LECHE DE CAMELLO: CARACTERÍSTICAS Y PERSPECTIVAS PARA USO EN CLÍNICA

CAMEL MILK: CHARACTERISTICS AND PERSPECTIVES FOR USE IN CLINICAL PRACTICE

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ABSTRACT

Camels are good milk producers and the selected animals are as good as the top cows for milk production. The camel milk has features that make it not only good as a supplement in the diet of humans, but in certain conditions such as allergies (does not contain beta-lactoglobulin, the cow's milk most important allergenic protein), lactose intolerance, general infections, diabetes, and even could be considered useful in the diet of patients with autism. Its use is, unfortunately, restricted to some populations where this animal is native. By its chemical composition does not clot in an acidic environment; it is rich in insulin, contains small dimeric immunoglobulins which suggest its use in molecular engineering. In conclusion, for its usefulness, camel farming should be encouraged, since these animals may become endangered animals.
Key words: Camel's milk; diabetes; milk allergy; immunoglobulins.

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INTRODUCTION

In most parts of the world, camelids are considered exotic animals which can only be seen in zoological gardens.

Even in places where there were previously large herds, and the animals had a social purpose, it is possible to notice a decline in their breeding grounds. Formerly used as a mode of transportation in desert regions and as a source of meat and milk, camels have been relegated to a secondary status with the advent of road construction for motor vehicles, migration of nomadic populations from deserts to urban zones and dominance of bovines as sources of meat and milk. The dwindling number of those animals seems irreversible.

Rehabilitation of this mammal should be considered, on account of its potential as a source of food and of genes for use in molecular biology. Their physical endurance, their huge adaptive capability, and the special properties contained in their milk support the argument for breeding them, instead of them being just objects of amusement.

THE CAMELIDS

Camels are mammals which ruminate, but they are not classified as ruminants. They belong to the order *Artiodactyla*, sub-order *Tylopoda*, family *Camelidae*. We will concentrate on the genus *Camelus*, species *C. dromedarius*, whose members have a single hump, short fur, and long legs, distinguishing them from *C. bactrianus*, which have two humps, long fur and short legs.

They originated in North America. Migrated, during the Tertiary Period, to Asia and Africa. Another group, the llamas (*Lama paca, L. glama e L. vicugna*), reached South America, in the last ice age, via Central America (1).

Camels are great economizers of water and food. They live in arid and semi-arid lands. Camels regulate body temperature on two levels: in the heat of the day their temperature reaches 40˚C and, at night, falls to 34˚C. In this way, they do not lose water as a result of thermal regulation. In only one situation does this mammal physiologically dehydrate: when the nourisher, without water for days, produces milk of lower density in order to keep the calf in a good state of hydration and nutrition.

A female camel is a good producer of milk, generating approximately 2-25 liters per day, depending on the quality of the food she takes in. The typical gestation period lasts about 13 months, and lactation varies between nine to eighteen months, the same as for bovines. In situations of poor rationing, the female camel is able to sustain a steady rate of milk production, distinguishing them from bovine females. In Kenya, a female camel can produce as much milk as four cows (1).

According to a report by U.N. Food and Agriculture Organization (FAO), camels number is around seventeen million, twelve million of them in Africa and 4,9 million in Asia. Fifteen million belong to the C. dromedarius species. This number is considered low and is quickly decreasing. In 1927 there were 1,3 million camels in Russia, and now there are just over two hundred thousand. Comparatively, there are 1,2 billion cattle in the world, making cattle 70,5 times more present than camels on the Earth (2).

Camel milk

Composition of camel milk. We will consider the following aspects: pH and density, mineral and vitamin contents, proteins, lipids, and the carbohydrates.

pH and density. Its pH varies from 6,5 to 6,82 (human milk: 7,12; bovine milk 6,7) and its density from 1,025 to 1,032 (human milk: 1.027; bovine milk 1,040) (3-5).

Mineral salts and vitamins. Except for sodium, they are the same as those found in bovine milk (sodium: 47 mg/100g in bovine milk and 69 mg/100g in camel milk) and in similar amounts. The content of mineral salts in camel milk varies in concentration by up to 5% in situations of water restriction. The comparison with the mineral contents found in human milk can be seen on table 1 (1,3,6,7).

A glass (250 ml) of camel's milk supplies 150 cal, contains a quantity of calcium identical to seven sardines with bones, and as much potassium as a banana.

Its vitamins are the same as those found in bovine milk, but in different proportions: vitamins A (0,15 mg/kg), C (24 mg/kg), B12 (0,002 mg/kg), thiamine (0,33 mg/kg), riboflavin (0,42 mg/kg), pyridoxine (0,52 mg/kg), niacin (4,6 mg/kg), folic acid (0,004 mg/kg), and pantothenic acid (0,88 mg/kg). Compared to bovine milk, camel milk contains four times less riboflavin, thirteen times less folic acid, four times less pantothenic acid, five times more niacin, and five times more vitamin C. There is no vitamin E in camel milk, in contrast to bovine milk, which contains about 0,6 mg/kg (1,3,8).

Proteins. Camel milk proteins are similar, in concentration and composition, to those contained in bovine milk (9). The protein concentration varies from 3,5 g/dL to 4,5 g/dL (human milk: 1,2 g/dL; bovine milk: 3,25 g/dL).A glass of camel milk contains as much protein as an egg.

When camel's milk casein precipitates, a liquid residue remains: the whey. It contains four protein fractions: two of them are identical to those found in whey from bovine milk, namely albumin (molecular weight: 66 kDa) and α-lactalbumin (molecular weight: 14 kDa). The other two fractions, with 23 and 43 kDa, are not yet

TABLE 1

Mineral elements per 100 g of camel and human milk *

Elements	Camel milk	Human milk
Phosphorus	51,5 mg	15,0 mg
Magnesium	14,2 mg	2,8 mg
Calcium	117,0 mg	35,0 mg
Potassium	60,0 mg	60,0 mg
Chlorine	163,0 mg	43,0 mg
Sodium	69,0 mg	15,0 mg
Copper	1,4 µg	39,0 µg
Iron	39,0 µg	76,0 µg
Zinc	121,0 µg	295,0 µg

*According references 1, 3 and 6.

completely identified.

As the human milk, the camel milk does not contain the β-lactoglobulin fraction, mostly responsible for the allergic symptoms provoked by bovine milk (10). This is the probable reason allergy to camel milk was not described until now. Some authors believe camel's proteins would not be recognized by other animals, among them, human beings, owing to phylogenetic differences (11). Camel milk would be, therefore, a naturally hypoallergenic product.

Concerning the immunoglobulins, the camelids, as so their milk, bring two repertoires: the usual tetrameric, found in the IgG1 (~160 kDA), with two different γ-isotypes, and a dimeric one, found in the IgG2 and IgG3 (~95 kDA), smaller than the humans, eliminated by the milk and easily absorbed, made up of just two heavy chains with a long hinge region. The absence of the CH1 domain where the light chain attaches, explains its absence in the dimeric immunoglobulins (12, 13).

Camelids' antibodies being smaller more easily reach their target points; have a quicker clearance and exert an exceptional neutralizing effect, as can be observed in the studies with tetanus toxin (14-16).

Contrary to what happens with humans, who suffer from severe deficiencies due to the high tendency of aggregation of immunoglobulin heavy chains (heavy chain disease), dimeric immunoglobulins of camelids have a low tendency to aggregate, providing these animals a high immune resistance.

The strong neutralizing effect of the camel immunoglobulins is evidenced by the selective inhibitory action on the enzymatic system of hepatitis C (14).

Dimeric immunoglobulins, similar to those of camelids, of low molecular weight, have been constructed in laboratory. They are highly specific, exceptionally thermostable, soluble and with good anti-enzimatic power. These immunoglobulins, cVH, are called minibodies, made up exclusively of heavy chains. Studies of camelids' immunoglobulins will likely lead to progress in molecular engineering with biochemical, diagnostic and therapeutic breakthroughs (13).

Dimeric immunoglobulins, formed only by two heavy chains, named VHH, acting on micromolar and nanomolar bases, have more ability to interact with antigenic epitopes than the conventional tetramerics. They have specific effects on haptens, proteins and peptidic ligants (15). Only in Tylopoda is the immune response achieved through activation of the conventional tetrameric chain or the dimeric, depending on the type of the responsible antigen (10,16).

Lipids. Camel milk has a fat content of 1,8 g/dL to 2,0 g/dL, largely consisting of unsaturated fatty acids (human milk and bovine milk: 4 g/dl). volatile fatty acids, mainly linoleic acid (18:3n-3), and polyunsaturated fatty acids.

A glass of camel milk (250 ml) contains less cholesterol than 100 g of fish and less fat than 250 g of beef. As with other types of milk, triacylglycerols constitute 97% of the fat in camel milk. The fatty acids, which form part of the fat, are different from those in bovine milk, in which short chain fatty acids prevail (C4 to C12), in contrast to those of camel milk, in which the predominant ones have a longer chain (C14:0, C16:0, C18:0, C18:1).

The phospholipids of camel milk are different from those found in the milk of other ruminants. They contain a great deal of linoleic acid, long chain unsaturated fatty acids and four times more phosphatidylethanolamine than bovine milk. Fat in camel milk appears as small globules (3 μm in diameter) covered by a membrane for emulsification of the fat - the fat globular membrane. That membrane is different from that found in bovine milk, because it has a lower protein content and a higher content of phospholipids. These are qualitatively the same as bovine milk (lysophosphatidylcoline, phosphatidyletanolamine, phosphatidylserine). The ability of camel milk to form cream is about ten times lower than that of bovine milk. The formation of the cream depends on the presence of adsorbed euglobulin in fat globules (17).

Carbohydrates. Lactose is the most important carbohydrate in milk and in only here is found. Camel milk contains 3,4 g/dL (human milk: 7 g/dL; bovine milk: 4,8 g/dL.). The lactose content of camel milk varies depending on water intake. When water is restricted, the lactose content decreases by up to 5%, as so the flavor of milk is less sweet in cases of dehydration.

Of the another properties of the camel milk are important to point out its enzymatic coagulation, antimicrobial activity, and the effect of the heat. As so:

Enzymatic coagulation. Camel milk does not form clot as firmly as bovine milk; rather, it coagulates into small flakes. Milk coagulation depends largely on the size of casein aggregates (mycelia). The larger they are, the more difficult is the process of aggregation. In bovine milk the mycelia are small, unlike those in camel milk, which are large. Consequently, it is difficult to make cheese with camel milk.

Antimicrobial activity: Camel milk whey can inhibit bacterial growth. The content of lysozyme, an enzyme with bactericidal activity and the capability to increase the action of antibodies, reaches 648 μg/dL in camel milk. A level similar to that found in egg whites, and higher than that found in bovine milk, which is 120 μg/dL, but less than the content found in human milk which is 40 000 μg/dL. Also, "protective proteins" have been found in camel milk, with bactericidal and viricidal action, such as lactoferrin, lactoperoxidase, NAGase, PGRP, IgG and IgA, as well as high levels of antibodies against rotavirus (1). The bactericidal action due to lactoferrin against Escherichia coli 0157:H7 is higher in camel milk than in human milk. Lactoferrin is the dominant protein in whey and each molecule of it is able to bind with two atoms of iron. It has bacteriostatic and bactericidal effects on Gram-positive and Gram-negative bacteria. These effects are mainly attributed to its chelating action on iron, thus depriving bacteria of that nutritional source. Camel lactoferrin has a higher degree of iron saturation than the human equivalent. It interacts with the bacterial cell membrane, changing its permeability, and causes release of lipopolysaccharides. Besides these actions, lactoferrin is important in the transport of iron. It works also as an antitumoral, anti-inflammatory, immunomodulatory and proteolytic substance. It displays enzymatic effects and plays a role in transcriptional regulation. Bovine lactoferrin is different from that found in humans and camels , because antibodies against the former ones do not react against the latter ones (18).

Effect of heat on camel milk. Camel milk is less stable at lower temperatures than bovine milk. In the process of pasteurization (63˚C for thirty minutes) 7% of whey proteins from bovine milk are denatured compared with 15% in camel milk. However, at 80˚C the result is inverted and the degree of denaturation of camel milk is 33% compared with 70% for bovine milk.

At 80˚C protein patterns observed in electrophoretic studies indicate a greater stability of camel milk proteins, when compared with the bovine milk. In the bovine milk seralbumin and immunoglobulins disappear in this temperature. This is not case with camel milk. (1)

The camel milk in human medicine

Following, we will point out the six most important aspects of the camel milk in human medicine.

1. Camel milk and alimentary allergies. Camel milk has been identified as assisting in the recovery processes of alimentary allergies (14). Improvement of the intestinal mucous membrane, promoted by camel milk, and particularly by camel yogurt (shubat), facilitates intestinal functions and this, in turn, prevents absorption of sensitizing molecules (19).

2. Camel milk and lactose intolerance. Lactose is the major energy source of milk. It facilitates absorption of calcium and the development of beneficial microflora, rich in bifidobacteria. Camel milk contains approximately the same amount of lactose as bovine milk but less than human breast milk. Nevertheless, individuals intolerant to lactose are able to accept camel milk without adverse symptoms (20). An explanation for this has not yet been found.. It was suggested that the lactose in camel milk is readily metabolized (14). If camel milk can be used by individuals intolerant to lactose, this will fill a major gap in their diet.

There is no allergy to lactose, and cases described as sensitivity refer to the residues of protein in lactose (21). All known milks contain lactose, except for Pinnipedia milk (sea lions and walruses).

3. Camel milk and infectious processes. Camel milk has been linked to improvement in cases of infectious diseases such as tuberculosis (22). This is the consequence that in camelids immunoglobulins with only the heavy chain, present a very high antigenic affinity, giving them more significant immune protection.

4. Camel milk and calcium metabolism disorders. Ingestion of camel milk quickly increases bone calcium (23).

5. Camel milk and diabetes. Papers have been published regarding camel milk antidiabetogenic activity. Its use could reduce by up to 35% the daily doses of insulin taken by patients with type-1 diabetes and there would be a reduction in the levels of anti-insulin antibodies (8,24). In populations where the use of camel milk is widespread, the prevalence of type-1 diabetes is showed as zero (19,25,26). The antidiabetogenic effect of camel milk could be linked to a number of factors. Thus: 1. the high concentration of insulin (118 to 128 units per liter) (8). Interesting was the fact the author found in the south american camelid milk, the Lama glama, just a small insulin content, 5,7 μU/ml. This finding contrasted with the 58,30 μU/ml found in the C. dromedarius milk; 2. the non-coagulation of camel milk in the acidic environment of the stomach makes transit of milk faster, and reduces the destruction of insulin in camel milk . A decrease in gastric emptying time is contested by some authors (27); 3. the immunomodulatory effect of camel milk on the function of beta cells; 4. the presence of half cystine in camel milk, which has some similarity to insulinic peptides; 5. the antioxidating action of vitamin C, which exists in large quantities in camel milk; 6. the dietary pattern of camels in the desert would make them produce phytochemical substances that would exert antidiabetogenic action (8,25).

In diabetics, the substitution of bovine milk by camel milk should be considered, in view of the similarity between bovine milk proteins and the pancreatic islets molecules. This cross-reaction would cause the formation of auto-antibodies which would harm the cells of the islets. It is also reported that an immunosuppressive substance, β-casomorfin-7, derived from the cleavage of β-casein from bovine milk, would perform and important role in the diabetogenic effect of bovine milk (18). The use of camel yogurt (shubat) has been considered to facilitate the restoration of good microflora and regulation of intestinal function due to the rapid recovery of the mucous membrane. For this reason it is recommended in the treatment of intestinal dysbiosis, by enabling reduced use of antibiotics. This in itself would also be important as a antidiabetogenic factor (27-29).

6. Camel milk and autism. The origin of many cases of autism is related to the autoimmune process. Casomorfin, an opioid, causes brain damage and, in experimental animals, produces signs typical of autism. This substance can be formed due to an enzymatic error from β-lactoglobulin, a substance which does not exist in camel milk, but present in the milk of other mammals (30). Therefore, it is advisable to avoid bovine milk in the diet of autistic patients (31).

Finally we believe that it is important to compare the camel milk with the milks used in the clinical practice as the bovine milk and the milk from another species, human breast milk, soy milk and the artificial milk formulas.

The camel milk, bovine milk and human breast milk. There are no reports in the literature describing adverse reactions or allergies to camel milk, unlike bovine milk. Approximately 5% to 15% of children suffer adverse reactions from bovine milk, and the incidence of allergies ranges from 0,3% to 7,5% (32-34), decreasing as age increases (35). Even human milk can cause allergic reactions, because allergens ingested by the nourisher can be eliminated through her milk. Therefore, 0,37% of children fed exclusively with breast milk react to bovine milk (36). The most important allergen in bovine milk is β-lactoglobulin, whose sensitization power increases if the milk is pasteurized (37), followed by casein. However, neither camel milk nor human milk contain β-lactoglobulin. Causal and differential diagnosis of an allergy to bovine milk is not always easy to obtain, and spontaneous remission usually occurs in 90% of cases, when the person is around three years old. Cutaneous or serological tests (RAST) do not allow accurate diagnosis because, in many cases, the reaction is not IgE-mediated, may or may not be associated to low levels of IgA and may depend on direct stimulation and the response of T cells to proteins from bovine milk. The gold standard for the diagnosis of an allergy to milk is the double-blind provocation test (32,34,38,39).

The camel milk and the milk from other animals. Buffalo, sheep, goat and horse milk are not perfect substitutes for bovine milk or human milk and are therefore far from being ideal options. They have cross-reactions to bovine milk and to each other. They contain β-lactoglobulin, which human milk and camel milk do not. Their α-caseins, extremely resistant to denaturation, share between 87% to 98% of the same amino acids and have little difference in their primary structures. Caseins, mainly α and ϰ-caseins, and whey proteins are major allergens. There have been reports of patients allergic to bovine milk casein who reacted to goat milk casein, but not to camel milk casein. This happens because, although camel milk proteins have similar amino acid chains, their three-dimensional structures are different, which prevents cross-sensitization. Milk from buffalo, goat, sheep, and horses do not supply all the nutritional requirements of children and does not have the ability to accelerate intestinal maturation as does human milk. Camel milk requires further studies about its qualities as a substitute for human breast milk in situations where the latter is difficult to obtain, although it is more similar to breast milk than milk of the other animals mentioned. Milk from other animal species is not recommended when the patient is allergic to bovine milk. Perhaps camel milk is an exception, though. It is already considered to be an excellent substitute in such cases (14). Human and camel milk have many similarities. Studies in patients allergic to bovine milk showed that the sera of those patients did not react with camel milk or human milk, but did react with milk from sheep, goats and buffalos (9,11,38,40-44).

The camel milk and the soy milk. Soybean was introduced in infant feeding by the Japanese and the Chinese many centuries ago. Soy milk became part of the human food chain in 1909 and, twenty years later, was proposed as an alternative source of nutrition for people who reacted adversely to bovine milk (45, 46). Currently, numbers indicating a prevalence of allergies to soy are not completely defined (47) and, although it is considered an important allergenic nutrient, data concerning its allergens are still controversial (48). In commercialized soybeans, proteins and amino acids are represented mainly by β-conglycin and glycin, the fat is a mixture of different types of vegetable oil, and the carbohydrates are a mixture of maltodextrins, sucrose and corn meal. All soy milk is free of lactose. Soy proteins are as sensitizing as those of bovine milk and can cause enteropathy with villous atrophy (49, 50). Denaturation by heat lowers, but does not eliminate its allergenicity. In their first days of life, 25% of children in the United States have used it, 13% in New Zealand, 7% in England, 5% in Italy and 2% in France. It is recommended for those intolerant to lactose and galactose, and in severe childhood gastroenteritis (38). Soy milk contains raffinose and stachyose, which are cleaved in the digestive tract under the action of bacterial galactosidases, producing galactose, which can contribute to the elevation of galactose-1-P in erythrocytes in galactosemic patients to their detriment. Soy milk, without additions, has no advantages over bovine milk. It is low in methionine, lysine and proline, and these must be added to it.

Cases of premature thelarche have been associated to soy milk use. This type of milk contains phytoestrogens and it is not unusual excess aluminum (50). From 10% to 50% of people allergic to bovine milk are also allergic to soy milk (32,34,39,42), and a large part of them with non-IgE mediated reactions. Five percent of individuals with atopic dermatitis are sensitive to soybean milk (39,51). The use of this milk in children under 6 months of age is not recommended without a specific reason, and its major indication is intolerance to lactose (34). Adverse reactions to soy milk are reduced if collagen and hydrolysates of soy are used (42). Comparative studies between soy milk and camel milk have not been performed but, in view of the negative aspects of soy milk, it is believed that camel milk, if available, will prove to be a more suitable choice.

The camel milk and the artificial milk formulas. Milk formulas are options for people allergic to bovine milk and soybean milk. However, only mixtures of amino acids are considered to be non-allergenic formulas and do not give cross-reactions to bovine milk. The other formulas, partially (pHF) and extensively hydrolized (eHF), always contain residues of bovine milk and can cause anaphylactic reactions in individuals sensitive to them. Ten percent of individuals sensitive to bovine milk proteins are sensitive to eHF (24,37,39,42). As for the formulas of amino acids (AAF), their cost is higher and their taste is not good. These, in some cases, will have to replace actual breast-feeding, as human breast milk allergens can be found in bovine milk and soy milk when the mother ingests them and is not able to conform to an absolutely restrictive diet (33,36). There are reasons not to consider these hydrolysates as ideal formulas. 1. All hydrolysates have molecules larger than 970 Da and the IgE can bind with molecules larger than 970 Da; 2. peptides with 13 to 17 amino acids with a molecular weight less than 1200 may associate with molecules of MHC class II to stimulate clones of T cells; those peptides are found in pHF and eHF; 3. reduction of molecular weight does not necessarily mean a reduction of allergenic potential and there is no way to know the exact moment at which to stop the hydrolysis; 4. the very process of hydrolysis can release biologically active peptides. In the European Union, these hydrolysates are controlled by demanding that immuno-reactive proteins amount to ‹1% of the total of the substances containing nitrogen (35,43). Given the limitations of pHF, eHF and AAF it is easy to imagine that camel milk would be a good substitute.

CONCLUSION

The camels are considered exotic animals in the most parts of the world. However, they have special characteristics, concerning their meat and milk, which need to be better studied. In this paper the author call to the attention to some of these aspects in the way to stimulate the research involving these animals.

RESUMEN

Los camellos son buenos productores de leche y los animales seleccionados para esta finalidad, la producen en cantidad y calidad excelentes. La leche tiene características que hace bien no sólo como complemento alimenticio en la dieta de los seres humanos, sino también en ciertas condiciones, tales como alergias (no contiene beta-lactoglobulina, la proteína más alergénica de la leche de vaca), intolerancia a la lactosa, infecciones en general, diabetes y incluso podría considerarse útil en la alimentación de personas con autismo. Su uso está restringido a algunas poblaciones donde este animal es nativo. Por su composición química no se coagula en un medio ácido. Contiene gran cantidad de insulina y sus proteínas especiales sugieren el uso en la ingenieria molecular. En conclusión, la crianza de camellos debería estimularse, dado que estos animales están en peligro de extinción.

Palabras clave: leche de camello, diabetes, alergia alimentar, inmunoglobulinas.

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