BAHRİ DAĞDAŞ
Hayvancılık Araştırma Dergisi

DERLEME

Cytokines and Growth Factors in Goat Colostrum: A Short Review

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Abstract

Distinctly milk, colostrum is a nutrient-rich and it plays vital role in most of mammary species. Basically colostrum consists 2 major factors; nutrient components and non-nutrient bioactive factors. Non-nutrient bioactive factors divide into two main components; immunological components and growth components. In the literature there are abundand studies on bovine and porcine colostrum and most of studies are related to nutrient factors of colostrum. Recent and former studies have shown that there are some clinical applications of colostrum in human medicine and ironically another convincing studies have revealed there might be relation between insulin-like growth factors in the milk and cancer developing in humans. Aim of present review is emphasize the importance of goat colostrum and its effectiveness in bioactive components and provide insight other researchers.

Keçi Kolostrumundaki Sitokinler ve Büyüme Faktörleri: Kısa bir derleme

Özet

Sütün aksine kolostrum besin maddelerinden zengindir ve çoğu memeli türünde hayati öneme sahiptir. Kolostrum temel olarak iki ana unsurdan oluşmaktadır; besin unsurları ve besin olmayan, biyoaktif unsurlar. Besin olmayan biyoaktif unsurlar ise iki ana grup bileşene ayrılır; immunolojik bileşenler ve büyüme faktörleri. Literatürde çok sayıda sığır ve domuz kolostrumu üzerine çalışmalar mevcuttur ve bunların büyük bir kısmı kolostrumun besin maddeleri ile ilgilidir. Yakın zamanda ve daha önceki çalışmalar, ruminant kolostrumunun insan hekimliğinde bir çok klinik uygulaması bulunduğunu göstermiştir. Ancak ironik bir şekilde diğer bir çok çalışma ise süt ve süt ürünleri tüketimine bağlı insülin benzeri büyüme faktörleri ile insanlarda kanser gelişimi arasında ilişki olabileceğini ortaya koymuştur. Sunulan derlemenin amacı keçi kolostrumunun önemini, biyoaktif bileşenlerinin etkinliğini ortaya koymak ve araştırmacılara yeni fikirler sağlamaktır.

1. Introduction

Colostrum is a nutrient rich fluid which secreted by mammary gland before parturition and it changes subsequently 24-48 hours after parturition (Bernabucci et al., 2013). It's not only nutrient rich but also contains some immunological factors such as IgG, IgA, IgG (Park, 2009) and Lactoferrin (Bulgan et al., 2020).

Mechanism of development and its genetical keys of placenta in goats are not known well yet (Luo et al., 2021). Due to the placental structure is epitheliocorial in goats, passage of maternal antibodies in transplacental way is not possible during pregnancy (Giguère and Polkes, 2005; Tizard, 2009); hence, it depends on passive immunity to intake adetuate colostrum in newborn kids after birth against gastrointestinal and respiratoric infections (Weaver et al., 2000; Argüello et al., 2004; Keskin et al., 2007).

It is thought that goat farming has a 10 thousand years evolution roots mountains of Iran which makes them one of the oldest domesticated animals (Haenlein, 2007). Today there is an increasing demand to goat milk and that increasing has 3 main reasons; home consumption, experting in goat milk and its derives and medical purposes such as lower digestive issues than the cow milk (Haenlein, 2004; Park and Haenlein, 2007). On the other hand, goat milk has an important ability to prevent several diseases in regard of different animal milks. And also provides strong nutritional and nutraceutical properties which make it more suitable for infants and elders (Kumar et al., 2016). Bovine and goat colostrum has been used not only for animal nutrition but also used for athlete nutrition, infant formulas, dietary supplements, functional foods, pharmaceuticals, and in cosmetics (El-Loly, 2022).

Although they are similar biological products, components of colostrum and milk secreted by different mechanisms (Quesnel and Farmer, 2019; Baumrucker et al., 2021). Basically colostrum consists 2 major factors; nutrient components and non-nutrient bioactive factors. Non-nutrient bioactive factors divide into 2 main components; immunological components and growth components. Eventually, all biological components of colostrum help the grow vital organs and ensure passive immunity of the offspring (Baintner, 2007; Agenbag et al., 2021).

Other crucial components of colostrum include growth factors (GFs); especially insulin-like growth factor-1 (IGF-1), transforming growth factor beta-2 (TGF-b2), hormones, cytokines and non-specifical antimicrobial factors (Puppel et al., 2019; Mondeshka et al., 2022). The composition of immune components in colostrum is significantly higher than the milk (Stelwagen et al., 2009; Ballard and Morrow, 2013; Ulfman et al. 2018). Most of studies on these components are well consisted in bovine, porcine, and human milk (Sangild et al., 2021).

In human colostrum, the presence of IL-1a, IL-1b, IL-6, IFN-γ, TNF-α and the anti-inflammatory cytokine IL-10 has been reported (Kim, 2021).

There are several factors those influence the production and the composition of colostrum; including species, breed, health status of the mammal, management and post partum time (Bernabucci et al., 2013).

Although immunostimulant components of it, goat colostrum also play anti-inflammatory effects (Daddaoua et al., 2006).

Table 1. Basic components of goat colostrum.

Type of Factor	Name
Nutrient	Proteins
	Fat
	Carbonhydrates
	Vitamins
	Minerals
	Antioxidants
Non-Nutrient	Immunoglobulins
	Lactoferrin
	Lactoferrampin
	Lysozyme
	Propilene-rich
	Polipeptides
	Cytokines
	Leukocytes
	T and B Lymphocytes
	Oligopolysaccharide
	Growth Components

Basically ruminant colostrum contains also insulin, thyroxine (T4), triiodothyronine (T3) and prolactin hormone (Campana and Baumrucker, 1995; Pan'kiv and Simonov, 2020).

2. Cytokines in Goat Colostrum

Cytokines are small peptide molecules (<40 kDa) and they have major immunmodulatory functions (Takeuchi and Akira, 2010); such as signals transducing to help immunoreactions (El-Loy, 2022). Those immunoreactions would be proinflammatory or antiinflammatory (Geginat et al., 2016) and they provide immunity against viruses and bacteria (Sienkiewicz et al., 2021). Cytokines in colostrum are exuded by leukocytes but also they are released in mammary glands in cows (Menchetti et al., 2016).

The cytokine levels in colostrum are related to capability of it ensure the immunomodulatory activity and neonatal immunity (Hagiwara et al., 2000). Lactoferrin, lactoperaxidase and lysozyme are antimicrobial components in the colostrum as well as cytokines (Bulgan et al., 2020; Zhou et al., 2023).

According to literature data upon goat milk, asserts the induction of proinflammatory and antiinflammatory cytokines help to maintain human immune homeostasis especially elders who have immunosupression (Jirillo et al., 2010).

Interleukins nowadays divided into 3 classes based on their structure and biological activities; Group 1, Group 2 and Group 3 (Akdis et al., 2011; Dinarello, 2018).

While proinflammatory cytokines are IL-1, IL-6, IL-16, TNF-α; antiinflammatory cytokines are IL-4, IL-10, IL-11, IL13 (Jun-Ming and Jianxiong, 2007). It's thought that ruminant colostrum contains some of cytokines but there is no study to estimate quantity of these cytokines in goat colostrum.

3. Growth Factors in Goat Colostrum

It is reported that there are important changes of IGF-1 levels in bovine colostrum at post partum 6 hours and later on (Elfstrand et al., 2002). There are approximately 50 different polypeptites in bovine colostrum known as growth factors (GFs) (Poonia and Shiva, 2022) but there is no such data about goat colostrum. Today there are several technologies developed to extract such bioactive molecules from bovine colostrum (Gomes et al., 2021).

GFs in colostrum consist these components: Epidermal growth factor (EGF), Transforming growth factor-α and β (TGF-α, TGF-β), Insulin-like growth factor-1 and 2 (IGF-1, IGF-2), Fibroblast growth factor (FGF), Platelet derivative growth factor (PDGF) and Growth hormone (GH) (El-Loy, 2022). Concentration of GFs show difference among species and within the species (Kráčmar et al., 2005; Poonia and Shiva, 2022).

IGF-1 and IGF-2 are also known as somatomedines that synthesized in the liver under lead of GH; their receptors are located on several tissues especially gastrointestinal tract (Kuemmerle, 2012). TGF and IGF stimulate skin growth and cell proliferation and regeneration directly act on DNA and RNA so improve wound healing (Sánchez-Macías et al., 2014). Once compared to milk, ruminant colostrum has high concentration of IGF-1 between 200 and 500 ng/mL (Odle et al., 1996; Pauletti et al., 2005).

TGF-β is produced by some type of cells and it regulates several cellular functions such as oncogenesis, control of immune responses and cell proliferation (Ihara et al., 2017). It also has antiinflammatory role and act like intestinal epithelial barrier (van Nerveen, 2014; Kelly et al., 2017). Another major function of TGF-β is modulation of immune cells and microbiota functions so it contributes maintaining intestinal homeostasis (Ihara et al., 2017). The function of TGF-β is inhibition to cell proliferation so it has an especial effect on neutrophils and it plays a role in the regenerative process by stimulating the migration of epithelial cells on the damaged area to epithelial regeneration (Nguyen et al., 2014).

EGF is a polypeptide which consisted 53 amino acid (6045 Da) and it's synthesised by matured salivary glands and Brunners glands in duodenum (Playford, 2001). EGF plays a role in mammary development (Dehnhard et at., 2000) and it helps to prevent against disease in infants, children and adults (Playford et al., 2000; Chatterton et al., 2013).

Another component of the colostrum is vascular endothelial growth factor (VEGF) that has reported in human colostrum (Nishimura et al., 2002; Özgürtaş et al., 2010). There are limited studies upon VEGF in goat milk but there is no study in goat colostrum.

4. Applications in Human Medicine

Multiple epidemiological, clinical and experimental studies are agreeable on the protective role of colostrum and milk against infectious diseases (Chantry et al., 2006; Gomes Fagundes et al., 2016) and prevention of allergic (Minniti et al., 2014) and chronic diseases (Kelishadi and Farajian, 2014).

TGF-β can inhibit or support the respiratoric inflammation and also there are some particular evidences its role maintain and develop immunity in children so this could ensure maintain of protection against some inflammations and allergies (Batista da Silva Galdino et al., 2021).

Table 2. Chemical composition of goat colostrum and goat mature milk (Niznikowski et al., 2006).

Biological Factor	Source	
	Colostrum	***Mature Milk***
Protein (g/100 g)	8.78	3.59
Fat (g/100 g)	6.61	4.02
Lactose (g/100 g)	2.64	4.51
Minerals (g/100 g)	0.94	0.72
Dry Matter (g/100 g)	19.14	12.57
IgG (µg/mL)	8123.33	1706.33

Table 3. Some clinical applications of colostrum in human medicine (Modified from Menchetti et al., 2016).

Clinical Condition	Reference
Acute infectious diarrhoea	Inagaki et al., 2013; Blais et al., 2014
Helicobacter spp. infections	Gomes et al., 2021
Drug-induced diarrhoea	Shen et al., 2015; Sponseller et al., 2015; Artym and Zimecki, 2023
Immunodeficiency diarrhoea	Pagnoncelli et al., 2022
Inflammatory bowel disease	Khan et al., 2002; Ragab et al., 2007
Necrotizing enterocolitis	Lee et al.,2004; Brooks et al., 2006
Surgery	An et al., 2009; Rathe et al., 2014
Viral influenza	Batista da Silva Galdino et al., 2021
COVID-19	Serrano et al., 2020

5. Conclusion

According to literature datas, goat colostrum contains significant cytokines and GFs alongside of milk.

Recent studies have shown goat milk oligosaccharides are more abundant than bovine milk oligosaccharides thus goat milk or colostrum are more potential to research other properties could be found in inovations (van Leeuven et al., 2020). Goat milk is an admitted protein source to infant formula and consequently higher levels in milk oligosaccharides it takes attention; with average concentrations reported of 60−350 mg/L in goat milk and up to 2.4 g/L in goat colostrum (Claps et al., 2014; Marziali et al., 2018).

On the other hand according to recent studies, there might be a relation between IGF-1 in milk and milk products and cancer developing in humans (Yu and Rohan, 2000; Qin et al., 2009; Simonov et al., 2021). Another opposite discourse is that goat milk has no certain nutritional adventage over bovine milk and it's not less allergenic (Turck, 2013).

There are studies on cytokine and GF levels in goat milk and especially bovine milk in the literature but studies in goat colostrum are limited. Thus it is suggested that there should be more studies on cytokines and GFs in goat colostrum.

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