Alternative views on the possible treatment of certain skin diseases with goat colostrum.

Bratislava, 20.07.2018

In this report we present new insights into new treatment of certain skin diseases with preparations containing goat colostrum.

We present new and available information about colostrum as such, especially about goat colostrum and we critically evaluate the possibilities of using goat colostrum preparations in human medicine.

Based on information obtained from PubMed (National Medical Library of the National Institutes of Health), which we then confronted with our own results obtained by clinical trials at the Institute of Clinical and Experimental Dermatovenerology, s.r.o. (IKEDV).

In conclusion, we describe a range of skin diseases, in the treatment of which we tested the preparations containing goat colostrum CAPRAMEDIC®.

We have had a therapeutic bath containing colostrum (Capraderm balnea M, Capraderm balnea S), a colostrum containing cream (Capraderm AD, Capraderm AR, Capraderm Scarfix, Capraderm Viticol, Capraderm AW) and capsules containing 200mg of colostrum in one capsule (Capramilk kolostrum caps).

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An examination of goat colostrum potential in dermatology.

Inflammatory and immune system-mediated diseases show a high prevalence in almost every population and relationship to medicine as such, internal medicine (in the broader sense) and not lastly in dermatovenerology.
Inflammation of the skin is the most common medical problem in dermatovenerology. It appears in various forms, ranging from occasional exanthema with various intensities of redness of the skin, accompanied by a feeling of itching of varying degrees to chronic inflammatory dermatoses, eczema-dermatitis, rosacea, seborrheic dermatitis and psoriasis.

Several scientific congresses and meetings of dermatovenerology experts (eg, The 2nd European Workshop on Skin Immune Mediated Inflammatory Diseases (SIMID), Verona, Italy, 11th-13th October 2018) confirm the severity and timeliness of inflammatory and immune system-mediated diseases of the skin.
The aim of these scientific meetings is to find new perspectives and explanations of the etiopathogenesis of inflammatory skin diseases on the basis of novel and progressive knowledge of molecular medicine and innate immunity, leading to new research into the pathogenetic basis of various diseases as well as to the discovery of new anti-inflammatory and immunomodulatory drugs.

Immune system-mediated diseases are conditions that result from abnormal host immune system activity. The immune system over-responds or attacks the various host tissues. Autoimmunity is the means of immune responses of the organism against its own healthy cells and tissues. Any disease resulting from such an aberrant immune response is called "autoimmune disease". Autoimmune diseases are a subset of immune-mediated diseases.

The skin, as the largest organ of the human body is a major defensive barrier against the external environment and provides the first defense line against pathogens, toxins and harmful environmental conditions. This functional barrier role is mechanical and immunological and promotes microbial settlement of the skin[1]. The immune defense barrier relies on the ability of the skin to act as a complete "immunological" organ.
A classic immune response, also referred to as an adaptive immune response, is characterized by the specificity that is caused by immunological memory (specific immunity). In addition, there is another simpler defense system that reacts quickly but less specifically. This is called congenital immunity (non-specific immunity). Adaptive skin immune responses, however, are not always defensive but can also cause harmful effects (allergic or autoimmune reactions). Numerous skin diseases are caused by T lymphocytes and are therefore immunologically mediated. As a result, many dermatoses respond favorably to immunosupresive therapy administered either globally or locally.

Skin inflammation can be characterized as acute or chronic. Acute inflammation may result in exposure to UV radiation, ionizing radiation, various allergens, or contact with chemical irritants (soaps, hair dyes, etc.). This type of inflammation usually subsides within 1 to 2 weeks and is accompanied by mild tissue destruction. In contrast, chronic inflammation is the result of cell-mediated immune-inflammatory response in the skin itself. This inflammation is long-lasting and can cause significant and serious tissue damage.
The process of skin inflammation is complicated and still not fully understood. When skin is exposed to a "trigger" stimulus, UV irradiation, irritants (such as soaps or perfumes) or different allergens, cells in the skin begin to produce various inflammatory factors called cytokines and chemokines. These factors bind to specific receptors on the target cells and

stimulate the production of other inflammatory signaling substances.
Some of them cause vasodilation, others activate nerve cells and others cause immune cells to leave blood and migrate into the skin, where they then produce more inflammatory factors, enzymes, free radicals, and chemicals that damage the skin. The end result of the initial triggering stimulus is the enhancement of the large inflammatory response, which, although originally created (congenital immunity) to help the skin fight a bacterial-induced infection, actually causes considerable skin damage.

Currently, the most effective and commonly used prescription drugs for the treatment of inflammation are corticosteroids, especially glucocorticoid-related steroids. They are effective in many forms of eczema, including atopic dermatitis, allergic contact dermatitis, seborrhoic dermatitis (containing an antifungal agent) and are also effective in relieving psoriasis symptoms. In current treatment regimens, topical or oral corticosteroids dominate the majority of inflammatory skin diseases, but are usually used only in the short term as they also have negative side effects on the skin. Based on the results of scientific research and understanding of cellular and biochemical processes involved in inflammation of the skin, new and more potent topical and injected drugs have been developed to treat inflammatory skin diseases.

Recently, "biological response modifiers" - "biologicals" have been introduced into the treatment of psoriasis and arthritis. Many of these biologicals act purposefully to stop the inflammation cytokine TNFα, which plays a key role in attracting and activating immune cells. These immune cells are responsible for many symptoms of psoriasis and their inhibition reduces the symptoms of psoriasis. Similarly, the suppressive effects of topical calcineurin inhibitors on the immune system have led to the development of topical dermatologicals for the management of atopic dermatitis. While these new drugs are effective, they can cause serious side effects in the long term due to their strong immunosuppressive effects.

In recent years, continuous research has been under way to identify natural compounds that may have anti-inflammatory effects, but without the negative effects observed with synthetic immunosuppressive drugs used to treat inflammatory skin diseases.
What makes a natural compound a "good" anti-inflammatory candidate depends primarily on the ability of the compound to block the key "inflammatory mediators" produced by skin and immune cells. Two of the most important inflammatory mediators involved in skin disorders are TNFα and PGE2.

Such naturally occurring antioxidant anti-inflammatory agents include various plant extracts as well as milk products from various livestock - e.g. goat colostrum.

Human skin microbiome (Skin microbiome, Skin microbiota)
Our skin is the home of millions of bacteria, fungi and viruses that make up the skin microbioma (formerly referred to as the normal microbial settlement of the skin). Like in our gut[2], skin microorganisms have an important role to play in protecting against pathogen attack, digesting our immune system, and disrupting natural products.[3,4]

As the largest organ of the human body, the skin is colonized by useful microorganisms and serves as a physical barrier to prevent the pathogen invasion. If the barrier is damaged or when the balance between commensal microorganisms and pathogens is disturbed, skin diseases or even systemic diseases may occur. Different places on the skin are categorized according to their physiological properties, ie they are sebaceous (greasy), wet or dry. Study of the composition of microbiom at various sites is valuable for elucidation of the etiology of

common skin diseases, which often have predilection sites, e.g. atopic dermatitis in cubic holes[5] and psoriasis on lactides.[6]

Traditionally, microbial settlement of the skin has been cultivated. However, this method favors growth by the kind of microorganisms that yield more in terms of artificial growth and underestimates the overall diversity of microbial settlement.

In order to capture the entire width of the microbial settlement (microbiom), sequential methodology was used. The sequential approach uses sequence variation in taxonomic markers as molecular fingerprints to accurately identify the entire width of microbial settlement.[7] For bacteria, the 16S ribosomal RNA gene (rRNA) is used, the inner transcribed region of the eucaryotic ribosome gene-spacer 1 (ITS1).[8]

Composition of skin microbial on healthy skin.
If we want to monitor the changes in the microbiome and its association with the disease state, we must first determine its condition in the skin of healthy individuals together with a possible normal deviation.

In healthy adult subjects, it has been found that microbial settlement of the skin primarily depends on the physiological characteristics of the locus of the skin being examined and changes in the relative amount of bacterial species bound to a moist, dry or sebaceous (sebaceous) microgeneous environment. Lipophilic Propionibacterium was dominated by sebaceous sites, while wetted bacteria such as Staphylococcus and Corynebacterium were preferentially detected in damp areas, including cubital and popliteal wells.

Unlike bacterial settlement, the composition of fungi settlement was similar throughout the human body regardless of the physiological characteristics of the site of the investigated skin. The Malassezia fungi predominated in the base of the body and arm while the legs were colonized by a more diverse combination of Malassezia spp., Aspergillus spp., Cryptococcus spp., Rhodotorula spp., Epicoccum spp. and others. Bacteria were found in large amounts at all sites of human skin, and the fungi were the smallest.[9]

The human microflora is starting to build up after birth. In addition to the method of delivery (vaginal delivery, section), breastfeeding is decisive for the profiling of the microbial community even though breast milk has long been considered sterile. In fact, the baby is the main source of probiotic bacteria representing the genera Lactobacillus, Enterococcus and Bifidobacterium.

The process of microflora building has stabilized in the first 2-3 years of life. In the course of life, the microbial composition changes, the diversity and the number of bacteria increase. The greatest complexity occurs during adulthood, with hundreds of phylotypes dominated by Bacteroidetes and Firmicutes. Each individual achieves a homeostatic stage of intestinal microflora composition, which remains a relatively stable majority of adulthood.[2]
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The relative abundance of cutaneous microbial species is being restructured during puberty when elevated hormone levels stimulate sebaceous glands to produce more sebum. Thus, the skin of post-pubertal individuals promotes the expansion of lipophilic microorganisms such as Propionibacterium spp. and Corynebacterium spp. and fungi of Malassezia spp.
In contrast, pre-pubertal infants have larger amounts of Firmicutes (Streptococcaceae spp.), Bacteroidetes and Proteobacteria and a more diverse fungal flora.[9]

Crosstalk between the immune system and the skin microbioma.
The immune system has evolved closely with resident microorganisms in the skin to ensure the coexistence of compensatory functions and the removal of possible pathogens. In order for this activity to be optimal, skin microbioma, epithelial cells and the innate and adaptive part of the immune system need to communicate effectively. This communication can trigger keratocytes by recognizing microorganisms, especially pathogen-associated molecular formulas (PAMP), by recognizing receptor patterns (PRRs).[10]

Skin commensal microorganisms are necessary for immune system maturation.[11] During the postnatal period immature immune system allows colonization by microorganisms without the presence of inflammatory reactions.[12] After this initial tolerogenic period, various microorganisms have been shown to produce distinct effects on the immune system. Staphylococcus epidermidis skin colonization has been shown to induce elevated cytokines interleukin-1α (IL-1α), which stimulates skin T cells to produce cytokines that contribute to host defense and skin inflammation.

Skin microbial and innate immunity.
Epidermal keratinocytes release antimicrobial peptides (AMPs) such as cathelicidins and β-defensins that make up most of these AMPs. AMPs, which also produce sebocytes (highly specialized epithelial cells producing sebum - skin sebum), provide microbicidal activity against pathogens and may also trigger an inflammatory response. Some of these AMPs are actually microbiologically controlled.

Further response of skin cells to the presence of bacterial pathogens is through pattern recognition receptors (PRR).

The IL-1 cytokine is necessary to trigger and amplify the immune responses, and it is believed that the acute immune response is affected by the interaction of the host skin of the commensal bacteria. Colonization of Staphylococcus aureus with barrier-induced skin increases the expression of IL-1β, IL-6 and TNF-α, demonstrating the key role of Staphylococcus aureus in promoting skin inflammation in atopic dermatitis.

Skin microbial and adaptive immunity.
The skin microbe is capable of supporting immune responses of both innate and adaptive immunity to limit pathogen invasion and maintain homeostasis.[13]

The adaptive immune response does not appear alone, it is only an extension of the innate immune response. The increase in IL-1 production is followed by the production of IL-17 and interferon-γ (IFN-γ) from dermal T cells.[11]

Lactoferrin.
Lactoferrin (LF) is a 80-kDa multiform protein from the group of iron-binding glycoproteins transferin.[14] This protein, composed of about 700 amino acids with high homology among

animal species, is considered to be a multifunctional glycoprotein, mainly found in colostrum, milk,[15] tears and saliva.[16]

Among its main physiological tasks, recently described, the regulation of iron homeostasis, host defense against a wide range of microbial infections, anti-inflammatory activity, regulation of cell growth and differentiation as well as protection against cancer and metastasis.[17] Lactoferrin has an antibacterial action, modulates the overall immune response and protects the host prior to viral infection. The concentrations of lactoferrin are locally increased in inflammatory diseases, arthritis and allergic inflammation.[18]

The role of lactoferrin in the host defense against microbial infection.
Lactoferrin is rapidly mobilized to help defend the host at the site of infection throughout the body. The ability of this protein to act as a broad spectrum antimicrobial on the basis of several different antimicrobial properties was demonstrated.

The first antimicrobial property of lactoferrin is a bacteriostatic action. Bactericidal activity is related to the ability of lactoferrin to bind directly to the outer membrane of Gram-negative bacteria, which causes rapid release of lipopolysaccharides (LPS), resulting in increased permeability and membrane damage of microorganisms.[19]

Isolation of iron with lactoferrin inhibits the formation of bacterial biofilm Pseudomonas aeruginosa (microbial bacterial formation) and loss of airway activity in cystic fibrosis (CF) patients who are particularly prone to chronic infection and Pseudomonas aeruginosa biofilm.

Lactoferrin can protect epithelial cells from microbial infection by inhibiting the intracellular invasion of pathogenic bacteria.[20] Lactoferrin can also protect against proteolytic activity of the protein or indirectly by stimulation of the host immune system. Until today it is unclear whether the antimicrobial properties of lactoferrin are related to its direct action against microbes or activation of the immune system, but both effects appear to be involved in the therapeutic effect.[21,22] We present a review of the lactoferrin immune response against pathogens (Table 1).

Antiviral activity.
Although lactoferrin generates antiviral activity against enveloped viruses, it is currently believed to have antiviral activity against a wide range of RNA and DNA viruses.[23]

Antifungal activity.
Candida albicans is one of the most common causes of vaginal infections.[24] The adhesion of this yeast to the vaginal epithelium can be prevented by the action of lactoferrin. Lactoferrin in vivo inhibits the growth of Trichophyton mentagrophytes and Trichophyton rubrum, the two main dermatophytosis developers.[25]

Antiparasitic activity.
Lactoferrin exhibits antiparasitic activity against Entamoeba histolytica, Trichomonas faetus, Trypanosoma cruzi, Trypanozoma brucei, Plasmodium falciparum, Toxoplasma gondii and Eimeria stiedai.

Anti-inflammatory function of lactoferrin.
Lactoferrin reduces the inflammation response caused by microorganism exposure. This protective effect of lactoferrin involves the inhibition of the production of several

proinflammatory cytokines including tumor necrosis factor alpha (TNFα), interleukin-1β (IL-1β) and IL-6 and an increase in anti-inflammatory cytokines including IL-10.[26,27]. The anti-inflammatory role of lactoferrin exceeds its activity against inflammation induced by microorganisms. Lactoferrin levels increase in various inflammatory diseases including neurodegenerative disease,[28] Inflammatory Bowel Disease,[29] allergic skin and lung diseases[18], and arthritis.

The anti-inflammatory activity of lactoferrin may result from a direct effect on the modulation of cytokine production by neutrophils, monocytes, macrophages and lymphocytes through receptor-mediated signaling pathways.

Immunomodulatory function of lactoferrin.
Lactoferrin has a strong modulating effect on the adaptive immune system by accelerating the maturation of T cell precursors to competent helper cells and differentiation of immature B cells into antigen presenting cells.

Development of microorganism-stimulated immunity.
The main stimuli that induce postnatal ripening of the mammalian immune system are signals from the microbial environment, the comensus microflora of the gastrointestinal tract, but also infections in the gastrointestinal and respiratory tract.[31] Lactoferrin is an important defensive component of colostrum and mature milk, which supports the hypothesis that its function protecting the intestinal barrier of newborns.[32]

The role of lactoferrin in the immune system - The interaction of lactoferrin with (APC).
Antigen presenting cells (APCs) are critical to maintaining tissue homeostasis and innate immune responses to macrophages, dendritic cells and B cells. This reaction takes place via the major histocompatibility complex II (MHC II) as well as the combination of the innate and adaptive immune response.

Macrophages are high-phagocytic cells that suppress infection by direct intracellular killing of microorganisms or cytokine secretion to inhibit their replication and participate in type II inflammatory processes and tissue repair processes.[33,34,35] Dendritic cells are a heterogeneous population of cells that are highly specialized in recognition of the antigen and play a key role in the immune system by controlling immunity and tolerance. B cells use specific surface receptors to capture foreign antigens and present their associated epitopes to T cells.[36,37]

Lactoferrin also contributes to the suppression of the production of proinflammatory cytokines and interferon-type I (IFNα/β), which affects the ability of macrophages to present antigens of antigen-specific CD4 + T cells in the adaptive immune system.[38] Lactoferrin may increase the phagocytic activity of infected or inactivated macrophages.[39] IL-12, one of the major cytokines produced by macrophages, is a key modulator of IFNα.

Dendritic cells form a group of functionally related phagocytic cells that control T cell differentiation and lead to the memory T cell function.[40]
Lactoferrin activates specific T cells by modulating dendritic cell function.[41] (Figure 1).

Lactoferrin modulates antigen-specific adaptive immune responses
The key immunomodulatory function (APC activation, maturation, migration and antigen presentation) that may be mediated by lactoferrin is the bridging of innate and adaptive cellular functions for T and B cell responses. Lactoferrin acts on B cells that are antigen

presenting cells to allow their subsequent interaction with T cells, which improves the increase in antibody response (Figure 1).

The effect of lactoferrin on the T cell population can be further subdivided in terms of cell subclasses. The adaptive immune response is dominated by T cell activity, which includes various functions.[42]

Lactoferrin may reduce allergic rhinitis, which reduces inflammatory responses as it increases the expression of Th2, Th17 and regulatory T cells, resulting in inhibition of T cell activation and decrease in the release of inflammatory factors (IL-5 and IL-17), and consequently to alleviate the inflammation.[43] Lactoferrin induces Th1 polarization in diseases where the ability to manage infection or tumor development depends on a strong immune response.[44]

Protection against cancer and metastasis.
Various in vivo studies also indicate that inhibition of tumor cell growth by lactoferrin may be related to the ability of this protein to induce apoptosis of cancer cells by activating the FAS signaling pathway in cancer cells.[45]

Lactoferrin as a regulator of organogenesis.
In recent years, information on new lactoferin activities in the regulatory function of bone morphogenesis is available. It has been shown that lactoferrin prevents bone resorption and by reducing apoptosis it promotes the growth and development of osteoblast cells by stimulating proliferation.[46] Furthermore, lactoferrin has been shown to increase osteoblast differentiation and inhibit osteoclastogenesis. These new findings suggest that administration of lactoferrin could potentially be of therapeutic use for the treatment of osteoporosis.[47]

Tab. 1 Lactoferrin immune response against pathogens. Modified by (48)

Mechanism of lactoferrin action	Target pathogen		Reference
Enhancing of phagocytosis	Gram-Positive bacteria:		21,49,50,51,38
		Streptococcus mutans	
		Staphylococcus epidermidis	
		Staphylococcus aureus	
	Gram-Negative bacteria:		
		Pseudomonas aeruginosa	
		Burkholderia cepacia	
		Burkholderia cenocepacia	
		Porphyromonas gingivalis	
	Virus:		
		VSV (Vesicular Stomatitis Virus)	
	Fungi:		
		Candida spp.	
		Aspergillus fumigatus	
	Parasites:		
		Entamoeba histolytica	
		Babesia caballi	
		Trypanosoma cruzi	
Biofilms inhibition	Gram-Positive bacteria:		
		Staphylococcus epidermidis	
	Gram-Negative bacteria:		49,23,25,52
		Porphyromonas gingivalis	
		Prevetella intermedi	
		Pseudomonas aeruginosa	
		Burkholderia cepacia	
		Burkholderia cenocepacia	
		Escherichia coli	
		Mycobacterium bovis	
Positive domain union with negative charges on microorganisms	Gram-Negative bacteria:		21,53
		Escherichia coli	
	Parasites:		
		Toxoplasma gondii	
		Eimeria stiedai	
Modification of the interactions of microbes, with the host cells, or with the extracellular matrix	Gram-Positive bacteria:		49,23
		Bacillus subtilis	
		Klebsiella pneumoniae	
		Streptococcus mutans	
	Virus:		
		Rotavirus	
		Enterovirus	
Inhibits LPS-mediated activation	Gram-Negative bacteria:		21,54,55
Induction of apoptosis	Fungi:		56
		Candida albicans	

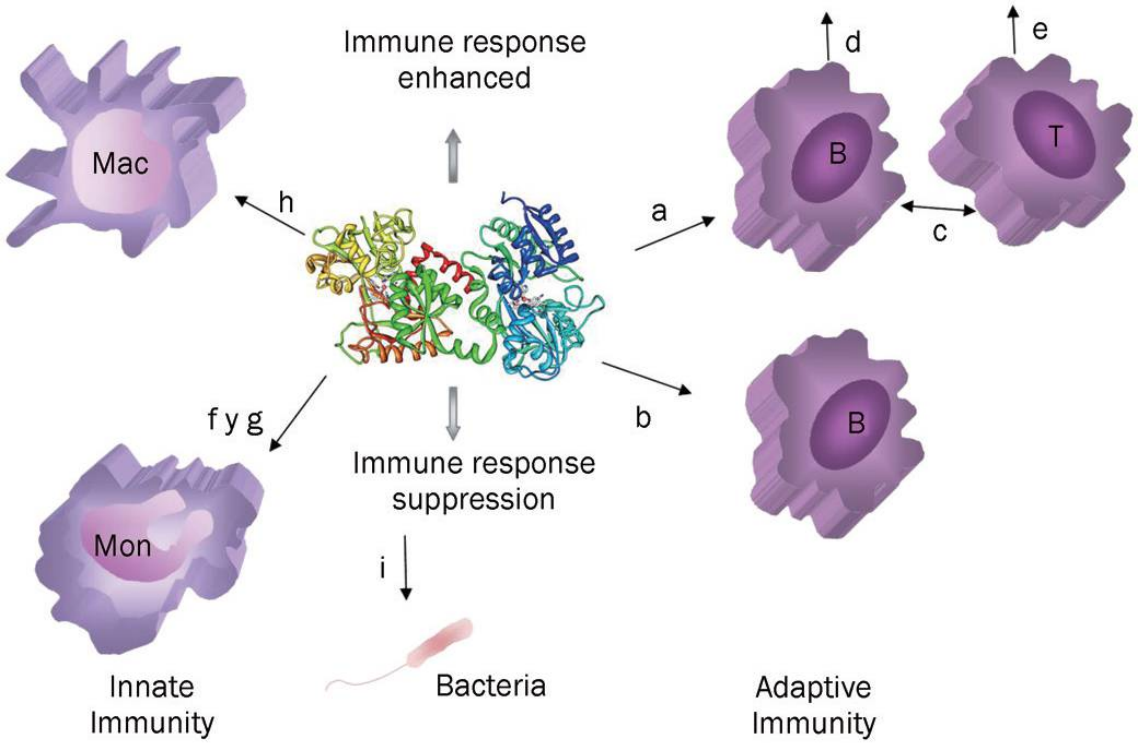

Fig. 1 Schematic representation of the effect of host lactoferrin on immune cells. (a) promotes maturation of B- and T-lymphocytes; (b) negative regulation of B-lymphocytes by binding to LPS; (c) interaction of B- and T-lymphocytes; (d) induces IgA and IgG secretion; (e) promotes proliferation of T-lymphocytes; (f) reduces the secretion of IL5 and IL10; (g) reduces NFκβ activation of monocytes; (h) enhances phagocytic macrophage activity; and (i) prevents the interaction between LPS and CD14 as TLR4. B, B lymphocytes; T, T lymphocytes; Mf, macrophages; Mon, monocytes; No, Neutrophils. Modified by (48)

Colostrum.

Colostrum is a light yellow color and also called "breast milk" is the precursor of milk that produces mammary glands of mammals immediately before and during the first hours after birth. About 2-5 days after birth he no longer produces and gradually converts it into full-fledged milk.[57]

In all mammals other than primates, colostrum is crucial for the survival of the offspring because high concentrations of immune factors are transmitted to the offspring only by colostrum. Colostrum contains many specific bioactive substances necessary for growth, such as immunoglobulins, antimicrobial peptides, and growth factors. Immunoglobulins regulate the immune response and protect against inflammatory diseases and autoimmune diseases and help to heal and restore damaged tissue. Anti-inflammatory agents reduce the irritation typical of autoimmune diseases. Colostrum is the only natural source of two growth factors that promote cell proliferation and regeneration.

Lactoferrin is one of the most effective biologically active substances contained in colostrum. The human colostrum concentration of lactoferrin is 5,3±1,9 mg/ml and after the first month of lactation this value is approximately 1 mg/ml.[58] Colostrum contained in breast milk contains all the immune factors necessary for activation and regulation of the response of the immune system.

In humans, some immunopaths are transmitted through the placenta. Human colostrum is particularly beneficial; but if a human newborn does not get colostrum, death is not the same as other mammals. As with other mammals, the first feeding of newborn colostrum significantly affects its health and well-being, and this effect lasts the rest of its life. Because the neonatal immune system is not yet fully developed, it is very prone to the adverse effects of pathogens, antigens and allergens. Colostrum plays a crucial role in supporting the immune system of the newborn during its development.[59]

The colostrum contains proline (amino acid) rich peptides, so-called colostrinin, a powerful immunomodulator that can reduce the exaggerated immune response typical of autoimmune diseases. Prevents lymphocyte overproduction and stimulates T-cell production.
The advantage is that the use of this substance is not species-dependent, and therefore that a person can also use goat colostrum.

Other important components of colostrum are the immunoglobulins and lactoferrin. They can inhibit both viruses and bacteria throughout the recipient's body. Autoimmune diseases can trigger and complicate attacks of various microorganisms. In addition, lactoferrin is capable of stopping the production of certain inflammatory agents (cytokines, interleukin IL-β1 and TNF-α). Relieving inflammatory irritation is another positive step against the development of autoimmune diseases by alleviating concomitant pain and complications.

Lactoferrin has some important properties and effects:

- antimicrobial effect
  - antibacterial effect
  - antiviral effect
  - antimycotic effect
  - antiparasitic effect
- anti-inflammatory effect (very strong)
- antioxidant effect (protects the organism against the harmful effects of chemicals)

- works against the development of some forms of cancer and metastasis

Growth factors present in colostrum also help repair tissue damage in autoimmune diseases. EGF (epithelial growth factor) can reverse skin cell destruction; TGF (transforming growth factor) present in colostrum in two forms can help prevent protein breakdown and induce tissue regeneration. IGF (insulin-like growth factor) promotes glucose transport in the blood of diabetics.

Growth factors in colostrum, therefore, primarily have anti-inflammatory effects, can help repair damaged cells and thus reduce intercellular spaces, which prevents further leakage of toxins into the body.[60,61,62]

The concentration of lactoferrin in goat colostrum is higher than in cow's milk (455,8-2058,3 mg/dl in goat colostrum and 575,0 mg/dl in cow colostrum).[63] The concentration of lactoferrin from goat colostrum is high in relation to the amount of goat colostrum, which is expressed in dry matter content (goat colostrum 25,43-38,96%, cow colostrum 18,30%).

Goat's milk contains milk ingredients such as lactoferrin, immunoglobulins, growth factors, and lactoperoxidase as an antimicrobial agent. Lactoferrin in milk is able to bind metal ions to microorganisms and thereby reduce microbial growth. Lactoferrin may be used to enrich or fortify milk. High lactoferrin levels in milk improve the quality and value of milk, especially its microbiological quality. The physiological functions of lactoferrin are mainly 1) the source of iron for infants and children, and 2) the antimicrobial factors in the gastrointestinal tract of infants and children.[65,66,67]

Because colostrum contains substances with immunomodulatory properties, it has come to the attention of some pharmaceutical and nutritional industries as a dietary supplement.[68] Lactoferrin, present in cow colostrum at a concentration of 500 mg/100 g, is referred to as GRAS (Generally Recognized As Safe, FDA), which is currently used in many countries as a nutritional supplement for infants. To date, no adverse effects on its use have been documented.[69] BF-L dry milk was first developed in Japan in 1986. Currently, lactoferrin is found in various products such as yoghurt, cream and milk and other beverages.[70]

Dairy goat breeding can provide valuable animal proteins with high biological and essential minerals and vitamins. In complex studies, goat's milk has been shown to have a similar nutritional value to cows' milk, and can be used as an alternative to cow's milk for the rehabilitation of children suffering from inadequate nutrition.[71]

A list of diseases for which local or total administration of the goat colostrum is recommended.

Tested preparations containing goat colostrum CAPRAMEDIC®.
Therapeutic bath containing colostrum (Capraderm balnea M, Capraderm balnea S)
Colostrum containing cream (Capraderm AD, Capraderm AR, Capraderm Scarfix, Capraderm Viticol, Capraderm AW)
Capsules containing 200mg of colostrum in one capsule (Capramilk kolostrum caps).

Dermatitis irritativa, Dermatitis contacta
Chronic inflammation of the skin by the accumulation of various harmful effects after exhaustion of skin protection mechanisms. Following the application of cream with goat colostrum, the rate of corticoid-like effect was relatively rapid, which was also observed in other inflammatory dermatoses.[72,73,74]

Dermatitis atopica (atopic eczema)
Atopic eczema (atopic dermatitis) is a chronic inflammatory and immune system-mediated skin disease that affects infants, children and adolescents in particular. The tendency for this disease is born from generation to generation along with a tendency to asthma asthma, allergic rhinitis and some other allergic reactions (the term atopy). Many internal and external influences are involved in its creation.[75]

Etiopathogenetically determined changes in stratum corneum may result in dysbiosis by a microbiome that alters the variety and variety of commensal species that disrupt the function of the skin barrier and trigger atopic dermatitis.[76,77]

Atopic eczema is among the most common skin diseases occurring in almost 20% of schoolchildren. If atopic eczema is present in both parents, the likelihood of eczema in the child is 81% if eczema is one of the parents, then 56%.[78]

The basic characteristic of the patient's skin with atopic eczema is excessive dryness caused by insufficient and incorrect function of the sebaceous glands, insufficient activity of sweat glands and reduced ability to bind water in the skin. We are talking about a broken barrier skin function in general. Increased dryness leads to itching, scratching and developing typical symptoms. An impaired barrier function is also associated with increased susceptibility to viral, bacterial or fungal infections of the skin.[79]

The course of the disease is divided into three phases:

- **Infant form**
  Typically, it begins in the 3rd month of life by sowing red puddings to blisters with scales or wetting in the middle of the cheeks, but it can spread to the flesh, limbs and the whole head. The illness is accompanied by a tingling to boutous itching that causes sleep disturbances.
- **Child form**

Eczema is gradually withdrawn from the face to the sites typical of this phase, i.e., j. into the elbow and underneath holes. The wrists start to show slight signs of roughing and cracking of the skin. Pruritus and subsequent scarring give rise to new skin manifestations.

- **Adult form**
  In 10% of patients, atopic eczema can only start in adulthood. Locations of affected skin are the same as for children, but skin and neck skin is affected and eczema changes throughout the skin (Erythrodermia).

Dermatitis seborrhoica

Seborrheic dermatitis is a chronic skin disease. It occurs in places with increased sebum production. The cause of seborrhoeic dermatitis is not known, but clinical manifestations aggravate stress, alcohol consumption, chocolate and climatic conditions. It is also contemplated the effect of reduced diversity (disbiosis) in the skin microbiome.
Symptoms of the disease vary, depending on the age of the patient and the localization of pathological changes, often occurring as red deposits with greasy yellow scales on the surface, sometimes also wetting with scratch formation. They appear mainly in the hair, on the face around the nose, behind the ears, in the armpits, under the breasts and chest, in small children and in the diaper area.[80]

Keratosis actinica (actinic keratoses)

Actinic keratosis is a rough, scaly patch on the skin that develops after exposure to the skin due to sunlight. The most common manifestations are on the face, lips, ears, backs, hands, forearms on the head and neck of older adults.
Bearings of actinic keratoses grow slowly, up to years, and usually do not induce any other subjective difficulty. A small percentage of lesions of actinic keratoses can eventually pass up to skin cancer. Clinically, actinic keratoses manifest as coarse, dry or scaly skin, usually less than 2.5 cm in diameter, with a slight elevation or bulge in the upper layer of the skin, or the formation of hard deposits on red to brown colored skin. Sometimes slight itching or burning in the affected area may be present.

Acne vulgaris (but also other forms)

It is a multifactorial chronic inflammatory disease of sebaceous glands and hair follicles, which is manifested in the most sebaceous glands, on the face and on the upper chest (in so-called seborrhoic areas). However, it may also penalize the shoulders and the entire back.
Acne affects almost all young people in puberty - about 85% of people aged 11-30 years, and about 3% of people over 30 years of age.
Genetic factors, sebaceous gland activity, endocrinological effects, microbial infection (Corynebacterium acnes I, Corynebacterium acnes II., Corynebacterium granulosum, cocci, especially Staphylococcus epidermidis, yeast microorganisms Pityrosporum ovale and Pityrosporum orbiculare), climatic influences, chemical factors. Most recently, it is thought of a reduced diversity (disbiosis) in the skin microbiome, which could be the trigger of the disease.[75]
Acne is characterized by the formation of comedones - papules - papules - red rashes, pustules - purulent rashes (even in depth), painful nodules - knots and hooves. The illness usually persists for several years. Acne superficialis heal without scar, deep acne with scar. Untreated or incorrectly treated acne can leave scars on the skin, causing psychological problems throughout life.[81,82,83]

Main Factors for Acne:
• genetic predisposition,
• increased sebum production,
• hormonal effects,
• bacterial settlement of the skin.

Candidosis (skin and mucous form)
Acute, subacute and chronic inflammation induced by the yeast microorganisms Candida albicans, C. tropicalis, C. guilliermondi, C. kruzei. Potential pathogenic factors for candidiasis include genetic predisposition, endocrinopathy, malignancies, immunodeficiency, pregnancy and oral contraception, hypochromic anemia, increased risk of exposure to the workplace, diabetes and oral application of broad spectrum antibiotics.

A particularly dangerous fungus is the presence of fungi or yeasts in the blood. Most commonly, it is caused by Candida species (also referred to as Candida or Invasive Candidiasis) but can also be caused by other fungi, such as Aspergillus or Cryptococcus. It usually occurs in patients with immunosuppression or immunodeficiency, in oncology patients or in patients with venous catheters. Recently a hypothesis has emerged that even patients taking infliximab (although otherwise immune system fully functioning) may be at risk of fungus.

Candidiasis infection is most often found in the place of a moist fume (intertriginous sites), and vaginal candidiasis is also common.[84,85,86]

Herpes infection
Herpes simplex virus (HSV) affects more than a third of the world's population and is responsible for a wide range of clinical manifestations, from mild manifestations, through discomfort to the death of the patient. There are 2 types of HSV - HSV1, which is found mainly on the face (Herpes simplex labialis), and HSV2, which is predominantly responsible for genital herpes (Herpes simplex genitalis).[87,88,89,90]

Xerosis cutis
Xerosis cutis is a medical term for abnormally dry skin. Dry skin occurs frequently, especially in older adults. This can be a small and temporary problem, but it can cause discomfort. It is more common in cold winter months and in diabetics. Older people are more prone to developing Xerosis cutis, because as we age, our sweat glands and sebaceous glands are less active mainly due to changes in hormone production. This makes Xerosis cutis a common problem for older people over 65 years of age.

Rosacea - Dermatitis perioralis
Rosacea is a chronic, inflammatory skin disease of the face (forehead, nose, chin and face). Skin inflammation - transient, later persistent redness, papules (nodules) and pustules (pus blisters), visible veins and / or facial swelling may be symptoms of rosacea. Often, however, they are confused with symptoms of allergy or acne.

According to today's understanding, inflammatory responses, disorders of natural immune mechanisms, dysregulation in the nervous system, as well as changes in blood and lymphatic vascular system regulation play a major role. Most recently, there is considered a reduced diversity (disbiosis) in the skin microbiome, which could be a trigger of the disease.[75] The effect of increased density of Demodex mites in hair follicles was also found to develop rosacea. Therefore, it is believed that high colonization of the skin by Demodex mites may be the cofactor of the inflammatory response underlying the disease.

Rhinitis allergica

Lactoferrin may improve the manifestations of allergic rhinitis, which reduces the inflammatory response as it increases the expression of Th2, Th17 and regulatory T cells, resulting in inhibition of T cell activation and (IL-5 and IL-17), and then to alleviate the degree of inflammation.[43] Lactoferrin induces Th1 polarization in diseases where the ability to manage infection or tumor development depends on a strong immune response.[44]

Psoriasis vulgaris (but also other forms)

Psoriasis is a non-infectious inflammatory and immune system-mediated skin disease. It shows up with the burning of lighted and flaky bearings on the skin. It occurs almost equally in both men and women and often occurs between the 15th and 20th years of life but also between the 40th and 50th years of life. The life of a patient with psoriasis is very demanding. Skin cells are renewed seven times faster than a healthy human. As a result, red scales of varying sizes, which can also bleed, may complicate blunted blisters. In chronic psoriasis, the disease deposits are most commonly found in hair, laces, knees, in the cross and in the wart area. A serious complication of patients with psoriasis is psoriatic arthritis. At other times, the view of etiopathogenesis is significantly altered, and there is a false assertion that psoriasis is an autoimmune disease.91 According to recent hypotheses, the trigger factor is change - dysbiosis in psoriatic lesions with reduced diversity of the microbe that triggers a cascade of IL-17A overproduction and TNF-α.[72,75,77,83]

Vitiligo

Vitiligo is a chronic skin disease with typical skin pigment loss without previous skin lesion. Skin manifestations result from the lack of melanin (brown skin dye) in the skin. The inability of melanocytes to produce a pigment on a certain part of the skin proves the presence of an active mechanism that prevents them from moving. However, the exact cause is not yet clear.

Vitiligo occurs in both sexes at any age. Origin may be blurred or suddenly after tanning, when circular or oval bearings of varying sizes are formed, and tend to collapse into large areas. It often occurs in places such as face, axilla, incites, areola mammae, genitalia. Bearings are milky-colored, normal relief and thickness, precisely bounded by hyperpigmented edges of 1-5 mm wide, which melts into the color of the normal skin into the periphery. Hair may be full or depressed (poliosis) only in the center, increased sensitivity to the sun's rays, and generalization may also occur.

Vitiligo has so far been considered a complex syndrome where various disorders lead to the same phenotype - melanocyte loss. Some studies indicate dysbiosis in vitiligo lesions with reduced microbial diversity, and firstly try to define a specific vitiligo microbe.77

Even keratinocytes (the main cell of the skin) affect melanocytes. Keratinocytes in depigmented skin can create a changed environment than those in normal pigmented skin. These changes may reduce the production of keratinocyte-derived melanocyte growth factor and thus the passive death of melanocytes and the development of vitiligo.[92]

Diabetic Foot, Diabetic Foot

Diabetic foot is a framework term for lower limb disorders that occur mainly in diabetics. According to WHO, a diabetic foot is characterized as ulceration (ulcers) or leg injury in diabetic patients caused by neuropathy and ischemia, which is usually accompanied by infection. Annual diabetic foot disorder of about 41 000 new patients.

In conservative treatment, the primary task is to strictly correct the disorder of glycid metabolism while avoiding hyperglycemia. The wounds are treated with suitable dry dressings or wet wound healing to accelerate the granulation and epithelization phase.[93,94,95] At the same time, antibiotics (against staphylococci, streptococci and anaerobic bacteria) are administered.[78,96,83]

The degree of disability in the diabetic foot is evaluated according to Wagner's classification.
Stage 1 - skin disorder (dermis)
Stage 2 - deeper subcutis (subcutis)
Stage 3 - deep fascia engagement (eg plantar fascia)
Stage 4 - local gangrene
Stage 5 - gangrene of the whole leg

Striae cutis distense

Wrinkles

A summary of the results of the clinical trials of preparations containing goat colostrum CAPRAMEDIC®, a summary of the current treatment and the pharmacoeconomics is given in Table 2.

Table 2. Summary of clinical trial results with goat colostrum anf pharmacoeconomics.

Disease	Current therapy options	Goat Colostrum therapy	Reference
Dermatitis irritativa, Dermatitis contacta	Local corticosteroids and antibiotics.	Nearly immediate healing effect - corticoid-like effect.	72,73,74
Dermatitis atopica	The disease can not be cured, it can only be managed (to get the patient into the symptom phase and keep it as long as possible). Healing spa, local corticosteroids and antibiotics, antibiotics overall, daily skin cleansing, antihistamines overall, UVB phototherapy, frequent hospitalization. Treatment is time-consuming, affects the entire family of the patient.	In light and moderate forms, after the first bathing with colostrum content, the feeling of itching is lost, the skin is preserved, it is trained, the need for antihistamines and antibiotics is reduced. Daily care is needed.	75,76,77,78, 79
Dermatitis seborrhoica	Local anti-inflammatory preparations, antibiotics, antimycotics, corticosteroids, magistraliter preparations, preparations against Malassezia furfur	Clinical improvement and withdrawal of itching after several applications of cream.	80
Keratosis actinica	Electrocoagulation, liquid nitrogen, Er: YAG laser, PDT (photodynamic therapy).	Relatively rapid clinical improvement and improved lession fading.	
Acne vulgaris	Treatment is both local as well as general, antibiotics, magistraliter preparations, local and total retinoids, in patient treatment.	There is a clinical improvement in the disease state. Local and general treatment.	75,81,82,83
Candidosis	Vaginal tablets, total treatment with antimycotics.	Already after the first application of the bath and cream improvement, the retreat of the itching.	84,85,86
Herpetic infection	Both local and general virostatic treatment.	Rapid healing of lesions (under clinical trials in IKEDV).	87,88,89,90
Xerosis cutis	Day care with moisturizing creams, antihistamines and neuroleptics	Rapid improvement after baths and topical application.	
Rosacea, Dermatitis perioralis	Local and generalized therapy, antibiotics, magistraliter preparations, *Demodex folliculorum* active substances, local and generalized retinoids, in patient treatment.	Clinical improvement after several applications	75
Rhinitis allergica	Antihistamines, Ketotifen.	Improvement while used orally	43,44
Psoriasis vulgaris	Keratolytic topical, magistraliter preparations, vitamin D3 derivatives, total retinoids, PUVA treatment, UVB phototherapy, XTRAC laser, frequent hospitalization, biologics.	Keratolytics, spa, cream as well as total colostrum treatment (under clinical trials in IKEDV).	72,75,77,83
Vitiligo	Local corticosteroids, calcineurin inhibitors, PUVA treatment, UVB phototherapy, XTRAC laser, pseudokatalase. Treatment is time consuming and financially demanding, PA only spends 20-25 exposure phototherapy a year, treatment takes up to several years, the results are not encouraging.	Very early onset of pigmentation in patients responding, after a few months, complete repigmentation may occur.	77,92
Diabetic foot	Daily application of medical aids for wet wound healing, antibiotics locally and globally, as well as surgical treatment of defects.	In clinical trials at the National Endocrinology and Diabetology Institute in Ľubochňa.	93,94,95, 78,96,83
Striae cutis distense	Various topical preparations to improve collagenogenesis	After 2 months up to 25% improvement.	
Vrásky	Various topical preparations to improve collagenogenesis	Improved skin texture, filling wrinkles.	

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