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REVIEW ARTICLE

Skin pH: From Basic Science to Basic Skin Care

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The "acid mantle" is a topic not only of historical interest, but also of clinical significance and has recently been linked to vital stratum corneum function. Despite compelling basic science evidence placing skin pH as a key factor in barrier homeostasis, stratum corneum integrity, and antimicrobial defense, application of the acid mantle concept in clinical care is lacking. We review recent basic science investigations into skin pH, discuss skin disorders characterized by aberrant pH, and finally discuss practical application for preservation of the acid mantle. Recognizing factors that alter skin pH and selecting products that preserve the acid mantle is of prime importance in treating dermatologic patients. ***Key words: skin pH; acid mantle; stratum corneum; barrier homeostasis; serine protease; atopic dermatitis; acne; intertrigo; diaper dermatitis; syndets.***

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Nearly a century ago, Schade and Marchionini first coined the term *Säuremantel* or "acid mantle" to describe the inherent acidic nature of the stratum corneum (SC) (1). In the last decade it has been demonstrated that skin pH largely influences barrier homeostasis, SC integrity and cohesion, and antimicrobial defense mechanisms (2–7).

In spite of mounting evidence that skin pH plays a vital role in SC function, application of the "acid mantle" concept in clinical care has lagged behind. The importance of preserving an acidic skin pH, especially in those affected by certain skin diseases, remains an under-recognized topic by practicing U.S dermatologists. This is evident by the scarcity of low pH soaps, cleansers, and moisturizers available in the US market.

The purpose of this article is to reintroduce the subject of the "acid mantle" and provide the reader with objective evidence that skin pH is intimately linked to vital SC function. It is impossible to ignore recent compelling basic science investigations placing the role of pH in the forefront of SC function (2–6). Aberrant pH has been noted in several skin diseases and these will be reviewed. Finally, practical recommendations will be discussed with respect to use of soaps, cleansers, and moisturizers that preserve the "acid mantle". At the very least, we hope to provide some "pH" ood for thought.

PHYSIOLOGIC SKIN pH

Skin pH is normally acidic, ranging in pH values of 4–6, while the body's internal environment maintains a near-neutral pH (7–9). This creates a steep pH gradient of 2–3 units between the SC and underlying epidermis and dermis. The physiologic role of an acidic skin surface, historically was thought to be a defense mechanism against invading organisms. More recently, it has been demonstrated that several key enzymes involved in the synthesis and maintenance of a competent skin barrier are largely impacted by pH. Hence, a broader view of the importance of pH in relation to function and integrity of the skin is emerging.

FACTORS INFLUENCING SKIN pH

A number of factors, including both endogenous and exogenous elements, affect skin pH. See Table I (10). Some of these endogenous factors will be discussed, and altered pH observed in these situations may partially explain certain clinical phenomena observed in these settings.

Age

Immediately after birth, skin surface pH of both full-term and preterm neonates is elevated compared to adults and older children. The mean pH value from 6 different body sites in the first day of life in full-term neonates was 7.08, which is significantly higher than in adult controls (pH 5.7) (11). pH decreases steeply in the first few days of the postnatal period and then more

Table I. *Factors influencing skin pH (adopted from Yosipovitch et al. 1996 (10))*

Endogenous factors	Exogenous factors
Age	Detergents, cosmetics, soaps
Anatomic site	Occlusive dressings
Genetic predisposition	Skin irritants
Ethnic differences	Topical antibacterials
Sebum	
Skin moisture	
Sweat	

gradually in the rest of the neonatal period (12–14). pH values later in infancy are similar to that of adults (15).

A decrease in pH occurs from day 3 to day 30 of the neonatal period and is most prominent in the volar forearm area compared with the forehead, cheeks, and buttocks (14). There is no disparity in pH values between different body sites in the neonate 1–2 days after birth (11). By day 90, pH is higher on the cheek and buttock and lower on the forehead and forearm (14). This apparent difference can be explained by exogenous factors, namely diaper occlusion in the buttock region and climatic factors in the exposed cheek skin (16). Eczema generally favors extensor areas in neonates, i.e. the cheeks, compared to the usual flexural distribution in adults. Extensor eczema and diaper dermatitis, commonly observed dermatoses in the infant, arise in areas with higher pH values.

A potential mechanism associated with enhanced desquamation observed in the first few days postpartum relates to the elevated pH levels. Elevated pH is known to increase activity of serine proteases, kallikrein 5 and 7, which are involved in desquamation and degradation of corneodesmosomes (5). Increased activity of these enzymes in the setting of higher pH levels likely explains the enhanced desquamation observed in the first few days postpartum, when the skin surface is more alkaline (16). Additionally, key enzymes involved in the synthesis of the permeability barrier, β-glucocerebrosidase and acidic sphingomyelinase, which require an acidic pH are not fully activated in the newborn period resulting in decreased skin hydration (17).

Increased skin pH and reduced buffer capacity has also been documented in skin of the elderly (9, 18, 19). Ceramide deficiency, observed in aged skin (20) has implications for barrier function and may be explained by elevated activity levels of certain enzymes that have alkaline optima. Alkaline ceramidase, which has a pH optimum of 9 and is involved in barrier lipid degradation, has higher activity in aged human skin (7).

Skin site

There are "physiologic gaps" in the acid barrier depending on skin site, particularly the interdigital spaces and intertriginous areas-axillae, groin, inframammary zone. The pH is higher in these regions compared to other skin sites (21). Higher pH in the axilla leads to colonization by certain odor-producing resident bacteria such as propionibacteria and staphylococci (22). Deodorants containing citrates reduce pH and inhibit bacterial activity (23). Candidal intertrigo also preferentially develops in the alkaline environment of the intertriginous areas.

Pigmented skin

Gunathilake et al. (4) demonstrated significantly more acidic surface pH in darkly pigmented individuals (Fitzpatrick IV–V) compared to lightly pigmented subjects (Fitzpatrick I–II) (pH 4.6 ± 0.03 vs. 5.0 ± 0.04). Additionally, superior SC integrity and barrier function were observed in darker skin. These qualities were attributed to increased epidermal lipid content, increased lamellar body density, and lower pH in the darkly pigmented group. Serine protease activity was reduced in the more acidic environment of the darker skinned group and increased in the higher pH setting of the lightly pigmented group. Furthermore, acidification of type I–II skin with topical polyhydroxyl acids to pH levels seen in type IV–V skin enhanced barrier function in the former group to levels comparable to the darkly pigmented group (4).

SKIN pH AND BARRIER FUNCTION

The stratum corneum's role as a permeability barrier hinges on its hydrophobic character, lipid distribution, and organization of lipids into a series of lamellar bilayers (24). The formation of the SC barrier, specifically generation of its lipophilic components, involves several pH-dependent enzymes. Two key lipid-processing enzymes, β-glucocerebrosidase and acidic sphingomyelinase have pH optima of 5.6 and 4.5, respectively (7). Both are involved in the synthesis of ceramides, critical components of the permeability barrier. Activity of β-glucocererbrosidase is 10 times lower *in situ* at pH 7.4 than at pH 5.5 (25). Processing of lipids secreted by lamellar bodies and formation of lamellar structures require an acidic environment (26). Additionally, free fatty acids in the extracellular space form lamellar liquid crystals at pH values of 4.5–6 through partial ionization (26–28).

Investigations in both mice and human models corroborate the assertion that pH impacts barrier function. *In vivo* studies in hairless mice exposed to acetone insult or adhesive film-stripping demonstrated faster barrier function recovery in the presence of acidic buffer solution compared to neutral buffer solution (25). Similarly, blockade or knockout of secretory phosholipase A2 or the sodium-proton exchanger, both of which are involved in acidification of the SC, resulted in compromised permeability barrier homeostasis and SC integrity (2, 3). Finally, studies have shown that elevations of pH in normal skin creates a disturbed barrier, linked to increased activity of serine proteases and reduced activities of ceramide-generating enzymes (5, 6).

Recently, Hatano et al. (29) demonstrated that maintenance of an acidic SC via application of polyhydroxyl acids prevented development of hapten-induced atopic dermatitis (AD) in at-risk mice. Lowering pH in these hapten exposed mice also reduced the inflammatory TH2 response, prevented epidermal hyperplasia, reduced tissue eosinophilia, and normalized epidermal structure (29). Their findings provide intriguing implications about the use of acidic topical preparations in altering

the course of inflammatory dermatoses. Applications of polyhydroxyl acids have been shown in earlier studies to improve barrier function in both neonatal and aged rodent skin (30, 31) and even to super-normalize barrier function in normal mice (32), and in humans (4).

SKIN pH AND STRATUM CORNEUM INTEGRITY

pH not only influences barrier homeostasis, but also affects SC integrity, cohesion, and desquamation. Serine proteases, kallikrein 5 (SC tryptic enzyme) and kallikrein 7 (SC chymotryptic enzyme), have neutral pH optima and are intimately linked to desquamation by degrading desmoglein 1 (33–35). As pH increases, these serine proteases are activated, while the enzymes responsible for generating ceramides which have an acidic optima are inactivated compromising SC structure and function. As serine protease activity is sustained, lamellar body secretion is blocked (6, 36). See Fig. 1 for summary.

SKIN pH AND ANTIMICROBIAL PROPERTIES

The microflora of the skin consists of transient, temporary-resident, and permanent-resident species, including coagulase-negative staphylococci (37). Normal flora growth is optimal at acidic pH levels, whereas pathogenic bacteria, such as *S. aureus*, thrive at a neutral pH levels (38). Dermicidin, an antimicrobial peptide found in sweat, demonstrates antimicrobial activity against a variety of pathogenic microorganisms. Incubation of *S. aureus* with a sweat fraction containing dermicidin induced >90% bacteriocidal effect when buffered at pH 5.5, and only 60% when buffered at pH 6.5 (39). Chikakane & Takashashi (40) have also postulated reduced antibacterial activities of cationic substances, such as certain basic proteins, due to reduced acidity. Nitrate secreted in sweat is converted to nitrite by bacteria. Nitrite then forms reactive nitrogen species which serve as a non-specific antibacterial defense mechanism. This occurs in an acidic milieu (41).

SKIN pH IN DISEASE

Permeability barrier homeostasis when functioning properly imparts the skin with the capability of withstanding external insults and retaining hydration. Stratum corneum pH and permeability homeostasis are co-dependent as earlier described. Several dermatoses characterized by disruption of the permeability barrier have altered pH and these will be discussed.

Atopic dermatitis

In a study of 100 children with AD, pH was observed to be significantly higher in eczematous skin and uninvolved skin in comparison to the skin of 21 healthy children (42). Others have documented similar findings of sequentially rising pH values in unaffected skin compared to perilesional skin and lesional skin in atopic patients (43, 44). Additionally, higher pH values have been measured in areas corresponding to more intense itching (44) and skin dryness in atopics (43).

Why is pH altered in atopic skin? Several contributing factors have been proposed. Free amino acids and urocanic acid, which are believed to be involved in creating the acidic milieu of the SC, are markedly reduced in atopic skin (45, 46). Filaggrin, a protein known to be deficient in AD, serves as an important precursor of free amino acids and urocanic acid. Sweat secretions, rich in lactic acid, also thought to contribute to the acid mantle, are reduced in AD (47). Finally, faulty secretion of lamellar bodies seen in AD (48), may have implications on acid pH, as exocytosis of lamellar bodies is a source of protons for SC acidification (49).

Impaired barrier function in AD can be explained in part by disturbed synthesis, excretion, and maturation of SC lipids (48, 49) processes that depend on enzymes with acidic pH optima. Aberrant lipid organization, namely increased gel phase relative to the crystalline phase of lamellar structures, has been described *ex vivo* in patients with AD (50). Lamellar liquid crystal formation occurs at pH values of 4.5–6. Serine proteases, specifically SC chymotryptic enzyme which has a pH optimum of 8 may also play a role in the pathogenesis of AD. Transgenic mice with increased serine protease activity exhibit an AD-like presentation (51). SC chymotryptic enzyme expression is dramatically increased in chronic eczema lesions (51). (Fig. 2). Moreover, serine proteases induce itch by activating PAR-2 receptors in keratinocytes and nerves in atopic skin further damaging the skin by inducing an itch scratch cycle (52).

In addition to impaired barrier, *S. aureus* colonization is a common feature of patients with AD and is considered a major pathogenetic factor in AD. Growth of staphylococcal strains is maximal at neutral pH (53) and markedly inhibited at pH values around 5 (53, 54). The 3 dimensional structure of Staphylococci enterotoxins is affected by pH. Staphylococci enterotoxin C2 has been shown to largely deviate from its normal 3-D

↑ SP activity → DSG degradation → loss of corneodesmosomes → abnormal integrity/cohesion
↑
↑ pH → ↓β-Glcer'ase / sphingomyelinase activity → ↓ lipid processing → abnormal permeability homeostasis

Fig. 1. Mechanism of pH altering permeability and stratum corneum integrity. SP: serine protease DSG: desmoglein.

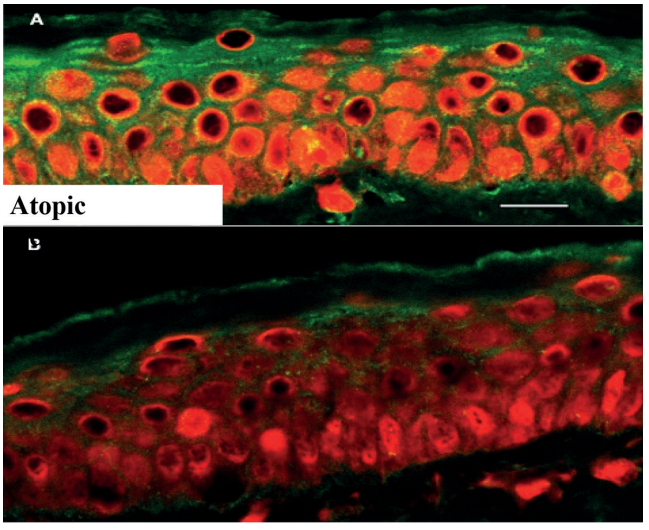

Fig. 2. Increased serine protease activity in atopic dermatitis (top) compared to normal (bottom). Orange fluorescence correlates to serine protease activity. Contributed by Dr. Peter Elias (unpublishd data).

structure at pH 5 compared to pH of 8 (55). *In vitro*, the adhesion of *S. aureus* to human keratinocytes increased with increasing pH (56). See Fig. 3 for summary of pH-related events in AD.

Ichthyosis

Öhman & Vahlquist (57), found significantly higher skin pH (5.3 ± 0.7) in patients with ichthyosis vulgaris compared to patients with X-linked ichthyosis (4.6 ± 0.4) and healthy subjects (4.5 ± 0.2). During tape stripping, a neutral pH of about 7 was reached in patients with ichthyosis vulgaris after half the horny layer was removed. In X-linked ichthyosis, a plateau of 6.2–6.6 in pH value was never exceeded with tape stripping. Filaggrin is known to be reduced in ichthyosis vulgaris and is also believed to play a role in acidifying the SC. Conversely, in X-linked ichthyosis, the aberration involves steroid sulphatase leading to accumulation of cholesterol sulphate and flattening of the pH gradient. Enzymes involved in desquamation are pH-dependent and alteration in pH disturbs normal desquamation (57). The use of acidic preparations with lactic acid promotes keratolysis and is effective in these ichthyoses.

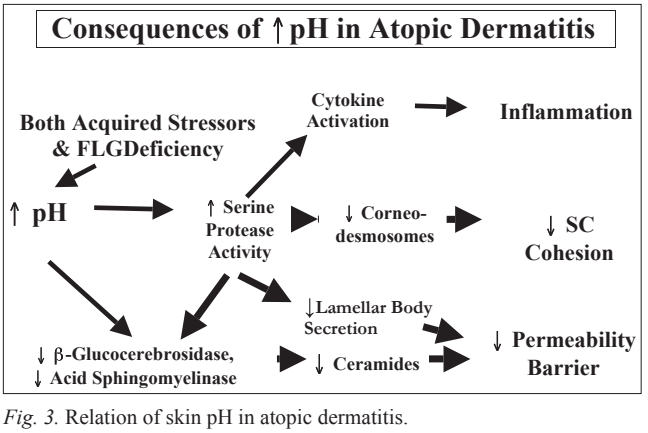

Fig. 3. Relation of skin pH in atopic dermatitis.

Candidal intertrigo

Candida albicans, a dimorphic yeast, is influenced by pH. An acidic pH favors the blastospore form and an increased pH promotes the mycelial phase (58, 59). The mycelial form is associated with pathogenicity (58, 60). In one study (61), solution with *C. albicans* was applied under occlusion to the left and right forearms of subjects, buffered at 2 different pH levels (6.0 and 4.5). Skin reactions 24 h later were more pronounced on the arm with the higher pH in 14 of the 15 subjects studied. An acidified nitrite cream has been reported to have antimycotic activity (62). Diabetics are particularly prone to develop candidal intertrigo. In a study involving non-insulin dependent diabetics, skin pH was significantly higher in the intertriginous zones of diabetics compared to intertriginous zones of healthy individuals (63). Interestingly, there was no difference in forearm pH of the two groups. Higher pH in diabetic intertriginous skin was interpreted as a possible factor promoting host susceptibility to candidal infection.

Diaper dermatitis

A number of factors play a role in development of irritant diaper dermatitis, including prolonged exposure to urine and feces, increased hydration and occlusion, changes in skin microbial flora, and altered skin pH (64). Significant correlation between severity of diaper dermatitis and elevated skin pH in the diaper area has been demonstrated (65). Exposure of urine and feces generates ammonia and produces an alkaline environment. Alkaline pH activates fecal proteases and lipases which breakdown the skin barrier. Elevated pH also influences susceptibility to *C. albicans* as earlier described, and *C. albicans* is the microorganism most commonly associated with diaper dermatitis. Recently, Beguin et al. (66) designed an adult diaper using acidic cellulose material in order to maintain a pH of 4.5–5.5 in the diaper area. Resolution of pre-existing irritant skin lesions was noted in 8 out of 12 patients after switching to the acidified diaper design (66). Development of cleansing wipes with increased pH buffering capacity to maintain physiologic skin pH has recently been under investigation (67).

Also, tampons that are purported to reduce the usual rise in vaginal pH during menstruation have been developed and are available for purchase. Vaginal pH in healthy, pre-menopausal women ranges between 3.5–4.5. The pH of blood is 7.4 and during menstruation vaginal pH increases. RepHresh Brilliant pH tampons are currently available and employ a pH-Reducing Micro Ribbon™ and contain citric acid and L-lactide (68).

Irritant contact dermatitis

Individuals prone to irritant contact dermatitis have been shown to have higher pH values compared to healthy individuals (69, 70). pH induced decline in SC integrity and barrier homeostasis further compounds the skin's susceptibility to injury from exposure to solvents, detergents, and mechanical forces (5).

Tinea pedis

In one study, mean skin pH values from the foot region of subjects with tinea pedis and those without tinea pedis were compared. Foot skin pH was significantly higher in patients with tinea compared to controls (40).

Acne

In vitro, *P. acnes* grows well at pH values between 6 and 6.5 and growth is markedly reduced at pH values less than 6 (71). In a study of acne-prone patients, the number of facial inflammatory lesions was compared in subjects using a conventional alkaline soap versus those using an acidic syndet bar. The number of inflammatory lesions increased in the alkaline soap group and decreased in the group using the acidic syndet at statistically significant levels by the 4th week of application (72).

Uremics

Skin surface pH has been shown to be significantly higher in patients on dialysis compared to healthy individuals (73), despite the fact that dialysis patients have chronic acidemia. Cutaneous infections, primarily fungal infections are common in patients on hemodialysis (74). The high pH may predispose this patient population to increased mycotic infections and may suggest a possible role in uremic pruritus (73).

PRACTICAL APPLICATION

It has been suggested that altered pH observed in the various dermatoses described earlier, is a "meaningful etiological component" and not merely an "epiphenomenon" of these conditions (75). Exposure to exogenous agents such as cleansers, creams, deodorants, and topical antibacterials affect pH and can further exacerbate underlying disease in these patients. Selection of topical agents that preserve an acidic environment seems relevant in these patients.

Cleansers

Cleansers can be classified according to the type of surfactant used. Cleansers with non-soap-based surfactants are known as "syndets" (synthetic detergent-based bars or liquids). Syndets are generally neutral or acidic (≤pH 7) compared to soap-based cleansers which are typically alkaline in nature (pH 10) (76). Soap-based cleansers are known to have a higher potential to irritate skin than syndets (77–82). Ananthapadmanabhan and colleagues (83) have demonstrated that high-pH solutions even in the absence of surfactants increase SC swelling and lipid rigidity. The higher pH of soap bars may be a contributing factor in the higher irritation potential of soap bars compared to syndet bars. Hand washing with soap causes the pH on the palms to increase by a mean of 3 units and remains altered 90 min after washing (7). Small and sustained pH increases, like those caused by daily use of soap-based cleansers multiple times a day, adversely influence the barrier repair mechanism (3). Baranda et al. (84) measured the pH of common cleansers (Table II). They found a significant correlation between alkaline pH of cleansers and skin irritation. In addition to information on pH of common cleansers, information regarding available low pH moisturizers is not readily accessible. Shi et al. (85) recently measured the pH of several moisturizers commonly used in the US some of which were found to have quite high alkaline pH (Table SI; available from http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1531).

Acidification of the stratum corneum

Topical alpha-hydroxy acids (AHA) are common agents used in treating disorders of keratinization. AHA, such as lactic acid have been shown to increase ceramide

Table II. *pH of cleansers (Adopted from Baranda et al. (84))*

Brand name	pH	Composition
Aderm	6.44	Syndet
Avecyde	3.61	Syndet
Avéne	6.94	Syndet
Cetaphil	7.72	Syndet
Dove white	7.53	Syndet
Dove baby	7.0	Syndet
Dove (liquid)	5.16	Syndet
Dove pink	7.23	Syndet
Johnson's baby	11.9	Soap
Johnson's baby oat	12.35	Soap
Nivea baby creamy	12.35	Syndet[a]
Nivea bath care	12.21	Syndet[a]
Nivea bath c. Almond	12.22	Syndet[a]
Nivea bath c. Oat	12.30	Syndet[a]
Zest neutral	9.85	Soap
Zest citrus sport	9.75	Soap
Zest herbal	9.97	Soap
Zest aqua	9.89	Soap
Palmolive green	10.18	Soap
Palmolive (white)	10.23	Soap
Palmolive botanicals	10.38	Soap
Palmolive botanicals/camomile	10.13	Soap
Camay classic	10.38	Soap
Camay gala	10.36	Soap
Camay soft	10.26	Soap

[a]plus mineral oil.

production by human keratinocytes by 300% *in vitro* (86). In one study, twice daily application of 4% l-lactic acid formulations (pH 3.7–4.0) led to significant improvement in barrier function as measured by TEWL and reduced sensitivity to sodium lauryl sulphate (SLS) after 4 weeks (86). *In vivo* the total ceramide fraction increased significantly. The ability of AHA to increase ceramide levels is beneficial in those individuals with reduced barrier function such as atopics who have reduced levels of ceramides (87, 88). Studies have shown beneficial effects of topical acidic electrolyte water (pH 2.0–2.7) on the severity of dermatitis and *S. aureus* colonization of the skin in children (89) and adults (90). Use of AHA in irritant dermatitis appears useful as evident by reduction in sensitivity to SLS.

Guidelines for dermatologists

In managing cutaneous diseases such as acne, AD, intertrigo, and irritant contact dermatitis the clinician has an armamentarium of prescription topicals and oral agents. Use of proper soaps and over-the counter creams that do not compromise the acidic pH of skin should become part of the treatment regimen of these patients. In recommending the ideal body wash, soap or cleanser, one that has a pH between 4.5–6.5, similar to the normal pH of the skin, should be selected. Syndets are less irritating and are preferred. Frequent use of alkaline medicated soaps containing benzoyl peroxide, sulfur, or resorcinol antibacterials (eg, triclocarban or triclosan), although excellent in eradicating Staphylococci and gram negative bacteria have a pH of 9–10 and cause skin irritation, so daily use should be discouraged. Often, patients with intertrigo or acne, believing that their dermatoses are related to poor hygeine, overuse harsh soaps exacerbating the condition and a vicious cycle of further cleansing ensues. Proper education and recommendations on appropriate topicals is crucial in these situations. In atopics, creating an acidic pH by selecting appropriate topicals is vital in restoring a pre-existing faulty barrier as earlier discussed. One may even consider measuring skin pH in clinic as a bedside measurement, which is a non-invasive, simple test. However the current available measurements using flat glass electrodes have limitations. The glass electrode needs calibration and measurement errors could be caused by surplus of water as well as dry electrode surface. Factors that can influence the results are sweat, washing procedures that can have alkalinizing effect on skin surface pH regardless of the pH of the solution (91).

CONCLUSION

In the last decade, the role of skin pH as a factor in vital SC function has been investigated. Likely, much remains to be learned about the complex relation of skin pH and downstream pH dependant events. We do know that many skin diseases characterized by faulty barrier function have aberrant pH values. This should prompt the clinician to focus on preserving or restoring an acidic milieu by selecting topical agents compatible with the acid mantle.

The authors declare no conflict of interest.

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