Chapter 10

Nutritional and Health Profile of Goat Products: Focus on Health Benefits of Goat Milk

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Abstract

Goat (*Capra hircus*) is one of the main sources of milk and meat products for human consumption. Goat milk differs from cow and human milk in both composition and nutritional properties. Goat milk and other goat-derived products contain several bioactive compounds that might be useful in patients suffering from a variety of chronic diseases. Several peptides, fats, and oligosaccharides present in goat's milk can be potentially useful in cardiovascular disease, metabolic disorders, neurological degeneration, or in promoting intestinal health. They have also shown chemopreventive properties in cancer. In addition, the oligosaccharides present in goat's milk have immunomodulatory properties, prevent adhesion of pathogenic bacteria, and have prebiotic, probifidogenic effects. Due to its potential health benefits, goat milk is particularly recommended for infants, older adults, and convalescing people. This chapter gives an overview of the biological activities of goat products and the effects of peptides, fats, and oligosaccharides present in goat milk on pathogenic bacteria, as well as their ability to regulate immunological, gastrointestinal, hormonal, and neurological responses in humans.

Keywords: goat milk composition, goat's products, nutritional value, bioactive compounds, health effects

1. Introduction: the importance of goat milk, dairy products, and meat as a potential functional food

Interest from the consumers as well as growing concerns for physical well-being and health have increased the demand for information about the consumption of healthier foods.

The intake of some active compounds present in food, the so-called nutraceuticals and functional foods, can be regarded as having beneficial effects (physical and mental) on certain functions in the human body, that go beyond their nutritional effects.

As technology and science advances, the fields of health and nutrition have focused on several emerging fields, namely nutrigenomics, or “personalized nutrition.” The study of the human genome in order to comprehend cellular response to nutrients and bioactive compounds is a promising field of work, which should lead specific dietary recommendations to prevent or aid in the treatment of certain diseases. In fact, stroke, cancer, and atherosclerosis and the general risk of diseases may be somehow minimized by introducing proper preventive nutrition and functional foods/foods as part of a healthier lifestyle that includes a balanced diet and physical activity [1]. Ingesting a wide variety of foods, namely fruits, vegetables, whole grains, milk, meat, and eggs is one way to ensure the intake of certain bioactive compounds that are present in its constitution such as carotenoids, dietary fiber, fatty acids, flavonoids, isothiocyanates, minerals, phenolic acids, plant stanols/sterols, polyols, prebiotics and probiotics, phytoestrogens, soy protein, sulphides/thiols, and vitamins [2].

Functional foods are growing in reputation across the globe and are becoming a part of daily diet of consumers who are concerned with their health. The global market potential for functional foods and beverages has been estimated to be worth $192 billion by 2020 [3]. However, the effectiveness of nutraceutical products in preventing diseases depends on preserving the stability, bioactivity, and bioavailability of the active ingredients [4]. Functional foods are found virtually in all food categories; however, some products are not widely available in the market [5].

Sheep and goat products (mainly meat and dairy) have interesting characteristics in their levels of flavor, taste, aromas, and leanness as well as the specific composition of fats, proteins, amino, and fatty acids and have been traditionally consumed in certain regions of the globe [6]. Additionally, the nutritional properties of goat milk and its lower allergenicity when compared to cow milk [7, 8] has sparked an interest in goat milk as a functional food, and it is now one of the current trends in healthy eating in developed countries [9]. Moreover, the use of milk with particular nutritional properties, alone or in combination with bacterial strains with probiotic properties and capable of producing physiologically active metabolites, might become one of the options for manufacturing new dairy functional beverages [10].

2. Materials and methods

The present chapter intends to give a comprehensive approach of the unique characteristics of goat-derived products, which have attracted the interest of researchers worldwide. This chapter aims to explore the nutritional value and bioactivity of the constituents of these products, with an emphasis in the reduction of the risk of chronic disorders by anti-inflammatory and anti-oxidative effects. The ability of goat’s milk and its derivatives to selectively encourage bacterial growth in intestinal microbiota and the beneficial effects in the metabolic, endocrine, and immune systems will also be a subject of this chapter.

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3. Composition of goat milk

Milk and derived dairy products are considered an important constituent of a balanced diet. Milk, as the first food for mammals, supplies all the energy and nutrients needed for the proper growth and development of the neonate. For all mammalians, the consumption of milk ends at the weaning period except in humans, which continue consuming milk throughout their life.

The physical characteristics and composition of milk vary between species. Chemically, milk is a complex oil-in-water emulsion containing proteins, fats, carbohydrates (mainly lactose), and lower amounts of minerals, enzymes, cells, hormones, immunoglobulins, and vitamins.

The information currently available on the composition of goat milk has been published in the form of reviews [11–13]. Authors are unanimous in recognizing that fresh milk composition has a dynamic nature that varies with several factors such as (a) genetics (e.g., species, breed, and individual); (b) stage of lactation; (c) health status of the individual animal; and (d) environmental factors (e.g., feed, climate, season, or method of milking) [14–16].

Approximate compositions of the milks of different animals are compared in **Table 1**.

The basic nutrient composition of goat milk resembles that of cow milk (**Table 1**). Both milks contain substantially higher amounts of proteins and minerals, but lower lactose content than human milk [17]. Nonetheless, goat milk has high concentrations of fat globules, which are smaller than those present in cow milk; these globule diameters average are approximately 3.6 and 3.0 μm against 4.0 μm, respectively [18, 19]. The smaller size of fat globules provides a smoother texture in goat's derived products. Furthermore, goat milk contains lower amounts of α1-casein conferring it a higher water-holding capacity and a lower viscosity [20, 21]. Despite all these properties, the flavor of goat's milk is peculiar and more intense in comparison to cow's milk, which can restrict the acceptance of its derivatives by consumers [21]. However, goat milk is more easily digested than cow milk due to the absence of agglutinins in the former [11].

Goat and cow milk differ essentially in their casein micelles (structure, composition, and size), the proportion of individual protein fractions and higher content of nonprotein nitrogen and mineral compounds found in goat milk.

Composition	Goat	Cow	Human
Energy (kcal)	70	69	68
Water (%)	87.5	87.7	86.7
Total solids (g)	12.2	12.3	12.3
Protein (%)	3.2	3.3	1.3
Fat (%)	4.0–4.5	3.8	4.1
Lactose (%)	4.6	4.7	7.2
Ash (g)	0.8	0.7	0.2

Table 1. Basic composition of different milks (mean values per 100g) (adapted from Yadav et al. [24]).

3.1. Proteins

The variability in milk composition, among individual animals of the same breed, is attributed to an extensive and complex genetic polymorphism of the goat milk caseins. The protein portion has a fundamental role on the nutritional and technological value of milk. Milk proteins are made of heterogeneous groups in terms of composition and properties and are divided into casein—the main group of proteins—and whey protein fractions to a lesser extent.

The total protein content in goat milk varies from 2.6 to 4.1 g/l. Casein is composed of four fractions: αS1-casein, αS2-casein, β-casein, and κ-casein [22]. The proportions of the milk casein fractions differ between ruminant species and the micelle characteristics also differ in regard to size, hydration, and mineralization. As reported by Grosclaude and Martin [23], in studies conducted using French Alpine and Saanen goats, milk from animals with low alleles FF had total casein and total protein contents of 22 and 27 g/l, respectively. These values increase to 27 and 32 g/l in milk from animals possessing strong alleles AA. Generally, goat milk contains less αS1-casein than other ruminants' milk. However, as allele frequency for this specific casein varies between breeds, its concentration in goat milk depends indirectly on the breed [23].

Other characteristics of goat milk proteins are their structural conformations and the amounts and subtypes of micelles, which are smaller (180 nm) than those of cow milk (260 nm) and similar to those of sheep milk (193 nm) [11].

It has been reported that beta casein comprises the largest fraction of total goat milk casein. Although αS2-casein is relatively higher in goat milk, the αS1 fraction of cow milk alone is higher than both the αS1 and αS2-casein fractions present in goat milk. These differences might help explain the soft curd-forming properties of goat milk, as well as its better digestibility and the lower frequency of allergic reactions in children [24].

The nutritional value of proteins present in milk depends on its essential amino acid content. Only small differences exist in milk amino acid levels per 100 g of protein between different species, which are most likely due to differences in total protein content [15, 25]. A comparison of amino acid content between different species can be seen in **Table 2**.

When compared to cow milk, goat milk has higher levels of essential amino acids: threonine, leucine, lysine, cystine, tyrosine, phenylalanine, valine, and nonessential proline and glutamic acid (**Table 2**) [26].

The importance of amino acid composition and polypeptides will be examined later in this chapter.

3.2. Fat

Fat content is the more quantitatively and qualitatively variable component of milk, depending on season, lactation stage, breed, genotype, and feeding. This last factor has been extensively studied, and Sanz Sampelayo et al. [27] examined the influence of feeding, roughage, and lipid supplementation on the fat content of both ewe and goat milk, and the presence of fatty acids of nutritional interest, such as rumenic acid or omega-3, as well as other fatty acids with potentially detrimental effects, such as trans fats. Chilliard et al. [28, 29] showed that goat's response

	Goat milk	Cow milk
Essential amino acids		
Thr	138.67	115.81
Ileu	160.54	128.04
Leu	341.01	266.23
Lys	342.86	252.59
Met	77.95	71.15
Cys	30.62	23.20
Phe	175.45	133.51
Tyr	162.51	159.99
Val	210.23	147.34
Total	**1639.84**	**1298.36**
Nonessential amino acids		
Arg	135.65	114.44
Hist	122.73	93.06
Asp	117.95	96.0.859
Ala	250.15	214.22
Glu	694.58	554.30
Gly	55.83	49.24
Pro	310.61	253.38
Ser	152.65	147
Total	**1840.15**	**1522.58**

Table 2. Amino acid composition of goat milk and cow milk (mg/100g milk) (adapted from Ceballos et al. [26]).

to lipid supplementation increased the fat content of goat milk without decrease in its protein content. Bovine, sheep, goat, and human milk fat consist of 97–98% of triglycerides, but have only low levels of phospholipids (0.5–1.5%) and free fatty acids (0.7–1.5%) [11].

The main characteristic of goat milk fat is the high content in short- and medium-chain fatty acids (MCFA). Average goat milk fat profile of fatty acids presented levels of butyric (C4:0), caproic (C6:0), caprylic (C8:0), capric (C10:0), lauric (C12:0), myristic (C14:0), palmitic (C16:0), and linoleic acids (C18:2) higher than those exhibited by cow milk. In contrast, goat's milk fat presented lower concentrations of stearic (C18:0) and oleic acid (C18:1) when compared to cow's milk fat. Average fatty acid composition (g/100g milk) of goat and cow milks are presented in **Table 3** [12]. Considering that these fatty acids have a different metabolism from that of long-chain fatty acids they present different functional proprieties [30]. Recent works of Núñez-Sánchez et al. [31] demonstrated that goat's milk exceeds cow's milk in its content of monounsaturated and polyunsaturated fatty acids and medium chain triglycerides. We will return to this subject later in this chapter.

Lipid profile	Goat milk	Cow milk
C4:0	66.55	116.44
C6:0	171.68	77.86
C8:0	192.20	57.80
C10:0	579.10	114.91
C11:0	7.46	7.29
C12:0	232.61	130.87
C14:0	518.56	384.41
C14:1	7.19	16.87
C15:0	28.11	35.23
C15:1	3.01	2.74
C16:0	1340.97	1102.72
C16:1	51.58	52.32
C16:2 n-4	1.57	0.57
C17:0	18.44	6.27
C17:1	4.32	2.85
C18:0	493.56	378.25
C18:1 n-9, trans	19.22	55.75
C18:1n-9, cis	1245.92	742.71
C18:2 n-6	142.39	82.31
CLA n-7, cis-9, trans-11	18.70	13.79
CLA n-6, trans-10, cis-12	3.53	1.82
CLA n-7, cis-9, cis-11	1.05	–
CLA n-5, cis-11, trans-13	12.42	–
CLA total	35.75	15.62
C18:3 n-3	27.72	8.55
C20:0	2.49	3.76
C20:1 n-9	1.57	1.03
C20:2 n-6	5.49	1.48
C20:3 n-6	-	0.80
C21:0	1.44	0.23
C22:0	4.05	3.99
C23:0	0.26	0.91
C24:0	0.66	0.68
C24:1 n-9	0.92	–
C6-14	1695.70	790.02
SFA	3683.10	2436.41

Lipid profile	Goat milk	Cow milk
MUFA	1342.67	874.27
PUFA	213.25	109.32
PUFA n-6	146.97	86.41
PUFA n-3	26.81	8.55
PUFA n-6/n-3	5.49	10.49

SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids.

Table 3. Fatty acid composition (mg/100g milk) of goat and cow milk fat (adapted from Ceballos et al. [26]).

3.3. Carbohydrates

Lactose is the main carbohydrate in milk: about 44% in goat milk and 49% in sheep milk. Its concentration does not vary excessively [32, 33]. However, goat milk lactose content is often largely increased by dietary plant oil supplementation in contrast to cow milk [34].

3.4. Minerals

Raynal-Ljutovac et al. [13] presented an update of the composition of goat and sheep milk products. In this document, authors complicated data available concerning the main mineral composition of goat and sheep milks (**Table 4**). Goat milk is distinguished by its high chloride and potassium content. A more recent study by Trancoso et al. [35], focusing on goat milk from the main Portuguese indigenous breeds (Serrana, Serpentina, Charnequeira, and Algarvia), also obtained similar results regarding mineral composition in the milk produced by these animals. Raynal-Ljutovac et al. [13] indicated that caprine milk provided a great amount of magnesium, calcium, and phosphorus with a normal Ca/P ratio in milk as 1.20.

	Goat (per L)	Sheep (per kg)
Calcium (mg)	1260	1950–2000
Phosphorus (mg)	970	1240–1580
Potassium (mg)	1900	1360–1400
Sodium (mg)	380	440–580
Chloride (mg)	1600	1100–1120
Magnesium (mg)	130	180–210
Ca/P (mg)	1.3	1.4
Zinc (μg)	3400	5200–7470
Iron(μg)	550	720–1222
Copper (μg)	300	400–680
Iodine (μg)	80	53–90
Selenium (μg)	20	31

Table 4. Mineral composition of goat and sheep milk (adapted from Balthazar et al. [19]).

As shown in **Table 4**, goat milk is characterized by its lower concentration of iron, zinc, and copper. López-Aliaga et al. [36] reviewed the mineral bioavailability, apparent digestibility coefficients, and the balance of calcium, phosphorus, magnesium, iron, copper, and zinc after the consumption of a goat milk diet compared with bovine milk diet in resected rats. In their work [36], they concluded that based on the particular biological, nutritional, and metabolic characteristics, goat milk can be an excellent natural food in cases of malabsorption syndrome and present a dietary alternative to bovine milk. Although goat milk has a low iron concentration, it has a higher bioavailability than in cow milk due to the presence of higher amounts of nucleotides that in turn increase absorption in the intestine [13].

As far as contaminant metals are concerned, concentrations differ between different studies and sampling (feeding, geographic areas, pollution…), and it is therefore difficult to compare species and breeds. According to Trancoso et al. [35], in goat milk from the main Portuguese indigenous breeds, the values for the potentially toxic elements such as Cd, Pb, Co, and Ni are well below the value stipulated by the Commission of the European Communities Directive EC n° 333 [37] for Pb in milk (0.02 mg/kg). Therefore, consumption of caprine milk does not constitute a risk for human exposure to toxic elements at present in Portugal.

3.5. Vitamins

Goat milk is an adequate source of vitamin A, thiamine, riboflavin, and niacin [11, 36, 38]. However, it presents low levels of folates, as well as vitamin B12, vitamin E, vitamin C, and vitamin D [11, 13] (**Table 5**).

	Goat milk	Cow milk
Fat soluble vitamins		
A		
Retinol (mg)	0.04	0.04
Beta-carotene (mg)	0.00	0.02
D (μg)	0.06	0.08
Tocopherol (mg)	0.04	0.11
Water soluble vitamins		
B1 Thiamin (mg)	0.05	0.04
B2 Riboflavin (mg)	0.14	0.17
B3 Niacin (PP) (mg)	0.20	0.09
B5 Pantothenic acid (mg)	0.31	0.34
B6 Piridoxin (mg)	0.05	0.04
B8 Biotin (μg)	2.00	2.00
B9 Folic acid (μg)	1.00	5.30
B12 Cobalamin (μg)	0.06	0.35
C Ascorbic acid (mg)	1.30	1.00

Table 5. Vitamin content of goat and cow raw whole milk (per 100g) (adapted from Raynal-Ljutovac et al. [13]).

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Compared to cow milk, goat milk has lower amounts of vitamin E, folic acid, and vitamin B12, which can result in "goat milk anemia" if additional sources for these vitamins are not present in the diets [13].

In conclusion, nutritionally, goat milk is comparable to cow milk as it contains similar levels of calcium, potassium, phosphorus, and many other nutrients that confer health benefits (see **Tables 1,2,3** and **5**). However, goat milk contains higher levels of 6 out of the 10 essential amino acids than cow milk [39]. It is also richer in monounsaturated and polyunsaturated fatty acids and medium-chain triglycerides [31], while containing less lactose than cow's milk.

The most appealing property of goat milk is its superior digestibility, which can make it particularly helpful in attenuating irritable bowel type symptoms [36].

4. Goat-derived products and nutritional value

The use of goat products was first closely related to a number of medical problems namely food allergies involving cow milk proteins. Cow milk allergy is relatively common during the first 3 years of life. Several studies report that the use of goat milk resolves 30 and 40% of the cases [12].

There are a number of unique physiological and anatomical differences between goats and cows which translate into differences in composition of goat milk and its products [40].

Goat milk products are considered dairy products with greatest marketing potential. Therefore, several characteristics of goat milk are currently the focus of increased research interest [24].

Two glasses (0.5 l) of goat milk or the equivalent amount of cheese or yoghurt can provide up to 94% of the recommended adult daily dietary allowance (RDA) of essential amino acids, 83% of calcium, and 78% of riboflavin needs, while also being a dietary source of other minerals and vitamins, albeit to a lesser extent [40].

4.1. Goat cheese

Literature is exiguous concerning the impact of technology (cheese-making) on every nutrient of cheese, other than fat and proteins. Most studies focus on the gross composition (fat, protein, and lactose contents) of Spanish, Italian, and Greek hard or semi-hard cheeses obtained from small ruminants. Gross composition is mostly dependent on the type of cheese and can be classified according to its dry weight. Although both caprine and ovine milk have been widely used in cheese-making, production of fermented caprine milk using probiotics has not yet been developed, despite the existence of studies showing the requirements for its production. Fermentation increases the nutritional value of caprine milk and improves its flavor, making it more tolerable to the average consumer than raw goat milk.

A review by Haenlein [41] focused on several aspects of yoghurt and cheese goat composition. The benefits for human digestion included proteins with different polymorphisms, forming a softer curd on digestion and cheese-making, and the high content in short chain, medium chain, and mono and polyunsaturated fatty acids.

Regarding cheese produced from goat milk, three categories can be distinguished: traditional cheeses (produced on farms) and prepared mainly for home consumption; cheese produced on farm scale under improved conditions (frequent, for instance, in France, which produces more than 90 varieties of goat cheese) and cheese produced with a mix of sheep and goat milks (produced in all Mediterranean countries, except France) [42].

The production of cheese from goat milk dates back to many centuries. In recent years, the production of cheese from goat milk has acquired commercial advantage in several Western European countries because legislation is not as restrictive for this kind of milk or its products as it is for cow milk products [42, 43]. In France, for example, the production of goat cheese increased approximately 13% (in the same year) while cow cheese increased only 1%. The consumption of goat cheese has been expanding at approximately 20% per year [44].

The composition and characteristics of cheese is highly affected by the characteristics of the milk used in its production. The substitution of sheep milk by goat milk in dairy products is a frequent problem because sheep milk has a higher price. The existence of mixed flocks of goats and sheep might result in accidental or fraudulent mix-ups, affecting profitability as well as the properties and quality of the resultant cheese [45].

Calf rennet was shown to hydrolyze goat casein forming characteristic breakdown of products from individual caseins: β-I to β-V derived from β-casein as well as other primary hydrolyzed products derived αs1-casein; para-K-casein formed from K-casein and other degradation products obtained from αs2-casein. Under the same conditions, both β-casein and αs1-casein present in goat milk seemed to be more sensitive to hydrolysis than their bovine counterparts [46].

Goats milk Gouda cheese is usually made in artisanal units by traditional technology passed on from generation to generation [47] and has a special taste and flavor [42]. However, cheese made under these conditions may not have the minimum hygiene and sanitary standards necessary to obtain a product with minimum quality [48]. In the Eastern Mediterranean, an area favorable to small ruminants, most of the cheese is also produced in small artisanal units, with high temperatures and a lack of refrigeration units. The majority of productions also do not include pasteurization leading to brucellosis, listeriosis, and food poisoning due to enterotoxin production by *Staphylococci*. Therefore, in these areas "white brined cheeses" (WBC), which are ripened and stored under brine until consumption, such as Feta, Domiati, and Beyaz-Peynir, are particularly common and constitute a large share of the cheese market (>50%). Whey cheeses (such as the Myzithra, Manouri, Lor, Anari, Urda, and Skuta) are also traditional products from the Eastern Mediterranean, as the whey obtained from producing sheep's and goat's milk cheese has a very high protein content. The addition of goat or sheep milk or cream to the whey improves the yield of this type of cheese [49].

Karagozlu et al. [50] studied the Cimi Tulum cheeses (made from goats' milk) during 90 days of ripening period. These cheeses contain 57.73% total solids; 30.01% fat; 3.51% salt; 22.27% protein; 2.92% water soluble nitrogen, and 1.75% lactic acid. During the ripening process, the amounts of total solids, fat, salt, protein, water soluble nitrogen, and free fatty acids have all been shown to increase, whereas the salt and fat ratios of the total solid content have decreased. The percentages of fatty acid composition of these cheeses were 31.73% of oleic acid, 24.19% of palmitic acid, and 9.32% of myristic acid.

El-Sheikh et al. [51] studied the effect of ripening conditions in blue cheese produced from cow's and goat's milk and concluded that blue cheese (Roquefort-style) had similar properties to the ones made from cow's milk.

Queiroga et al. [52] evaluated the nutritional, textural, and sensory characteristics of *coalho* cheese made from goat's (CGM) or cow's milk (CCM) and their mixture (CCGM) during cold storage for 28 days. The choice of milk only seemed to have influenced the moisture, fat, and salt contents of the cheeses. CGM and CCGM showed higher amounts of short and medium-chain fatty acids (such as C6, C8, C10, and C12), and long-chain polyunsaturated fatty acids C18:2n6c. They also showed lower C16 and C16:1 contents. Their properties seem to have been maintained throughout storage time.

Main goat cheese types can be classified as follows [53]:

1. Fresh and soft cheese: Gibna Beida (Sudan), Feta (Greece), and Saint Mareá and Camembert (France). Fresh type is prepared by acid curdling with a small dose of rennet. It is consumed the day after being prepared, and it contains 60–80% moisture. It has a texture similar to Queso-Blanco (Latin America). Soft cheese is produced as fresh cheese, but it is ripened for 10–30 days, and it has 55–60% moisture. For instance, Saint Moreé is surface-ripened cheese prepared by a 24 h coagulation step at 17–20°C after addition of mesophilic lactic culture (20 ml/L) and a rennet solution (6 ml/100L) and has a specific goat cheese aroma and has seven acid compounds present: hexonoic, octanoic, nonenoic, decanoic, 3-methylbutanoic, 4-methyl octanoic, and 4-ethyl octanoic acids; some were already of value in 2 days-old cheese, whereas some others only reached this value after 31.
2. Blue-veined cheese: Savoy (France), Roquefort (France), and Cabrale (Spain). Curd of this cheese is prepared with lactic acid culture and rennet. It has a greenish or bluish marbled appearance after 1–2 hours of curdling and inoculated with penicillium. After salting and piercing, the cheese is ripened for 1–4 months at 9–10°C and 90–95% RH.
3. Semi-hard cheese: Edam (the Netherlands). It contains 40–50% moisture and is prepared by using mesophilic started and rennet. After curdling, cutting the curd, scalting, molding, pressing, and salting, the curd is waxed and ripened for 1–5 months at 8–10°C and 90–95% RH.
4. Hard cheese: Chevrotin (France), Kefalotili (Greece), Ras (Egypt), and Manchego (Spain). It contains 30–40% moisture and is produced in warm countries or in mountainous area. Regarding Chevrotin cheese, it is prepared by culture and rennet curdling. It is preserved for 1–3 months submerged in olive oil.

Hassan et al. [44] fortified goat cheese with caramel, cocoa, and cocoa with walnuts, and these cheeses were prepared in order to be directed to children feeding, given its protein content. The ω-6/ω-3 ratios were at levels 6.0, 7.7, and 4.7, respectively.

The study made during ripening by Niro et al. [54] compared the physicochemical, microbiological, and sensorial characteristics of Caciocavallo cheeses, made from cow milk and a mixture of cow with ewe or goat milk. Different percentages of goat milk added milk to cow milk influenced compositional and nutritional characteristics of these cheeses.

4.2. Goat yoghurt

The preparation of goat yoghurt is made using similar processes to those used in the production of cow milk yoghurt, but it has different organoleptic properties as well as nutritional composition. It presents less viscosity, has softer consistency flavor and higher acidity, during storage [55]. Goat yoghurt has free caproic, caprylic, lauric, and myristic acids. While palmitic and stearic acids were approximately equal, oleic, linolenic, and palmitic acids were lower when compared with cow yoghurt [44]. Regarding amino acid content, goat yoghurt showed about 4 mg/100g of Gly and Pro; 2 mg/100g of Lys, Thr, Ser, Glu, and Ala; and 1–2 mg/100g His, Asp and Leu. Regarding Arg, Val, Meth, and Phe, their concentrations were inferior to 1mg/100g [56].

There are significant changes in gross nutrients between fresh goat milk and yoghurt. Eissa et al. [57] found a decrease in lactose content and pH of the yoghurt after fermentation. Cold storage also resulted in significant changes in gross composition of goat yoghurt. The number of total bacteria and yeast increased significantly within 10 days of storage, decreasing thereafter. Goat milk yoghurt showed in this study lower sensory scores than cow milk yoghurt.

Bano et al. [58] concluded that mixing 75% of goat milk and 25% sheep milk in manufacture of yoghurt improved color, flavor, and texture scores of the resultant yoghurt.

Uysal-Pala et al. [59] showed that drinkable yogurts made from different goat breeds' milk and made with normal and probiotic cultures were evaluated for their sensory characteristics. Yoghurt manufacture with cows and with goats' milk (100, 75, 50 and 25%) substitution blend with cow's milk revealed that goats milk yoghurt (100%) had the highest protein content (4.2%), fat (4.3%) and caproic (c6), caprylic (c8) capric (c10), and total solids (16.2%). Generally, goat's milk yoghurt samples (100, 75, and 50%) were mostly significantly preferred to 25% goat's milk yoghurt sample at ($P > 0.05$).

Al-Abdulkarim et al. [60] studied a sample of dried fermented goat's milk product (Oggtt) obtained from the local market of Riyadh (Saudi Arabia), which was stored for 6 months at 4°C and subjected to chemical composition analysis before and after storage. After storage, total ash decreased nonsignificantly ($P < 0.05$) from 8 to 7.6%, total carbohydrates decreased nonsignificantly ($P < 0.05$) from 35.5 to 33.8%, protein increased nonsignificantly ($P < 0.05$) from 16 to 16.1 g/1, fat content was found to have the same values in all samples before and after storage at 5%, lactose increased nonsignificantly from 28.4 to 29%, acidity decreased ($P < 0.05$) significantly from 0.45 to 0.39%, and pH decreased nonsignificantly from 4.3 to 4%. On the other hand, mineral composition showed ($P < 0.05$) nonsignificant results before and after storage. Ca concentration decreased from 118 to 114 mg/kg and K concentration increased from 185.8 to 188.8 mg/kg. This is a stable product and presents good nutritional value in comparison to daily requirements for healthy human life.

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4.3. Goat butter

The production of butter from goat milk is not very common, and sometimes it is artificially colored in order to look similar to cow butter [61]. There is a difficulty in cream separation, a softer texture, and it presents high tendency to hydrolytic rancidity. Idoui et al. [62] studied a traditional butter from Eastern Algeria. The results showed the presence of lactic acid bacteria (3.51 × 105 + 2.44 cfu/g), psychotrophic bacteria (1.11 × 105 + 1.31 cfu/g), moulds and yeasts (39.08 × 102 cfu/g), lipolytic bacteria (4.41 × 103+5.91 cfu/g) and the absence of total coliforms except in one sample. An analysis of fatty acids was made by GC-MS that showed a prevalence of saturated fatty acids, namely palmitic acid with a low rate of unsaturated fatty (oleic acid).

4.4. Goat meat

Goats are animals with fairly low-fat content. Several authors have indicated that the fat content of goats is 47–54% lower than that of cattle and sheep. The introduction of goat meat in diet may become an important measure for the prevention of cardiovascular diseases

Banskalieva et al. [63] also pointed out that further experimentation is needed to characterize interactions between factors such as race, age, and nutritional status in the lipid profile of goat for a better understanding of their meat quality. Little is known about the lipid profile of goat meat, but some studies indicate that oleic, palmitic, stearic, and linoleic are the predominant acids in muscles. Rhee [64] reported that goats have higher concentrations of desirable fatty acids than cattle and sheep, but at levels similar to lean meat of pigs.

Several factors such as race, gender, stress, environment, management, diet, weight, and health condition affect the chemical composition of goat meat. Studies have shown that the average composition of meat obtained from Serbian white goats to be estimated around 75.42% water, 3.55% fat, 19.95% protein, and 1.06% minerals, whereas meat obtained from Balkan goats had a similar composition, with a water content of 74.51%, 3.92% fat, 20.55% protein, and 1.04% minerals. The energetic value was similar in both breeds and is around 580 kJ per 100 g of meat [65].

The quality of goat meat is influenced by its water content. The muscles contain approximately 75% water, which is distributed within the myofibrils, between themselves, between the cell membrane (sarcolemma), and between the muscle bundles. The cooling or freezing mode after slaughter, especially during the rigor, is of great importance for the percentage of water that will remain in the meat.

Adipose tissue of slaughtered animals contains 50–95% fat, 3–35% water, 2–15% protein, and 0.1–0.6% mineral matter. The composition of adipose tissue is highly variable and depends of nutritional status, breeding, age, and type of animal. In each cell, there are 40–50 types of fats, which represent about 5% of the organic matter present in cells. The amount of fat per cell varies from tissue to tissue, for instance, cells of the nervous system are extremely rich in fats. Diet influences the deposition of fat in the muscular tissue, as well as the saturated (SFA) and polyunsaturated fatty acid (PUFA) concentrations in cattle.

In ruminants, lipids from meals suffer hydrolyzation and biohydrogenation processes in the rumen, resulting in absorption of saturated fatty acids in the digestive tract. This fact could help explain the higher percentage of saturated fats in meat products obtained from ruminants. Several studies have been conducted in an attempt to determine the fatty acid profile of goat meat [66]. However, the role of certain processes such as biohydrogenation, transition of unsaturated into saturated fatty acids, elongation of fatty acid chains, metabolism, and deposition rate are yet to be fully understood.

The composition of the fat in goat meat and other ruminants differs from that of monogastric animals, having larger amounts of SFA and lower quantities of PUFA, with C18:1 and C18:2 *trans* and *cis* isomers of FA are also present in goat meat. In animals, the main PUFA (C18:2n-6 and C18:3n-3) are obtained from the diet. However, in ruminants, these products suffer biohydrogenation processes in the digestive tract, originating saturated fats as well as other intermediate products, which include *cis* and *trans* C18:1 isomers and C18:2 *trans* isomers, conjugated or unconjugated [67]. While grain feeds are a food source of C18:2n-6, green grass on pastures are richer in C18:3n-3 [68], which is more desirable as it could lead to higher contents of omega-3 fatty acids in meat products.

Meat products derived from ruminants are a dietary source of CLA. C18:2 *cis*-9, *trans*-11 is the most frequent isomer of CLA, and is also present in higher amounts in the meat of ruminants fed on pasture than in the meat of ruminants fed with grain. Despite the fact that a fraction of this fatty acid occurs in the rumen, about 70–80% of the acid present in the tissues results from endogenous transformation C18:1 *trans*-11 by the enzyme Δ9 desaturase [69]. Therefore, the difference in CLA concentration in the tissues results mainly from the amount of C18:1 *trans*-11 absorbed in the rumen.

5. Nutrient functionality

Nowadays, nutrients have emerged as an important research topic in food and nutrition sciences as they appear to be able to modulate the inflammatory status of humans [70]. Dairy products represent a particularly interesting food type to study in the context of inflammation, mostly because of milk's ability to support the development of the immune system of the newborn, to inhibit bacterial growth, and to provide anti-oxidative and anti-inflammatory protection [71]. Some of these properties might still be maintained in the context of the consumption of dairy products by human adults. Additionally, the ability of milk and milk-products to deliver supplements to the human organism able to modulate the gut microbiota, a key regulator of immunity, is another factor which might help influence immune and inflammatory processes [72, 73].

Recently, reviews by Hsieh et al. [74, 75] have described the effects of different bioactive components of milk and dairy products in preventing low-grade systemic inflammation and in acting as coadjutants in conventional therapies.

In the following sections, after a brief overview structure and function of the immune system, we will focus on the effects of several bioactive compounds found mainly in goat milk and their effects in low-grade systemic inflammatory diseases and immunity.

5.1. Overview of immune system: low-grade systemic inflammation and gut-systemic inflammatory associations

Inflammation is one of the main biological processes involved in response to potentially detrimental stimuli to the body and can be classified as acute or chronic with different processes involved in each of these types. Acute inflammation is an immediate and short-lasting response to irritation, injury, or infection which leads to the activation of mechanisms such as increased blood flow, greater blood vessel permeability, and movement of white blood cells to the affected site. These mechanisms are responsible for the classic signs of inflammation: redness, edema, heat, pain, and decreased function [76]. Chronic inflammation is a long-lasting response to factors such as poor nutrition, stress, environmental toxins, and processes related to aging [76]. These prolong the inflammatory response, leading to destructive reactions which, coupled with inappropriate repair processes, eventually lead to the clinical symptoms of disease [77].

The human immune system possesses innate or nonspecific and adaptive mechanisms that work synergistically to protect the body against injury and infection. Innate immunity constitutes the first line of defence, providing immediate response albeit unspecific response to localized injury or invasion by an infectious agent. Innate immunity is triggered when the inflammasome (a large sensor protein produced by bone marrow) detects a toxic substance and stimulates the production of macrophages to destroy harmful stimuli. Macrophages are able to recognize different types of pathogens and are able to react either by producing several mediators that activate other elements further downstream inflammatory cascade (these include, for instance, toll-like receptors, cytokines, or transcription factors); or by eliminating them directly through a process known as phagocytosis. Innate immunity, however, has a limited duration and is not able to stop all pathogenic stimuli. When overtaxed, the body's adaptive immunity mechanisms are activated [78].

Adaptive immunity or acquired immunity is based in highly specialized responses directed at specific antigens [77]. It can be divided into two types: humoral immunity, in which the B lymphocytes, produced in the bone marrow, generate antibodies targeting specific antigens present in the pathogen in question; and cell-mediated immunity, in which T lymphocytes, matured in the spleen and lymph nodes, recognize antigens present on infected cells and lead to their destruction. Memory cells are also a part of the adaptive immunity response and recognize and react to repeated exposures to specific antigens [77].

When, in the human body, the mechanisms of innate and adaptive immunity are ineffective in eliminating a harmful stimulus, illness occurs. Normal function of the cells is disrupted by processes that include leukocyte proliferation, oxidative reactions, and fibrosis caused by repeated or uncontrolled inflammatory responses. A chronic low-grade inflammatory state as a pathological feature of a wide range of chronic conditions, such as metabolic syndrome (MetS), nonalcoholic fatty liver disease (NAFLD), type 2 diabetes mellitus (T2DM), atherosclerosis, cardiovascular diseases (CVD), cancer, neurological diseases, among others, has been recognized [79–81]. The numbers of illnesses, which are related to molecular mediators of inflammation, are large and expanding.

Inflammation constitutes one of the basic mechanisms of the innate immune response. In general, inflammation is a local response to cellular injury that aims not only to eliminate the toxic agents but also to promote repair of damaged tissue [78].

The microbiota present in our bodies also plays an important yet often under looked part in maintaining systemic metabolism and cardiometabolic health [82, 83]. Increasing evidence indicates that a relationship between microbiota, the immune system, and inflammatory processes exists. When chronic disease (such as obesity or processes related to aging) occurs, microbiota loses "richness" altering gene expression diversity and increasing low-grade chronic inflammation [83]. According to Kurashima et al. [84], gastrointestinal tract-microbiota interactions influence immune function by maintaining the function of the mucosal immune system, protecting against invasion by pathogens, and maintaining the integrity of the barriers present in gastrointestinal tract. The permeability of the walls of the gastrointestinal tract to the lipopolysaccharides (LPS), found on the outer membrane of Gram-negative bacteria, can also induce low-grade systemic inflammation, as LPS is a powerful proinflammatory. In the elderly, a higher count of bacteria that produce LPS in the colon, coupled with a lower amounts of bifidobacteria [85], increases gut permeability, leading to higher amounts of LPS entering the bloodstream, which in turn aggravates inflammation [86]. One of the mechanisms through which LPS may be an important trigger in the development of inflammation and metabolic diseases is an interaction with the Toll-like receptor 4 present on the surface of mononuclear cells [87]. Moreover, in addition to its role in low-grade systemic inflammation, emerging evidence suggests that the gut microbiota can also have an influence in the risk of high-grade autoimmune inflammatory conditions such as type 1 diabetes mellitus, celiac disease, inflammatory bowel disease, and rheumatoid arthritis [88–90].

5.2. Food allergy

Specific immune response also plays a lead role in food allergy. The term "allergy" can be used to define an abnormal adaptive immune response directed against noninfectious environmental substances (allergens), including noninfectious components of certain infectious organisms. After antigen contact, the body responds with an excessive reaction (IgE antibodies, histamine release). The symptoms are dramatic and acute. In allergic disorders, such as some food allergies, these responses are characterized by the involvement of allergen-specific IgE and T helper 2 (T_H2) cells that recognize allergen-derived antigens [91].

Recent studies suggest that the consumption of dairy products is inversely associated with low-grade systemic inflammation [92]. The cross-sectional nature of these studies precludes definite conclusions on the cause-and-effect relation between dairy food consumption and inflammatory outcomes. Considering distinctive proprieties of goat milk, we will summarize some of the bioactive compounds present in goat's milk and dairy products and their effects on health.

6. Anti-inflammatory effects of goat milk and its derivatives

6.1. Bioactive peptides

Bioactive peptides (BP) have been defined as specific protein fragments that have a positive impact on body functions or conditions and may ultimately influence health [93]. According to Atanasova and Ivanova [94], goat milk is as "close to perfect food as possible in nature."

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As we have previously described, the protein present in goat milk is comprised of about 80% caseins and 20% whey proteins. Some of the peptides and proteins in milk present direct biological activity, while other proteins have a latent biological activity, which is activated only upon proteolytic action. For example, the active forms of caprine calmodulin (calcium-binding protein) are the soluble C-terminals obtained as a by-product from the action of chimosin on k-casein during the milk clotting process of cheese-making. These peptides are also important sources of bioactive ACE-inhibitory and anti-hypertensive peptides [95, 96]. Moreover, goat milk possesses other minor proteins including immunoglobulins, lactoferrin, transferring, ferritin, protease peptone, prolactin, and folate-binding protein with biological activity.

Furthermore, a variety of naturally formed bioactive peptides have been found in fermented dairy products, such as yoghurt and cheese. The main bioactive peptides of goat milk and its derivatives will be described below.

6.1.1. Biopeptides that lower blood pressure

Several epidemiological studies have linked dietary intake of milk and dairy foods with a decreased risk of hypertension [97]. Their high mineral content (in calcium, potassium, and magnesium) and certain proteins present in these products (as well as their hydrolysates) have been thought to be involved in the anti-hypertensive effect of these products [98]. Angiotensin-converting enzyme (ACE) is a multifunctional enzyme that acts as one of the main regulators of blood pressure. ACE inhibition, restrain the formation of angiotensin II or block its receptors leading to arteriolar vasodilation and a reduction of total peripheral resistance. Therefore, ACE inhibition is currently considered as one of the best strategies for hypertension treatment [99].

Inflammation and oxidative stress play an important role in the pathophysiology of hypertension; however, the description of the mechanisms involving all interplays between them is behind the scope of this chapter, nevertheless, we might consider the link between angiotensin II and immune system. Nosalski et al. [100], in a recent revision, state that the bulk of mechanistic model studies clearly indicate that a complex network of interactions between T cells, dendritic cells, monocytes, and B cells may be involved in hypertension. The lack of this immune response has a blunt response to angiotensin II-simulated hypertension and may promote hypertension by potentiating vascular dysfunction. Consequently, hypertension is associated with significant activation of immune and inflammatory systems and shares several functional differences with other immune-mediated diseases [101, 102].

Several studies have been done to investigate the bioactivity of goat milk protein hydrolysates and the release of ACE-inhibitory and anti-oxidant peptides with individual proteases such as thermolysin, trypsin, subtilisin, papain, and pepsin or their combinations [95, 103]. Espejo-Carpio et al. [95] and De Gobba et al. [104] identified many casein-derived peptides from hydrolyzed proteins of goats' milk, which were enzymatically liberated by a combination of subtilisin and trypsin. Among them, many peptides contained tyrosine in their sequence and had anti-oxidant and ACE-inhibitory activities. More recently, Ibrahim et al. [105] have shown that ACE-inhibitory peptides can be released from goat milk caseins and whey proteins after gastric pepsin digestion. In their study, they found one peptide from whey β-lactoglobulin, PEQSLACQCL and two peptides from caseins, ARHPHPHLSFM (fragment 96–106 κ-casein), and QSLVYPFTGPI (fragment 56–66 β-casein). These peptides displayed ACE-inhibitory activity that compares favorably with the activity of anti-hypertensive drugs with ACE-inhibitory action. These peptides as well as other hydrophobic peptides additionally exert anti-oxidant and anti-inflammatory activities. Therefore, goat milk and goat whey bioactive peptides present anti-hypertensive activity through inhibition of ACE, but considering all the mechanisms involved in the pathophysiology of hypertension, the existence of multifunctional peptides must be considered [106].

6.1.2. Antimicrobial peptides

The antimicrobial activity of milk is mostly attributed to the presence of immunoglobulins and other proteins, such as lactoferrin, lactoperoxidase, and lysozyme. It is generally accepted that the total antibacterial effect in milk is greater than the sum of the individual contributions of immunoglobulin and nonimmunoglobulin defensive proteins. This might be because naturally occurring proteins and peptides act synergistically with peptides that result from metabolization of inactive protein precursors [107]. The proteins present in milk proteins have been proven to act as antimicrobial peptide precursors, thus improving the ability of natural defences to eliminate invading pathogens. Consequently, food proteins can be considered components of nutritional immunity [94]. A paper by Budiarti et al. [108] demonstrates the presence of Alpha-S2 casein in Ethawah goat milk and yoghurt. This protein contains eight bioactive peptides, with different effects, such as anti-osteoporotic or anti-inflammatory effects, and it was not found in cow fresh milk [109, 110]. More recently, Triprisila et al. [111] reported the effect of antimicrobial activity from CSN1S2 protein as a member of casein protein from Ethawah breed goat milk and yoghurt against pathogen Gram-positive bacteria (*Listeria monocytogenes*, *Staphylococcus aureus,* and *Bacillus cereus*) and Gram-negative bacteria (*Escherichia coli*, *Salmonella typhi,* and *Shigella flexneri*). The results of their work showed a greater inhibitory effect on Gram-positive bacteria than on Gram-negative bacteria. They also demonstrated that milk has a higher antimicrobial activity than yoghurt [111].

Goat lactoferrin has been studied after the beneficial effects demonstrated by both human and bovine lactoferrin. The levels of this protein in sheep and goat milk are slightly higher than in cow milk with values of approximately 0.107 ± 19 mg/mL [112]. The concentrations of lactoferrin in goat milk during various stages of lactation have been shown to vary in direct proportion with the number of somatic cells present in the milk samples. These parameters are influenced by a number of physiological processes [112]. Another study, which compared the glycosylation of goat milk lactoferrin with that of other glycoproteins present in human and bovine milk, demonstrated similarities in glycans present in both human and goat milk samples. However, some novel glycans were also identified goat milk, which did not exist in the human milk samples [113]. Considering its high digestibility, immunological properties, and high mineral concentration as well as the similarities between human and goat lactoferrin, goat milk can be considered an attractive candidate for use in infant formula supplementation. Lactoferrin plays an important role in both innate and adaptive immunity responses. Not only pathogens have high affinity toward the iron present in lactoferrin, it also induces changes in leukocytes, involved in innate immune system, by increased activity of NK cells and increasing the phagocytic activity of neutrophils and macrophages [114].

In the same way, caseins seem to be good antimicrobial peptides against Gram-negative bacteria [115]. Esmaeilpour et al. [116] investigated the antimicrobial action of goat milk casein hydrolysates produced by the proteolytic enzymes trypsin and ficin and by combination of both enzymes. The authors obtained fractions with significant antimicrobial activities against Gram-negative and Gram-positive bacteria.

6.1.3. Cytomodulatory and anticancer peptides

Goat milk lactoferrin demonstrates not only to possess antimicrobial action but also to induce apoptosis in a human cervical cancer cell line [117]. Considering the resemblance with other lactoferrins, goat lactoferrin might be able to present protective activity against other cancers. However, the research in this area is only in its infancy. The mechanisms by which this molecule might exert its activity were recently reviewed by Zhang et al. [118]. These properties of lactoferrin constitute an interesting alternative to chemoprevention, and the currently used anticancer drugs. In addition, its stability through the gastrointestinal tract is beneficial if oral administration is envisaged.

It seems that intact and hydrolyzed goat whey protein concentrates, blood serum albumin, and skim milk inhibited lymphocyte proliferation in dose-dependent reactions [119]. Su et al. [120, 121] reported that an anticancer bioactive peptide (ACBP) extracted from goat spleens significantly inhibited the growth of human gastric cancer line BGC-823 in vitro in a dose-dependent manner. In vivo, ACBP-inhibited human gastric tumor growth in a *xenograft* model with no apparent cytotoxicity to host. The study suggested that ACBP could be a powerful anticancer biological product through induction of cell apoptosis and cell cycle arrest. Furthermore, Yu et al. [122] found using in vitro and in vivo samples that the bioactive peptide-3 (ACBP-3), a peptide isolated from goat liver, presented antitumor properties on gastric cancer stem cells (GCSCs). ACBP-3 was also found to decrease CD44 (+) cells and suppress proliferation of SC (spheroid colonies) cells and their clone-forming capacity alone or in combination with cisplatin, in a dose-dependent manner [122].

6.1.4. Antioxidant peptides

Antioxidant peptides are particularly interesting because they can potentially prevent or delay oxidative stress as well as low-grade systemic inflammation associated chronic diseases [74, 94]. In this sense, milk proteins as well as milk-derived proteins have been considered as potential carriers for the delivery of antioxidant peptides in the gastrointestinal tract, where they may exert direct protective effects by scavenging reactive oxygen species and reducing the oxidative stress [123]. Only a few studies on the antioxidant properties of goat milk protein-derived peptides have been performed. Silva et al. [124] identified three antioxidant peptides in a water extract from a goat cheese-like system made using an extract from *Cynara cardunculus*. Nandhini et al. [125] found that goat milk fermented with *Lactobacillus plantarum* had potent radical scavenging and lipid peroxidation inhibition activity, although they did not identify the active peptides. Li et al. [126] identified antioxidant peptides in a goat's milk casein hydrolysate made using two enzymes (alcalase and pronase), although some of which did not match with the goat casein sequences available in protein databases. De Gobba et al. [104] isolated and identified antioxidant peptides formed from goat's milk protein fractions by enzymatic hydrolysis using trypsin and subtilisin, both individually and in combination. They found hydrolysates with high radical scavenging activity attributed to the presence of short peptides. Furthermore, an abundance of tyrosine in novel casein-derived peptides seems to play an important role in the radical scavenging capacity of the peptides. Also, peptide fractions with a high abundance of phenylalanine showed the ability to prevent the formation of secondary lipid oxidation products.

6.1.5. Immunomodulatory/anti-inflammatory peptides

As stated above, some peptides can present more than one function. Antimicrobial action of goat lactoferrin and some goat caseins is not only antimicrobial but also acts in the immune system.

A proline-rich polypeptide complex, named colostrinin (CLN), was isolated from ovine colostrum [127]. Cell culture and in vivo studies have shown colostrinin to have anti-inflammatory and antioxidant properties. It also was found to play a regulatory role in growth and differentiation of lymphocytes. Colostrinin also inhibits pathological conditions associated with β-amyloid aggregation in neurons [128, 129]. The CLN complex was also found to present neuroprotective activity, inhibiting nerve cell apoptosis induced by the deposition of toxic amyloid [130]. Colostrinin improves learning and memory in rats, delays the progression of dementia, and loss of long-term memory in aging animals [131, 132]. In humans, positive results of preliminary clinical trials have been found [133, 134].

Zhang et al. [135] also found DPP-IV-inhibitory peptides in goat milk casein-derived hydrolyzed with a combination of trypsin and chymotrypsin thus conferring moderate antidiabetic properties to goat's peptides.

The works of Jirillo et al. [136] recently investigated the effects of goat milk on human blood cells in terms of cytokine release and nitric oxide (NO). The results of their work demonstrated that goat milk was able to trigger cytokine production (IL-10, TNF-α, and IL-6) as well as activate NO release from blood cells. It is well known that NO release can be useful in the prevention of cardiovascular disease being a strong vasodilator and an effective antimicrobial agent. Furthermore, NO possesses other antiatherogenic activities, such as (i) inhibition of influx of atherogenic monocytes and LDL into the wall of arteries; (ii) inhibition of adhesion to the vascular wall of proliferating smooth muscle cells; (iii) inhibition of platelet aggregation; (iv) inhibition of the expression of genes involved in atherogenesis [137]. Goat milk can be helpful in maintaining inflammatory homeostasis by stimulating production of multiple cytokines with a variety of effects, such as TNF-α (a proinflammatory cytokine), IL-6 (an acute phase reactant and growth factor for B cells), and IL-10 (an anti-inflammatory cytokine) [138].

Nowadays, the modulator effect of the diet on the gastrointestinal tract functions has been accepted as essential for maintaining and improving the general health of the host [139]. Dairy proteins, hydrolysates, and peptides have been demonstrated to transform the dynamics of mucus mainly via influencing the mucin secretion and expression and the number of goblet cells. The β-casein-derived peptide β-casomorphin 7 produced the same effects that have been suggested to be mediated by interaction with opioid receptors [140]. Also, this peptide, another β-casein fragment (identified in commercial yoghurt), whey proteins hydrolysates and β-lactorphin have been reported to stimulate the expression of mucin Muc2 and Muc3 genes [141, 142]. Additional gut-protective effects, exerted by a cheese whey protein diet and a diet supplemented with Thr, Ser, Cys, and Pro residues, have been demonstrated by Sprong et al. in colitis and chemical-induced ulcerative gastric lesions [143, 144]. The enhancement of the mucosal immune response is also a dietary modulating strategy of the defense systems protecting the gastrointestinal tract. Kitamura and Otani showed that ingestion of cakes enriched with casein phosphopeptides increased fecal IgA content in healthy individuals, suggesting a positive effect on mucosal immunity [145].

Imbalances in both oxidative and inflammatory status are involved in the etiology of several human chronic diseases that affect the digestive tract, such as ulcerative colitis and Crohn's disease. This has encouraged the search of natural preventive treatments against these imbalances and, consequently, against disease [146].

The minor constituents of goat milk, namely lysozyme and transforming growth factor-β (TGF-β), seem to offer additional protection against intestinal cell damage/inflammation [147]. Several authors have shown that oral administration of TGF-β has anti-inflammatory effects at the intestinal level in animal models of colitis [148]. Schiffrin et al. showed that TGF-β administration lowered leucocytes in the blood stream, as well as the levels of the acute phase reactants fibrinogen and orosomucoid. Colonic weight and thickness and mRNA synthesis for IFN-γ production were also reduced. Finally, TGF-β supplementation also increased mucin-2 production in the caecum and normalized muscle proteolytic activity [149]. Goat milk has a much higher level of growth factor activity than that of cow milk [140], thus making goat milk a possible nutraceutical for gastrointestinal disorders [150].

6.1.6. Prevention of milk allergy

Cow's milk allergy is a common disease of infancy and childhood, and its prevalence is about 2.5% during the first 3 years of life [151]. It is an IgE-mediated allergy, meaning that body produces IgE antibodies against certain protein (allergens) in cow milk. Repeated ingestions of milk lead to identification of antigens present in milk by these IgE antibodies, triggering an immune response that causes symptoms such as eczema, respiratory symptoms (wheezing or asthma), gastrointestinal symptoms, or anaphylaxis. Some proteins, namely αS1-casein and β-lactoglobulin (the structures and composition of which vary between animal species) are known to be important allergens in cow's milk allergy. The allergy-causing properties of β-lactoglobulin can be partially eliminated by heat denaturation [11]. However, caseins maintain the capability of binding to lgEs even after a strong denaturing process [39]. Because the content of αS1-casein is low in goat milk, it is plausible that for children with high sensitivity to αs1-casein of cow milk, goat's milk could be considered an alternative source of milk. More recently, several studies report extensive cross-reactivity between cow and goat milk, caused by cow milk-specific IgE antibodies [152]. Because of the cross reactivity, all scientific reports dissuade persons with cow milk allergy to ingest goat milk. Interestingly, allergy to goat's and sheep's milk without allergy to cow's milk has been reported [153]. However, this food allergy develops later in childhood and not in early childhood as cow's milk proteins allergy, and all the children tolerated cow's milk. Cow milk proteins have been shown to have higher binding capacity to lgE and lgG than proteins present in goat milk. In animal models, cow milk has induced higher lymphocyte proliferation, IL-4 production, histamine secretion, and IgG production [154], which indicates a more exacerbated allergic response.

As described above, peptides present in goat products have been claimed to be active on a wide spectrum of biological functions or diseases, including blood pressure and metabolic risk factors (coagulation, obesity, lipoprotein metabolism, peroxidation, gut and neurological functions, immunity, and cancer). **Figure 1** presents a schematic representation of these different active biological functions.

6.2. Bioactive lipid components of goat milk

Milk lipids have a complex composition, consisting of a variety of bioactive substances with various health effects. Lipids in milk are organized in unique structures: milk fat globules. These structures are important in delivering essential nutrients to the neonate, as they increase bioavailability of lipids. Fat globules have also recently an object of interest in food science, namely their use as a method of delivering other beneficial bioactive nutrients. As previously

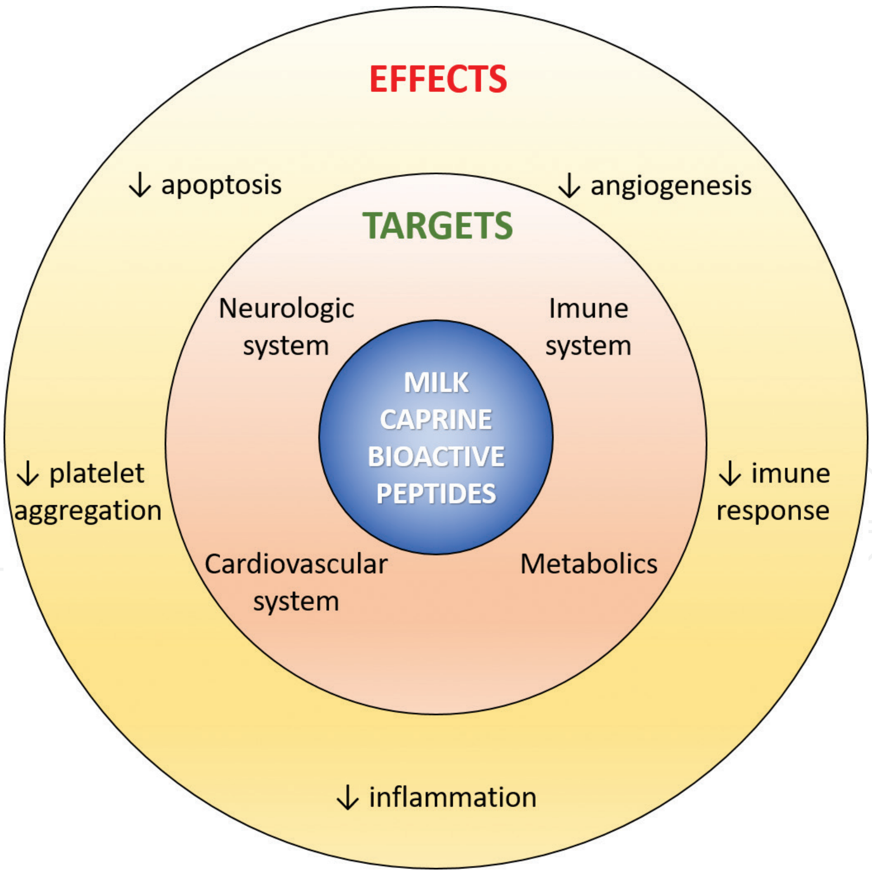

Figure 1. Schematic representation of the wide spectrum of biological functions of caprine biopeptides.

described, caprine milk has more fat globules than cow milk, with a smaller size. These characteristics are important, as they increase the surface area of the globules in contact with pancreatic lipase in the intestinal tract. This allows for better digestibility and a more efficient lipid metabolism, when compared with cow milk fat [155]. Goat milk is therefore recommended for infants, elderly, and convalescing people.

There are several lipid components that have bioactive functions, such as short- and medium-chain fatty acids (MCT), phospholipids, cholesterol, gangliosides, and glycolipids, etc. Goat milk has a relatively high amount of saturated fatty acids (SFAs; 53–72%) and a relatively low content of polyunsaturated fatty acids (PUFAs; 2–6% of fatty acid composition); the remaining fat is constituted by monounsaturated fatty acids (MUFAs) [156].

Table 3 demonstrates that the fatty acid content of goat milk differs from that of cow milk, the former having much higher amounts of butyric (C4:0), caproic (C6:0), caprylic (C8:0), capric (C10:0), lauric (C12:0), myristic (C14:0), palmitic (C16:0), linoleic (C18:2) acids, but lower stearic (C18:0) and oleic acids (C18:1) contents. Three of the medium-chain fatty acids (caproic, caprylic, and capric) represent 15% of the total fatty acid content, compared to only 5% in cow milk [12].

According to Ceballos et al. [26], goat milk also has higher proportions of n-3 and n-6 polyunsaturated fatty acids (PUFA) as well as conjugated linoleic acid (CLA). The work of De La Fuente et al. [157] demonstrates that flock, day of testing within each flock, lactation stage, age of ewe, and season had a significant effect on fatty acid content in dairy sheep milk. They also show that the three quantitatively most important sources of variation in fatty acid content were flock, season, and circumstances of testing within each flock. The most important variations related to testing within each flock and season effects occurred in rumenic (CLA) and linolenic acids. These two fatty acids were higher in spring-summer than in winter. Moreover, lactation stage and age of ewe had a significant effect on some FA. As the age of ewe increased, monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA) decreased and sum of short-chain saturated fatty acids (C4 to C10, SCFA), sum of medium-chain saturated fatty acids (C12–C15, MCFA) increased. Despite the fact that the work of De La Fuente et al. [157] focused on ovine milk, the same factors can also influence goat milk.

Conjugated linoleic acids (CLA) are naturally occurring isomers of linoleic acid. They are a result of biohydrogenation in the rumen of ruminants and influence the concentration of fatty acids in milk [29]. The conjugated linoleic acid found in goat milk fat comes from two sources: ruminal biohydrogenation of linoleic acid (C18:2 n-6) that leads first to vaccenic (trans-11 C18:1) and finally, to stearic acid (C18:0); and synthesis from trans-11 C18:1, an intermediate product of biohydrogenation of unsaturated FA, in animal tissues. Therefore, the conjugated linoleic acid contents in food products derived from ruminants are derived from incomplete biohydrogenation of unsaturated fatty acids in the rumen. Ruminal biohydrogenation, combined with the mammary lipogenic and Δ-9 desaturation pathways, modifies the profile of dietary fatty acids and consequently milk composition [29]. Food products obtained from ruminants, such as milk, cheese, and meat, contain more CLAs than foods of nonruminant origin [158].

Many researchers have investigated the effect of goat milk fatty acids in human research. The short- and medium-chain fatty acids in goat milk exhibit several bioactive effects in digestion, lipid metabolism, and treatment of lipid malabsorption syndromes. The important bioactive lipid components in goat milk have been explored in a recent review by Park [140].

Short- and medium-chain fatty acids are transported directly from the intestine to portal circulation after hydrolysis of the parent triglyceride, without undergoing resynthesis of triacylglycerols. Therefore, they can be used for instant energy production for muscles, heart, liver, kidneys, blood platelets, and the nervous system and are not available for adipose formation. The consumption of a wide range of fermentable carbohydrates can lead to the synthesis of butyric acid, a well-known modulator of genetic regulation, by endogenous microbiota in the lower intestine. This fatty acid is also present in milk, and its properties have prompted various investigators to target this mechanism in an attempt to reduce cancer risk [159]. Butyric acid, by binding short-chain fatty acid receptors, also manages to reduce the inflammatory response in the intestine [160].

Capric and caprylic acids have similar antimicrobial effects. Caprylic acid lowers salmonella infection in chickens [161] and both caprylic and capric acid have antiviral activity. Monocaprin, their monoglyceride form, has been shown *in vivo* to possess antiviral activity against infection by retrovirus [162]. The release of lauric acid in the stomach may have direct antimicrobial activities toward *Helicobacter pylori* [163]. The above fatty acids do not increase blood lipid levels, and they do not contribute to the risk of obesity. Palmitic acid has shown to improve intestinal absorption not just of the palmitic acid but calcium as well as stimulated the expression and activities of the transcription coactivator PGC-1b and by so doing promoted the transcriptional regulation of biosynthesis of lipoproteins from the liver [164, 165].

Milk fat contains essential fatty acids (EFAs) that are not synthesized by the body and therefore have to be supplied with food. Polyunsaturated fatty acids have beneficial health effects by increasing the synthesis of eicosanoids, molecules that regulate cardiovascular function, blood pressure, coagulation, plasma triacylglycerol concentrations, immune response, inflammation, neoplastic proliferation, hormone, and neurotransmitter activity, gene expression, renal function, and pain. Eicosanoids boost immunity, lower cholesterol levels in peripheral blood by stimulating lipid transport, thus reducing the risk of ischemic heart disease [166]. Fatty acids from the n-3 family, commonly known as omega-3 fatty acids, can be useful in the management of inflammatory diseases, such as rheumatoid arthritis, as well as in decreasing symptoms of mental disorders and dementia. DHA was found to be effective in late-stage Alzheimer's disease [167].

Conjugated linoleic acid was recognized as having anti-oxidative and anti-carcinogenic properties in animal model studies [158]. CLA has important functional properties, such as inhibiting the growth of skin, gastric, breast, and colorectal cancer cells [168]. The *cis*-9, *trans*-11 isomer shows the biological activities, but other isomers seem to have beneficial effects as well, such as *trans*-10, *cis*-12, which is believed to prevent the development of obesity [169]. CLA helps prevent osteoporosis, reduces blood sugar levels, boosts immune system function, lowers total cholesterol and LDL cholesterol levels, and improves the LDL/HDL ratio in the blood plasma, thus contributing to the prevention of ischemic heart disease and atherosclerosis [170].

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Furthermore, sphingolipids and their digestion products, ceramides and sphingosines, have been associated with a variety of health benefits, namely anti-carcinogenic effects, immune regulation, prevention of food-borne infections, and reduction of serum LDL cholesterol [170].

As it was described above, milk is not only the main source of energy for the neonate of each species, but its components also have the potential to influence many aspects of physiology from the central nervous system to the immune system, while also exerting both antibacterial and antiviral effects.

6.3. Biological activity of oligosaccharides

Lactose is the major carbohydrate in milk with an average content of 4.1 g/100 mL in goat milk [11]. This disaccharide is a valuable nutrient because it favors the intestinal absorption of calcium, magnesium, and human milk oligosaccharides phosphorus, and the utilization of vitamin C. On the other hand, milk oligosaccharides possess prebiotic and anti-infective properties. The amount of oligosaccharides in caprine milk ranges from 250 to 300 mg/ml. Sialic acid, a general name for N-acetylneuraminic acid (Neu5Ac) and N-glycolylneuraminic acid 355 (Neu5Gc), exists in many of these oligosaccharides and is important in promoting the development of the brain during infancy, among other beneficial effects [140]. Although goat milk is the richest source of oligosaccharides among the different types of milk from farm animals, its content is significantly lower compared to human milk (21–24 g/l for human colostrum; 12–13 g/l for mature human milk) [11]. However, from a structural point of view, among the oligosaccharides found in different types of milk, goat milk oligosaccharides are the most similar to human milk oligosaccharides [171].

While a wide range of biological functions has been attributed to human milk oligosaccharides, less information is available regarding the biological activities of ruminant's milk oligosaccharides and complex oligosaccharides. In short, human milk oligosaccharides are considered to have mainly prebiotic and anti-infectious properties, thus being beneficial for humans, especially for the human-milk-fed neonate [172]. Goat milk seems to be a very appealing candidate for a natural source of human-like oligosaccharides due to its concentration and structure. However, research data on the bioactive oligosaccharides of goat milk is still scarce.

Based on the above, goat oligosaccharides have gained lately much attention as potential nutritional supplements or therapeutic agents. Therefore, they have been used in a number of studies in order to evaluate their health-promoting effects.

6.3.1. Prebiotic and antipathogenic activity

A healthy gut microbiota, composed primarily of bifidobacteria and lactobacilli, which are bacteria presenting saccharolytic activity, has been linked with multiple health benefits. This can be explained by the interactions of intestinal bacteria with metabolic processes and the endocrine and immune systems of infants and adults. Intestinal colonization with a balanced microbiota is of major importance for the appropriate development of the immune system, and there is an enormous scientific and commercial interest in modifying the microbiota for health promotion [173]. As the gut is sterile at birth, it is an organ sensitive to environmental influences. Furthermore, there is an intensive crosstalk between gut microbes and the intestinal epithelium throughout life [174, 175]. The species present in intestinal microbiota, once established, appear to be difficult to modify. Two strategies have been developed to promote a healthy microbiota: the administration of live bacteria (probiotics); or substances (prebiotics) which pass through the gastrointestinal tract undigested, but constitute substrate for desirable bacteria in the gut. The ability of saccharolytic bacteria to break the bonds present in carbohydrates make them able to use these substances to proliferate in detriment of other bacteria which do not possess enzymes to degrade these products. These bacteria provide additional benefits by producing important nutrients, such as vitamins, amino acids, or short-chain fatty acids, which can then be absorbed by the host. The mechanisms by which the intestinal mucosa perceives and responds to microbes, both pathogenic and commensal, are not completely known yet. Based on the literature and considering the analogy between human and goat milk oligosaccharides we might hypothesise a goat oligosaccharides metabolism and potential functions (**Figure 2**).

One of the main features of oligosaccharides is that they can only be consumed by very specific bacteria strains that possess the appropriate set of enzymes to cleave their complex structure. This prebiotic effect is associated with improved health outcomes because it allows specific changes, both in the composition and/or in the activity in the gastrointestinal microflora [176]. Considering that oligosaccharides are only partially digested in the small intestine, they can reach the colon intact where they selectively stimulate the development of lactobacilli and bifidobacteria. Oliveira et al. [177] evaluated the prebiotic activities of the natural oligosaccharides recovered from caprine milk whey and reported that the natural oligosaccharides from caprine milk whey favored the development of *Bifidobacterium* spp. and produced

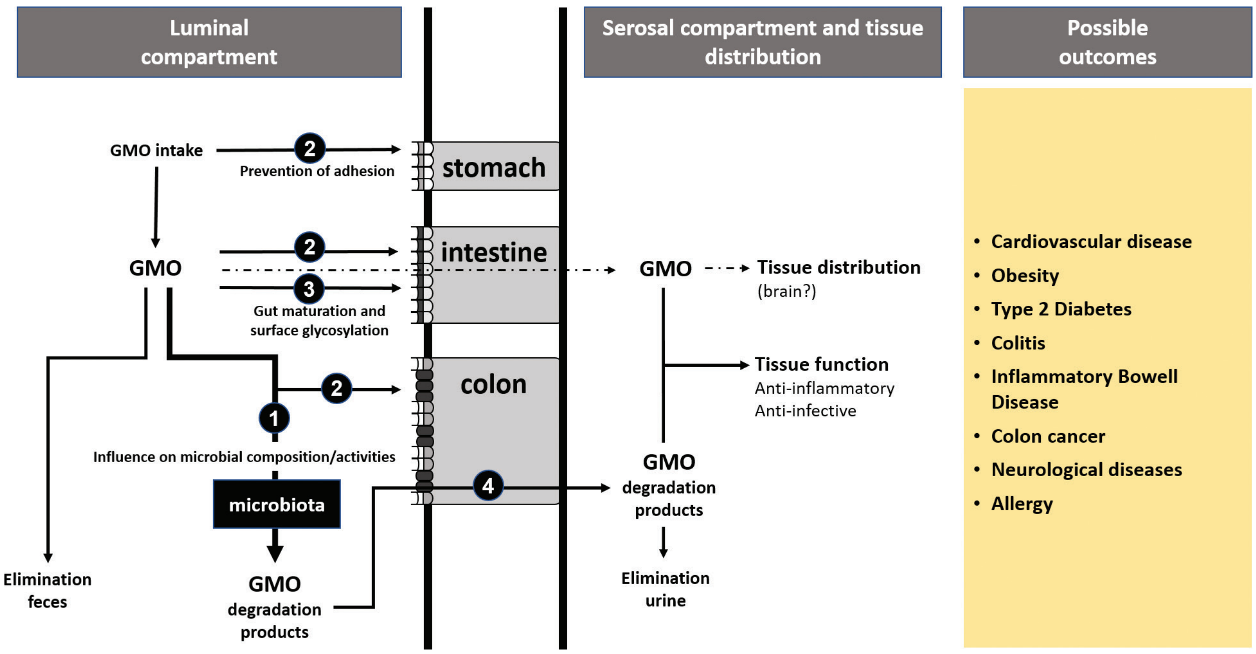

Figure 2. Metabolism of goat milk and milk derivates oligosaccharides and potential functions (1—influence on the microbiota composition and/or activity; 2—prevention of pathogens adhesion; 3—direct effects on epithelial cells; 4—systemic effects) (adapted from Kunz et al. [172]).

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short-chain fatty acids such as lactic and propionic acids. However, there was no inhibition of *S. aureus* and *E. coli* grown in human feces.

The ability of oligosaccharides to reduce the pathogen binding to the intestinal mucosa is another feature that should be considered. Certain bacteria and viruses are able to recognize some types of fucosylated and sialylated oligosaccharides (which are present in milk) and adhere to them [178] reducing their adhesion to intestinal cells and consequently the occurrence of infection. Acidic oligosaccharides containing sialic acid are able to block adhesion of *H. pylori* [179], *S. aureus*, and *Clostridium botulinum* [180]. More recently, Thum et al. [181] investigated catabolism and fermentation of caprine milk oligosaccharides by selected bifidobacteria isolated from four breastfed infants. Results show that dietary consumption of caprine milk oligosaccharides (sialyloligosaccharides) may stimulate the growth and metabolism of intestinal *Bifidobacteria* spp., including *Bifidobacterium bifidum*, typically found in the large intestine of breastfed infants.

6.3.2. Anti-inflammatory activity

Martinez-Ferez et al. [182] suggested that goat milk oligosaccharides may have an anti-inflammatory action. Their research aimed to investigate whether goat's milk oligosaccharides could inhibit the adhesion of monocytes to human umbilical vein endothelial cells. The results of this research indicated that goat's milk oligosaccharides may in fact act as anti-inflammatory agents in the newborn infant, an effect that had already been demonstrated for human milk oligosaccharides and that can be attributed to the structural similarities between goat and human milk oligosaccharides.

6.3.3. Prevention of inflammatory bowel disease (IBD) and colitis

The studies of Lara-Villoslada et al. [183] and Daddaoua et al. [184] have evaluated the effects of oligosaccharides isolated from goat milk in rat models of induced colitis. Lara-Villoslada et al. [183] found that goat milk oligosaccharides are actively involved in the repairing process after a DSS-induced colitis. Moreover, the development of the intestinal flora can be stimulated by oligosaccharides containing N-acetylglucosamine that enhance the growth of *B. bifidum* [185]. Daddaoua et al. [184] reported that animals previously treated with goat milk oligosaccharides showed decreased colonic inflammation and fewer necrotic lesions compared to the respective controls. The authors suggested that the observed upregulation of the trefoil factor 3, which is involved in tissue repair, could indicate a possible mechanism of action. Although further research is needed in order to validate this approach, the use of goat milk oligosaccharides as part of a therapeutic strategy against inflammatory bowel disease seems promising.

Research data suggests that goat milk may be a very appealing source of human-like oligosaccharides The high amount of oligosaccharides in goat milk, as well as their structural profile, as opposed to other domestic mammals, place goat's milk oligosaccharides as the best source for animal-derived oligosaccharides. However, there is still a lack of data concerning the variation of the oligosaccharides profile of goat milk depending on the season, diet, lactation stage, breed, and number of lactation.

The beneficial effects of goat milk oligosaccharides are summarized in **Figure 3**. The increasing interest in healthy diets is stimulating development of new products in the food industry, and many studies have been conducted on fermented milk [138]. Taking into account the health benefits from goat milk, this could be a future trend in the field of probiotic fermented milk products. A lack of information still exists regarding traditional goat cheese and its health properties. However, the incorporation of selected lactic acid bacteria in simple and mixed cultures in goat cheese production is an example of recent innovation in this field. Furthermore, caprine milk whey could be an important source of bioactive compounds for the dietary supplement industry.

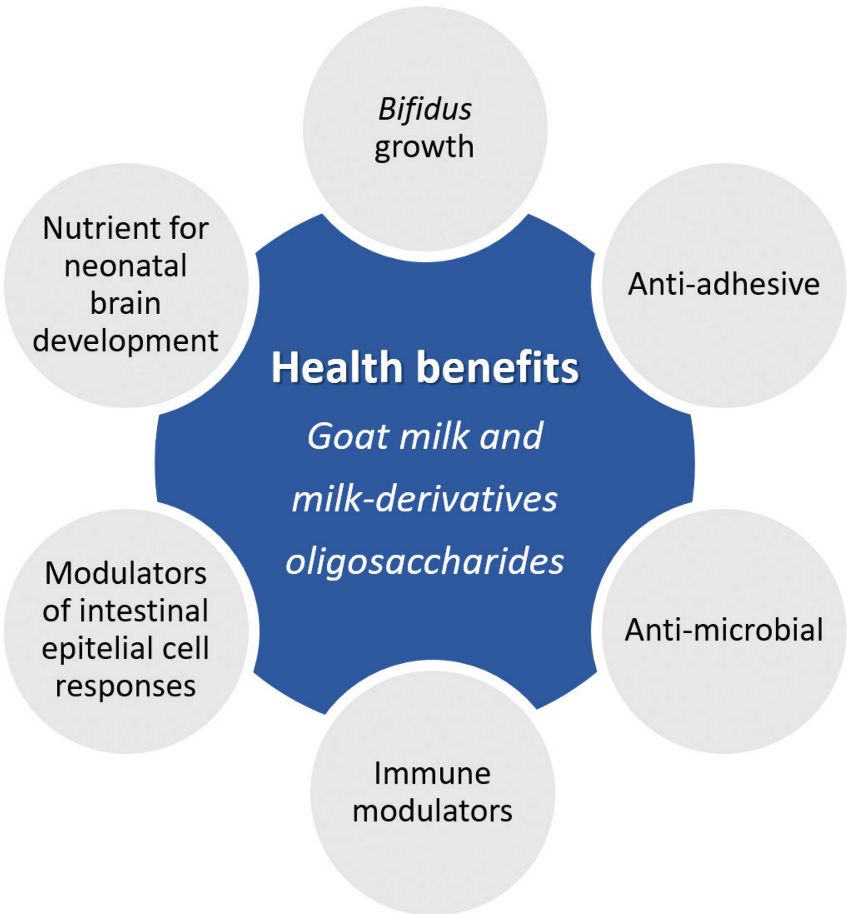

Figure 3. Main health benefits of oligosaccharides present in goat milk and its derivatives.

7. Conclusions and future prospects

Goat milk and other goat-derived products present unique characteristics and their nutritional value, as well as their potential health effects, have been the object of a fair amount of investigation. The composition of goat milk does not differ remarkably from that of cow milk, while presenting more similarities with human milk, making it more easily tolerated. Moreover, the superior digestibility of goat milk, its fatty acid composition, and the presence of various bioactive compounds in its constitution make goat milk potentially helpful in the treatment or even the prevention of certain medical conditions.

Several studies conducted on animal models have shown that goat milk can have beneficial effects on inflammatory bowel disease and disorders characterized by malabsorption. Goat milk, its whey, and fermented goat products may reduce the risk of chronic disorders by anti-inflammatory and anti-oxidative effects. Additionally, goat milk and its derivatives can encourage the selective growth of bacteria that are part of the intestinal microbiota, with potential benefits on the metabolic, endocrine, and immune systems. All these mechanisms suggest that the bioactive compounds present in goat's products might have pleotropic effects. The main health effects of goat-derived products are summarized in **Figure 4**.

Taking all of this into account, goat's milk and other goat derivatives have the potential to act as health-promoting food and to improve overall therapeutic success in the management of chronic diseases, in conjunction with conventional medical treatment. Goat milk is particularly recommended for infants, the elderly, and convalescing people. Therefore, goat milk and dairy products offer exciting opportunities in the area of functional foods. However, this field of research is only in its infancy, as more and more nutrients with physiological effects are being discovered. More studies and clinical trials are necessary, exploring various new fields of study, going as far as to the molecular level, in order to confirm the beneficial effects of such compounds. This will allow for the identification of important pathways in the cells and tissues of the organism and the discovery of new and accessible biomarkers that are indicative of the health benefits promoted by functional foods and their bioactive compounds.

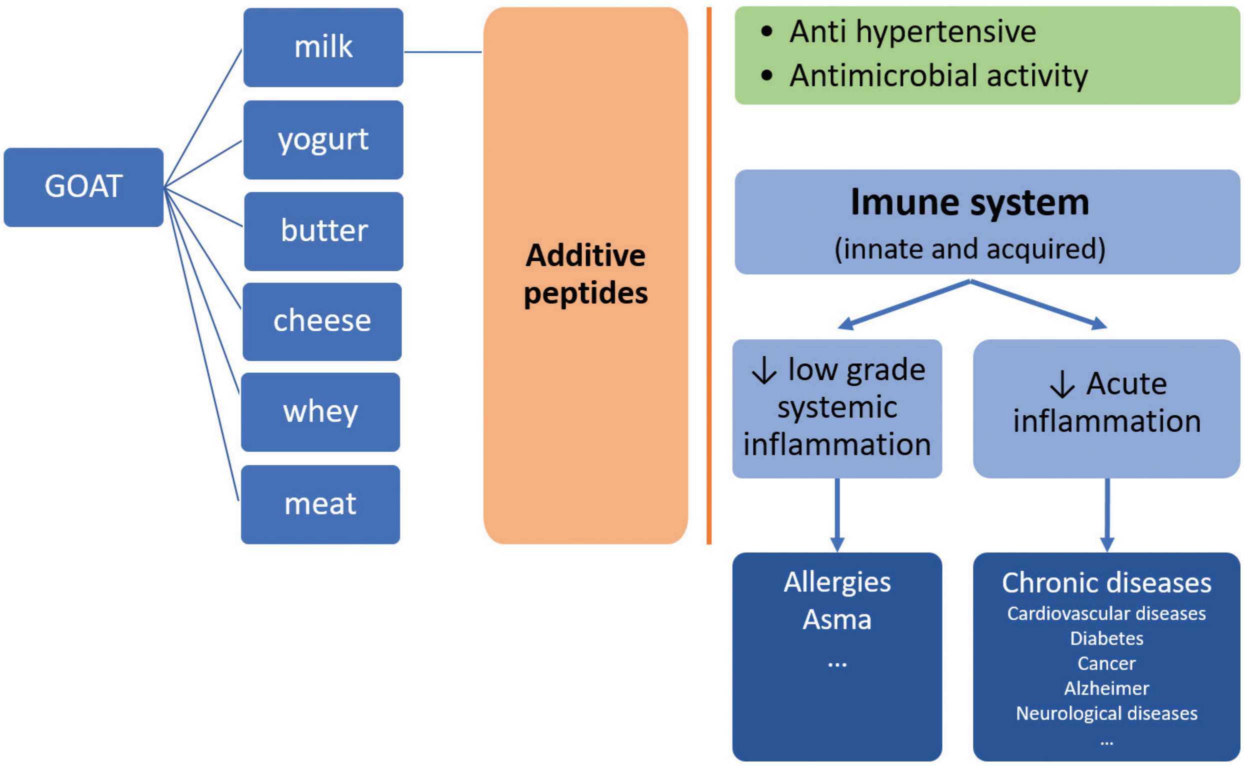

Figure 4. Schematic representation of the main health effects of goat's products.

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