Colostrum Functional Properties in Puppies and Kittens

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Colostrum is the secretion of the mammary gland at the time of the final third of pregnancy. The main source of energy is provided by lipids and carbohydrates. The protein fraction is principally constituted by casein and immunoglobulins, whose role is fundamental for passive immune transfer to newborns.

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1. Nutritional Function and Composition

The exact colostrum composition of carnivores is not extensively known, and data reported in the literature are characterized by high variability [1]. Considering calories, the colostrum energy is nearly equally provided by proteins (50% of colostral calories) and by lipids (40% of colostral calories), and the energy concentration (kcal/mL) is similar in colostrum and in milk, but the pattern during lactation differs slightly between bitches and queens [2]. In dogs, the energy value progressively decreases by 20% during the two first weeks postpartum, whereas in queens, it rapidly drops (−30% over the first 3 days) and then increases progressively over the whole lactation period [3][1][4]. Considering carbohydrates, lactose represents, as in other animal species, the principal sugar source, although its concentration in bitch and cat milk is about 30% lower if compared to cows' milk. The lactose concentration in queen and bitch colostrum was 29.9 g/L and 16.6 g/L, and approximately 35–42 g/L in mature milk [3][1]. Lactose is the only glucose source for a puppy during the first month of life, as the pancreatic activity of amylase is practically nonexistent and, therefore, other carbohydrates cannot be digested. The digestion of lactose remains constant up to two months of age, and then, there is a sharp decline in intestinal lactase. This sharp decline is responsible for outbreaks of diarrhea in patients over 2–3 months of age who are given a large amount of milk [5]. Vitamin E is required to protect the newborn against oxidative stress and vitamin A is fundamental for growth and development. Furthermore, colostrum of livestock animals was found to contain higher concentrations (approximately 80% more in cows' milk) of vitamins A and E compared to mature milk [4]. Vitamin A is essential for cellular differentiation, vision, skin health and protein synthesis. A lack of vitamin A causes depression of immune function, mainly cell-mediated function, and alteration of nonspecific defenses. Vitamin A deficiency can lead to metaplasia and keratinization in skin and mucous membranes [6]. Vitamin D is essential for blood calcium regulation through intestinal absorption, which is fundamental for bone development, and is also implicated in a properly functioning immune system. Vitamin D must be supplemented with the diet since puppies and kittens cannot convert dehydrocholesterol in the skin to a more active form of vitamin D [7]. In addition to calcium absorption, in the

intestine, vitamin D also acts on phosphate absorption, influencing bone growth, mineralization and remodeling [8]. Calcium-phosphorus ratio is generally stable over time in a bitch's colostrum and milk (1.5) and rises from colostrum to milk in queens [1]. The micronutrient content of colostrum strongly contributes to puppies' and kittens' health and growth.

2. Immune Function

Colostrum contains approximately a double concentration of proteins compared to milk, and most of these (20–30%) are represented by immunoglobulin (IgG, IgM, IgA), which provide systemic and local immunization of the newborn. Immunoglobulin intake is vital for carnivore neonates as it provides partial humoral protection to complement the limited placental transfer of immunoglobulins during gestation [9]. Carnivore species have an endotheliochorial placenta in which there are four cell layers (comprising maternal endothelium and the chorionic epithelium), allowing the passage of approximately 10–20% of the mother's IgG [10]. Generally, it is accepted that only 10% of the maternal circulating antibodies pass by the transplacental way in the carnivores, such that the newborn puppy or kitten has a serum IgG concentration of approximately 5% compared to the adult level [11]. Colostrum is particularly rich in IgG and also contains IgA and IgM antibodies that are produced locally in the mammary tissue [2][12]. Total IgG concentration is about 20–30 g/L in bitch colostrum and 50–70 g/L in queen colostrum [2], but they drastically decrease, especially during the first 24 h, so colostrum must be ingested as soon as possible (within the first 16 h) after birth by newborn puppies and kittens to fulfill its immunizing role. For this reason, the absence of colostrum intake can cause several disorders and impairs immune system development [13].

For dogs, 10–20% of IgG transferred from the mother to the newborn is via the placenta; the remainder is supplied by the colostrum [14]. By this passive transfer, immunoglobulins can pass the intestinal barrier of newborn animals. According to Poffenbarger et al. [14], the maximum effectiveness of absorption of colostral immunoglobulins occurs eight hours after birth and needs to be completed within 16–24 h [15]. Other authors showed that immunoglobulins cannot pass the digestive barrier beyond a 15 h deadline [16] or after the first 24 h of life [13]. After this time, the gut epithelium becomes impermeable preventing immunoglobulin absorption [5].

In the cat, immunity transfer must be completed within 12 h postpartum to obtain a maximum rate of immunoglobulin serum in the kitten. Absorption becomes impossible between 16 and 36 h of life. During normal development, absorption of undigested proteins occurs until the concentration of the trypsin inhibitors of colostrum decreases and protein digestion begins, namely toward 24–36 h of life in the cat [17]. Rapid ingestion is necessary not only due to the reduction in immunoglobulin concentration in mammary secretions, but also because of the decrease in its intestinal absorption. Colostral immunoglobulins are transferred to the blood by the small intestine [18]. Within the 24 h after birth, in the intestines of puppies, there is a nonselective macromolecular transport which allows the transfer of immunoglobulins and other proteins from the intestinal lumen to the bloodstream without degradation. Once this absorption period is completed, humoral immunity is acquired [19]. Furthermore, newborns are characterized by a low production of pancreatic enzymes, which facilitates the absorption of intact immunoglobulins from colostrum. Macromolecule absorption capacity is related to the presence of intracellular

vacuoles, less numerous in cats than in dogs [20]. The ability of intestinal absorption, experimentally evaluated by polyvinylpyrrolidone (PVP) supplementation, resulted lower in kittens than puppies. This was also reflected by a lower concentration of serum antibodies. PVP has non-selective macromolecular absorption. It is used as a model protein, as its absorption occurs from 10 to 14 days in kittens [20]. Physiologically, the characteristics of eosinophilic droplets absorption of undigested proteins are histologically visible in kittens up to 36 h of life and the antitrypsin activity of colostrum leads to the maintenance of these droplets for up to five days. Therefore, enterocytes retain their ability to absorb larger proteins if enzymatic digestion is inhibited [21]. A recent work in dogs, instead, highlighted that the absorption ability is reduced by 50% at 4 h after birth, although the absorption continues over 48 h [15].

3. Bioactive Compounds

Colostrum also contains bioactive proteins and peptides that improve local immune defense (**Table 1**). Growth factors and hormones present in the colostrum play a crucial role in the development and health of young animals [22]. Growth factors can be transferred from the digestive tract toward the circulation and involve tissue development in other parts of the organism. For example, insulin-like growth factors (IGF) persist in the digestive tract and have local effects on cell growth [23]. These factors are generally found to be more concentrated in bovine colostrum and are likely biologically important for the survival of newborns and help the maturation of the digestive tract, as suggested in other livestock [24]. Several studies have clarified the role of these compounds, showing that during the transition to milk feeding, the development of the small intestine undergoes a noticeable decline [25][26][27]. This decline should not be interpreted as a stop, as even so-called mature milk (day 21 of lactation), although less so, has a trophic effect on the small intestine [28]. Indeed, milk possesses several bioactive substances including immunomodulatory, anti-inflammatory, and antimicrobial agents.

Table 1. Bioactive compounds and growth factors of colostrum.

Bioactive Compounds	Function	Reference
ß-lactalbulin	Potential antiviral, prevention of pathogen adhesion anticarcinogenic and hypocholesterolemic, and hydrophobic components binding ability, including retinol and long-chain fatty acids.	[29]
α-lactalbulin	Calcium metalloprotein, in which Ca plays a crucial role in the folding and structure. Effector of lactose synthesis in mammary gland, calcium carrier, immunomodulatory, precursor for bioactive peptides potentially anticarcinogenic.	[30]
Lactoferrin	Antimicrobial, antioxidative, anticarcinogenic, anti-inflammatory, iron transport, cell growth regulation, precursor for bioactive peptides, immunomodulatory, stimulation of osteoblast proliferation.	[31]
Lactoperoxidase	Antimicrobial, synergistic effects with immunoglobulins, lactoferrin, and lysozyme.	[27]

Bioactive Compounds	Function	Reference
Lysozyme	Antimicrobial, synergistic effects with immunoglobulins, lactoferrin, and lactoperoxidase.	[32]
Growth factors	**Function**	**Reference**
Epidermal growth factor (EGF)	Stimulation of cell growth, intestinal cell protection and repair, regulation of immune system.	[33]
Binding proteins (IGFBP)	Marked anabolic characteristics, gastrointestinal maturation, and wound healing contribution.	[34]
Transforming growth factor -alpha (TGF-α) and beta (TGF-ß)	Cellular proliferation and tissue growth, maturation, and repair activation. Inductive effect on IgA production in Peyer's patch lymphocytes and spleen lymphocytes.	[35]
Insulin-like growth factor 1 (IGF-1).	Maintenance of adult muscle mass depending on satellite cells activation, proliferation, survival, and differentiation, processes. Lean muscle growth and beta oxidation of fats.	[36]
Hepatocyte growth factor (HGF).	Produced by macrophages, important factor for intestinal cells growth in neonates after birth. DNA and proteins synthesis and nutrient uptake enhancement, particularly in muscles and cartilages.	[37]
Platelet derived growth factor (PDGF)	Gastrointestinal development and maturation.	[38]
Vascular endothelial growth factor vascular (VEGF)	Gastrointestinal growth and perivascular maturation.	[39]
Growth hormone (GH)	Maturation of gastrointestinal mucous membrane development and closing of antibody transport at intestinal level.	[40]

Even if the available studies have been conducted in ruminants, the nutraceutical proprieties of colostrum could be translated to other animal species. Colostrum is characterized by a high content of different growth factors and bioactive molecules that positively influence health status [41]. Trophic factors in mammalian colostrum promote the growth of the small intestine of neonates. Colostrum enhances the maturation decline in lactase activity and the expression of sucrose activity [42]. Small peptides and proteins of the innate immune system are increasingly valued for their potential as antimicrobic and immunomodulators [43][44]. Colostrinin (CLN), a proline-rich polypeptide complex, originally isolated from ovine colostrum, has been studied as a nontoxic natural preparation for the prevention of Alzheimer's disease (AD), observing encouraging results [45].

The lactose concentration in canine and feline colostrum is low compared to milk, about 1.5% and 3.0%, respectively. Mammalian milk and colostrum usually contain, in addition to lactose, a plethora of neutral and acid oligosaccharides [46]. Oligosaccharides play an important role, as they may inhibit the adhesion of pathogenic

microorganisms to the intestinal and urinary tract by acting as receptor analogs, thus preventing gastric and urinary infections [47][48]. In addition, milk oligosaccharides may act as prebiotics, promoting the growth of beneficial microorganisms, such as *Bifidobacterium bifidum*, within the lower gastrointestinal tract, and inhibiting pathogenic organism proliferation [49]. The immunomodulatory effects of livestock animal colostrum in humans have been demonstrated in several studies, including infectious diseases [50][51], exercise-induced immune suppression [52][53], wound healing involving gastrointestinal damage [27][54][55] and bone density [56]. This has led to several investments in antimicrobial molecules that are currently at various development stages by biotechnology companies [57]. With the use of milk as a food on one side, and the development of novel drugs based on isolated colostrum compounds on the other, the nutraceutical use of colostrum extracts in health management is an expanding niche [58] and is receiving interest as a complement to or substitutes for vaccines and pharmaceutical drugs [59][60]. Despite the commercial application of colostrum and colostrum by-products, it represents an indispensable nutraceutical for newborns. In polytocous species, those bearing multiple offspring in a litter, such as dogs and cats, the degree of passive immunization is often variable within the same litter due to colostrum absorption variability. Indeed, the last born could potentially ingest an insufficient amount of colostral immunoglobulins, and this represents an important risk for pathology development [61].

4. Conclusions

The neonatal period is crucial for puppies' and kittens' survival as dramatic systemic changes may occur if their management is not properly approached. Colostrum administration is pivotal to minimize neonatal failure. Maternal colostrum provides high amounts of nutrient as well as functional compounds that promote immune system and intestinal maturation. Immunoglobulin transfer plays a pivotal role for puppies' and kittens' survival. Colostrum is the first source of nutrients for the newborn, and it fulfills all nutrient requirements while also providing several bioactive compounds fundamental for puppies' and kittens' long-term development.

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