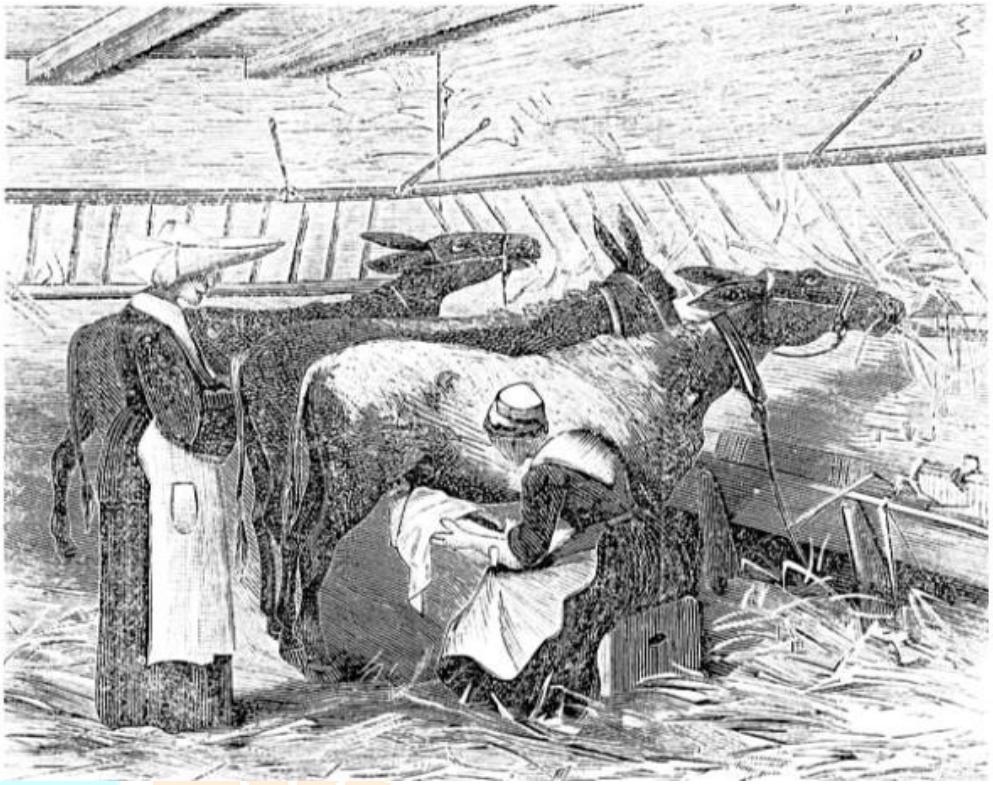
According to legend, Cleopatra, the final active Pharaoh of Egypt, purportedly indulged in a daily bath enriched with donkey (ass) milk to safeguard her skin's beauty and youthful appearance. The myth suggests that it took as many as 700 donkeys to meet the required milk quantity. This practice was thought to enhance skin delicacy, maintain its fairness, and diminish facial wrinkles

Pliny the Elder, the ancient historian, documented that Poppaea Sabina, the wife of Emperor Nero from 30 to 65 AD, endorsed the use of ass milk for her skincare regimen. She even had entire groups of donkeys accompany her during her travels to ensure a constant supply of ass milk for her baths. Similarly, Pauline Bonaparte, Napoleon's sister, who lived from 1780 to 1825 AD, was also known to have utilized ass milk for her skincare routine [53].

Donkey milk as a cure-all

Throughout the centuries, the medicinal virtues of donkey's milk persisted. During the 1800s, a hospital in Paris caring for children with congenital or contagious illnesses employed donkeys to contribute to the recuperation of these young patients. This practice was documented in Volume 22 of "The Popular Science Monthly."

Initially, the infants were being fed goat's milk, but it became evident that donkey's milk was a more suitable choice for them. Consequently, all the infants were switched to receiving milk directly from the donkey's teat. The procedure involved presenting one, two, or sometimes even three children simultaneously to the donkey, with the nurse holding them at the teat, and this process was executed with remarkable ease.



Nurse holding a baby to suckle directly from a donkey at the hospital for assisted children in Paris, 1882-1883

The outcomes vividly illustrate the method's success. Over a span of six months, a total of eighty-six children afflicted with congenital and contagious diseases were cared for in the nursery. Among the initial six who received cow's milk from a bottle, only one recovered. Out of the forty-two nursed at the teat of a goat, eight survived, while thirty-four did not. In contrast, thirty-eight children nursed at the donkey's teat resulted in twenty-eight recoveries and ten fatalities. Given these compelling results, there is little doubt that, especially within hospital settings, the most effective approach for feeding new-borns who, for various reasons, cannot be placed in the care of a nurse is to allow them to suckle directly from a donkey's [53].

Immunomodulatory effect

Donkey milk (DM) is notably abundant in lysozyme (LZ), an enzyme that can disintegrate the peptidoglycan layer found in Gram-positive bacteria. On average, DM contains approximately 1.07 grams per liter (13% of the total protein content), which is comparable to human milk (HM) with concentrations ranging from 0.3 to 1.1 grams per liter. In contrast, cow's milk (CM) contains negligible amounts of LZ. The lysozyme activity in DM varies widely, ranging from 1670 to 11,531 units per milliliter (U/mL), whereas CM has a barely detectable LZ activity of 0.0292 U/mL. HM boasts the highest LZ activity, with approximately 39,000 U/mL [54].

Mao et al. suggested that the White Protein fractions, which include Lysozyme (LZ), are accountable for the Immunomodulatory impact of DM. It is yet to be determined if other constituents, like α-lactalbumin (α-LA) and lactoferrin, contribute to this effect. Notably, α-LA appears to influence the overall immune function in

infants. Recent investigations into milk oligosaccharides have also demonstrated positive effects on immune system development. However, it's worth mentioning that research on oligosaccharides primarily focuses on HM, with less emphasis on DM [54].

Donkey Milk has demonstrated immunological activity in both in vitro tests and randomized controlled studies in animal models and humans. In these studies, DM has been observed to stimulate the release of certain cytokines, which are proteins that regulate the inflammatory and immune response to infections. Specifically, DM has been shown to increase the levels of cytokines associated with the regulation of innate immunity and the initiation of local acute inflammatory responses, such as interleukin 1 (IL-1), interleukin 6 (IL-6), and tumor necrosis factor α (TNF-α), both in laboratory settings and within living organisms.

On the contrary, Jiang et al. have reported an inhibition of TNF-α in mice with inflammatory bowel disease (IBD) [54].

Potential Antioxidant and Antihypertensive affect

The antioxidant efficacy of DM has been assessed in double-blind randomized trials conducted on animal models (Table 4). Rats administered DM exhibited an enhancement in their antioxidant defense mechanisms and detoxifying enzyme activity. Specifically, Li et al. observed that DM consumption tended to elevate the superoxide dismutase (SOD) activity in the plasma of diabetic rats when compared to rats that received no treatment. SOD enzymes, in turn, facilitate the dismutation of superoxide radicals (O2−) into ordinary molecular oxygen (O2) and hydrogen peroxide (H2O2). Furthermore, Li et al. demonstrated that the overall antioxidation capacity was also heightened in diabetic rats treated with DM, approaching levels observed in healthy (control) rats

In mouse models, there were observed enhancements in the liver's glutathione/glutathione disulfide ratio, which is an indicator of oxidative stress. Additionally, the activities of liver detoxifying enzymes like glutathione-S-transferase and NAD(P)H:Quinone Oxidoreductase were increased.

The antioxidant activities measured in Donkey Milk (DM) and fermented DM (kefir) using ABTS and DPPH assays were higher in kefir compared to raw DM. Furthermore, these antioxidant properties increased after undergoing in vitro simulated gastrointestinal digestion. This improvement in DM's antioxidant activity is attributed to the presence of bacteria, especially Enterococcus faecium DM 33, which was found in kefir and contributed to the strongest antioxidant activity observed in the fermented milk [54].

Future prospect

While donkeys were once disregarded for their 'asinine' qualities, their milk is now esteemed as the elixir of life. With a growing body of global research reports, donkey milk is increasingly regarded as a potential "gold mine" for the future. In contrast to prosperous Western societies, in India, donkeys play a crucial role in the livelihoods of landless, small, and marginalized farmers. The majority of donkeys are in the possession of nomads and laborers at brick kilns who lack knowledge of how to derive economic benefits from these animals beyond their use as pack and load carriers. If these donkey owners and marginalized farmers can be

educated about the advantages and the range of products derived from donkey milk, this could represent a significant financial windfall for them. The future prospects are truly vast, achievable through proper breeding, milking practices, and effective product marketing

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