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## **The Future of Innovation: Unveiling the Science of Skin Diversity to Drive Cosmetic Advancements**

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### **1. Introduction**

In the current Gender Theory, there are three attributes that define an individual's sexual identity profile: sex, gender, and sexual orientation. Gender has a psychosocial scope, with the term "transgender person" referring to a group of individuals who identify themselves within socially established gender identities. Thus, "trans person" is the name given to an individual who identifies themselves through social behaviors that differ from those attributed to their biological sex at birth (SILVA et al, 2020). The term cisgender applies to a gender identity that is consistent with the sex assigned at birth (HUANG et al, 2022).

Transgender individuals can transition to their identified gender through social, hormonal, and procedural methods. It is worth highlighting the various factors involved in the transition; in this sense, a multidisciplinary team is essential to monitor the individual and provide the necessary health care. Hormone therapy is often the first medical step that initiates the process of feminization or masculinization in transgender people, which induces changes in the anatomy and physiology of the skin. Feminizing hormones such as estradiol and antiandrogenic agents induce the redistribution of fat and a decrease in the diameter of body hair, in addition to improving acne and stimulating neocollagenesis (DHINGRA et al, 2019). Giacomoni et al (2009) found that topical application of estrogen increases skin thickness by almost 10%.

Treatment with estrogen and antiandrogens decreases sebum production, which can lead to generalized xerosis, eczematous changes, and pruritus.

Masculinizing androgenic hormones, particularly androgens, regulate the sebaceous gland and hair growth by activating epithelial sebocytes and the dermal papilla of the hair follicle. Adverse reactions to hormone therapy can occur on the skin, such as eczema, pruritus, increased hair growth, and acne vulgaris (DHINGRA et al, 2019; ALMAZAN, 2016).

Recent articles have highlighted the relevance of specific dermatological knowledge about the skin health of transgender individuals and emphasize how important their skin care is for dermatology. Scientific literature shows the main changes in the skin of transgender people due to the use of hormone therapy. However, information about this is essential for a better understanding of the skin of transgender individuals.

The morphological and physiological differences between non-pigmented and pigmented skin significantly affect how different skin tones age. However, despite growing societal awareness of diversity, much of the research on skin aging has predominantly focused on non-pigmented Caucasian skin. Studies addressing racial and ethnic variations in skin function remain limited and often controversial.

In this context, our study utilized the Fitzpatrick skin phototype scale, a widely recognized classification system that categorizes skin types based on their response to UV radiation, such as susceptibility to burning or tanning. Pigmented skin includes types V (brown skin) and VI (black skin), which are less prone to burning and tan more readily. These categories encompass a wide range of racial and ethnic groups, providing a basis for exploring ageing in diverse Brazilian populations.

The aim of this work was to characterize skin diversity by obtaining clinical, molecular, and metrological data, providing insights for the development of cosmetic products that meet the needs of diverse population

## **2. Materials and Methods**

### **2.1. Ethical compliance**

The clinical trials were conducted under Resolution 466/12 of the National Council of Health on Regulatory Guidelines and Standards for Research Involving Humans. The research protocol received approval from the Institutional Ethics Committee. Only participants who voluntarily consented to participate by signing the Informed Consent Form, after receiving a complete explanation of the study, the risks involved, and the necessary procedures for adherence to the study, were included. The citation of participants was carried out through anonymized codes, maintaining the confidentiality of personal information and complying with the guidelines of LGPD. The study's data collection and processing were conducted in compliance with current Brazilian legislation on data protection and other applicable Brazilian regulations for clinical trials, always respecting the confidentiality of the data, privacy, and non-stigmatization of participants.

We have considered: Trans women and trans men, aged between 18 and 65, healthy. Participants could not present any type of skin lesion, nor any report of allergy to moisturizers and/or perfumes. Participants were duly informed about the experiment and signed the Free and Informed Consent Form. Also, we have included Healthy women, aged 35 to 65 years, with phototype II, III, V, or VI were enrolled in four groups: (A) subjects between 35 and 49 years old, phototype II and III, (B) subjects between 35 and 49 years old, phototype V and VI, (C) subjects between 50 and 65 years old, phototype II and III, and (D) subjects between 50 and 65 years old, phototype V and VI. Non-inclusion criteria included other dermatological diseases, intense sun exposure, and allergic reactions to the cosmetic product.

### **2.2. Assessment of the aqueous content of the stratum corneum**

The stratum corneum (SC) hydration was assessed using the device Corneometer® (Courage & Khazaka, Germany). This device is based on the electrical capacitance measurement, specifically the variation of the dielectric constant of water. At each instance, five measurements were taken, and the mean of these values was then calculated

### 2.3 Measurement of transepidermal water loss (TEWL)

The Tewameter® TM 210 device (Courage & Khazaka, Germany) was employed to measure transepidermal water loss (TEWL), which is indicative of skin barrier integrity. This measurement is based on the diffusion principle described by Adolf Fick, and the values are expressed in  $\text{g m}^{-2} \text{h}^{-1}$ . The mean value of thirty measurements was utilized for the subsequent calculations 6,7.

### 2.4. Assessments of skin viscoelastic properties

The mechanical properties of the epidermis were determined using a no-invasive in vivo suction skin elasticity meter equipped with a 2 mm measuring probe. The time/strain mode 1 was used with the 3 seconds application of a constant negative pressure of 500 mbar followed by a 3-second relaxation. The average values of 3 measurements were taken for each test region and determined time, performed by the same operator 8. The selected parameters evaluated and their possible interpretation according to the fabricant (Courage-Khazaka, Germany) were described below:

$R0 = Uf$ . Amplitude at the end of the suction phase of the first curve. This parameter reflects the firmness/pliability of the skin. This parameter represents the passive behaviour of the skin to force. Result = distance in mm. Improving skin firmness normally shows a decrease in the value of  $R0$ .

$R7 = Ur/Uf$ . Proportion of the immediate recovery compared to the amplitude after suction. The higher the value, the better the elastic properties of the skin. Result = %.

### 2.5. Measurement of skin pH

The skin pH value was measured using the Skin pH Meter® equipment (Courage-Khazaka, Germany). The pH electrode was calibrated prior to each measurement using two standard buffers at pH 4.0 and 7.0. The electrode was washed with distilled water before each measurement. The measurements were performed three times and the average of the three measurements was used for the results.

### 2.6 Reflectance confocal microscopy (RCM) image acquisition

The evaluation of the cellular characteristics of the different layers of the skin was performed by reflectance confocal microscope (RCM) using the Vivascope® 3000 equipment (Caliber Imaging & Diagnostics, US), which uses a laser source with a wavelength of 830 nm and an immersion objective capable of detecting 20 images per second. The microscopic images of  $5 \text{ mm}^2$  at successive depths were performed using the imaging system, Vivastack, which generates multiple confocal images at successive depths at a certain location in the tissue in the malar and forearm regions in quintuplicate. The methodology for the acquisition of images followed the protocol established by Andrade et al. (2015) 10.

### 2.7 Statistical analysis

All statistical analyses were performed with the GraphPad Prism 8 programme (GraphPad, San Diego, US). The differences between the groups regarding the instrumental parameters were analysed using a two-way repeated measures analysis of variance (ANOVA) and Tukey's test for multiple comparisons ( $\alpha = 0.05$ ).

### 3. Results and Discussion

#### 3.1 Characterization of pigmented dry skin

According to Table I, the stratum corneum water content presented a significant ( $p < 0.05$ ) difference between Groups A and B. Both represent subjects between 35 to 49 years, but different skin phototypes ranges. The TEWL values showed no statistical difference ( $p > 0.05$ ) between all the groups. Regarding pH, the parameter was significantly different when comparing Group A with Group B, as well as when comparing Group C with Group D ( $p < 0.05$ ). In the same age ranges, differences were identified between the skin phototype groups. Additionally, a difference was identified between Groups B and D, both groups represent skin phototypes V and VI, but different age ranges.

To better characterize the difference between non-pigmented and pigmented skin, Figure 1 and 2 show the RCM images focusing on the deepest layers of the epidermis and the papillary dermis for Group C and D, respectively. Additional images of the epidermis and dermal papilla from groups A, B, C, and D were obtained by RCM methodology (Figure 1.).

Regarding the measure of skin firmness, a significant difference ( $p > 0.05$ ) in the R0 parameter (total deformation) was observed in Group A in relation to group C, and Group C in relation to Group D (Table I). Moreover, regarding the measure of skin elasticity, a statistical difference ( $p > 0.05$ ) was noticed between groups A and C, B and D, and C and D. Differences between non-pigmented and pigmented skin were found only in the older age group.

The corneometry results for subjects aged 35 to 49 (Groups A and B) indicated that non-pigmented skin showed higher SC water content compared to the pigmented skin group. However, for individuals aged 50 to 65, no statistically significant difference was observed. The lipid matrix of the SC—composed predominantly of ceramides, free fatty acids, and cholesterol—forms an essential barrier for water retention, preventing skin dryness. A study with females' subjects between the ages of 18 and 45, revealed that the proportion of ceramides in African Americans skin (IV to VI skin phototype) is lower compared to Caucasian skin (II and III skin phototype), and the amount of this lipid is directly correlated with SC water content 11.

The presence of xerosis in pigmented skin is more pronounced, causing significant discomfort for individuals with this skin type. Dry skin results in a greyish appearance, which culturally contributes to greater visual discomfort 12. Additionally, black skin tends to have higher rates of desquamation, making it prone to dryness in specific areas of the body 12.

In general, age-related impairment of barrier function has been associated with reduced epidermal renewal, a decrease in natural moisturizing factors in the stratum corneum, a decline in moisture-binding glycosaminoglycans, and increased MMP hyaluronidase activity, which is exacerbated by UV exposure 13,14. Studies suggest that black skin has a superior barrier function compared to other skin tones 5,12. However, in the present study, no statistically significant difference was observed between the pigmented and non-pigmented skin groups.

Table I. Comparative analysis of the parameter of aqueous content, TEWL, pH, R0, and R7 for the groups with participants of phototype II and III and for the group of phototype V and VI, divided into different age groups.

	Groups with $35 \leq x < 50$ years				Groups with $50 \leq x < 65$ years				P values			
	Group A Phototype II and III		Group B Phototype V and VI		Group C Phototype II and III		Group D Phototype V and VI		A vs. B	C vs. D	A vs. C	B vs. D
	Mean (N)	SD	Mean (N)	SD	Mean (N)	SD	Mean (N)	SD				
Aqueous content of the SC (UA)	33.00 (46)	1.34	32.22 (49)	1.09	33.17 (100)	1.31	32.86 (25)	1.37	*	0.7061	0.8877	0.1809
TEWL ( $\text{g}^1\text{m}^2\text{h}^{-1}$ )	11.78 (20)	1.26	12.18 (36)	1.65	12.07 (28)	1.8	12.6 (29)	1.75	0.8297	0.6232	0.9347	0.7358
pH	4.99 (48)	0.23	5.16 (105)	0.29	5.09 (66)	0.34	5.27 (99)	0.31	**	***	0.2852	*
R0 (mm)	0.28 (12)	0.04	0.27 (36)	0.05	0.34 (9)	0.04	0.30 (32)	0.07	0.5931	*	*	0.0503
R7 (%)	68.86 (12)	6.07	65.31 (36)	6.43	49.63 (9)	2.38	60.35 (32)	8.58	0.1331	***	****	**

Abbreviations: AU, arbitrary unit, TEWL, transepidermal water loss, SD, standard deviation, SC, stratum corneum, N, sample size.

Note: Values that were found to be different are indicated with an asterisk, p-value<0.05 (\*), p-value<0.01 (\*\*), p-value<0.001 (\*\*\*), and p-value<0.0001 (\*\*\*\*), (two-way repeated measures ANOVA followed by Tukey's multiple comparison test).

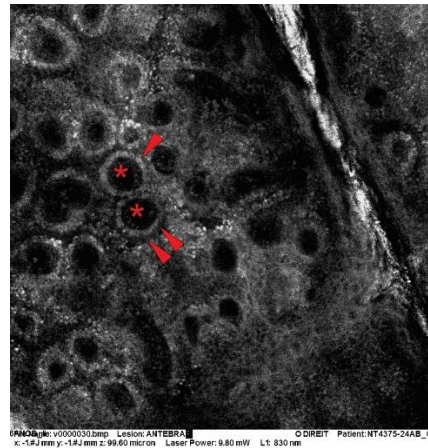
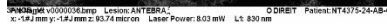


Figure 1. Sample of skin imaging using reflectance confocal microscopy (RCM), showing the main skin alterations caused by phototype and aging. RCM skin image was obtained from the inner part of forearms from a 66-y-old woman skin phototype II (Group C). The dermal papillae correspond to dark round to oval areas (asterisks) circumscribed by refractive cells (arrows), corresponding to melanocytes and melanin-rich keratinocytes.



Additionally, the use of male hormones revealed a direct and significant impact on oiliness levels in the frontal region of the skin. The measured values exceeded 130  $\mu\text{g}/\text{cm}^2$ , again approaching patterns observed in trans women. Such data corroborate the participants' subjective perception of increased skin oiliness after the initiation of hormone therapy, culminating, in some cases, in acne episodes.

These objective findings are in full concordance with qualitative information reported in scientific literature, which describes dermatological changes in individuals undergoing masculinizing hormone therapy. The convergence between quantitative data and anecdotal evidence reinforces the validity and robustness of the conclusions. In summary, this study elucidates crucial aspects of dermatophysiology in trans men, contributing to a deeper understanding of skin modifications induced by hormone therapy.

#### **4. Conclusion**

This study emphasizes skin diversity, noting variations in hydration and pH across different phototypes and ages. It highlights how hormone therapy impacts skin in transgender individuals, affecting water content and oiliness. The findings advocate for personalized cosmetic development and dermatological care to address these unique skin needs.

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