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A Randomized, Double-blind, Placebo-controlled Study on the Clinical Efficacy of Oral Treatment with DermaVite™ on Ageing Symptoms of the Skin

E THOM

ETC Research, Oslo, Norway

In this double-blind, placebo-controlled study, 40 women with ageing symptoms of the skin were randomized to receive DermaVite™, a new preparation containing marine proteins, α-lipoic acid, pine bark extract, vitamins and minerals (*n* = 20), or placebo (*n* = 20) twice daily for 6 months. Objective measurements of skin thickness and elasticity, together with subjective clinical assessments of various parameters (fine wrinkles, coarse wrinkles, tactile roughness and teleangiectasia) were used to evaluate changes after 2, 4 and 6 months' treatment. Self-evaluations were also made by the study participants. There was a significant improvement in skin quality in both objective and subjective parameters after treatment with Dermavite™ compared with placebo. Participants' self-evaluations also showed a statistically significant difference in favour of the active treatment. The treatment was very well tolerated. Based on this efficacy and tolerability study, DermaVite™ can be considered a suitable therapy for ageing symptoms of the skin.

KEY WORDS: MARINE PROTEINS; α-LIPOIC ACID; PLACEBO; AGEING SKIN; SKIN ELASTICITY; SKIN THICKNESS

Introduction

Various therapies are available for treating ageing symptoms of the skin: prescription drugs, cosmeceuticals and cosmetic agents, as well as food supplements, have all been claimed to have anti-ageing effects on the skin. For most of these agents, particularly for cosmeceuticals and cosmetic products, acceptable scientific efficacy and safety documentation is lacking. Selling highly priced preparations that have no effect is an unethical approach that has been heavily criticized, and even prohibited, by consumer authorities in some countries. One exception, however, is retinoic acid, which has been convincingly documented to have an effect on skin-ageing symptoms in several well-performed clinical studies.[1 – 4] In most countries, retinoic acid is a prescription drug, and it is thus not possible to advertise it directly to consumers or obtain it without a prescription from a physician.

DermaVite™ (Biovite Ltd, Poole, Dorset, UK) is a food supplement based mainly on marine proteins obtained from a deep-water

fish found along the Norwegian coastline. A previous study of the effects of these marine proteins on ageing skin showed favourable results.[5] In addition to marine proteins, DermaVite™ contains various minerals and vitamins plus α-lipoic acid and pine bark extract. α-Lipoic acid and pine bark extract are powerful antioxidants, with the ability to reduce the level of free radicals,[6 – 8] and are found in a number of antioxidant preparations for oral use. Topical application of α-lipoic acid has been shown to have a significant effect on ageing symptoms of the skin.[9]

To date, no controlled studies on skin-ageing symptoms have been carried out with DermaVite™. This double-blind, placebo-controlled study was therefore undertaken to investigate the efficacy and tolerability of DermaVite™ in females with ageing symptoms of the skin.

Subjects and methods

SUBJECTS

Females with ageing symptoms of the skin were recruited to this randomized, double-blind, placebo-controlled study. All subjects received verbal and written information about the aims of the study before giving informed consent. The study protocol was not required to be approved by a human ethics committee as the preparation used is classified as a dietary supplement and, as such, falls outside the mandate of the regional ethics committee.

TREATMENT

Subjects were randomized to receive the active preparation DermaVite™ or placebo. Blinding of the treatment was achieved by using active and placebo tablets with identical appearance. Dermavite™ and placebo tablets were supplied by Med-Eq AS (Tønsberg, Norway). The study participants were asked to take two tablets per day (one in the morning and one in the evening) with food, and to swallow them with water. The composition of the active preparation is given in Table 1. Treatment was continued for 6 months.

EVALUATION OF SKIN-AGEING SYMPTOMS

The ageing symptoms of the skin were evaluated clinically using a five-point scale: 0, absent; 1, very modest; 2, modest; 3, moderate; 4, pronounced. A score was recorded for each of the following symptoms: fine wrinkles, coarse wrinkles, tactile roughness and teleangiectasia.

The study participants returned for follow-up visits after 2, 4 and 6 months. At follow-up, the effect of the treatment on each of the four symptoms studied and as a global evaluation was recorded using a 10 cm visual analogue scale (VAS) with endpoints of 'no change' and 'pronounced change'.

In addition, an overall rating of extrinsic ageing was performed using a three-point scale: 0, modest; 1, moderate; 2, pronounced.

TABLE 1:
Constituents of a DermaVite™ tablet

Marine protein complex	350 mg
α-Lipoic acid	100 mg
Vitamin C	90 mg
Red clover extract (8%)	62 mg
Tomato extract (5% lycopene)	40 mg
Pine bark extract (95%)	30 mg
Vitamin E	18 mg
Vitamin B_3	18 mg
Soya extract (40%)	12 mg
Zinc	12 mg
Vitamin B_5	8 mg
Copper	2 mg

The subjects also performed global self-evaluation of skin-ageing symptoms using a VAS with endpoints of 'no change' and 'very pronounced change', at each of the follow-up visits.

EVALUATION OF SKIN THICKNESS AND ELASTICITY

Objective measurements of skin thickness and skin elasticity index were made at the start of the study and at each follow-up visit on the right and left sides of the face, at the lateral angle of each eye. Measurements were carried out using Dermascan A® and Dermaflex® instruments (Cortex, Århus, Denmark). Each measurement was performed in duplicate and the mean value recorded.

In order to avoid inter-observer variability, all objective skin measurements were carried out by the same person.

STATISTICAL ANALYSIS

The mean was used for the analysis of continuous and near-continuous variables; for skin thickness and skin elasticity, the mean of the values from the right and left sides of the face was used. Student's *t*-test was used for constructing the confidence interval of the mean. The one-sample *t*-test was used for analysing change over time within groups. Analysis of covariance and two-sample tests were used to compare groups with regard to continuous variables.

Categorical variables were reported using contingency tables. Fisher's exact test was applied when testing 2×2 tables. A network algorithm for performing Fisher's exact test in $r \times c$ contingency tables was used when testing tables larger than 2×2.

A two-tailed P-value < 0.05 was considered to be significant in all the tests.

Results

A total of 44 females aged from 30 to 64 years of age were included in the study; 22 received the active preparation and 22 were randomized to receive placebo. Of these, 40 subjects concluded the study according to the protocol, 20 in the active group and 20 in the placebo group. Four subjects withdrew from the study at the first follow-up visit; one subject in the active group withdrew due to gastrointestinal problems. These four subjects were not included in the statistical evaluation.

Table 2 shows the age and overall rating of skin-ageing symptoms at the start of the study in the two treatment groups. The two groups were comparable initially with respect to age and the severity of skin-ageing symptoms. No statistically significant differences were detected between the groups.

TABLE 2:
Age and overall rating of skin-ageing symptoms at the start of the study in females receiving DermaVite™ (n = 20) or placebo (n = 20)

	DermaVite™	Placebo
Mean ± SD age (years)	44.1 ± 5.2	46.3 ± 5.0
Grading of skin-ageing symptoms		
Modest	10	8
Moderate	7	10
Pronounced	3	2

GLOBAL EVALUATION OF SKIN-AGEING SYMPTOMS

The results of the global evaluation of the effects of treatment are shown in Table 3. After 6 months' treatment, compared with baseline evaluations, there was no significant difference in the global evaluation in the placebo group, whereas a significant change ($P < 0.05$) was seen in the group receiving the active preparation.

OBJECTIVE SKIN MEASUREMENTS

Table 4 shows the skin thickness and elasticity values recorded during the study. A significant increase ($P < 0.05$) between the initial skin thickness value and the value seen after 6 months was found in the group treated with the active preparation, but not in the placebo group. The difference in the increase in skin thickness between the groups was also significant ($P < 0.05$).

There was a significant increase ($P < 0.05$) between the initial skin elasticity and the value seen after 6 months in the group treated with the active preparation, but not in the group treated with placebo. The difference in the increase in skin elasticity between the groups was also significant ($P < 0.05$).

SELF-EVALUATION

Self-evaluation of the effect of treatment by the study participants revealed a significant difference ($P < 0.05$) in favour of the active group after a treatment period of 6 months, as shown in Table 5. Of the 20 subjects in the active group, 18 reported an improvement in their skin quality on self-inspection,

TABLE 3:
Global evaluation of changes in skin-ageing symptoms measured using a visual analogue scale (VAS) in females treated with DermaVite™ (n = 20) or placebo (n = 20) according to treatment duration

	Mean ± SD VAS measurement of skin-ageing symptoms (cm)	
	DermaVite™	Placebo
After 2 months' treatment	0.6 ± 0.7	0.3 ± 0.5
After 4 months' treatment	1.6 ± 0.9	0.7 ± 0.6
After 6 months' treatment	6.2 ± 1.6	0.5 ± 0.7

TABLE 4:
Mean ± SD skin thickness and elasticity index in females treated with DermaVite™ (n = 20) or placebo (n = 20) according to treatment duration (there were no significant differences after 2 months' treatment)

	Skin thickness (mm)		Skin elasticity (%)	
	DermaVite™	Placebo	DermaVite™	Placebo
Before treatment	0.85 ± 0.12	0.91 ± 0.15	47 ± 8.1	48 ± 7.6
After 4 months' treatment	0.94 ± 0.15	0.90 ± 0.13	50 ± 8.5	46 ± 8.2
After 6 months' treatment	1.14 ± 0.17	0.87 ± 0.12	62 ± 8.4	45 ± 8.5

TABLE 5:
Self-evaluations of the effect on their skin-ageing symptoms measured using a visual analogue scale (VAS) in females treated with DermaVite™ (n = 20) or placebo (n = 20) according to treatment duration

	Mean ± SD self-evaluation VAS measurement of skin-ageing symptoms (cm)		
	DermaVite™	Placebo	*P*-value
After 2 months' treatment	0.5 ± 0.7	0.4 ± 0.7	NS
After 4 months' treatment	1.9 ± 1.0	0.5 ± 0.7	< 0.05
After 6 months' treatment	6.5 ± 1.7	0.6 ± 0.8	< 0.001

NS, not significant.

while only one of the 20 subjects treated with placebo reported a small improvement.

After 4 months of treatment, a number of the participants in the active group (approximately 30%) did not report any visible change in skin quality on self-evaluation. On studying this subgroup further, however, there was a smaller but still significant ($P < 0.05$) positive change in skin thickness and elasticity, as compared with those reporting a positive visible self-evaluation.

All 20 subjects in the active group had a positive effect from the treatment, measured as improvement in skin elasticity and skin thickness. All 20 subjects also expressed a desire to persist with the treatment, even though two of the participants could not detect any visible changes. None of the placebo-treated subjects wished to continue.

TOLERABILITY

The overall tolerability was good. One subject in the active group stopped the treatment due to gastrointestinal problems. None of the subjects receiving placebo reported any side-effects. Two participants in the active group were of the opinion that the tablets were hard to swallow and should have been coated.

Discussion

In this study, the active capsules of DermaVite™ had a significant positive effect on skin quality in middle-aged females with skin-ageing symptoms, compared with placebo. This positive effect seemed to develop over time, being less pronounced after 2 months than after 6 months. Based on previous experiences in similar studies that we have undertaken, no pronounced effect of the active treatment was expected before the treatment had been taken for at least 4 months.[5] The efficacy of the treatment was reflected in the results of the clinical observations, the objective measurements of skin thickness and skin elasticity, and the participants' own evaluations of skin-ageing symptoms.

The reasons why some subjects did not respond to the active treatment are unclear. There were no significant differences between the responders and non-responders in terms of age or grade of skin-ageing symptoms. We have no reason to believe, after asking about compliance, that the non-responders had not taken the preparation as recommended. It may be that a longer treatment time is required in some subjects than in others to produce a similar effect.

Although the mode of action of DermaVite™ is unclear, the results of the present study indicate that this preparation seems to have a favourable effect on degenerated elastin and collagen tissue of the dermis. Several of the patients in the active group reported that their skin was much smoother after treatment, and a few also expressed that the pigmentation was more even, with reduced pigmentation spots. Based on this efficacy and excellent tolerability, DermaVite™ can be considered an attractive therapy for the treatment of ageing symptoms of the skin.

Conflicts of interest

No conflicts of interest were declared in relation to this article.

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Address for correspondence
Dr E Thom
Stasjonsveien 5A, 0774 Oslo, Norway.
E-mail: erlingthom@etc.as