

Evaluation of the IN VIVO COSMETIC EFFICACY of MF III of Switzerland PE Softgels

1740mg

(Swiss Original Dietary Supplement)
A four-month randomized
placebo-controlled Double-blind study

Clinical Study Report Nr. CTE23A



Independent Clinical Study directed & headed by:

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September, 2005 – January, 2006



Demography

- Venue of study: Neuchâtel Switzerland
- Time: September, 2005 to January, 2006
- 2 groups of volunteers: Test group, Placebo group
- 28 volunteers in each group
- Healthy women, Caucasian skin type, Various races
- Skin phototype II (Fitzpatrick)
- Ages: Group ranging from 20-60 years, mean 41
- Volunteers nor research conducting personnel are aware which is the real PE Softgels nor its name or a Placebo as softgels looks totally alike.





Demography (Continued)

*Homogeneous distribution of ages
within the groups:*

- Test group

Age Group 20-24	Age Group 25-29	Age Group 30-34	Age Group 35-39	Age Group 40-44	Age Group 45-49	Age Group 50-54	Age Group 55-59
Nic (20*)	Gir (27*)	Bio (33*)	Dem (36*)	Cal (42*)	Aes (47*)	Bor (52*)	Bod (59*)
Nis (20*)	Lou (29*)	Don (30*)	Pet (37*)	Hei (41*)	Bau (45*)	Gra (53*)	Mer (59*)
Pap (24*)		Mon Pa (32*)	Rot (38*)	Mai (40*)	Cla (48*)	Mon Ir (55*)	Rer (55*)
		Vol (31*)	Tar (38*)	Spi Fa (44*)	Coi (46*)	Rol (51*)	
					Kon (47*)		

- Placebo group

Age Group 20-24	Age Group 25-29	Age Group 30-34	Age Group 35-39	Age Group 40-44	Age Group 45-49	Age Group 50-54	Age Group 55-59
Bar (21*)	Dal (25*)	Bug (32*)	Ban (37*)	Dea (42*)	Gut (47*)	Feu (54*)	Dre (59*)
Cor (23*)	Guy (27*)	Dep (34*)	Con (38*)	Dek (42*)	Noi (48*)	Sto (50*)	Rac (56*)
Duc (22*)	Mon (25*)	Gai (33*)	Mel (39*)	Dub (44*)	Sch (48*)	Wic (50*)	Spi (58*)
	Sca (29*)			Jab (41*)			Vau (55*)
				Sei (43*)			

* Code numbers of each different women.



Measurement and treatment schedules



Schedule1	Skin measurement	Treatment sessions at home	Questionnaire hand-over	Questionnaire back hand-over
First day of the study/ first measurement session (Sep. 20-30, 2005)	●			
First month of treatment		● (28)		
Meeting after 1 month (Oct. 18-28, 2005)	●			
Second month of treatment		● (28)		
Meeting after 2 months (Nov. 15-25, 2005)	●		●	
Third month of treatment		● (28)		
Meeting after 3 months (Dec. 13-23, 2005)	●			●
Meeting after 4 monts (Jan. 10-20, 2006)	●			





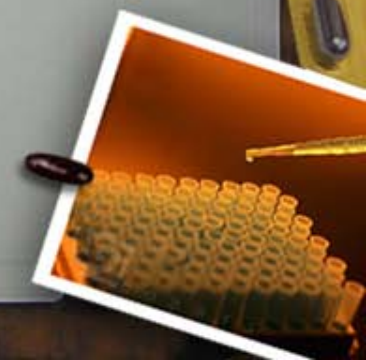
Room conditions

Protocol:

- Room temperature = $(22.5 \pm 1.5) ^\circ\text{C}$
- Relative air humidity = $(50 \pm 10) \%$

	Measuring conditions (mean values \pm SD)									
	Day 1		Day 29		Day 57		Day 85		Day 113	
	Temp ($^\circ\text{C}$)	RH (%)	Temp ($^\circ\text{C}$)	RH (%)	Temp ($^\circ\text{C}$)	RH (%)	Temp ($^\circ\text{C}$)	RH (%)	Temp ($^\circ\text{C}$)	RH (%)
Measured values (Means \pm SD)	21.7 \pm 0.8	56.1 \pm 1.9	21.5 \pm 0.6	55.2 \pm 3.3	21.4 \pm 0.6	52.1 \pm 4.9	22.3 \pm 0.7	51.2 \pm 3.8	21.9 \pm 0.8	50.9 \pm 4.7
Legend:	Temp: temperature; RH: relative humidity; SD: Std. deviation									

The measuring conditions were ensured at each visit conforming to the protocol.



Test Parameters

- Test Parameters No.

1. Transepidermal water loss
2. Skin sebum content
3. Erythema index (*skin colour*)
4. Skin microrelief, average roughness, forearm
5. Dermis density
6. Skin moisture

- Skin Measurement Devices :

- Corneometer® CM 825
(*Courage & Khazaka, skin moisture*)
- Sebumeter® SM 810
(*Courage & Khazaka, skin sebum content*)
- Mexameter® MX 16
(*Courage & Khazaka, erythema index*)
- Dermalab® TEWL
(*Cortex Technology, TEWL*)
- DermaScan® C
(*Cortex Technology, dermis density*)
- Visioscan® VC 98
(*Courage & Khazaka, skin microrelief*)





Measurement Areas and sequences



Sebum
(forehead)



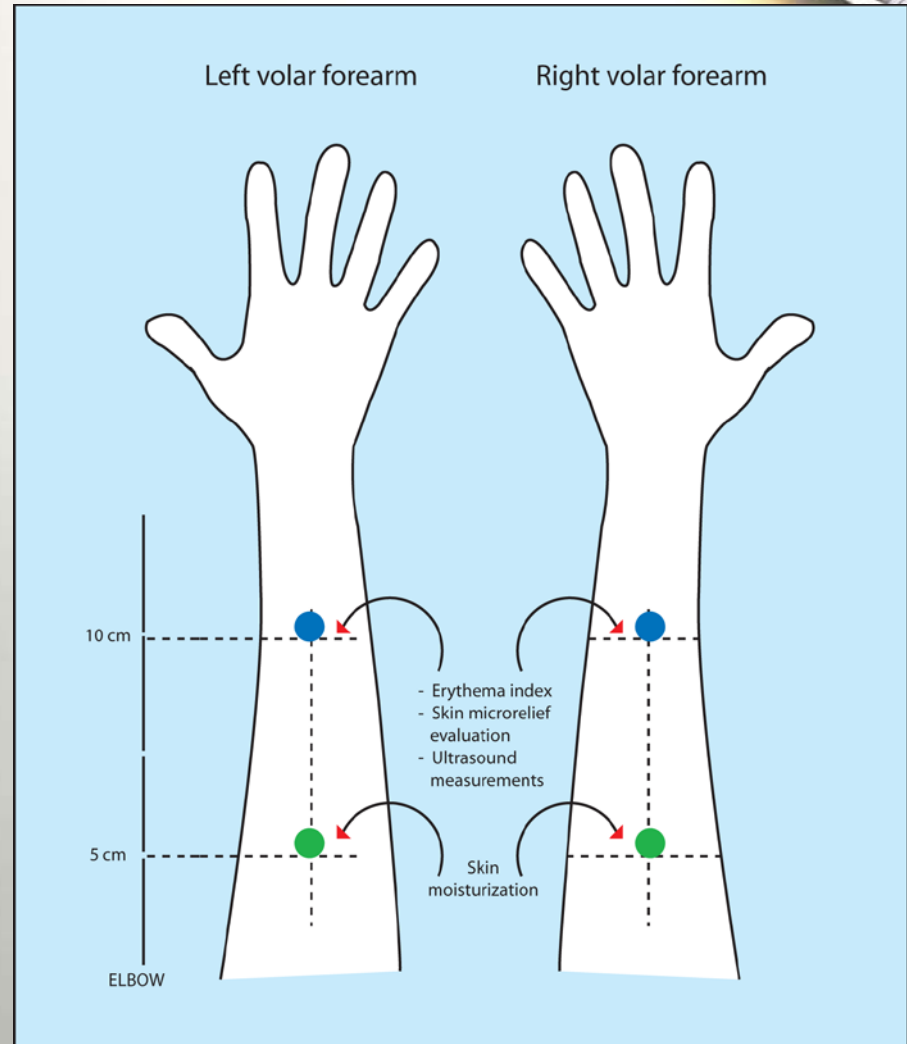
**Ultrasonography
measurements
on the face**
(left cheek)



Measurement Areas and sequences *(continued)*

Other measurements on the left and right volar forearm:

- Transepidermal water loss
- **Moisture**
- Skin microrelief
- **Erythema index**
- Dermis density





Measurement areas and sequences *(continued)*

Sebum

- left forehead (1x)
- right forehead (1x)



Moisture

- left forearm (5x)



Skin microrelief
(roughness)

- left forearm (3x)



Erythema index

- right forearm (5x)



Measurement areas and sequences *(continued)*

Firmness

– right forearm (2x)



TEWL

– right forearm (1x)



**Epidermis + dermis
density** *(forearm)*

– right forearm (1x)



**Epidermis + dermis
density** *(cheek)*

– left cheek (1x)





Selected Measurement Devices



Combi-3
(Courage & Khazaka)

- *Moisture*
- *Sebum*



DermaScan C
(Cortex Technology)

- *Dermis density*



Selected Measurement Devices *(Continued)*



Visioscan

(Courage & Khazaka)

- Skin microrelief



Dermalab TEWL

(Cortex Technology)

- Transepidermal water loss

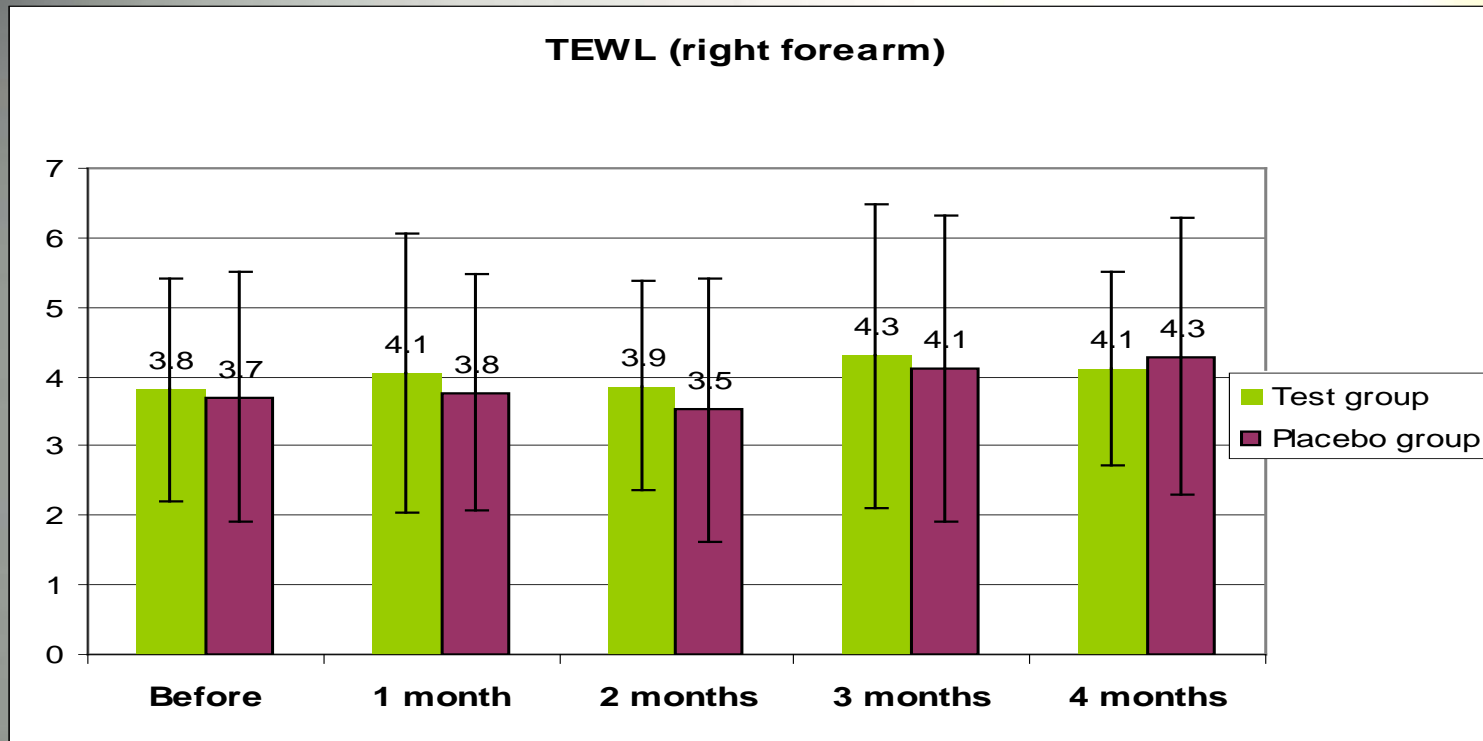


Test Parameter No:1 (on transepidermal water loss, forearm) **RESULTS**

	TEWL: Mean values (\pm SD; g/m ² x h)				
	Day 0	Day 28	Day 56	Day 84	Day 112
Test group	3.8 \pm 1.6	4.1 \pm 2.0	3.9 \pm 1.5	4.3 \pm 2.2	4.1 \pm 1.4
Placebo group	3.7 \pm 1.8	3.8 \pm 1.7	3.5 \pm 1.9	4.1 \pm 2.2	4.3 \pm 2.0
Ratio to Day 0 (treated)	0.1	0.3	0.3	0.2	-0.2
Ratio to Day 0 (treated) (%)		4.5%	6.2%	2.1%	-7.9%
Statistics (permutation)	p = 0.402 (ns)	p = 0.283 (ns)	p = 0.220 (ns)	p = 0.376 (ns)	p = 0.342 (ns)



Test Parameter No:1 (on transepidermal water loss, forearm) RESULTS



Transepidermal water loss before and during once daily supplementation



Test Parameter No:1
(on transepidermal water loss, forearm)
CONCLUSION ON RESULTS

- **The test product did not influence TEWL, which shows that it was very well tolerated by the skin and the organism.**



Test Parameter No:2 (on sebum casual level, forehead)

RESULTS

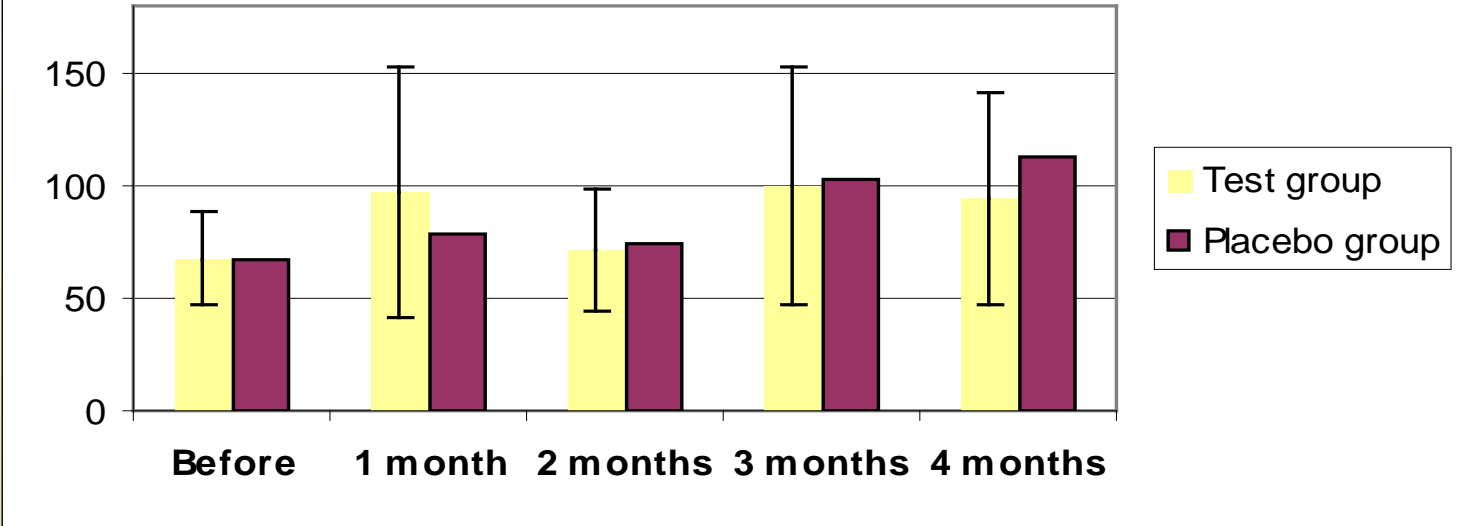
	Sebum casual level: Mean values (\pm SD; $\mu\text{g} / \text{cm}^2$); dry subgroup				
	Before	1 month	2 months	3 months	4 months
	Day 0	Day 28	Day 56	Day 84	Day 112
Test group (17 subjects)	67.7 ± 20.7	97.4 ± 55.5	71.5 ± 27.0	99.7 ± 52.8	94.0 ± 47.1
Sebum casual level difference [D0 - Dx]/D0], % (Test group)	-	-43.9%	-5.6%	-47.3%	-38.9%
Placebo group (15 subjects)	66.6 ± 20.3	77.9 ± 30.9	74.1 ± 34.3	102.7 ± 56.6	112.9 ± 52.6
Sebum casual level difference [D0 - Dx]/D0], % (Placebo group)	-	-16.9%	-11.2%	-54.1%	-69.4%
Mean difference (test vs. placebo, $\mu\text{g} / \text{cm}^2$)	-	-27.0%	5.6%	6.9%	30.5%
Stat. results (test group, permutation test for paired data)	-	p = 0.017 * significant	p = 0.265 (ns) unsignificant	p = 0.010 ** Very significant	p = 0.018 * significant
Stat. results (placebo group, permutation test for paired data)	-	p = 0.078 (ns) unsignificant	p = 0.232 (ns) unsignificant	p = 0.014 * significant	p = 0.004 ** Very significant





Test Parameter No:2 (Continued) (on sebum casual level, forehead) **RESULTS**

Sebum casual levels (test group, lower sebum subgroup, forehead)



Forehead sebum, casual levels before and during once daily supplementation



Test Parameter No:2 (on sebum casual, forehead)

CONCLUSION ON RESULTS

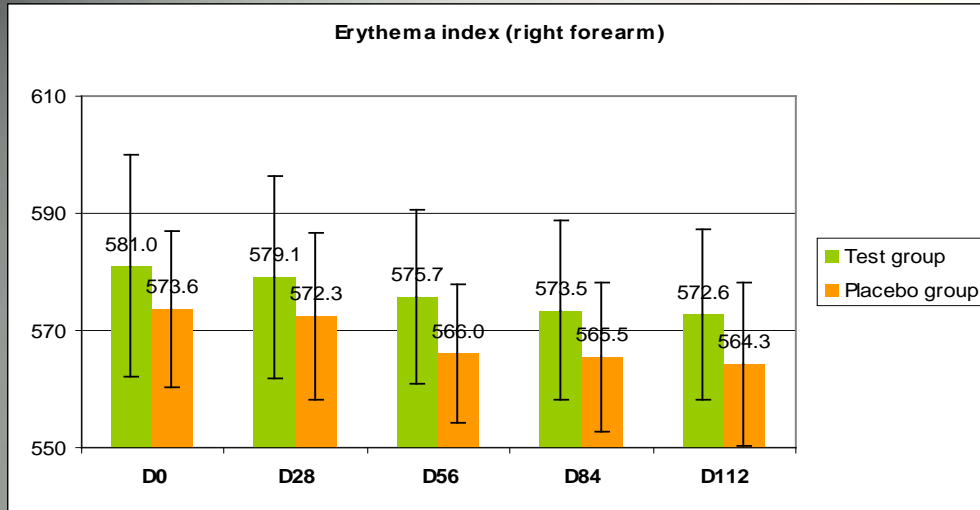
- **A seboregulation process was noted for low sebum-containing skins.**
- **Mean sebum values increased to normal levels, at 3 months.**
- **The test product significantly normalises too low sebum values on the forehead.**



Test Parameter No:3 (on erythema index, forearm) RESULTS

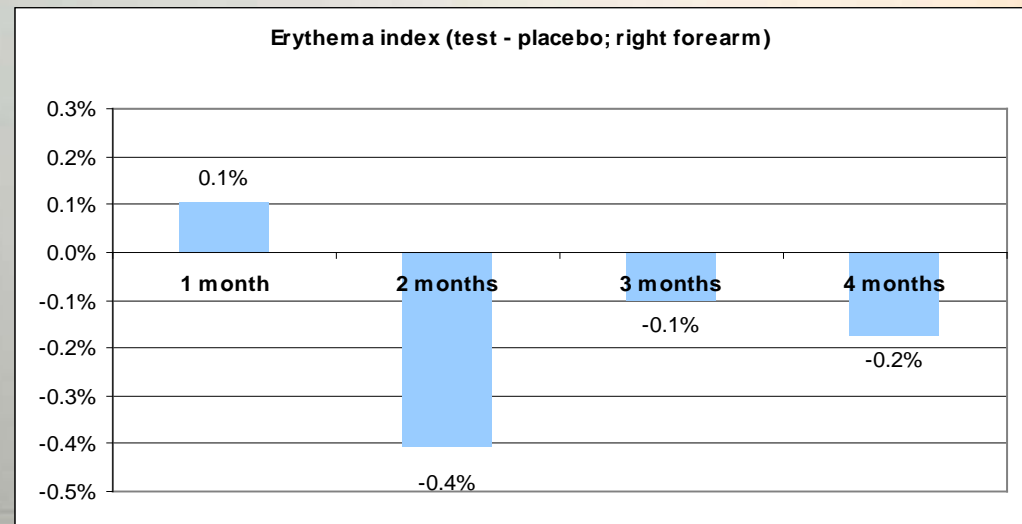
	Erythema index: Mean values (\pm SD; Mexameter units)				
	Before	1 month	2 months	3 months	4 months
	Day 0	Day 28	Day 56	Day 84	Day 112
Test group (30 subjects)	581.0 \pm 19.0	579.1 \pm 17.2	575.7 \pm 14.9	573.5 \pm 15.2	572.6 \pm 14.6
Erythema index difference [D0 - Dx]/D0], % (Test group)	-	+ 0.3%	+ 0.9%	+ 1.3%	+ 1.4%
Placebo group (28 subjects)	573.6 \pm 13.4	572.3 \pm 14.2	566.0 \pm 11.8	565.5 \pm 12.8	564.3 \pm 13.9
Erythema index difference [D0 - Dx]/D0], % (Placebo group)	-	+ 0.2%	+ 1.3%	+ 1.4%	+ 1.6%
Mean difference (test vs. placebo, μ g / cm ²)	-	+ 0.1%	-0.4%	-0.1%	-0.2%
Stat. results (test group, permutation test for paired data)	-	p = 0.107 ns unsignificant	p = 0.0004 *** extr. significant	p = 0.0003 *** extr. significant	p < 0.0001 *** extr. significant
Stat. results placebo group, permutation test for paired data)	-	p = 0.423 ns unsignificant	p < 0.0001 *** extr. significant	p = 0.0001 *** extr. significant	p = 0.0001 *** extr. significant
Stat. results test vs. placebo, permutation test for independent data)	p = 0.0501 ns unsignificant	p = 0.061 ns unsignificant	p = 0.005 ** very significant	p = 0.019 * significant	p = 0.016 * significant

Test Parameter No:3 (Continued) (on erythema index, forearm) RESULTS



**Forearm erythema indexes,
before and during once
daily supplementation**

**Graphical display of
Erythema index evolution
(test group – placebo group)**





Test Parameter No:3
(on erythema index, forearm)
CONCLUSION ON RESULTS

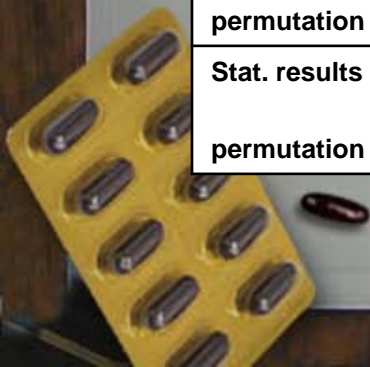
According to erythema index results, the test product was considered as non irritant to the skin during the study.



Test Parameter No: 4 (on skin microrelief, average roughness, forearm) **RESULTS**



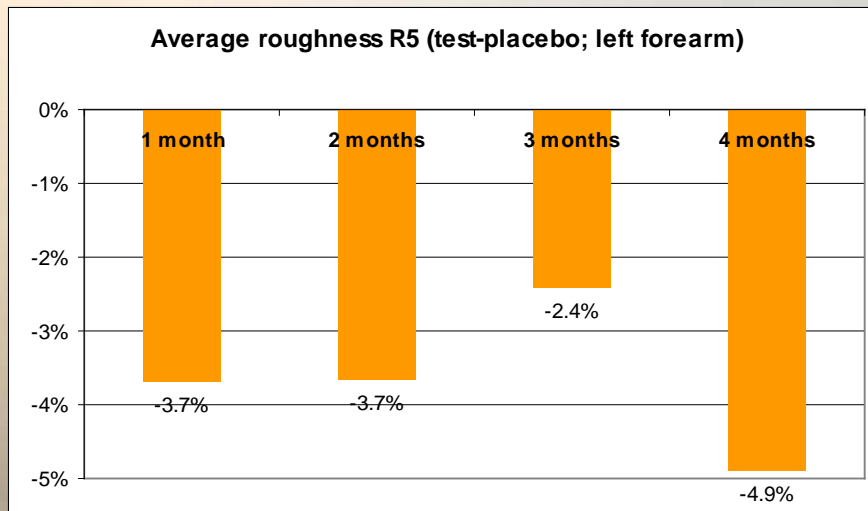
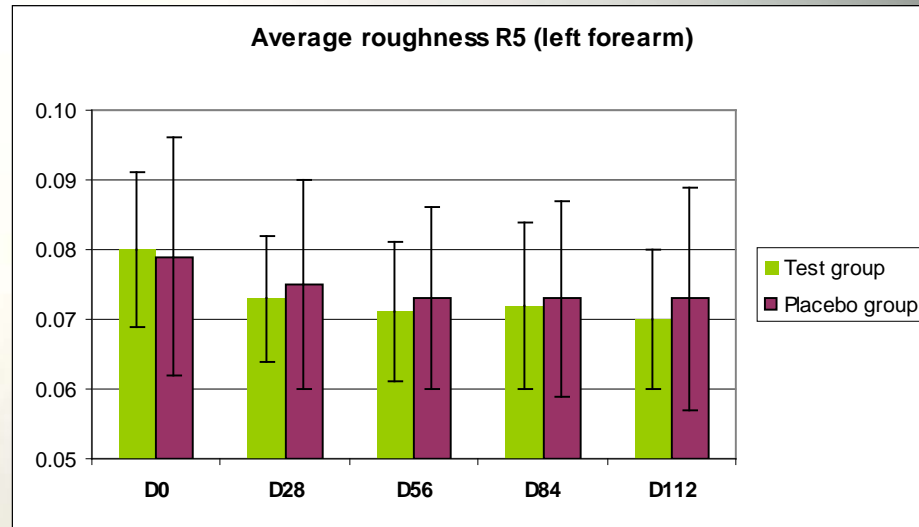
	Average roughness R5: Mean values (\pm SD; Visioscan units)				
	Before	1 month	2 months	3 months	4 months
	Day 0	Day 28	Day 56	Day 84	Day 112
Test group	0.080 \pm 0.011	0.073 \pm 0.009	0.071 \pm 0.010	0.072 \pm 0.012	0.070 \pm 0.010
Average roughness R5 Difference [D0 - Dx]/D0, % (Test group)	-	-8.8%	-11.3%	-10.0%	-12.5%
Placebo group	0.079 \pm 0.017	0.075 \pm 0.015	0.073 \pm 0.013	0.073 \pm 0.014	0.073 \pm 0.016
Average roughness R5 Difference [D0 - Dx]/D0, % (Placebo group)	-	-5.1%	-7.6%	-7.6%	-7.6%
Mean difference (test vs. placebo)	-	-3.7%	-3.7%	-2.4%	-4.9%
Stat. results (test group, permutation test for paired data)	-	p = 0.0002 ** extr. significant	p < 0.0001 *** extr. significant	p = 0.0004 ** extr. significant	p < 0.0001 *** extr. significant
Stat. results (placebo group, permutation test for paired data)	-	p = 0.028 * significant	p = 0.045 * significant	p = 0.008 ** very significant	p = 0.002 ** very significant





Test Parameter No: 4 (Continued) (on skin microrelief, average roughness, forearm) **RESULTS**

Forearm average roughness, before and during once daily supplementation



Graphical display of the evolution of average roughness (test group – placebo group)







Test Parameter No:4
(on skin microrelief, average roughness, forearm)

CONCLUSION ON RESULTS

The test product showed to
Induce a significant skin
roughness reduction during
the treatment period.

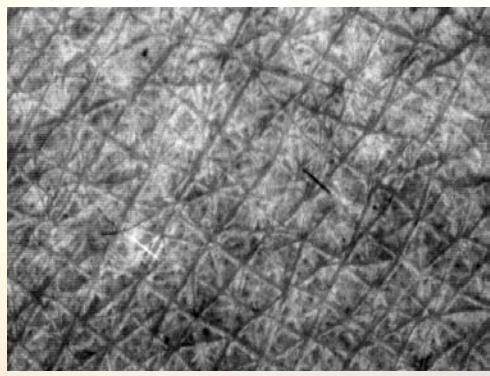




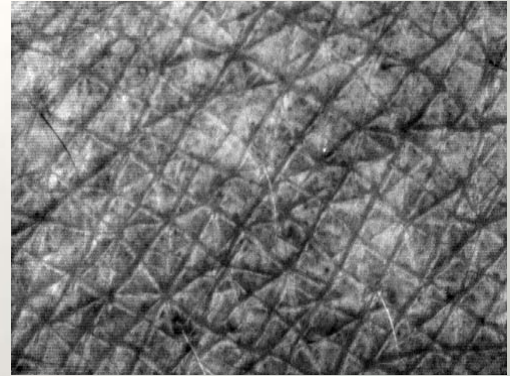
Test Parameter No: 4 (continued)
(on skin microrelief, average roughness, forearm etc)

CONCLUSION ON RESULTS

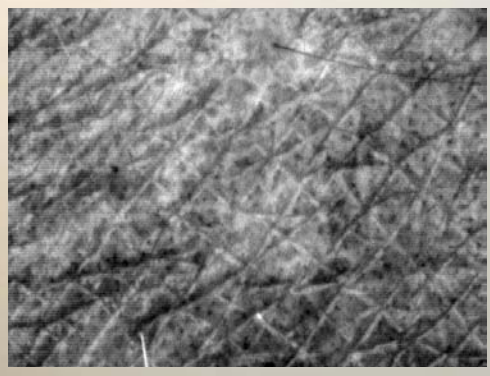
Selected example of skin surface smoothing
(vol. #12, age 46) :



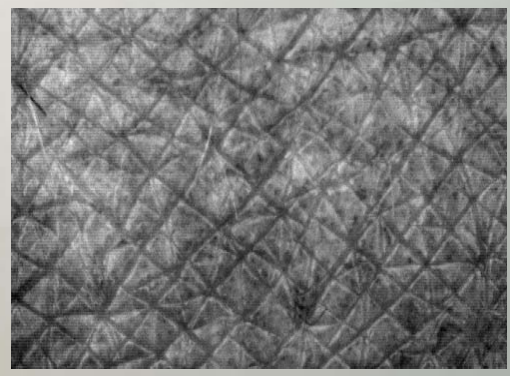
Before



2 months



1 month



3 months

A stepwise skin surface improvement can be followed up visually:

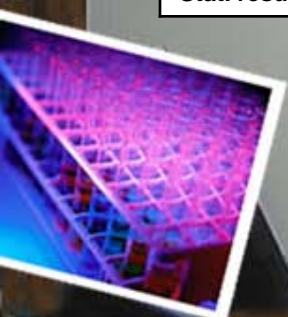
- smoother skin!**
- less dry skin!**
(less white areas!)



Test Parameter No: 5 (on epidermis + dermis density by ultrasonography, forearm) **RESULTS**



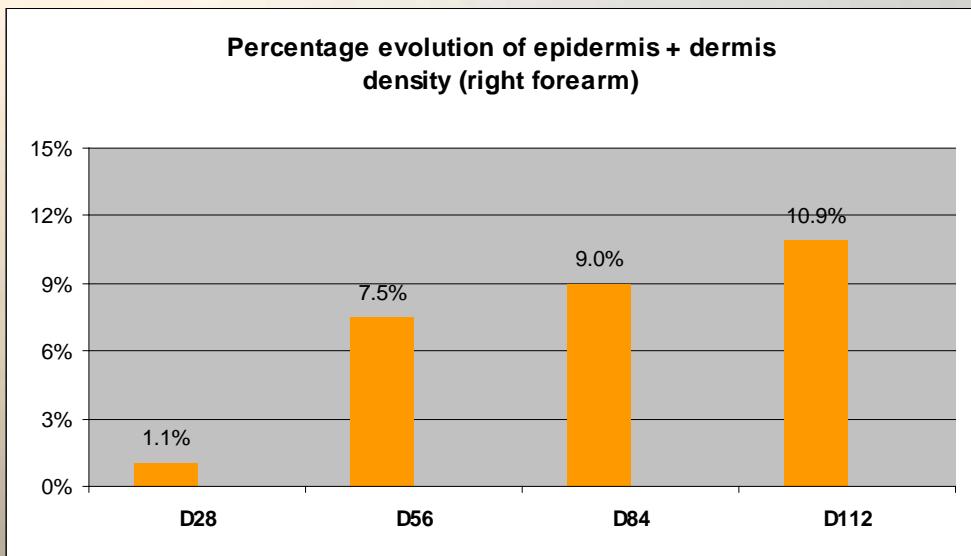
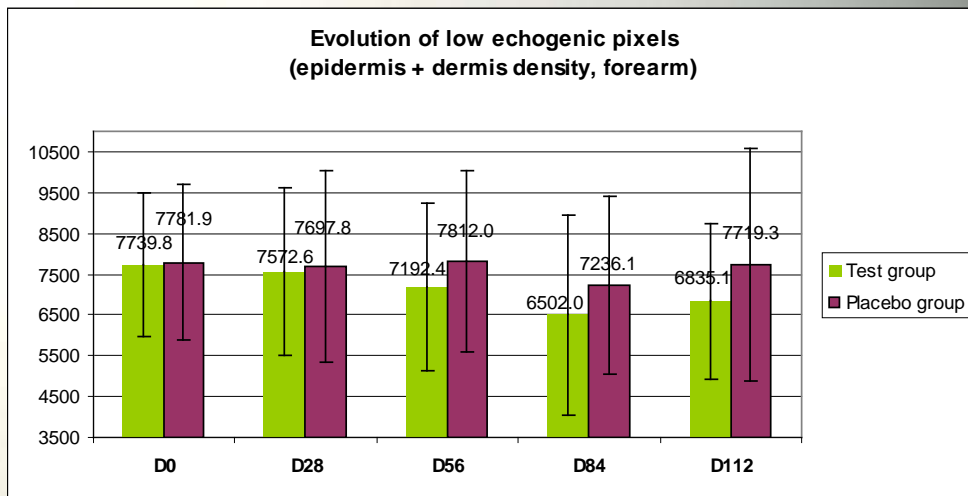
	Epidermis+dermis density on the right forearm: Mean values (\pm SD; LEPs Units)				
	Day 0	Day 28	Day 56	Day 84	Day 112
Test group	7740 \pm 1773	7573 \pm 2061	7192 \pm 2043	6502 \pm 2464	6835 \pm 1909
Density difference [D0 - Dx]/D0], % (Test group)	-	2.2%	7.1%	16.0%	11.7%
Placebo group	7782 \pm 1909	7698 \pm 2358	7812 \pm 2230	7236 \pm 2185	7719 \pm 2844
Density difference [D0 - Dx]/D0], % (Placebo gr.)	-	1.1%	-0.4%	7.0%	0.8%
Mean % change (Test - Placebo)	-	1.1%	7.5%	9.0%	10.9%
Stat. results (test group, permutation paired data)	-	p = 0.303 (ns)	p = 0.048 *	p = 0.005 **	p = 0.007 **
Stat. results (placebo gr., permutation paired data)	-	p = 0.428 (ns)	p = 0.476 (ns)	p = 0.073 (ns)	p = 0.324 (ns)





Test Parameter No.5 (continued) (on epidermis + dermis density by ultrasonography, forearm) **RESULTS**

**Low echogenic pixels
before and during once
daily supplementation
(forearm)**



**Graphical display of the
evolution of density (test
group – placebo group)
versus baseline (forearm)**

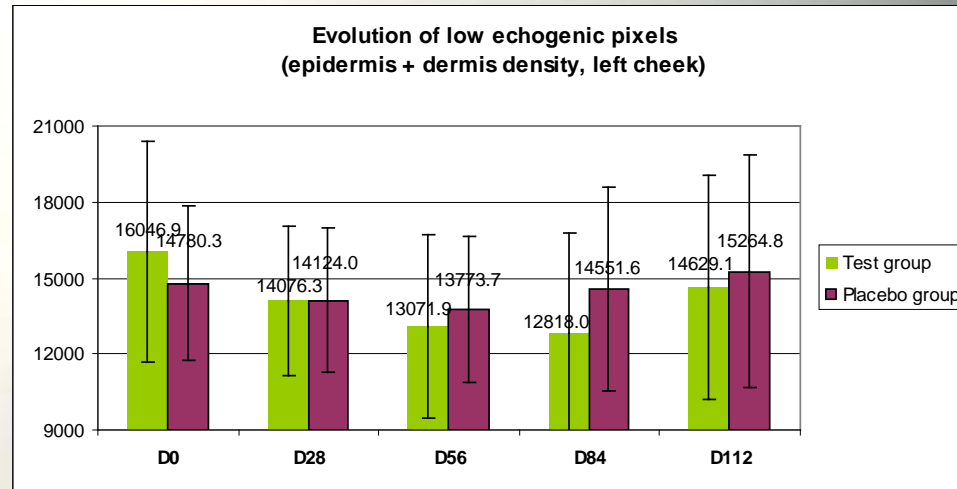


Test Parameter No: 5 (continued)
(on epidermis dermis density by ultrasonography, cheek)
RESULTS

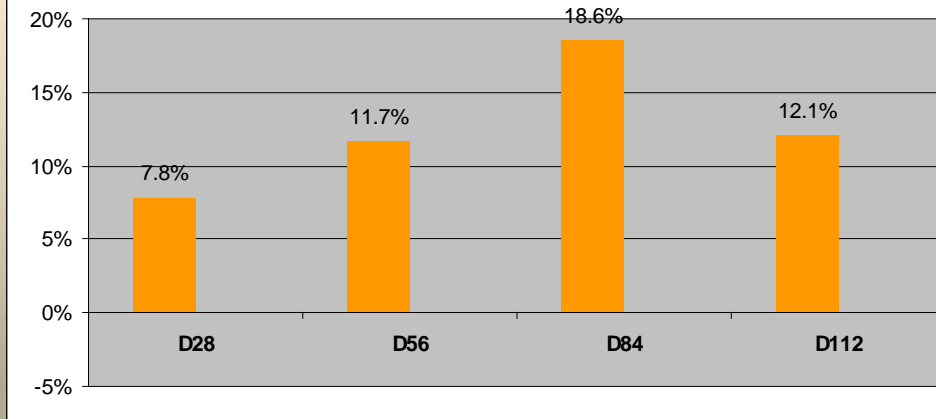
	Epidermis+dermis density on the left cheek: Mean values (± SD; LEPs Units)				
	Day 0	Day 28	Day 56	Day 84	Day 112
Test group	16047 ± 4370	14076 ± 2942	13072 ± 3612	12818 ± 3988	14629 ± 4398
Density difference [D0 - Dx]/D0], % (Test group)	-	12.3%	18.5%	20.1%	8.8%
Placebo group	14780 ± 3045	14124 ± 2833	13774 ± 2865	14552 ± 4006	15265 ± 4568
Density difference [D0 - Dx]/D0], % (Placebo gr.)	-	4.4%	6.8%	1.5%	-3.3%
Mean % change (Test - Placebo)	-	7.8%	11.7%	18.6%	12.1%
Stat. results (test group, permutation paired data)	-	p < 0.0001 ***	p < 0.0001 ***	p < 0.0001 ***	p = 0.022 *
Stat. results (placebo gr., permutation paired data)	-	p = 0.101 (ns)	p = 0.064 (ns)	p = 0.326 (ns)	p = 0.339 (ns)

Test Parameter No: 5 (continued) (on epidermis dermis density by ultrasonography, cheek) RESULTS

Low echogenic pixels before and during once daily supplementation (cheek)



Percentage evolution of epidermis + dermis density (left cheek)



Graphical display of the evolution of density (test group – placebo group) versus baseline (cheek)





Test Parameter No: 5

(on epidermis + dermis density by ultrasonography, forearm and cheek)

CONCLUSION ON RESULTS

- On the forearm dermis density increase difference test-placebo was +8%, after 2 months. Result was significant versus placebo.
- On the cheek dermis density difference test-placebo kept increasing between 1 and 3 months. Difference test-placebo was +17% after 3 months.





Test Parameter No: 5 (on epidermis + dermis density by ultrasonography, cheek, age subgroups, <41 years)

RESULTS

	Epidermis+dermis density: Mean values (± SD; LEPs Units; cheek; age < 41 years)				
	Day 0	Day 28	Day 56	Day 84	Day 112
Test group <41y	13788 ± 3174	13041 ± 2701	12747 ± 3172	11625 ± 4134	14131 ± 4555
Density difference [D0 - Dx]/D0], % (Test group <41y)	-	5.4%	7.5%	15.7%	-2.5%
Placebo group <41y	12977 ± 2825	12742 ± 2907	12818 ± 3072	13042 ± 4679	13133 ± 4803
Density difference [D0 - Dx]/D0], % Placebo gr. <41y)	-	1.8%	1.2%	-0.5%	-1.2%
Mean % change (test group - placebo group, <41y)	-	3.6%	6.3%	16.2%	-1.3%
Stat. results (test group <41y, permutation test for paired data)	-	p = 0.053 unsignificant	p = 0.030 * significant	p = 0.001 ** very significant	p = 0.463 unsignificant
Stat. results placebo gr. <41y, permutation test for paired data)	-	p = 0.197 unsignificant	p = 0.327 unsignificant	p = 0.358 unsignificant	p = 0.281 unsignificant



Test Parameter No: 5 (continued)
(on epidermis + dermis density by ultrasonography,
cheek, age subgroups, >41 years)



RESULTS

	Epidermis+dermis density: Mean values (\pm SD; LEPs Units; cheek; age \geq 41 years)				
	Day 0	Day 28	Day 56	Day 84	Day 112
Test group \geq 41y	17883 \pm 4425	15043 \pm 2910	13356 \pm 4039	13713 \pm 3756	15065 \pm 4356
Density difference [D0 - Dx]/D0], % (Test group \geq 41y)	-	+ 15.9%	+ 25.3%	+ 23.3%	+ 15.8%
Placebo group \geq 41y	16103 \pm 2535	15321 \pm 2219	14602 \pm 2483	15860 \pm 2870	17069 \pm 3618
Density difference (D0 - Dx)/D0), % Placebo gr. \geq 41y	-	+ 4.9%	+ 9.3%	+ 1.5%	- 6.0%
Mean % change (test group-placebo group, \geq 41y)		+ 11.0%	+ 16.0%	+ 21.8%	+ 21.8%
Stat. results, test group \geq 41y, permutation test for paired data	-	p = 0.001 ** very significant	p = 0.0001 *** extr. significant	p < 0.0001 *** extr. significant	p = 0.004 ** very significant
Stat. results, placebo gr. \geq 41y, permutation test for paired data	-	p = 0.119 unsignificant	p = 0.018 * significant	p = 0.288 unsignificant	p = 0.424 unsignificant

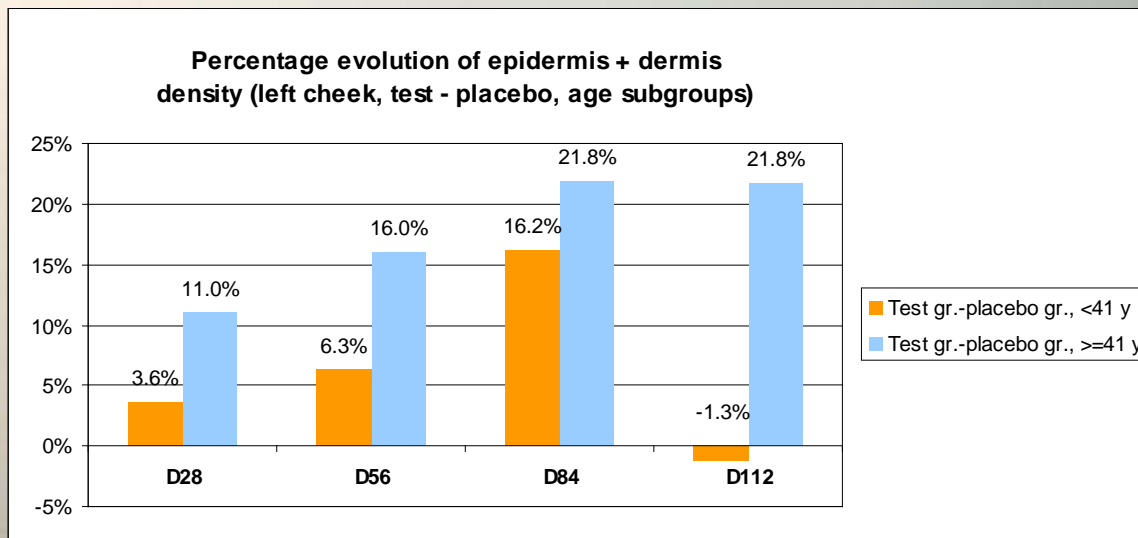
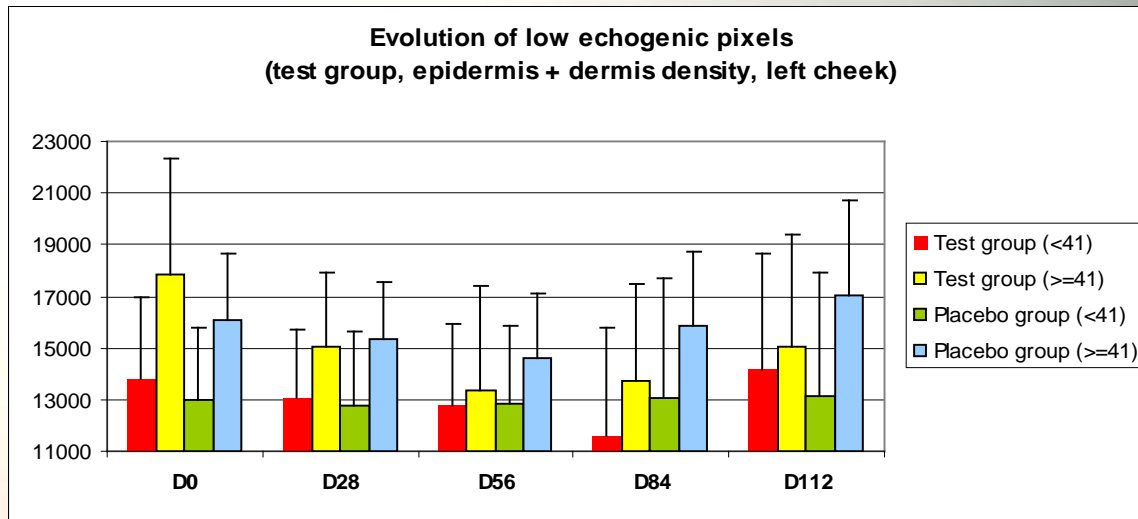




Test Parameter No: 5 (continued)

(on epidermis + dermis density by ultrasonography, cheek, age subgroups)


RESULTS





Test Parameter No: 5 (continued)
(on epidermis + dermis density by ultrasonography, cheek, age subgroups)

RESULTS

- **Older subjects (≥ 41 y, mean age 50) showed an average lower skin density at the beginning, than younger subjects (< 41 y, mean age 30).**
 - **The percentage of density increase was more important in the older age group (yellow bars) than in the younger one.**
 - **The average starting skin density value of the younger group was reached by the older group after 2 months of supplementation.**
- 

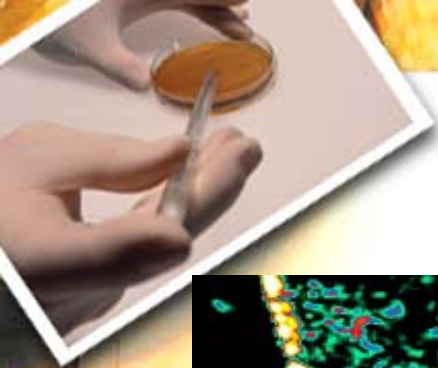


Test Parameter No: 5 (continued)
(on epidermis + dermis density by ultrasonography, cheek, age subgroups)

RESULTS

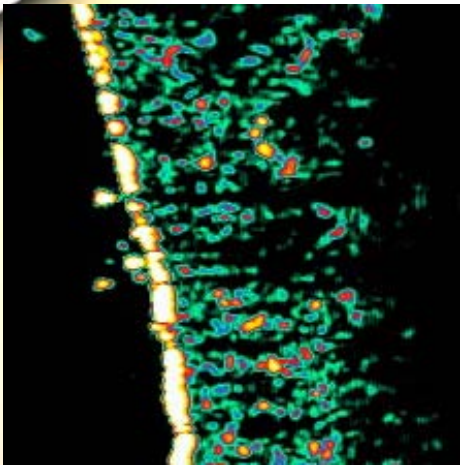
- **Results show that a dramatic increase of skin density was achieved in the older group during the months #1 (+11%), #2 (+16%), and #3 (+22%). In the younger group an important increase took place especially during month #3 (+16%).**
- **The results of the test groups were globally statistically significant, whereas placebo results were in most cases insignificant.**



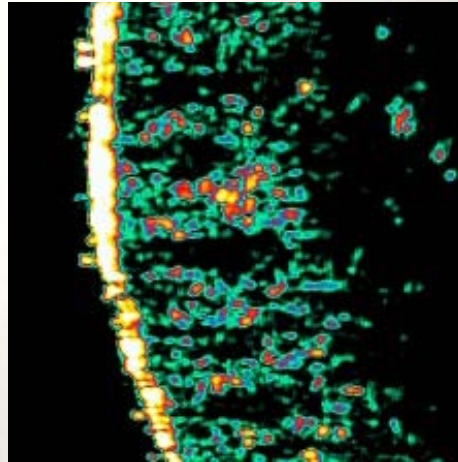


Test Parameter No: 5 (continued)
(on epidermis + dermis density by ultrasonography, cheek)

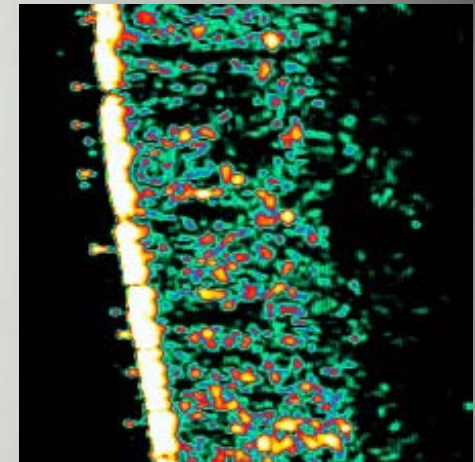
RESULTS



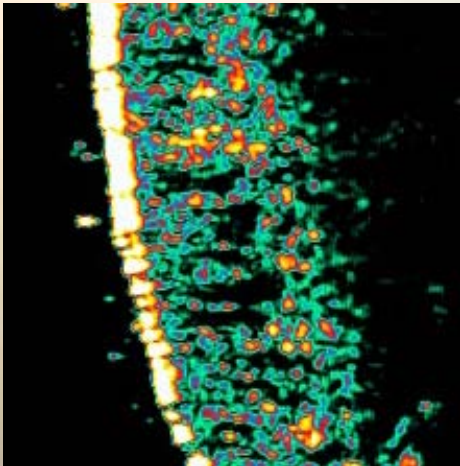
Day 0



Day 28 (+8% density)



Day 56 (+26% density)



Day 84 (+40% density)

Example of dermis density increase on the right, treated forearm (volunteer #57, Vol, age 31)

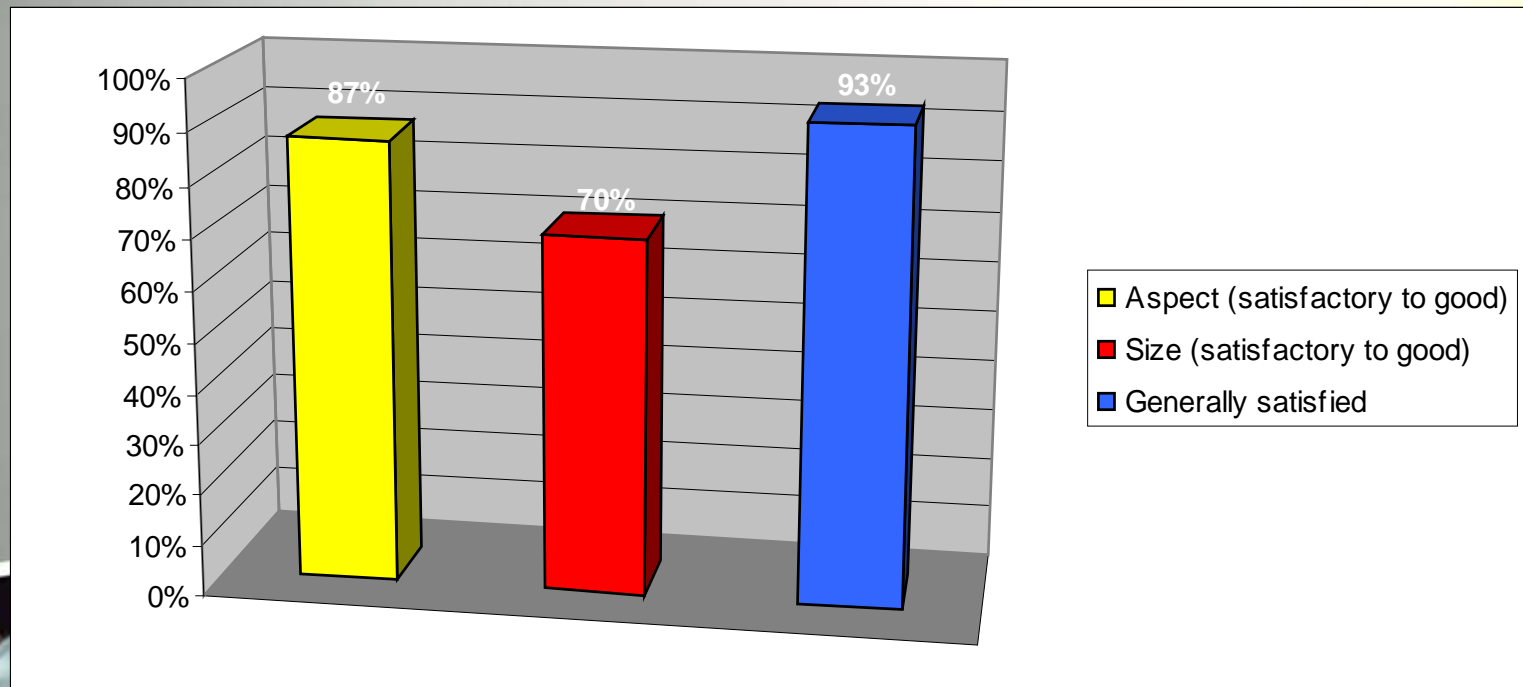


Test Parameter No: 5 (on sensory evaluation) RESULTS

87% of the participants appreciated the aspect of the test product.

70% of the participants appreciated the size of the test product.

Over 90% of them are generally satisfied by the product and the treatment.



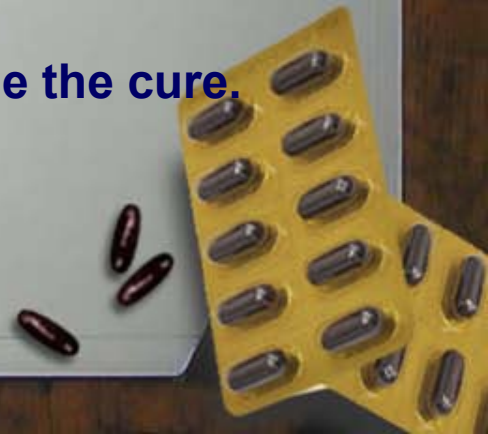
Selected sensory evaluation results



Test Parameter No: 5 (*continued*) (on sensory evaluation) **RESULTS**

A few sentences expressed by the participants (test group):

- "The product made my facial skin less dry. It regulated the T-zone (*forehead, nose, chin*), which was sometimes either too dry or too oily. I didn't notice any unwanted effect." (*Mrs. Pap Ma, age 24*)
- "My skin (body and face) seems to be less dry, smoother, more replenished. I hope that these positive effects will last for a while !" (*Mrs. Rer Is, age 55*)
- "I appreciated the fact that my skin became less oily and smoother." (*Mrs. Lou De, age 29*)
- "I totally appreciate this product and I wish to continue the cure. How to do it ?" (*Mrs. Mer Fr, age 59*)





CONCLUSION ON RESULTS

In conclusion:

- A significant reduction of skin roughness took place during the treatment, and was observed versus placebo.
- An interesting seboregulating process was observed for low sebum-containing skins: mean values were increased to normal levels at 3 months. The test product significantly normalises too low sebum values on the forehead, versus placebo.
- The study results showed an interesting difference in dermis density between the test group and the placebo group. The overall difference was +17% after 3 months of treatment.
- Interestingly, after 3 months older subjects above 41 years showed a more important average increase in dermis density (+22%) than younger subjects below 41 (+16%).
- The test product is safe, non irritating and non allergenic. No TEWL increase and no increase in erythemas were observed during the clinical study.



Thank You

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