

A population-based study of the stratum corneum moisture

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Background: The stratum corneum (SC) has important functions as a bound-water modulator and a primary barrier of the human skin from the external environment. However, no large epidemiological study has quantified the relative importance of different exposures with regard to these functional properties. In this study, we have studied a large sample of individuals from the Brazilian population in order to understand the different relationships between the properties of SC and a number of demographic and self-perceived variables.

Methods: One thousand three hundred and thirty-nine individuals from a rural Brazilian population, who were participants of a family-based study, were submitted to a cross-sectional examination of the SC moisture by capacitance using the Corneometer® CM820 and investigated regarding environmental exposures, cosmetic use, and other physiological and epidemiological measurements. Self-perception-scaled questions about skin conditions were also applied.

Results: We found significant associations between SC moisture and sex, age, high sun exposure, and sunscreen use frequency ($P < 0.025$). In specific studied sites, self-reported race and obesity were also found to show significant effects. Dry skin self-perception was also found to be highly correlated with the objective measurement of the skin. Other environmental effects on SC moisture are also reported.

Keywords: investigative dermatology, stratum corneum moisture, Corneometer, sun exposure, familial data modeling

Introduction

Formed mainly by corneocytes surrounded by a very organized insoluble lipid envelope¹ and low-molecular-weight molecules responsible for moisture properties (the natural moisturizing factor),² the stratum corneum (SC), the outermost layer of the skin, is responsible for both water retention and the permeability barrier of the skin, serving as a bound-water modulator³ and also as a primary barrier of the body for pathogens, toxic components, and part of the radiation striking the organ.⁴ Previous studies have reported that the characteristics of the human SC show several variations according to the body region,⁵ sex, and also the external and internal temperatures.⁶ Changes on this layer have been correlated with several topical pathologies of the skin, such as psoriasis,⁷ dermatitis,⁸ and other (including genetic) disorders.⁹

The search for new methods that avoid the use of animal testing in experiments has brought new noninvasive devices for in vivo measurements of the human skin. Several devices are commercially available for the measurement of the moisture of the SC using different approaches, including biochemical, electrical, chemical, and imaging methods.¹⁰

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One of these is the Corneometer® CM820 (Courage + Khazaka Electronic, Cologne, Germany), which uses the capacitance principle to measure the water content of the SC.^{11,12}

Factors that modify the moisture of the SC are not completely explained in the literature. However, it is known that environmental exposure, individual habits, and several extrinsic and intrinsic factors can modify the state of the layer and its expected behavior.¹³ This knowledge is of great importance to the cosmetic industry for the development of products that take into account intrinsic and extrinsic variations of the organ, in the explanation of causal effects that act upon the skin, in the full comprehension of skin pathologies, and in the improvement of topically administered drug. Yet, the relative proportion of contribution due to each factor is not well described, which can lead to inaccurate experiments or treatments. In order to measure these quantities, a population-based study is needed, with adequate estimation procedures and considering the confounding factors related to the main measurement. The Brazilian population presents optimal conditions for this work, mainly due to the high admixture that occurred in the region since the end of the 18th century, assembling different ancestralities in the same country.^{14,15}

This study presents the results of the largest cross-sectional population-based study to date on the determinants of skin moisture. This was conducted in a Brazilian sample using a noninvasive method. Here, we describe the associations of this measurement with epidemiological, environmental, and cosmetic variables.

Materials and methods

Study population and sample design

All the subjects of this study were participants of the Baependi Heart Study, a genetic epidemiological study of cardiovascular disease risk factors with a longitudinal design in the Brazilian population. The main sampling was designed in a familial scheme in five primary steps consisting of 1) sampling design and selection of census districts, 2) sampling familial structure enrollment, 3) main data recording and physiological measurement, 4) initial analysis, and 5) follow-up.¹⁶ Baseline enrollment occurred between December 2005 and January 2006 by selecting 1,857 individuals from 95 families in the municipality of Baependi, a city in the state of Minas Gerais in the southeast of Brazil. The population has typical characteristics of a small-sized Brazilian city, with urban and rural regions, and a wide range of age-groups. The study covers ~10% of the total adult population of the city.

Probands were randomly selected from the community at large in eleven census districts. Once the probands were enrolled, all their first-degree, second-degree, and

third-degree relatives as well as those of their spouses living in the surrounding cities and who were at least 18 years old were invited to participate. To elect the participants, the study was advertised through provincial, religious, and municipal authorities, in local radio, television and newspapers, through physicians and also by phone calls. A clinic was established in an easily accessible sector for physical examination.¹⁷

Main pieces of information, such as family relationships, sociodemographic characteristics, medical history, physiological measurements, and other epidemiological data (smoking and alcohol abuse), were obtained through a closed questionnaire based on the instrument recommended for the WHO MONICA project¹⁸ and filled by trained research assistants. For this study, an additional questionnaire was applied concerning the presence of environmental exposure to sunlight, hormone replacement therapy, as well as cosmetic use and its frequency. In addition, questions based on self-perception concerning several characteristics of the skin, such as the texture, aging signs, and perceived hydration of the skin, were also performed. From 1,339 subjects who were subjected to this additional protocol simultaneously with SC moisture measurement, 1,176 individuals were identified in one of the pedigree lineages organized until now on the main research sample.

The study protocol was approved by the ethics committee of the Hospital das Clínicas, University of São Paulo Medical School, São Paulo, Brazil (project #297/12), and all subjects provided informed written consent before participating in the study. The list of variables collected in this study is found in the [Supplementary materials](#) section. The present work followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.¹⁹ All ethical proofs are available upon request.

Corneometer measurement

The biophysical measurement was performed with a calibrated Corneometer CM820 probe at three different sites: anterior forearm, posterior hand, and submalar region, previously trimmed. Ten technical replicates were performed for each site. Temperature and relative humidity of the air in the application room were previously stabilized and were also recorded. All the participants were instructed not to use any kind of cosmetic or topical drug in the last 24 hours of the measurement in order to verify the extended effect of these products after their use was stopped. All data collection was made between March 2013 and August 2014.

Statistical analysis

Statistical procedures were used to test and quantify the association between objective measures of the SC moisture

(obtained by the Corneometer) and the environmental and epidemiological factors as well as the collected self-perception variables of the skin. An initial data consistency check was performed (illegal values checking, invalid answer deletion, cross-checking, and missing data deletion) followed by a descriptive analysis and a confounding analysis. The descriptive analysis aimed to investigate data distribution and possible methodologies for the subsequent statistical modeling. Confounding analysis was intended to verify any possible influence of room temperature and relative humidity in SC measurements for subsequent consideration in the analysis, since there are occasional random variations in room conditions with time.

After preliminary analysis, statistical models were proposed to study the risk and protecting factors for the skin layer moisture. Linear mixed models were used with a kinship matrix for the covariance structure due to parental correlation between subjects, due to the familial sampling scheme, which required an explicit definition of the response covariance behavior.^{20,21} All computations were performed in the R statistical environment (R Foundation for Statistical Computing, Vienna, Austria),²² implemented with the `lmekin` function in the `coxme` library.²³ Parallel computing procedures were applied in order to optimize the computation time. The R scripts are available upon request.

Initially, each exposure as well as the epidemiological and perception variables was fitted with age, sex, and confounding covariates (temperature and air humidity) to explain the SC moisture levels of the sample. Two different models were proposed in order to measure both regional and overall effects of covariates in SC moisture: one regression procedure for each body region and a general model with all observations, considering the body site as a random effect due to its different properties is described in the literature.²⁴

Final additive and interaction models were constructed considering the main significant variables in previous modeling, intending to verify the effects of covariates in the presence of other significant effects. Ordinal categorical variables were treated as numerical scales when possible.

Results

Descriptive measures for main variables of the sample are shown in Table 1. Respondents were in the age range of 18–89 years, with an average of 47 years. Eight hundred and forty-seven (63.25%) participants were women, and 492 (36.74%) participants were men. Of the 1,339 individuals, 10.8% were self-attested as smokers, 42% confirmed regular exposure to sunlight, and 21% declared

Table 1 Main descriptive table

Variables	Women (n)	Men (n)	All, N (%)
Age (years)			
Mean	46.773	48.539	47.422
Median	48	49	48
SD	15.594	17.251	16.238
BMI (kg/m ²)			
Mean	26.106	25.826	25.926
Median	25.195	24.988	25.076
SD	5.388	5.024	5.157
Ethnicity (self-reported)			
White	555	338	893 (66.7%)
Black	40	17	57 (4.3%)
Mixed	140	81	221 (16.5%)
Smoking			
No	559	227	786 (58.7%)
Former smoker	204	188	392 (29.3%)
Social smoker	9	8	17 (1.3%)
Yes	75	69	144 (10.8%)
Smoking history			
Never	558	227	785 (58.6%)
Until 5 years	81	67	148 (11.1%)
6–10 years	43	34	77 (5.8%)
11–15 years	26	28	54 (4%)
>15 years	138	136	274 (20.5%)
Alcohol abuse score (0: abstinent and 6: heavy drinking)			
Mean	1.79	2.113	1.998
Median	0	0	0
SD	4.093	5.197	4.832
Sun exposure			
Always	532	186	718 (53.6%)
Sometimes	46	17	63 (4.7%)
Never	269	289	558 (41.7%)
Sunscreen use			
Daily	241	33	274 (20.5%)
Sometimes	184	53	237 (17.7%)
Occasionally	76	82	158 (11.8%)
Do not use	346	324	670 (50%)
Hormone replacement therapy			
No	753	0	753 (56.5%)
Not currently	78	0	78 (5.8%)
Yes	14	0	14 (1%)
Antiaging treatment	106	6	167 (2.7%)
Total, N (%)	847 (63.256%)	492 (36.744%)	1,339 (100%)

Abbreviations: SD, standard deviation; BMI, body mass index.

using sunscreen products daily. For self-reported race/color, 893 (66.7%) self-declared as white, 57 self-declared as black (4.3%), and 221 self-declared as mixed (16.5%). Detailed descriptive tables, missing rate, and other measures are listed in [Tables S1–S3](#).

For the self-perception variables, it is possible to note that 42% of the subjects declared their own skin appearance as “regular”, while 26% of the subjects expressed the perception of good skin appearance. When asked regarding the self-perception of the skin moisture, 28% of the participants affirmed not having a hydrated skin.

Corneometer observations indicated a symmetric distribution for both sexes and body sites. This fact supports a normally distributed assumption modeling for the presented data (Figure S1). Also, the Pearson correlation coefficient was computed, aiming to check possible confounding effects of room temperature and air humidity in the SC measurement. The procedure provided small correlation values but gave statistical evidence for an association between the Corneometer values and temperature ($Rho = 0.082$; $P = 0.000015$) and humidity ($Rho = 0.177$; $P < 0.00001$). These effects were also added to the modeling in order to check their influence in the final analysis (Figure S2).

Initial modeling

For the proposed initial additive modeling (SC outcome explained by each response plus sex, age, and confounding variables), Figure 1 describes main epidemiological and exposition covariates related to the SC moisture. From the model, it is possible to note that men presented smaller values of skin moisture than women (the reference level). High sun exposure leads to a higher loss of skin moisture for all investigated sites of the body. Age affects the SC moisture, mainly at the sites of hand and anterior forearm. In addition, body mass index and weight show a slightly negative relation with the Corneometer values for the anterior forearm. Self-reported black and mixed races present a strong intrinsic protective factor for different body sites compared to self-declared white skin color (the reference level).

Also in this approach, the self-perception modeling coefficients are shown in Figure 2. Analysis shows that individuals who reported having dry or very dry skin, in fact, present smaller measured moisture values. The same inference is possible for subjects who declared poor skin moisture. Also, relevant relationships were found between the Corneometer readings and skin softness, texture, and luminosity perception. The less perceived these perceptions are, the less is the actual skin moisture measure.

Final modeling

For the multiple regression approach, which includes all the covariates that found relevant to the previous analysis (still considering body site as a random effect), male sex, age, high sun exposure, and sunscreen use still presented significant relationship with SC moisture. Yet, room temperature and air humidity showed evidence of an association with the Corneometer measures, indicating a small (and here treated as) confounding effect. Modeling also confirms the direct

proportional protective factor of darker tone of self-reported skin color for SC moisture. The log-likelihood ratio test²⁵ provided evidence for this approach against basal models. The estimates are listed in Table 2. Additional coefficients and P -values are listed in Table S4.

The computation of a final model with several covariates is justified by the need to verify joint effects of each regressor in the presence of others. This modeling can provide some additional measures to the inference of the SC moisture variation in the population. Generalized R^2 proposed by Nagelkerke²⁶ gives an appropriate quantity to measure the proportion of the total variance explained by the model. In the present case, 18.23% of the SC moisture measurement variation is explained by the previously mentioned factors, not considering self-perception variables. Genotypic variants and metabolic or other environmental variables can be responsible for unexplained variance. A discussion about these findings is given in the next section. Residual analysis was performed to check the distribution assumptions of the proposed models (Figure S3).

Discussion

Intrinsic factors associated with SC moisture

Our findings describe men as more prone to dry skin (in 6.9 moisture units) compared to women. Generally, it is well described, and the literature agrees with the hypothesis of distinct skin properties for each sex,²⁷ including SC moisture.²⁸ Statistical evidence was found for an association between self-declared race and SC moisture; compared to white race/color (the reference level), black and mixed individuals were found to have a “protective gradient” for the layer property (six moisture units for blacks vs two moisture units for mixed race). Previous works reported no relationship or only a small relationship between skin surface hydration and race.^{29–31} However, most previous studies²⁹ were conducted in small samples. In addition, the Brazilian population has a high admixture degree³² that differs from most of the studies performed with small samples from specific ethnic groups. In the final modeling, even with the effect of solar exposure, the data presented strong evidence for this fact, which tempts us to suggest that this relationship is a product of genetic ancestry variations modulating SC moisture with reciprocal action on epidermal melanin photoprotective properties.

Concerning the effect of aging on SC moisture properties, Marrakchi and Maibach³³ have affirmed that previous works

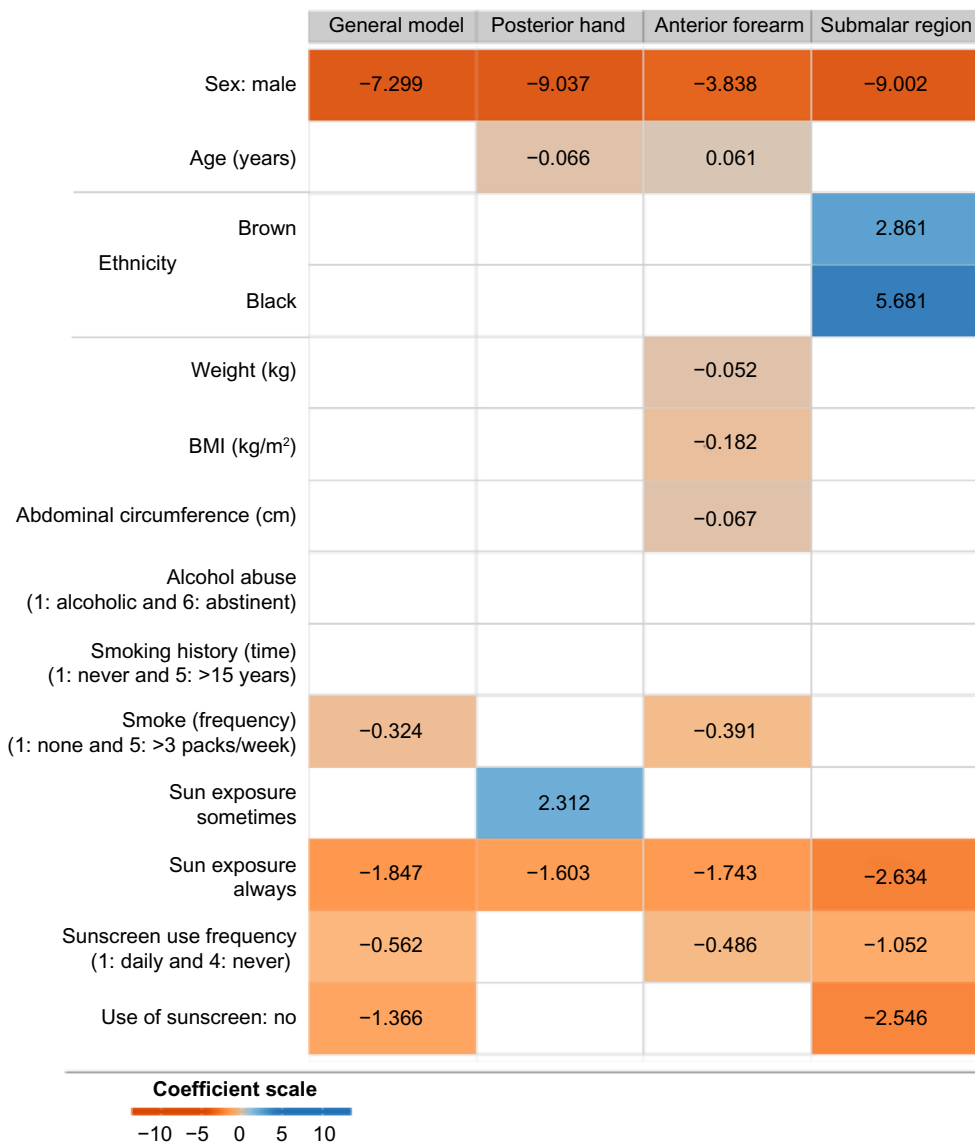


Figure 1 Diagram displaying effect intensity on stratum corneum moisture of each mainly studied covariate in initial modeling.

Notes: Values in the boxes show estimated coefficients of each model. Negative effects are displayed in red scale, while positive effects are shown in blue tones and values next to zero (nonsignificant) present gray tone. Empty boxes represent no significant relationship (critical P -value >0.025). One can see strong inverse association between the Corneometer measurement and the male sex and high sun exposure. In this model, the reference level for sex is female, and the reference level for sun exposure is never exposed. Alcohol abuse, smoking time, and frequency are taken as numerical scale.

showed conflicting results concerning the effect of aging on skin surface moisture, and suggested studies in homogeneous groups in order to reduce race and sex effects in the results. Tagami³⁴ underlined relevant differences in the perioral surface hydration according to age in a group of Chinese women. Darlenski and Fluhr reported an increased skin dryness with age in the photoexposed areas, while Diridollou et al³⁵ emphasized this fact for lighter skin tones. In this study, no effect was found for the influence of age on the SC moisture for the submalar region even in the presence of race or sex effects. However, significant effects were found in others sites.

This difference can be explained by the structural variance found in the facial skin according to the region.³⁶

Extrinsic factors associated with SC moisture

Solar ultraviolet (UV) radiation exposure has been described by several authors as harmful for several skin processes and properties. Bonté³⁷ related skin dryness with damage due to chronic sun exposure, and Humbert³⁸ reported its effects on the skin's youthfulness. In fact, this study shows smaller values of SC moisture for subjects who referred to frequent

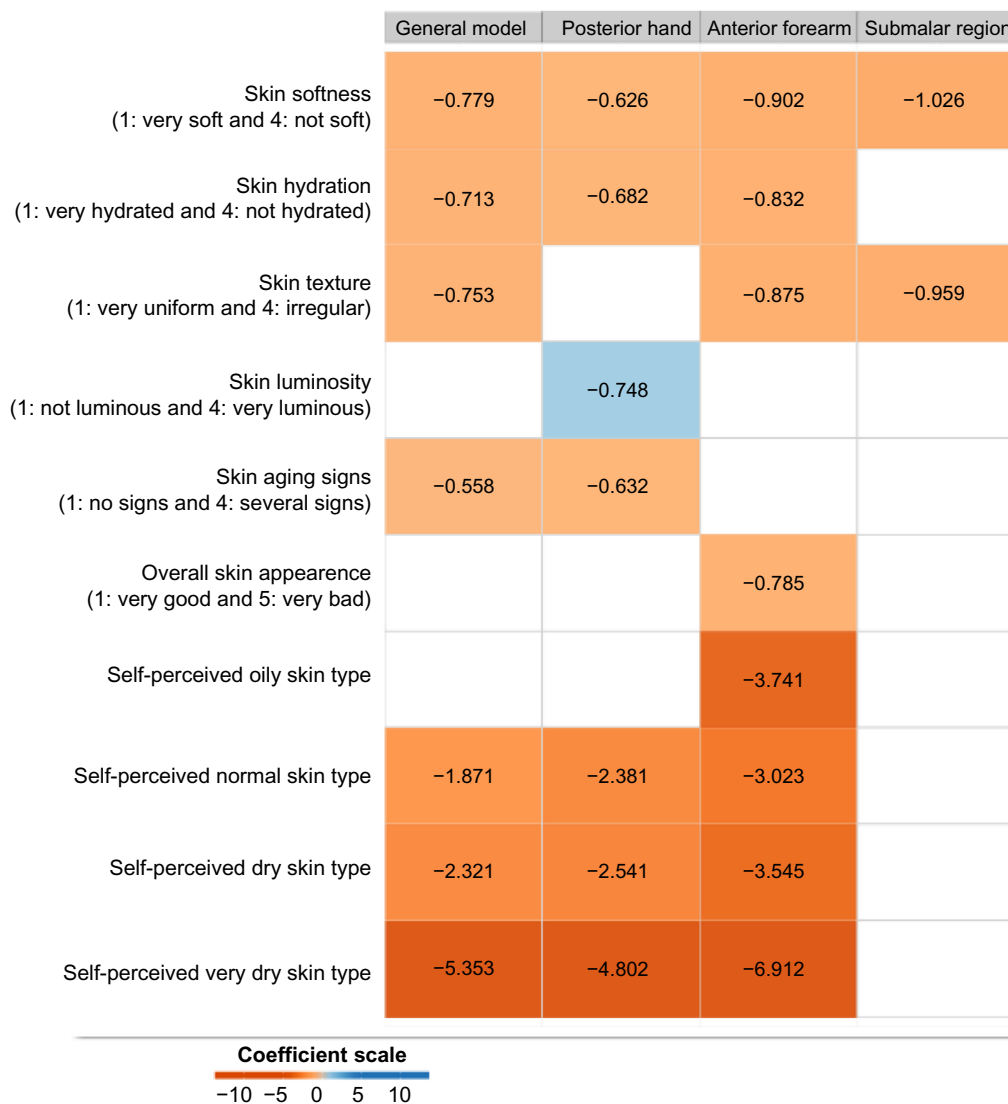


Figure 2 Diagram displaying effect intensity on stratum corneum moisture of each self-perception question in initial modeling.

Notes: Values in the boxes show the estimated coefficients of each model. Negative effects are displayed in red scale, while positive effects are shown in blue tones and values next to zero (nonsignificant) presents gray tone. Empty boxes represent no significant relationship (critical *P*-value >0.025). One can see strong association between the Corneometer measurement and the self-perceived dry and very dry skin of the participants. It is also possible to note this relation for perception of skin softness, hydration, texture, and luminosity. In this model, the reference level for self-perceived skin type is mixed skin.

sun exposure, in all the studied body sites. Most studies describe this fact through clinical experiments; we confirm the role of solar exposure based on the epidemiological point of view, leading to high evidence that the aftereffects of excessive solar exposure influence this skin property in the general population.

The literature presents relevant associations between smoking and skin damage or related diseases,³⁹ mainly for events centered on the epidermis. Despite the small number of studies investigating changes on SC properties, the authors agree with the hypothesis that smoking leads to several changes in the organ,⁴⁰ including less water content on SC.^{41,42} In the present case, smoking frequency shows

evidence for an action in SC moisture for the anterior forearm.

Derraik et al⁴³ showed a high association between body weight and skin thickness, and Kim et al⁴⁴ showed the relation between the thickness and moisture of SC in an animal sample of hairless mice. Our results indicate that body mass index and weight are associated with forearm SC moisture. This finding suggests that moisture of the skin is a product not only of the molecular processes of the layer but also of the structural organization of the stratum, where the moisture level is proportional to the thickness, with changes occurring due to increased weight in specific body sites. In fact, Guida et al⁴⁵ showed higher transepidermal water loss in obese

Table 2 Coefficient estimates and associated *P*-values for covariates for final proposed model

Covariate/level	Coefficient	Standard error	<i>P</i> -value
Intercept	5.807821	4.185529	0.17
Temperature	0.867252	0.129443	<1×10E-10
Air humidity	0.204178	0.019874	<1×10E-10
Sex			
Male	-5.94138	0.427233	<1×10E-10
Age	0.032517	0.012337	0.0084
BMI	-0.07749	0.038641	0.045
Ethnicity			
Brown	0.976346	0.507066	0.054
Black	2.387815	1.025978	0.02
Sun exposure			
Eventually	1.145759	0.878445	0.19
Always	-2.05304	0.393892	<1×10E-10
Sunscreen use	-0.52107	0.163704	0.0015

Notes: *P*-values in bold indicate significance at 0.05. Reference level for sex is female, reference level for smoking is not smoking, reference level for sun exposure is never exposed, and reference level for self-perceived skin type is mixed skin.

Abbreviation: BMI, body mass index.

individuals, linking this fact with metabolic changes in this group. Further investigations covering the link between metabolism variations and SC moisture and thickness properties are warranted.

After 24 hours without using any type of cosmetics, weak evidence was found for extended effects of the products on the SC moisture for this sample. This implies that most moisturizers or other products present only short-term effects on skin hydration properties. The dynamics of the layer poses difficulties for the development of protective agents for the skin. Nevertheless, sunscreen use presented a high association with the SC moisture levels as a protective factor against sun exposure, according to its frequency of use, showing lower moisture levels in individuals who used sunscreen irregularly. It is also important to note that the coefficients found in modeling present higher values of sun exposure effect than the coefficient for sunscreen use, indicating that, on average, even subjects who use sunscreen regularly present a significant influence of sun exposure on skin moisture.

Only a few studies relate self-perceived dryness with skin surface hydration.^{46,47} The proposed models present very significant coefficients for the relation between poor skin moisture self-perception and small values for Corneometer measurements. This relation is still significant when individuals respond having dry or very dry skin or refer lower levels of softness, texture, and luminosity of the skin. These results show that the condition of the SC moisture, different from other skin properties, is easily perceived by the individual.

Evidence for the influence of air humidity and temperature with the Corneometer measures confirms the sensitivity of the capacitance-based equipment by external factors, which needs to be considered in all experimental designs in this area, as stated by previous authors.^{48,49}

Based on the additional results, 18.23% of the total variation of the SC moisture could be explained by the variables presented in this study. This implies that several other intrinsic and extrinsic effects can also modify skin surface moisture, including genetic variants, metabolic covariates, physiological covariates, and other environmental covariates, interacting and modifying each other, a fact that explains the complexity to improve the technology based on the layer, such as cosmetic formulation and topical drug delivery systems.⁵⁰

The discovery that self-perception of skin dryness is related to real skin condition can be applied in several ways from the development of products based partially on a self-reported skin history to automated systems based on a self-reported score of the skin moisture for the prediction of diseases linked to the layer.

Conclusion

Special attention is needed for the fact that solar UV exposure is a potential public health issue, concerning the cumulative sun damage caused in skin and the excessive unprotected sun exposure in several segments of the population. Since SC plays an active role in protecting the body from photodamage, quantified by Young and Sheehan⁵¹ as on the order of 66%, the risk of diseases related to changes in the organ, such as xerosis⁵² and eczema,⁵³ dramatically increases associated with individual habits and traits described in this study, such as smoking and obesity.

Based on the present results, we propose that experimental design in this area must be performed in different age- and sex groups and also in different skin tones and layer thicknesses to cover different responses of the skin due to structural changes in SC sites. We also propose that chemical formulation of products must present properties of stability toward exogenous processes (such as smoking and pollution), high photostability, and a broad spectrum action in the mentioned groups.

Based on a large sample from a highly admixed population, this study corroborated the literature concerning the effects of sex, age, sun exposure, sunscreen use, and other epidemiological factors on SC moisture and discussed about the effects of age and other covariates on this property. This study also established the concordance between objective skin

moisture measures and the self-perception of skin dryness. The presented work showed that the variation of measured moisture is due to several factors, including the environmental temperature and relative humidity.

Disclosure

The authors report no conflicts of interest in this work.

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