

THE EFFECT OF A NEW SKIN OINTMENT ON SKIN THICKNESS AND ELASTICITY

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Summary

The present open pilot study was carried out in order to investigate a new patented concept for skin treatment. The new concept is intended for use in treatment of ageing skin. The ointment contains conjugated linoleic acid (CLA) and retinyl palmitate (RP). Both ingredients are conjugated with the biopolymer chitosan in order to improve water solubility, increase skin penetration and inhibit oxidation of the active substances. A number of studies have previously been carried out with conjugated retinyl palmitate, where the conjugation mostly has been done using β -cyclodextrin.

We included 20 females in our study and the treatment period was three months. Objective measurements of skin-thickness and elasticity were carried out initially and after three months. Subjective observations and scores were performed by the participants themselves using visual analogue scales (VASs) initially and at the end of the study.

The results showed a significant improvement in skin quality both with regard to objective as well as in subjective parameters after treatment with the new ointment. In comparison to our previous studies with ointments containing only conjugated RP the effects on skin thickness and elasticity were more pronounced with the new formulation showing an average improvement in skin thickness of 51% and in skin elasticity of 27%. The self evaluation scores of the participants were also highly favourable and significant, and all of the participants would like to continue with the ointment after the formal study was closed. The tolerability of the treatment was excellent and all subjects concluded the study according to the protocol.

Riassunto

Questo studio pilota è stato condotto per verificare una nuova e brevettata metodologia di trattamento per l'invecchiamento cutaneo.

La crema contiene acido linoleico (LLA) retinil palmitato (RP) complessati tra loro. Entrambi gli ingredienti sono complessati con biopolimeri di chitosano per aumentarne la solubilità in acqua, la penetrazione transcutanea e per impedirne l'ossidazione.

Alcuni studi preliminari sono stati condotti utilizzando il retinil palmitato complessato con β -ciclodestrina. Nello studio clinico sono state inserite 20 donne per un periodo di tre mesi durante il quale è stato valutato lo spessore e l'elasticità della pelle. Le stesse pazienti hanno espresso il loro parere personale utilizzando una scala analogica.

I risultati ottenuti hanno dimostrato un netto miglioramento della qualità della cute sia con la metodica soggettiva che con quella oggettiva.

La nuova formulazione è risultata migliore della RP utilizzata in precedenza sia per quanto riguarda lo spessore (+51%) che l'elasticità (+27%).

Il prodotto è risultato ben tollerato con soddisfazione piena di tutto il gruppo.

INTRODUCTION

We have for a number of years been interested in investigating the efficacy of different topical treatments on the skin structure, especially skin thickness and elasticity, in humans.

We have published a number of studies on water soluble retinyl palmitate showing that by conjugating this Vitamin A ester with β cyclodextrin a significant better effect on these two skin parameter is obtained than after using the unconjugated ester. In fact, the effect after using the unconjugated ester is not significantly different from using the ointment vehicle (placebo) (1-3). However, still a number of ointments containing the unconjugated Vitamin A esters are available in the market.

We have also made a double - blind comparison of Retinoic acid (RA) and the conjugated ester (RP). The strength was 0,025% for RA and 0,2% for ester. In these concentrations the two preparations were equipotent and the effect was good for both preparations. However, the tolerability was significant improved by using the RP ointment (3).

Others have confirmed our results that by using a «tween» together with the ester is essential for having a good skin penetration (4,5)

A new ointment has been developed by Jan Wadstein MD; Ph.D., who previously has been involved in the development of the conjugated RA ointments we have tested. The new ointment contains two new agents, chitosan and CLA (conjugated linoleic acid) in addition to retinyl palmitate.

CLA is a polyunsaturated fatty acid with unique properties. The effects of CLA on body composition have been studied in animals and humans. CLA is a naturally occurring substance also detected in the tissue and body fluids in humans and is as such regarded as non-toxic. We were interested in investigating the effect of CLA on the skin. However, CLA is easily oxidised and for oral use it is enclosed in amber capsules to

prevent oxidation. The application of CLA to many food systems as an ingredient has a limitation due to its limited solubility in water and oxidation by O_2 . To solve this problems inclusion complexes with β - cyclodextrin (CD) have been studied. Oxidation of CLA complexed with CD was greatly reduced as compared to uncomplexed CLA (6) Conjugation is a proper method for inhibiting oxidation and has been used with success in inhibiting retinyl palmitate and other sensitive substances from being oxidised. We decided therefore to try to use chitosan as a conjugation agent instead of the more conventional β cyclodextrin. From a structural point of view these two substances have similarities both being complex polysaccharides. In this way we felt that it should be possible to combine the potential effect CLA and the documented and positive effect chitosan has on the skin.

Chitosan is well documented as a cosmetic ingredient through improvement of skin compatibility and the capacity to release bioactive cosmetic ingredients (7).

The decision was taken to test the new ointment after the same method we have used in our previous studies. As this was a pilot study the decision was taken to run it open before doing a formal randomised double - blind placebo controlled study.

MATERIAL AND METHODS

The study was carried out as an open study in 20 females who applied the ointment on the right volar (protected part) of the right forearm. The left forearm was used as a control and was not treated. The total treatment period was 3 months and administration was bid (in the morning and in the evening) during the study period. The study was carried out in accordance with the revised Helsinki declaration. All subjects received information about the aim of the study before inclusion and participate voluntarily in the study and signed an informed con-

sent before being included.

THE INVESTIGATIONAL FORMULATION

The formulation used in this study was made according to a formula developed by one of the authors (JW). A patent application has been filed for this formulation. Norwegian application No. 20005718 the conjugation is made as follows: 100 g of CLA (Tonalin, 80, Natural ASA Norway) is heated to 70°C under pressure with 30 g Chitosan (Chitoclear, 400 Primex AS Norway). When conjugation has taken place (milky appearance of the solution) it is cooled down to 50°C and the other ingredients are added. Retinyl palmitate is conjugated with chitosan in the same way as for CLA. The cream base is of a standard type comprising of soybean oil and peanut oil in a suitable concentrations to achieve an acceptable cosmetic formulation. Other ingredients are Vitamin E as stabilisator and preservatives. The pH is adjusted to 6,5 using lactic acid. To our knowledge this is the first ointment containing these two active ingredients Chitosan and CLA conjugated.

MEASUREMENTS OF SKIN THICKNESS AND SKIN ELASTICITY

The measurements of skin thickness and skin elasticity were performed by ultrasound using Dermalcan and Dermaflex instruments, respectively (Cortex Inc. Aarhus, Denmark). Measurements were carried out at baseline, after 1 months and after 3 months, by the same person (ET) on both occasions and measurements were performed at the mid - region of the volar part of the forearm. All measurements were in triplicate and average values used for statistical evaluation.

SELF-EVALUATION BY THE PARTICIPANTS

At the same time as the objective measurements were carried out, participants made a self-evaluation of skin quality using visual analogue scales of 10 cm with end -points of «no change» and « very pronounced change ». Subjects were asked to score the global change in skin quality by placing a mark on the line between the end-points. The distance from the end-point (0 cm) to the mark was used as the score for the subject.

STATISTICAL METHODS

A significance level of 5% was used in the tests and two-tailed tests were applied. The one-sample test was used analysing change over time within groups. Two -sample t-test were used to compare arms with regard to continuous variables.

RESULTS

20 females aged between 40 and 60 years (mean 49,2 yrs) were included in the study and all participants were compliant with the protocol.

EFFICACY PARAMETERS, SKIN THICKNESS AND ELASTICITY

The results from the skin thickness measurements are shown in Table 1. As can be seen from the table the ointment gave an increase in skin thickness of 51% as compared to no change for the untreated arm. This change is highly significant ($p < 0.01$).

Table I

Change in skin thickness (mm) after administration of the ointment and no treatment for 3 months in 20 females.

		Initially	After 1 month	After 3 months
Ointment	Mean (SD)	0.89(0.13)	1.10(0.20)	1.35 (0.19)
No treatment	Mean (SD)	0.90 (0.10)	0.91(0.11)	0.89 (0.12)

The viscoelastic properties of the skin is shown in table 2.

Table II

Change in skin elasticity (%) after administration of the ointment for 3 months in 20 females

		Initially	After 1 month	After 3 months
Ointment	Mean (SD)	59.0 (8.0)	70.0 (7.9)	75.2 (8.5)
No treatment	Mean (SD)	61.0 (7.5)	60.0 (8.0)	61.5 (8.1)

The results show that the elasticity is improved by 27% on the ointment treated arm while no change is observed on the control arm.

EFFICACY PARAMETERS, SELF-EVALUATION BY USE OF VAS.

The self - evaluation shows impressing results. The average score was 7.9 cm for the ointment treated arm. This is highly significant ($p < 0.001$) as compared to the control arm where »no change« was reported. The participants felt that they got a smoother and more elastic skin. They also expressed that they were highly satisfied with the cosmetic properties of the ointment. The rapid penetration of the ointment into the skin was highly appreciated by the participants.

TOLERABILITY

No tolerability problems were reported during the study. The tolerability was excellent. All participants would like to continue with the ointment.

DISCUSSION

The results from this study shows very good effects in improving skin thickness and elasticity. As compared to our previous studies with conjugated Vitamin A esters the results are better showing an average improvement in skin thickness of 51% and in elasticity of 27%. This should be compared with around 32% and 19 % with the conjugated creams we have tested previously using the same measuring devices. The average global score on the satisfaction of the cream is also impressive with an average final