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Full Length Research Paper

Efficacy of the MFIII placenta extracts softgels supplementation: a randomized double-blind placebo-controlled study

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ABSTRACT

Placenta consumption (placentophagy) is a widely encountered phenomenon in animal kingdom and also is accepted in certain communities as one of the means to increase mother's energy, stimulate milk production, balance the hormonal level, reduce postpartum depression and insomnia, and achieve anti-aging effect. Cosmetic industry has successfully developed various products based on animal placenta. In this article we study efficacy of MFIII Placenta Extract supplementation in cosmetology. The following parameters are studied: skin surface roughness, skin elasticity and firming effect, skin radiance, regenerative improvement of epidermis+dermis density, skin hydration-moisturization, skin surface sebum level, melanin index, erythema index, transepidermal water loss.

Keywords: placenta extracts, placenta supplements, rejuvenation, revitalization, cosmetology supplements.

INTRODUCTION

In all times and cultures people tried to find effective ways of rejuvenation and revitalization by creating products based on the organic source able to strengthen the inner power and resources of human body, improve stamina and fitness, and invigorate the skin. In animal kingdom placenta consumption is a normal widely encountered phenomenon and even human placentophagy is accepted in certain communities as one of the means to increase mother's energy, stimulate milk production, balance the hormonal level, reduce postpartum depression and insomnia, achieve anti-aging effect, etc (Coyle et al., 2015).

Cosmetic industry has successfully developed various products based on animal placenta. However most of it vary in quality and are lacking of scientific substantiation.

It is the responsibility of the cosmetic industry to provide the consumer with safe products they can trust in, which meet their requirements. Regulatory authorities request a number of conditions to be met, should a cosmetic product be put on the market. Particularly, product claims must be vindicated, as far as this is compatible with the constitution and quality of the product and with the claim praised. Proof of the claims is considered to be an additional safety factor for consumers and regulatory authorities. Furthermore, tests in human beings are increasingly encouraged for cosmetic products and their ingredients, and especially for finished products, instead of animal tests (Phillip and

Nigel, 2007; FDA, 1999).

In view of this, our special attention was attracted to a supplement by MFIII™ brand "PE SOFTGELS", containing ovine placenta extract and vitamin C. Currently there is an ongoing study on the efficacy of the MFIII™ "PE SOFTGELS" successor - MFIII™ "PE SOFTGELS advanced formula", a next generation of the supplement which, in spite of sheep placenta nutrients, comprising of over 200 various growth factor and biologically active ingredients, dermal bio-activators, vitamins and minerals, also contains highly polymerized marine DNA, M-polypeptides, Collagen-Elastin HME, and five superior botanical ingredients, including glutaredoxin, grape seed extracts, alpha lipoic acid, Co-enzyme Q10 and resveratrol.

Therefore, the objectives of this study were to verify the specific cosmetic efficacy of the MFIII™ "PE SOFTGELS", i.e. skin surface (roughness), skin elasticity and firming effect, skin radiance, regenerative improvement of epidermis+dermis density, skin hydration (moisturization), skin surface sebum level, melanin index, erythema index, transepidermal water loss. Secondary criteria was the feedback from the users and evaluation of product's tolerance.

Healthy female volunteers were recruited, they were informed about the objectives of the study and gave their informed consent.

Inclusion criteria

- Age 20 to 65 years old;
- Caucasian, gender female;
- If not Caucasian: subjects with South-East Asian skin characteristics;
- Healthy with no significant concurrent illness;
- Presenting any of the following skin types: normal, oily, mixed, dry, sensitive, or in any combinations;
- Signed informed consent form after receiving the volunteer information and after the nature of the study has been fully explained.

Exclusion criteria

- Non-caucasian with exception of South-East Asian origin;
- Participation in any other clinical study/use of experimental drug(s) involving the test area within the previous 8 weeks;
- Use of any topical (drug containing) or cosmetic product on the test areas within 5 days before beginning the study;
- Use of any topical or systemic medication likely to interfere with the study (such as corticosteroids or immunosuppressive drugs);
- Any skin disease, known allergy or intolerance to any component of the test products;
- History or evidence of alcohol or drug abuse;
- Severe systemic or dermatological disease;
- Impaired cooperation possibilities or unwillingness to satisfactorily participate in the study;
- Other considered relevant by the investigator (e.g. too many hairs or colour disturbances of the skin impairing visual scoring).

Design of the study

The study was a double-blind placebo-controlled randomized trial with healthy female volunteers. 64 women (20-60 years old, mean age 40-41 y.o.) were selected and recruited for the study. They were randomly divided in two groups of 32 persons of equivalent age distribution, forming test group and placebo group.

For each volunteer the duration of the study was 4 months (16 weeks). The supplementation period was 3 months (12 weeks). The study was terminated after the bioengineering measurements at the end of the fourth month.

The test product, as well as the placebo, were taken once daily in the morning with some cold liquid (water, fruit juice, etc.). The use of standard skin care products was allowed during the study (non-specific moisturisers, cleansers, day creams and night creams). No specific products such as anti-wrinkle treatments or strong moisturising products were allowed during the study.

Methods used

The following equipments and methods were used for bioengineering measurements:

- Skin hydration (moisturization): Corneometer® CM825PC; Courage and Khazaka, Cologne, Germany. The Corneometer® evaluates the capacitance of the upper layers of the skin. The value of this parameter is dependent on the hydration of the measured layers.
- Skin barrier function (transepidermal water loss; TEWL): DermaLab® TEWL; Cortex Technology, Hadsund, Denmark. The TEWL represents the passive diffusion of water vapour escaping the body through the skin into the surroundings. Generally speaking, if the skin barrier is intact, then TEWL is low. The higher the TEWL, the more damaged the skin barrier. However, the TEWL also depends on the water content of the upper layers of the skin. An increase in this water content, e.g. after application of a strong moisturizer, will lead to an increase of TEWL despite an intact skin barrier.
- Skin elasticity/firmness: Cutometer® SEM575; Courage

and Khazaka, Cologne, Germany. The Cutometer® evaluates the mechanical properties of the skin by applying stress to the skin (vacuum). A negative pressure is created and the skin is drawn into the aperture of the probe to then relax upon establishment of normal pressure. Among the different parameters calculated from the measured deformation curves, the following are of importance: R2 (also called “biological elasticity”), F2 (area above the upper envelope curve; “dynamic fatigue”) and F3 (area within the envelope curves; “dynamic elongation”).

- Skin firmness: DermaScan® C, 20 MHz, medium focus, B-mode; Cortex Technology, Hadsund, Denmark. The instrument consists of three main parts: the C probe, the elaboration and visualization system and the data storage system. Ultrasound images were recorded and further processed by image analysis software (GIPS, Cortex Technology). The velocity of ultrasound in the skin was set at 1580 m/s and a depth of signal penetration of about 7 mm enabled visualization of the epidermis, dermis and subcutaneous fatty tissue. The system evaluates dermal density by measuring echogenicity of single image elements (pixels) on a numerical scale extending from 0 to 255. The low echogenic area extends from 0 to 30. The number of low echogenic pixels (LEPs) was determined in the epidermal and dermal region between the entrance echo and the interface with the subcutaneous fat layer. It has been postulated that the number of LEPs is proportional to the water content, to the amount of collagen and to its configuration.

- Skin surface properties/Fine lines and wrinkles: SELS 2000/Visioscan® VC 98; Courage and Khazaka, Cologne, Germany. The SELS measurements are conducted with a Magnifying camera operating under UV-light. The geometry of the lighting system, which is integrated in the camera, ensures a homogenous illumination of the skin surface. The wavelength of the light (long wavelength UV-A light) has been chosen to enhance in particular the fine structures of the skin. The parameters are calculated by image analysis of grey levels and concern only the fine and/or microstructures of the skin surface. They are not applicable to more coarse structures such as deeper wrinkles due to consistent changes of dermal structures.

- Skin surface sebum level: Sebumeter® SM810; Courage and Khazaka, Cologne, Germany. The Sebumeter® measurements are based on grease-spot photometry. A special tape becomes transparent in contact with the sebum on the skin surface. The transparency of the tape is measured by photocell behind a light source sending light through the tape. The light trans-mission is correlated to the sebum level of the measured surface. The device is calibrated for µg sebum /cm2 skin surface.

- Measurements of the melanin and erythema index: Mexameter® MX 16; Courage and Khazaka, Cologne, Germany. Hemoglobin is mainly responsible for the pink-red component of skin colour. Melanin is the mainly responsible for the tan. The measurement is based on the absorption principle. The Mexameter MX 16 emits light of three defined wavelengths, at 568, 660 and 880 nm, respectively. A receiver measures the light reflected by the skin. As the quantity of emitted light is defined, the corresponding quantity of light absorbed can be calculated. The higher the values, the more erythema, respectively melanin is detected The measurements were conducted under air-conditioned conditions (temperature 22.5 ± 1.5°C; relative humidity 50 ± 10%) after an acclimatization period of at least 20 min.

Anatomical locations of the bioengineering measurements

Face: Measurements were conducted on the cheeks (area defined at the crossing of a vertical line from the eye corner with a horizontal line from the mouth corner) on both sides of the face.
Forehead: Measurements were conducted on both sides of the forehead.
Forearms: Measurements were conducted in the middle of each forearm between wrist and elbow.

Subjective assessments: Questionnaire

The secondary criteria (opinion of the users during the duration of use and evaluation of the tolerance of the test product and placebo) were performed by means of a questionnaire adapted to the particular claims of food supplements. Informations were gathered about products’ efficacy on claims such as skin firmness, skin radiance, moisturization, skin surface improvement.

Possible skin reactions to the products were scored on a scale that describes the amount of erythema, scaling and fissures. Any other features indicative of irritation were also registered. table 1.

If a grade of 2 or more is attained on the erythema scale or a cumulative score of 5 or more by adding all three scales, the corresponding test product was not be re-applied.

Any other adverse event and/or subjective observation such as e.g. burning, itching or stinging was recorded at the assessment times and noted in the case record forms.

The results of the bioengineering measurements and of the subjective and visual assessments were collected directly in the forms. The collected data was summarized by usual methods (calculation of means, medians, and standard deviations) and descriptively evaluated. A

Table 1. Visual evaluation of the tolerance

Erythema	Scaling	Fissures
0 No evidence of irritation	0 No evidence of irritation	0 No evidence of irritation
0.5 Minimal spotty erythema, barely perceptible	0.5 Minimal dry surface, barely perceptible	0.5 Slight, very superficial epidermal separation, barely perceptible
1 Minimal homogeneous erythema	1 Minimal dry surface	1 Slight, superficial epidermal separation
2 Slight but definite erythema, readily visible	2 Slight but definite dryness, glazing	2 Definite epidermal separation
3 Moderate erythema	3 Fine scaling	3 Individual superficial fissures
4 Strong erythema	4 Moderate scaling	4 Individual wide or several fissures
5 Strong erythema, oedema, and papules	5 Strong scaling, erosion	5 Deep fissures, bleeding, exudation

Table 2. Skin hydration: Mean values (± SD; Corneometer units)

	Day 0	Day 28	Day 56	Day 84	Day 112
Test group	34.2 ± 9.3	34.2±8.3	36.6±8.3	35.5±9.0	36.5±8.5
Placebo group	32.1±8.1	36.0±8.0	32.9±6.1	35.3 ±8.1	37.3±7.2
Mean difference	2.2	-1.8	3.7	0.2	-0.9
(test vs. placebo, Corneometer units)	P = 0.178	p = 0.202	p = 0.030	p = 0.475	p = 0.348
Ratio to D0 (treated) (%)	6.3%	-5.4%	10.2%	0.5%	-2.3%

nonparametric statistical calculation was used to report on statistical significance of the different pairs before / after treatment (permutation test for independent data).

OBTAINED RESULTS OF THE STUDY AND DISCUSSIONS

Skin hydration was measured on the forearm with the Corneometer CM825 from Courage and Khazaka. The results of the measurements are summarized in Table 2.

From the data at D0 in Table 2 it may be first concluded that the volunteers had dry skin on forearms (mean values < 35 Corneometer® units). Looking at the test group values, we can see that there is a continuous increase of moisturization until D56 (3 months). Then, the moisture levels keep stable until the 4-month measurement session. In the placebo group, values are slightly increasing too. Most significant difference between both groups was shown at 2 months (D56), where the moisture level in test group exceed the placebo value by 10% (p value = 0.030 *).

The dermal density was evaluated on the left cheek and the right forearm with the DermaScan® C from Cortex Technology. The results of the evaluation of low echogenicity pixels (LEPs) on the forearm are summarized in Figure 1 below and on the left cheek in Figure 2 below.

From these data it may be concluded that the supplementation with MFIII™ PE Softgels gives steady decrease of LEPs, corresponding to an increase of epidermis+dermis density, as compared to placebo results, where LEPs did not decrease at all or decreased in a marginal proportion. This epidermis+dermis density increase may represent a decrease in tissue water and a possible increase in collagen content and stiffness. A younger skin also displays less LEPs than older skin.

The epidermis+dermis density increase on the forearms after two months (+7.5%) was about seven times the value at 1 month. This shows that supplementation with the test product has a beneficial effect on the deeper skin layers of the forearms, starting around 5-6 weeks after supplementation began. Moreover, statistical significance was obtained for the two-month results (significant), and the three- and four-month results, as well (very significant in both cases). In the placebo group, the whole series of results was insignificant.

On the cheeks epidermis+dermis density kept increasing between one and 3 months (difference MFIII™ PE Softgels vs. placebo = +17% at D84). When the supplementation process was stopped, epidermis+dermis density was slightly reduced to reach the value corresponding to 2-months of supplementation.

Efficacy claims was successfully supported in a visual way. An additional interesting approach was to separate both test and placebo groups into subgroups, in order to assess about possible differences in the dermal density on the face.

Hence, older subjects are usually lacking dermal density due to reduction of the extracellular matrix - elastin and collagen fibers in the dermis. This situation is mainly due to photoageing processes (solar elastosis),

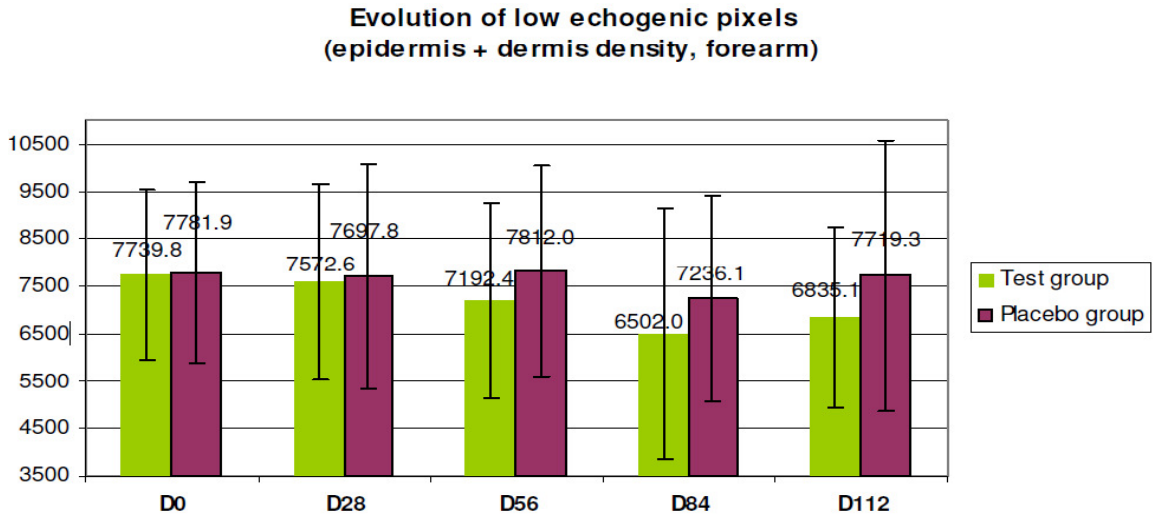

Figure 1. Low echogenic pixels (LEPs) before (D0) and during once daily supplementation with the MFIII^{TM} PE Softgels / the placebo (Dermascan pixel units; forearm; Means ± SD)

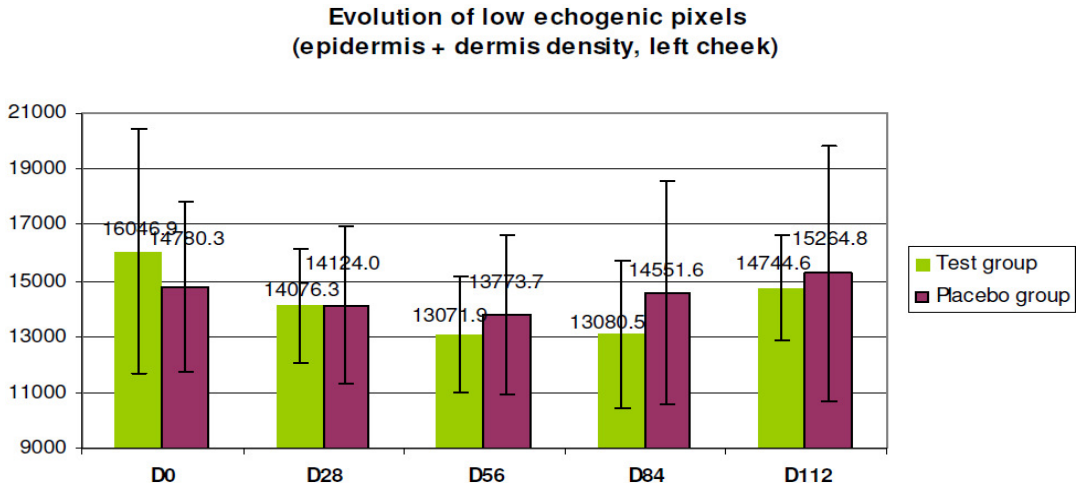

Figure 2. Low echogenic pixels (LEPs) before (D0) and during once daily supplementation with the MFIII^{TM} PE Softgels / the placebo (Dermascan pixel units; cheek; Means ± SD)

and to some extent the density can be improved as a regenerative and reversible process.

The test group and placebo group were both separated into two subgroups:

- volunteers younger than 41 years (subgroup I; 14 subjects in the test group, mean age 31 y.o. ± 6.5 y; 13 subjects in the placebo group, mean age 30 y.o. ± 6 y).
- volunteers that are 41 years old or more (subgroup II; 16 subjects in the test group, mean age 50.5 y.o. ± 6 y; 15 subjects in the placebo group, mean age 49 y.o. ± 6 y).

A comparative evaluation of the epidermis+dermis density results on the cheeks was made within the subgroups, by comparing them as test subgroup versus placebo subgroup. Results are given in Figure 3.

Out of these results, obviously older subjects show lower density in the skin at the beginning (Fig. 3). Remarkably, during the treatment, the percentage of density increase was stronger in the older subjects (yellow bars) than in the younger ones (red bars). Placebo subjects were only marginally decreased during the same period (blue and green bars). The results of test group were statistically significant all through the measurement sessions, excepted in the younger group at the beginning (D28 vs. D0) and at the end (D112 vs. D0).

The placebo subgroups showed in almost all cases

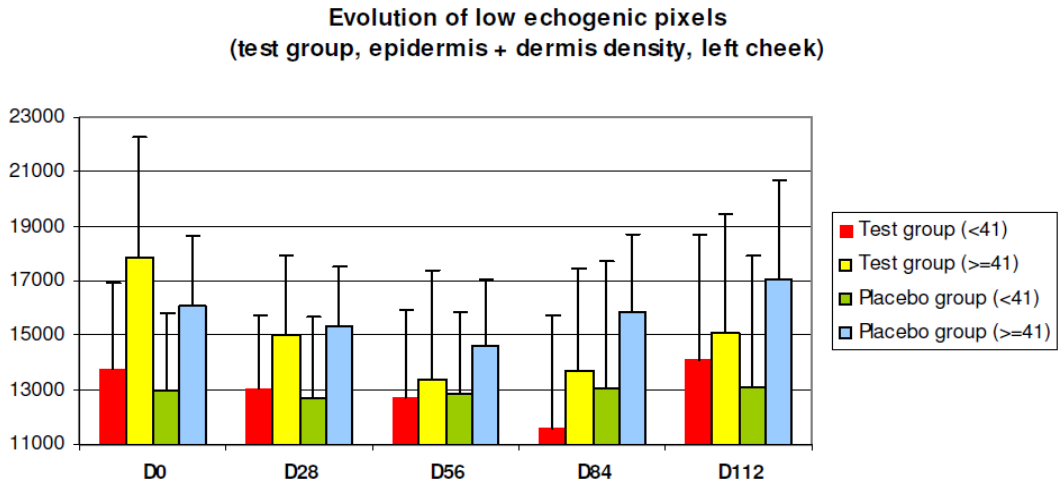

Figure 3. Comparative evaluation of low echogenic pixels (LEPs) before (D0) and during once daily supplementation with the MFIII^{TM} PE Softgels / the placebo [test group and placebo group; subgroups I (<41y.o.) and II (>=41y.o.), Dermascan pixel units; cheek; Means ± SD]

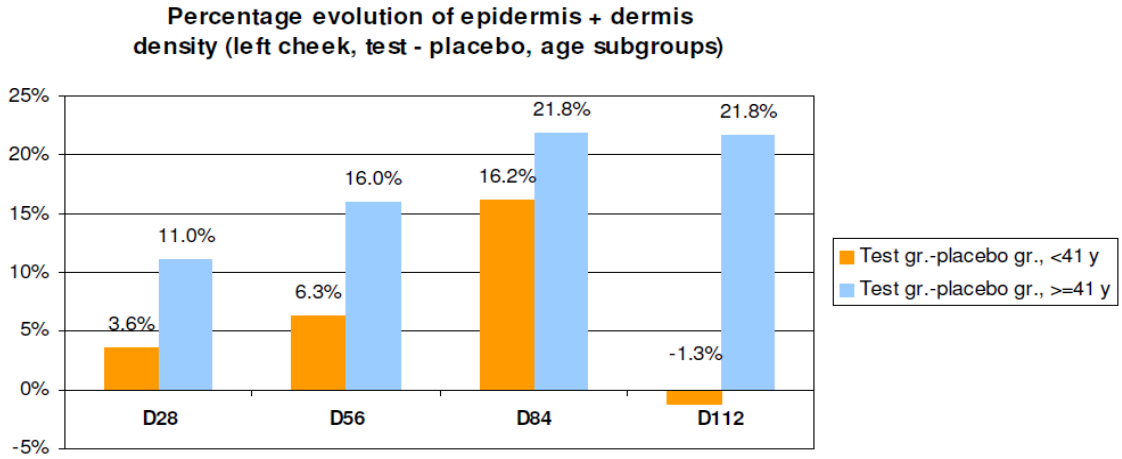

Figure 4. Comparative % changes in the LEPs of the skin ultrasound imaging during once daily supplementation with the MFIII^{TM} PE Softgels / the placebo [test group - placebo group; subgroups I (<41 y.o.) and II (>=41 y.o.), cheek; Means ± SD]

insignificant results.

The average epidermis+dermis density of younger test subgroup was reached by the older test subgroup after 2 months of supplementation. This result shows that supplementation of older subjects (mean age 50) brought more intense results than supplementation of younger subjects (mean age 30).

Moreover, the synoptic figure 4 shows that the relative differences test – placebo are stronger within the older subjects than within the younger ones. Concerning epidermis+dermis density, a steady increase was noted towards the end of the study. This increase was not measured in the placebo group. This effect may represent a decrease in tissue water and a possible increase in collagen content and stiffness. It is known that younger skin also displays a decreased dermal density as compared to older skin. This shows that treatment with the test product has a beneficial effect on the deeper skin layers starting at least 4 weeks after treatment begin. The most impressive epidermis+density changes were noted in older subjects (mean age 49), especially on the face. The 4-month measurement session (= 1 month after supplementation was stopped) showed in the test group a residual effect: the epidermis+dermis density was still as high as after 1 month of supplementation.

The skin surface sebum levels were evaluated on the right and left forehead sides with the Sebumeter SM 810 from Courage and Khazaka. Among both the 30

Table 3. Biggest roughness R2: Mean values (± SD; Visioscan units)

	Before	1 month	2 month	3 month	4 month
	D0	D28	D56	D84	D112
Test group	0.444 ± 0.060	0.401 ± 0.053	0.397 ± 0.059	0.398 ± 0.068	0.382 ± 0.055
Biggest roughness R2 difference [D0-Dx)/D0], % (Test group)	-	-9.7%	-10.6%	-10.4%	-14.0%
Placebo group	0.457 ± 0.082	0.423 ± 37.7	0.420 ± 55.4	0.396 ± 47.2	o.401 ± 71.0
Biggest roughness R2 difference [D0-Dx)/D0], % (Placebo group)	-	-7.4%	-8.1%	-13.3%	-12.3%
Mean difference (test vs. placebo)	-	-2.2%	-2.5%	3.0%	-1.7%
Stat. result (test group, permutation test for paired data)	-	P <0.0001*** extr. significant	P <0.0001*** extr. significant	P =0.0003*** extr. significant	P <0.0001*** extr. significant
Stat. result (test group, permutation test for paired data)	-	P <0.003** very significant	P =0.025* significant	P <0.0001*** extr. significant	P <0.0001*** extr. significant

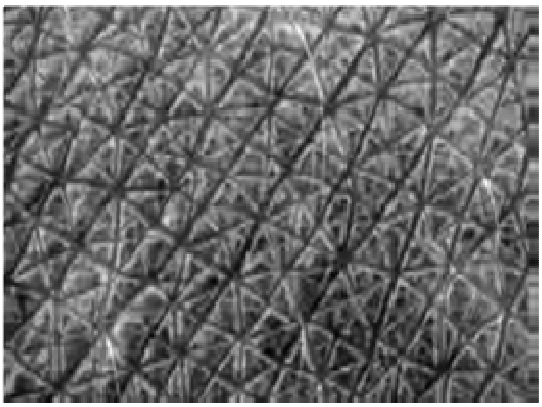

Figure 6. Skin surface evaluation by Visioscan VC98 D0.

volunteers of test group and the 28 volunteers of placebo group, 3 categories of persons were outlined, according to their sebum levels (SL) at the beginning of the study: (a) Volunteers with SL ≥ 150 µg sebum/cm^2 (oily skin, higher sebum level, 5 subjects in test group and 9 subjects in placebo group); (b) Volunteers with SL range 100 - 150 µg sebum/cm^2 (normal sebum level, 8 subjects in test group and 4 subjects in placebo group); (c) Volunteers with SL < 100 µg sebum/cm^2 (generally dry skin low sebum level, 17 subjects in test group and 15 subjects in placebo group).

The most significant decrease of sebum casual levels was measured on the forehead of the study participants in oily subgroup. A seboregulation process shows that after 3 months of supplementation mean values of sebum level normalized. The mean differences 'test – placebo' are positive for the three first months, which shows that within the oily subgroup the treated people show a stronger sebum decrease (up to 11%) than those who took placebo.

The skin surface properties were evaluated on the left forearm with the Visioscan® VC98 from Courage and Khazaka. The following parameters were calculated: R2, which is the biggest roughness of all measured segments, and R5, which is the average roughness.

The dynamics represented in Table 3 reflect the efficacy of MFIII^{TM} PE Softgels supplementation in reduction of skin roughness. All the results are statistically significant. Corresponding to the measured reduction in the biggest roughness R2, the average roughness was diminished too by the supplementation with MFIII^{TM} PE Softgels. The measured R5-changes were more important than those measured on R2. This discrepancy is likely to be due to the moisturizing effect of the test product, which was increasingly apparent from week 4 onwards. Indeed, moisturizing of the upper layers

Figure 7. Skin surface evaluation by Visioscan VC98 D84.

Figure 8. Skin surface evaluation by Visioscan VC98 D112.

of the skin leads to a swelling of the corneocytes and therefore to a decrease of the biggest roughness. Taken together, these figures allow concluding that treatment twice daily with MFIII^{TM} PE Softgels reduced skin roughness. As this roughness was measured with the Visioscantechnique, this result is to be interpreted as the decrease and/or disappearance of fine lines and fine wrinkles. Interestingly, this effect was rapid, being seen already after 4 weeks of treatment, and increased slowly but steadily over the 8 weeks of treatment duration (Figure 6-8).

The melanin index was evaluated on the right forearm with the Mexameter® MX16 from Courage and Khazaka. The results of measurements are summarized in Table 4 and Figure 9 below.

Differences observed between the test group and the placebo group were at 1 month, 2 months and 4 months. Melanin reductions was more prominent in the test group, supplemented with MFIII^{TM} PE Softgels than within the placebo group. Statistical significance, as the nonparametric permutation test for two independent variables, was able to support this evidence.

The erythema index was evaluated on the right forearm with the Mexameter® MX16 from Courage and Khazaka. The results of measurements are summarized in Table 5 below.

Most differences were observed between the test group and the placebo group at 2, 3 and 4 months. Statistically significant erythema reductions was noted within the test group than within the placebo group.

The results of the questionnaire and the fact that participants of the sudy did not use any AHAs-containing products prove that the measured improvement of skin surface (fine lines and wrinkles) was indeed due to the test product MFIII^{TM} PE Softgels. Regarding participant's subjective evaluation of product's tolerance, only few participants did quote that they have some special intolerance reactions to cosmetic products.

The results of this study prove that the MFIII^{TM} PE Softgels was rated in different ways from participants, whether they belonged to the test group or to the placebo group. In the test group 80% of the volunteers rated the aspect as excellent or good, versus 36% (good) and 40% (satisfactory) in the placebo group. Everyone reported

Table 4. Melanin index: Mean values (± SD; Mexameter units)

	Before	1 month	2 month	3 month	4 month
	D0	D28	D56	D84	D112
Test group (30 subjects)	499.6 ± 17.2	496.2 ± 15.4	493.5 ± 14.0	489.1 ± 13.4	487.4 ± 8.5
Melanin index difference [D0-Dx)/D0], % (Test group)	-	0.7%	1.2%	2.1%	2.4%
Placebo group (28 subjects)	493.4 ± 12.7	488.2 ± 12.2	486.7 ± 10.9	483.5 ± 10.1	480.8 ± 7.2
Melanin index difference [D0-Dx)/D0], % (placebo group)	-	1.0%	1.4%	2.0%	2.6%
Mean difference (test vs. placebo, µg/cm^2)	-	-0.4%	-0.1%	0.1%	-0.1%
Stat. result (test group, permutation test for paired data)	-	P =0.0009*** extr. significant	P <0.0001*** extr. significant	P <0.0001*** extr. significant	P <0.0001*** extr. significant
Stat. result (placebo group, permutation test for paired data)	-	P =0.0009*** extr. significant	P <0.0001*** extr. significant	P <0.0001*** extr. significant	P <0.0001*** extr. significant
Stat. result test vs. placebo, permutation test for independent data)	P =0.070 insignificant	P =0.021* extr. significant	P =0.026* significant	P =0.040* significant	P=0.017* significant

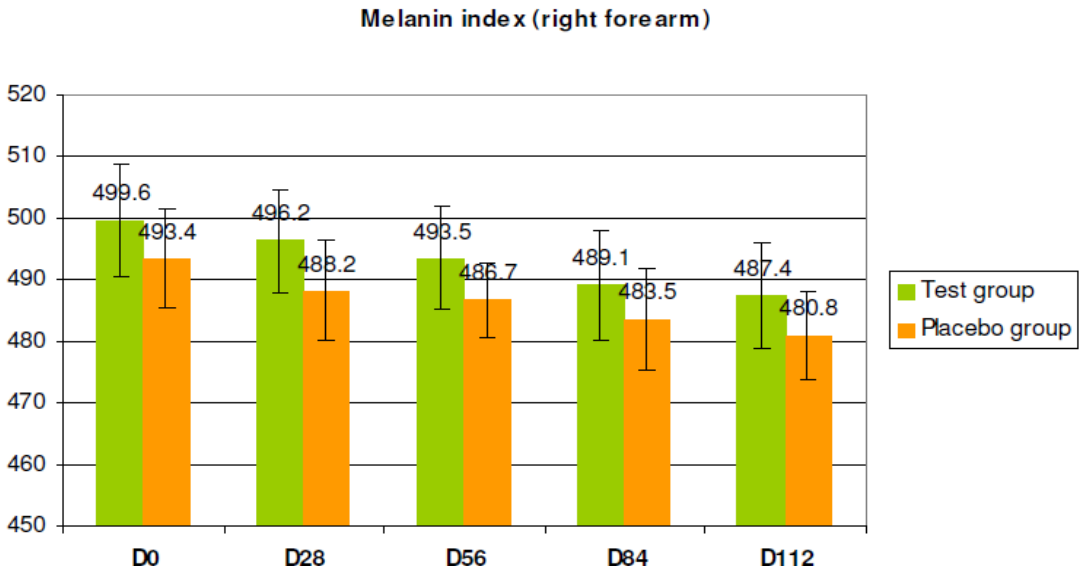

Figure 9. Melanin index: before (D0) and during once daily supplementation with MFIII^{TM} PE Softgels / the placebo Mean values (± SD; Mexameter units; right forearm)

Table 5. Erythema index: Mean values (± SD; Mexameter units)

	Before	1 month	2 month	3 month	4 month
	D0	D28	D56	D84	D112
Test group (30 subjects)	581.0 ± 19.0	579.1 ± 17.2	575.7 ± 14.9	573.5 ± 15.2	572.6 ± 14.6
Erythema index difference [D0-Dx)/D0], % (Test group)	-	0.3%	0.9%	1.3%	1.4%
Placebo group (28 subjects)	573.6 ± 13.4	572.3 ± 14.2	566.0 ± 11.8	565.5 ± 12.8	564.3 ± 13.9
Erythema index difference [D0-Dx)/D0], % (placebo group)	-	0,2%	1.3%	1.4%	1.6%
Mean difference (test vs. placebo, µg/cm^2)	-	0.1%	-0.4%	-0.1%	-0.2%
Stat. result (test group, permutation test for paired data)	-	P =0.107 ns insignificant	P =0.0004*** extr. significant	P =0.0003*** extr. significant	P <0.0001*** extr. significant
Stat. result (placebo group, permutation test for paired data)	-	P =0.423 ns insignificant	P <0.0001*** extr. significant	P =0.0001*** extr. significant	P =0.0001*** extr. significant
Stat. result test vs. placebo, permutation test for independent data)	P =0.0501 ns insignificant	P =0.061 ns insignificant	P =0.005* very significant	P =0.019* significant	P=0.016* significant

that softgels are easy to swallow. No smell is perceptible in standard Softgel packaging in blisters. 25 volunteers (78%) perceived a smoother skin after the supplementation period in the test group (versus 12, 37% in the placebo group). More than half of the participants of the test group supplemented with MFIII^{TM} PE Softgels advanced formula noticed an improvement of the skin on the face. For the several reasons mentioned above, 85% of the test group's participants would purchase the test product. Only 29% of the placebo group's participants would purchase the placebo.

CONCLUSION

After 3 months of supplementation, the MFIII^{TM} PE Softgels showed an important increase in epidermis+dermis density, as measured by ultrasound. The most impressive epidermis+density changes were noted in older subjects (mean age 49), especially on the face. Simultaneously, a reduction in skin roughness was noted, as well as reduction of wrinkles, melanin index and significant reduction of erythema index, that overall greatly contributed to the dramatic improvement of skin visual appearance. Besides high efficacy concerning skin improvements and smoothness, a good tolerance of the product was attested by the majority of the volunteers.

It is important to remember that the climatic conditions are totally different in Switzerland from those in South-East Asia countries. Temperature and relative humidity are totally different, being much higher in South-East Asia countries than in Switzerland at the time of study conduction. This is most likely the reason why product efficacy may differ under outdoor conditions with a relative high humidity, as this is likely to be the case in many Asian countries. For that reason, there is an ongoing study on the efficacy of MFIII^{TM} PE Softgels advanced formula in South-East Asia, results of which will be submitted shortly.

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