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Review

The Potential Applications of Natural Colostrum in Skin Health

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Abstract: Skin is a crucial organ for preserving the body's equilibrium. Like other parts of the body, skin also ages due to extrinsic and intrinsic factors, leading to several signs such as wrinkles, spots, and a decline in elasticity, causing a range of issues similar to those seen elsewhere in the body. Some of these factors include ultraviolet (UV) radiation, hormonal disorders, genetic factors, loss of moisture, metabolic disorders, exposure to chemicals, and smoking. Colostrum, which is the initial foremilk, has shown positive effects on the consequences of these factors. Its content is richer than mature milk and contains several beneficial components. For instance, it includes hyaluronic acid, a molecule that binds water and keeps the skin hydrated; lactoferrin, with high antimicrobial properties; immunoglobulins, which are responsible for immunity; growth factors, which increase the amount of collagen, the main protein type of the skin; and, finally, the telomerase enzyme, which maintains the telomere's length and, thus, decelerates the aging process. It has recently become apparent that using skin products with natural ingredients is essential. Considering its nature, contents, and effects, colostrum stands out as an excellent material for the cosmetic industry, especially for the aging sector. Therefore, the aim of this review article is to demonstrate the potential application of natural colostrum in skin health and its usage in natural cosmetic products in the cosmetic sector.

Keywords: colostrum; skin repair; wound healing; skin aging; natural solution; cosmetic; dermatology

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1. Skin Aging

Skin aging is a natural phenomenon that develops in different cells, tissues, or organs at separate times and stages. Human skin ages due to the accumulation of several factors, considered either intrinsic or extrinsic [1]. Intrinsic factors include hormonal disorders, reactive oxygen species (ROS), moisture loss, metabolic events, cell metabolisms, genetic factors, and many others, contributing to skin aging and the deterioration of its natural balance [2]. The primary extrinsic factors include pollution, chemicals, and especially the damaging effect of sunlight (UV) on the external appearance of the skin (Figure 1). Additively, UV light is the most common factor to join with other factors, leading to skin damaging and aging [3]. UV light acts as a mutagenic agent, leading to skin cancer in severe cases. Furthermore, UV light causes oxidative damage to the DNA, lipid tissues, and proteins in the body, forcing these molecules into cell apoptosis [4]. Conditions such as laxity, wrinkles, black spot formation (spotting), thinning, and loss of elasticity and brightness in the skin are visible signs of aged skin. These symptoms arise as a consequence

of the skin repair mechanism progressing slower than the degradation mechanism over time [5]. Simultaneously, the degradation of the collagen molecule, which provides brightness, flexibility, and supports the skin's connective tissue, increases the skin's sensitivity to aging [6].

Figure 1. Schematic representation of skin aging factors.

As presently known, the diet is crucial for numerous physiological processes, including the aging process. Studies have revealed that a high-fat diet is correlated with skin aging and delayed wound-healing processes due to increased oxidative stress [7]. Similarly, a high-sugar diet may cause an increased level of skin aging due to the accumulation of advanced glycation end products. Moreover, the consumption of spicy, salty, and extremely vegetarian foods may be harmful to the skin [8]. Therefore, it is crucial to opt for a nutritious diet to maintain health and prevent skin aging. In normal dermatologic functioning, nutritional factors play an important role; however, one's diet also affects skin aging and its appearance. A study was performed with 4025 women between 40 and 74 years old to show the effect of one's diet on skin appearance [9]. The findings of the study demonstrated that a higher consumption of vitamin C and linoleic acid can provide a lower intake of carbohydrates and fats. These resulted in fewer wrinkles, less senile dryness, and reduced skin atrophy, leading to better skin appearance. A different, large population-based cohort study was performed with 2753 elderly participants [10]. The study aimed to consider facial wrinkling, dietary patterns, and healthy lifestyle parameters, leading researchers to suggest that a healthy diet was related to less facial wrinkling. Also, a high intake of animal products, carbohydrates, and fats stimulated skin aging. Additionally, a high fat intake could induce skin inflammation by increasing the expression of inflammatory and tumor necrosis factors as a response to UV-B exposure. Moreover, some studies have demonstrated a strong link between carbohydrates, food processing methods, and skin aging due to the formation of advanced glycation end (AGE) products. A high intake of carbohydrates and the consumption of barbecued or fried foods led to

the accumulation of AGE products, stimulating the skin aging process. Briefly, the high intake of fats, carbohydrates, and barbecued or fried foods can affect skin aging processes, inducing oxidative stress and inflammatory skin damage [11,12]. Tobacco smoking is another critical issue that significantly affects the skin. It can cause acne, deceleration in wound healing, psoriasis, premature skin aging, eczema, and, especially in women, crow's feet and glabellar lines [13]. It damages the epidermis and the dermis layers in a similar way to UV radiation [14]. Like tobacco smoking, alcohol can also contribute to skin aging as an extrinsic factor [13]. It can cause oxidative stress, which is related to aging [15]. On the other hand, drinking an adequate amount of water every day has a positive impact on the skin, keeping it moisturized [16].

Apart from all these factors, when the beauty and hygiene products (cosmetics) used for personal care today penetrate the skin, they may cause disorders such as allergic or contact dermatitis, leading to a deterioration in skin texture [17]. These cosmetic products are composed of different chemical ingredients that may not be safe for human use, and the interaction of different ingredients can cause a cocktail effect on skin cells [18]. Also, cosmetics may alter the bacterial balance of the skin, known as the skin microbiota, which may cause certain skin problems [19]. For this reason, the interest in using natural components rather than products with chemical components is increasing day by day.

To date, new strategies have been trialed to repair skin damage and induce regeneration. Among these, the stem cell approach has been the subject of many efforts, but the low retention probability of transplanted stem cells and the inability to control their differentiation have made this approach difficult to use [20]. However, extracellular vesicles, also known as exosomes, a type of membrane-enclosed extracellular vesicles derived from various types of stem cells [21], are able to provide therapeutic benefits in skin repair without the risks of stem cells [22]. Therefore, they have attracted attention as additional alternatives to stem cell therapy in the healing and repair of skin damage. Currently, the number of studies on natural compounds that are safe for human use is on the rise [23]. With current knowledge about its characteristics, colostrum, for instance, has gained importance as a therapeutic product. Due to the positive effects of the active ingredients in colostrum on skin defects, it has recently found a place in the cosmetic field, making it the main subject of this article, which aims to explore its potential applications and usage in the cosmetic industry as a cocktail of bioactive factors.

2. Colostrum: Cocktail of Bioactive Factors

2.1. Colostrum as a Natural Compound

Colostrum, also known as initial milk, is the first form of foremilk secreted by Mammalia (bovine, sheep, mare, etc.) in the early postnatal period [24]. It contains the same nutrients as mature milk but with remarkably higher levels of fat, protein, peptide, vitamin, mineral, hormone, growth factor [25], cytokine, and immunoglobulin, and lower lactose content [26–28] (Table 1). According to the studies referenced in Table 1, it is shown that colostrum of different species contains different concentrations and ratios of components. Colostrum finds applications in supporting and strengthening the immune system [29] and promoting intestinal health in humans [30,31]. Additionally, it serves as a food supplement in sports nutrition, being a rich source of carbohydrates and fat (macronutrients), vitamins and minerals (micronutrients), peptides with antimicrobial activity, subcomponents, and growth factors [32,33]. Research on these components has shown that colostrum facilitates the reproduction of skin cells, stimulates differentiation, supports the repair of skin wounds, and reduces allergic inflammation on the skin [34].

Table 1. Different colostrum types and their contents.

Colostrum Type / *Colostrum Content*	*Bovine Colostrum*	*Sheep Colostrum*	*Mare Colostrum*	*References*
Total Protein	7.1–22 g/100 mL	2.7 g/100 g	15.2 g/100 g	[35,36]
Oligosaccharides	70–120 mg/100 mL	n.a.	n.a.	[35]
Total Lipids	5.35–6.7 g/100 mL	3.3 g/100 g	1.7 g/100 g	[35,36]
Lactose	2.03–2.5 g/100 mL	6.8 g/100 g	2.5 g/100 g	[31,32]
Immunoglobulins				
IgG	32–113 mg/mL	n.a.	84 g/L	[35,37]
IgM	4.3–4.9 mg/mL	n.a.	n.a.	[35]
IgA	1.6–4.4 mg/mL	n.a.	n.a.	[35]
Growth Factors				
EGF	248–1850 µg/L	1.0–1.24 ng/mL	249–269 µg/L	[35,38,39]
IGF-1	n.a.	n.a.	n.a.	
TGF-α	n.a.	n.a.	n.a.	
TGF-β	n.a.	n.a.	n.a.	
Lactoferrin	0.3–2.2 mg/mL	n.a.	n.a.	[35]
			Vitamins	
Vitamin A	0.25 µg/mL	n.a.	0.88 mg/kg	[35,40]
Vitamin D	0.89–1.81 IU/g of lipids	n.a.	0.0054 mg/kg	[35,40]
Vitamin E	2.92–5.63 µg/g	n.a.	1.342 mg/kg	[35,40]
Vitamin B1	0.58–0.90 µg/mL	n.a.	n.a.	[35]
Vitamin B2	4.55–4.83 µg/mL	n.a.	n.a.	[35]
Vitamin B3	0.34–0.96 µg/mL	n.a.	n.a.	[35]
Vitamin B12	0.05–0.60 µg/mL	n.a.	n.a.	[35]
			Minerals	[35,40,41]
Calcium (Ca)	2.6–4.7 g/kg	9.03–9.32 g/kg	748–847 µg/g	
Phosphorus (P)	4.5 g/kg	7.32–7.62 g/kg	389–742 µg/g	
Potassium (K)	1.4–2.8 g/kg	7.3–7.52 g/kg	928–1143 µg/g	
Magnesium (Mg)	0.4–0.7 g/kg	0.77–0.84 g/kg	140–473 µg/g	
Iron (Fe)	21.2 mg/kg	4.02–4.32 mg/kg	1.00–1.31 µg/g	

n.a.: not assessed.

Beyond these, colostrum has hyaluronic acid, which is a molecule also found in the nature of the body, playing a crucial role [42,43]. It keeps the skin hydrated under favor of its ability to bind to water molecules and also plays a part in the wound repair

mechanism [42]. Additionally, lactoferrin, a subcomponent of colostrum, is a glycoprotein with the capacity to bind to iron [44]. This capacity enables it to exhibit various biological activities, such as antimicrobial, antioxidant [45], and anti-inflammatory properties [46]. The lactoferrin molecule also demonstrates anti-inflammatory characteristics by regulating the production of T and B lymphocytes [47]. Moreover, thanks to its anti-inflammatory and antimicrobial properties, lactoferrin is beneficial for addressing skin problems such as infections or allergic acne lesions by combating the lesions on the skin. Furthermore, evidence suggests that when patients with HIV-associated diarrhea use bovine colostrum supplements rich in bovine lactoferrin, it can significantly reduce diarrhea and reduce negative symptoms such as vomiting. Additionally, it may inhibit HIV-1 replication due to its broad-spectrum antiviral abilities [48].

Because of its rich composition, colostrum has a pivotal role in the development of newborns. Its immunoglobulin (Ig) A, G, and M content can protect newborns against bacteria, viruses, and fungi [33]. Since Ig A and G can be synthesized in human epidermal cells, they support skin immunity [49]. Colostrum has been observed to balance the proliferation of keratinocytes, the cells located on the outermost surface of the skin [34]. Together with epidermal growth factor (EGF) and platelet-derived growth factor (PDGF), which are found in high amounts in colostrum, it supports normal skin growth, plumping, and antiaging with DNA-RNA repair activity by stimulating the synthesis of fibroblasts like collagen and elastin proteins that form the skin tissue [50]. Transforming growth factor (TGF) takes an important role in the healing and repair mechanisms of skin sores [51]. Cytokines, another important component of colostrum, are crucial proteins that facilitate communication between skin cells during the aging process. Cytokine molecules prevent the system of structures that inhibit collagen synthesis, thereby maintaining collagen synthesis and ensuring that the skin retains its plump structure [52]. Another intriguing finding is the relationship between colostrum and telomerase enzyme, which is crucial for the aging process. According to a study, bovine colostrum prevents telomere shortening, and this effect might be due to the positive contribution of bovine colostrum to telomerase activity [53]. Additionally, colostrum is very rich in A, B, C, and E vitamins, minerals (Zn, Cu), and amino acids, which are referred to as microcomponents. When combined with other major components, these microcomponents have even stronger effects on human skin [54].

A research study was performed to show the induction effect of bovine colostrum on the differentiation of human primary keratinocytes [34]. This study demonstrated that colostrum properties can be utilized in the treatment of skin diseases caused by impaired barrier function and altered differentiation. According to the results of this study, bovine colostrum can increase the expression of cyclin-dependent kinases inhibitors (P21/WAF1 and P27/KIP1), which are involved in the regulation of cell cycle control in the position of G1/S phase transition. Therefore, it can promote keratinocyte cells from a proliferating state to a differentiating state. Thus, cutaneous dryness or UVR-exposed skin defects might be treated with colostrum.

A case study was performed with a 41-year-old Japanese male patient with severe erythema and a rare photosensitive disease that commonly affects elderly men, chronic actinic dermatitis [55]. During the research process, the patient took 1 mg oral bovine-colostrum-macrophage activating factor (Colostrum-MAF), which is a health food containing degalactosylated/desialylated bovine colostrum. After 2 weeks, erythema and symptoms of skin defects disappeared. According to the result of this study, colostrum-MAF can provide immune modulation by activating type 2 macrophages with regulation function.

A biochemical study aimed to show the biological activity of mare's colostrum on fibroblast growth [56]. The results of this study showed that the mare's colostrum biological action is located in the fat globule; thus, colostrum globules stimulated fibroblast cell growth and improved wound healing. In this study, an 83-year-old man had a chronic ulcer in the external perimalleolar area and was treated with colostrum globule emulsion. After 6 weeks of treatment, the size of the wound was reduced.

A combined research study including in vitro and in vivo experiments was conducted to show wound healing properties of colostrum and colostrum-derived substances [57]. In this study, extracellular vesicles (EVs) of colostrum and bovine milk were used. The first experiment conducted in this study evaluated the wound closure properties of EVs from colostrum obtained in the early stage of lactation and EVs obtained from normal pasteurized milk. Expression of IL-4 cytokine, which can promote anti-inflammation, was increased, and also a large number of tissue remodeling factors were highly expressed. According to the results of the experiment, the wound closure rate of 100 µg/mL colostrum EVs was higher than the normal bovine milk EVs, and inflammation to proliferation phase of fibroblast cell transition was improved. Additionally, in the second experiment, 100 µg/mL EVs derived from colostrum were used for the in vivo excisional wound mouse model. Subcutaneously injected EVs improved wound healing after 4 days of application.

A research study aimed to demonstrate the mitogenic and proliferation-supporting effect of bovine colostrum on the human keratinocyte HaCaT cell line [58]. A scratch wound assay was performed with varying concentrations (0.5–20%) of colostrum, and better results for cell growth were provided with 5% and 10% of bovine colostrum in the first hour after birth. Additionally, bovine colostrum promoted migration of the human keratinocytes and re-epithelialization at the wound site.

A different in vitro study investigated the effect of fermented bovine colostrum whey on the proliferation of keratinocytes [59]. *L. bulgarious*, *S. thermophilus*, and *L. rhamnosus* were used for the fermentation of colostrum, and the human skin keratinocyte cell line (HaCaT) was used for proliferation assay. As a result of the study, upregulation of the aquaponin-3 (AQP3) protein, which can facilitate water and glycerol transport for skin hydration in the cell migration process, cell proliferation, and accelerating cutaneous wound healing, was demonstrated.

Colostrum as a natural cocktail is used with its nanofibrous conjugated (PCL-PEG) form to investigate stimulation and supporting wound healing [60]. The study design involved in vitro cell migration, antioxidant, antibacterial/antibiofilm, and in vivo wound healing assays. A mouse fibroblast cell (NIH3T3) was used, and a scratch was created on the cell layer. Colostrum- and colostrum-conjugated treated groups were compared, and the colostrum-conjugated group demonstrated higher cell migration and full-wound closure than the normal colostrum-treated group. To induce oxidative stress, H_2O_2 was added to evaluate the antioxidant properties, and samples that were colostrum-conjugated showed a reduction in ROS production. Infections are one of the major factors that make it difficult for wounds to close. Lactoferrin and immunoglobulins in colostrum can inhibit bacterial growth. According to the results of antibacterial assays performed in this context, it was shown that conjugated colostrum inhibited the growth of *Escherichia coli* and *B. subtilis* bacteria, and very little bacterial growth was observed. In addition, in an in vivo wound healing histological assay, Wistar albino rats were used, and a thick skin wound was created. The produced conjugated colostrum was placed on the wound and covered with surgical adhesive tape. On day 14, the wounds were shown to be completely closed. In addition, there was a study in which colostrum albumin-based formulations seemed to be an effective solution for skin staining, which is one of the signs of aging. The study showed that colostrum can whiten skin color [54].

It is important to highlight that among the natural compounds that have recently gained attention, colostrum stands out for each of its components having a different healing effect on the skin (Figure 2). 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.

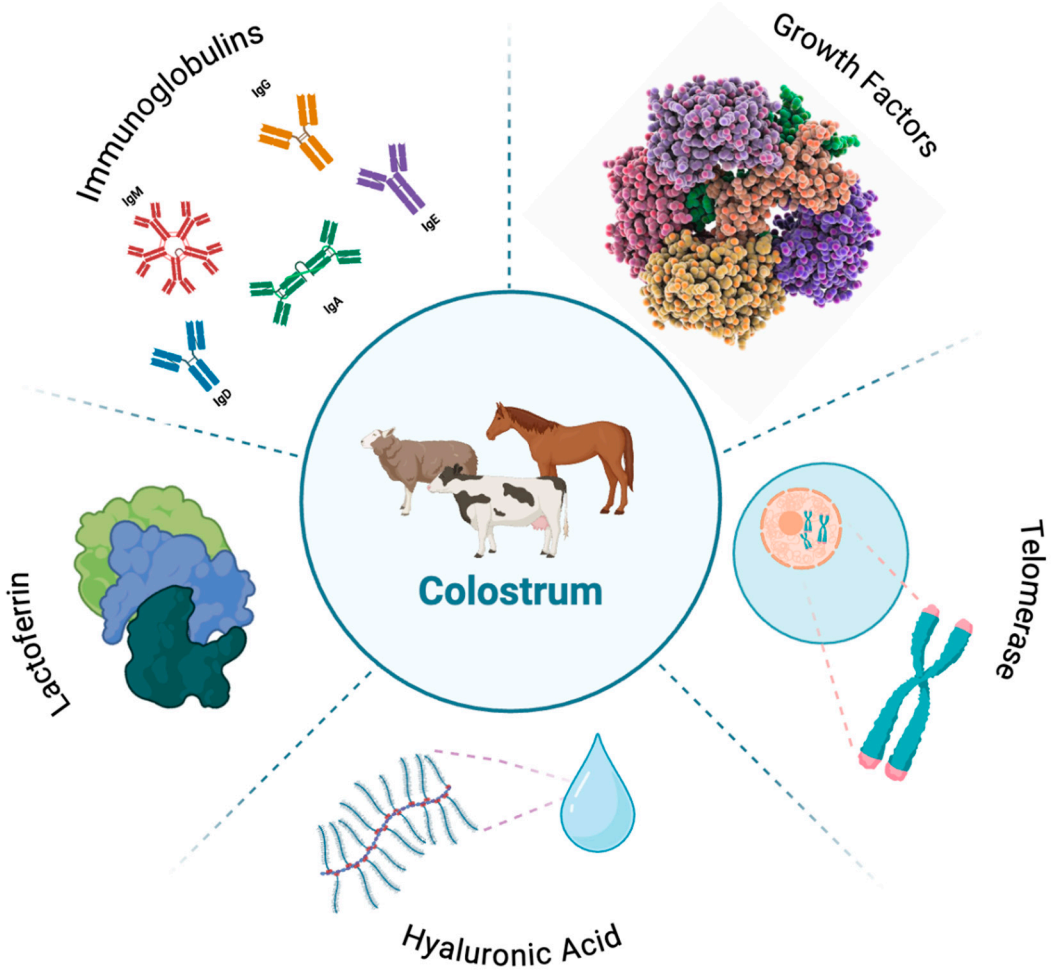

Figure 2. Schematic representation of the biological components of colostrum.

2.2. Usage as Cosmetics

While cosmetics are supposed to have hygiene effects and health benefits that can be tracked back to ancient Egyptian times, today they are being linked to skin aging and are being shown to provide medical treatment [61]. Known for improving the appearance and odor of human skin, today's cosmetics have become globalized with the cosmetic industry. Today, individuals are encouraged to use beauty and personal care products that promise to protect from sun rays, give skin elasticity, brighten and whiten the skin, moisturize the skin, and more; however, today's cosmetic products contain heavy chemicals, allergens, and toxin components that trigger the intake of carcinogenic substances in the human body when used while ignoring the limits [62,63]. These cosmetic products contain different chemical components, and the interaction of different product components can cause a cocktail effect on skin cells. Therefore, there is an increasing interest in cosmetics made from natural bioactive ingredients or natural bioactive compounds instead of harmful products with predominant chemical compositions [18]. Currently, colostrum is one of the natural compounds of growing interest. With its multiple biologically active molecules, it is a new approach to improving and maintaining skin health. In addition, there are studies in the literature investigating the place of colostrum in the cosmetic sector and its effects on the skin as a result of application and supplementation. In line with this, a recent study examined the potential of exosomes derived from bovine colostrum to heal and repair damaged and aged skin cells. In the study, it was shown that exosomes increased the rate of absorption into human fibroblast skin cells, showed antioxidant effects on keratinocyte cells, reduced melanogenesis after UV damage, and improved skin elasticity [64]. A different study demonstrated that cow colostrum extract had the ability

to decrease melanin production by the regulation of the cAMP signaling pathway; thus, researchers proposed that cow colostrum extract is a potential therapeutic agent for skin whitening [65].

A randomized placebo control research study aimed to study the effect of cosmetic preparation containing 15% of lyophilized sheep colostrum on mature skin aging problems [66]. Patients of this study were divided into two different groups: cream with sheep colostrum and placebo cream group. According to the authors, topical application of sheep colostrum cream reduced the redness of skin and smoothed skin pores. Additionally, the study demonstrated that the application of sheep colostrum can improve skin hydration, regeneration, tone, and softness. Among the sheep colostrum cream group, sebum secretion was reduced in patients with oily skin when compared to a placebo cream. Another communication study investigated the effect of the same cosmetic product containing sheep colostrum on acneic skin [67]. In the study, a cream containing 15% sheep colostrum cream was prepared and used for the treatment of acne on 30 different volunteers with acne-prone skin. This communication study examined the potential dermatological benefits of colostrum on mild or moderate acne skin. According to the results, sheep-colostrum-containing cream could lower sebum production, and provide adequate hydration. Additionally, cream could prevent or improve skin lesions caused by acne. A different in vitro study was performed to demonstrate how sheep colostrum potentially improves skin health and would be a good choice as an active component in cosmetic preparation [68]. For the goal of the study, two different cell types were used: diabetic human skin fibroblast cells and neonatal epidermal keratinocytes. According to the study, topical treatment of colostrum increases the proliferation rate of diabetic human fibroblast cells. In addition to this result, researchers performed a scar test to show the wound-healing property of colostrum and demonstrated that colostrum increased wound closure rate.

From all these studies, colostrum, a cocktail of bioactive molecules, could be a new ingredient for natural cosmetics and therapeutics products. Apart from these studies, investigating the place and properties of all colostrum types in the cosmetic sector is necessary.

3. Biological Components of Colostrum

3.1. Hyaluronic Acid (Hyaluronan)

Currently, it is known that human skin ages because of many environmental factors, such as UV rays, hormonal imbalances, ROS, moisture loss, and more. In short, skin aging is a multifactorial process and may result from independent mechanisms or causes [69]. The most important of these factors that cause the aging of the human skin is the loss of its own moisture. Youthful skin is firm, more resilient, and pliant, due to its higher water (moisture) content than aged skin [69]. Hyaluronic acid (HA), or hyaluronan, a component of colostrum, is the key molecule that can bind and retain water molecules, promoting skin moisture [70,71]. Hyaluronan, also known as glycosaminoglycan (GAG), is also found in the extracellular matrix fluid [70]. HA is widely present, from prokaryotic cells to eukaryotic cells, mostly found in the skin and vitreous tissue of the eye in humans, but it can also be found in other tissues of the body [69]. HA was first discovered in the vitreous tissue of the eye [71]. It is a nonsulfated GAG that contains two repeating different sugars; these are D-glucuronic acid and N-acetyl-glucosamine, linked by a glucuronidic β 1-3 bond [72]. These two distinct sugars repeat more than thirty thousand times [73]. The two most important functions of hyaluronic acid in human skin are hydration and wound healing [74]. Additionally, HA regulates the healing of wounds by increasing its synthesis during injury [75]. Synthesis of HA occurs in the presence of the HA synthase enzyme (HAS), which includes HAS 1-2-3 membrane-bound enzymes with different enzymatic characteristics. HA is synthesized at the interior of the plasma membrane and then extruded into extracellular space [76]. HA, one of the valuable components of bovine colostrum, is a gel-like (viscous) molecule that can be synthesized in the body. Today, it is used in many cosmetic products.

3.2. Lactoferrin

Lactotransferrin, also known as Lactoferrin (Lf), is an iron-binding multifunctional glycoprotein naturally present in colostrum and milk [77]. It consists of approximately 700 amino acids and has a molecular weight of about 80 kDa [78,79]. Lf has numerous biological functions, particularly prominent in inflammatory diseases, but it also holds a crucial place in cosmetics due to its positive effects on the treatment of skin disorders. According to studies, Lf has been shown to improve skin tissue deteriorated by acne, psoriasis, tinea pedis, and environmental conditions, thereby eliminating skin disorders [80,81]. For instance, acne vulgaris, an inflammatory skin condition, is a common skin disorder affecting almost 80% of adolescents [80]. Acne can occur in two different forms: open inflammatory lesions, which are papules, nodules, and cysts; or closed noninflammatory lesions (comedonal acne), which are blackheads. In addition, acne formation is associated with bacteria called *Propionibacterium acne* or *Cutibacterium acne* [80,81]. In a study investigating the effects of lactoferrin on acne lesions and its antibacterial and anti-inflammatory properties, one group of 56 patients received a daily supplement of 200 mg lactoferrin mixed with fermented milk for 12 weeks, while the other group received a placebo. The study revealed that fermented milk enriched with lactoferrin reduced the formation of acne vulgaris on the skin [80]. Generally, the *Staphylococcus aureus* bacteria type is a cause of wound infections and leads to localized suppurative lesions, affecting wound healing processes. Therefore, developing an efficient antimicrobial and healing result is crucial. Based on this issue, a new study was performed to demonstrate the antibacterial effect of hydrogel form of lactoferrin (Lf/NZ2114/LMSH) on *Staphylococcus aureus*-infected wound tissues in a mouse model. First, in this study, the injectable hydrogel lactoferrin was prepared and tested. The *Staphylococcus aureus*-infected Balb/c mouse wound models were set up with treatment of 1% Lf/NZ2114/LMSH. After 4 days of treatment, skin homogenates were collected and coated on plates, and the bactericidal rate was over 99.92%. Also, wound images were observed at 4, 8, 12, and 14 days, and wound size was calculated. According to observations, the wound healing increased with time but slightly increased from day 12 to day 14. Good treatment with 1% Lf/NZ2114/LMSH was shown at around 12 days. The result of the analysis showed that the 1% Lf/NZ2114/LMSH mixture provided a strong inhibition of 99.99% against *Staphylococcus aureus* bacteria. It is emphasized that a 1% Lf/NZ2114/LMSH mixture can be used as an effective wound dressing for the treatment of wound infections. Additionally, after 1% Lf/NZ2114/LMSH treatment, the number of inflammatory response cells was diminished, and the structure of the tissue looked clear and regular with a large number of neovascularizations. Along with the decrease in inflammatory cells and restoration of structure of tissue, 1% Lf/NZ2114/LMSH showed an anti-inflammatory and prohealing effect [82]. Furthermore, a similar study was performed to show the antibacterial effect of lactoferrin-containing hydrogel against methicillin-resistant *Staphylococcus aureus*, which causes chronic skin wounds. In this animal study, lactoferrin-containing hydrogel was injected, and it significantly inhibited the growth of *Staphylococcus aureus* on chronic skin wounds. Also, the antibacterial activity was tested with in vitro assays and demonstrated a strong antibacterial effect [83].

In a recent study, oral administration of bovine Lf was researched to show its protective role against skin damage [84]. The study was performed on 7-week-old male hairless mice with UV-B-induced skin photodamage, and mice were supplemented with bovine lactoferrin for 6 weeks. To complete the study, the activity of bovine lactoferrin was evaluated by four different assays, including transepidermal water loss (TEWL) and hydration histological changes, superoxide dismutase (SOD) activity, and UV-stimulated IL-b levels. Administration of bovine lactoferrin could suppress TEWL and induce skin hydration. Histological change analysis: mouse skin samples were tested to demonstrate epidermal thickness. Then, epidermal thickening was suppressed in the Lf-administrated group. Additionally, SOD-like activity was tested to understand induced ROS, which might be one of the specific factors in skin defects. According to SOD assay results, the Lf-supplemented group could reduce ROS formation in UV-damaged skin. Also, UV-irradiation induced

the expression of proinflammatory cytokines like IL-b. Lf was demonstrated to have the potential to inhibit the production of IL-b and prevent dysfunction of the skin barrier.

Moreover, bovine lactoferrin promotes hyaluronan and collagen synthesis in normal human dermal fibroblast (NHDF) cells [85]. In this in vitro study, which used NHDF cells, the production of hyaluronan, a major component of tissue hydration, was increased by enhancing HAS2 mRNA transcription and protein expression. Increasing the amount of hyaluronan could regulate the proliferation of fibroblast cells and stimulate wound healing. In addition to this, a collagen assay was performed in this study. Normally, collagen is a special component in the dermis and promotes wound healing. According to the collagen assay, bovine lactoferrin could induce the expression of the COL1A1 gene and type-1 collagen transcription. Apart from this study, supporting collagen metabolism an in vitro study was performed with lactoferricin, isolated from an active peptide of Lf [86]. Because of this study, isolated lactoferricin was demonstrated to have anti-inflammatory and anticatabolic roles in preventing collagen degradation in human synovium and cartilage fibroblast cells.

A clinical trial was conducted including randomized, double-blind, placebo-controlled experiments to evaluate the efficacy and safety of oral treatment of lactoferrin with vitamin E and zinc for improving mild to moderate acne vulgaris [87]. For 12 weeks, each patient took one capsule (containing 100 mg bovine lactoferrin) twice a day, and after 12 weeks, sebum levels and the number of acne lesions were reduced. Another clinical trial included open-label, single-arm experiments involving 43 patients with mild to moderate acne vulgaris [88]. All patients took one bovine lactoferrin tablet formulation twice a day for 8 weeks. As a consequence of the study, total acne lesion counts were reduced. A total of 76.9% of the patients demonstrated a reduction in total lesions. None of the patients experienced a problem related to the administration of bovine lactoferrin.

3.3. Immunoglobulins

One of the challenges of the cosmetic industry is the requirement for soothing impacts against skin problems caused by bacteria, fungi, and viruses. Immunoglobulins (Ig), also known as antibodies, are produced by B lineage cells, responsible for recognizing and counteracting pathogens directly or through other immune cells [89]. Also, immunoglobulin G glycosylation is well known for its heterogeneity and varies considerably within species. The composition of IgG glycosylation is influenced by genes and environment, thus serving as a biomarker for general health status and biological age. Changes in IgG glycosylation patterns have been observed in aging and various diseases. These changes have been shown to modulate IgG effector functions and may play a role in disease development or progression, representing a mechanism involved in disease pathology [90]. The main classes of Ig are IgA, IgM, IgG, IgE, and IgD [89]. On the other hand, for the last decade, some studies have shown that in addition to B lineage cells, certain gland epithelial cells, germ cells, cardiomyocytes, and neurons can also express Ig [49]. Epidermal cells in humans can encode IgG and IgA, potentially providing immunity for the skin [49]. This is especially crucial for neonates who do not have major immune characteristics and are vulnerable to viruses, bacteria, fungi, and other antigens. They acquire some immunity sources from their mother's placenta and foremilk. Colostrum is richer in Igs rather than mature foremilk. It contains IgG, IgA, and IgM at a high level, and Igs constitute 70–80% of the whole protein in colostrum [91] or. In particular, IgE possesses antiviral properties and has a soothing impact on allergic reactions in the skin [92]. Ultimately, colostrum is a source of Ig that supports skin immunity and makes the product a natural fighter against pathogens.

3.4. Growth Factors

Growth factors (GFs), commonly classified as a subset of cytokines, are signaling molecules that regulate intracellular communication and stimulate various cellular processes such as cell growth, inflammation, tissue repair, and wound healing [54]. GFs are found naturally in colostrum, and studies have revealed that colostrum exhibits more cellu-

lar stimulation compared to mature milk, probably due to its higher content of GFs [93]. These GFs include insulin-like growth factors 1 and 2 (IGF 1-2), transforming growth factor-βI and βII (TGF-β1-2), platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor 1 and 2, and betacellulin growth factor [54].

Within the dermal extracellular matrix, aging and its visible signs, such as wrinkles, are mainly related to decreasing collagen synthesis, which is a key protein type of the skin [70]. Regarding gender differences, collagen levels are lower in females than in males, which is why females generally tend to have more wrinkles and other signs of aging at the same age as males [94]. Today, it is known that growth factors increase the amount of collagen by stimulating dermal collagen synthesis and reversing the effects of collagenases [95].

Moreover, GFs and cytokines play a crucial role in skin rejuvenation and wound healing in the cosmetic industry [96]. Numerous clinical trials have shown that the application of growth factors with topical routes reduces fine lines and wrinkles, stimulates collagen formation, and promotes the healing of chronic and normal wounds [96,97]. An example of a study in this area is of epidermal growth factor (EGF), which has a molecular weight of 6 kDa and is an important polypeptide due to its effect on wounds. In this study, 29 participants who were 30 years old applied EGF serum for 3 months, twice a day, resulting in improved brown and red spotting, pore size, skin texture, and wrinkles compared to the baseline [97]. In conclusion, cytokines and growth factors have similar effects on skin aging, and their cell-regenerating properties hold significant potential for the cosmetic industry.

3.5. Telomerase Enzyme

A visible symptom of aging is the physical change in the skin due to endogenous and exogenous factors. One of these factors of molecular outputs is the telomere shortening rate [98]. Telomeres are regions found at the ends of chromosomes that prevent their degradation. In vertebrates, telomeres include TTAGGG repeats, and, especially in humans, they are generally 10–15 kb long. With every cell division in a human somatic cell, telomeres shorten due to the end replication problem. Additionally, the telomere sequence can be easily affected by oxidative stress, alkylation, and UV irradiation because of its high G quantity. If telomeric regions of DNA are critically shortened, this may cause chromosome destabilization and replicative senescence by blocking cell replication with activated DNA damage checkpoints [99]. To delay senescence, it is important to maintain telomere length and high expression of telomerase [98]. The eukaryotic ribonucleoprotein (RNP) enzyme complex, telomerase, is responsible for the replication of these telomeric regions and the addition of TTAGGG repeats to stabilize the telomeres using its intrinsic RNA as a template for reverse transcription [100]. Thus, it decelerates the shortening of telomeres.

When colostrum is applied topically, cytokines, growth factors, and other bioactive components are known as inducers for collagen biosynthesis, wound healing, and skin rejuvenation. In an in vitro study, liposomal bovine colostrum is used on human fibroblast cells to estimate the skin antiaging effect based on telomere length alterations [53]. According to the study design, human fibroblast cells were cultured with different concentrations of colostrum (0.125%, 0.25%, 0.50%), and for oxidative stress attack, H2O2 was added. As a consequence of the study, proliferation rates, telomere length, and telomere shortening were analyzed, and it was found that colostrum-containing culture protects the cell from telomere length erosion. Researchers suggested that bovine colostrum is an enhancer of the protection of skin health. Keeping telomeres long is an important aspect of delaying the aging process at the cellular level, and for the cosmetic industry, further research about colostrum, telomeres, and the telomerase enzyme is crucial.

4. Conclusions

In conclusion, skin aging is triggered by intrinsic and extrinsic factors, and the on-demand use of chemical-containing cosmetic products can contribute to skin aging and damage. For these reasons, colostrum, which is considered a natural solution, holds an

important place in today's cosmetics. Colostrum is a unique compound that effectively combats all signs of skin aging, thanks to its components such as hyaluronic acid, lactoferrin, immunoglobulin, growth factors, telomerase enzyme, and many other microstructures. Additionally, it serves as a multifunctional initial milk that protects the skin from skin dryness caused by harsh conditions, aids in wound healing and skin tissue repair, fights microbial infections caused by bacteria and viruses in the skin tissue, and increases skin elasticity by stimulating collagen production. It plays a crucial role as a strong and natural resource in the cosmetic industry.

In the field of cosmetics, products containing colostrum generally support skin regeneration, 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. Clinical studies for the application of colostrum and colostrum-based formulations are very limited. Further clinical studies showing the antiaging, anti-inflammatory, antimicrobial, antioxidant, anticancer, and other therapeutic effects on skin defects should be included in the literature. These studies will provide more objective answers regarding the health benefits of colostrum. It is predicted that this natural content will play an even greater role in the cosmetic industry in the future, leading to a decrease in skin defects. In addition, further studies on the effect of colostrum-based cosmetic products after long-term use will add value to the place of colostrum in the cosmetic industry. Furthermore, since different types of colostrum have different concentrations of components, it is important to add the skin health benefits of different types of colostrum samples to the literature. Further research to compare the therapeutic effects of different colostrum types on similar skin defects will add diversity to the development of colostrum-based formulations in the cosmetic industry and will fill the gaps in the literature in this field.

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