

SKIN pH IN THE ELDERLY AND APPROPRIATE SKIN CARE

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ABSTRACT

The acidic skin surface pH (pH_{SS}) plays a crucial role in the maintenance of a vital stratum corneum (SC) and an intact epidermal barrier. However, ageing affects the pH of the skin, both pH_{SS} and the pH of the stratum corneum (pH_{SC}). The purpose of this article is to review the physiological function of skin pH and the effects of an age-related increase of skin pH. Moreover, the consequences for the development of skin care products, specifically for the elderly, will be discussed. Reported pH_{SS} values of the skin range between 4 and 6 in non-intertriginous areas. The acidity of the outer surface of the skin is essential regarding the following functions: epidermal barrier homeostasis, integrity/cohesion of the SC, support of proteolytic processes leading to desquamation, metabolism of extracellular lipids, and microbiological colonisation of the SC. Exogenous, as well as endogenous factors, affect skin pH (especially pH_{SS}), thereby influencing its functions. Age is one important endogenous factor. Interestingly, pH_{SS} of adults slightly increases with age. This increase of pH_{SS} influences several functions in ageing skin. Increased pH_{SS} may impair epidermal barrier permeability, integrity/cohesion of the SC, and even antimicrobial capacity. Hence, ageing skin shows an increased vulnerability, not only towards mechanical stress. Moreover, aged skin often appears rough and dry, which is sometimes associated with itching. However, so far only a few studies have investigated the effect of skin care products on ageing skin. In addition, normalising the increased skin pH in the elderly by appropriate skin care products formulated with a lower pH, e.g. 4, may improve impaired skin functions, which are impaired.

Keywords: Stratum corneum, acidic, emulsion, epidermal barrier, antimicrobial.

INTRODUCTION

The acidic character of the skin was described in 1892 by Heuss.¹ In this context, it is important to discriminate between skin surface pH (pH_{SS}) and stratum corneum (SC) pH (pH_{SC}). In this paper, skin pH denotes both pH_{SC} and pH_{SS} , whereas we discriminate between the latter two whenever necessary. Schade and Marchionini² verified a direct correlation between pH_{SS} and bacterial colonisation. This is still known as the 'acid mantle' of the skin,² which consists of a thin viscous mixture of sweat and sebum covering the outer layer of the SC. Skin pH plays a crucial role for the maintenance of physiological epidermal barrier functions.

Exogenous factors (e.g. skin care products) and endogenous factors (e.g. age) may, however, affect pH_{SS} .³⁻⁷ The aim of this review is to focus on the importance of a physiological skin pH for a healthy skin, and on the consequences of an age-related increase of pH_{SS} . Furthermore, the effects of acidic skin care products for the elderly are discussed.

FORMATION AND MAINTENANCE OF SKIN SURFACE pH

The physiological pH_{SS} ranges between 4 and 6 in non-intertriginous areas. Tape stripping experiments revealed an increase up to a pH of ~7.5 after complete removal of the SC. This is the

normal pH of the interstitial space, indicating a high regulatory effort in a distance of only 10-15 μm (thickness of the SC).⁸⁻¹¹ Differences in the measured values can partially be attributed to the investigation of different skin areas.¹²⁻¹⁶ Several studies demonstrate further differences based on circadian rhythm, gender, ethnicity, and age.⁴⁻⁶ Although differences are reported, the underlying mechanisms of formation and maintenance of pH_{SS} and pH_{SC} and its physiological functions are well known.

The SC, as well as the skin surface, are acidified primarily by amino acids (AAs), free fatty acids (FFAs), by enzymatic mechanisms (in particular the sodium-hydrogen exchanger 1, NHE1), and the secretion of the content of lamellar bodies. It was shown that AAs are important factors in regulating skin pH.¹⁷ About 70-100% of the free AAs of the SC are derived from histidine-rich proteins of the keratohyalin granules, such as filaggrin.¹⁶ Filaggrin is expressed during terminal differentiation of the epidermis and is essential for the regulation of epidermal homeostasis.¹⁸ It is hydrolysed in the upper SC to the AAs histamine, glutamine, and arginine,^{19,20} which (among others) are metabolised to urocanic acid, contributing significantly to skin pH regulation.²¹ Additionally, FFAs derived from phospholipids play an important role in regulating skin pH. Inhibition of epidermal secretory phospholipase (sPLA2), which hydrolyses membrane phospholipids and generates FFAs via topical application of bromphenacylbromide, and 1-hexadecyl-3-trifluoroethylglycero-sn-2-phosphomethanol on murine skin increases pH_{SS} .^{22,23} In contrast, an increase in skin pH may result in defective lipid processing and delayed maturation.²⁴ This is mediated by two key lipid-processing enzymes, β -glucocerebrosidase and acidic sphingomyelinase, which generate a family of ceramides from glucosylceramide and sphingomyelin precursors, and exhibit low pH optima.²⁵

However, recent studies in mice, as well as on human skin and cultured keratinocytes, melanocytes, and melanoma cells, support the role of NHE1 as probably the most important transporter in SC acidification. NHE1 is expressed ubiquitously in keratinocytes.^{8,26,27} Its expression is upregulated under physiological acidic skin pH.²⁸⁻³¹ Experimental knockout studies in mice indicate a delay in recovery of barrier function, which support a crucial role for NHE1 in the maintenance of the

physiologic skin pH.^{32,33} A recent study in humans has shown that NHE1 regulates wound surface pH and that the pH of the wound fluid governs epidermal barrier recovery in wounds.³⁴

Other transporters, such as monocarboxylate transporter 1 (MCT1) seem not to play such a pivotal role. MCT2-expression is very low in human tissues (with the exception of testis), MCT3 is restricted to the retina and the choroid plexus, and MCT4-expression is generally limited to tissues which use glycolysis for their energy metabolism (e.g. white skeletal muscle fibres, astrocytes, white blood cells, chondrocytes, certain tumour cells, and cells under severe hypoxia).³⁵ Furthermore, exocytosis of lamellar bodies depends on skin pH and participates in skin pH regulation.²⁵⁻³⁷ These specific organelles exhibit an acidic pH maintained by ATPases.³⁸ Fusion of lamellar bodies with the intercellular membrane of the SC contributes to the acidification of the extracellular space and lowers the intercellular pH of the SC significantly, as proven in atopic individuals.^{36,37} The coordinated interaction of the aforementioned molecular mechanisms is crucial for the proper formation and maintenance of a physiological skin pH and, consequently, for healthy skin (Figure 1).

PHYSIOLOGICAL FUNCTIONS OF SKIN pH

It is well known and proven by many studies that acidification of the skin surface is crucial for healthy skin protecting the body from environmental influences. The acid mantle of the skin maintains functions of the skin which are:

- Integrity/cohesion of the SC;
- Homeostasis of the epidermal barrier;
- Antimicrobial defence.

The proper regulation of these functions is important for keeping the skin smooth, to prevent infections, and to keep the skin insensitive to irritation. The permeability of the epidermal barrier depends on its hydrophobic character, lipid distribution, and distribution of these lipids into a series of lamellar bilayers.³ It is suggested that the distribution is regulated by pH-dependent mechanisms: the generation of lipophilic components and lipid-lipid-interactions.²⁵ Two key lipid-processing enzymes are β -glucocerebrosidase and acidic sphingomyelinase,

which both exhibit highest activity at acidic pH. These enzymes generate a family of ceramides from glucosylceramide and sphingomyelin precursors,³⁹ and an increased pH leads to reduced activities of these enzymes.^{25,40} Pretreatment with α -hydroxy acid shows a significantly higher resistance towards barrier disorders in mice.⁴² This may result in a reduced exposure of epidermal cells to irritants, allergens, and pathogens.

SC integrity and cohesion of corneocytes is mediated by corneodesmosomes and by extracellular lipids.⁴³⁻⁴⁵ The controlled loss of corneocytes (=desquamation) is highly regulated and associated with the degradation of corneodesmosome proteins such as desmoglein, desmocollin, and corneodesmosin.⁴⁵⁻⁴⁷ This degradation, which induces desquamation, is mediated by chymotryptic and tryptic serine proteases, kallikrein 5 and 7.^{3,25,39,44,46,48-54} Most importantly, these enzymes require neutral pH-values. In the elderly - with increased skin pH - the structure and function of the SC is impaired by altered serine protease activity but also the secretion of lamellar bodies is inhibited.^{3,25,55} This can lead to an increased desquamation, which becomes visible as rough skin.

The skin and skin surface exhibit antimicrobial properties, which play a key role in the prevention

of colonisation by pathogens.^{2,56,57} Microorganisms that colonise the skin belong to either transient, permanent-resident, or temporary-resident species.^{25,58,59} The physiological microbiota of the skin depends on different factors; however, pH is very likely the most important one.^{57,60-63} Microorganisms that colonise the skin as commensals require acidic pH-values for optimal growth, whereas some pathogenic bacteria grow better at neutral pH levels. *Staphylococcus aureus*, a pathogen associated with different skin diseases, has its growth optimum at pH 7.5, whereas under physiological acidic pH_{SS} growth rates are reduced.^{58,59,64} In addition, antimicrobial peptides (such as cathelicidin [LL-37], dermcidin, cationic substances, and nitrates that are found in human sweat) develop their antimicrobial activity only at acidic pH, whereas a dermcidin containing sweat fraction showed a reduced bactericidal effect when buffered at pH 6.5.^{25,65}

All these physiological functions depend heavily on the proper regulation and maintenance of an acidic skin pH. Thus, any alteration of skin pH, either endogenously or exogenously, impairs physiological skin functions.³ Endogenous factors besides age are diseases (e.g. diabetes), and exogenous factors are, in particular, skin cleansers and skin care products, which are generally preserved and not adjusted to skin pH.⁶⁶

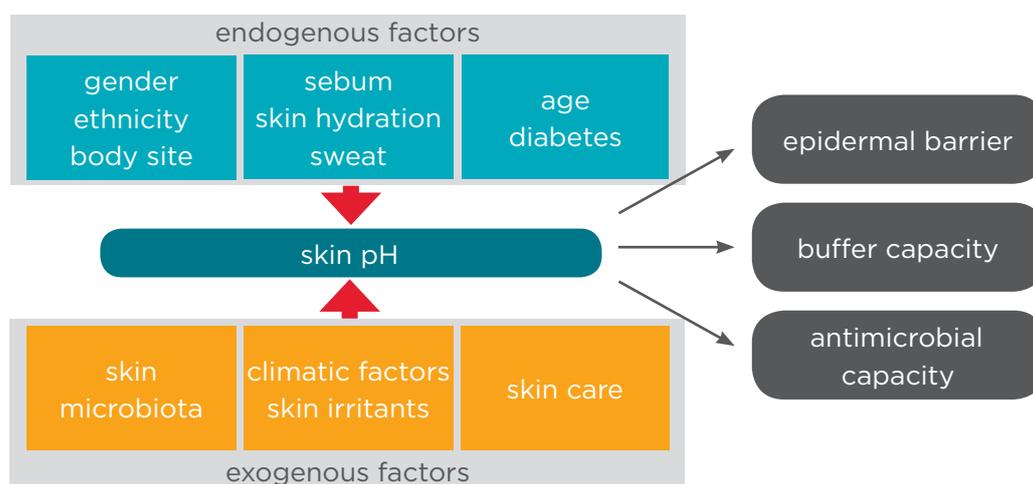


Figure 1: Skin pH is influenced by endogenous and exogenous factors.

Skin surface pH (pH_{SS}) is controlled by endogenous and exogenous factors. Exogenous factors include skin microbiota, dressings, and skin care products. Gender, ethnicity, body site, sebum production, sweating, and age belong to the endogenous factors. All these factors have an impact on the acidification of the skin, which influences the permeability of the epidermis, the integrity/cohesion of the stratum corneum, and antimicrobial defence mechanisms.

Modified from Schreml et al.⁶⁷

In particular, leave-on products (e.g. lotions and creams) not optimised with respect to pH and used on a regular basis may disturb skin pH or affect the normal skin flora, which could be shown in various clinical studies.^{3-5,8,39,67-76}

AGE-RELATED CHANGES IN SKIN pH

The pH_{SS} of neonates is neutral to alkaline immediately after birth. The acidification process starts within the first 24 hours, and during the first weeks a switch to moderately acidic pH_{SS} occurred.⁴² During early infancy of the child, pH_{SS} reaches normal acidity after approximately 6 months.⁶² Previous studies demonstrated that pH_{SS} increases slightly with age.⁶ Even though there is no United Nations (UN) standard numerical criterion for the different classes of age, the UN agreed on a cut-off at 60 years in the developed world to refer to the old age or elderly population, and in this paper we refer to this classification. In general, a linear correlation between pH_{SS} and age was observed by two independent groups.^{6,73}

Three molecular mechanisms responsible for the acidification of skin appear to be disturbed with increasing age: a decreased NHE1 expression, a reduced breakdown of phospholipids into acidifying FFAs, and a reduced breakdown of filaggrin into natural moisturising factors.^{24,69,24} In addition, sebum and sweat production are decreased in the elderly, thereby further decreasing the buffer capacity of the skin.^{78,79} The age-related pH_{SS} increase alters several functions in the skin of the elderly, and therefore may have negative effects. An increased pH_{SS} impairs SC function, which may cause disturbed lipid processing, putatively via influencing the two key lipid-processing enzymes β -glucocerebrosidase and acidic sphingomyelinase, which both exhibit highest activity at low pH. Therefore, their activity will be reduced with increasing age.^{25,40}

Moreover, the maturation of lamellar membranes is delayed.^{69,76,24,79-82} It has been proven that barrier recovery in aged, compared to younger, human epidermis is reduced.^{83,84} Furthermore, an increased skin pH will lead to premature degradation of corneodesmosomes and increased desquamation because activity of serine proteases increases parallel to pH of the skin.^{68,24} Therefore, the SC can be easily removed by tape stripping, and a higher amount of protein will be removed per stripping, supporting the notion of a disturbed integrity/

cohesion of the SC in the elderly. Additionally, aged epidermis exhibits abnormal growth factor signalling and reduced synthesis of epidermal lipids such as ceramides, cholesterol, and fatty acids.^{85,86} This is assigned to reduced activity of the key and rate limiting enzymes for each of these lipids (serine palmitoyltransferase, 3-hydroxy-3-methylglutaryl-coenzyme A reductase, and acetyl CoA carboxylase).⁸⁶ Lipid synthesis and enzyme activities are not only constitutively reduced, but are also not sufficiently upregulated after acute barrier disruption.⁸⁶

Furthermore, the microbial defence mechanisms of the SC are impaired due to an increased skin pH. As mentioned above, physiologic pH-values ensure normal microbial colonisation of the skin, whereas aged skin exhibits an increased susceptibility to pathogens facilitating bacterial infections.^{88,89} Thus, an age-dependent increase of pH_{SS} very likely promotes the colonisation of the skin surface with an altered microbial flora, contributing to the development of a characteristic body odour.^{90,91}

In aged skin, lipid processing mechanisms are impaired and the lipid content decreases. Lipids are able to slow the penetration of topical substances and they are necessary to maintain the buffer system of the skin.^{39,69,73,80,82} In aged skin, topical products may penetrate more easily into the epidermis and, thus, are also potential irritants and allergens.^{69,83} With increasing age, the buffer capacity of the skin surface is impaired, resulting in less resistance towards endogenous and exogenous pH changes. Therefore, aged skin is more sensitive towards contact irritants and allergens, partially explaining the increase of contact dermatitis in the elderly.^{3,39,69} Hence, ageing skin exhibits increased vulnerability, not only to mechanical stress because of atrophic changes, but also because of an increased skin pH. Furthermore, the skin of elderly people appears rough and dry, which is sometimes associated with itching, probably related to an increased pH_{SS}. Thus, we assume that appropriate skin care products (leave-on as well as rinse-off products) for the elderly should be formulated to normalise the age-related pH increase.

SKIN CARE OF MATURE SKIN

In general, skin care products for the elderly should contain emollients and moisturising ingredients to prevent dehydration of the skin.

In addition, water-in-oil formulations are more effective compared to oil-in-water formulations because of prolonged skin hydrating effects.⁹² Furthermore, it is known that skin pH increases immediately but only transiently (up to 1 or 2 days) if the skin is rinsed with tap water.³⁹ Hand washing with alkaline soap causes an increase in pH_{SS} of up to 3 units, lasting for >90 minutes.^{4,39,93} Furthermore, topical products not adjusted to a physiological pH of the skin, such as deodorants, affect pH_{SS} for a few hours.⁴ For example, sodium lauryl sulphate, a contact irritant, leads to a significant increase of pH_{SS} and to a disturbed skin barrier function.^{39,94} Thus, numerous studies in humans have addressed changes of pH_{SS}, following the use of rinse-off as well as leave-on skin care products.^{67,93-99} However, only a few studies have investigated the effect of skin care products on old aged skin exhibiting increased pH-values.^{100,101}

It could be shown that washing hands with acidic mineral water, or a balneotherapeutic application of acidic spring water (pH 2), can inhibit bacterial growth, reduce pH_{SS} for a prolonged time, and decrease levels of resident *Staphylococcus aureus* in 76% of the cases.^{95,102-104} Repeated application of carbonated water (pH 5.4) or of lactic acid formulations (pH 3.7-4.0) led to a highly significant reduction of skin pH_{SS} and reduced transepidermal water loss, as well as to a significant improvement in barrier function.^{105,106} Washing sensitive skin with a mild acidic emulsion (pH 5.5) revealed only a mild damage of SC function compared to washing with water (pH 7.0).⁹³ In another study, pH_{SS} was significantly decreased for 3 hours after application of a 10% α -hydroxy acid oil-in-water emulsion.⁶⁷ Furthermore α -hydroxy acid seems to be effective in reducing dry skin conditions and enhancing the skin barrier function.¹⁰⁷ Administration of a combination of glycolic acid and α -lipoic acid (glypoic complex) on sun and age-damaged skin even improved skin texture, tone, discolouration, and led to less pronounced wrinkles.¹⁰⁰ One of the underlying mechanisms was found in an *in vitro* study investigating the effects of glycolic acid on human SC.⁹⁸ In this study, activities of proteinases regulating desquamation were shown to be remarkably increased at pH 3.⁹⁸

It is recommended that skin care products should exhibit a pH <5.5 to not disturb the physiological pH of the skin.^{97,100} However, according to the literature, there is an increase of skin pH with increasing age, leading to impaired SC function and

to reduced buffer capacity. These negative effects of an age-dependent increase of skin pH may be reverted by exogenous acidification of the skin surface.^{67,77,108} Therefore, skin care products for aged skin should be formulated so that they normalise the age-dependent increase of skin pH to ameliorate the impaired SC function. Thus, rinse-off as well as leave-on products for the elderly should be formulated with a more acidic pH as compared to normal skin care products. A clinical trial showed a positive effect of topically applied oil-in-water emulsions with different pH of 3.5 or 4.0: pH_{SS} in people older than 80 decreased significantly after a single application of either emulsion to a pH_{SS} <5.0 for more than 7 hours.¹⁰⁸ Furthermore, topical α -hydroxy acid, containing emulsions (either water-in-oil or oil-in-water), with a pH of 4 have recently been shown to reduce pH_{SS} over a number of hours (own data). Moreover, even lower levels of the SC exhibited markedly reduced pH_{SC} over hours.¹¹ Yet, our own unpublished data have revealed that long-term application (4 weeks) of a water-in-oil emulsion adjusted to pH 4.0 can reduce pH_{SS} significantly. After 14 days, pH_{SS} was reduced by about 0.38, and after 28 days even by 0.52 pH units (see [Figure 2](#)), suggesting long-term instead of short-term treatment. This finding is not in contrast to an independent study by Buraczewska and Lodén.⁹⁴ They failed to prove the superiority of a cream of pH 4.0 over a cream of pH 7.5 regarding the promotion of skin barrier recovery after a short-term treatment of only 7 days.

Investigating effects on skin collagen metabolism was not part of our study. However, Ditre et al.,¹⁰⁹ among others, showed an increased skin thickness caused by increased synthesis of collagen and possibly elastic fibres after treatment with a pH 3.5 lotion in a placebo-controlled trial. Therefore, based on our findings, it is recommended that skin care products for continuous application (e.g. daily) should be formulated taking into account age-related changes of the skin, in particular increased pH and reduced hydration. This has already been suggested by Maibach and Levin⁶⁹ in an article published in 2011 in *Cosmetics and Toiletries*.⁶⁹ Such products with an acidic pH to normalise the age-dependent increase may very likely improve not only cosmetic appearance but also physiological skin function. Taking all these into account, practical suggestions regarding the suitable skin care of the elderly were summarised in [Table 1](#).

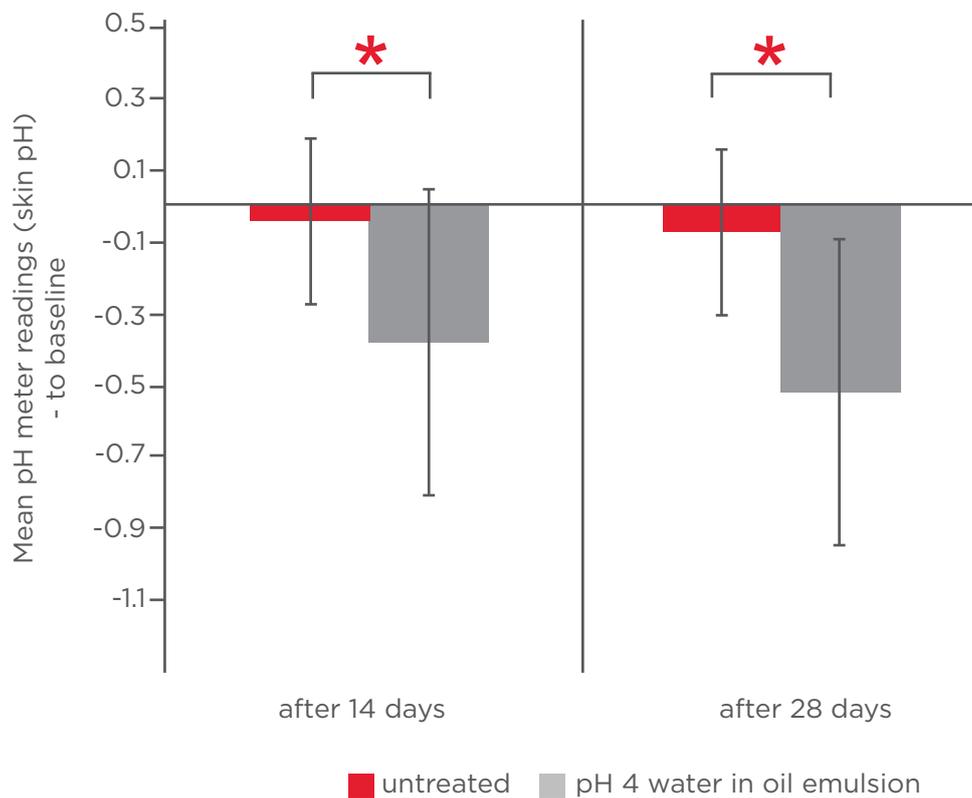


Figure 2: Reduction of skin surface pH after 14 and 28 days of application of pH 4 emulsion.

A water-in-oil emulsion adjusted to pH 4 significantly reduces skin surface pH after 14 days, further reducing pH after 28 days of application. 30 individuals with an average age of 70.9 years were topically treated two to four times daily with a water-in-oil emulsion adjusted to a pH of 4. After 14 days of treatment, a significant decrease of skin pH was observed compared to baseline values. In the treated group, the pH-value decreased about -0.38 ± 0.33 after 14 days of treatment to -0.52 ± 0.58 after 28 days of treatment. Mean \pm SD; * $p < 0.05$ in Wilcoxon Signed-Rank Test.

Table 1: Practical suggestions regarding suitable skin care for maintenance of a physiological and healthy skin pH in aged skin.

Practical suggestions regarding the suitable skin care of aged skin	
Cleansing	Better to shower than to bath; duration: 5-10 minutes
	Water temperature should not exceed 35 °C
	Use of mild, soap-free syndet-based products
Moisturising	Preferential use of water-in-oil emulsions
	Only few ingredients to reduce risk of sensitisation
	Regular use prevents from itching and scratching

Modified from Abels et al.¹¹⁰

CONCLUSION

Physiological pH_{SS} of the skin ranges between 4 and 6. The acidity of the skin surface is crucial for physiological skin functions. A decline in SC

acidity, as it is observed in aged skin, may negatively affect physiological skin functions, such as barrier permeability, integrity/cohesion of the SC, and antimicrobial capacity. Following the suggestions of Maibach and Levin,⁶⁹ and based

on our own clinical data, skin care products for the elderly (either rinse-off or leave-on products) should be formulated with a pH, e.g. of 4, which may

normalise the age-related increase of skin pH and thereby help to maintain physiological skin functions and a healthy skin.

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