

A NEW COSMETIC SOLUTION FOR A MILD TO MODERATE XEROSIS

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Summary

As it is known, ceramides, together with cholesterol and fatty acids making up the lamellar layers, play a key role in maintaining balanced the lipid barrier of the skin.

PCA, fundamental agent of the NMF, and the glycine, main agent of the collagen, behave as "cutaneous sponges" able to link water for long term at a deep cutaneous level. Hyaluronic acid and some chitosan-derivatives, contribute to cutaneous superficial hydration, acting both as topical protectors and as active principles able to link high quantities of water.

Based on the aforementioned facts, it was controlled the activity of a special multilamellar structure based on phospholipids, ceramide-6 and phytosphingosine enriched with hyaluronic acid, a chitosan derivative, vitamin C, PCA, glycine and arginine.

The trial was a randomized double-blind placebo-controlled study, carried out at two dermatological in-offices on 40 very dry skinned female volunteers aged 23-35.

The product activity was controlled by a clinical score method and measuring hydration and superficial skin lipids by the 3C System (Dermotech, Rome, Italy) for a three month period.

Skin tolerability was also controlled.

This 12-week study, has shown multi-lamellar structure to be significantly superior to placebo in the treatment of mild to severe xerosis.

In fact, both the hydration and the surface lipids increase quickly on the area treated from 70% to 80% ($p < 0.005$), and reached higher values of about 20% ($p < 0.005$) with the active cream, if compared to its own vehicle. Moreover, there was a significant correlation ($r = 0.94$) between the results recorded by the clinical score method and these obtained by the 3C System.

The product was generally well tolerated and no side effects were detected during the study.

Riassunto

Come è noto, le ceramidi assieme al colesterolo ed agli acidi grassi rivestono un ruolo fondamentale nel mantenere in equilibrio la barriera cutanea. Il PCA, componente chiave dell'NMF, e la glicina

na, aminoacido basilare del collagene, agendo come "spugne" cutanee, che trattengono l'acqua a livello cutaneo profondo, assieme all'acido ialuronico ed ai derivati del chitosano, che la trattengono al contrario a livello superficiale, svolgono tutti un'azione idratante contribuendo a mantenere l'omeostasi cutanea.

Si è voluta, così, controllare l'attività chimica svolta da una struttura cosmetica multilamellare basata sull'uso di fosfolipidi, cerammide 6 e fitosfingosina, arricchita con acido ialuronico, un chitosan-derivato, glicina, arginina, e soprattutto vitamina C.

La vitamina C era presente sia tal quale che sottoforma di un suo nuovo derivato liposolubile.

Lo studio è stato condotto presso un centro dermatologico su 40 donne di età compresa tra 23 e 35 anni, affette da evidente xerosi del viso.

L'azione svolta dal prodotto è stata controllata sia clinicamente, mediante punteggio, che misurando l'idratazione ed i lipidi cutanei di superficie con il 3C System, durante un periodo di tre mesi di trattamento.

Sia i lipidi di superficie che l'idratazione cutanea è aumentata dal 70% all' 80% in tutte le pazienti trattate sia con il veicolo che con la crema attiva, risultando un maggiore incremento del 20% ($p < 0.005$) per la crema attiva.

E' stata riscontrata una completa correlazione ($r=0,94$) tra i dati clinici ed i dati ottenuti con l'uso del 3C System, e sia il veicolo che la crema attiva sono risultati ben tollerati senza che si siano verificati effetti collaterali negativi.

BACKGROUND

As it is known, ceramides together with cholesterol and fatty acids making up the lamellar layers, play a key role in maintaining the lipid barrier of the skin balanced(1-4).

The barrier function, indispensable for water homeostasis, is closely linked to skin health and disease (5-9).

The PCA, fundamental agent of the NMF, and the glycine, main agent of the collagen, behave as "cutaneous sponges" able to link water for long term at a deep cutaneous level, while the hyaluronic acid and the new chitosan-derivative used contribute to cutaneous superficial hydration, acting both as topical protectors and as active principles able to link high quantities of water (10-13).

Moreover, one of the best known human antioxidant is vitamin C which has been shown to be effective in photodamage and in skin ageing (10-15).

AIM

Based on the aforementioned facts, it was controlled the activity of a special multilamellar structure based on phospholipids, ceramide-6 and phytosphingosine enriched with hyaluronic acid, a chitosan derivative, vitamin C, PCA, glycine and arginine.

It was used free l-ascorbic acid together with its liposoluble derivative.

MATERIAL AND METHODS

Cosmetic Preparation

A cosmetic preparation was formulated using liposomes composed of an high proportion of lipophilic phospholipids able to encapsulate and protect both hydrophilic and amphiphilic substances.

The liposomal fraction contained: ceramide-6,

Tradename: Idroskin® C

phytosphingosine, cholesterol, linoleic acid, ascorbic acid and all the other active compounds. This cosmetic formulation forms in water a continuous and stable multi-lamellar structure (Active A)¹.

The vehicle was deprived of all the actives, such as l-ascorbic acid, hexyldecanoyl-l-ascorbic acid (VC-IP), ceramide-6, phytosphingosine, hyaluronic acid, chitosan, PCA, glycine and arginine (Vehicle B).

STUDY DESIGN

Protocol

The trial was a randomized double-blind placebo-controlled study carried out on 40 very dry skinned female volunteers, aged 25-35, and with a minimum of xerosis, severity of grade 6, according to Dahl and Dahl (16) :

0 Normal skin:	no sign of dryness
1-3 Mild xerosis:	ashy appearance and appearance of minute skin flakes
4-6 Moderate xerosis:	defined scales
7-9 Severe xerosis:	heavy scaling and deep erythematous fissures included eczema craquelè

Treatment

The cream containers were identified by the letters A (the active), B (the vehicle), volunteer number and the notation on (right or left). The volunteers received two different creams to use for the right or left side of face and neck. Each subject was used as her own control. All were instructed to use the cosmetic products twice a day (morning and evening) on the assigned area (right or left) for 12 weeks, after using as cleansing agent *Kera® Idroschiuma* and abundant water rinsing. All the subjects gave their written informed consent in conformity with the ethics of cosmetic experimentation.

Conduct of the study

The study included the first evaluation, using clinical scores, and the second one, using an instrumental method.

Scoring Method

The clinical evaluation, according to Dahl (16), was carried out at the beginning of the treatment (baseline value) and after weeks 2, 4, 6, 8, and 12 (end of treatment).

Instrumental Method

Surface lipids and skin hydration were detected by the 3C System® (Dermotech, Rome, Italy) (17) (Fig.1), carrying out five separate measure-



Fig.1 3C System

ments (right and left) on forehead, crow's feet area, cheeks, medio-facial region and neck. The mean of the obtained results for each of the five areas are reported on Fig. 2 and Fig. 3.

Tolerability

Skin tolerability was evaluated by expert dermatologists after 2, 4, 6, 8 and 12 weeks of treatment.

Statistical Analysis

A two-tailed student's *t* test on paired series was used to analyze the differences between the values obtained before the treatment and after 2, 4, 6, 8, and 12 weeks of treatment.

The difference was considered to be significant when $p < 0.05$.

The correlation coefficient *r* and its level of significance *p* were calculated in order to determine the correlation between the results recorded by the scoring method, and those obtained by the 3C System.

RESULTS

Clinical Observation

The treatment by this multi-lamellar-based cosmetic, induced significant and progressive improvement on all the skin's signs of dryness.

The mean of the scores obtained for all the subjects at each control visit is given in Table I. How is clearly visible, the improvement starts to be evident after 4 weeks of daily treatment, even if remarkable differences between the skin surface treated with vehicle and the controlateral treated with the active cream, were not so strong.

Probably that's due to the specific activity of the phospholipids which surely improve the skin appearance for their hydrating and restructuring properties.

At the beginning of the week 6 of treatment till the week 12, the presence of vitamin C, and surely that of the ceramide-6 together with phyto-sphingosine, and the other moisturizing compounds makes the active cream much more effective if compared to the phospholipidic vehicle alone.

However, the phospholipidic base alone gives a remarkable improvement of xerosis, which tends to ameliorate in a visible way.

From fig. 2 and 3, it is possible to observe a mo-

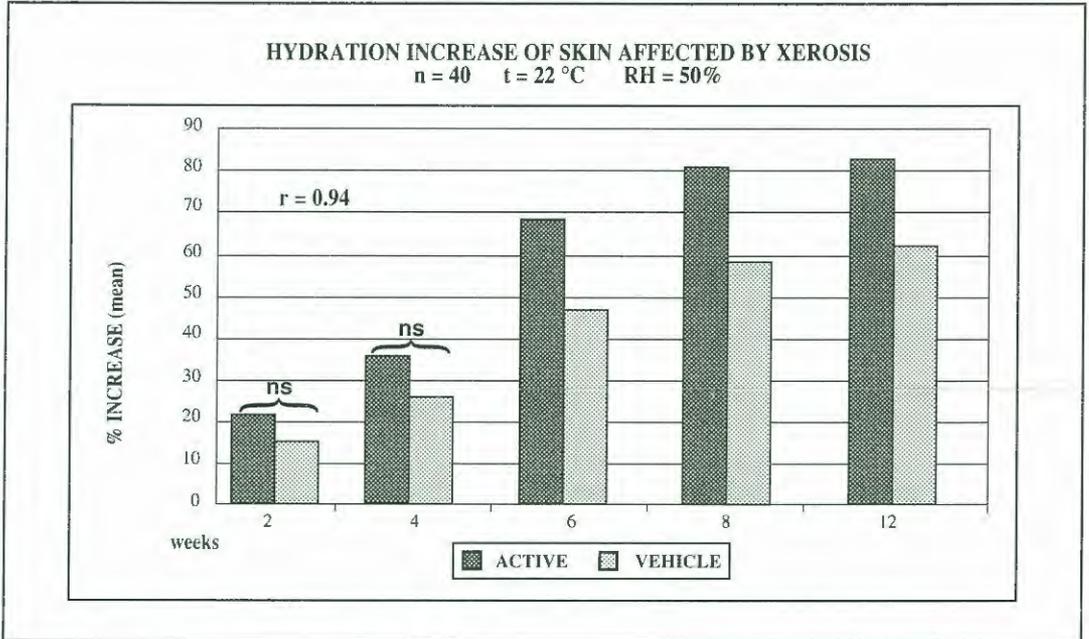


Fig.2 All *p* values are highly significant ($p < 0.005$) as baseline an as to groups from the weeks 6.

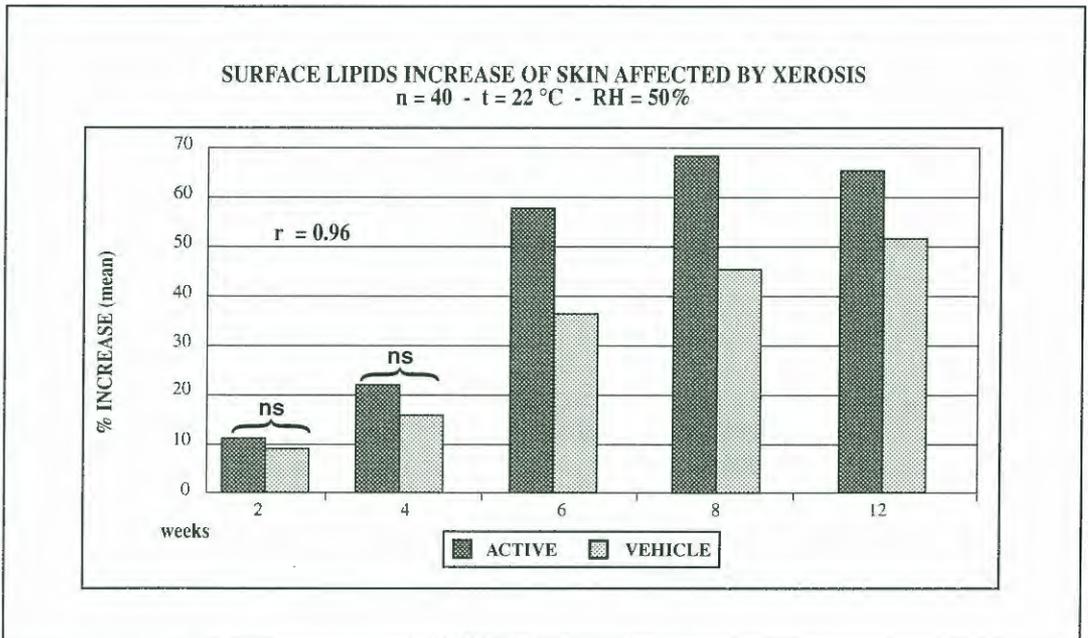


Fig.3 All *p* values are highly significant ($p < 0.005$) as baseline an as to groups from the weeks 6.

re evident improvement due to the active principles used: vitamin C, ceramide-6, phytosphingosine, hyaluronic acid, chitosan, PCA, glycine and arginine. In fact, both the hydration and the surface lipids increase quickly from 70% to 80% ($p < 0.005$), on the area treated with the active cream compared with the vehicle, and reach higher values of about 20% ($p < 0.005$).

Considering the starting values and the vehicle's activity all the results obtained are very significant just from the first month of treatment.

Tolerability

No undesirable cutaneous reaction was observed during the use of the product and the tolerability was excellent during the whole treatment period.

CONCLUSIONS

According to the results already obtained, both from our work team (12) and by other authors (18-19), the phospholipids combine hydrating, restructuring and soothing properties.

Moreover, they are known as penetration enhancers of many active ingredients but mainly they are to be considered as physiological lipids which either form or can be integrated into the membrane bilayers of the skin.

What is important to underline is that they seem to be able to allow the penetration of the ceramides (skin barrier fundamental components) and to protect for long time vitamin C from the oxidative process, as our study still in progress seems to demonstrate (20).

TABLE I

REDUCTION OF SKIN XEROSIS TREATED BY A MULTILAMELLAR LIPID STRUCTURE ENRICHED WITH VITAMIN C AND CERAMIDE-6

t = 22 °C RH = 50% n = 40

XEROSIS SEVERITY SCORES	WEEKS		2	4	6	8	12
	FIRST AREA	ACTIVE	6.0 ± 0.3	5.1 ± 0.2	3.3 ± 0.2	2.0 ± 0.2	0.5 ± 0.2
MEAN BASELINE VALUE	6.6		↕ ns	↕ ns	↕ p < 0.05	↕ p < 0.05	↕ p < 0.05
	SECOND AREA	VEHICLE	6.1 ± 0.2	5.3 ± 0.3	3.8 ± 0.3	3.0 ± 0.2	1.2 ± 0.2

All p values are significant ($p < 0.005$) as baseline and to groups. First area vs second area is significant only from 6 th to 12 th week

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