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Date: 10.12.2010

Efficacy Test Conducted With "Callous Cream (LAD-041, X-11)"

(Cosmetic Study)

Summary

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

Date of Order.....: 15.10.2010

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

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

A. Callous Cream (LAD-041, X-11)
(13 October 2010 / 26 October 2010)

Subjects .....: Number of individuals. : 20
Sex.....: female
Age range (completing) ..: 38-62 years (average: 47,9)

Test Area .....: Feet (test against initial condition)

Application.....: Duration.... : 28 days of application
Frequency . : twice daily

Test Period .....: November / December 2010

Test Parameters .....: Determination of *skin thickness* by means of COLLAGENOSON® ICU (Minhorst GmbH & Co., Meudt, Germany) – *measured on the heel (callus)*

Design of Study.....: **Day 0**
Measurement & first test product application

Day 28
Measurement 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 Thickness**

The test product was found to statistically significantly reduce skin thickness (callous) as measured on the heel; after 28 days of treatment a mean reduction by 15% was detected and a positive effect of the product treatment was observed in 90% of the study participants.

Methods

Measurement of Skin Thickness (Ultrasound Echography)

Skin thickness (epidermis + dermis) was assessed by echographic evaluation of the skin using COLLAGENOSON® "ICU" (Minhorst GmbH & Co., Meudt, Germany). The ultrasound device is equipped with a 22 MHz ultrasonic transducer, which enables a high definition examination of the skin up to a depth of approximately 6 mm. Distilled water was employed as coupling medium between the probe and the skin surface. During each measurement of 1 second, where the probe is manually moved at constant speed across the skin surface, 208 A-images (one-dimensional) were taken and merged to a B-image (two-dimensional) depicting a cross-section of the skin. A high gain curve (25) was selected to compensate the hyperecho of the dense horned skin layer. Per subject and time point, 3 measurements were conducted. Data evaluation was conducted at the end of the study.
Skin thickness (epidermis + dermis) was measured as the distance between the first flank in the averaged A-image and the flank between the dermis and hypodermis. COLLAGENOSON® "ICU" used in this study: S/N 7097 (Software: Collagenoson USM, version: 021007.2). As total thickness in the measurement area is dominated by the horned layer, any change in the measurement value of total skin thickness (epidermis + dermis) can be interpreted as reduction of the horned layer (callus reduction). COLLAGENOSON® "ICU" used in this study: S/N 7097 (Software: Collagenoson USM, version: 021007.2).

Performance of Test

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

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

for exclusion from study:
- skin diseases
- pregnancy
- mechanical or chemical removal (pedicure) within past 2 month

A reserve subject to replace potential drop-outs started the study with a delay of 2 days (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). Pedicure and the use of abrasives on the foot sole and heel was not allowed during the entire test.

Prior to the first application of the test product, measurements were taken at clearly defined sites on the lateral heel (skin thickness; randomized side selection). 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) once daily in a manner corresponding as largely as possible to that to be practised by the future consumer for a period of 28 days on their feet at home. They then returned to the test institute for a concluding measurement (8-12 hours following the last daily application). All measurements were conducted under standardized environmental conditions (room temperature: 21±1°C, relative humidity: 50± 5%) with an adaptation time of 30 minutes – without wearing shoes or socks and without placing the heels onto any hard surface.

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 16 dropped out of the study due to an unrelated medical condition and was replaced by the reserve subject. The data collected on the initial visit 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 38-62 years of age (average: 47,9).

Skin Thickness

Evaluated are the changes in the skin thickness measured by ultrasound on the heels (callus) in comparison to the respective initial condition. The absolute values by time point are shown below in figure one, the changes in figure two.

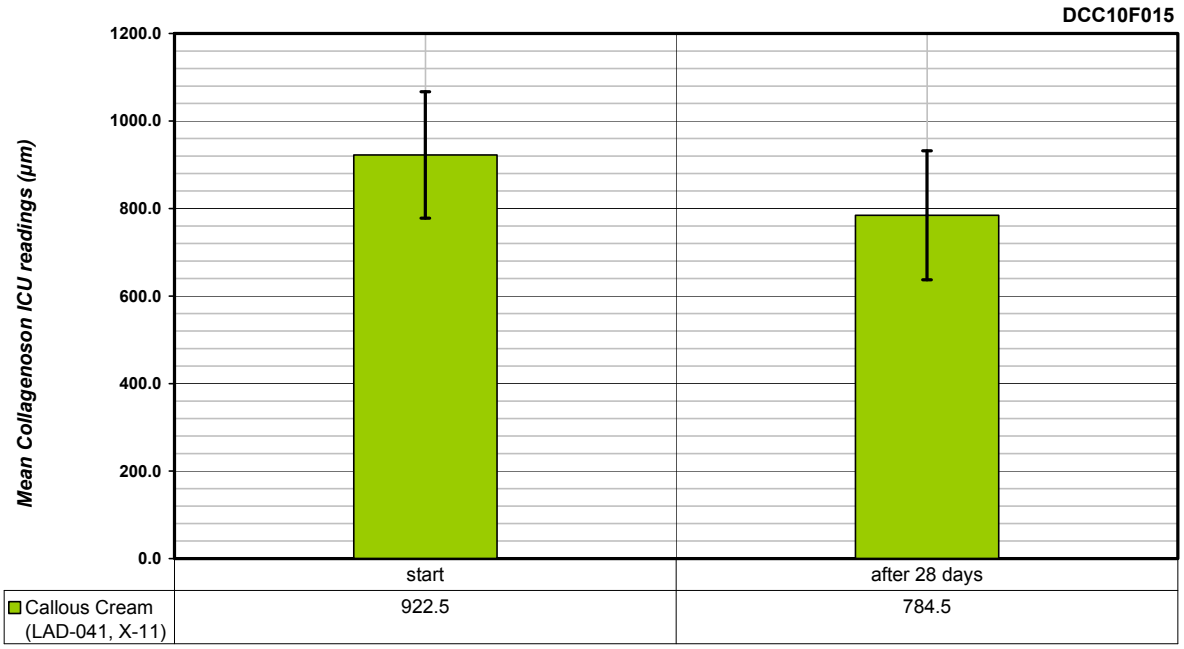


Fig. 1: Skin thickness (µm)

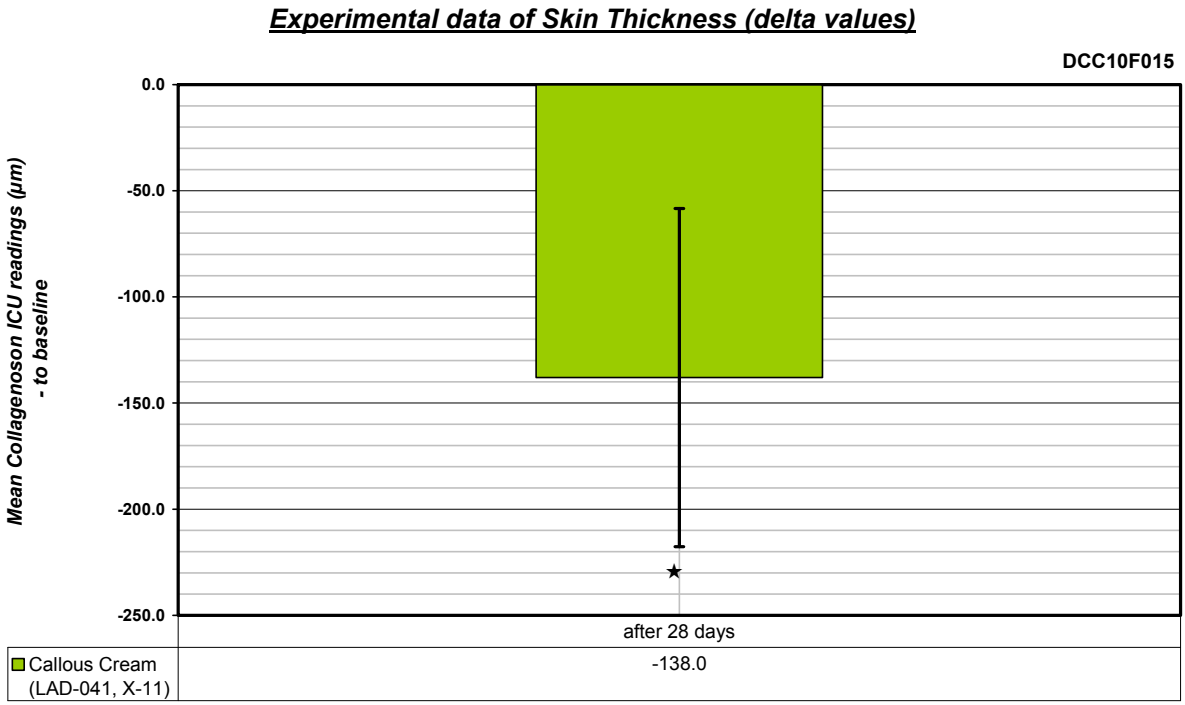


Fig. 2: Δ Skin thickness

After 28 days of treatment, the absolute measurement values show a statistically significant ($p<0,05$) average decrease in skin thickness as compared to the initial condition; a positive effect of the product treatment could be detected in 90% of the volunteers.
The skin thickness decrease expressed as a percentage is shown below in figure three. Ultrasound before / after images from two subjects (1 and 10) of the study are depicted in figures four to seven below. Horned skin is shown in light yellow (very dense).

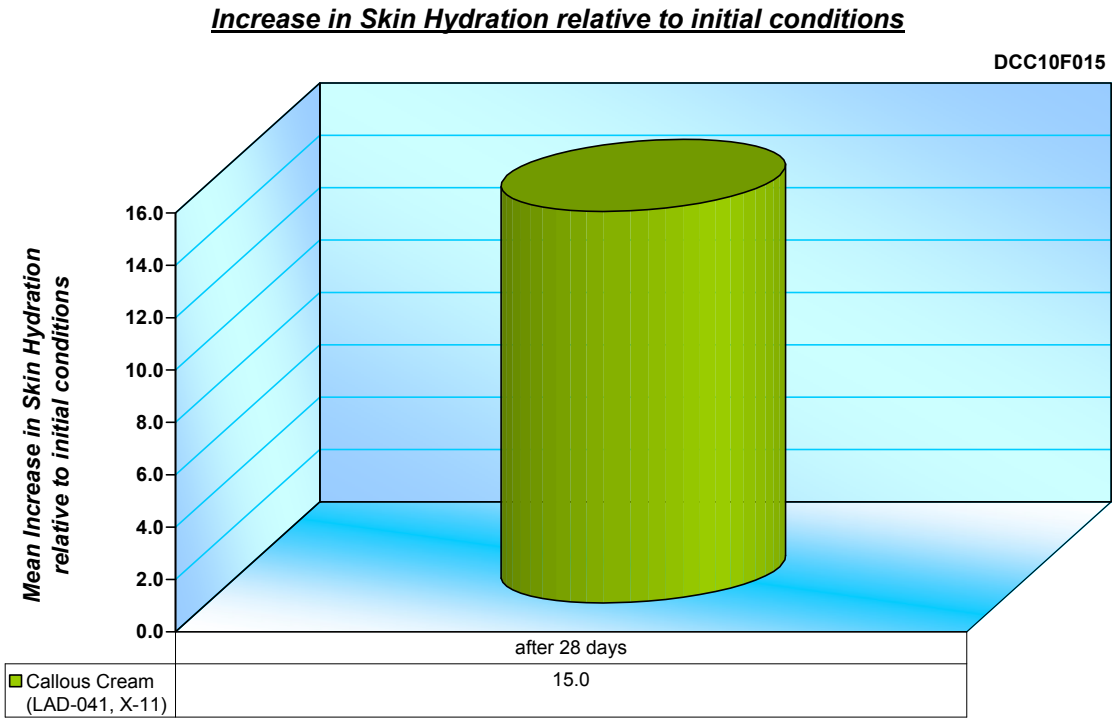


Fig. 3: Decrease in Skin thickness (%)

Start (subject 1)

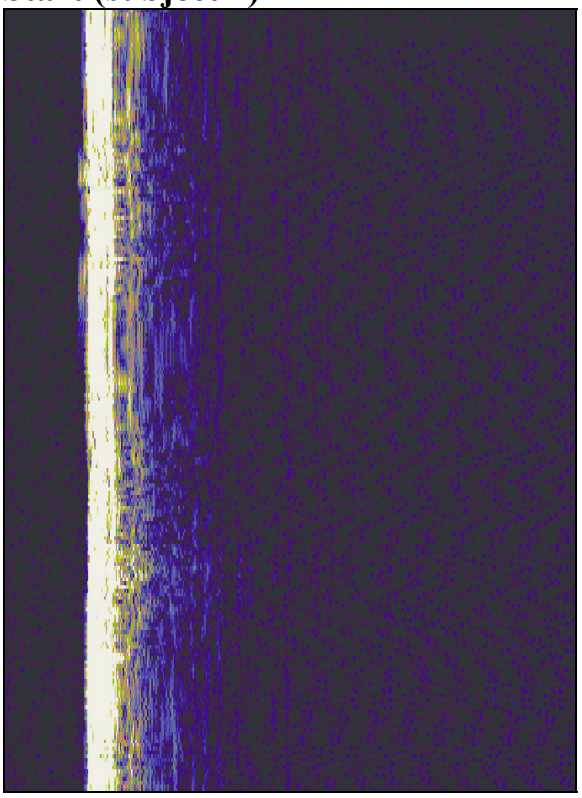


Fig. 4

28 days (subject 1)

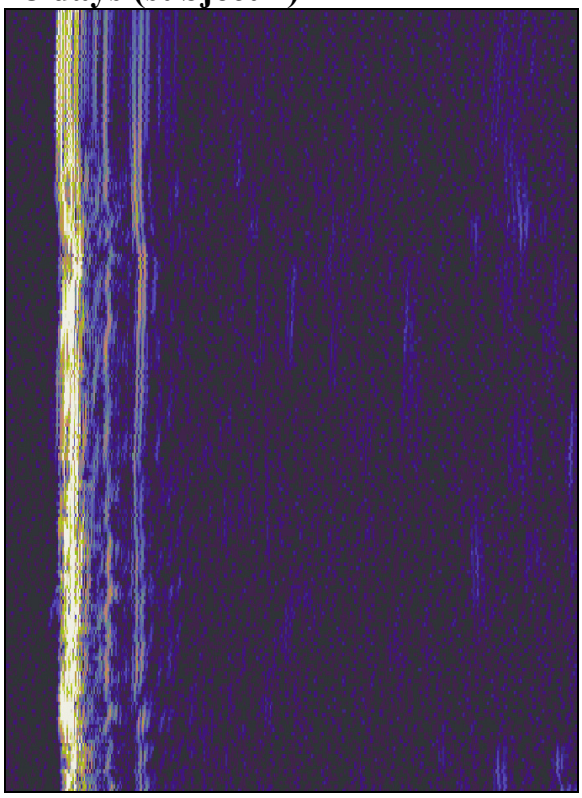


Fig. 5

Start (subject 10)

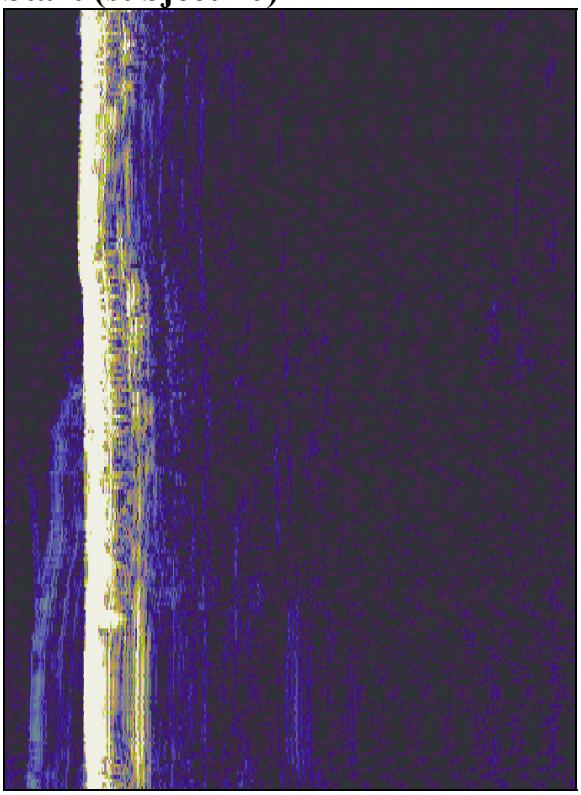


Fig. 6

28 days (subject 10)

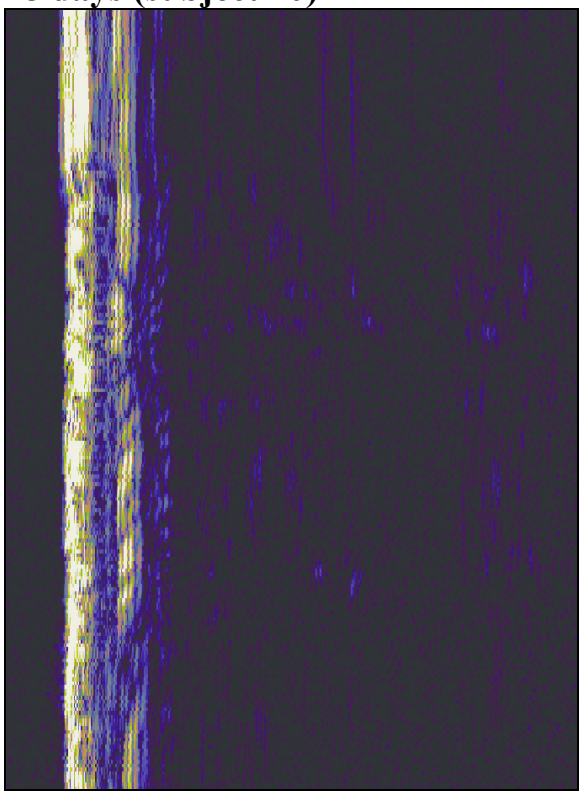


Fig. 7

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 Thickness, DCC10F015

Collagenoson ICU readings (μm)

	start	after 28 days
	A	A
1	796.7	583.3
2	973.3	780.0
3	1183.3	946.7
4	990.0	1010.0
5	796.7	693.3
6	1003.3	846.7
7	1010.0	846.7
8	983.3	720.0
9	1006.7	936.7
10	696.7	530.0
11	906.7	823.3
12	1140.0	1023.3
13	770.0	773.3
14	966.7	776.7
15	843.3	666.7
16	613.3	596.7
17	890.0	693.3
18	1043.3	966.7
19	810.0	610.0
20	1026.7	866.7
Average	922.5	784.5
S.D.	144.5	147.3
Median	970.0	778.3

Experimental data of Skin Thickness, DCC10F015

delta Collagenoson ICU readings (μm)

after 28 days

t1-t0

	A
1	**-213.3**
2	**-193.3**
3	**-236.7**
4	**20.0**
5	**-103.3**
6	**-156.7**
7	**-163.3**
8	**-263.3**
9	**-70.0**
10	**-166.7**
11	**-83.3**
12	**-116.7**
13	**3.3**
14	**-190.0**
15	**-176.7**
16	**-16.7**
17	**-196.7**
18	**-76.7**
19	**-200.0**
20	**-160.0**
Average	**-138.0**
S.D.	**79.7**
Median	**-161.7**

Increase in Skin Hydration relative to initial conditions, DCC10F015

corrected Collagenoson ICU readings (µm) [%]

after 28 days

	A
1	**-26.8**
2	**-19.9**
3	**-20.0**
4	**2.0**
5	**-13.0**
6	**-15.6**
7	**-16.2**
8	**-26.8**
9	**-7.0**
10	**-23.9**
11	**-9.2**
12	**-10.2**
13	**0.4**
14	**-19.7**
15	**-20.9**
16	**-2.7**
17	**-22.1**
18	**-7.3**
19	**-24.7**
20	**-15.6**
Average	**-15.0**
S.D.	**8.8**
Median	**-15.9**
Impr.*	**90**

* % of subjects with relative improvement in test area as compared to initial condition

Descriptive Statistics of Skin Thickness, DCC10F015

start

	A
Valid cases	20.0
Mean	922.5
Std. error of mean	32.3
Variance	20873.5
Std. Deviation	144.5
Variation Coefficient	0.2
Minimum	613.3
Maximum	1183.3
Median	970.0

after 28 days

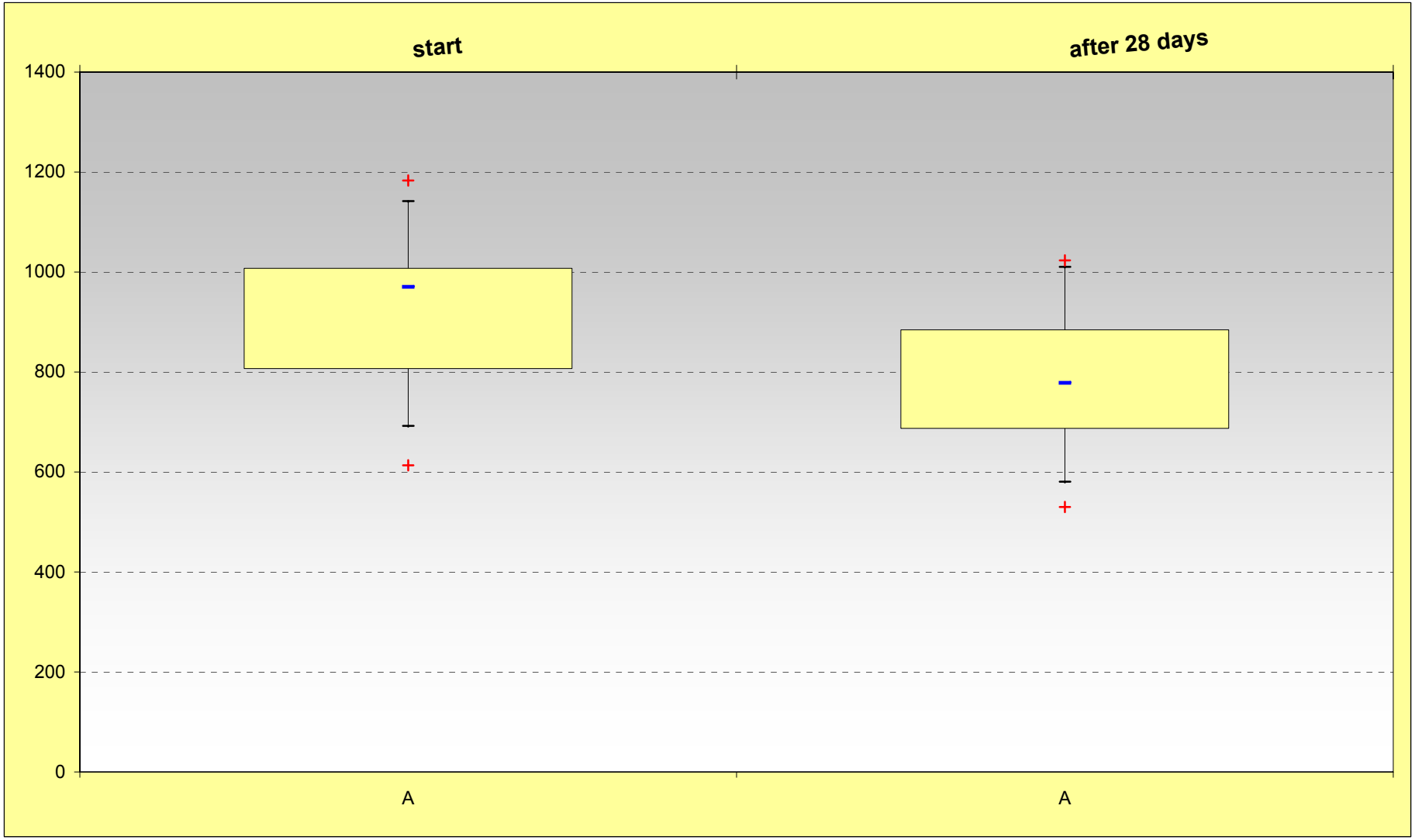
	A
Valid cases	20.0
Mean	784.5
Std. error of mean	32.9
Variance	21703.2
Std. Deviation	147.3
Variation Coefficient	0.2
Minimum	530.0
Maximum	1023.3
Median	778.3

Wilcoxon Rank Test of Skin Thickness, DCC10F015

start - after 28 days

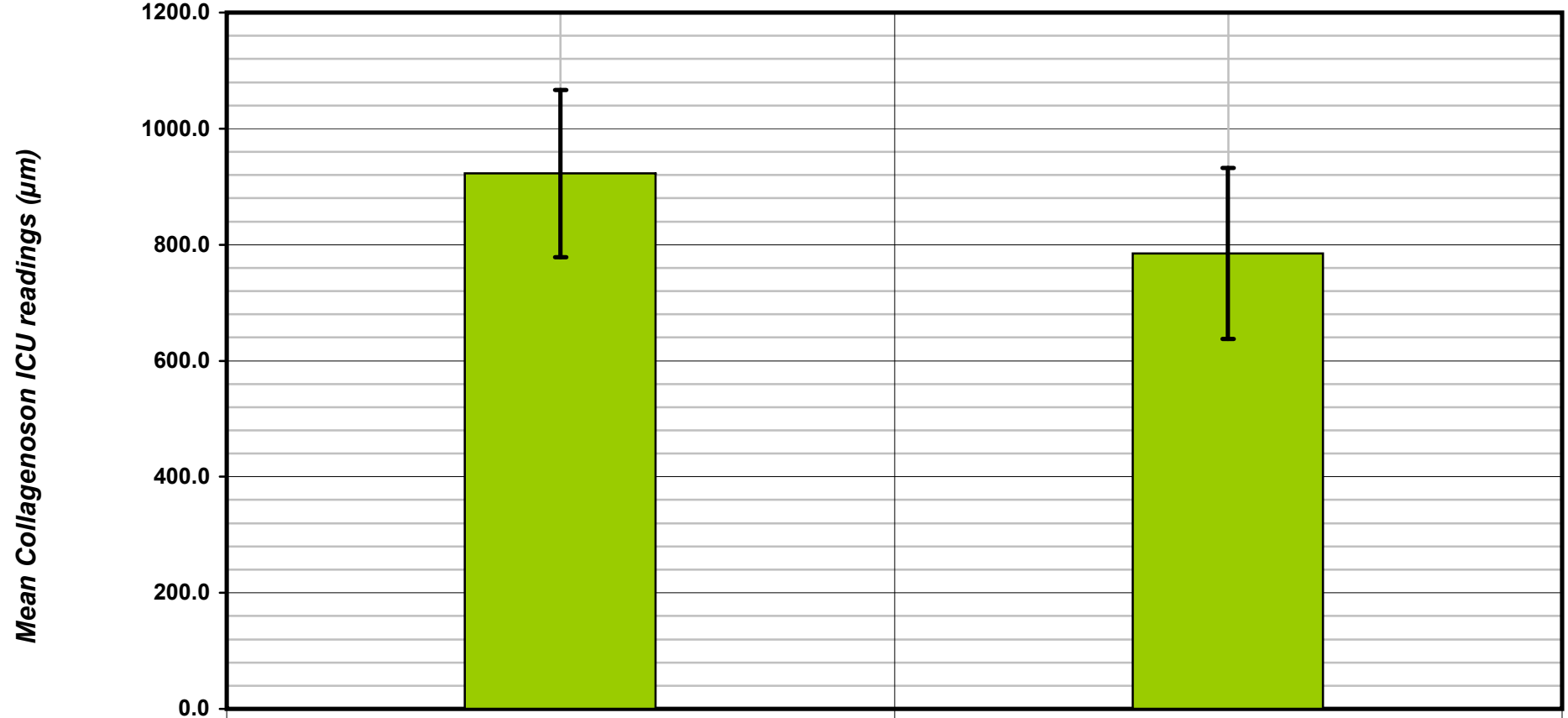
	A
Rank sum (positive)	206
Z-value	3.7519
Significance	0.0000
non-zero observations	20

Box & Whisker Plot of Skin Thickness, DCC10F015



Experimental data of Skin Thickness

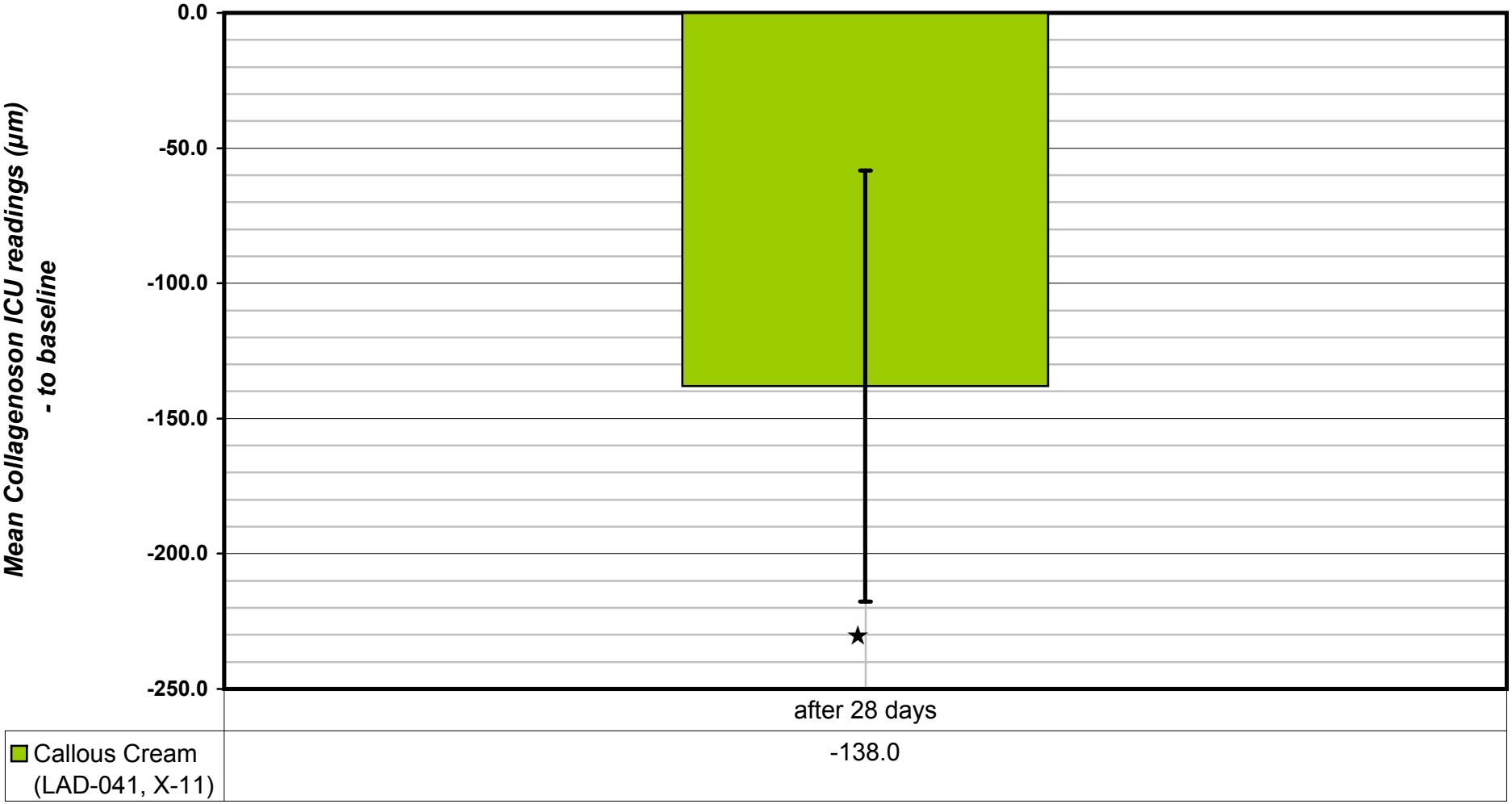
DCC10F015



	start	after 28 days
Callous Cream (LAD-041, X-11)	922.5	784.5

Experimental data of Skin Thickness (delta values)

DCC10F015



Increase in Skin Hydration relative to initial conditions

DCC10F015