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BOVINE COLOSTRUM: FROM NUTRITION TO DERMAL THERAPY

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ABSTRACT

Colostrum is the first secretion of milk after delivery, which contains a variety of bioactive molecules such as immunoglobulins, growth factors, vitamins and minerals. Bovine colostrum (BC), also referred to as "liquid gold," contains higher levels of proteins, cytokines and antimicrobial peptides when compared with mature milk. These constituents help support the neonatal immune system, healing of tissues and cellular growth. In cosmetics, BC exhibits a number of advantages, including: anti-ageing effects through an increase in collagen synthesis and prevention of telomere loss; increased skin elasticity as a result of improved hydration by hyaluronic acid released from nylon/BC films and antibacterial effect via action of lactoferrin and lysozyme, which helps to fight acne and infection. BC also promotes wound healing and antioxidant activity against reactive oxygen species. In addition, hydrolysed colostrum extract is also said to work effectively in skin lightening by controlling melanin production. As a therapeutic, industrial use of the approach may be limited by stability and standardisation. Further investigation and better formulation approaches will make BC a versatile ingredient for effective and natural skin care agents.

KEYWORDS: Colostrum, Cosmetic, Bovine Colostrum, Anti-ageing, Lactoferrin, IGF.

1) INTRODUCTION

The initial milk produced during pregnancy and immediately after delivery, for about five

days, by milking an animal is known as colostrum or Liquid Gold. The colour of colostrum is yellow, it has a pH of about 6.4, which is slightly acidic, and its density is slightly higher than later milk. It has a much higher content of biologically active substances that affect and heal the immune system, which is the reason for its purposeful use.[1,2] A healthy cow can produce approximately 5–10 L of colostrum per milking. The name was given due to its excellent contribution to cosmetics as well as pharmaceuticals, from skin care to nutraceuticals.[3] There are many different factors which affect the composition and physical properties of colostrum, like individuality, breed, parity, pre-partum nutrition, length of the dry period of cows, and time post-partum and others. Generally, colostrum has less lactose compared to mature milk content and more fat, protein, peptides, non-protein nitrogen, ash, vitamins and minerals, hormones, growth factors, cytokines, nucleotides. The concentration of components starts decreasing rapidly in the first 3 days of lactation, excluding lactose content.[4,5]

1.1) Clinical and Long-term Benefits[6,7]

- Accelerates wound healing through growth factors (TGF-α/β, IGF-1/2, EGF)
- Shows positive effects in skin disease treatment and UV-exposed skin
- Protects cells from reactive oxygen species (ROS) damage
- Decreases skin lesions (blackheads, papules, pustules)
- Shows anti-ageing effects by improving skin elasticity
- Reduces fine lines and wrinkles through collagen stimulation.
- Protects against UV-induced skin damage

1.2) Types Of Colostrum

Although milk and colostrum are traditionally known as key ingredients in the food industry, it's now gaining popularity in the pharmaceutical and cosmetic fields because of their powerful biological benefits as well as due to their natural origin and non-toxicity. Researchers have also taken a close look at its individual components and the unique properties they offer. They show various antibacterial, antifungal, antiviral, anticancer, antioxidant, and immunomodulatory properties etc. The different types of colostrum which are used in the cosmetic field are:

a. Bovine Colostrum
b. Goat Colostrum
c. Sheep Colostrum

d. Mare Colostrum

Some formulations are also made with fermented colostrum (Hydrolysed Colostrum) and with the help of specific bioactive which are extracted from the colostrum.[1,8,9,10]

1.3) Comparison

It is found that the composition of milk or colostrum varies for different species. Colostrum in some species contains the same nutrients but in higher levels of fat, protein, vitamins, minerals, hormones, growth factors, immunoglobulins and low lactose levels. As per the research values, we can observe, the largest difference is seen in the concentration of protein content in different individuals due to their genetics, environmental conditions, and dietary factors. Bovine colostrum is richer in caseins, β-lactoglobulins, α-lactalbumin, immunoglobulins, GMP (glycomacropeptide), lactoferrin, and growth factors than normally produced milkand is listed in the following table 1.

Table 1: Comparison between different components of colostrum in different species.[1,8,9,10]

COMPONENTS	BOVINE	GOAT	SHEEP	MARE	MATURE MILK
LACTOSE (%)	2-3	4.1-4.7	3.2-4.2	6.37	4.7-5
MINERAL (%)	0.71	0.77	0.59	n.a	4.10 - 4.71
PROTEINS (%)	14-16	3.4-8.8	6.4-13.6	2.14	3.1-3.2
FATS (%)	6-7	4.1-4.9	8.2-9.1	1.21	3.6-4
LIPID (%)	22.3%	n.a	2.7 g/100 g	n.a	n.a

1.4) Properties

Bovine Colostrum- A Natural solution to all skin-related problems is the Bovine Colostrum that helps improve skin elasticity by reducing the fine lines and wrinkles. Its growth factors, proteins, anti-microbial and anti-ageing growth hormone (HGH, or human growth hormone) help in cellular regeneration, tissue healing, wound healing, antioxidant properties and many more when used daily. The chemical messengers target the dermal layer of the skin and stimulate cell growth, which then helps improve skin thickness and elasticity. Colostrum fat is found to be richer in carotene and vitamin A than normal milk, making it a great source of vitamins for cosmetic products. Additionally, it acts as a multifunctional milk that protects the skin from skin dryness caused by harsh conditions, aids in wound healing and skin tissue repair, fights microbial infections in the skin tissue, and makes the skin more elastic by increasing collagen production. It plays a crucial role as a strong and natural resource in the cosmetic industry. In the area of cosmetology, products containing colostrum generally

support skin renumeration, collagen production, wrinkle reduction, skin moisture, and skin elasticity, as well as soothe irritated skin due to colostrum's multifunctional properties. To address the literature gap on cosmetics and colostrum mentioned in our paper, further research is required beyond the existing studies.[1,8,11]

Sheep Colostrum- The research for goat colostrum is very low compared to bovine colostrum. One research published focuses on the total protein level and lipid compositions of goat colostrum, which are vital for its therapeutic efficacy, particularly in skin care and human health. In conclusion, sheep colostrum may exhibit anti-ageing, regenerative, and anti-inflammatory effects on the skin and accelerate wound healing. But there are further tests which are to be performed to confirm those activities. One study examined the efficacy of a cosmetic preparation containing sheep colostrum on acne-prone skin, with particular emphasis on the potential dermatological benefits arising from its bioactive components. The tested colostrum-based cream was found suitable for the care of acne-prone skin. It maintained the skin in good condition by reducing sebum secretion and providing adequate hydration. It shows the result of a reduced number of skin lesions typical of acne-influenced skin. It was found to be useful in completing the care of acne skin during dermatological therapies.[11,12]

Goat Colostrum- Goat colostrum is again a pure natural product containing a large amount of biologically active substances such as proteins, vitamins, minerals, antimicrobial peptides, and immunoglobulins. Therefore, it is also used for formulating therapeutic and cosmetic products based on its colostrum. The colostrum shows properties like skin protection from ageing, dermatological problems, and harmful effects of the environment. An analysis performed by the scientists comparing goat's and cows' milk found that goat's milk substances penetrate deep layers of skin more easily, since they contain oleic or caprylic fatty acid, and saturate the skin with vitamins, phospholipids, and fatty acids more quickly. This property of goat's milk is due to its high content of fatty acids.[9,13]

Mare Colostrum- Mare's milk has different major components of milk as compared to other breeds of animals. It has low content of fat and proteins and a high content of lactose. It helps detoxify the body, slows down cell ageing and has bactericidal, anti-viral, and anti-inflammatory properties. It stimulates the growth of granulation tissue in skin diseases and promotes wound healing. Aside from the nutritional content, other advantages of mare's milk are the presence of more health-promoting compounds, such as lactoferrin, orotic acid, and

lysozyme. Lactoferrin has immunomodulatory (inhibits disease activity), antibacterial, antiviral, anti-inflammatory, and antifungal properties. Orotic acid (vitamin B13) is one of the few vitamins to prevent the aging of skin. Furthermore, lysozyme is responsible for one of the mechanisms of the immune response, and it shows antibacterial properties.[14]

In today's world, skin health and personal care products are very generalised, but the components present in the cosmetic products contain harmful chemicals, allergens and toxic elements. Therefore, it is necessary to focus on cosmetic products to be manufactured from natural bio-ingredients. One such ingredient is bovine colostrum, which is now gaining interest in cosmetology. In the following sections, we will examine Bovine Colostrum in detail.

2) Chemical Constituents Of Bovine Colostrum

BC contains similar nutrients to mature bovine milk; the only difference is the variable rates of bioactive components, making BC a key component for biological processes. BC offers a rich compositional similarity, which makes BC a suitable alternative source compared to HC. BC includes higher amounts of IgG content, growth factors, and protein content, promoting muscle growth, tissue repair, and adaptive immunity (Fig. 1). As compared to HC, BC is less species-specific. Its more abundant contents result in the particularly effective general wellness and recovery of important systems.[8,9,15]

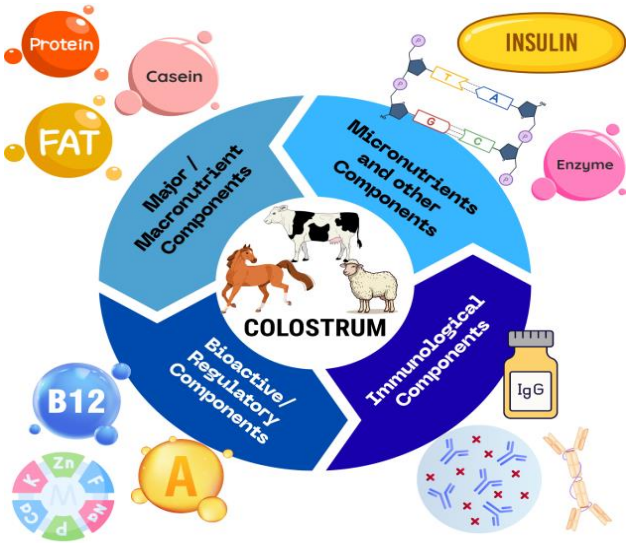

Fig. 1: Different constituents of colostrum.

2.1) Major / Macronutrient Components

These are nutritional constituents, similar to milk but in enriched form.[16]

Table 2: List of macronutrients present in colostrum.

CATEGORY	EXAMPLE	DESCRIPTION
Proteins/ Nitrogenous Compounds	Casein, Whey proteins, Peptide, Amino acid, Non-casein nitrogen	BC has higher total protein and non-protein nitrogen compared to mature milk.
Carbohydrates	Lactose (lower than in mature milk), oligosaccharide, glycoproteins, glycans	BC is relatively lower in lactose and enriched in oligosaccharides and glycan structures compared to mature milk
Lipids / Fats	Fatty acids (saturated, unsaturated), triglycerides, phospholipids, polar lipids	BC contains lipids in enriched forms; the lipid fraction carries fat-soluble vitamins and helps in the absorption of lipophilic bio-actives.

2.2) Micronutrients and other Components

These are "supportive" nutritional constituents.[11]

Table 3: List of micronutrients present in colostrum.

CATEGORY	EXAMPLE	DESCRIPTION
Vitamins	Vit A, B1, B2, B3, B12, Vit D, Vit E	Important for many metabolic processes, including bone growth and antioxidant activity. Most vitamins are higher in concentration within BC as compared to mature milk.
Minerals	Calcium, Phosphorus, Potassium, Sodium, Magnesium, Zinc	The mean concentration of many important minerals is found more in colostrum than in mature milk

2.3) Bioactive/Immunological/ Regulatory Components

These are what make colostrum distinct from regular milk. Many of these are present in relatively low concentrations but play a crucial role.[9]

Table 4: List of bioactive or regulatory compounds present in colostrum.

CLASS	EXAMPLE	DESCRIPTION
Immunoglobulins/ Antibodies	IgG(dominant), IgA, IgM	A key marker of colostrum quality confers passive immunity
Antimicrobial peptides/ Proteins	Lactoferrins, Lysozyme, Latoperoxidase, Defensins, Cathelicidins	These help inhibit the growth of pathogens and modulate microbial ecology in the gut
Cytokines, Chemokines, Growth regulators	IL's, TNF, TGF	Involved in immune modulation, Inflammation regulation
Growth factors/ Peptide hormone	EGF, IGF-1, IGF-2, TGF-β, FGF, PDGF, Insulin	These support cell growth, repair, gut maturation, tissue remodelling
ProlinePolypeptides (PRP/ Colostrinin/ Transfer factors)	Mixtures of small peptides, often Proline	Modulate Immune function, possibly via regulatory signalling pathways
Oligosaccharides/	Neutral and acidic	Serves as a prebiotic, modulates

Glycans	oligosaccharides, complex glycoconjugates	microbiota, and acts as a decoy for pathogens
Nucleotides/ Nucleosides/ RNA/DNA fragments	Free nucleotides, nucleoside precursors	These can support cell proliferation, immune response, and gut development
Hormones/Signalling Molecules	Insulin, Leptin,	May exert systemic or local regulatory effects
Antioxidants/ Enzymes/ Protective factors	Glutathione, superoxide dismutase, and catalase	Help protect the cell from oxidative stress

3) Dermal Therapies

It is important to note that among the different natural compounds that have recently gained attention, colostrum is unique for each of its components, having a different healing effect on the skin. Thanks to all these active biological components, colostrum holds an important place in skin healing, skin health, and personal care, as well as in cosmetics. (see Fig.2)

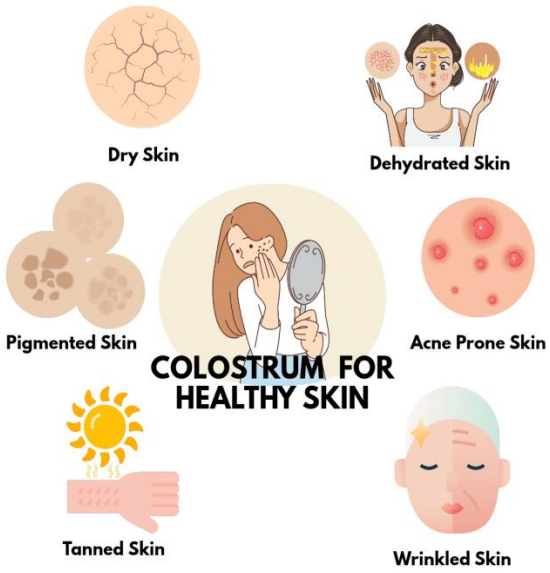

Fig. 2: Properties of colostrum.

3.1) Anti-Ageing Property

Currently, it is observed that human skin ages due to many environmental factors, such as UV rays, hormonal imbalances, ROS, moisture loss, and more. Therefore, skin ageing is multifactorial, which may result from independent causes. The most important factor that causes the ageing of the human skin is moisture loss. Youthful skin is firm, more resilient, and pliant, due to its higher water (moisture) content than aged skin. The body's production of growth hormones and antioxidants decreases with the ageing of the body, damaging the DNA, proteins, and lipids, which accelerates ageing. Telomeres help maintain the DNA

structural integrity, which is a major factor in ageing. As DNA strands shorten with age, reproduction of new cells decreases, leading to an increased risk of mortality. Telomere inhibits cell divisions, which get too damaged to generate new cells, making them inactive. To help with ageing constituents like Hyaluronic acid, Igf1, Igf2, and TGF-β show anti-ageing activity.[17,18]

3.1.1) Hyaluronic acid (HA) is a component of colostrum that can bind and retain water molecules, which helps restore the skin's moisture. HA, also known as glycosaminoglycan (GAG), is also found in the extracellular matrix fluid, widely present in prokaryotic cells to eukaryotic cells, mostly found in the skin and vitreous tissue, but also found in other tissues of the body.

3.1.2) Growth factors like IGF-1 and IGF-2 are present within the dermal matrix. Visible signs, such as wrinkles, are related to decreased collagen production in the body. Since collagen levels are lower in females than in males, they tend to have more wrinkles and other signs of ageing at the same age as males. Researchers have concluded that growth factors can stimulate dermal collagen synthesis and reverse the effects of collagenases, which help increase the amount of collagen. GFs and cytokines play an important role in skin regeneration and wound healing and are now widely used in the cosmetic industry. Numerous clinical trials show that the topical application of growth factors helps reduce fine lines and wrinkles, stimulate collagen formation, and promote the healing of chronic and normal wounds.[19,20,21]

3.1.3) Increased level of insulin-like growth factor or IGF helps improve skin ageing and can also boost collagen production through the enzyme prolidase and help reduce photo-ageing. IGF-2 activates the PI3K/mTOR pathway, which slows down the ageing of skin fibroblasts and shows faster wound healing. Low level of aquaglyceroporin 3 (AQP3) is linked to skin ageing; this pathway also increases the level of AQP3 in liver cells, which helps maintain healthy skin.

3.1.4) TGF-β Transforming Growth Factor is a group of proteins that regulate many cell processes and are strongly associated with ageing. It functions by regulating genes and proteins involved in cell proliferation, the cell cycle, reactive oxygen species (ROS), DNA repair, telomere length, protein folding, autophagy and also shows an impact on cellular senescence and stem cell ageing, which help maintain the skin from all the

factors.[22,23,24,25,26,27]

3.2) Anti-Microbial / Acne Property

Acne affecting the pilosebaceous follicles of the skin is an inflammatory disease which can be caused due to many factors. Acnes are prone to affect teenagers, but it is not uncommon among adults as well. This requires consistent and gentle care with effective treatment for such sensitive skin. The pathogenic factors of acne include higher sebum secretion, hypercornification of the follicular epidermal layer, Cutibacterium acnes colonisation, and inflammation; the condition can be characterised by the development of blackheads, inflammatory pimples, papules, and scars. Acne treatment typically includes both topical and systemic approaches, which are decided on the basis of symptom severity. Although acne is not deemed an infectious disease, the regimen often includes antibiotics which have enhanced potential for bacterial resistance, such as erythromycin, tetracycline and others. Currently, the need to developalternative non-antibiotic therapies for acne has escalated due to the growing concerns over antibiotic resistance and the adverse effects of treatment. As an anti-microbial component of colostrum and milk, lactoferrin and lysozymes are suggested to help reduce acne or microbial activity and can be used in the field of cosmetology.[28,29]

3.2.1) Lactoferrin are secreted by neutrophils in the inflammatory response, enhances the vulnerability of lysozyme and antibiotics similar to polycationic membrane-active agents, such as poly-L-lysine and the peptide antibiotic polymyxin B, by damaging the outer membrane of Gram-negative bacteria, which leads to the loss of lipopolysaccharide. Recent studies show that antimicrobial peptides, called lactoferricin B or H derived from lactoferrin, have more potent activity than lactoferrin. They are generated after the enzymatic cleavage of this protein. This work has led to the identification of the structural region responsible for the membrane-disruptive properties and its lethal effect against various microorganisms. Lactoferricin binds directly to lipopolysaccharide and disrupts the permeability barrier of the outer membrane of Gram-negative bacteria which shows its affinity for cell membranes and its lethal effect, which is exerted by disruption of essential membrane functions.

3.2.2) Lysozyme is another essential antimicrobial protein found in colostrum, which hydrolyses the microbial β-glycosidic linkages and initiates bacterial cell wall lysis by triggering platelet-activating factor and Interleukin-10 (IL-10). Lysozyme is active against both Gram (+) and Gram (−) bacteria and kills Gram (−) microorganisms, whereas it inhibits

the growth of Gram (+) microorganisms. Lysozyme assists synergic bacteria growth , and higher concentrations of lysozyme show superior antibacterial and anti-inflammatory activities.

3.3) Wound HealingProperty

Other than immunological support, colostrum also has incredible musculoskeletal repair and growth capabilities. Studies found that the only natural source for two major growth factors, transforming growth factors alpha and beta (TGF-α and B) and insulin-like growth factors 1 and 2 (IGF-1 and 2).[30,31]

3.3.1) TGF-A/B and IGF-1/2 have significant muscle and cartilage repair characteristics that are biochemically outstanding and promote wound healing with excellent implications. Not only these, but another study found that lactoferrin or stem cells present in colostrum can be used in wounds of different etiologies. An increase in the collagen content has proven its enhancement in the cosmetic field.

3.3.2) EGF and TGF-β1 play a specific role in wound healing. A clinical study found that EGF decreases inflammation and speeds up wound healing by stimulating granulation tissue development. While TGF-β1 acts as a pro-inflammatory mediator and then changes to an anti-inflammatory role, which is important for tissue repair and immune cell activation.

3.3.3) Membrane-enhanced vesicles like EVs are secreted from most of the cells present in biological fluids, playing a crucial role in intercellular communication. EVs derived from milk have gained attention due to their anti-inflammatory activity. Recent studies are being conducted and have shown that EVs can contribute to pathogenesis, tissue regeneration, diagnosis and drug delivery. Research concluded that EVshave increased IL-4 cytokine, which helps promote anti-inflammation, and large numbers of remodelled tissues were highly expressed, proving that the EVs derived from bovine colostrum helped in the wound healing at a faster rate.[32,9,33,34,35]

3.4) Antioxidant Property

Colostrum also contains antioxidative systems with nutrient and immunological components, which are necessary for the protection against reactive oxygen species. Researchers have evidence that proteins like lactoperoxidase (LPO), lactoferrin (LF) and ceruloplasmin (CP), other than well-known antioxidative enzymes like glutathione peroxidase, superoxide

dismutase, catalase or low molecular antioxidants, can show antioxidative properties in colostrum.

3.4.1) Lactoferrin have shown directreduction in the intracellular levels of reactive oxygen species, and pre-treatment with lactoferrin decreases the production of ROS in human mesenchymal stem cells (hMSCs), helping protect cells from excessive ROS and oxidative damage. This suggests that lactoferrin can help maintain cell function and viability under oxidative stress. Bovine lactoferrin has shown decreased plasma hydrogen peroxide levels, which are elevated due to oxidative stress-induced conditions. Lastly, its ability to regulate iron metabolism is essential during an iron imbalance. It acts by mitigating the oxidative stress, helping maintain cellular health and through clathrin-mediated endocytosis.[11,36,37]

3.5) Anti-Tanning/ BrighteningProperty

There are studies conducted which show anti-melanin synthesis effects are observed not from the original bovine colostrum but from hydrolysed cow colostrum extract (BCFM).

3.5.1) Alpha-MSH-induced B16F1 cells were examined for anti-melanogenesis mechanisms. Treatment of cells with BCFM resulted in lower concentrations of factors MC1R and cAMP, andphosphorylation levels of CREB, PKA phosphorylated MITF were decreased. Simultaneously, the expression of TRP-1 and tyrosinase was also decreased in B16F1 cells. BCFM shows an effect on melanogenesis progression by regulating the MC1R-cAMP signalling pathway, as well as suppressing the expression of TRP-1 and tyrosinase by regulating the CREB/MITF signalling pathways. This proved that hydrolysed cow colostrum extract (BCFM) is suitable for use as a novel active agent for skin whitening or pharmaceutical applications.[38]

3.5.2) The bovine colostrum's Ribonuclease 4 and Ribonuclease 5 (angiogenin) may specifically regulate the melanin synthesis of B-16 cells, which are melanoma cells and may cause skin lightening. Even at a concentration of roughly 0.15 micrograms/ml, the angiogenin demonstrated a substantial inhibitory effect on the synthesis of melanin. As a result, it is frequently utilised in skin-lightening cosmetics.[39]

4) Marketed products

4.1) PerCōBa® Colostrum Rejuvenating Cream by PerCōBa

4.2) Colostrum Luminous Glow Cream® by Epicuren

4.3) Travel Size Colostrum Luminous Glow Cream® by Epicuren

4.4) Colostrum Hydrating Mist by Epicuren

4.5) Environ Vita-Enriched Colostrum Gel by Environ

5) Gaps Observed

Recent scientific articles and reviews show that while colostrum has long been established in nutraceuticals and medicinal products, there is a noteworthy gap and growing scientific interest in its application within the cosmetic industry. Bovine colostrum, or the first milk of mammals, has many varieties of benefits. The restricted technical and hygienic problems along with the unstable physicochemical nature of colostrum, have resulted in minimal utilisation of colostrum on an industrial scale, which can be alternatively used for cosmetic preparations. It is an amazing source of substances necessary to support the development and repair of cells and skin tissue. Colostrum-based cosmetics can work at a cellular level to enhance skin health and beauty. It can be foreseen that in the future, the first milk (bovine colostrum) may play a significant role as an effective functional cosmetic ingredient.[39]

6) CONCLUSION

As an example of multifunctional secretion, colostrum has an unexcelled therapeutic and nutritional value. Bovine colostrum is of special importance among other species because of its high concentration of immunoglobulins, growth factors, vitamins and its minerals and antimicrobial peptides. Bovine colostrum's physiological and dermatological benefits are attributed to these factors. These polyfunctional bioactive components modulate immunity and assist in tissue repair and in addition, colostrum has anti-ageing, antioxidant, anti-inflammatory, and wound-healing properties, making it a bioactive ingredient of great potential in pharmaceuticals and cosmetics.

Research has shown that the potential use of colostrum is not only limited to nutrition but can also be applied to the revitalisation of skin in dermatology and skincare, moisturising, softening the skin, and protecting the skin from oxidative and microbial damage. Formulation concerns at the mass, stability, and standardisation levels of colostrum products need to be addressed to create guaranteed, effective and quality products. The full potential of colostrum as safe, effective, and versatile in health and dermatology can be harnessed by a more integrated approach to research and the development of colostrum products in extraction,

storage, and application in skin and health.

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