

## Innovative Non-Invasive Techniques in Skin Pharmaceutics as Valid Complements in Cosmetic Dermatology Practice

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### ABSTRACT

Non-invasive tools for measuring various skin parameters are widely used as research tools in the area of skin pharmaceutics to evaluate the cutaneous effects of topically applied skin care products. They provide objective and quantitative data of various skin attributes as compared with subjective clinical grading and allow detection of differences that are not apparent to the eye. On the other hand, typical dermatological practice is based on the skills and trained eyes of dermatologists to evaluate the skin conditions of patients and their response to various treatments. This study aims at showing the feasibility of using three non-invasive instruments as complementary tools in dermatology practice to evaluate and monitor quantitatively relevant cutaneous treatment effects.

Mexameter®, Corneometer®, and Tewameter® were used to evaluate quantitatively the degree of pigmentation, hydration, and barrier integrity, respectively, at baseline and 1, 7, 14, and 30 days after one session of superficial TCA peel treatment of melasma on the face of a female patient. The results show the ability of these devices to aid the dermatologist in quantifying and comparing the changes in skin attributes over time.

**Keywords:** Skin Bioengineering, Cosmeceutical Efficacy, Superficial Chemical Peel

### INTRODUCTION

Recently, many non-invasive skin analysis tools have been developed for measuring various skin parameters; these tools are widely used for assessing the cutaneous effects of topically applied cosmetic products for claim substantiation<sup>1</sup>.

This kind of non-invasive evaluation provides some distinct advantages over visual assessment and clinical grading for *in vivo* product efficacy testing since it presents more information about the different modes of product interaction with the skin in the form of objective and quantitative data<sup>1</sup>.

Diagnosis and treatment in dermatology have strong elements of art as they rely mainly on the clinical expertise of dermatologists. Subjectivity, inaccuracy, and inconsistency are the main limitations of clinical evaluation as a research and diagnostic tool<sup>2</sup>.

A logical step for the dermatological practice would be the utilization of objective, quantitative and non-invasive tools of skin bioengineering. However, a dermatologist may be overwhelmed by the relatively large number of innovative skin bioengineering instruments developed to measure a wide variety of skin attributes (elasticity, color, hydration, permeability, cutaneous blood flow, etc.) and may find it difficult to judge whether an instrument can be of real use or not<sup>3</sup>.

The aim of this study was to evaluate three pieces of technology in skin bioengineering that are widely used in

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Received on 25/8/2010 and Accepted for Publication on 5/1/2011.

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skin pharmaceuticals as potentially useful instruments in clinical dermatology practice. To evaluate their usefulness in clinical dermatology, these three instruments were used to evaluate and monitor quantitatively the effects of superficial peeling using Trichloroacetic acid (TCA) for the treatment of melasma on various skin attributes.

Superficial peeling by using a 20-35% solution of TCA is a commonly used procedure to aid in the management of pigmentation disorders of the face including melasma<sup>4</sup>.

## METHODS

### Patient

A female patient with melasma in her face and Fitzpatrick skin type IV, but otherwise healthy, underwent a single 20% TCA peel. The study was conducted in compliance with the ethical principles of the Declaration of Helsinki and the subject was fully informed about study aim, procedure outcomes, and measuring principle of the non-invasive devices used.

### Peeling Procedure

After degreasing the skin with 70% ethanol, one layer of 20% TCA was applied using a cotton-tipped applicator until an even white frosting was seen. Immediate post peel care included washing the skin with water, and the patient was instructed to avoid sun exposure and to use a moisturizing sunscreen regularly.

### Skin Parameters Measurement

Patient face was evaluated using non-invasive methods at baseline and 1, 7, 14, and 30 days post peeling. The measurements were performed on the forehead and both cheeks. For each parameter, twelve measurements were performed by measuring four different points on each selected area of the face. Measurements have been performed following an acclimation period of approximately 30 minutes at a temperature of  $23 \pm 2$  C° and a relative humidity of  $45 \pm 5\%$  according to guidelines pertaining to these techniques<sup>5,6,7</sup>. The parameters monitored were as

follows:

- Hydration: water content of the stratum corneum was measured by the widely used Corneometer® CM 825 (CK electronics GmbH, Germany) which registers the electrical capacity of the skin surface<sup>6</sup>. The probe was perpendicularly applied to the skin surface with a constant pressure for one-second recording time, and the readings were expressed in arbitrary units which are proportional to the skin hydration level.

- Color: the color of the skin is mainly due to two pigments: melanin and hemoglobin. Mexameter® (CK electronics GmbH, Germany) is widely used to measure the content of melanin and haemoglobin (erythema) in the skin. Its probe measures the absorbed and reflected light at specific wavelengths corresponding to the spectral absorption peak of each pigment. Melanin and erythema index is computed from the intensity of the absorbed and the reflected light. The probe was applied on the skin surface with a constant pressure using a spring and the results of both parameters are immediately shown as index numbers<sup>8</sup>. Both index values range from 0 to 999.

- Barrier permeability: the permeability of skin barrier was determined with the Tewameter® TM 300 (CK electronics GmbH, Germany). The measurement is based on measuring Transepidermal Water Loss (TEWL) through the skin surface by two pairs of sensors (relative humidity (RH) and temperature) placed in a cylindrical probe. TEWL represents the rate of evaporation of water from the skin surface and reflects the integrity of the skin since the stratum corneum function as the main barrier to water loss<sup>3</sup>. The probe head was placed gently on the skin, and measurement is started by pressing a button in the probe. The TEWL readings were taken 40s after the application of the probe to the skin, when the TEWL level had stabilized. TEWL values were recorded in g/m<sup>2</sup>h.

### Data Analysis

The measurements made for each parameter are presented as the Mean value  $\pm$  SEM. The paired student's

t-test was used to determine the statistical significance of the differences between post peeling time points and baseline values for each skin parameter. Values of  $p < 0.05$  were considered statistically significant.

**RESULTS AND DISCUSSION**

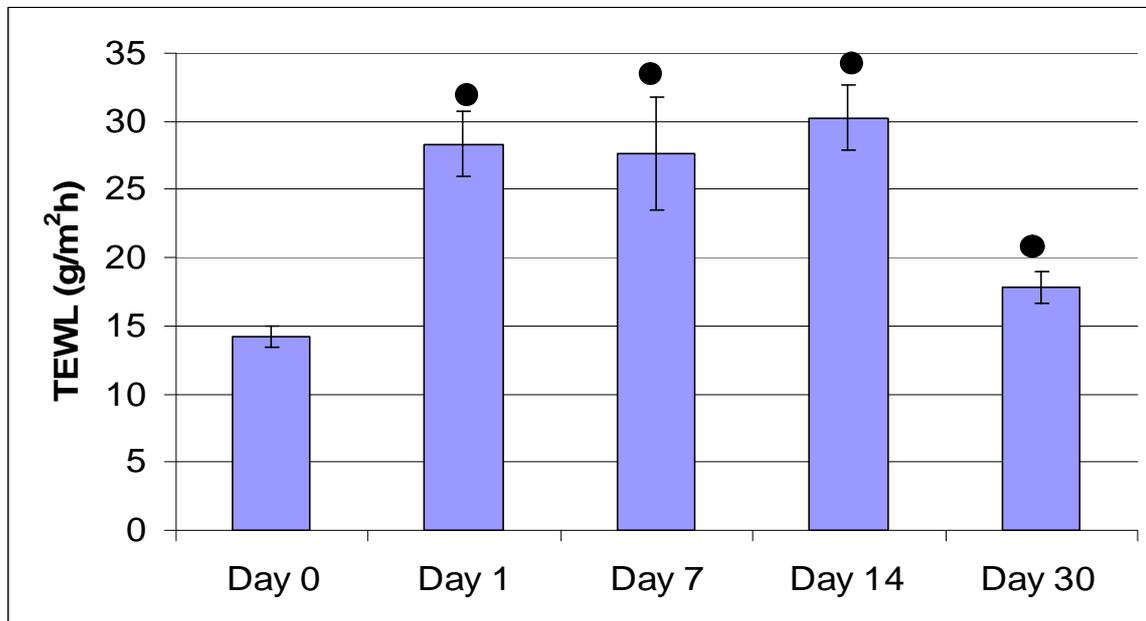
Chemical peeling is a popular procedure employed by physicians for cosmetic and therapeutic treatment of skin<sup>4</sup>. It is defined as the application of a chemical irritant onto the skin, producing a controlled destruction of the epidermis and the upper dermis followed by regeneration of new epidermis and dermal tissues<sup>4</sup>.

Transepidermal water loss increased significantly 24 hours after the use of 20% TCA, and it needed more than 1 month to return to baseline level (Figure 1). Elevated TEWL values are known to result from damage to stratum corneum by acute or chronic exposure to irritants as well as certain skin diseases<sup>9</sup>.

Thus, the increase in TEWL confirmed the impairment of stratum corneum barrier function by TCA

application. This was followed by regeneration of the stratum corneum as evidenced by the return of TEWL value back to almost pre-peeling level. The stratum corneum needed more than 30 days to acquire its barrier integrity and adequately function as a barrier to excessive water loss.

It is recommended in peeling practice that peeling solution not to be reapplied to skin that is not re-epithelized<sup>4</sup>. In addition, superficial peeling is meant to wound the epidermis and papillary dermis<sup>10</sup> without affecting the lower reticular dermis. Uncontrolled penetration of the peeling agent to the deeper layers of the skin is a major cause of scarring as a post-peeling dreadful complication<sup>11</sup>. Our TEWL values showed that patient's skin barrier needed almost 1 month to gain its barrier integrity and thus repeating the chemical peeling at one or two weeks interval might affect the deeper dermis by the topically applied TCA and could negatively affect the desired outcome.



**Figure 1. Transepidermal Water Loss pre-peeling and at different time points post-peeling. Values represent Mean ± SEM (● significantly different from baseline value P < 0.05).**

Skin hydration level declined significantly from 24 hour up to 7 days post-peeling (Figure 2). The reduction

correlates with dryness and crusting of the skin that is known to occur in 2 or 3 days post-peeling due to tissue necrosis<sup>4</sup>. This is followed by improvement in skin hydration in a time dependent manner. The hydration of the skin returned to pre-peeling level two weeks post-peeling after sloughing and shedding of the dead skin flakes that are known to occur during the first 10 days post peeling<sup>4</sup>. At 14 and 30 days time points, although not statistically significant, the skin hydration was higher than the pre-peeling baseline level. Two factors may play a role in this improvement. The regeneration of new stratum corneum, thus, the progressive regain of skin's barrier integrity and its ability to control excessive water loss as shown in Figure 1 and the daily application of a moisturizing sunscreen lotion by the patient throughout the study.

Pigment density of melasma was evaluated via Mexameter® pre- and post-peeling (Figure 3). Melanin index demonstrated a significant increase in the degree of pigmentation 24 hour post-peeling as a result of destruction and desiccation of the old stratum corneum. This is followed by a gradual decrease in pigment density that reached a significant reduction on day 14 post-peeling which correlates to the pigment density of the newly regenerated skin after the sloughing and peeling of the old TCA treated skin. However, the reduction in skin pigmentation during the healing process is followed by a significant increase in pigment density of the treated areas after the stratum corneum has regenerated and healed. This increase in skin pigmentation is a common sequel of TCA superficial peel<sup>4</sup>.

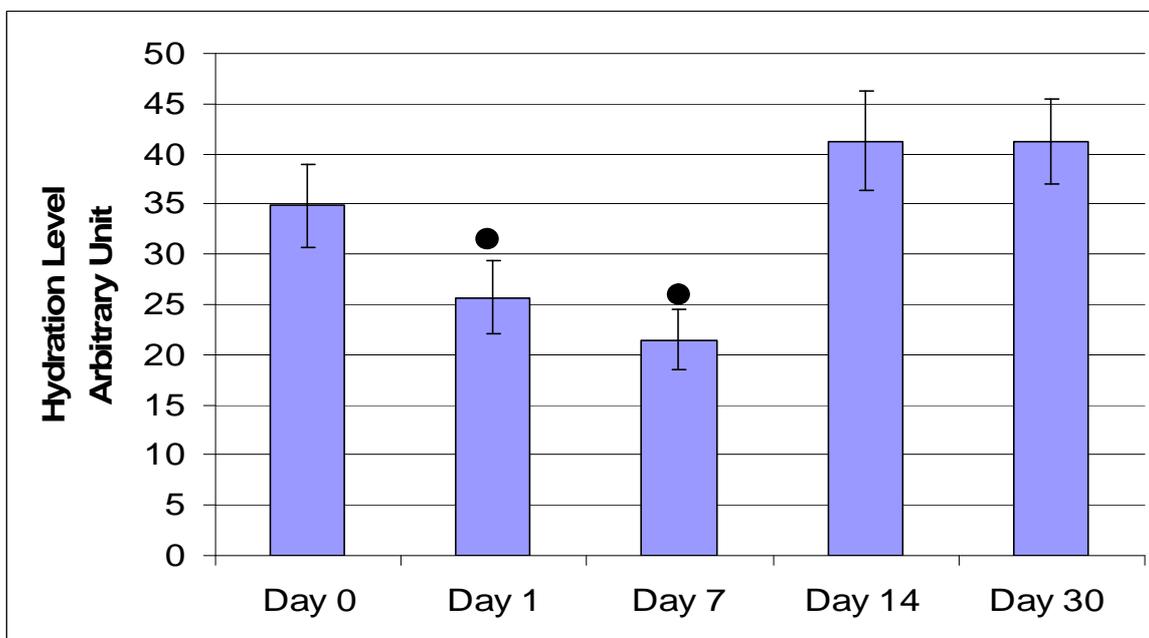
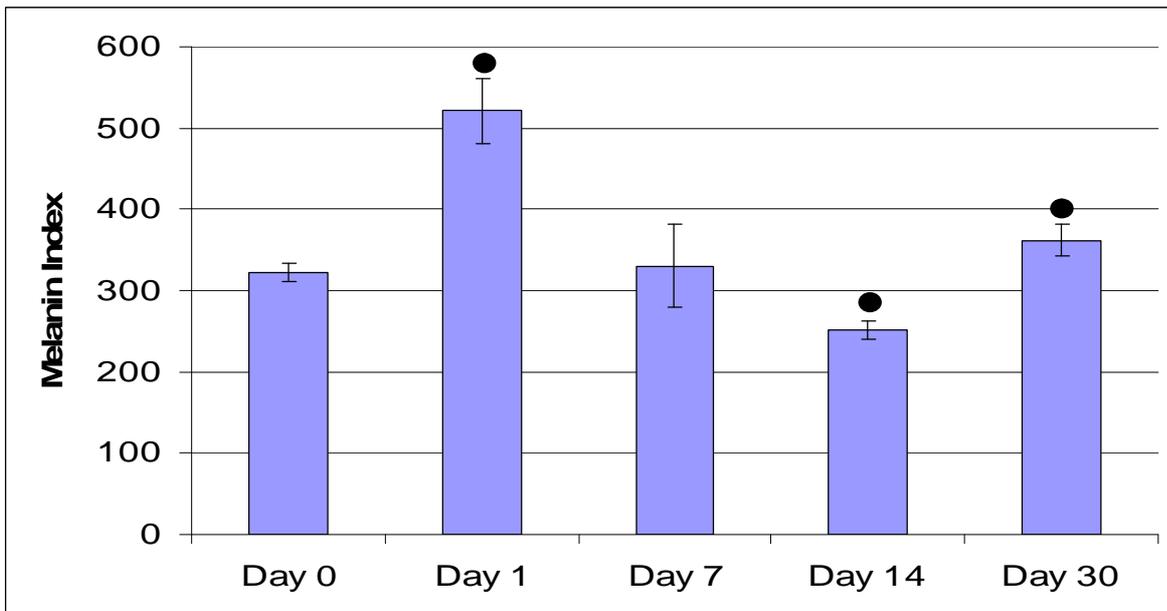


Figure 2. Skin hydration pre-peeling and at different time points post-peeling. Values represent Mean  $\pm$  SEM (● significantly different from baseline value  $P < 0.05$ ).



**Figure 3: Melanin content pre-peeling and at different time points post-peeling. Values represent Mean ± SEM (● significantly different from baseline value P < 0.05).**

The above measured skin aspects may not be adequately appreciated and compared by sensory perception or subjective clinical scoring using melasma area and severity index score and taking pre- and post-treatment photographs; two popular subjective clinical evaluation parameters that are routinely used by dermatologists to evaluate changes consequent to a chemical peel.

### CONCLUSION

The study demonstrates quantitatively that one session of superficial peel is insufficient to treat melasma.

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In clinical practice, superficial TCA peeling (20-35% TCA) is used repeatedly on weekly, biweekly, or monthly intervals to aid in lightening of hyperpigmentary disorders such as melasma<sup>4</sup>.

This study shows the feasibility and applicability of three skin non-invasive analysis devices; Corneometer®, Tewameter®, and Mexameter® as an adjunct to chemical peeling in-office procedure. Although these devices will not replace the intuition and experience of the dermatologist; their use in cosmetic dermatology practice could complement the art and expertise of the dermatologist with objective data that can be tracked over time.

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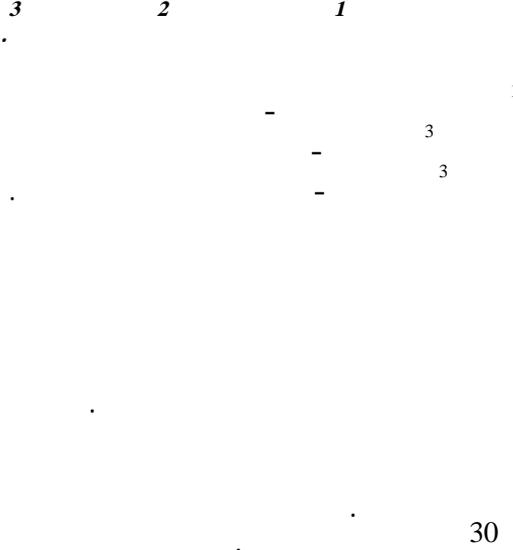
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## تقنيات الهندسة الحيوية السطحية المبتكرة في مجال صيدلانيات الجلد و أهميتها في طب الجلد التجميلي



الكلمات الدالة: الهندسة الحيوية للجلد، التقشير الكيميائي السطحي ، فعالية مستحضرات الجلد الصيدلانية

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