

## Literature List

### CutiScan

*A. Charpentier, How testing innovations is meeting beauty trends, PERSONAL CARE Magazine, June 2022, p. 25-28*

For many years now, every cosmetic product launched on markets around the world has been validated for its safety and efficacy in accordance with the cosmetic regulations of each country. Product performance is changing along with consumer expectations, shopping habits, beauty routines and lifestyles. For the past two years, the health crisis has had an impact on the use of hand hygiene products specifically and on care and make-up products with new products resistant to the conditions of wearing a mask and the increase on the surface of the skin of temperature, humidity, CO<sub>2</sub> and friction. In addition, after the decrease in human activities related to confinement, large cities are regaining significant levels of pollution that have a significant impact on the condition of the skin.

*S. Faloni de Andrade, E. José Pinheiro, C. Pereira Leite, M. do Céu Costa, L.M. Rodrigues, Cymbopogon citratus essential oil: Unraveling potential benefits on human skin, ISBS Congress Berlin, June 2022*

*Cymbopogon citratus* (DC.) Stapf, commonly known as lemongrass, is an important aromatic medicinal plant cultivated in different regions of the world. Its essential oil is widely used for the production of fragrances, cosmetics, detergents, and pharmaceuticals. However, there is no clear evidence of the alleged effects of *C. citratus* (EOCC) on human skin. Thus, the aim of this study was to evaluate the effects of one formulation containing EOCC on skin's physiology in healthy volunteers. A Carboxymethyl cellulose (CMC) gel containing 5% EOCC (Cantinho das Aromaticas, Portugal) was prepared. Twelve healthy volunteers (4 men and 8 women) mean age  $36.2 \pm 16.3$  years old were selected after informed written consent. All procedures were conducted respecting all principles of good clinical practice and approved by the institutional Ethics Committee (approval reference ECTS 04/13). Two areas (3cmx3cm) were drawn in forearm. In one area one formulation containing EOCC was applied with a spatula while in the other only gel (control) was applied. This procedure was repeated for 14 days twice/day (morning and night). In the beginning and by the end of the experiment, transepidermal water loss (Tewameter® CK electronics), hydration (Moisturemeter® DTec), and biomechanics skin (Cutiscan® CK electronics) parameters were measured. Images from High Resolution Sonography (HRS) were also taken at those sites with the Dermascan C (Cortex Tec). A methylnicotinate-provocation test was applied and followed with Laser Doppler Flowmetry (LDF, Perimed AB). A significant decrease in Transepidermal Water Loss (TEWL), as well as a significant increase in epidermal hydration, were observed at these areas treated with the formulation containing EOCC. An increase in firmness and elasticity was also noted. The HRS showed that epidermis is more echogenic after the application of formulation indicating that essential oil penetrates only the most superficial layers of the skin. Noteworthy, the site previously "protected" with the EOCC formulation revealed a reduced microinflammatory reaction following the methylnicotinate challenge. In conclusion, our results suggest that this formulation with EOCC is safe for topical application showing an interesting potential to be applied in skin care.

*M. Anthonissen, E. van den Kerckhove, P. Moortgat, I. Geraerts, N. Devoogdt, T. de Vrieze, A. de Groef, Can the CutiScan CS 100® measure anisotropy and viscoelasticity in scar tissue after mastectomy? A reliability and validity study, Skin Res Technol. March 2022;28: p. 246–253.*

Background: Scars have different biomechanical characteristics, including anisotropy and viscoelasticity compared to healthy skin. To assess these characteristics, the CutiScan CS 100® can be used. The aim of the present study is to investigate reliability and validity of this device in breast cancer patients. Materials and methods: Thirty female patients, with scar adhesions following

mastectomy were assessed with the CutiScan CS 100®. Maximal distensibility (pixels) (V1), after-suction return rate (pixels) (V2), and their ratio (%) (V3) at three points on and around the scar were assessed as measures of viscoelasticity. For intra- and interrater reliabilities, the intra-class correlation coefficient (ICC) and its 95% confidence intervals were calculated. The standard error of measurement (SEM) was calculated to interpret reproducibility of these measurements. To investigate criterion validity of the measurement of anisotropy, measurements in the direction of healthy skin were compared with measurements in the direction of the scar, using a paired t-test. Results: V1, V2, and V3 show poor to moderate intrarater reliability (ICC 0.00–0.72) and interrater reliability (ICC 0.00–0.53). The maximum displacement (V1) on the measurement point above the scar shows the best reliability (ICC 0.33–0.72). The SEM is about the same for all parameters at all three points. The paired sample t-test showed a significant difference ( $p < 0.05$ ) between V1 in the direction towards the scar versus the measurement towards healthy tissue, on the point below the scar. Conclusion: These first reliability and validity results of the CutiScan CS 100® for measuring anisotropy and viscoelasticity in scar tissue adhesions after mastectomy seem promising. Further research is needed addressing the limitations of the present study design.

*A. Elouneq, A. Bertin, Q. Lucot, V. Tissot, E. Jacquet, J. Chambert, A. Lejeune, In vivo skin anisotropy dataset from annular suction test*, Data in Brief 40 (2022)

To characterize the anisotropic and viscoelastic behaviors of the skin, we conducted an experimental campaign of *in-vivo* suction tests using the CutiScan®CS100 device from Courage and Khazaka electronics. In this data paper, we present the raw acquired data of the tests and their respective treated data. The tests were performed 30 times on the anterior forearm of a 28-year-old Caucasian male at different pressure set-points, ranging from 100 to 500 mbar with an increment of 20 mbar, at ambient temperature in a windowless room. The primary dataset consists of videos recorded by a probe camera associated with the CutiScan® device during the tests. After data treatment with DIC (Digital Image Correlation) technique and based on a homemade Python program, we have obtained secondary data tables and 2D displacement for all mapped grid nodes.

*I. Micek, J. Nawrot, A. Seraszek-Jaros, D. Jenerowicz, G. Schroeder, T. Spizewsk, A. Suchan, M. Pawlaczyk, J. Gornowicz-Porowska, Taxifolin as a Promising Ingredient of Cosmetics for Adult Skin*, Antioxidants 2021, 10, 1625

Active substances, effective in the reduction in or delay of skin changes caused by aging occurring in natural compounds, are desirable. Taxifolin (TXF), a flavonoid of strong antioxidant activity found in the plant *Stizolophus balsamita* (*S. balsamita*), has been tested for its biological effects on adult human skin. The aim of the study was to investigate the effects of two creams: 3% *S. balsamita* extract and 3% TXF on the function of adult skin. In total, 97 Caucasian women with clinical signs of skin aging were investigated. The biophysical and biomechanical skin parameters were measured before and after applying the creams, using Colorimeter CL400, Mexameter MX16, Skin-pH-Meter PH900, Skin-Thermometer ST 500, Glossymeter GL200, and Cutiscan SC100. Patch tests were performed with the investigated products to assess their potential irritant properties. The percutaneous penetration of creams was examined with the use of electrospray ionization mass spectrometry (ESI-MS) and confocal Raman spectroscopy. The 3% *S. balsamita* extract cream reduced hyperpigmentation, erythema, and elevated pH. All the tested preparations were proven to be nonirritant. A higher penetration rate was revealed for the 3% TXF cream than for the 3% *S. balsamita* extract cream. A total of 3% TXF cream improved skin viscoelasticity. The obtained results suggested that *S. balsamita* extract and TXF may be considered as ingredients of skincare products for adults.

*M.A. Kim, Y.C. Jung, E.J. Kim, Evaluation of anisotropic properties of striae distensae with regard to skin surface texture and viscoelasticity*, Skin Res Technol., March 2020; Volume 26, Issue 2, p. 220-225

Background: Striae distensae (SD) are skin lesions of parallel streaks, which mostly occur during rapid tissue expansion. Considering the etiological mechanism of SD, including dermal network ruptures and alignment to mechanical stretch, structural directionality or anisotropy could be expected. Non-invasive objective methods for measuring the anisotropy of SD have not been suggested yet. Therefore, we evaluated the anisotropic properties of SD with regard to skin surface texture and viscoelasticity, to verify them as new objective evaluation parameters of SD. Methods: Thirty-two healthy subjects with SD on their body participated. Anisotropy of skin surface texture and biomechanical

properties of SD-involved skin and adjacent normal skin was assessed and compared. Results: Analysis of skin surface texture, based on the x60 magnified images, revealed that SD have more disordered patterns compared to the regular honeycomb patterns seen in the normal surrounding skin. SD have bigger sizes of each blob than normal skin. The overall anisotropy of skin texture was significantly higher in SD. Skin biomechanical parameters, measured using Cutiscan<sup>®</sup>, indicated the less deformable, less recovered, and less viscoelastic properties of SD. When comparing viscoelastic properties over 360°, SD were more anisotropic than the adjacent normal skin as well. Conclusion: We observed that SD were significantly more anisotropic than adjacent normal skin with regard to skin surface texture and viscoelasticity. Therefore, anisotropy could be an objective evaluation parameter to represent the distinctive features of SD. It can be applied for evaluation of the SD severity and clinical efficacy of various treatments.

*A. Charpentier, Clinically supporting ‘antiage’ and ‘pro-age’ claims, Personal Care Europe, June 2020*

Claims of personal care evolve following trends and various innovations in the field of the active ingredient development, the finished product formulation and the way both are evaluated, demonstrating their performances. Since 2014, the cosmetics industry is gradually leaving the era of anti-ageing behind. Today, most consumers are more in the mood for a well ageing, slow ageing or pro ageing approach. The philosophy of the ‘pro-ageing’ movement has sought to remove all ‘anti’ claims because, according to this concept, women over 50 are not interested in looking younger; they want to look healthy and be honest about their age. Some brands have used the idea of “improves the appearance of skin quality”, and “restore the skin comfort”, for example. A new vocabulary of renewal, regeneration, plumpness and “glow” now dominates the language of the beauty industry.

*F. Perin, K. Chalothorn, P. Tachalerdmanee, Mechanical properties of skin and exploration methods, PERSONAL CARE ASIA PACIFIC, May 2020*

Our skin constitutes the interface between the interior of the body and the outside world, covering between 1.5 and 2.0 m<sup>2</sup> and weighing almost 4 kg in adults. Its thickness ranges between a few tenths of millimeters and 5-6 mm for areas submitted to high stresses and loads such as the soles of the feet. This organ (encompassing cells, fibres, sebaceous and sweat glands, hairs, nerves, blood vessels) ensures numerous essential functions such as maintaining homeostasis and protecting the organism from external aggressions (mechanical, thermal, chemical, bacterial, etc.) It is sometimes said that it is the silence of organs that defines their health. This is probably why we almost forget the mechanical function of the skin. This is unfair when we consider its incredible ability to absorb shocks, to support all internal body tissues, to stretch so as to allow movements, changes of posture and variations of body volume in the case of pregnancy for instance. This article aims to bring light to this critical mechanical function and to present the different methods which can be used for its exploration and measurement.

*L.M. Rodrigues, J.W. Fluhr, EEMCO Guidance for the in vivo Assessment of Biomechanical Properties of the Human Skin and Its Annexes: Revisiting Instrumentation and Test Modes, Skin Pharmacol Physiol 2020;33:44–59*

Biomechanics of the skin is an important subject in skin research. It has been studied for many decades involving various technologies and methods to characterize and quantify mechanical properties of the skin under different in vivo conditions. The present EEMCO paper reviews the current relevant information, providing practical orientation to researchers dedicated to in vivo assessment of biomechanics of skin and its annexes. We discuss the available noninvasive instruments, including their principles and variables. A correspondence between the descriptors nomenclature proposed by Agache and the designation for the suction-based standard instruments is proposed. The addressed properties include skin softness/stiffness, firmness, elasticity, elastic and viscoelastic properties, extensibility, resilience, anisotropy, acoustical shock wave hardness, friction (in relation to topographic properties), thickness, fiber/stress-mechanics (bending, cyclic, tensile, fatigue, or torsion), and hardness. We provide the relation of these properties to biomechanical descriptors and in some cases to SI units. Practical guidance for the proper use of these instruments, limitations, and possible interpretations are provided, while discussing the meaning of descriptive or “phenomenological” variables. For studies intended to quantify the effect of an intervention with regard to mechanical properties, we recommend a minimum of 30–40 participants, based on normal distribution of the data sets. Some important limitations are recognized, including the lack of standardization of procedures and calibration of instruments, which compromises the relevance and real nature of the descriptors/parameters obtained with these devices. The present work highlights an approach to a better practice and a sciencesupported biomechanical assessment of human skin, hair, and nails.

*P. Barlier, V. Couturaud, Évaluation de l'effet antirides et des propriétés biomécaniques*, in: A.-M. Pénse-Lhéritier (Editor): *Évaluation des produits cosmétiques*, Lavoisier Paris, Tec & Doc, chapter 4, p. 58-81, 2016

En vieillissant, les organes du corps humain, dont la peau fait partie, se mettent à fonctionner de façon moins efficace. Ce processus, programmé par notre profil génétique, peut être amplifié par l'environnement et par nos habitudes de vie.

*H. Silva, F.F.C Rego, C. Rosado, L. Monteiro Rodrigues, Exploring Human Skin Anisotropy by 3D Plotting*, Poster Presentation at ISBS Conference San Diego, May 2018

Introduction: The CutiScan® is a recent device apparently capable of quantifying skin viscoelastic behavior in a 360° topography. Here we propose a new 3D representation of CutiScan's data and parameters obtained from 13 healthy female foreheads (n=7 20.0±1.2 y.o., an n=6 50.2±2.4 y.o.). Methodology: The CutiScan® quantified the height of displacement, after suction, for each of the 360 angles. From a 3D polar data representation (time-displacement-angle), several 2D plots were constructed, from which other parameters - stretchability, stretching speed, stretching time and rise time were calculated and graphically represented. Results and Conclusions: These representations shown that older subjects display larger displacement heights, as well as larger height max slopes, higher rise and stretching times, irrespective of orientation. Results suggest that these new parameters are sensible and useful for the characterization of in vivo skin biomechanics.

*J. Comas, O. Laporta, M. Ollagnier, S. Venkataraman, R. Delgado, A firmer skin from the elixir of life mushroom*, PERSONAL CARE EUROPE, November 2017, p. 85-87

Shiitake mushroom has been recognised throughout history for its youth-promoting benefits, even being acknowledged as an elixir of life. In terms of its application in skin care, a shiitake mushroom-based extract has been recently selected to provide rejuvenating and firming effects to the skin of the face, neck and décolleté. More specifically, Actifcol advanced botanical ingredient has shown to offer a holistic care of the collagen protein, by helping increase its synthesis, improve its quality, through the PLOD1 gene, and reduce its deterioration process caused by carbamylation. When evaluated on mature skin, it showed to enhance firmness and to achieve a more isotropic skin behaviour, typical of a younger skin.

*C. Rosado, F. Antunes, R. Barbosa, R. Fernando, M. Estudante, H.N. Silva, L.M. Rodrigues, About the in vivo quantitation of skin anisotropy*, Skin Research and Technology 2017; 23: 429-436

Background/purpose: Human skin anisotropy is difficult to quantify. The Cutiscan®, is allegedly, the first biometrical system to provide information on the elastic and viscoelastic properties, as well as on anisotropy and directionality of the human skin *in vivo*. Thus, this study aims to contribute to characterize this new device and its applicability, and to compare its behavior with two other well-known devices— the Cutometer® and the Reviscometer®. Methods: Measurements were conducted with each device in three different anatomical sites (forehead, forearm and leg) of 20 female volunteers engaged after informed consent. The participants in the study were aged 19-73 years (mean age 37 ± 18.7 years old), and were divided in two groups (n = 10), based on their age - Group I, mean age 22 ± 1.3 years; Group II, mean age 52 ± 13.7 years. Results: All devices were useful tools to explore the anatomical and the age dependant changes in biomechanical terms, showing different discriminative capacities. Interesting correlations were established between the variables provided by the equipment. Conclusion: The Cutiscan® descriptors delivered excellent relationships with those from Cutometer® and Reviscometer®, while providing more detailed information about skin anisotropy through a full 360° analysis.

*J. Comas, C. Davi, E. Canadas, M. Vincendet, R. Delgado, Firmed Face, Neck and Décolletage*, COSSMA 5, 2017, p. 24-27

Actifcol\*, Lipotec's new botanical active ingredient, is based on shiitake mushroom - considered to be an elixir of life. Designed to offer complete care for the collagen lifecycle, the ingredient's new approach helps provide high levels of quality protein while decreasing the deterioration of collagen for visible firming effects on the face, neck and décolletage.

*H. Silva, F.F.C Rego, C. Rosado, L. Monteiro Rodrigues, Novel 3D "active" representations of skin biomechanics*, Biomed Biopharm Res., 2016; (13) 2: p. 219-227

Skin exhibits unique biomechanical properties that enable unrestricted body movements without tearing. Several devices have been used to quantify skin mechanical properties, but techniques, in general, do not concern this multidirectional capacity, only allowing measurements in a few angles.

CutiScan® is a new device that quantifies skin elasticity over 360°. It uses a suction method to induce skin deformation and a video camera to quantify its displacement. This work aims to assess these properties through the analysis of 3D time-angle-height of displacement representations. 20 female subjects (37.0 ± 18.7 years old) were enrolled in this study after informed consent, grouped by age in group 1 (22.0 ± 1.3 years old), and group 2 (52.0 ± 13.7 years old). The in vivo mechanical profile of each volunteer was assessed in the forehead, forearm and in the leg. Significantly higher surface area and volume under the curve values were found in the forehead of the subjects of group 2. Significant differences were also found between the forehead and forearm and between the forehead and leg among each group. These results suggest that these 3D representations are useful in distinguishing the viscoelastic profile of differently aged subjects and of different skin sites.

*C. Rosado, F. Antunes, R. Barbosa, R. Fernando, L. Monteiro Rodrigues, **Cutiscan® - A new system of biomechanical evaluation of the skin in vivo - comparative study of use depending on the anatomical site***, Biomed Biopharm Res., 2015; (12) 1: p. 49-57

Skin is a complex biomaterial. One of its characteristics is anisotropy due to fiber alignment, resulting from prolonged exposure to a surrounding stress state. This property is important in experimental studies of skin biomechanics and in experimental dermatology. During the last decades, several devices have been developed to study the cutaneous physiology. The CutiScan®, one of the latest, provides information not only about the elastic and viscoelastic properties, but also on anisotropy and directionality of the skin. The aim of this study is to investigate the changes in the biomechanical properties of human skin due to the anatomical site, combined with a study on the benefits and limitations of the CutiScan®, and also comparing it with other more studied devices - the Cutometer® and the Reviscometer®. 20 volunteers were engaged in this investigation after an informed consent. Measurements were conducted in three different anatomical sites (forehead, forearm and leg) with each device. Results showed that devices were able to identify significant differences among anatomical sites. The CutiScan® enabled a more complete assessment of skin's biomechanical properties, since it provides real-time images and 360° elasticity curves that allowed the simultaneous study of viscoelasticity and anisotropy.

*M. Higuchi, K. Kitahara, K. Shimizu, K. Hirai, T. Matsumoto, M. Takahashi, **Analysis of the Facial Skin Pores with a Video Microscope with Concerning the Relationship between the Pore direction and the Cutaneous Mechanical-Anisotropy***, J. Soc. Cosm. Chem. Jpn. (Article in Japanese)

Recently a number of studies on the facial skin pores are reported. The shape of pores is ellipsoidal but non-circular, and its elliptic distortion increases with age. Many factors such as menstrual cycle, ultraviolet irradiation, sebum secretion, and dry skin affect the size of pores. However, few studies focus on the relationship between the direction of pores (the angle of the long axis of ellipse) and the cutaneous mechanical-anisotropy. This study examined the pore size and its direction at six different sites on the face by image analysis with a video microscope and software (Integral, Tokyo, Japan). The directions of pores in the forehead, jaw, and upper and lower cheeks of the both sides of the face run along the Langer's lines. The size of pores in the upper cheek was larger than those of other sites. This study also measured the cutaneous mechanical-anisotropy with CutiScan (C+K, Cologne, Germany). The low extensible direction of the skin was found to correspond to those of the pores and the Langer's lines. Finally, this study investigated the effect of a 4-week treatment with skincare products on the shape of pores. The total area of pores significantly decreased with improving the skin condition, which was confirmed by increase in water content in the stratum corneum and decrease in the transepidermal water loss. However, the direction of pores was unable to be changed.

*C. Rosado, R. Barbosa, R. Fernando, F. Antunes, L. Monteiro Rodrigues; **Use of the Cutiscan CS100 to quantify cutaneous cutaneous anisotropy and viscoelasticity***, Skin Forum Prague September 2014

Introduction: Skin is a complex biomaterial with anisotropy, due to preferred fiber alignment resulting from prolonged exposure to a surrounding stress state. Several devices were developed to quantitatively assess skin biomechanics. The CutiScan CS 100® aims to provide information not only about the elastic and viscoelastic properties but also on anisotropy and directionality of the skin. This device contains a probe that combines mechanical force (suction) with imaging (Fig. 1). During the suction and recovery time a high-resolution CCD camera inside the probe monitors the displacement of each pixel by an optical flow algorithm in a video. From that video an overall graph (Fig.2) is generated, as well as measurement parameters.

*C. Rosado, R. Barbosa, R. Fernando, F. Antunes, L. Monteiro Rodrigues, **New Approaches to Quantify Cutaneous Anisotropy and Viscoelasticity***, Physiology 2014 London

Introduction: Skin is a complex biomaterial. One of its characteristics is anisotropy due to preferred fiber alignment in the skin, resulting from prolonged exposure to a surrounding stress state. Skin anisotropy is an important issue for plastic surgeons, as well as cosmetics science. In the last decades, several devices have emerged as indispensable tools in the study of the cutaneous physiology, as well as in the assessment of the efficacy and safety of topical formulations. The CutiScan CS 100<sup>®</sup> (Courage and Khazaka, Köln, Germany) is designed to provide information not only about the elastic and viscoelastic properties but also on anisotropy and directionality of the skin. This device contains a probe that combines mechanical force with imaging in a unique way. It consists of a suction ring (14 mm diameter) that draws the skin uniformly in all directions with a constant negative pressure. During the suction and recovery time a high-resolution CCD camera inside the probe monitors the displacement of each pixel by an optical flow algorithm in a video. From that video an overall graph is generated, as well as interesting measurement parameters.