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4

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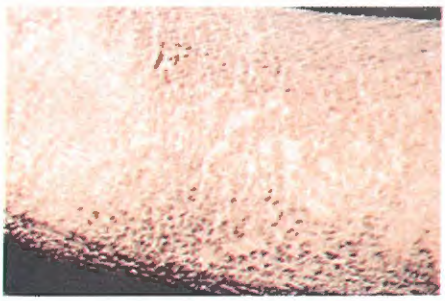

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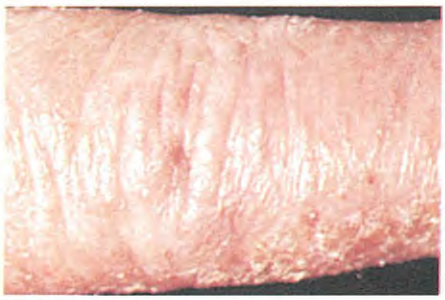

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- Effective for initial and maintenance therapy [1,2,3]
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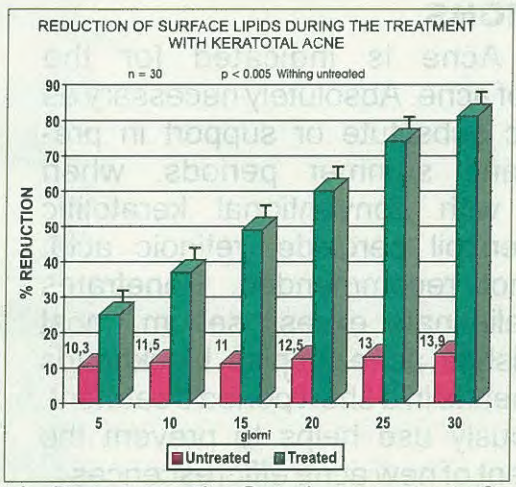
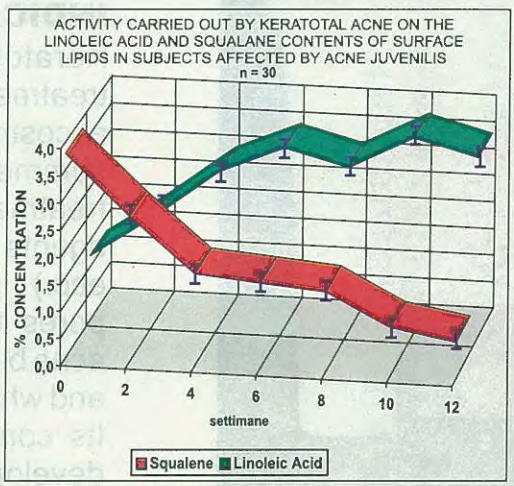
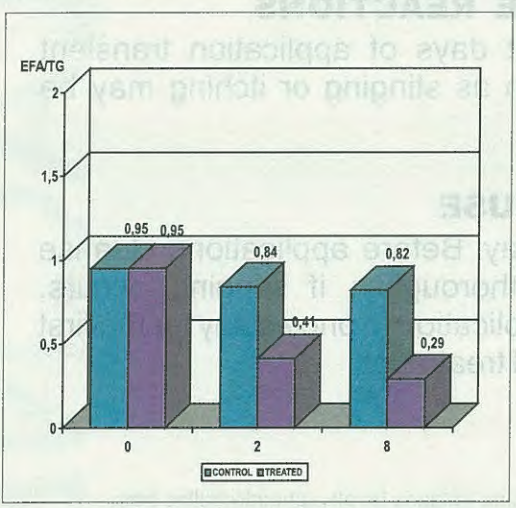


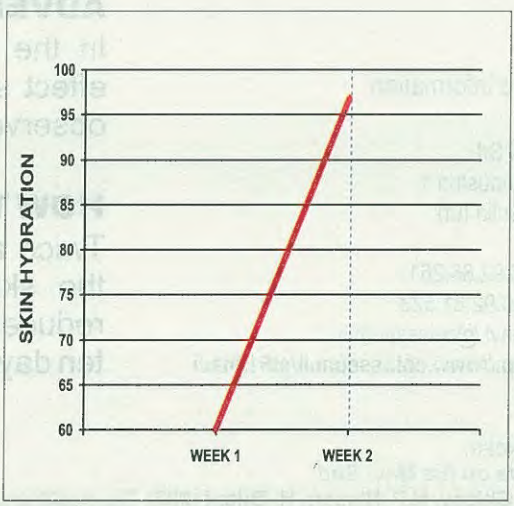
⇒ *Decreases the Squalene content of acne affected skin*



⇒ *Reduces excess lipids*



⇒ *Significantly reduces EFA/TG ratio*



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ADVERSE REACTIONS

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HOW TO USE

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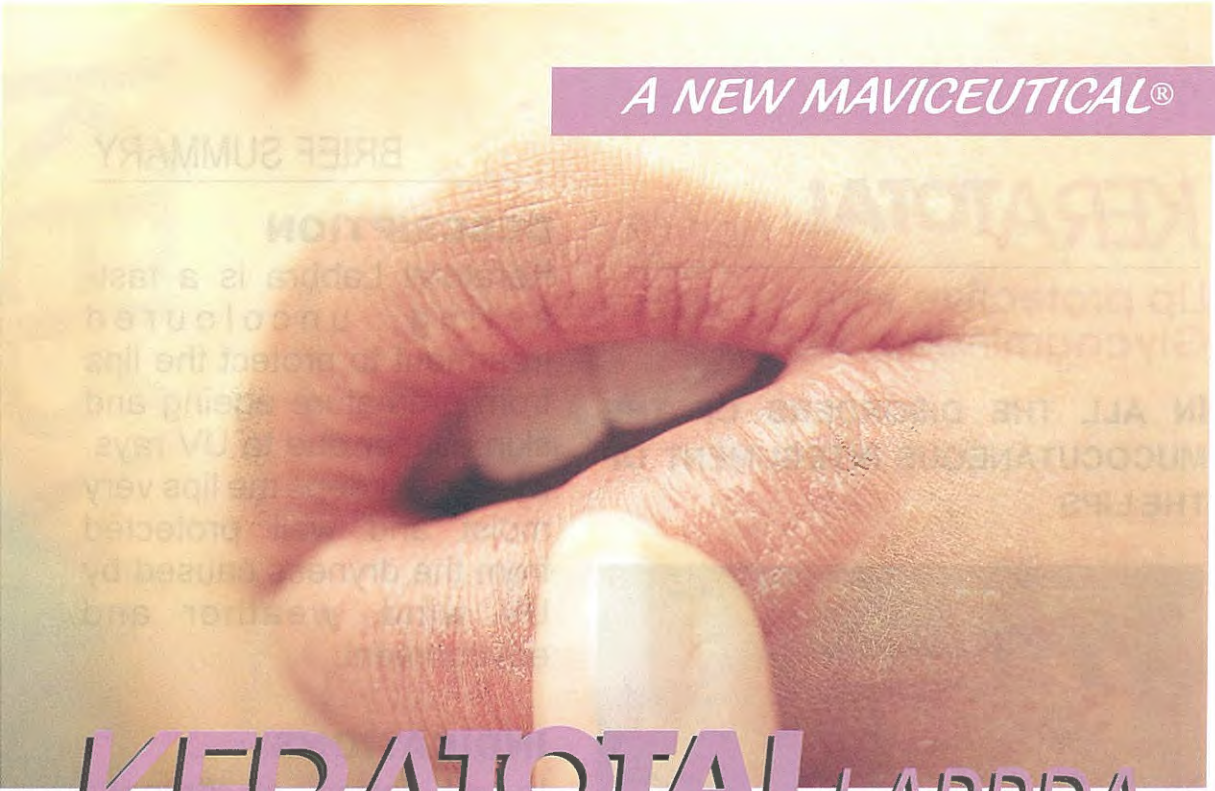
*1,2 - **Data on file Mavi Sud***
3 - **M. Ghiczy, H.P. Nissen, H. Biltz (1996)** The treatment of Acne Vulgaris by phosphatidilcholine from Soybeans, with a high content of linoleic acid. *J. Appl. Cosmetol.* **14,** 137-145



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• Wind	Allergic cheilitis
• Weather	Exfoliative cheilitis
• Environmental pollutants	Angular cheilitis

HOW TO USE

Use day and night as a regular lipstick

(*) partially neutralized by a special patented blend of aminoacids

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KERATOTAL LABBRA™

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IN ALL THE DISORDERS OF THE MUCOCUTANEOUS INTEGUMENT OF THE LIPS

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BRIEF SUMMARY

DESCRIPTION

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INDICATIONS

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ADVERSE REACTIONS

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HOW TO USE

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what?
when?
where?
why?

why not?

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what?

Dietary supplement with Folic Acid, Magnesium and Polyunsaturated Fatty Acids omega-6 and omega-3, which have a high content of DHA (docohexaenoic acid).

when?

Fundamental for an optium development of the brain and retinal structures in the fetus.

where?

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- optimizes membrane formation by protecting the internal structures of cells;
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why?

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and to reduce the risk of

- functional neurologic disorders in the fetus;
- spina bifida;
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- uterine hypercontractility;
- skin diseases (psoriasis, atopic eczema, alopecia, etc.);
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journal of applied cosmetology

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Quarterly Review of Cosmetic Dermatology

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Trimestrale di Dermatologia Cosmetologica
Quarterly Review of Cosmetic Dermatology

Contents

J. Appl. Cosmetol. 15, 115-123 (October-December 1997)

BIOLOGICAL FUNCTIONS AND THERAPEUTIC PROPERTIES OF UREA

W. Raab*
*Allergy Clinic "Innere Stadt" in Vienna, Austria

Received: *October 25, 1995*

Key words: Urea, Dry skin, Atopy, Glucocorticoid, Moisturizer.

Synopsis

Although urea is know for about 50 years, its use as a topical drug or as an adjunct is obtaining more and more attention in topical dermatotherapy. Urea is absolutely non-toxic, undesirable actions occur only, if skin state and concentration of urea are on a disbalance. Urea proved to be a most valuable substance for restoring hydration in dry skin and in eczemas due to skin dryness. Therefore, urea ranks among the standards in atopy, for the treatment of eczema as well as for the interval care.

Riassunto

Sebbene si conosca l'urea già da circa 50 anni, il suo uso come farmaco o cosmetico topico sta ottenendo sempre più attenzione nella dermoterapia topica.
L'urea è assolutamente atossica e si possono verificare effetti indesiderati solo nel caso in cui le condizioni della pelle e la concentrazione di urea siano sbilanciate.
L'urea ha provato di essere una sostanza di grande valore per il ripristino dell'idratazione nella cute secca e negli eczemi causati dalla cute secca. L'urea si colloca quindi tra le scelte standard nei casi di atopia, per il trattamento degli eczema e per le terapie di intervallo.

INTRODUCTION

Urea (carbamide), the diamide of carbonic acid, is a naturally occuring degradation product of various proteins in man. Up to 30 g were produced daily. Urea is found in all organs and body liquids. On the skin surface, urea is an important component of the natural moisturizing factor contained in the hydrolipid emulsion.

About 50 years back, urea was reccommended for the topical treatment of hand eczema but only 30 years back, the first experimental data were collected on its biochemical and pharmacological activities. The moisturizing capacity of urea in the stratum corneum, especially in xerotic states, was discovered. In 1988, a symposium was held in Salzburg, Austria, the proceedings of which contain all the information available on the various actions of urea in dermatology and cosmetology (1). The more recent publications are compiled in a review article published 1993 (2).

Today, urea belongs to the standard substances used in dermatological therapy and skin care.

TOXICITY

Urea lacks any systemic toxicity. Urea formerly was used as a diuretic drug; doses up to 1.0 g/kg bodyweight were given intravenously, without any undesirable action.

Therefore, following absorption from external preparations, no toxic effects of urea can be found.

The tolerance of urea depends on the state of the skin and on the concentration of urea. The vehicle applied may influence the tolerance, too. On healthy skin, urea may be used in concentrations up to 20%. Most products, however, contain 5-10% of urea, only, as irritating effects on slightly damaged skin should be avoided. Such effects might develop as a consequence of osmotic activity.

BIOCHEMICAL FUNCTIONS OF UREA ON THE SKIN

Urea is an important component of the natural moisturizing factor of the stratum corneum. Water is bound by an inclusion in the crystal structure of urea and only slowly liberated. Urea stems from the sweat and from the process of keratinization. The natural moisturizing factor consists of various ions (24%), pyrrolidone carboxylic acid (12%), various other carboxylic acids (50%), amines and amides (17%) and urea (7%). One should not understimate the amount of natural moisturizing factors in the stratum corneum wich make up about 25% of the dry weight of the total horny layer.

Stratum corneum of healthy skin contains about 40 M urea per lo M amino acids which corresponds to about 28 µg/2.5 cm^2 (2). In dry skin, urea content is significantly lower (50% in some instances, only). Clinically normal skin of atopic individuals contains only 30% urea compared to normal values. In clinically diseased skin (atopic eczema), urea content is lowered to 20% of normal values (Fig. 1, 2).

From these data the conclusion may be reached that urea is one of the most important components of the natural moisturizing factor of human skin.

MOISTURIZING ACTIVITY OF UREA

Urea exerts a wide ranges of pharmacological activities when applied on the skin:

- moisturizing activity,
- desquamating action (lysis of cementing substance),
- antimicrobial action (uptake of water interferes with the growth requirements of microorganisms),

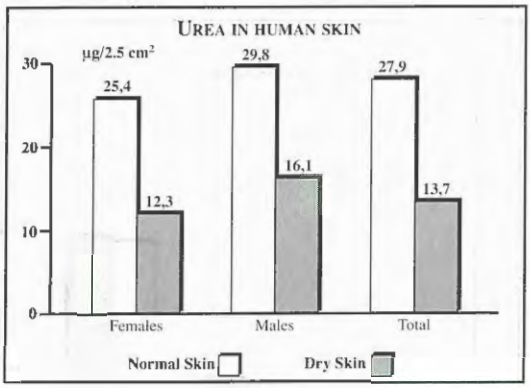

Fig. 1

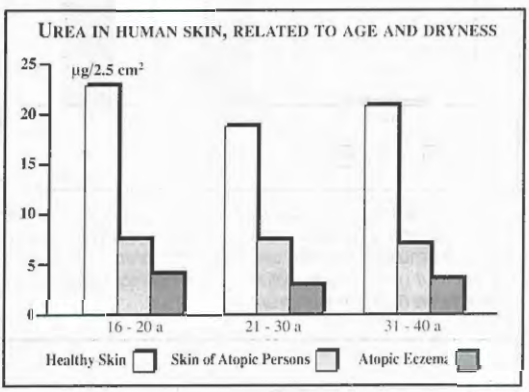

Fig. 2

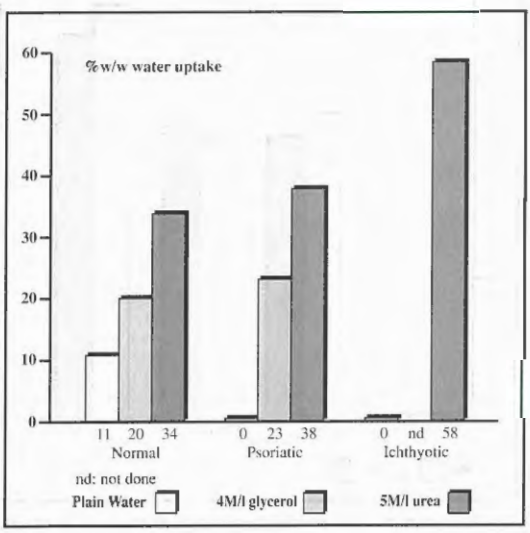

Fig. 3: Water uptake of normal, psoriatic, and ichthyotic stratum corneum following immersion in various solutions (Swanbeck, from 3).

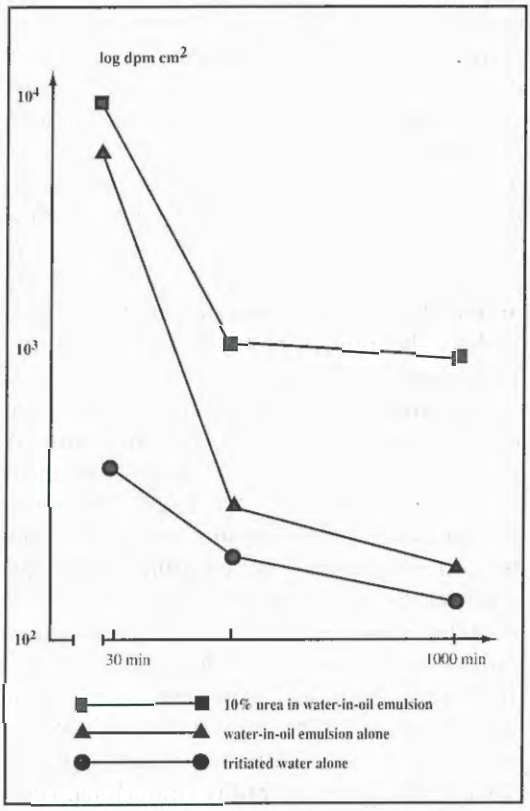

Fig. 4: The influence of urea on the water binding capacity of human stratum corneum (Wohlrab from 3).

- "antiinflammatory" action (antiproliferative, antiedematous, antipruritic).
- enzyme inhibiting action (mostly against proteases) and
- keratolytic action (true keratinolysis occurs under the influence of urea in a concentration of 40%).

The most important (and therapeutically most widely used) action of urea is its moisturizing capacity. By immersing stratum corneum from dry skin (psoriatic, ichthyotic) in 5 M urea/l, the uptake of water could be significantly increased. In these experiments, urea showed definitely higher activity than glycerol, a humectant which is widely used in cosmetic products. In another series of experiments, tritiated water was applied on the skin surface in the form of a water-in-oil

emulsion with 10% urea. The water retention, judged by how long tritiated water could be detected and in which amount, was significantly higher than in the controls with the vehicle alone. (Fig.4).

The application of urea containing emulsions decreases skin roughness due to the moisturizing action of urea; maybe, the desquamating action of urea contributes to this effect. In atopic skin, this decrease in roughness, judged by the replica method, was expecially pronunced. (Fig. 5, 6).

A vast number of experiments has been conducted to ascertain the moisturizing property of urea (figures 3, 4, 5, 6). Various methods have been used to probe this effect: corneometry, measurement of conductivity, evaporimetry and profilometry. By electron microscopy, a loosening of the layers within the stratum corneum could be demonstrated, indicating a moisturizing effect (2). Cf. Fig. 7, 8, 9.

In diseased skin, too, experimental investigations have been performed to demonstrate the moisturizing (and antieczematous) action of urea. In the European Study (Barcelona, Hamburg, Vienna) a statistically significant increase in moisture and a statistically significant decrease in TEWL occurred following a four week treatment of atopic eczema with a preparation containing 10% urea (4). Cf. Fig. 10.

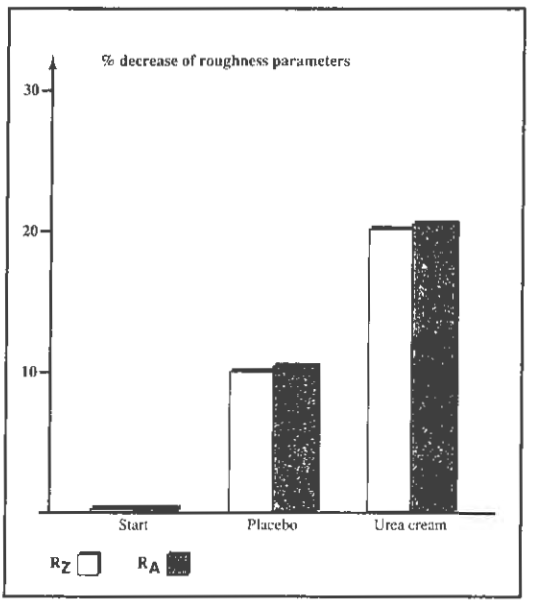

Fig. 5: Decrease of skin roughness parameters RZ and RA 60 min. after the application of a silicone-containing water-in-oil emulsion with 5% urea as compared to the vehicle without urea. Mean values of ten normal individuals were given (Puschmann from 3).

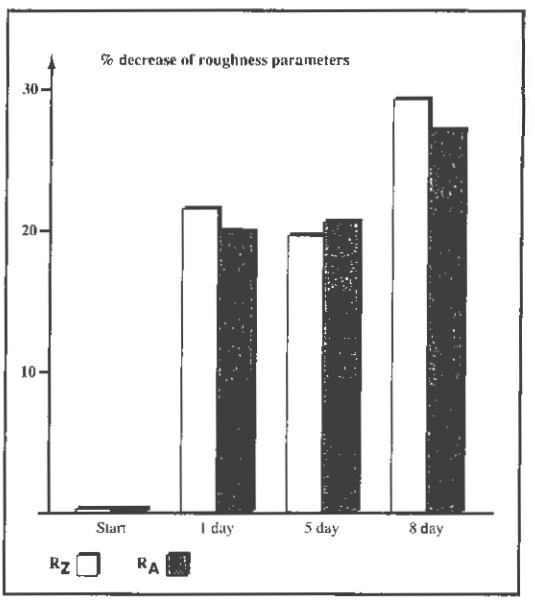

Fig. 6: Decrease of skin roughness parameters RZ and RA following the use of a silicone-containing water-in-oil emulsion with 5% urea. Mean values of 9 atopic individuals were given (Puschmann, from 3).

KERATOLYTIC AND DESQUAMATING PROPERTIES OF UREA

In concentrations up to 20%, urea exerts a concentration-depending desquamating action on the stratum corneum. By this effect, skin penetration is facilitated. Cf. Fig. 10, 11.

In a 40% concentration, urea has been shown to exert true keratinolytic properties. Nail plates in fungal diseases may thus be dissolved.

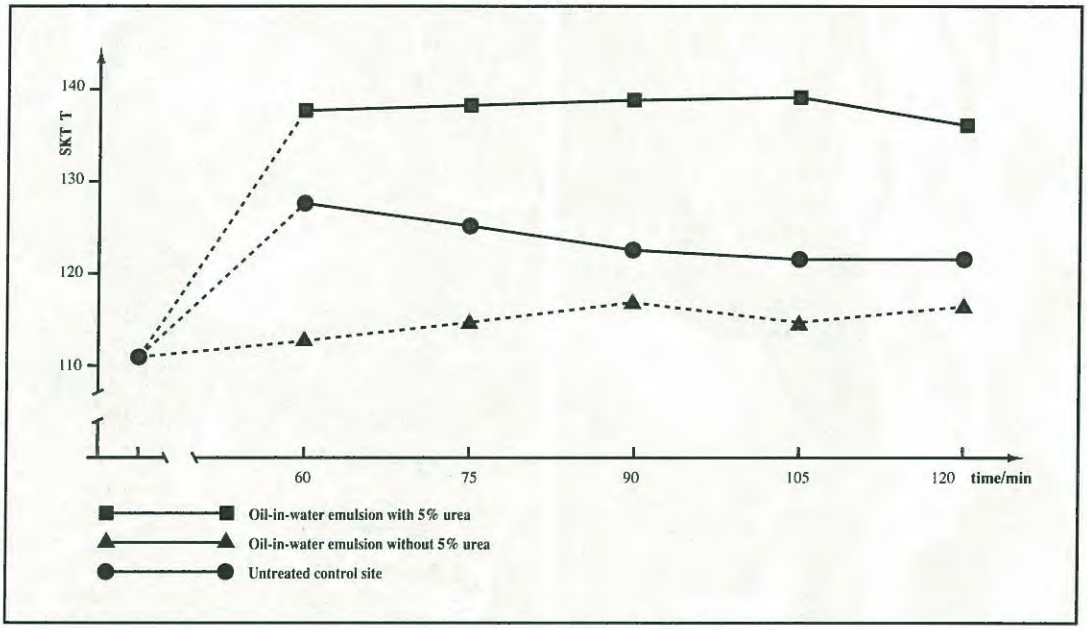

Fig. 7: Skin moisture after application of a silicone-containing oil-in-water emulsion with and without 5% urea, measurement by determination of the dielectric constant. Mean values of 35 healthy individuals were given. (Puschmann, from 3).

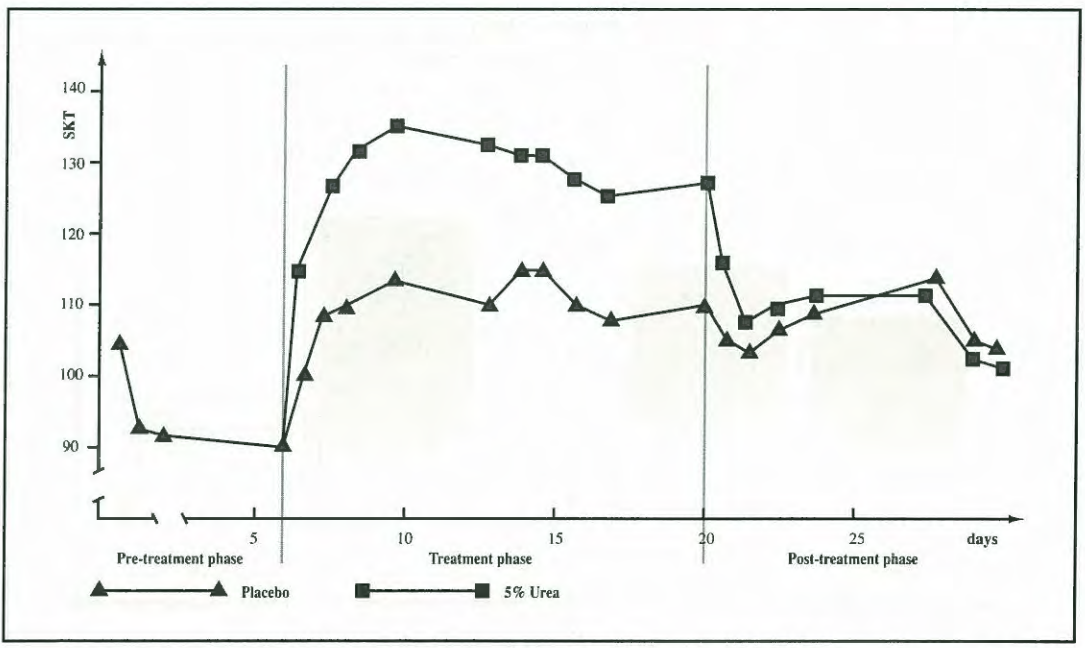

Fig. 8: Skin moisture following the application of a silicone-containing oil-in-water emulsion with and without 5% urea for two weeks. Mean values of 6 healthy individuals were given (Puschmann, from 3).

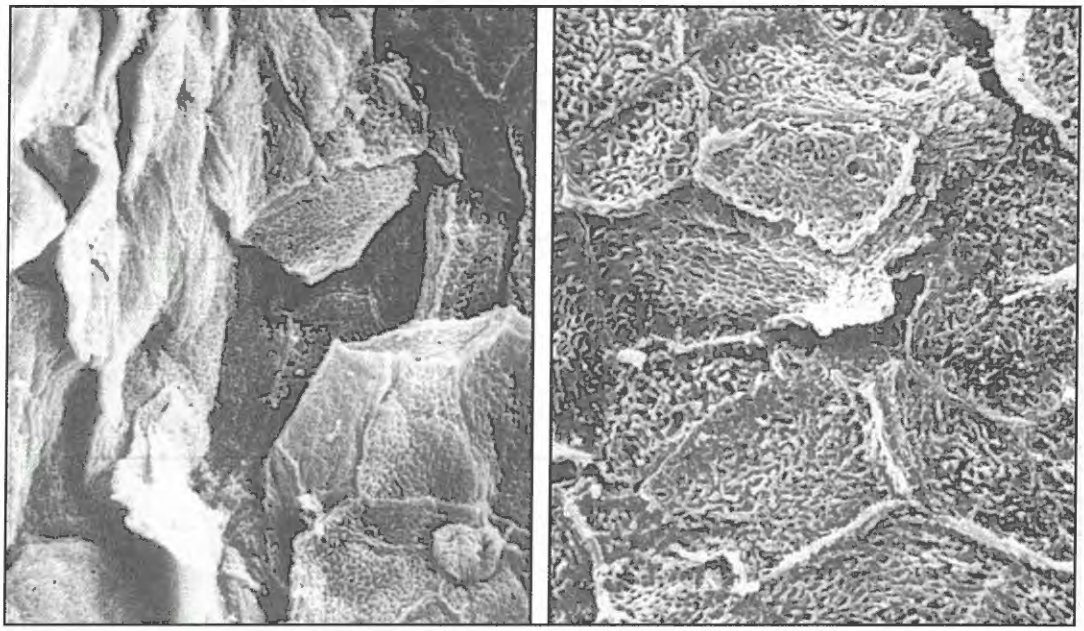

Fig. 9: Hyperkeratotic skin in chronic eczema before and after the application of urea 10% + salicylic acid 5% for 10 days. REM, material from biopsies, magnification 2.500 x.
From 2, with the permission of the autors Plugshaupt and Früh.

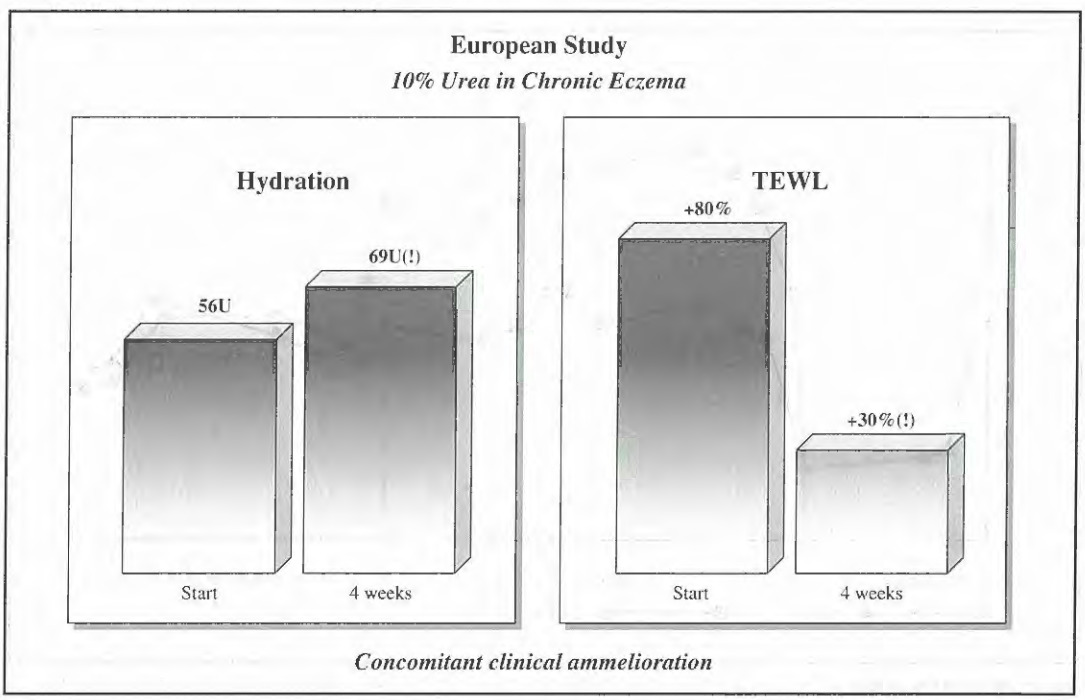

Fig. 10

ANTIINFLAMMATORY ACTIONS OF UREA

An antiproliferative effect of urea has been demonstrated in states of accelerated cellular turnover (e.g. psoriasis vulgaris) but no atrophogenic effect in normal skin could be observed.
The antiedematous action of urea is connected with its diuretic activity. In states of lymphostasis, a dramatic response can be evoked by topical applications of 10% urea.
The antipruritic activity of urea mainly is due to its moisturizing capacity. On the other hand, a directed influence of urea on those enzymatic activities which provoke itch could be demonstrated.

ANTIMICROBIAL ACTIVITY OF UREA

By its strong water binding capacity, urea inhibits the growth of microorganisms. Therefore, urea may be regarded as a preservative-saving substance.

UREA COMBINED WITH OTHER DRUGS

Via three mechanisms, urea increases the pharmacological activities of other simultaneously applied drugs:
- via its moisturizing capacity (increased absorption),
- via its desquamating properties (increased absorption) and
- via the formation of hydrophilic adducts (increased release from the preparation and increased uptake by the skin).

Lastly, synergistic effects much be mentioned between urea and some topically applied drugs with antiinflammatory or keratolytic action. An example is shown in Fig.9.

USES OF UREA IN DERMATOLOGY

Urea alone

Dry skin, old skin, photodamaged skin.
Atopic skin, (therapy and interval skin care).
Psoriasis vulgaris and other scaly dermatoses.
Ichthyosis and ichthyosiform skin conditions, hyperkeratoses, keratoses.
Onycholysis (40%!)

Urea in combinations

With glucocorticoids (hydrocortisone, halcinonid): atopic eczema, chronic dry eczema, Psoriasis vulgaris, all old, hyperkeratotic, scaly, resistant inflammatory skin lesions. (5-10% urea, 0,1-1% steroid).

With anthralin (17% urea + 0,5-2% anthralin): Psoriasis vulgaris, prolonged applications or short contact therapy.

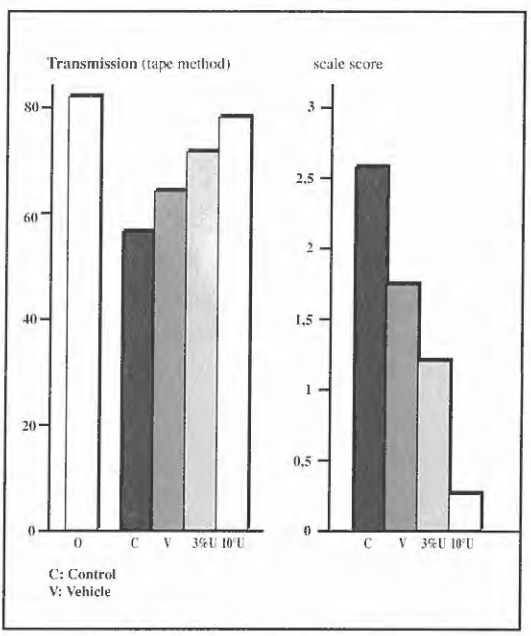

Fig. 11 - Desquamating action of urea

With polydocanol (5% urea + 3% polydocanol): atopic eczema, treatment and interval skin care.

With tretinoin (10% urea + 0,03% tretinoin): non-inflammatory, non-erythrodermic ichthyosis.

With salicylic acid (10% urea + 5% salicylic acid): stubborn hyperkeratosis, corns, eventually warts.

With bifonazole (40% urea + 1% bifonazole): onychomycosis.

Among the combinations of urea with other drugs, the preparations containing urea and a glucocorticoid have found widest application. Urea increases the biovailability of the steroid ("hydrocortisone develops into triamcinolone") but does not alter the incidence and severeness of undesirable effects.

REFERENCES

1. **Raab, W. (Editor) (1989)**, Harnstoff in der Dermatologie, *Hautarzt* **40**, Suppl. IX.
2. **Raab, W. (1993)**, Harnstoff in der Dermatologie, *TW Dermatologie* **23**: 257-269.
3. **Raab, W. (1990)**, Use of urea in cosmetology, *Cosmet. Toiletr.* **1054**: 97-102.
4. **Vilaplana, J. et al. (1994)**, Internationale, multizentrische Prüfung der Wirksamkeit und Verträglichkeit der externen Therapie chronischer Ekzeme mit einem 10% igen Harnstoffpräparat, *Akt. Dermat.* **20**: 227-231.

Author Address:

Univ. Prof. Dr. W. Raab
Walfischgasse 3
A - 1010 Vienna, Austria

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PRACTICAL TREATMENT OF DRY SKIN

W. Raab*
*Medical Director, Allergy Clinic "Innere Stadt" Vienna, Austria

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Key words: Dryness, Moisture, Ultraviolet, Age, Photodamage, Atopy.

Synopsis

Dry skin may result of exogenous or of endogenous factors. Exogenous factors may be excluded by informing the patient of his false behaviour. If endogenous factors are the cause of the dry skin state, reasonable measures of skin cleansing, skin care and skin protection should be considered.

Riassunto

La pelle secca può essere il risultato di fattori esogeni o endogeni. I fattori esogeni si possono eliminare facendo presente al paziente il suo comportamento errato. Nel caso invece in cui siano fattori endogeni la causa della secchezza della pelle, dovranno essere prese in considerazione misure adatte per la sua detersione, cura e protezione.

INTRODUCTION

Water is the softener of the horny layer and secures smoothness, elasticity and suppleness. Under normal conditions, water enters the horny layer via transdermal diffusion (TEWL). The evaporation of water from the skin surface is prevented by the action of the natural moistourizing factors (NMF). The water balance of the horny layer is depicted in figure 1, the composition of the NMF is shown in figure 2.
Dry skin is either caused by external factors or by endogenous changes.

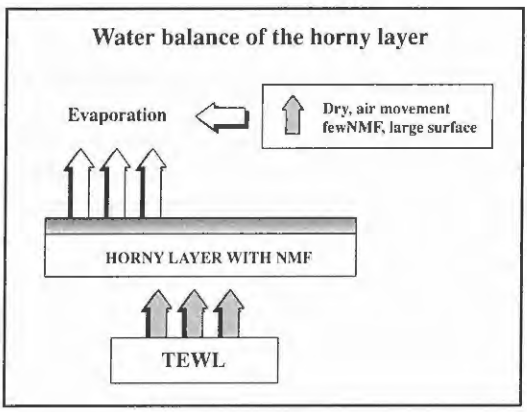

Fig. 1

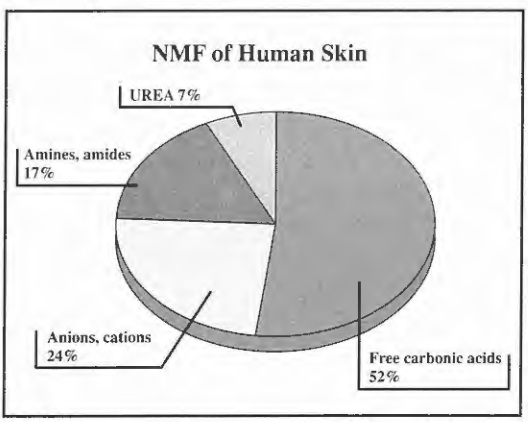

Fig. 2

EXTERNAL CAUSES OF DRY SKIN

Among the external causes of dry skin, abuse of soaps and detergents must be mentioned on the first hand.
But often a prolonged contact with water is the reason for skin dryness, as the NMF is dissolved and rinsed off.
For facial skin, prolonged exposure to a dry environment causes skin dryness, unless the water loss is prevented by the application of moisturizing skin care products.

ENDOGENOUS REASONS FOR DRY SKIN

There are three endogenous reasons for dry skin:
- constitution, especially atopy,
- genetic ageing and
- photodamage.

In atopy, the disturbed barrier function must be regarded as the main reason for skin dryness. Furthermore, there is almost always some inflammation present which causes skin dryness.
In senile skin, water loss is increased due to the numerous wrinkles and folds which increase the surface. Furthermore, water supply is decreased as general circulation is reduced and an atrophy of rete plugs occurs (reduced size of the contact area with the supplying dermal tissues).
In photodamage, the surface is even more increased than in senile skin as there are numerous wrinkles and deep folds (elastosis); solar keratoses provoke a further increase in water loss. - The mechanisms for endogenous dry skin are depicted in figure 3.

SIGNIFICANCE OF DRY SKIN

For the patient, dry skin causes an unpleasant "old and neglected" appearance. Steady application of skin care products is needed to counteract

itch and tension. From the dermatological point of view, dry skin often is the cause of eczemas and infections, especially in older persons.

REGIMEN IN DRY SKIN

Three important measures have to be taken to counteract dry skin and to prevent the disturbing consequences of this skin state:
- mild, non-alkaline skin cleansers,
- regular application of O/W or W/O-emulsions with moisturizing compounds, and
- skin protection against all kinds of environmental influences (ultraviolet, heat, cold).

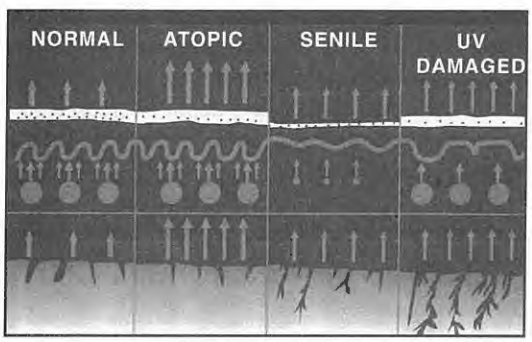

Fig. 3

CLEANSING MEASURES IN DRY SKIN

Skin cleansing may be effectuated by the application of
- natural (soaps) and synthetic detergents (syndets),
- adsorptive cleansing agents (e. g. oatmeal),
- desquamating agents ("exfoliation") and peeling agents,
- dermabrasive agents, e. g. polyethilene granules (cf. 2,5).

The best way of cleansing dry skin is the use of slightly acid, mild detergents. In cases of very sensitive skin, in atopy or in atrophic skin, the use of adsorptive complexes should be preferred. Oatmeal extracts, prepared for cleansing purposes, contain complexes consisting of polysaccharides, oligosaccharides, oils and proteins. That means that the complex exhibits lipophilic and hydrophilic groups on its surface thus permitting the removal of lipophilic and hydrophilic "dirt" (substances from the environment, decomposition products of sweat, sebum and topically applied preparations) by adsorption.
Figure 4 demonstrates the roughness of the skin surface following the use of soaps, detergents or adsorptive cleansing agents with smoothing additives.

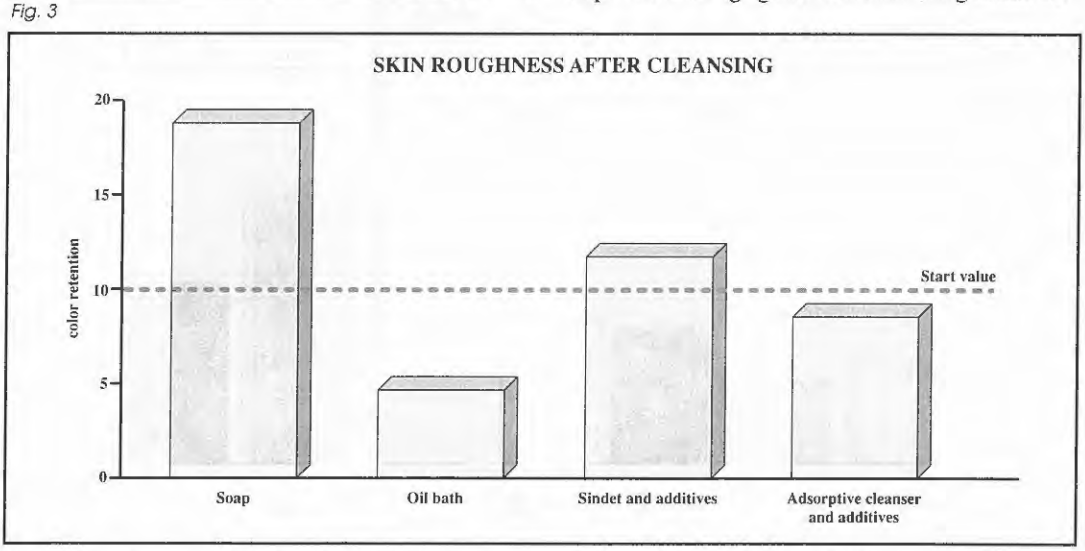

Fig. 4: Skin roughness after different forms of cleansing, determined by the colour retention method

SKIN HYDRATION

Skin hydration may be effectuated by the application of emollients (pseudo-occlusive effect closing small clefts on the surface of the stratum corneum), by the application of moisturing compounds, or by the increase of oxygen tension in the stratum corneum. The various possibilities of increasing hydration in the stratum corneum are depicted in figure 5.

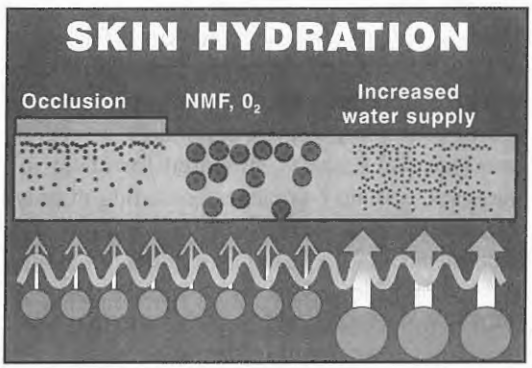

Fig. 5

Among the moisturizers, humectants (e. g. glycerol) and moisturizers have to be mentioned. Moisturizers such as mucopolysaccharides (hyaluronic acid) are preferable as they retain water even in a dry environment and offer it to the horny layer. Under such unfavorable conditions, humectants may even withdraw water from the skin (cf. figure 6).

The observation that oxygen tension in the horny layer decreases steadily with increasing age (figure 7) has provoked investigations of the changes in dry skin following the application of oxygen delivering preparations (1).

In fact, applications of a cream containing oxygen (4,5%) in 10% perfluordecaline significantly increases oxygen tension in the horny layer as compared to the vehicle (6,7). Cf. figure 8. Parallel to the increase in oxygen tension an increase in moisture was noted (figure 9). Furthermore, wrinkle number and depth decreased under the influence of an oxygen delivering cream (figure 10).

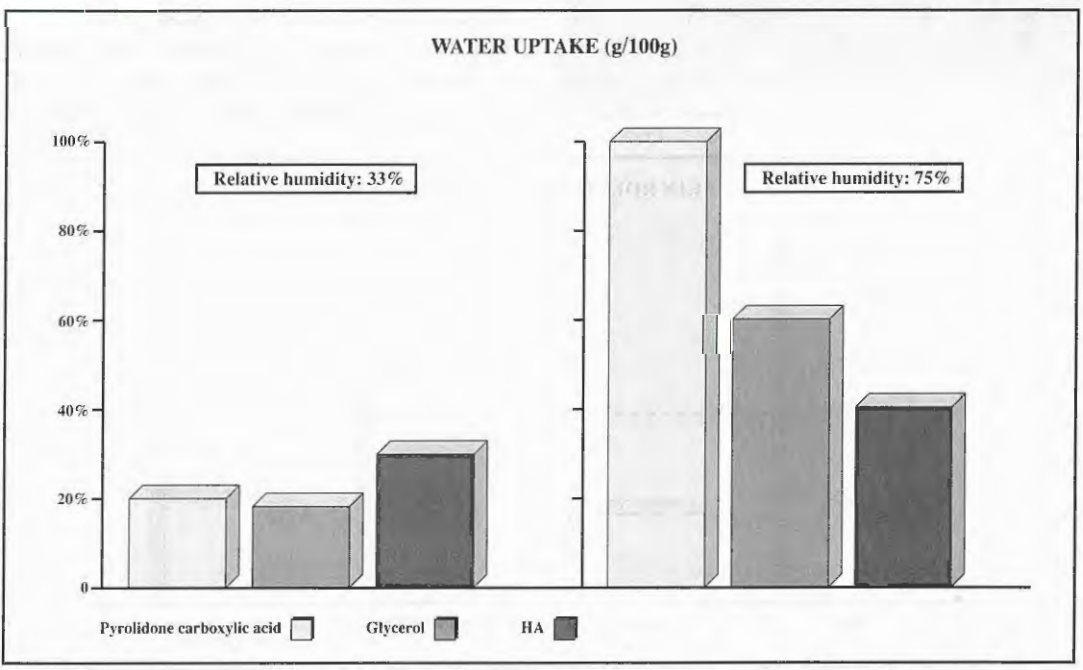

Fig. 6: Water uptake by different moisturizing compounds, hmuectants and true moisturizers depending upon the humidity in the environment

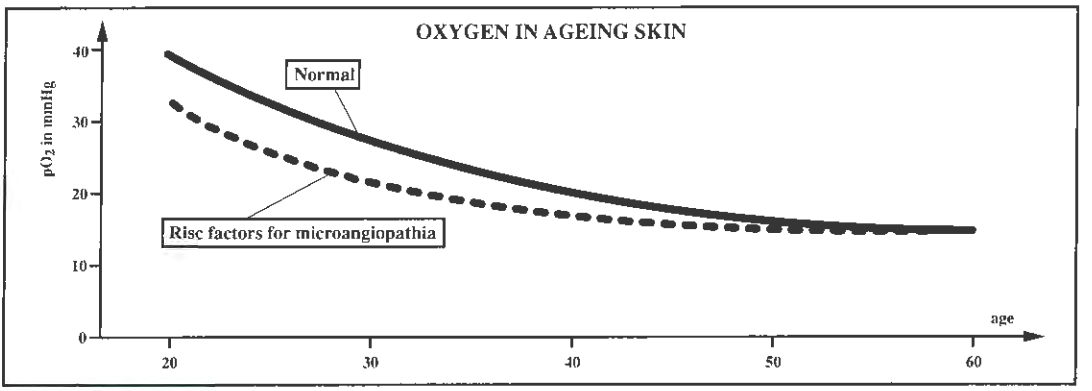

Fig. 7: Oxygen pressure in the skin, depending upon age. Note the reduced oxygen pressure in persons with risk factors for micorangiopathis such as cigarette abuse

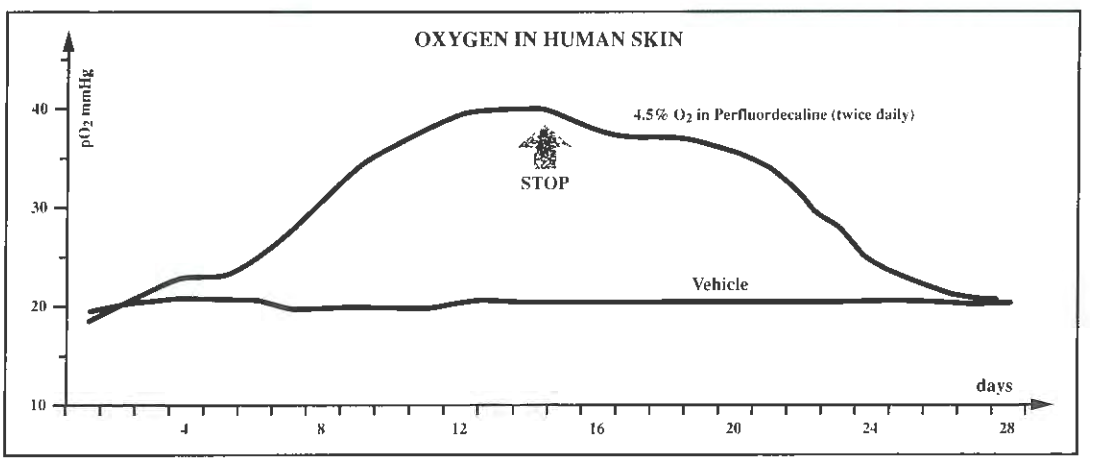

Fig. 8

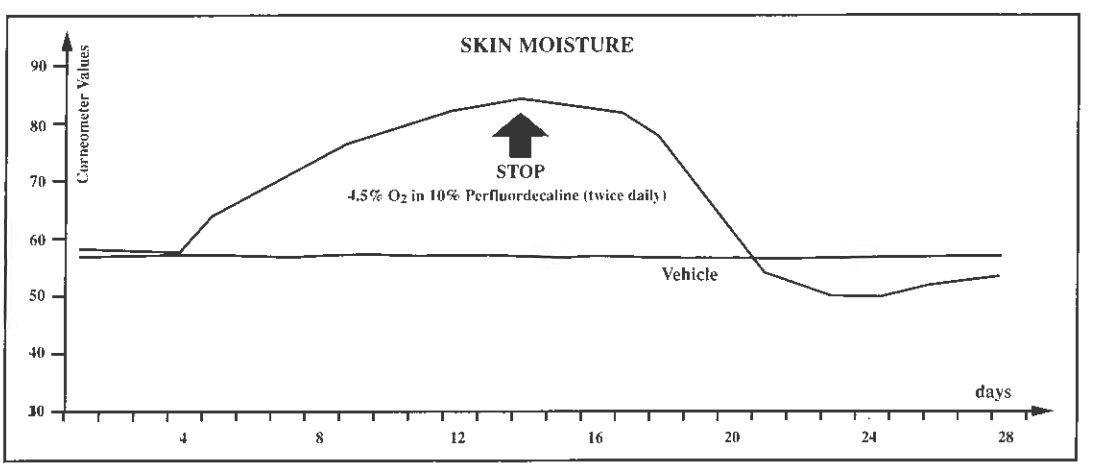

Fig. 9

SKIN PROTECTION

Most forms of environmental stress increase skin dryness. Therefore, protection against physical influences or, even better, avoivance of those plays an important role in treatment and prophylaxis of dry skin states. Ultraviolet irradiation, UVB as well as UVA, provokes skin dryness due to alterations of the epidermis and the dermis over the years (3, 4). As it is non realistic to try to keep people out of the sun, doctors should advise their patients to apply sun protecting creams in a reasonable manner.

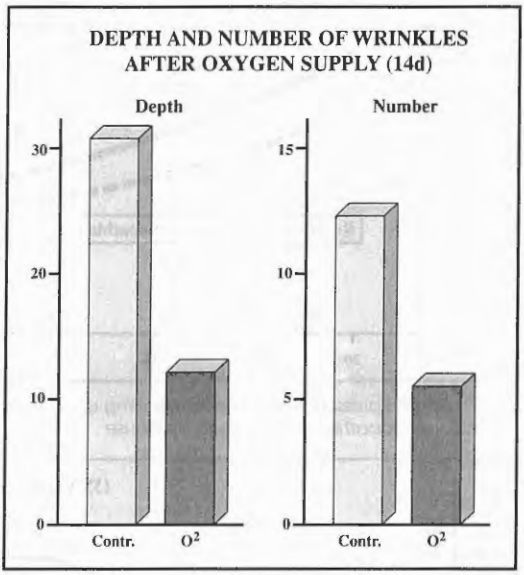

Fig. 10

REFERENCES

1. **Artmann, C. et al.(1993)**, Sauerstoff in der Haut. Ein neuer Parameter der Hautalterung, *SÖFW Journal 1993* **15**, 1-5.
2. **Raab, W. (1990)**, Skin cleansing in health and disease, *Wien. Med. Wschr.* **140**, Suppl. 108.
3. **Raab, W.**, Zeitalterung und Umweltalterung der Haut, *hautnah 6/1994 Dermatologie*, 589-594.
4. **Raab, W. (1994)**, Reinigung, Pflege und Schutz der Altershaut, *Handbuch der Gerontologie. Bd.* **7**, 365-388, *Fischer, Stuttgart, Jena, New York.*
5. **Raab, W. und U. Kindl (1997)**, Pflegekosmetik. *Fischer und Govi, Stuttgart und Eschborn (2nd ed.).*
6. **Stanzl, K. et al.(1993)**, A new cosmetic product containing molecular oxygen, *Eurocosmetics 1993* **1**, 1-6
7. **Zastrow, L. et al.**, The effectiveness of molecular oxygen in cosmetic formulations, *In press.*

Author Address:

W. P. Raab, M. D., FAAD
Professor in Dermatology
3, Walfischgasse
A-1010 Vienna, Austria

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A COMPARATIVE DOUBLE-BLIND WITHIN SUBJECT STUDY OF THE EFFICACY AND TOLERABILITY OF TWO DIFFERENT DERIVATIVES OF VITAMIN A ON SKIN THICKNESS AND ELASTICITY: RETINOIC ACID AND CONJUGATED RETINYL PALMITATE

Erling Thom, Ph.D.*
*Medstat Research Ltd, Lillestrøm, Norway

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Key words: Retinyl palmitate, Retinoic acid, Comparative study, Skin elasticity, Skin thickness.

Synopsis

A randomized comparative double-blind within subject study of topical administration of two different Vitamin A preparations - conjugated retinyl palmitate, RP (0,2%) and retinoic acid, RA (0.025%) for 3 months in 20 females caused significant changes in skin thickness and elasticity as well as in the participants own judgment of skin improvement using visual analogue scales.
The results indicate that both galenical formulations exert a comparable effect, while the tolerability of the RP formulation was significantly better. It might be of great importance for the efficacy of the RP cream that the compound is conjugated and thus having a better skin biovalability than unconjugated RP has. Whether the clinial effect is due to metabolism of RP to RA or retinol in the skin can not be answered by this study, but should be subject to further percutaneous absorption studies. Other studies indicate that the mechanism of action for RP creams might be due to biotransformation to retinol rather than to RA.

Riassunto

Uno studio randomizzato a doppio-cieco è stato condotto per tre mesi su 20 donne utilizzando due diversi preparati a base di vitamina A: retinil palmitato coniugato (RP 0,2%) ed acido retinoico (RA 0.025%). Le due formulazioni hanno provocato cambiamenti significativi sia nello spessore che nella elasticità della pelle .
I risultati indicano che entrambe le formulazioni galeniche svolgono un'attività paragonabile, ma la tollerabilità della formulazione RP è stata significativamente maggiore. Potrebbe essere di grande importanza per l'efficacia della formulazione RP il fatto che la miscela sia coniugata ed abbia perciò una biodisponibilità cutanea migliore rispetto ad un RP non coniugato. Questo studio non ha potuto rispondere al quesito se l'effetto clinico sia dovuto al metabolismo dell'RP che si trasforma in RA o in retinolo nella pelle. Questo argomento dovrebbe essere oggetto di ulteriori studi sull'assorbimento percutaneo. Altri studi indicano che il meccanismo d'azione delle creme RP può essere dovuto alla biotrasformazione in retinolo, piuttosto che in RA.

INTRODUCTION

Data has previously been reported on the efficacy and tolerability of a skin cream containing conjugated Retinyl palmitate (RP) (1,2). The aims of these two studies were to investigate the effect of the cream on skin thickness and elasticity and in addition to study the duration of the effect after treatment was stopped. From these studies we have clearly documented that use of conjugated RP results in an increase in skin thickness and an improvement in skin elasticity. These observations have been confirmed by others (3,4) using other measuring techniques.

RP is a widely used ingredient in cosmetic formulations. Because it is the most stable of the available vitamin A esters it can be directly incorporated into an anhydrous base or the oil base of a cosmetic cream or lotion. RP is lipophilic and photostable. Ofter products containing RP are advertised as having benefical effects on the appearance of the skin. A great number of products containing RP are marketed. Previous studies suggest that enzymes present in the skin metabolize RP during skin absorption. Esterase activity hydrolyzes RP to retinol (Vitamin A), wich is oxidized in many tissues to Retinoic acid (RA) primarly by alcohol dehydrogenase. RP can therefore be classified as a prodrug where the inactive RP is transformed to active substances by metabolic biotransformation reactions in the skin.

Recently a number of studies have been carried out with RA creams showing that this compound has a positive effect on photo-aged skin (5-8). Preparations containing RA have been registered in some countries as ethical drugs for treatment of aging skin. However, one main drawback with this type of treatment is that a number of patients (4-10%) develop soreness in and miscolouring (redness) of the skin (6).

As mentioned above RA has been convincingly documented as having an effect on the treatment of the aging skin and retinol is also a compound with know pharmacological activity (9). Previous studies have shown the formation of all-trans-retinoic acids after topical application of all-trans-retinol in vivo in hairless mouse skin (10). Recently, however, a study showed that retinol was the only detectable metabolite following administration of RP both in guinea pig and human skin, while no retinoic acid was detectable (11). About 30 and 18% of topically applied RA were absorbed from an acetone vehicle by hairless guinea pig and human skin, respectively. Less than 1% of the applied dose of RP diffused from the skin into the receptor fluid. In human skin, 44% of the absorbed RP was hudrolyzed to retinol.

An essential prerequisite for an optimal penetration of the lipohilic RP into the skin is to modify the solublity of the compound by the use of tweens (12,13). The producer of the RP preparation used in this study has developed a process where RP in conjugated with a complex polysaccharide thereby making the compound water soluble. In this way the penetration of RP through the skin and into the diffusion cell receptor fluid is enhanced. The same technique has been used succesfully to enhance the bioavailability of drug substances both administered perorally as well as topically (14).

Based on the abovementioned information and our previous experiences with conjugated RP, we decided to carry out a clinical comparison on skin thickness and skin elasticity following treatment with an cream containing either RA or conjugated RP in order to gain an indirected impression of the bioequivalency of these two substances.

MATERIAL AND METHODS

The study was carried out as a randomized double-blind study in 20 females with each participant using both formulations one on the right and the other the left volar (protected) part of the forearm, respectively. The administration of the formulations was randomized, such that half of the participants used formulation A on the

right arm and formulation B on the left arm and vice a versa for the other women. The total treatment period was 3 months and administration was b.i.d. (in the morning and evening) during the study period. The study was carried out in accordance with the Declaration of Helsinki.

The investigational formulations

The two formulations used in this study were: A conjugated RP cream made by Pedersens Laboratorium, Vejle, Denmark, containing 0.2% RP and a cream containing 0.025% RA made with the same cosmetic properties and apperance as the conjugated RP cream. Formulation A is identical to the marketed preparations Sincera®, Demelle®, Luscinia® and Rebilt®. The investigational products were packed in identical packages in order to keep the study blinded.

Measurements of skin thickness and skin elasticity

The measurements of skin thickness and skin elasticity were performed by ultrasound using Dermascan A and Dermaflex instruments, respectively (Cortex Inc. Aarhus, Denmark). Measurements were carried out at baseline, after 1 month and after 3 months, by the same person (ET) on all three 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 evaluations.

Self-evaluation by the partecipant

At the same time as each ultrasound measures was made, participants made a self evaluation of skin quality using visual analogue scales of 10 cm with endpoints of "no change" and "very pronunced change". Subjects were asked to score the global change in skin quality by placing a mark on the line between the endpoints. The distance from the zero point ("no change") 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. Mean was used for estimation of continous and near continous variables, and Student procedure was used for construction of confidence interval of the mean. The one-sample t-test was used analysing change over time within groups. Analysis of cavariance and two-sample t-test were used to compare arms with regard to continous variables.

RESULTS

20 females aged between 40 and 60 years (mean 51.4 yrs) were included in the study and all participants were compliant with the protocol. All participants gave their informed consent to take part in the study after having received written and verbal information about the study.

Efficacy parameters, skin thickness and elasticity

The results from the skin thickness measurements are shown in Table I. Formulation A resulted in a average increase in skin thickness of 31% compared with 33% for formulation B. This increase in skin thisckness was significant ($p<0.01$) for both formulations, while the difference between the two formulations was not significantly different.

In Table II the viscoelastic properties of the skin following administration of formulations A and B, respectively, are presented. The results show that formulation A improved the elasticity by 19% on average, compared with 20% for B.

Both formulations improved the elasticity of the skin significantly ($p<0.01$), but again the difference in elasticity improvement between the two formulations was not significant.

Efficacy parameters, self-evaluation by use of VAS

The VAS results are shown in Table III.
A significant improvement ($p<0.01$) in skin quality was reported for both forearms. The difference in skin improvement between the two formulations is, however, not significant.

Table I
Changes in skin thickness (mm) after administration of conjugated RP (A) and RA (B) creams for 3 months, respectively (N=20)

	Formulation	Initially	After 1 month	After 3 months
A	Mean (SD)	0.90 (0.12)	1.01 (0.17)	1.18 (0.15)
	Range	0.71-1.24	0.74-1.27	0.90-1.34
B	Mean (SD)	0.88 (0.15)	1.02 (0.15)	1.17 (0.17)
	Range	0.70-1.25	0.76-1.30	0.90-1.37

Table II
Changes in skin elasticity (%) after administration of conjugated RP (A) and RA (B) creams for 3 months (N=20)

	Formulation	Initially	After 1 month	After 3 months
A	Mean (SD)	59.3 (7.9)	65.2 (8.2)	70.6 (8.4)
	Range	44.3-81.0	50.2-81.2	51.3-85.0
B	Mean (SD)	60.0 (7.5)	67.2 (8.0)	71.2 (8.6)
	Range	45.4-80.8	46.4-81.6	52.4-86.0

Table III
Changes in VAS scores (cm) after administration of conjugated RP (A) and RA (B) creams for 3 months (N=20)

Formulation		After 1 month	After 3 months
A	Mean (SD)	1.8 (1.2)	6.3 (1.6)
	Range	0.0-3.5	1.0-8.3
B	Mean (SD)	1.9 (1.5)	6.5 (1.8)
	Range	0.3-3.4	1.2-8.6

Tolerability

At each visit subjects were asked if they had had any problems and/or side-effects with the treatments they had used.

Seven of the subjects reported skin soreness after using the RA formulations and 2 of these also reported a considerable redness in the skin 1/2-1 hour after application. The reported side-effects are, however, transient and none of the subjects stopped the treatment due to the side-effects. One subject reported redness of the skin following administration of the conjugated RP formulation.

The tolerability was significantly in favour of formulation A, the conjugated RP formulation. This is also revealed in the preference choice from the users (see below).

Preference choise from the subjects

On completion, subjects were asked to give a preference for one of the two creams they had used taking into account the effect, the tolerability and the cosmetic properties of the creams.

Thirteen subjects prefered the conjugated RP cream, formulation A, while 4 prefered the RA cream, and 3 subjects had no preference. The difference in preference is significantly in favour of the conjugated RP formulation.

DISCUSSION

In recent years knowledge of the effect and metabolism of vitamin A derivatives in the human skin (15,16) has been accumulating.

The results from the present study indicate that both, the 0.025% RA cream and a 0.2% conjugated RP cream bring about a comparable effect in skin composition and morphometry. No significant differences could be detected either in skin thickness or elasticity improvement between the two creams. As the tolerability of the conjugated RP is significantly better than the RA, the conjugated RP may represent a valuable alternative to RA.

As have been stressed by other investigators (3,4) it is of utmost importance that the RP is in a form allowing skin penetration. In a previous comparative study we reported a significant difference between conjugated and non-conjugated RP in the effect on the skin parameters (1). The change in solubility of the RP is probably essential for making the ester available in sufficient concentration.

To our knowledge no percutaneous absorption and metabolism studies have been carried out with conjugated RP. Such studies are needed in order to explain the mechanism of action behind the effect seen in skin parameters measured. The minimal conversion of retinol to RA may not be relevant to the application of formulations containing RP to the human skin.

Both retinol and RA can have pharmacological effects on human skin. Retinol is about 50% as potent as RA in inducing epidermal hyperplasia in the hairless mouse (11).

It has, however, been shown that retinol is formed in hairless guinea pig and human skin after topical application of RP, but if further metabolism to R occurs, it is to small to detect. Any biological response of skin treated with retinyl palmitate formulations may be due to ester hydrolysis of the parent compound to retinol. The use of RP in cosmetic formulations may result in a significantly improved delivery of retinol into the skin.

REFERENCES

1. **Thom E (1993)**, Skin treatment with two different galenical formulations of retinyl palmitate in humans, *J.Appl. Cosmetol.* **11**, 71-76.
2. **Thom E (1994)**, Long-term effects after topical application of active retinyl palmitate, *J.Appl. Cosmetol.* **12**, 45-50.
3. **Counts DF, Skreko, Mcbee J, Wich G (1988)**, The effect of retinyl palmitate on skin composition and morphometry, *J.Soc.Cosmet.Chem.* **39**, 235-240.
4. **Fthenakis CG, Maes DH, Smith WP (1991)**, In vitro assessment of skin elasticity using ballistometry, *J.Soc.Cosmet.Chem.* **42**, 211-222.
5. **Kligman AM, Grove GL, Hirose R, Leyden JJ (1986)**, Topical tretinoin for photoaged skin, *J.Am.Acad.Dermatol.* **15**, 836-859.
6. **Weiss KS, Ellis CN, Headington JT, Hamilton TA, Vorhess KK (1988)**, Topical tretinoin improves photoaged skin: a double-blind vehicle controlled study, *JAMA* **259**,527-532.
7. **Bhawan J, Gonzales-Serva A, Nehal K, Labadie R, Lufrano, Thorne G et al. (1991)**, Effect of tretinoin on photodamaged skin, *Arch.Dermatol.* **127**, 666-672.
8. **Rafal FS, Griffiths CEM, Cherie MRCP, Ditre M, Finkel LJ, Hamilton TA et al. (1992)**, Topical tretinoin (retinoic acid) treatment for liver spots associated with photodamage, *New Engl J Med.* **6**, 368-374.
9. **Gilchrest BA (1992)**, Retinoid pharmacology and the skin. In H. Mukhtar (ed.) Pharmacology of the skin, *CRC Press, Boca Raton*, 167-181.
10. **Connor MJ, Smit MH (1987)**, The formation of all-trans-retinoic acid from all-trans-retinol in hairless mouse skin, *Biochem Pharmacol* **36**, 919-924.
11. **Boehnlein J, Sakr A, Lichtin Leon J, Bronaugh RL (1994)**, Characterization of esterase and alcohol dehydrogenase activity in skin. Metabolism of retinyl palmitate to retinol (Vitamin A) during percutaneous absorption, *Pharm Res* **8**, 1155-1159.
12. **Jarrett A, Jackson RJ (1980)**, The effect of vitamin A on the skin and istrole as a cosmetic agent. *Abstract 11th International IFSCC Congress Research and Technology. Venice 23-26 Sept.*
13. **Spearman RIC, Jarret A (1974)**, Biological comparison of isomers and chemical forms of vitamin A (retinol), *Br J Dermatol.* **90**, 553-560.
14. **Paginton JS (1987)**, Beta-cyclodextrin: the success of molecular inclusion, *Chemistry in Britain* **23**, 455-458.
15. **Wolf G (1996)**, A history of vitamin A and retinoids, *FASEB J* **10**, 1102-1104.
16. **Fisher GJ, Voorhees JJ (1996)**, Molecular mechanisms of retinoid actions in skin, *FASEB J* **10**, 1002-1013

Author Address:

Erling Thom, Ph.D.
P.O. Box 210
N-2001, Lillestrøm, Norway
*Fax: (+47)*63.81.92.50

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A NEW COSMECEUTICAL FOR THE "ORANGE PEEL" SKIN

P. Morganti*, S.D. Randazzo, G.Fabrizi*** ond C. Bruno******

* President/Director, R & D Mavi Sud S.r.l., Viale dell'Industria 1, 04011 Aprilia (LT), Italy.
Department of Dermatology, Dermatologists Training School, II University of Naples, Italy.

** Department of Dermatology, University of Catania, Italy.

*** Department of Dermatology, Cathalic University of Rome, Italy.

**** Physiology Institute, University of Urbino, Italy.

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Key words: TCDS, Cellulitis, Orange-peel skin, Skin hydration, TEWL, 3C System®, Dermoscan® C.

Synopsis

"Cellulitis" represents an unaestheticism capable of modifying the harmony of the figure referring to modern rules. The skin opaque, arid, scabrous and painful to the touch is characterized by a rugged appearence known as "orange peel skin".
The present study was designed to evaluate the activity of a new Transdermal Cosmetic Delivery System (TCDS) on the anterior lateral surface of the thighs of 30 female volunteers (aged 18-30) presenting cutaneous signs of "cellulitis" of different degrees of intensity, treated each night for 21 days with this special patch in a double blind study.
Before and after the study the thickness of the cutaneous tissue was controlled by the Dermoscan C® (Denmark, version 3 at 20-MHz) and skin hydration and TEWL by 3C System® (Rome, Italy). The TCDS caused a both a decrease of skin thickness, and of the cellulitic layer thickness and a contemporary high increase of skin hydration and TEWL ($p<0.005$).
No adverse reactions were observed. The obtained results seem to prove the validity of this new cosmeceutical device for the treatment of the so called "cellulitis".

Riassunto

La "cellulite" rappresenta un inestetismo capace di modificare l'armonia della figura secondo i parametri moderni. La pelle opaca, arida, scabra e dolorante al tatto è caratterizzata da un aspetto ruvido noto come "pelle a buccia d'arancia".
Con il presente studio si è voluta valutare l'attività di un nuovo cerotto transdermico denominato Transdermal Cosmetic Delivery System (TCDS). La valutazione é stata effettuata sulla superficie antero-laterale delle coscie di 30 donne volontarie (di età compresa tra i 18 e i 30 anni), che presentavano segni cutanei di una cellulite con diversi gradi di intensità, trattate ogni notte per 21 giorni

con questo speciale cerotto in uno studio a doppio cieco.
Lo spessore della pelle è stato controllato prima e dopo lo studio tramite il Dermoscan C® (Denmark, versione 3 a 20 MHz), l'idratazione della pelle e la TEWL per mezzo del 3C System®. Il TCDS ha provocato una diminuzione dello spessore della pelle, una diminuzione dello spessore dello strato di cellulite ed un contemporaneo aumento sia dell'idratazione cutanea globale ($p<0.005$) da addebitarsi essenzialmente all'attività occlusiva esercitata dal cerotto, che del TEWL.
Non sono state rilevate reazioni collaterali.
I risultati ottenuti sembrano provare la validità di questo nuovo mezzo cosmetico per il trattamento della cosiddetta "cellulite".

INTRODUCTION

"Cellulitis" represents an unaestheticism capable of modifying the harmony of the figure referring to modern rules. The skin opaque, arid, scabrous and painful to the touch is characterized by a rugged appearence known as "orange peel" skin (1-3).

STUDY DESIGN

The present study was designed to evaluate the activity of a new Transdermal Cosmetic Delivery System (TCDS) on the anterior lateral surface of the thighs of 30 female volunteers (aged 18-30) presenting cutaneous signs of cellulitis at different degrees of intensity, localized on the anterior-lateral surface of thighs, treated each night for 21 days with this special patch (4x4 cm) in a double blind study.
In order to eliminate possible external influences 15 women were randomly treated on the right or on tbe left thigh with both the active-patches or with the vehicle-patches (control), the other side serving as untreated control. In this way both the active and the control patches were indifferently applied both on the right and the left tigh.
The selected subjects were not taking drugs for systemic administration or anti-cellulitis topic products and, moreover, had not undergone specific diets before and during the clinical trial's period.

MATERIALS AND CHEMICALS

1. 4x4 cm patch with acrylic base (vehicle-control B);
2. 4x4 cm patch enriched with centella asiatica and fucus vesicolosus extracts so that each plaster contains a total of 10 mg active compounds, 0.2 mg/cm^2 of which are centella triterpens (4-9).

INSTRUMENTAL MEASUREMENTS

Ultrasound-B-mode imaging

This two-dimensional B-scan procedure gives ultrasounds single lines (A-Scan lines) corresponding to a cross-sectional image of the skin. In fact when a beam of ultrasounds passes through the different layers of the skin, different echoes are produced depending on the acoustic characteristics of the examined areas ; those echoes are recorded by the instrument and visualized on the screen as peaks (A-Scan). By measuring the distance among the peaks, it is possible to determine the thickness of the different structural components of the skin (10).
Before and after the study the thickness of the subcutaneous tissue was controlled on 3 points of skin surface for both the tbighs by the Dermoscan C®, (Denmark) version 3, at 20-MHz. Skin hydration and TEWL were controlled by 3C System®, (Rome, Italy) which was previously used by our team (11).

3C System®

This computerized system through the capacitative resistance permits a simple and quick control of surface lipids, skin hydration and TEWL. The 3C System® collects up to 10/15 measure-

3C System®

ments over 25 seconds sampling period and records the mean value automatically standardizing the environmental conditions (RH=50%, T=22°C). Measurements were performed on 1st day (baseline) and after 7, 14, 21, 28, 35 days. TEWL is expressed as the amount of water evaporated per unit of surface in 1 hour gr/m^2/h and the system collects up 10/15 measurements over 25 second sampling period and record the mean value automatically (11).

Statistical analysis

Differences in TEWL, skin hydration and subcutaneous tissue thickness were examined for statistical significance using the non-parametric Friedman test. When the Friedman test revealed significant values between the treatments, multiple comparisons of all groups were conducted by the Wilcoxon-Wilcox tests.

RESULTS

The obtained results are reported in Fig. 1, 2 and 3.

COMMENTS

As already proven by our group and by other authors the scan-ultrasound tecnique seems to be the best methodology feasible for measuring the variations of the cellulitic layers during an anti-cellulitis treatment (12-18).

As it can be seen on Fig. 1 patch application on day 21 highlights a remarkable change in the thickness of the cutaneous layer ($p<0.005$) before and after the treatment. This change is surely due to the activity carried out by the used active ingredients, since the sole vehicle has proved to be ineffective.

It is also interesting to point out that the patch-

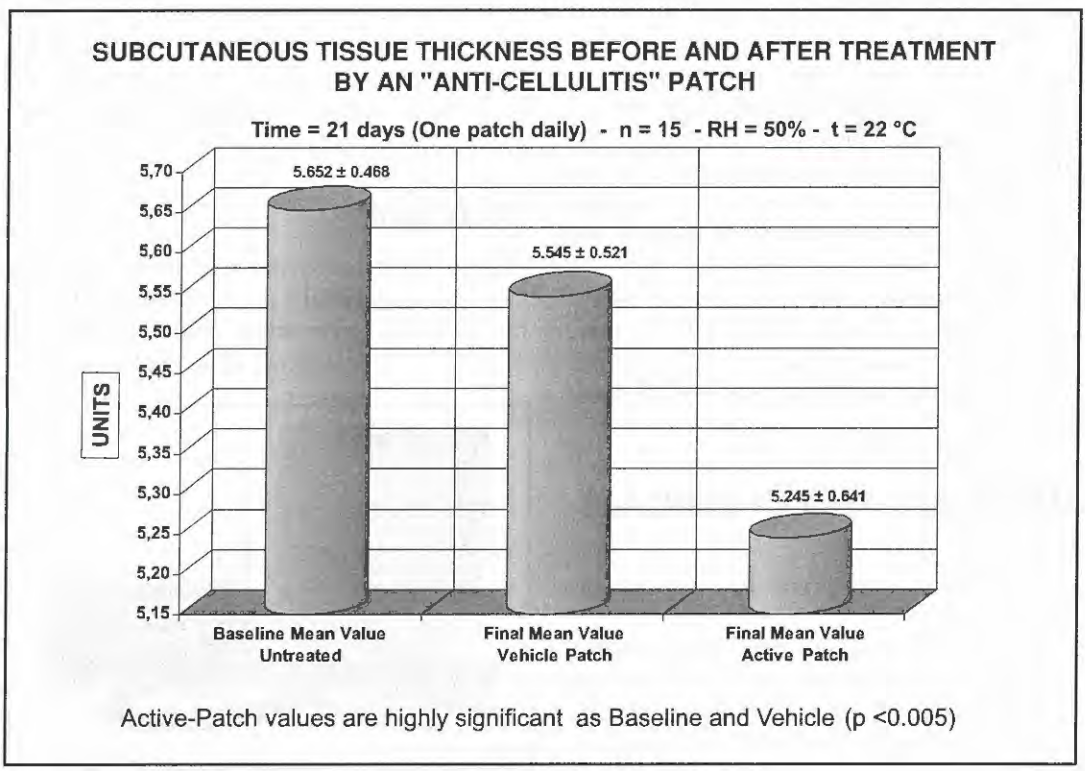

Fig. 1

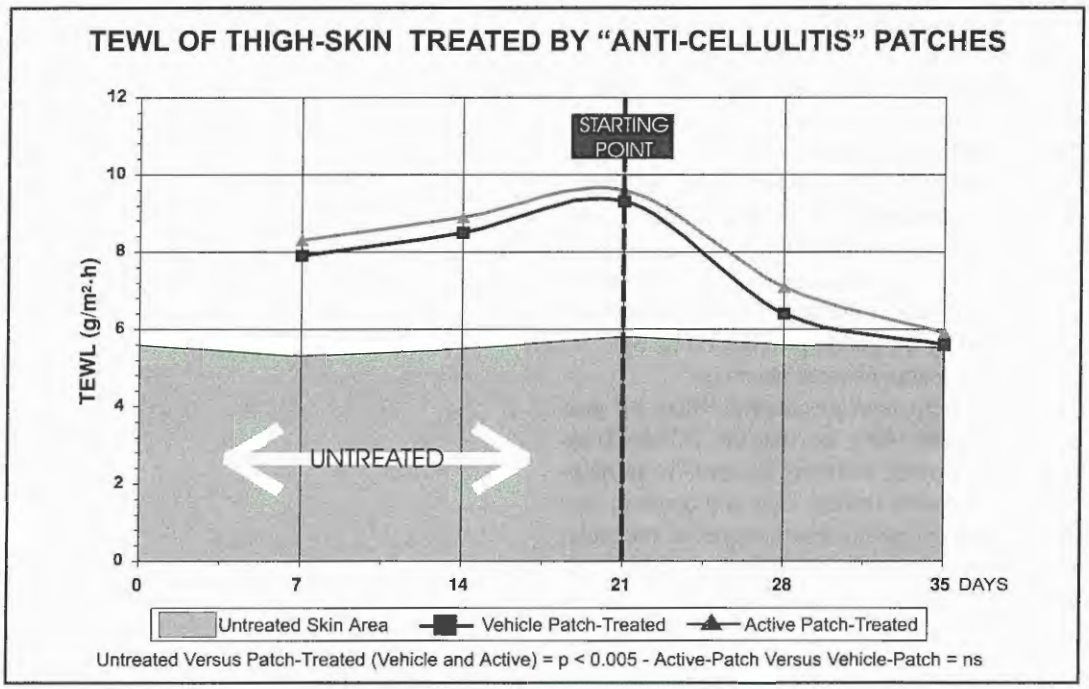
TEWL OF THIGH-SKIN TREATED BY "ANTI-CELLULITIS" PATCHES
TEWL (g/m².h)
12
10
8
6
4
2
0
STARTING POINT
UNTREATED
0
7
14
21
28
35 DAYS
Untreated Skin Area
Vehicle Patch-Treated
Active Patch-Treated
Untreated Versus Patch-Treated (Vehicle and Active) = p < 0.005 - Active-Patch Versus Vehicle-Patch = ns

Fig. 2

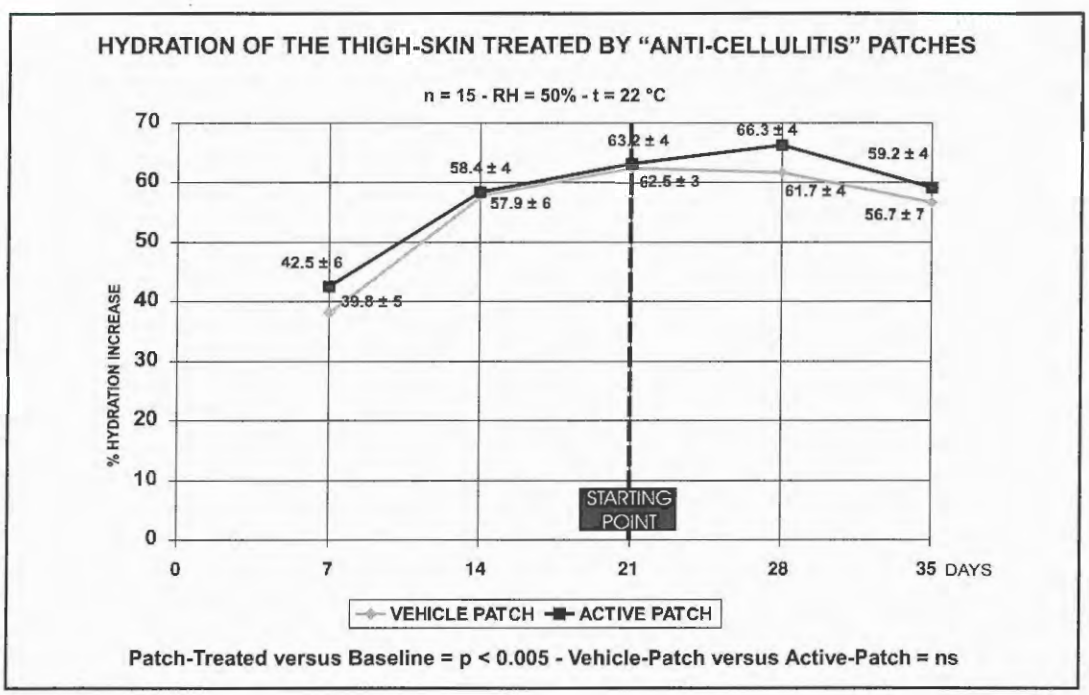
HYDRATION OF THE THIGH-SKIN TREATED BY "ANTI-CELLULITIS" PATCHES
n = 15 - RH = 50% - t = 22 °C
% HYDRATION INCREASE
70
60
50
40
30
20
10
0
42.5 ± 6
39.8 ± 5
58.4 ± 4
57.9 ± 6
63.2 ± 4
62.5 ± 3
66.3 ± 4
61.7 ± 4
59.2 ± 4
56.7 ± 7
STARTING POINT
0
7
14
21
28
35 DAYS
VEHICLE PATCH
ACTIVE PATCH
Patch-Treated versus Baseline = p < 0.005 - Vehicle-Patch versus Active-Patch = ns

Fig. 3

treatment causes the TEWL to increase considerably ($p<0,005$), indipendently from the presence of the active ingredient. This means that it acts by changing the stratum corneum barrier. That should be the reason why the active ingredients seem to be able to easily reach the hypoderm. By interrupting the treatment TEWL gets back to normal values ($p<0.005$) (Fig. 2).
Also concerning the cutaneous hydration the increasing problem is due also to the occlusive effect caused by the patch ($p<0,005$) (Fig. 3).
No adverse reactions were observed.
Obtained data seem to confirm what we previously proved (4-8), i.e. that the TCDS (Transdermal Cosmetic Delivery System) is an helpful cosmeceutical device, easy and quick to use, and capable of giving good results in the treatment of the cutaneous unaesthetism called "cellulitis".

Author Address:

P. Morganti, PhD - Research and Development
MAVI Sud srl - Via dell'Industria 1,
04011 Aprilia (LT), ITALY
Phone: + 39 06 9286261
Fax: + 39 06 9281523
E-mail=mavi@colosseum.it
URL=http://www.colosseum.it/st81/mavi

REFERENCE

1. **Braun Falco O., Scherwitz C. (1972)**, Histopathologie der Sog. *Zellulitis. Hautartz*, **23**, 71-75
2. **Binazzi M., Papini M. (1983)**, Aspetti chimico-istomorfologici. In: (Ribuffo-Bartoletti eds) *La cellulite*, Ed. Salus Internazionale, Roma, Italy
3. **Scherwitz C., Braun Falco O. (1978)**, So-called cellulitis, *J.Dermatol.Surg.Oncol.* **4**, 230-234
4. **Morganti P., Celleno L. and Vasselli A. (1995)**, A new Transdermal Delivery Cosmetic System to control the skin localized lipodystrophy, *J.Appl.Cosmetol.* **13**, 15-20
5. **Morganti P. (1995)**, Nuove applicazioni di principi attivi vegetali: il cerotto cosmetico, *Cosm. News*, 107-109
6. **Morganti P., Tiberi L., Vasselli A., Tolaini M.V., Serafini G., Celleno L. (1995)**, Transdermal Cosmetic Delivery System: a new device for cosmetic use. Evaluation of its effects in the treatment of so called "cellulitis", Presented at IFSCC Congress, Montreux, Switzerland, 18-21 September 1995
7. **Morganti P. (1996)**, The cosmetic patch: a new frontier in Cosmetic Dermatology, *Soap, Cosm. Chem. Special.* (February), 48-50
8. **Morganti P, Fionda A., Tiberi L. (1996),** The Transdermal Cosmetic Delivery System: A new cosmeceutical device, Presented at Active Ingredients Conference, Paris 13-14 November 1996, in print on *Cosmetics & Toiletries.*
9. **Morganti P., Fionda A., Tiberi L., Icare M., Rusch F., Elia U. (1996)**, Extraction, analysis by HPLC of cosmetic active ingredients from an anti-cellulitis transdermal delivery system, *Submitted for pubblication.*
10. **Seidenari S. (1995)**, Ultrasound B-mode imagine and in-vivo structure analysis. In: Non invasive methods and the skin (Serup and Jemec Edrs.), *CRC Press Inc.*, Bocaraton, Florida, p. 257
11. **Cardillo A., Morganti P. (1994),** A fast non-invasive method for skin hydration control, *J. Appl.Cosmetol.* **5**, 105-120
12. **Webb S. (1990),** "The Physics of medical imaging", Ed. Adam Hilger, Bristol.
13. **Edwards C. (1988)**, Non invasive in vivo measurement of dimensions and properties of stratum corneum and epidermis by A-Scan ultrasound, *15th IFCC International Congress* **4**, 263-4
14. **Pugliese P.T. (1989)**, Use of ultrasound in evaluation of skin care products, *Cosm. Toil.* **104**, 61-76
15. **Armengol R., Girones E., Belles A. et al. (1992)**, Quantitative evaluation of the anti-cellulitis efficacy by scan-ultrasound and its relation with clinic studies, *17th IFCC Int. Congr.* Vol. 3, 1218-1240
16. **Fornage B.D. and Anderson M.D. (1995),** Ultrasound examination of the skin and subcutaneous tissues at 7.5 to 10 MHz. In: Non-invasive methods and the skin (Serup and Jemec Eds.), CRC Press Inc., Bocaraton, Florida, p. 279
17. **Agner T. (1995)**, Ultrasound A-mode measurement of skin thickness. In: Non-invasive methods and the skin (Serup and Jemec Eds.), CRC Press Inc., Bocaraton, Florida, p. 289
18. **Morganti P. (1997),** A new peloid mask of Etruscan origin. Presented at IN-COSMETICS Conference, Düsseldorf, May 6. Published on the Conference Proceedings "Modern challenges to the Cosmetic Formulations", p.451-456, *J. Appl.Cosmetol.* **15**, 109

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ENHANCING THE GLYCOLIC ACID EFFICACY BY PIEZOELECTRIC VIBRATIONS

P. Morganti*, S.D. Randazzo and G.Fabrizi*****

* President/Director, R & D - Mavi Sud S.r.l., Viale dell'Industria 1, 04011 Aprilia (LT), Italy.
Department of Dermatology, Dermatologists Training School, II University of Naples, Italy.

** Department of Dermatology - University of Catania, Italy.

*** Department of Dermatology, Catholic University of Rome, Italy.

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Key words: Glycolic acid, Piezoelectric vibration, Skin Master®, Skin ageing, 3C System®, Skin elasticity, Skin hydration, Surface lipids, TEWL.

Synopsis

As it is well known, AHAs improve skin hydration by binding water to the stratum corneum.
In addition, when applied topically in concentration between 8% and 70% they decrease corneocyte cohesion and stratum corneum thickening, including various levels of epidermal separation. Among the various AHAs available, glycolic acid has enjoyed the greatest popularity.
Its higher concentrations (from 50% to 70%) are being used for superficial skin peeling,meanwhile, low concentrations (from 8% to 30%) have been reported to act as moisturizing agent capable of causing a decrease in corneocyte attachment. The glycolic acid activity is always correlated to some degree of irritation, and stinging or burning is its common side effect-especially at the begining of treatment. This study investigates and compares the effect of a 20% glycolic acid product, partially neutralized at 4,5 pH with a special blend of aminoacids, used as "lunch time peel" on skin degreased by a cleansing lotion combined with or without a new "piezoelectric technology" called "Skin Master®". Skin Master® activity is based on mechanical energy trasmitted to the skin by a series of ultrasound vibrations. Through the Skin Master® device, a significant exfoliation of the horny layer is obtainable together with a contemporary micromassage of the skin with an evident hyperemia. In this way, it is possible to enhance the glycolic acid absorption and its activity at medium/low concentrations. In order to explore the activity of this 20% glycolic acid-containing product and to verify the real use of the Skin Master®, Skin Elasticity (RER by Dermaflex®), Clinical Scoring (CS) (according to Effendy et al.), Stratum Corneum Turnover Time (SCTT) by the Dansylchloride Methodology (Jansen at al.), TEWL, Superficial Skin Lipids and Skin Hydration were controlled by 3C System® Technology (Rome, Italy) on 30 women aged 35-56 who were observed weekly for 3 months. No significant adverse reactions were noted during the 90-day study.
The obtained results indicate a significant reduction ($p<0.005$) of SCTT (+ 20%), substantial modification of TEWL, and an increase of superficial skin lipids (+ 27%), skin hydration (+70%) and skin elasticity (+12%).
These benefits were significantly ($p<0.05$) improved (+ 25%) when the Skin Master® was used.

Riassunto

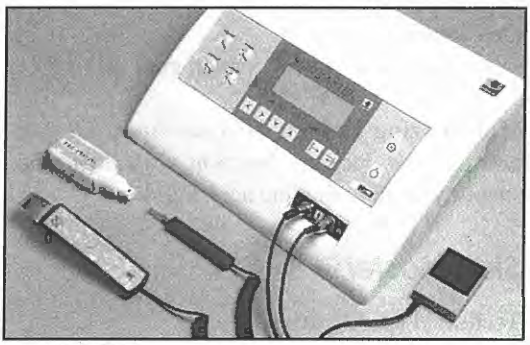
Come è noto gli alfaidrossiacidi aumentano l'idratazione cutanea legando l'acqua allo strato corneo. Inoltre, quando sono applicati topicamente in concentrazioni tra l'8% ed il 70% fanno diminuire la coesione dei corneociti e l'inspessimento dello strato corneo, accelerando a vari livelli la divisione cutanea. Tra i vari AHA disponibili, l'acido glicolico è quello che gode della più grande popolarità. Le sue alte concentrazioni (dal 50% al 70%) sono utilizzate per il peeling cutaneo superficiale, mentre le basse concentrazioni (dall'8% al 30%) sono risultate agenti idratanti in grado di causare anche una diminuzione nella coesione dei corneociti.
L'attività dell'acido glicolico è sempre correlata a qualche tipo di irritazione, ed il prurito e l'arrossamento ne sono comuni effetti collaterali, soprattutto all'inizio del trattamento.
Con questo lavoro si sono voluti valutare gli effetti di un prodotto contenente una percentuale del 20% di acido glicolico, parzialmente neutralizzato ad un pH 4,5 tramite una speciale miscela di aminoacidi. Il prodotto viene utilizzato come "lunch time peel" sulla pelle precedentemente detersa con una lozione detergente, in combinazione o no con la nuova tecnologia piezoelettrica denominata "Skin Master©".
L'attività dello Skin Master© è basata sulla energia meccanica trasmessa alla pelle da una serie di vibrazioni ad ultrasuoni.
Con l'uso dello Skin Master© si ottiene una significativa esfoliazione dello strato corneo, insieme ad un contemporaneo micromassaggio della pelle con evidente iperemia. In questo modo è possibile aumentare l'assorbimento dell'acido glicolico e la sua attività a concentrazioni medio / basse.
Per analizzare l'attività di questo prodotto e per verificare il reale uso dello Skin Master©, sono state controllate settimanalmente e per tre mesi 30 donne di età compresa tra i 35 e i 56 anni con la tecnologia del 3C System© (Rome, Italy). I valori controllati riguardavano l'elasticità della pelle (RER Dermaflex©), il grado di eritema della cute (Clinical Scoring - CS secondo Effendy et al.), il rinnovo delle cellule cutanee, Stratum Corneum Turnover Time (SCTT) con la Dansylchloride Methodology (Jansen et al.), la TEWL, i lipidi cutanei di superficie e l'idratazione della pelle.
Durante la durata dello studio (90 giorni) non sono stati riscontrati significativi effetti collaterali.
I risultati ottenuti indicano una riduzione significativa ($p<0.005$) dello SCTT (+ 20%), una modifica sostanziale della TEWL, ed un aumento dei lipidi cutanei di superficie (+27%), dell'idratazione cutanea (+70%) e dell'elasticità della pelle (+12%).
La positività dei dati è risultata significativamente più elevata (+ 25% $p<0.05$) nelle aree trattate con lo Skin Master©.

As it is well known AHAs improve skin hydration and photo-induced skin ageing by binding of water to the stratum corneum (1-17).
In addition, when applied topically in concentration between 8 and 70% they decrease corneocyte cohesion and stratum corneum thickenig, including various levels of epidermal separation. Among the various AHAs available, glycolic acid has enjoyed the greatest popularity. Its higher concentrations (from 50 to 70%) are beeing used for superficial skin peeling meanwhile low concentrations (from 8 to 30%) have been reported to act as moisturizer agent capable also to cause a decrease in corneocyte attachment (18-21).
The glycolic acid activity is always correlated to some degree of irritation and stinging or burning is its common side effect, especially at the beginning of treatment (22).
These side effects are linked to its own irritant properties as acid, but are also based on the following factors: concentration, pH, percentage and type of neutralizers used to adjust acidity, vehicle formulation, cleaning and/or degreasing treatment used, period of time the acid remains on the skin, skin area and skin type (23).
Because of glycolic acid known ability to be effective on some photodamage, pigmentation, scarring condition and fine wrinkles improvement, physicians and aestheticians are using it primarily in high/medium concentrations. For these reasons the use as "refresher peel" of a glycolic acid solution at medium degree concentration of simpler use should be interesting fot both the medical community and aestheticians, particularly if without side effects.
This study investigates and compares the effect of a 20% glycolic acid-peel, partially neutralized at 4.5 pH with a special blend of aminoacids (*), used as "lunch time peel", on skin degreased by a cleansing lotion or by a new "piezoelectric technology" called Skin Master®.

(*) Trade name: Keratotal® Peel

STUDY PROJECT

In order to verify the real use of the Skin Master® and to explore the activity of this 20% glycolic acid-peel, Stratum Corneum Turnover Time (SCTT). Skin elasticity, Clinical scoring and TEWL were controlled on upper forearm; Skin lipids and Hydration were controlled on the face.



Skin Master®

3C System®

CHEMICALS

Gel A:
water gel of glycolic acid 20% (1ml = g 0,224 of GA) partially neutralized by Na OH (pH 4.5) GA.

Gel B:
water gel of glycolic acid 20% (1ml = g 0,224 of GA) partially neutralized by aminoacids (pH 4.5) GA-Arg/Gly (*).

Cleansing Lotion:
(pH 4.5) Aqua, Ceteareth-6, Isopropyl myristate, Octyl stearate, Lactic acid, Sorbitol, Propylene glycol, Glycerin, Gelatin-Glycine[1], Hydrolyzed collagen, Tocopheryl acetate, Retinyl palmitate, Linoleic acid, Linolenic acid, Disodium EDTA, Imidazolidinyl urea, Methylparaben, Parfum (*).

Gel-Vehicle:
water, propylene glycol, xantan gum (pH 4.5).

Moisturizing Lotion: Soybean liposome containing 10% lecithin fraction with 80% phosphatidylcholine linoleic acid-rich.

Skin Master®

Technical specifications
Actuator frequency: 25.000 Hz +/- 10%
Vibration at time actuator: 30 micron pp
Frequency: 0.1 - 1000Hz
Work cycle: 5 sec.
Maximum of current: 10-600 microA

Skin Master®'s activity is based on mechanical energy transmitted to the skin by a series of ultrasound vibrations of its special actuator.
The extreme part of the actuator, induced to vibrate by piezoeletric device, produces compression and decompression on the skin surface.
The outcome of this treatment is a smooth relaxed and cleaned skin and toned musculature.

3C System®

This computerized system through the capacitative resistance permits a simple and quick control of surface lipids, skin hydration and TEWL.
The 3C System® collects up to 10/15 measurements over 25 seconds sampling period and records the mean value automatically standardizing the environmental conditions (RH=50%, T=22°C) (11).

TEST PROCEDURE ON THE FACE

Patients

Fourthy healthy women volunteers, age range 35 to 56, skin type III/IV, participated in the study. Each woman had at least a moderate degree of photodamage as defined by an overall score of 5 with separate scores for each side of the face on a visual analogue scale of 0 (none) to 10 (severe).
The number of actinic keratoses and wrinkling improvement were also counted.
No topical retinoid use or other topical medications or cosmetic antiaging products were allowed for 1 month prior to study initiation.
The subjects were observed daily or weekly for three months (January-March) always by the same investigator.
Patients were randomly divided into four treatment groups of 10 individuals. After baseline evaluation, one group was treated twice a week by a 20% glycolic acid "refresher peel" (partially neutralized by aminoacids at pH 4.5) (Gel B) for 2 months, after cleansing the face with a Cleansing Lotion (TS Gentle Cleansing) (Group 1).
The second group was treated with the same peel, after cleansing the skin, previously wetted with distilled water, by using the Skin Master® (Group 2).
The thirth and the fourth group were respectively treated as the first and the second but used also a phospholipid-based moisturizing lotion twice daily.

Procedure

To perform the peel the following procedure was utilized: the Gel B (glycolic acid peel) was applied uniformly over the entire face after the skin was cleansed with Gentle Cleansing or Skin Master®.
Application times were started at 15 minutes for each peel treatment.

(*) Trade name: TS Gentle Cleansing

(1) USA patented n°4806525/Feb.2, 1989

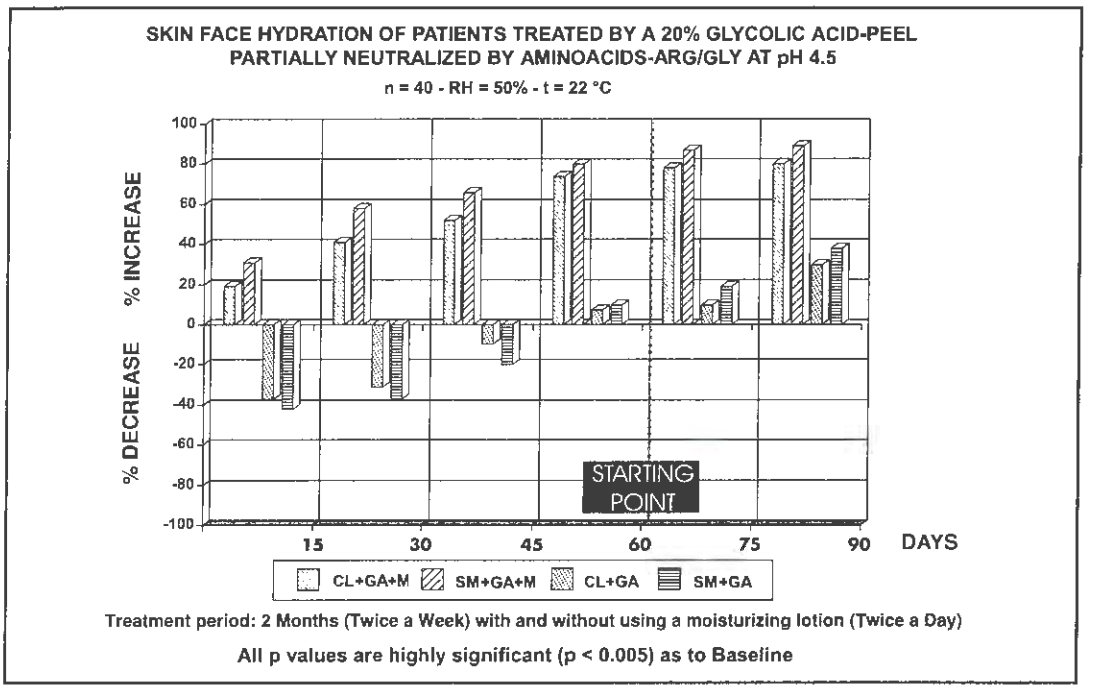


Fig. 1 *Abbreviations*: CL=Cleansing Lotion, GA=Glycolic Acid, M=Moisturizing Lotion, SM=Skin Master

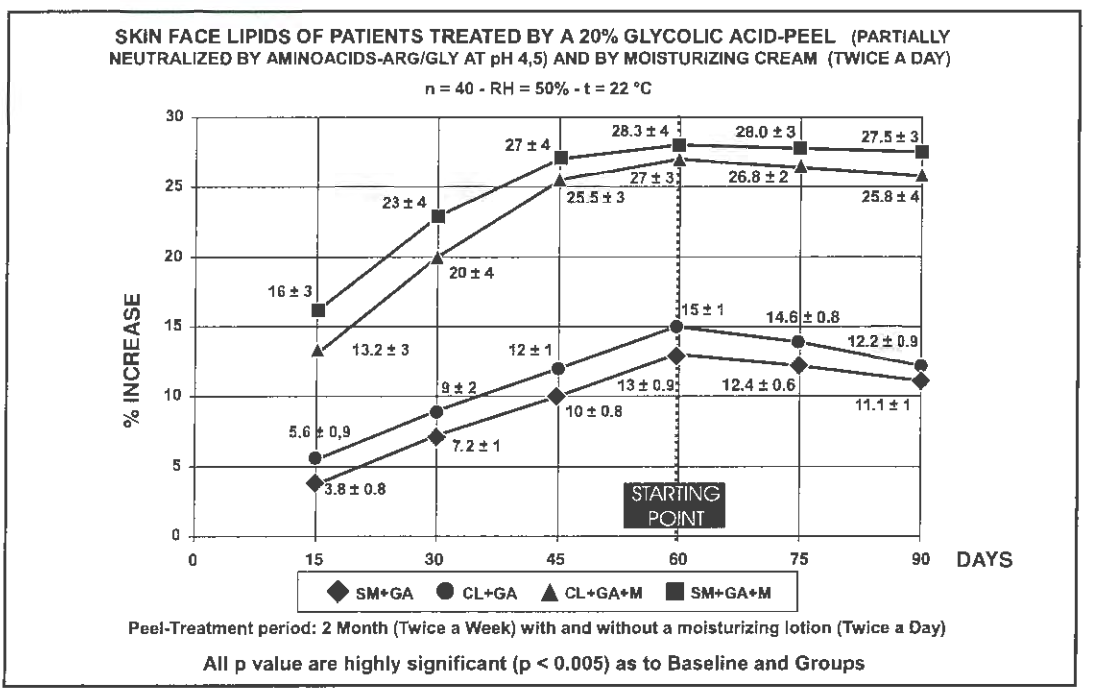


Fig. 2 *Abbreviations*: CL=Cleansing Lotion, GA=Glycolic Acid, M=Moisturizing Lotion, SM=Skin Master

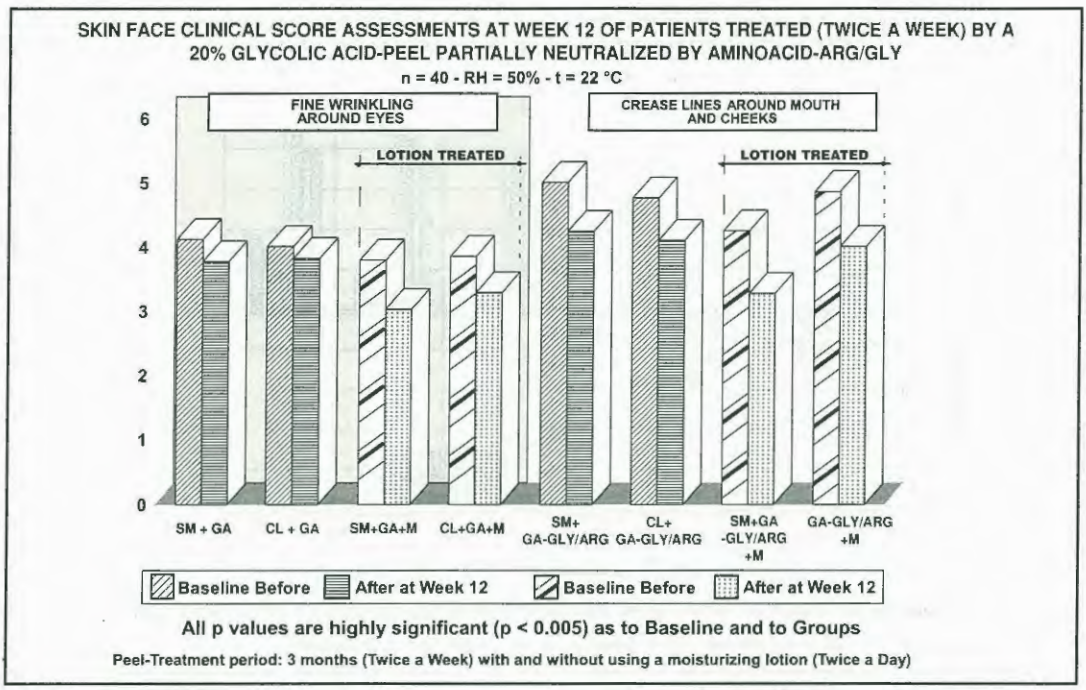


Fig. 3 *Abbreviations*: **CL**=Cleansing Lotion, **GA**=Glycolic Acid, **M**=Moisturizing Lotion, **SM**=Skin Master

Every two weeks at 10.00 a.m. surface lipids, skin hydration, the number of crease lines and the degree of wrinkling improvement were controlled. The obtained results are reported in Fig 1,2,3.

TEST PROCEDURE ON THE FOREARM

Stratum corneum turnover time (SCTT)

The right or left forearm was marked with 7 areas of 2cm² each, treated in this way:

AREA 1	Cleansed	with	Cleansing	Lotion	+ Gel A
AREA 2	"	"	"	"	+ vehicle Gel
AREA 3	"	"	Skin Master		+ Gel A
AREA 4	"	"	"	"	+ vehicle Gel
AREA 5	"	"	Cleansing	Lotion	+ Gel B
AREA 6	"	"	Skin Master		+ Gel B
AREA 7					UNTREATED

Areas treated by Skin Master® were previously wetted with distilled water.

Prior to treatment the stratum corneum was labelled with dansyl chloride according to Jansen et al. (24) methodology. According to Effendy et al. (25) dansyl chloride was finely triturated into white petrolatum at 5% (w/w) and applied to right volar forearm of the volunteers under semi-occlusive dressing for 24 h. Subsequently, after remove of any excess material with soft tissue paper, and after cleansing the area by cleansing lotion or by Skin Master®, test substances were applied. The clearance of the fluorescence was examined under UV illumination. SCTT was the time in days between staining (day 0) and fluorescence disappearance.

0,1 ml. of glycolic acid-Gel-B (pH 4.5), glycolic acid-Gel-A (pH 4.5) and vehicle (pH 4.5) were applied respectively to the dansyl chloride-labelled areas pre-treated by Cleansing Lotion or Skin Master® volar forearm areas using polypropylene chambers (19 mm

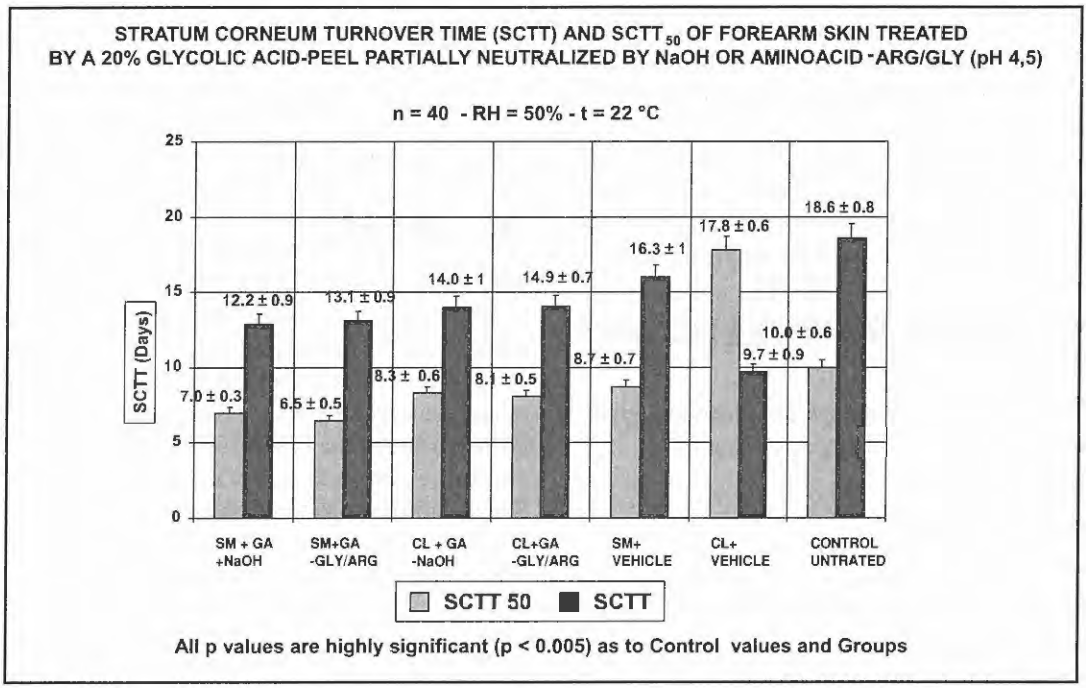


Fig. 4 *Abbreviations*: **CL**=Cleansing Lotion, **GA**=Glycolic Acid, **M**=Moisturizing Lotion, **SM**=Skin Master

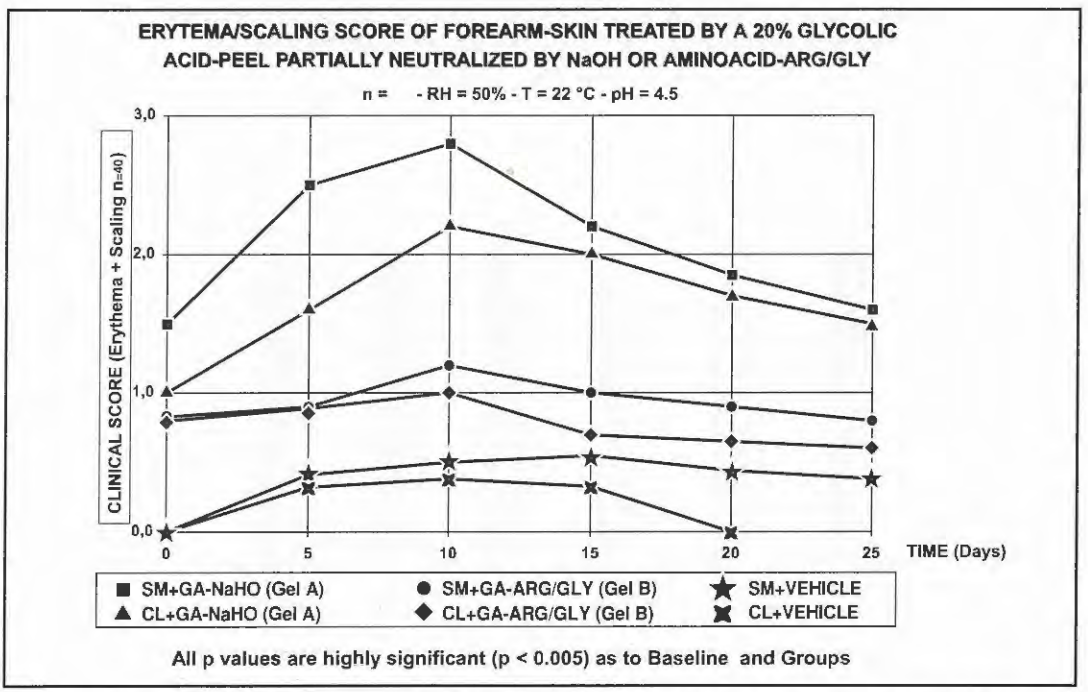


Fig. 5 *Abbreviations*: **CL**=Cleansing Lotion, **GA**=Glycolic Acid, **M**=Moisturizing Lotion, **SM**=Skin Master

diameter) on paper adhesive tape for 15 min. Once daily (5 consecutive days for 2 weeks) according to the method described by Effendy et al.
Chambers with an erythema score of 3.0 or greater were not reapplied. Vehicle Gel served as control. Untreated skin served as a control site. The obtained results are reported in Fig. 4 and 5.

ERYTHEMA SCALING SCORES

Each test site was always examined and graded for erythema and scaling according to:

ERYTHEMA:
0 = no erythema
0.5 = equivocal reaction
1 = slight erythema
2 = moderate, uniform erythema
3 = intense
4 = fiery redness with edema

SCALING:
0 = no scale
1 = minimal, fine
2 = moderate
3 = large flakes, intense peeling

Skin elasticity

Skin elasticity has been controlled weekly 10 a.m. to all patients on a marked forearm area by Dermaflex® A((Cortex Technology, Hadsund, Denmark) (26). The evaluation of the skin was determined electronically by measuring electric capacitance between the marked skin surface and the electrode placed in the top of the suction chamber. The parameters used were: suction 450m bar, suction period 20s, number of cycles 5.
The obtained results are reported in Fig. 6 and 7.

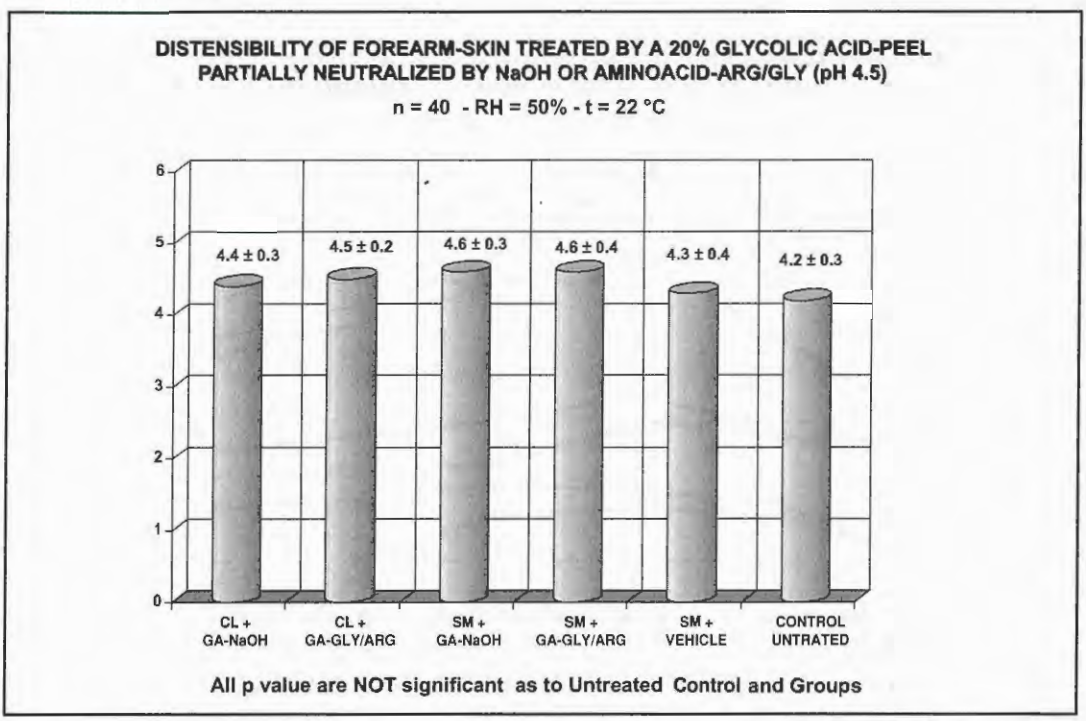


Fig. 6 *Abbreviations*: **CL**=Cleansing Lotion, **GA**=Glycolic Acid, **M**=Moisturizing Lotion, **SM**=Skin Master

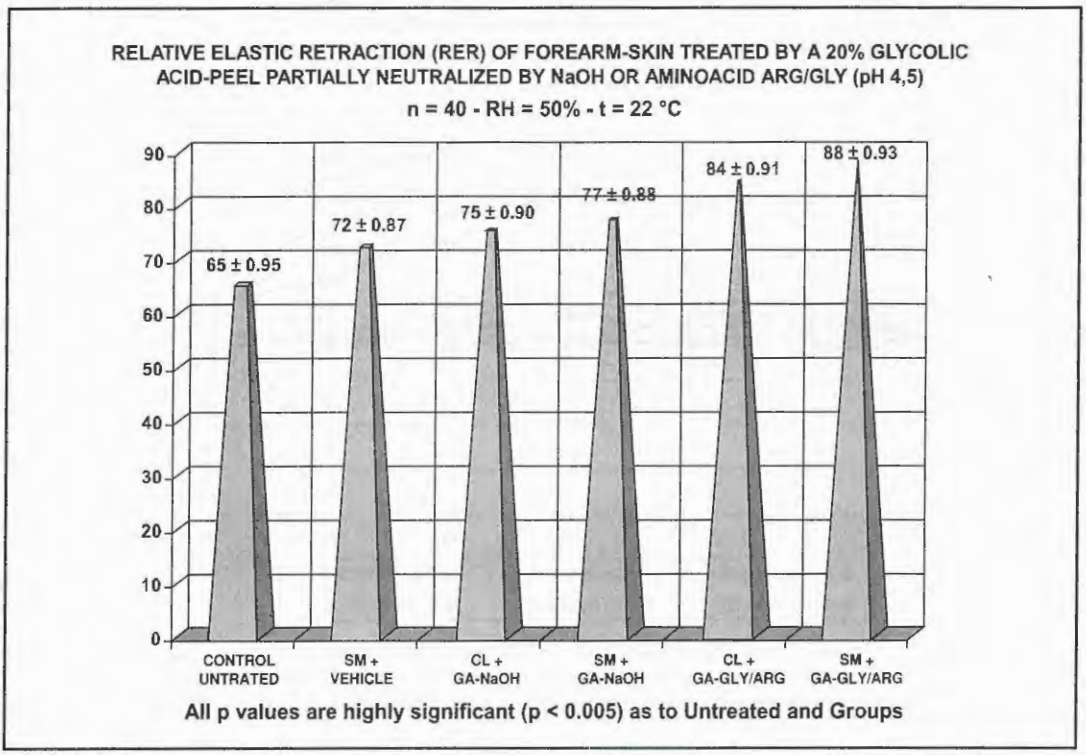


Fig. 7 *Abbreviations*: **CL**=Cleansing Lotion, **GA**=Glycolic Acid, **M**=Moisturizing Lotion, **SM**=Skin Master

TEWL, SUPERFICIAL SKIN LIPIDS AND SKIN HYDRATION

TEWL, skin lipids and hydration were controlled weekly on the skin face by the 3C System® methodology (Dermotec, Rome, Italy) (27).
This computerized system permits a simple and quick determination of TEWL, superficial skin lipids, hydration and pH, while the environmental conditions are automatically standardized (50% RH and 22°C) by the use of proper correction factors.
TEWL is expressed as the amount of water evaporated per unit of surface in 1 hour gr/m2/h and the system collects up 10/15 measurements over 25 second sampling period and record the mean value automatically.
The obtained results are reported in Fig. 1, 2 and 8.

RESULTS AND DISCUSSION

Erythema and Scaling

As expected the Gel A application (20% glycolic acid partially neutralized by NaOH at pH 4.5), compared to its vehicle ($p<0.005$), caused a strong erythema (2nd degree) from the second day of treatment on the cutaneous area already cleansed with cleansing lotion. This erythema turned out even stronger when the cleansing was carried out by using Skin Master® (3 degree), that, as expected, allowed the glycolic acid to pass through the cutaneous layers even quicker.
The Gel B application (20% glycolic acid partially neutralized at pH 4.5 by aminoacids) has recorded, on the contrary, only a slight erythema from day 8 to day 10 as compared to its vehicle

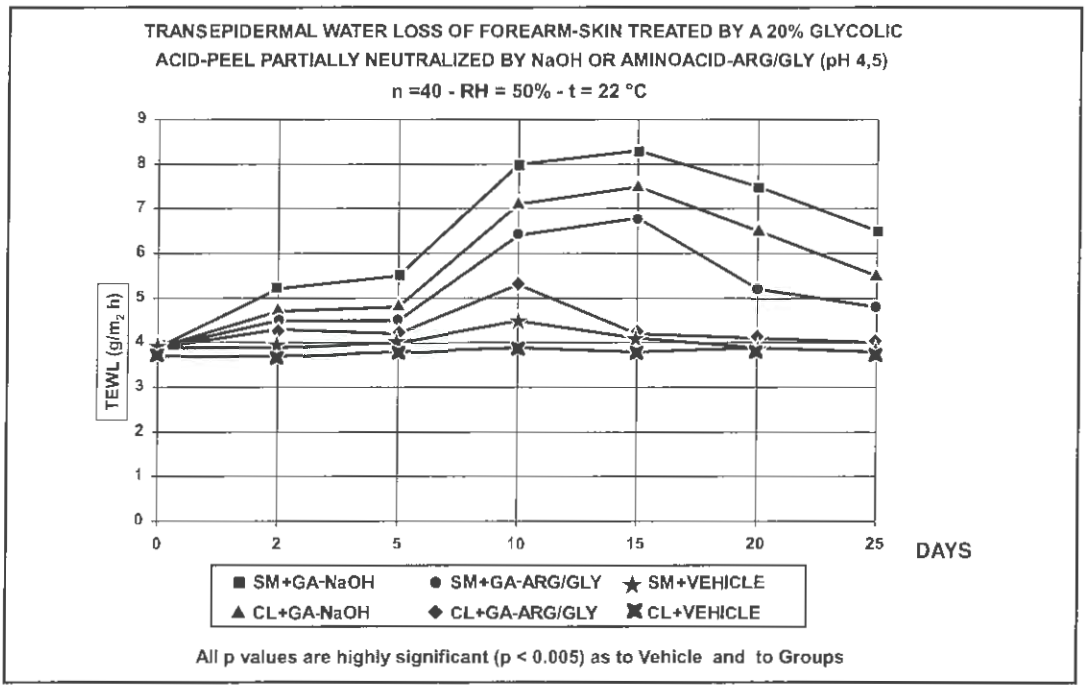


Fig. 8 *Abbreviations*: **CL**=Cleansing Lotion, **GA**=Glycolic Acid, **M**=Moisturizing Lotion, **SM**=Skin Master

(p< 0.005), and produced evident scaling from day 10 to day 18. This did not occur with the vehicle (Fig. 5).

TEWL

In accordance with Effendy et al. TEWL at the GA-treated area increased on day 10 and maintained significantly higher levels than the untreated or vehicle-treated skin (p<0.005). Only the areas treated with glycolic acid partially neutralized with ARG/GLY aminoacids showed TEWL levels similar to the vehicle.

These levels were higher only when the skin was pre-treated by Skin Master®, and when glycolic acid (GA) partially neutralized with NaOH was used, implying that the water barrier of Stratum Corneum is altered by the glycolic acid treatment more or less clearly not only in relation to the quantity of free glycolic acid, but also to the kind of used neutralizer and to the intensity of the cleansing treatment used. What seems even more interesting is the fact that the alteration of the barrier seems not to be dependent from the pH, as often asserted by different authors (15,19, 21-22), but from the kind of neutralizer used (Fig. 8). The glycolic acid used, neutralized by a mixture of aminoacids, acted in a way fairly similar to the vehicle (Fig. 8), unlike the same glycolic acid neutralized by NaOH.

SCTT

Glycolic acid has significantly reduced SCTT and SCTT-50 with respect to the vehicle and the control (Fig. 4), both when partially neutralized with NaOH (14.0±7, p<0.005) and by aminoacids (14.0±1, p<0.005)), after cleansing previously the skin with Cleansing Lotion. The use of the Skin Master® has furtherly reduced the SCTT (GA-Arg-Gly 13.1±0.9 and GA-Na OH 12.9±0.9) (p<0.005), proving that this type of cleansing helps the absorption and therefore the activity of glycolic acid and of

active ingredients in general. These results prove, as already verified by ourselves and other authors, that glycolic acid acts as Stratum Corneum cell renewal accelerator, and that the intensity of activity and the the erythema degree is strictly related also to the means of cleansing used and to the used chemical neutralizers (Fig. 4 and 5). It seems not to depend, therefore, only on the free glycolic acid.

Superficial skin lipids, hydration and elasticity

As it is known and as can be seen the every-two-week treatment with glycolic acid, considerably improves the skin elasticity (RER) (Fig. 7) ($p<0.005$ with regard to control), but not the skin distensibility (Fig. 6).
Concerning hydration and surface lipids (Fig. 1 and 2) it is evident that the peeling reduces the skin hydration and seems to have an influence also on superficial skin lipids thanks to the exfoliating activity caused by glycolic acid if used in 20% concentrations without the use of emollients. When the treatment is integrated by the use twice a day of an emollient cream results invert.

Clinical score assessment

Before (Day 0) and after 12 weeks of treatment clinical score assessment was checked by the same dermatologist for all patients GA-treated ($p<0.005$). The individual signs of fine wrinkling around eyes and crease lines around mouth and cheeks were scored on 0-10 visual analogue scales with separate scores for each side of the face. The patients treated also with the post-peel moisturizing cream (twice a day)and pre-treated by Skin Master® demonstrated the highest improvement on wrinkling and crease lines also at week 4 and 8 ($p<0.05$) in respect to other groups (Fig. 3).

CONCLUSION

As already supported by several authors glycolic acid carries out an interesting biological activity, which is not completely explained yet. From these first data, however, it seems possible to say that it obtainable an interesting increase of cell turnover by using lighter and simpler peeling, that can be performed also by expert aestheticians. It is of extreme importance to perform before the treatments a careful cleansing, and it is fundamental not only the product's pH and the neutralizing degree, but the kind of neutralizer used, that affects also the erythemigenic components and the stinging activity carried out by this AHA.
It is also fundamental the use of moisturizing creams after the peeling treatments, in order to improve the appearance of photoaged skin by reducing fine wrinkling and crease lines and to enhance the radiance of the skin giving complexion a fresh, youthful glow.
Finally, we found highly interesting the use of the Skin Master® as new cleansing means, to be used to deeper cleanse the skin when there is a need to accelerate and improve the absorption and the activity of AHAs or other cosmetic active ingredients.

Author Address:

P. Morganti, PhD - Research and Development
MAVI Sud srl - Via dell'Industria 1,
04011 Aprilia (LT), ITALY
Phone: + 39 06 9286261
Fax: + 39 06 9281523
E-mail=mavi@colosseum.it
URL=http://www.colosseum.it/st81/mavi

REFERENCES

1. **Van Scott EJ, Yu RJ. (1974),** Control of keratinization with alpha hydroxy acids and related compounds: 1.topical treatment of ichtyotic disorders, *Arch.Dermatol.* **110**, 586-590.
2. **Van Scott EJ, Yu RJ. (1984),** Substances that modify the stratum corneum by modulating its formation. In: Principles of Cosmetics for the Dermatologists. (Frost, SN Horwitz, eds.) CV Mosby Co., St. Louis, p.70-74
3. **Van Scott EJ. (1988),** The unfolding therapeutic uses of alpha hydroxy acids, *Med guide to Dermatol.*, **3**, 1-5.
4. **Van Scott EJ, Yu RJ. (1989),** Alpha hydroxy acids: therapeutic potentials, *Canadian J. Dermatol.* **1**, 108-112.
5. **Dahl MV, Dahl AC. (1983),** 12% lactate lotion for the treatment of xerosis, *Arch Dermatol.* **119**, 27-30.
6. **Buxman M, Hickman J, Ragsdale W, et al. (1986),** Therapeutic activity of lactate 12% lotion in the treatment of ichthyosis. Active vehicle and active vs. a petroleum cream, *J. Am. Acad. Dermatol.* **15**, 1253-1258.
7. **Van Scott EJ, Yu RJ. (1989),** Alpha hydroxy acids: treatment of the Aging Skin with Glycolic Acid procedures for use in clinical practice, *Cutis.* **43**, 122-128.
8. **Moy LS. (1990),** The use of glycolic acids in the treatment of various skin disorders. Communication at the 17th Annual Clinical and Scientific Meeting of the American Society for Dermatologic Surgery. Reported in *Canadian Medical News*, July 27.
9. **Dial W.F. (1990),** Preparations prescribed in anti-wrinkling therapy, *Cosmet Dermatol.* **3**, 32-34
10. **Ridge J.M., Siegle R.J., Zuckerman J. (1990),** Use of alpha hydroxy acids in therapy for photoaged skin, *J. Am. Acad. Dermatol.* **23**, 932
11. **Hermitte R. (1992),** Aged skin, retinoids and alpha hydroxy acids, *Cosmet. Toilet.* **107**, 63-66
12. **Vilaplana J. (1992),** Clinical and non-invasive evaluation of 12% ammonium lactate emulsion for the treatment of dry skin in atopic and non-atopic Subjects, *Acta Dermatol. Venerol.* **72**, 28-33
13. **Wehr F.R. (1991),** A controlled comparative efficacy study of 5% ammonium lactate lotion vs. an emollient control lotion in treatment moderate xerosis, *J Am. Acad. Dermatol.* **25**, 849-851
14. **Morganti P., Persechino S. and Bruno C. (1994),** Effects of topical AHAs on skin xerosis, *J.Appl. Cosmetol.* **12**, 85-90
15. **Smith W.P., Smith W. (1994),** Hydroxy acids and skin aging, *Cosmet. Toilet.* **109** (9), 41-48.
16. **Morganti P., Randazzo S.D., Bruno** C. **(1996),** Alpha hydroxy acids in the cosmetic treatment of photo-induced skin aging, *J.Appl. Cosmetol.* **13**, 1
17 **Morganti P., Bruno C. and Randazzo Sd (1997),** Stratum corneum turnover time in aged skin, *Cosmet. & Toilet* **112**, July, 61
18. **Moy L.S., Murad H., Moy R.L. (1993),** Glycolic acids peels for the treatment of wrinkles and photoaging, *J.Dermatol. Surg-Oncol.* **19** (3), 243-6
19. **Di Nardo J.C., Grove G.L.,Moy L.S. (1996),** Clinical and histological effects of glycolic acid at different concentrations and Ph levels, *Dermatol. Surg.* **22** (5), 421-4
20. **Clark C.P. (1996),** Alphahydroxy acids in skin care, *Clin.Plast.Surg.* **23** (1), 49-56
21. **Becker F.F., Langford F.P.,Rubin M.G. Speelman P. (1996),** A hystological comparison of 50% and 70% glycolic acid peels using solutions with various pH, *Dermatol.Surg.* **22** (5), 463-5
22. **Harris D.R. (1994),** Treatment of the aging skin with glycolic acid. In: Evaluation and treatment of the aging face (Elson Ed.) Springer-Verlag, New York, p.26

23. **Brody H.J., Hailey C.W. (1986),** Medium depth chemical peeling of the skin: a variation of superficial chemosurgery, *J.Dermatol. Surg. Oncol.* **72**, 1268-75
24. **Jansen L.H., Hojyo-Tomoko M.T., Kligman A.M. (1974),** Improved fluorescence staining technique for estimating turnover of the human stratum corneum, *Br.J.Dermatol.* **90**, 9-12
25. **Effendy I., Kwangsukstith C., Lee J.Y. and Maibach H.I. (1995),** Functional changes in human stratum corneum induced by topical glycolic acid: comparison with all-trans Retinoic Acid, *Acta Derm.Venereol.* (Stochk) **75**, 455-458
26. **Elsner P.E. (1995),** Skin elasticity. In: Bioengineering of the skin: methods and instrumentation. (Beradesca et al. Eds) CRC Boca Raton, USA p.58
27. **Cardillo A., Morganti P. (1994),** A fast, non invasive method for skin hydration control, *J.Appl. Cosmetol.* **12**, 11
28. **Morganti P., Fabrizi G. Randazzo S.D. and Bruno C. (1996),** Decreasing the stinging capacity and improving the antiaging activity of AHAs, *J.Appl.Cosmetol.* **14**, 79-91

1997 AWARDS

1997 can be considered particularly successful by Pierfrancesco Morganti, Ph.D., Editor in Chief of our Journal. Dr. Morganti, leading an outstanding team of cosmetic and pharmaceutical scientists, accepted two coveted awards during this year.

Their work, "The transdermal cosmetic delivery system: a new cosmeceutical device" was awarded "The Elegance Engineering Innovation Award" by Cosmetics & Toiletries magazine. This award was announced and publicly presented to Dr. Morganti during the 1997 Advanced Technology Conference in Dusseldorf, Germany on May 3, 1997.

The European Academy of Dermatology and Venereology (E.A.D.V.) Poster Prize was awarded and presented to Dr. Morganti by Prof. W.J.Cunliffe during the 6° E.A.D.V. Congress in Dublin, Ireland on September 15, 1997. The title of the poster was "A new cosmeceutical for all year round acne therapy".

Congratulation from the entire editorial staff of the Journal to the Secretary General of International Society of Cosmetic Dermatoly for such outstanding success. This reflects well on both the Society and the Journal. Many of our membership may have equally significant honors, and we would be pleased to announce them here, also.

Editorial Staff of the Journal of Applied Cosmetology

Dr. P.Morganti receiving his Award from T.J.Malafronte President of Amerchol

MECHANISM OF TRANSDERMAL DRUG DELIVERY
Drug and Pharmaceutical Sciences. Series/8

Russel O. Pohs and Richard H. Guy Editors

Published by Marcel Dekker, New York - 376 hard bound, illustrated
ISBN: 0-8247-9863-5 • US$ 150.00 Price subject to change without notice
Marcel Dekker Inc., 270 Madison Avenue - New York, NY 10016-0602

This new book about transdermal delivery has surely hit the target, providing the readers with a full survey of the mechanisms that are at the basis of Transdermal Delivery. This relatively new methodology was developed, as it is known, through three steps or generations, that gradually led to the realization of a better regulation, a better dosage and a better end-user comfort. The objective of the development was the improvement of the transfer and absorption mechanisms through the use of particular ingredients (or enhancers), the redaction of the patch's dimensions, the improvement of the outward appearance to the advantage of portability.

This new book edited by Pohs and Guy in the "Drugs and Pharmaceutical Sciences" series of Marcel Dekker highlights "what is known", giving a "summary of what is happening now", together with "a perceptive look at what is to come in the area of mechanism and enhancement of molecular transport accross the stratum corneum" It begins by highlighting all the most sophisticated technologies used to enhance the path ways of transdermal Stratum Corneum penetration including the usage of Penetration Enhancers, as new chemical molecules, of Orthophoresys and Sonophoresys, based on the use of ultrasonic energy. It is necessary to remind the reader that the need to stay in depth, improve and widen the knowledges and practical uses of drugs with controlled release arises from different requirements, and among those from the request of chemists of improving client's compliance towards the drugs (e.g. by decreasing the number of daily administrations) and making more steady the hematic and topical level of active ingredients. For these purposes patches are used to obtain a steady release of the drug in the space of a day or more, and an extreme user-friendly product. Naturally, it is necessary to evalute the safety of this new device and to determine the degree of risk connected to its use.

All the methodologies this interesting book deals with, those concerning the control of Stratum Corneum's bilayers lipids, as well as those about th newest systems for the control of the drug release at cutaneous level, are described with plenty of details and bibliographic notes. This book makes a useful reading for researchers who know the technological development which patches have undergone in these last years, for graduates in medicine, biologists, pharmacists and students willing to learn the basis and the mechanisms of activity that regulate cutaneous absorption and the release of drugs and cosmetics through the organ skin.

P. Morganti, Ph.D
Editor in Chief

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Rome, September 14 - 18, 1999

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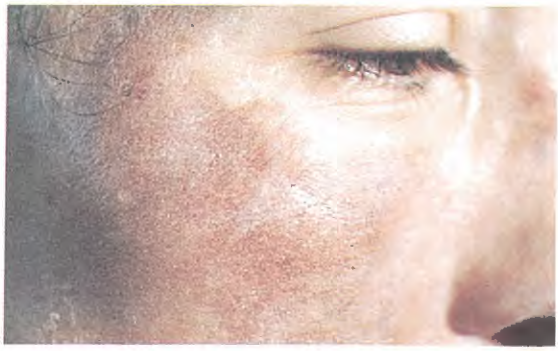

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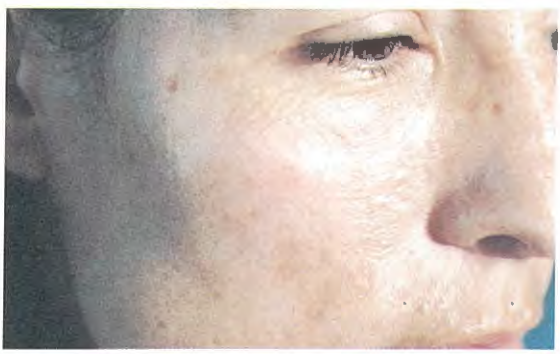

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SKIN LIGHTNER WITH HYDROQUINONE, GLYCOLIC ACID AND NON-CHEMICAL UVA SCREEN

Una risposta ottimale alle ipermelanosi cutanee

Indicazioni:

Ipermelanosi acquisite di origine metabolica, endocrina, nutrizionale, chimico-fisica, ecc.

Modo d'uso:

1-2 volte al dì per non meno di 8 settimane

mavi

La Ricerca Scientifica nella Dermocosmesi

MAVI SUD s.r.l. Aprilia (LT) - Italy

THE EVOLUTION IN COSMETIC SCIENCE

GRAFO - ROMA