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# Efficacy Test Conducted With "Flexitol Very Dry Skin Balm 12.5% Urea "

## Summary

Study Sponsor .....: **Laderma Trading Pty Ltd.**
205 Victoria St.
Beaconsfield, NSW 2015
Australia

Date of Order.....: 03.02.2010

Performance of Test .....: Derma Consult Concept GmbH
and Evaluation by Von-Weichs-Str. 9A
53121 Bonn

Supervisors of Study .....: Dr. H. Prieur, Dermatologist – Allergist
Drs. B. Nissen

Study Code .....: DCC10W012

Test Product .....: The test product, which was coded as follows, was provided by Laderma Trading Pty Ltd.:

B. Flexitol Very Dry Skin Balm 12.5% Urea
(Project: 1231; Date 3/12/2009)

Subjects .....: Number of individuals.: 20 (+ 1 reserve subject)
Sex.....: female
Age range (completing) ..: 37-65 years (average: 45,8)

Test Area .....: Inner sides of forearms

Application.....: Duration....: 14 days
Frequency.: twice daily

Test Period .....: February / March 2010

| | | |
|---|---|---|
| Test Parameter | : | Determination of *skin hydration* with Corneometer MPA 5 CPU (Courage & Khazaka GmbH, Cologne) |
| Design of Study | : | **Day 0**<br>Determination of the parameters in the test areas<br>First test product application<br><br>**Day 7**<br>Determination of the parameters 8-12 hours following the last daily test product application<br><br>**Day 14**<br>Determination of the parameters 8-12 hours following the last daily test product application |
| Evaluation | : | Descriptive statistics (average, median, minimum, maximum, variance, standard error, standard deviation); Wilcoxon Rank test |
| Results | : | **Skin Hydration**<br>The test product was found to statistically significantly increase skin hydration. After 14 days of treatment, a mean increase by 52% (B) was observed and a positive effect of the test product was detected in 100% (B) of the volunteers. |

## Methods

### *Measurement of Skin Hydration (Corneometry)*

The Corneometer MPA 5 CPU (Courage and Khazaka, Cologne, Germany) registers the electrical capacitance of the skin surface. The capacitance is expressed digitally in arbitrary units (a.u.). The probe head (7x7 mm) consisting of a condenser was applied to the skin surface at constant pressure (3.5 N). The measuring principle is based on distinctly different dielectric constants of water (approximately 81) and most other materials (less than seven). Five measurements were performed on each test area and the mean was used to define the hydration state of the stratum corneum. Corneometer used in this study: S/N 08114012; probe S/N 01040160.

## Performance of Test

The subjects were selected from the Derma Consult Concept GmbH database. They were informed about importance and meaning of the study; they could withdraw from the study at any time without giving any reason. Written informed consent was obtained from all the subjects prior to entry into the trial. The following criteria were used for selection of subjects:

for inclusion in study:
- female (≥ 18 years of age)
- clinically healthy

for exclusion from study:
- skin diseases
- pregnancy

A reserve subject to replace potential drop-outs started the study with a delay of 1 day (final reading only taken in case a drop-out needed to be replaced). The subjects were instructed not to use any topical preparations on the test areas starting from seven days prior to testing and until the end of the test. For cleansing, water or a mild syndet (Eubos® flüssig – blau; manufacturer: Dr. Hobein, D-53340 Meckenheim-Merl, Germany) was allowed only (whole study inclusive the run-in phase).
Prior to the first application of the test product, measurements were taken at clearly defined sites of the inner sides of the forearms (skin hydration). One area remained untreated and served as control. Further measuring was performed after 7 and 14 days of application 8-12 hours following the last daily application (adaptation time: 30 min, room temperature: 21±1°C, relative humidity: 50± 5%). After a demonstration of the correct product application procedure by a Derma Consult staff member, the subjects used the test product (approximately 2 mg/cm²) twice daily (in the morning and evening) and in a manner corresponding as largely as possible to that to be practised by the future consumer.

## Biometry

Measurement data is automatically computerised and after validity check and quality assurance stored centrally in a database. Evaluation is conducted using the software NAG® Statistical Add-Ins for Excel – NAG Ltd., United Kingdom.
The data were analyzed by Wilcoxon Rank test. The 0.05 level was selected as the point of minimal acceptance of statistical significance.

## Results

During the second week of treatment, original subject 5 dropped out of the study due to an unrelated medical condition and was replaced by the reserve subject. The data collected on the initial and interim visits from the drop-out was discarded and hence the entire evaluation is based on the complete results from 20 volunteers. The completing subjects of this study were between 37-65 years of age (average: 45,8).

## *Skin Hydration*

Evaluated are changes in the hydration values in the treated area in comparison to the changes in the untreated area. An increase in the measurement value corresponds to an increase in skin hydration. The absolute changes by area and time point are displayed in figure one below.

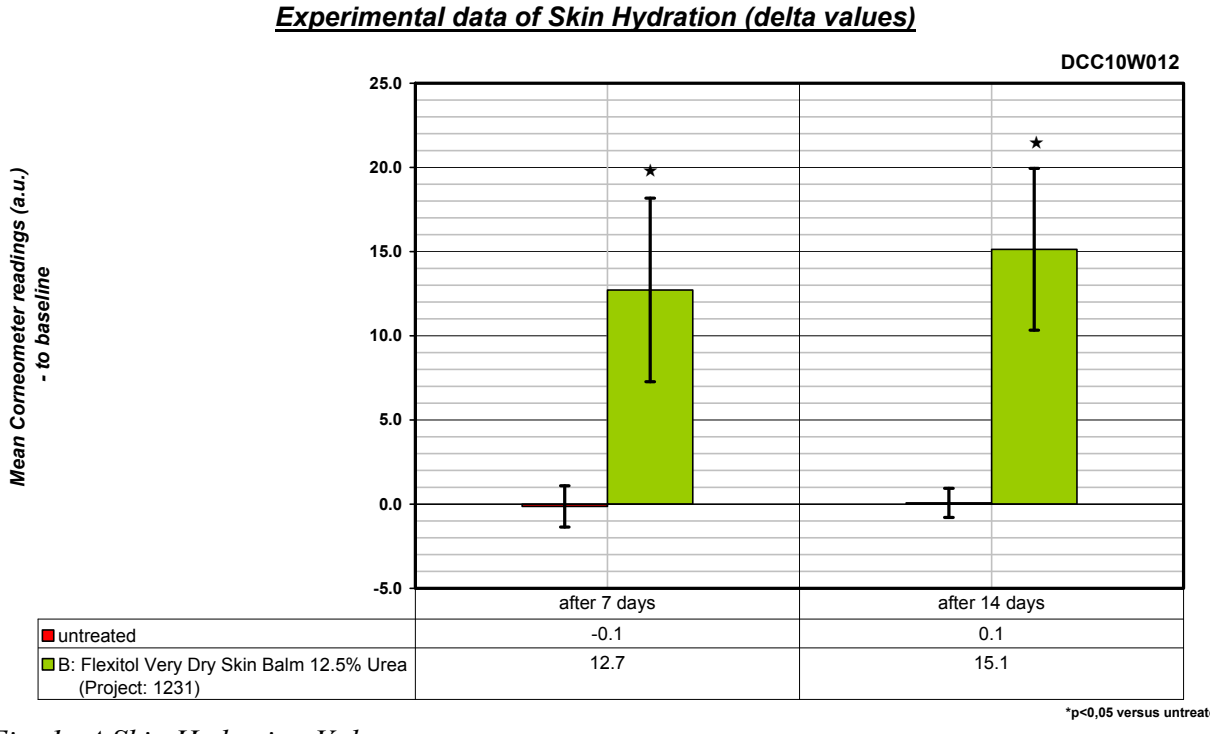



*Fig. 1: Δ Skin Hydration Values*

After both 7 and 14 days of treatment, a statistically significant ($p<0.05$) increase in skin hydration was observed in the product treated test area as compared to the changes in the untreated area.

The test product was found to increase skin hydration; after 7 & 14 days of treatment a positive effect could be detected in 100% of the study participants. The respective measured changes as percentages relative to the initial condition and with consideration of the changes in the untreated area are reported in figure two below.

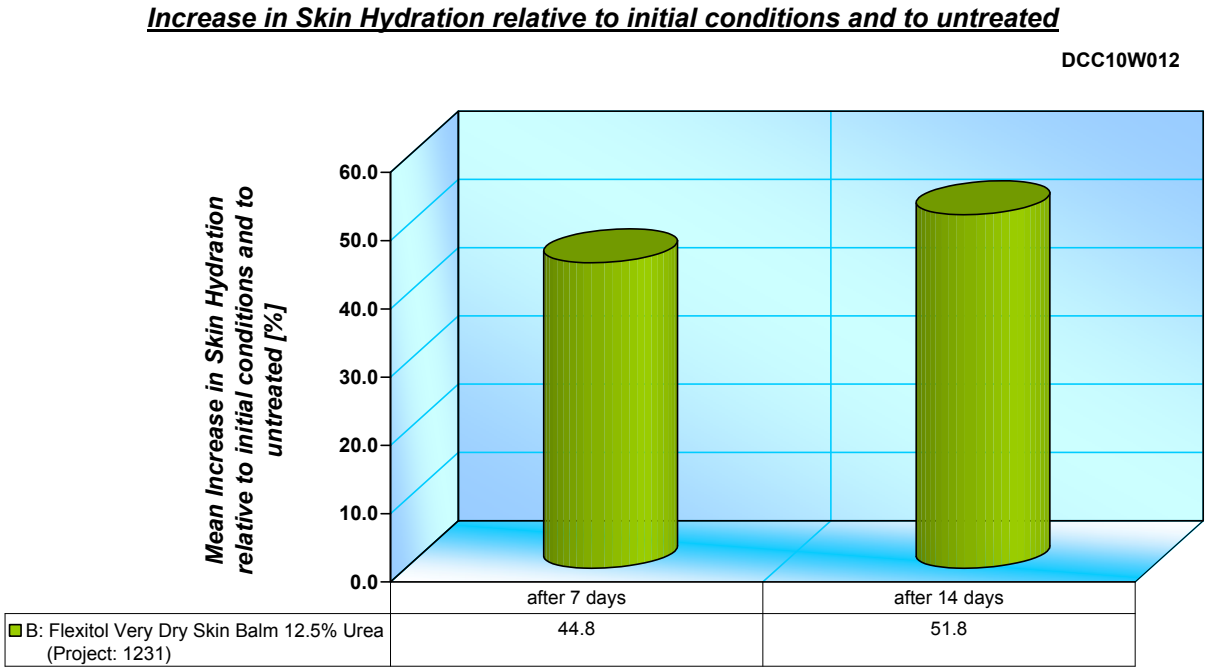



*Fig. 2: Increase in Skin Hydration in %*

## Incompatibility

No incompatibility was observed in or reported by any of the volunteers.

Signature:

Drs. B. Nissen
Manager Derma Consult Concept

Signature:

Dr. med. H. Prieur
Dermatologist - Allergist

Enclosures: Measuring values, statistics, summary statistics, graphic representations

**Experimental data of Skin Hydration, DCC10W012**

Corneometer readings (a.u.)

| | start | | after 7 days | | after 14 days | |
|---|---|---|---|---|---|---|
| | untr. | B | untr. | B | untr. | B |
| 1 | 27.2 | 27.5 | 26.5 | 34.5 | 26.5 | 34.7 |
| 2 | 29.5 | 28.1 | 27.7 | 49.7 | 28.4 | 53.4 |
| 3 | 32.0 | 35.1 | 33.7 | 53.3 | 32.2 | 51.1 |
| 4 | 31.2 | 34.8 | 30.6 | 41.5 | 30.7 | 45.7 |
| 5 | 33.4 | 35.0 | 32.0 | 40.9 | 34.0 | 52.5 |
| 6 | 32.3 | 28.2 | 33.4 | 43.6 | 32.9 | 42.7 |
| 7 | 26.9 | 25.2 | 25.3 | 41.9 | 25.6 | 44.4 |
| 8 | 33.1 | 35.5 | 32.1 | 41.8 | 32.7 | 42.5 |
| 9 | 25.1 | 21.9 | 24.7 | 37.1 | 26.9 | 43.7 |
| 10 | 33.9 | 33.2 | 33.8 | 36.4 | 33.2 | 42.4 |
| 11 | 35.1 | 33.8 | 35.2 | 45.5 | 34.6 | 46.7 |
| 12 | 30.8 | 30.3 | 31.1 | 45.3 | 31.0 | 46.4 |
| 13 | 32.6 | 35.1 | 34.2 | 43.4 | 33.2 | 45.3 |
| 14 | 32.2 | 34.0 | 30.5 | 43.3 | 31.6 | 51.1 |
| 15 | 27.6 | 26.6 | 28.0 | 44.7 | 28.5 | 45.8 |
| 16 | 26.0 | 24.5 | 28.2 | 40.8 | 26.5 | 38.7 |
| 17 | 23.2 | 25.8 | 24.3 | 46.9 | 24.0 | 45.3 |
| 18 | 34.5 | 31.5 | 32.8 | 41.7 | 35.9 | 48.3 |
| 19 | 34.4 | 33.0 | 33.9 | 44.3 | 33.6 | 44.7 |
| 20 | 25.4 | 27.1 | 25.8 | 44.0 | 26.2 | 43.5 |
| **Average** | 30.3 | 30.3 | 30.2 | 43.0 | 30.4 | 45.4 |
| **S.D.** | 3.7 | 4.3 | 3.6 | 4.3 | 3.5 | 4.5 |
| **Median** | 31.6 | 30.9 | 30.8 | 43.4 | 31.3 | 45.3 |

**Experimental data of Skin Hydration, DCC10W012**

delta Corneometer readings (a.u.)

| | after 7 days t1-t0 | | after 14 days t2-t0 | |
|---|---|---|---|---|
| | untr. | B | untr. | B |
| 1 | -0.7 | 7.0 | -0.7 | 7.2 |
| 2 | -1.9 | 21.7 | -1.2 | 25.3 |
| 3 | 1.7 | 18.2 | 0.1 | 16.0 |
| 4 | -0.6 | 6.7 | -0.5 | 10.9 |
| 5 | -1.4 | 5.8 | 0.6 | 17.5 |
| 6 | 1.1 | 15.4 | 0.6 | 14.5 |
| 7 | -1.5 | 16.7 | -1.2 | 19.2 |
| 8 | -1.0 | 6.3 | -0.5 | 7.1 |
| 9 | -0.3 | 15.2 | 1.8 | 21.8 |
| 10 | -0.1 | 3.2 | -0.7 | 9.2 |
| 11 | 0.1 | 11.7 | -0.5 | 12.9 |
| 12 | 0.3 | 15.0 | 0.2 | 16.1 |
| 13 | 1.6 | 8.3 | 0.6 | 10.2 |
| 14 | -1.8 | 9.3 | -0.7 | 17.1 |
| 15 | 0.4 | 18.0 | 0.8 | 19.2 |
| 16 | 2.2 | 16.3 | 0.5 | 14.3 |
| 17 | 1.0 | 21.2 | 0.8 | 19.6 |
| 18 | -1.8 | 10.1 | 1.4 | 16.8 |
| 19 | -0.5 | 11.3 | -0.8 | 11.6 |
| 20 | 0.4 | 16.9 | 0.8 | 16.3 |
| **Average** | -0.1 | 12.7 | 0.1 | 15.1 |
| **S.D.** | 1.2 | 5.5 | 0.9 | 4.8 |
| **Median** | -0.2 | 13.4 | 0.1 | 16.0 |

**Increase in Skin Hydration relative to initial conditions and to untreated, DCC10W012**

corrected Corneometer readings (a.u.) [%]

| | after 7 days | | after 14 days | |
|---|---|---|---|---|
| | untr. | B | untr. | B |
| 1 | -2.4 | 27.9 | -2.6 | 28.9 |
| 2 | -6.4 | 83.6 | -3.9 | 94.1 |
| 3 | 5.2 | 46.7 | 0.4 | 45.1 |
| 4 | -1.9 | 21.0 | -1.5 | 32.8 |
| 5 | -4.1 | 20.7 | 1.8 | 48.1 |
| 6 | 3.4 | 51.1 | 1.9 | 49.4 |
| 7 | -5.7 | 72.2 | -4.6 | 80.9 |
| 8 | -3.1 | 20.8 | -1.4 | 21.3 |
| 9 | -1.4 | 70.8 | 7.3 | 92.1 |
| 10 | -0.4 | 10.1 | -2.1 | 29.9 |
| 11 | 0.3 | 34.3 | -1.4 | 39.6 |
| 12 | 0.8 | 48.8 | 0.5 | 52.7 |
| 13 | 4.8 | 18.8 | 1.7 | 27.5 |
| 14 | -5.5 | 33.0 | -2.0 | 52.3 |
| 15 | 1.5 | 66.1 | 3.0 | 68.9 |
| 16 | 8.4 | 58.4 | 2.0 | 56.3 |
| 17 | 4.4 | 77.8 | 3.4 | 72.6 |
| 18 | -5.1 | 37.2 | 4.1 | 49.1 |
| 19 | -1.5 | 35.6 | -2.3 | 37.6 |
| 20 | 1.7 | 60.5 | 3.1 | 57.1 |
| **Average** | -0.3 | 44.8 | 0.4 | 51.8 |
| **S.D.** | 4.1 | 22.1 | 3.0 | 20.9 |
| **Median** | -0.9 | 42.0 | 0.5 | 49.3 |
| **Impr.*** | - | 100 | - | 100 |

* % of subjects with relative improvement in test area as compared to initial condition and corrected by changes in untreated area

## Descriptive Statistics of Skin Hydration, DCC10W012

**start**

| | untr. | B |
|---|---|---|
| Valid cases | 20.0 | 20.0 |
| Mean | 30.3 | 30.3 |
| Std. error of mean | 0.8 | 1.0 |
| Variance | 13.4 | 18.4 |
| Std. Deviation | 3.7 | 4.3 |
| Variation Coefficient | 0.1 | 0.1 |
| Minimum | 23.2 | 21.9 |
| Maximum | 35.1 | 35.5 |
| Median | 31.6 | 30.9 |

**after 7 days**

| | untr. | B |
|---|---|---|
| Valid cases | 20.0 | 20.0 |
| Mean | 30.2 | 43.0 |
| Std. error of mean | 0.8 | 1.0 |
| Variance | 12.7 | 18.5 |
| Std. Deviation | 3.6 | 4.3 |
| Variation Coefficient | 0.1 | 0.1 |
| Minimum | 24.3 | 34.5 |
| Maximum | 35.2 | 53.3 |
| Median | 30.8 | 43.4 |

**after 14 days**

| | untr. | B |
|---|---|---|
| Valid cases | 20.0 | 20.0 |
| Mean | 30.4 | 45.4 |
| Std. error of mean | 0.8 | 1.0 |
| Variance | 12.4 | 20.1 |
| Std. Deviation | 3.5 | 4.5 |
| Variation Coefficient | 0.1 | 0.1 |
| Minimum | 24.0 | 34.7 |
| Maximum | 35.9 | 53.4 |
| Median | 31.3 | 45.3 |

## Wilcoxon Rank Test of Skin Hydration, DCC10W012

**start - comparison of absolute values**

| | untr. - B |
|---|---|
| Rank sum (positive) | 99 |
| Z-value | -0.2053 |
| Significance | 0.8408 |
| non-zero observations | 20 |

**after 7 days - comparison of changes from initial condition**

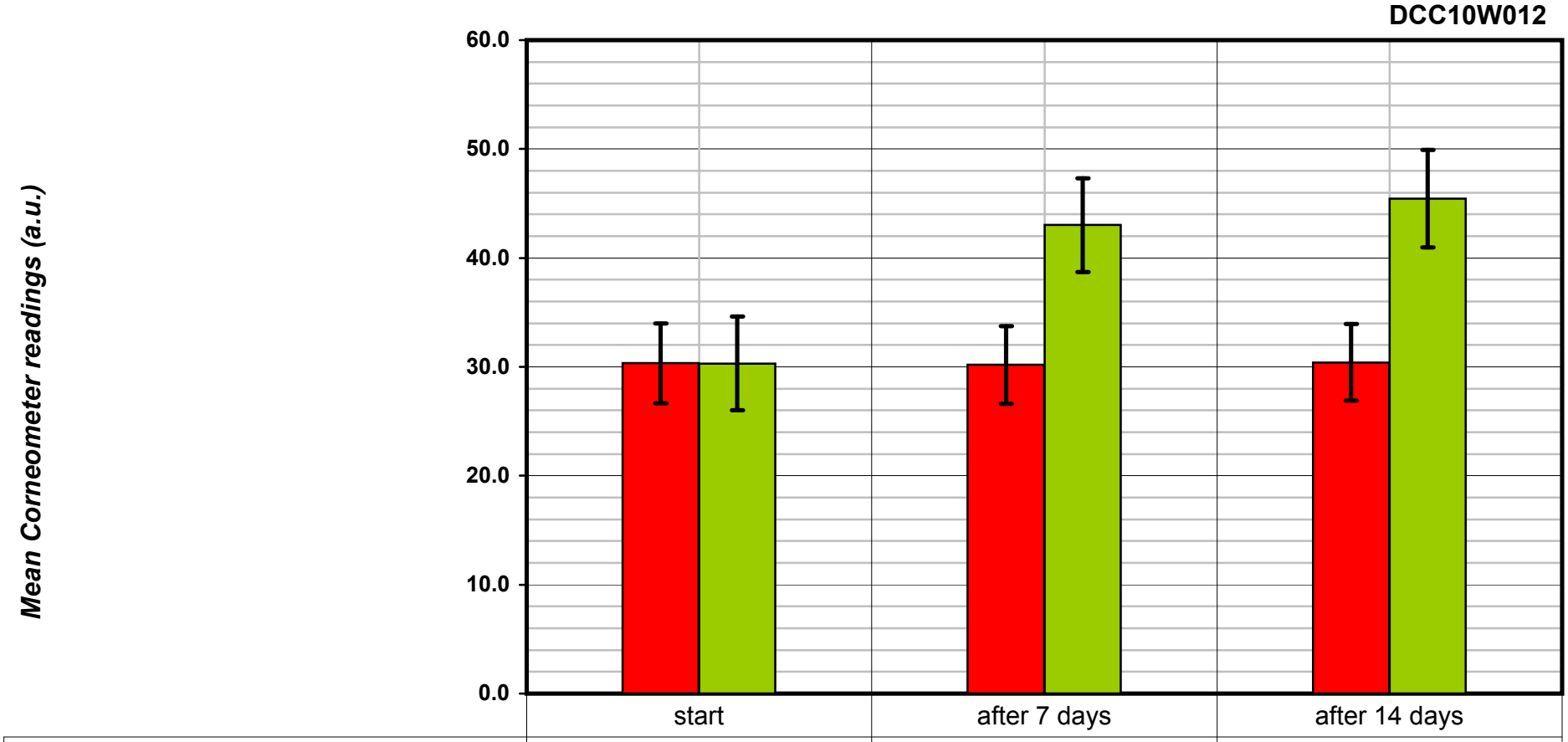
| | untr. - B |
|---|---|
| Rank sum (positive) | 0 |
| Z-value | -3.9013 |
| Significance | 0.0000 |
| non-zero observations | 20 |

**after 14 days - comparison of changes from initial condition**

| | untr. - B |
|---|---|
| Rank sum (positive) | 0 |
| Z-value | -3.9013 |
| Significance | 0.0000 |
| non-zero observations | 20 |

## ***Experimental data of Skin Hydration***

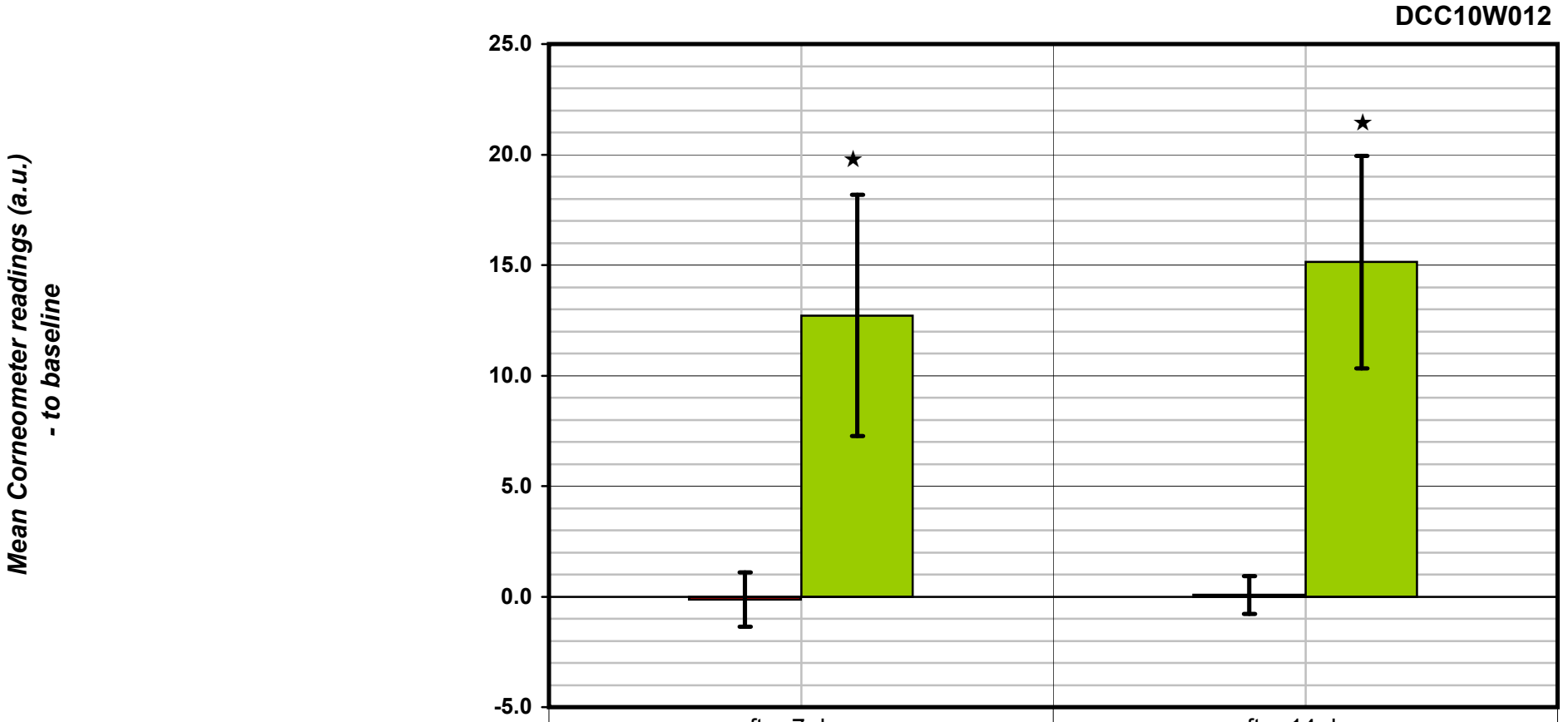
**DCC10W012**




| | start | after 7 days | after 14 days |
|---|---|---|---|
| untreated | 30.3 | 30.2 | 30.4 |
| B: Flexitol Very Dry Skin Balm 12.5% Urea (Project: 1231) | 30.3 | 43.0 | 45.4 |

# ***Experimental data of Skin Hydration (delta values)***

**DCC10W012**

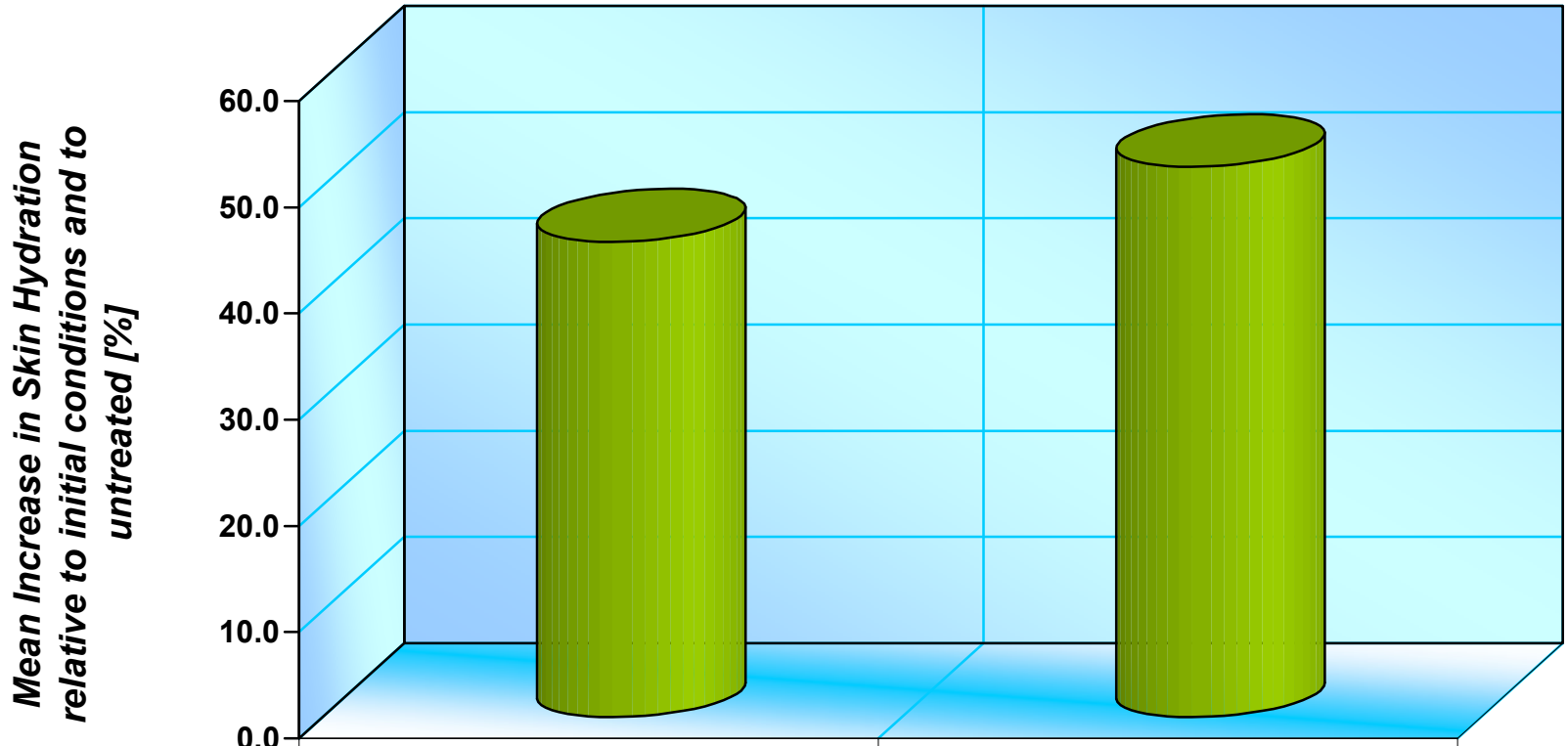



| | after 7 days | after 14 days |
|---|---|---|
| untreated | -0.1 | 0.1 |
| B: Flexitol Very Dry Skin Balm 12.5% Urea (Project: 1231) | 12.7 | 15.1 |

***p<0,05 versus untreat**

## ***Increase in Skin Hydration relative to initial conditions and to untreated***

**DCC10W012**




| | after 7 days | after 14 days |
|---|---|---|
| B: Flexitol Very Dry Skin Balm 12.5% Urea (Project: 1231) | 44.8 | 51.8 |