STUDY PROTOCOL
CWY PROTOCOL VERSION 1

Hydration, TEWL and Roughness Test on Human Skin

DEF-HSPIT050(14)-15106

DERMAPRO SKIN RESEARCH CENTER

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1. OBJECTIVE

To evaluate anti-aging effect (wrinkle, sagging, elasticity, lifting, texture, luminosity and hydration) of the test product on human skin

2. STUDY SPONSOR AND MONITOR

Organization	Coway
Location	J platz, 1104-1, Gasan-dong, Geumcheon-gu, Seoul, Korea
Telephone No	02-6711-3224
Fax No	02-6711-3250
E-mail Address	mrkim@coway.co.kr
Monitor	Myeong Rae Kim

3. INVESTIGATIVE ORGANIZATION AND PERSONNEL

Organization	DERMAPRO Ltd.
Location	30, Bangbaejungang-ro, Seocho-gu, Seoul 06684, Korea
Telephone No	82-2-597-5435
Fax No	82-2-597-5430
Investigator	Da Jung Jo
Scientific Director	Jae Sook Koh, Ph.D.
Dermatologist	Min kyung Shin, M.D., Ph.D

4. CLINICAL RESEARCH STANDARD

The study will be conducted in compliance with Good Clinical Practice (GCP) Regulations, Standard Operating Procedures (SOPs) of the DERMAPRO SKIN RESEARCH CENTER
The DERMAPRO SKIN RESEARCH CENTER was validated by receiving a “QUALITY MANAGEMENT SYSTEM CERTIFICATE” (C*ertificate No.5855*) from the KOTRIC Certification Center for providing contract research and consulting services on human skin safety and efficacy.

5. ETHICAL CONSIDERATION

This study will be reviewed and approved by an Institutional Review Board (IRB). The IRB will review the study including protocol and CRF before any significant change in the protocol is initiated. After the

review, the IRB's approval will be documented in a letter to principal researcher and a copy of the IRB approval letter will be forwarded to the sponsor.

6. INVESTIGATIVE PRODUCT

The study sponsor will supply products to all subjects for the duration of the study.

6.1. PRODUCT SPECIFICATION

No.	Formulation type	Name of the product
1	Skin	Re:NK essential moisture rebalancing skin softner
2	Emulsion	Re:NK essential moisture rebalancing emulsion
3	Essence	Re:NK cell to cell essence
4	Cream	올빛 Revital cream

6.2. APPLICATION

Application will be done twice a day under normal conditions of use according to sponsor's recommendations. The product will be applied twice a day (in the morning and evening) in the order of skin, lotion, essence, cream.

7. STUDY POPULATION

7.1. NUMBER OF SUBJECTS

The subjects will be selected on the basis of inclusion and exclusion criteria and consist of 20 healthy Korean healthy females.

7.2. SUBJECT RECRUITMENT AND SELECTION

The investigator will select potential study subjects satisfying the inclusion and exclusion criteria. The investigator will fully explain the purpose and procedures of the study, schedule, compensation, and anticipated adverse reactions or side effects. After fully understanding such explanations on the research, study subjects voluntarily decide whether or not to participate as a research subject and fill out an informed consent form.

7.2.1. INCLUSION CRITERIA

i. Healthy females; 20 to 60 years of age
ii. Being classified as the test group if the skin hydration value is lower than 50, and control group if the value is higher than 51 by Corneometer® CM 825
iii. The subject is apprised regarding the purpose and the protocol of the study; signed informed consent is obtained.
iv. Volunteers should be cooperative and available for follow-up during the study period.

7.2.2. EXCLUSION CRITERIA

i. Pregnancy, nursing condition.
ii. Treatment of skin external application containing steroid more than one month
iii. Participation in a previous study without an appropriate intervening period (one month) between studies.
iv. Sensitivity or hypersensitivity skin.
v. Any abnormal opinion as judgement of the investigator, which includes dot, acne, erythema or capillary expansion on the test site
vi. Use of similar cosmetics or medicine on the test site within 3 months
vii. Chronic disease (diabetes, asthma, high blood-pressure).
viii. In case of atopic dermatitis
ix. Any difficult which may interfere with the aim of the study as the judgment of the investigator

7.2.3. PROHIBITION AND RESTRICTION

i. No other test article should have been applied to the application areas during the entire study.
ii. No excessive exposure to sunlight or UV radiation.
iii. During this testing period, other than the application of the test article, the use of any cosmetic products, beauty tools, and any skin care procedures, should not be used.

7.3. SUBJECT WITHDRAWAL

After admission to the study, the subject may withdrawal at any time for any reason, but must report such reason fairly and accurately.

Subjects failing to complete the study will be identified, and whenever possible, a reason will be given. Subjects who drop out of the study will not be replaced.

i. They do not follow the conditions of the Study Information Sheet or they no longer wish to participate in the study
ii. They suffer of any side effect occurred by test material during the study.
iii. They suffer any illness or accident or develop any condition during the study which could affect the outcome of the study
iv. They could be dropped off from the study by investigator when they affect the outcome of the study.

8. STUDY PROCEDURE

8.1. DESCRIPTION OF THE STUDY PROCEDURE

The procedures included:
1) A preliminary interview during which volunteers were informed of the purpose and the protocol of study, the study timetable, the compensation modes, the possible benefits, the constraints linked to the study and the foreseeable risks;
2) Obtaining written informed consent from the subjects, thus ascertaining that study participants made their decisions fully aware of the purposes and conditions of this study prior to participation.

During the course of the 4 weeks study, 3 examinations will be performed, i.e. at before treatment, 2 weeks and 4 weeks after the start of treatment. All objective and subjective results will be recorded in the case report form. The following will be examined in all there examinations:

i. Assessment of skin hydration
ii. Assessment of skin TEWL
iii. Assessment of skin roughness
iv. Assessment of questionnaires by subjects
v. Product safety

8.2. ENVIRONMENTAL CONDITION

The entire study will performed under the environmental conditions of specific relative temperature and humidity, controlled and maintained identically for each volunteer. The ambient temperature is maintained at 22±2℃ and the relative humidity is maintained in the range of 50±5%.

8.3. EVALUATION

8.3.1. ANALYSIS OF SKIN HYDRATION

Skin hydration of the stratum corneum is measured by Corneometer® CM 825 (Courage+Khazaka, Germany). Owing it to the high resistance of electrical resistance in the stratum corneum of the epidermis, the current wave AC conductance is measured by the reciprocal of the resistance moisture content when applied in the skin. Therefore, dried stratum corneum represented a weak electrical conductivity, and hydrated stratum corneum represented strong electrical conductivity. The skin hydration will be measured using Coreometer® (C+K, Germany) before treatment, at 2 and 4 weeks after treatment (Fig. 1).

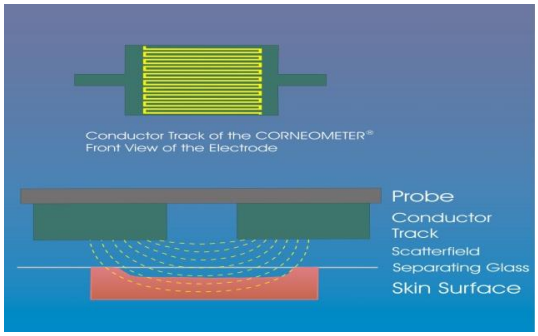


Figure 1.Principle of Corneometer® CM 825

8.3.2. ANALYSIS OF SKIN TEWL

Skin TEWL (Transepidermal water loss) is measured by Tewameter® TM 300 (C+K, Germany). A certain evaporation of water from the skin takes always place as part of the normal skin metabolism. As soon as the barrier function of the skin however is slightly damages, the water loss will increase (even with smallest damages invisible to the human eye). The measuring principle is to measure the density gradient of the water evaporation from the skin indirectly by the two pairs of sensors (temperature and relative humidity) inside the hollow cylinder. This is an open chamber measurement. The open chamber measurement method is the only method to assess the TEWL continuously without influencing its micro environment. A microprocessor analyses the values and expresses the evaporation rate in $g/h/m^2$ (Fig. 2.). In this study, TEWL on frontal cheek will be measured and analyzed before, at 2 and 4 weeks after treatment. TEWL is measured 3 times on every occasion and the average is used for the analysis.

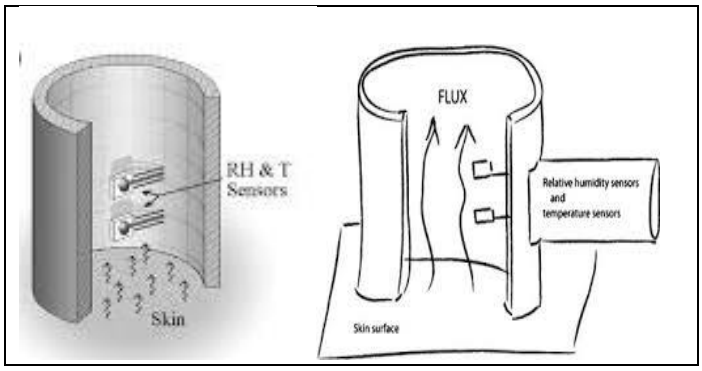
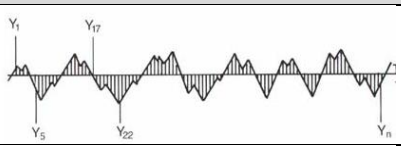
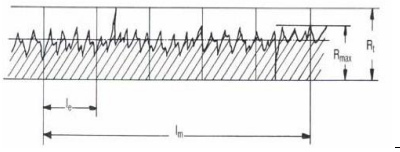
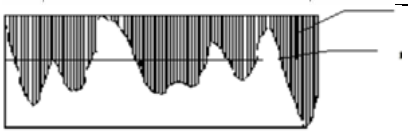
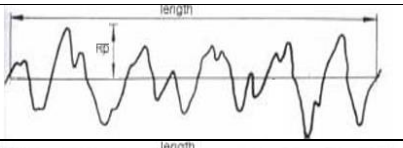
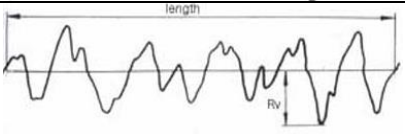


Figure 2. Principle of Tewameter® TM300

8.3.3. ANALYSIS OF SKIN ROUGHNESS PARAMETER

Skin roughness is measured by PRIMOS® Premium (GFMesstechnik GmbH, Germany). This system allows the quantitative analysis of the roughness of the skin surface, the depth, area and the volume of protruding on the skin surface. The skin roughness parameter will be analyzed using PRIMOS® Premium (GFMesstechnik GmbH, Germany) before treatment, at 2 and 4 weeks after treatment in terms of R-parameters (Table 1).

Table 1.R-parameters of skin roughness on cheek

Parameter	Definition	Profile
Ra	Arithmetic average value of profile peaks within the total measuring length	
Rmax	Maximum of all peak-to-valley values St, measured over the assessment length	
Rz	Average maximum height of the profile	
Rp	Maximum profile peak height	
Rv	Maximum profile valley depth	

8.3.4. ASSESSMENT OF QUESTIONNAIRES BY SUBJECT

The subjects will be completed self-questionnaires for efficacy at 2 and 4 weeks after treatment. The subjects also will be completed self-questionnaires for usability at 4 weeks.

9. SKIN ADVERSE REACTION

An adverse event is defined as any unusual event, which, in the researcher's opinion, is related to the study. The safety of the product will be assessed a clinical observation (subjective and objective signs) by two researchers in charge of efficacy and safety in this study. The frequency, the duration and the intensity of the sign and a possible or probable relationship with the test product will be investigated. Subjective signs included itching, prickling, tickling, burning, stinging, stiffness and tightness, etc. Objective signs included redness, edema, desquamation and papule, etc.

If an adverse event occurs, the subject, under the direction of the principal researcher, may be referred to DERMAPRO SKIN RESEARCH CENTER's dermatologist for treatment. All adverse events will be monitored by DERMAPRO SKIN RESEARCH CENTER researcher until resolution. DERMAPRO SKIN RESEARCH CENTER will report all serious adverse events to the study sponsor within 24 hours.

10. STATISTICAL ANALYSIS

Statistical analysis will be conducted using the SPSS® software program. To determine whether variables followed a normal distribution or not, we use the Shapiro-Wilks test or Kurtosis & Skewness for normality test. Statistical analysis of variables for parametric are conducted using the Repeated Measures ANOVA. If value was non-parametric, all of them are initially compared by the Wilcoxon signed rank test. Statistical analyses for comparison between groups are analyzed by the RM ANOVA or Independent t-test. A statistically significant difference was set at $p<0.05$.

11. REPORT

The study report will be reviewed to assure that it correctly describes the methods of testing and that the reported results accurately reflect the data obtained during the clinical study.

12. STORAGE OF THE DOCUMENTATION

The final report summarizes the method, data and conclusions (when applicable) relative to the product and the subjects. Source data will be retained on file by the testing facility. The original source data will be

maintained according to the investigator's standard operating procedure. A copy of the source documents may be obtained upon request of the Study Sponsor.

13. STUDY TIMELINE

Study Phase	Date
First Subject In	22th June. 2015 ~ 3th July. 2015
Last Subject Out	20th July. 2015~ 31th July. 2015
Draft Study Report	24th August. 2015
Final Study Report	When you confirm the draft

14. PROTOCOL APPROVAL

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