



The effect of probiotics on colostrum quality: A concise review

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Abstract

Colostrum, the first nutritional source for newborns, not only provides essential nutrients for growth but also contains immunological factors that activate the immune system against harmful microorganisms encountered in the environment. Colostral components form initial intestinal barriers in newborns. A healthy intestinal barrier can eliminate harmful pathogens, such as mesophilic aerobic bacteria, by promoting the growth of probiotic microorganisms, thereby enhancing immunity through increased colonization. This review aims to explore the potential of probiotics in improving the immunological quality of colostrum and developing more effective methods for its enhancement.

Keywords: Colostrum, probiotic, immunity, immunoglobulin

1. INTRODUCTION

Colostrum, the first food of newborns, is produced in the mammary gland at the end of pregnancy and supports the growth and development of the offspring to form an immunity against pathogens during the most vulnerable first 72 hours of life.¹ Colostrum is composed of nutritional factors generally expressed as protein, carbohydrate, fat, mineral and vitamin, immunological factors such as immunoglobulins (especially IgG, IgM and IgA), lactoferrin, lactoperoxidase (LP), lysozyme, cytokines (IL-2, IL-6, IL-10), chemokines, cathelicidin and growth factors. Immunoglobulins and other immunologic factors support the development of the gastrointestinal system, increase the resistance of the offspring against diseases and initiation of antimicrobial activity, as well as the acquisition of native and adaptive immunity of the organism.¹ In addition to these compositions, colostrum also contains many beneficial microorganisms, especially *Bifidobacterium* and *Lactobacillus*. These microorganisms are resistant to bile and pancreatic enzymes, inhibit the affinity of bacteria, viruses or protozoa to the host's intestinal propria, have no toxic side effects and have health-promoting effects.² Probiotic microorganisms and other components of colostrum are directed to the mammary glands of the lactating mother via intestinal lymphoid cells and peripheral blood, and thus this rich content is taken up by the offspring.³

The aim of this review is to present the studies evaluating the improvement of the quality of colostrum through the synergistic effect of probiotic microorganisms present in the colostrum and strengthening the immunological factors present in its content.

2. COLOSTRUM

Colostrum is secreted from the mammary gland during

late pregnancy and helps newborns adapt to the environment, gain immunity against pathogenic microorganisms and support their development. The first and most important study in its history reported that colostrum contains antibodies against polio and that the risk decreases when babies take this food, and a vaccine was developed from colostrum given to calves. Based on this research, it was suggested that immunological factors may be transmitted from mother to calf through colostrum and that calves may gain immunity against many diseases in this process.⁴⁻⁶ Tyrell et al.⁷ reported that these immunological factors in colostrum are present in the intestinal tract of the living organism and that they contribute to healthy microflora.

Colostrum, which is taken within 24-48 hours after birth, is different from normal milk where it has a higher concentration of constituents and its content is similar to blood, contributing to the adaptation of the offspring to extrauterine environment.⁸ It contributes to the development of the gastrointestinal system and maturation of the body with the immunological factors, nutrients and growth factors in its composition.^{9,10} It has a unique composition and has higher albumin, globulin, vitamins A, E and K and fatty acids, but lower lactose content compared to lactation milk.¹¹ In addition, being rich in polyunsaturated fatty acids known as linoleic acid 18:2 and omega-3 has been found to positively affect the development of vision and consciousness in children.¹²

Immunological factors (also known as antimicrobial peptides) in colostrum provide passive immunity by destroying Gram-negative bacteria such as *Escherichia coli*, *Salmonella*, *Klebsiella* and Gram-positive bacteria such as *Bacillus*, *Staphylococcus*, *Listeria* and therefore, colostrum intake of 10% of the live weight of newborns contributes to the acquisition of this immunity.^{1,13} In addition, it has immunomodulatory, nutraceutical, antihy-

pertensive, antithrombotic and antioxidative properties in terms of its ability to prevent and treat diseases¹⁴

2.1. Mechanism of Action of Colostrum against Pathogens

Placenta types are important in the transfer of passive immunity from mother to offspring. It is evident that humans and primates exhibit the highest rate of antibody transfer from mother to offspring, a phenomenon attributable to the presence of a hemochorial placenta. In contrast, the placenta of carnivores is characterised by an endotheliochorial structure, resulting in its permeability to antibodies being limited to one-third of the pregnancy. This phenomenon is referred to as hypogammaglobulinemia in these animals. Conversely, ruminants possess a syndesmo-chorial placenta, while pigs and horses exhibit an epitheliochorial type. These animals are designated as agammaglobulinemic, hypothesising their inability to permit antibody penetration.¹⁵ Therefore, it is evident that the colostrum ingested by the offspring from their mothers via the placenta contains immunological factors that provide both native and adaptive immunity. These factors are recognised as pathogens that cause bacterial, viral and protozoal diseases, thereby reducing their activity. However, the permeability of antibodies through the placenta is minimal or non-existent.¹⁶

The acquired immune response is driven by T and B lymphocyte cells and responds rapidly to the threat of a pathogen to which it has been previously exposed. However, since it is late to respond to a pathogen to which it has not been exposed, native immunity forms the first defense cascade to protect the body from pathogenic microorganisms by generating a series of signals before acquired immunity kicks in.¹⁷ A series of signaling proteins (chemokines and proinflammatory cytokines), Toll-like receptors (TLRs), transcription factors such as nuclear kappa beta (NF- κ B) and Interferon Regulatory Factor 3 (IRF3), which localize to the plasma membrane or endosomes of mammary epithelial cells and recognize specific motifs on the surface of pathogens; Tumor necrosis factor alpha (TNF- α), Interleukins (IL-2, IL-6, IL-10, IL-12) and interferons (IFN- α and IFN- β , IFN- γ). With the activation of signaling proteins, secretion of antimicrobial peptides such as Lysozyme, Lactoferrin, Lactoperoxidase, β -defensin and Cathelicidin increases bacteriocidal permeability and directly inactivates pathogens.¹⁸

Immunoglobins are the main component of passive transfer immunity.¹⁶ Even if the mammary epithelium does not synthesize immunoglobulins directly, it transports a small amount of Ig into colostrum and blood serum through tight intercellular connections, while the majority of IgG is transported to the mammary gland through the neonatal Fc receptor (FcRn), the special receptor of IgG, and IgA and IgM through the polymetric immunoglobulin receptor (pIgR) and the effect of hormones. When they bind to these receptors, their antigen recognition is enhanced and they phagocytize the agents by increasing the response of T and B lymphocytes against microorganisms.¹⁹

Researchers administered immune boosting supplements to mothers in late pregnancy and examined their effects on colostrum quality. The first of these is levami-

sole, an anthelmintic drug with immunomodulatory and stimulating properties, which increases lymphokine production and stimulates antibody production from B lymphocytes, thus stimulating the cellular immune system and increasing colostrum antibody levels and contributing to passive immunity of the offspring against infections.²⁰ Kamada et al.²¹ observed that the addition of selenium, an important mineral substance involved in the antioxidant defense system and immune functions, directly activates physiological pinocytosis in the intestinal propria and causes IgG absorption in pregnant cows to increase the immunological quality of colostrum. They also suggested that the addition of selenium to colostrum substitute food containing immunoglobulin may significantly increase IgG transfer to the piglet. Recently, carnitine supplementation, which has been observed to positively affect the growth and development of piglets, also has immunomodulatory properties, did not show the expected difference in lactose, lipids, IgG, IgA and IgM in colostrum compared to the control group, but an increase in the growth of piglets receiving carnitine supplementation was observed and it was concluded that this was due to the prolongation of sucking time.²² In recent years, probiotics have started to be evaluated as an alternative in studies to improve colostrum quality.

3. PROBIOTICS

It is known as a community of living microorganisms that, when taken in appropriate amounts, have a positive effect on the health of animals and humans and provide immunity against pathogens.²³ Fermented oligosaccharides that increase the growth and activity of bacteria in the colon are called prebiotics. These microorganisms, which are beneficial for the body, can be alone or in combination.²⁴

In the intestinal microbiota of living organisms, probiotics have five different special effects that make nutrients usable and useful, regulate sensory and motor neurons and maintain their transmission, restrict the life of pathogenic microorganisms thanks to their bacteriostatic effect, strengthen the mucosal barrier layer by increasing mucin production, and regulate the immune system by reducing the formation of proinflammatory cytokines.²⁵

These microorganisms were first isolated from the feces of colostrum-fed pups and it has been shown that whether the mother receives food containing probiotic microorganisms or not, the mode of birth, the first food material of the puppy (colostrum or commercial food) or environmental factors affect the intestinal flora and cause the decrease or increase of many microorganisms.²⁶⁻²⁸ Mehrnia et al.²⁹ observed that while *Bifidobacterium* and *Lactobacillus* were dominant in the intestinal flora of colostrum-fed pups, *Enterobacter* species were dominant in commercial formula-fed pups and less microbial flora distribution was determined compared to colostrum-fed pups. In line with this study, it was determined that the risk of developing diseases was high in puppies fed with commercial formula and not receiving colostrum.

3.1. Mechanisms of Action of Probiotics on Immunity

It has been suggested that the immune system may be

beneficially influenced by surface recognition receptors on the surface of intestinal epithelial cells in the presence of probiotics.³⁰ TLRs located in the mucosa of the intestinal lumen exert their effects by affecting immune system cells such as macrophages and dendritic cells (DC), B cells, T cells and NK cells, as well as non-immune system cells such as fibroblasts and mucosal epithelial cells. In the innate immune system, these cells recognize lipopolysaccharides and lipoteichoic acids in pathogens and facilitate the detection of these microorganisms by triggering defense mechanisms such as the production of cytokines. The activation of TLRs is initiated by the response of DC, inducing both innate and acquired immunity.^{31,32}

In the intestinal lamina propria, probiotics of the genus *Lactobacillus*/*Bifidobacterium* can directly inhibit some viral microorganisms by producing lactic acid, hydrogen peroxide, bacteriocins and other inhibitors; they also maintain the integrity of the epithelium and compete with pathogens for its receptors. *Lactobacillus* capture viruses via lectin molecules to prevent infection and act as microorganism killers via nitric oxide. *Bifidobacteria* produce short-chain fatty acids (SCFA) through DC development; induce Fas-mediated T (Treg) uncoupling (death receptors); decrease IL-12 production and increase IL-23 production and bind to TLRs through DC. In intestinal lamina propria secrete mucin and antimicrobial peptide (AMP) in response to probiotic microorganisms and stimulate activated B plasma cells such as BAFF (B cell activating factor) and APRIL (a proliferation-inducing ligand) to produce IgA secretion (sIgA) that limits microbial interaction. Under equilibrium condition in the intestinal lamina propria, probiotics promote the development of antigen-presenting cells and stimulate the secretion of cytokines (thymus-stimulating lymphoprotein, IL-33, IL-23, IL-25 and Transforming growth factor (TGF)). Antigen-presenting cells induce regulatory T cell formation through TGF- α and retinoic acid-dependent mechanisms and reduce TGF- α and IL-10 responses; induce lymphoid tissue by increasing IL-22 responses; and NK and T cells regulate the expiration of tight junction proteins to maintain the anti-inflammatory microbiota of the intestinal lamina propria.³³⁻³⁶ They also found that lactic acid probiotics maintained the increase in IL-10 regulated by bifidobacteria through DCs formed in the intestinal lamina propria, while the production of IL-12 decreased. Therefore, it was observed that the proinflammatory cytokine response may change in the presence of different variations of probiotics.^{37,38}

The response of the immune system to a probiotic is weaker than in the presence of Gram-positive bacteria and DCs respond differently to these bacteria.³⁹ Braat et al.⁴⁰ when *Klebsiella pneumoniae* from the *Enterobacteriaceae* family and *Lactobacillus rhamnosus*, a probiotic, were compared, it was found that both species induced DC maturation; however, *Klebsiella pneumoniae* activated Th1 signal expression and *Lactobacillus rhamnosus* decreased the production of TNF- α , proinflammatory IL-6, IL-12 by immature DCs and IL-12 and IL-18 by mature DCs. Thus, the different immunological response of Gram-positive and probiotic was confirmed and it was concluded that probiotics do not affect the living body in the same way as a pathogen.

3.2. Probiotics to Improve the Immunological Quality of Colostrum

Beneficial microorganisms found in colostrum of pregnant animals prevent resistant microbial colonization and reduce their inflammatory power through mechanisms such as providing native and acquired immunity in offspring, enhancing antimicrobial activity and reducing intestinal permeability.⁴¹ Studies have shown that goat colostrum contains more bioactive components than milk and sheep colostrum, and a high proportion of *Lactobacilli* and *Bifidobacterium* have a positive immunological effect on colostrum.⁴² Diaz-Ropero et al.⁴³ found that *Lactobacillus salivarius* and *Lactobacillus fermentum* in colostrum tended to increase the production of Th1 signaling proteins such as IL-2, IL-12 and TNF- α in the absence of a stimulus, and to decrease Th1 release in the presence of a lipopolysaccharide. Fernández⁴¹ also examined the effect of these bacteria on both native and acquired immunity by activating NK and regulatory T cells and observed that probiotic microorganisms in colostrum affected IL-10 and IL-1 production more. They showed that mannan-oligosaccharides and fructooligosaccharides, a combination of pro-prebiotics, increased fecal *Lactobacillus* in pregnant dogs, so ideal IgA concentrations in colostrum could be achieved. Since these pro-prebiotics have a synergistic effect with immune compounds, they found that the longer the supplementation, the more pronounced the increase in serum and colostrum may become.⁴⁴ In humans, detectable levels of IFN γ in cord blood of *Lactobacillus* supplements have been associated with a protective association to allergens such as asthma, while high levels of TNF- α and IL-4 have been associated with a lower risk of atopy. They also observed high levels of TGF- β in women's colostrum and explained that it is a critical factor in the development of allergen-specific tolerance.⁴⁵

After *Lactobacillus* supplements administered to pregnant pigs, high levels of lymphocytes were observed in the intestinal mucosa, suggesting that probiotic microorganisms induce an immune response associated with the activation of T cells and that colostrum supplementation after birth will contribute to the passive immunity of the offspring by increasing IgG and IgA concentrations. It was also found that the *Saccharomyces cerevisiae* in its content induces the production of Th1 and Th2 signaling pathways, thus increasing the synthesis of immunological factors and protecting the cell against possible infection.⁴⁶ Beldjouhar et al.⁴⁷ reported an increase in colostrum IgG as a result of *Saccharomyces cerevisiae* supplementation to pregnant cows. This is in agreement with the study in sows by Jang et al.⁴⁸ who observed that yeast significantly improved colostrum quality due to its synergistic effect on immunity. In mares, in which passive transfer failure is most frequently observed, it was observed that when *Saccharomyces cerevisiae* was used, IgG was present even at low levels for seven hours and significantly improved the quality of persistence.⁴⁹ When the serum concentration status of *Bacillus* genus probiotic supplements in pregnant cows in different lactation groups was examined, it was observed that cows in the fourth lactation group increased immunoglobulin concentrations compared to other groups and may be successful in increasing the resistance of young animals against pathogens.⁵⁰

5. CONCLUSION

As a result, many studies have explained the mechanisms of action of probiotics such as competing with pathogens for the receptor that binds to the intestinal propria, contributing to the formation of an epithelial barrier by promoting mucin and antimicrobial peptide secretion, and activating lectin molecules and phagocytosing carbohydrates, which are the energy source of pathogens, and exposing them to death. Recent studies have investigated the use of probiotics not only to improve colostrum quality but also to increase immunologic factors in the blood serum of pregnant animals. In the light of these studies, it has been determined that probiotics increase the immune components in colostrum and develop an immunity against pathogens. However, it was concluded that no statistical difference was found or ignored in maternal serum levels and therefore a more detailed study should be conducted on this subject.

Ethical approval

This study does not require approval from the Ethics Committee for Animal Experiments.

Authors contribution

HME and SKS: Research, planning, article scanning, writing original draft & review. All authors contributed to the article and gave final approval of the version to be submitted.

Conflict of interest

There are no conflicts of interest associated with this research publication, according to the authors.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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