

ALPHA HYDROXY ACIDS IN THE COSMETIC TREATMENT OF PHOTO-INDUCED SKIN AGEING

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Synopsis

The continuous adverse effects of light over the years add to normal ageing processes. This increases the number and severity of wrinkles, reduces the efficiency of cell mechanisms responsible for the reparation of damaged genes due to UV rays in photo-exposed areas, causes actinic keratosis, slows down epidermic cell turnover and reduces surface lipids, the moisture level and, as a result, the suppleness of the skin.

The noticeable adverse effects generally decrease with the use of retinoic acid-based drugs or cosmetic-based products including various active components, from collagen to sodium lactate and aminoacids, from gelatine-glycine to Pyrrolidone Carboxylic Acid (PCA) and the newly-used Alpha hydroxy acids (AHAs), such as, for example, glycolic acid.

This double-blind study aims to control the activity of 8% AHAs and gelatin-glycine-based cosmetic emulsions over 90 days clinically evaluating the number of thin wrinkles.

Furthermore, the surface lipid film, the pH value and the skin moisture level were tested with the computerized methodology 3C System[®]. Finally, the cell turnover was tested with the "Scrub technique".

Riassunto

La continua attività negativa svolta dalla luce durante gli anni si sovrappone ai normali processi di invecchiamento, - aumentando il numero e la profondità delle rughe, - riducendo l'efficienza dei meccanismi cellulari preposti alle riparazioni dei geni danneggiati dalle radiazioni UV a livello delle zone fotoesposte, - provocando la comparsa di cheratosi attiniche, - rallentando il turnover delle cellule epidermiche e riducendo i lipidi di superficie, l'idratazione e conseguentemente l'elasticità della pelle.

Per ridurre questi danni cutanei evidenti si utilizzano generalmente prodotti cosmetici nella cui composizione sono presenti i più svariati principi attivi, dal collagene, al lattato di sodio, agli aminoacidi; dalla gelatina-glicina, all'acido Pirrolidon Carbossilico (PCA) e ai più recenti Alfaidrossiacidi (AHAs) quale, ad esempio, l'acido glicolico. Con questo studio a doppio cieco si è voluto controllare in un periodo di 90 giorni, l'attività svolta da emulsioni cosmetiche contenenti alfa-idrossiacidi all'8% e gelatina-glicina, valutandone il numero di rughe sottili.

È stato, inoltre, controllato il film lipidico di superficie, il pH e l'idratazione cutanea utilizzando una nuova metodica computerizzata denominata 3C System[®]. Il turnover cellulare è stato controllato con la tecnica cosiddetta "Scrub".

FOREWORD

The skin gradual ageing is known to depend on two main factors: intrinsic ageing due to genetic factors, which, as such, is relentless, and extrinsic ageing, which is basically linked to the amount of environmental pollutants, UV rays and IR rays we are exposed to throughout our life. These agents act by speeding up changes in the skins biological characteristics (1-4).

The continuous adverse effects of light over the years add to normal ageing processes. This increases the number and severity of wrinkles, reduces the efficiency of cell mechanisms responsible for the reparation of damaged genes due to UV rays in photo-exposed areas, causes actinic keratosis, slows down epidermic cell turnover and reduces surface lipids, the moisture level and, as a result, the suppleness of the skin (5-9). This noticeable adverse effects generally decrease with the use of retinoic acid-based drugs or cosmetic products including various active components, from collagen to sodium lactate and aminoacids, from gelatin-glycine to Pyrrolidone Carboxylic Acid (PCA) and the newly-used Alpha hydroxy acids (AHAs), such as, for example, glycolic acid (10-17).

PURPOSE

This double-blind study aims to control the activity of 8% glycolic acid and gelatin-glycine-based cosmetic emulsions over 90 days in a group of 60 volunteer women aged 45 to 60, who showed clear sun-induced skin changes.

After assessing the major role of the vehicle, the pH value and the concentration necessary for AHAs optimum performance (17-18), a visual analogic scale (19) was used to clinically evaluate the number of thin wrinkles on the face and back of the hands, actinic keratosis and the cheek telangiectasis before and after treatment as compared to the placebo group.

Furthermore, the surface lipid film, the pH value and the skin moisture level were tested with

the computerized methodology 3C SYSTEM® (20).

Finally, the cell turnover was tested with the Scrub technique (21-23).

MATERIALS AND METHODS

Materials

CLEANSING LOTION QM

Distilled water, Cetareth-6, Isopropyl myristate, Octyl stearate, Sorbitol, Glycerin, Propylene glycol, Glycolic acid, Gelatin-glycine, Tocopheril acetate, Rethynil palmitate, Imidazolidyn urea, Linoleic acid, Methyl paraben, Hydrolized collagen, Sodium EDTA.

QM 5 H BASE (A1M control)

Distilled water, Decyl oleate, Propylene glycol, Glycerin, Cethyl Phosphate, DEA-cethyl phosphate, Hydrolyzed collagen, Sodium PCA, Micronized titanium dioxide, Gelatin-glycine, Carbomer, Imidazolidynil urea, Tocopheryl acetate, Butyl methoxy dibenzoilmethane, Methyl paraben, Propyl paraben.

QM 5H/AHAs (A2M active)

QM 5 H BASE + 8% AHAs (glycolic and lactic acid)

QM 5 N BASE (A3S control)

Distilled water, Cetareth-6, Isopropyl miristate, Sodium PCA, Octyl stearate, Propylene glycol, Glycerin, Tocopheryl acetate, Hydrolized collagen, Gelatin-glycine, Linoleic acid, Retinyl palmitate, Disodium EDTA, Imidazolidynil urea, Methyl paraben.

QM 5 N/AHAs (A4S active)

QM 5 N BASE + 8% AHAs (glycolic and lactic acid)

Methods

Previous tests (17, 18, 22) showed the major role of the cosmetic vehicle used and the pH va-

lue of the finished product, which are essential for clear positive results at skin level.

For example, it was possible to show that an acid environment seems to promote the AHAs activity whereas the concurrent presence of gelatin-glycine seems to enhance AHAs action.

Selection of volunteer patients

This study was performed in 60 volunteer women aged 45 to 60, who had chronic skin damage due to a continuous exposure to sun rays and the so-called high-pressure lamps.

All selected women showed various signs of photoageing on their face, such as telangiectasis on the cheeks, thin wrinkles around the eyes and lips, actinic keratosis, wrinkles and hyperpigmented spots on the back of the hands. All suffered from dryness and clear dehydration of the skin of the face.

Cosmetic treatment

A double-blind cosmetic treatment was performed after teaching patients how to apply the A1M and A2M creams in the morning to the right or left half of the face (including the eye area) and to the right or left back of the hand respectively. The A3S and A4S creams were used always on the right or on the left, but in the evening. The creams marked with odd numbers had to be always applied to the same skin area.

Thirty minutes before applying the creams, the areas concerned were cleaned only with QM Cleansing Lotion that we supplied.

Fifteen women applied the 3AS product and 15 other women the 4AS product also to the inner part of the right forearm, whereas the left forearm was used as a control.

The cosmetic treatment lasted 12 weeks between January and March 1994, and tests were made always by the same researcher at 0, 4, 8 and 12 weeks, with a further test a month later, during which no cream was applied. The researcher

also checked that the creams be regularly applied according to instructions. During the treatment, no other cosmetic product was used. Thirty days before starting the study both topical and systemic treatments were discontinued.

Methods for skin mark detection

All photoageing-induced skin marks, which were separately detected in the various face areas, were examined before, during and after the cosmetic treatment using an analogic scale with 0 to 10 points, according to the Lever at all method (19). Results are shown in tables I - III.

Measurement of the moisture level, pH value and surface lipid film

These factors were measured before (0 weeks) and after 4, 8 and 12 weeks of treatment, always in the morning from 10.00 to 12.00 on skin cleansed the night before. According to instructions, no cream was applied the night before the measurement. A measurement was performed also on the 16th week. Values were obtained using the 3C SYSTEM® a new computerized equipment which automatically compares values always read at 22° C with 50% RH (20) (Fig. 1). Results are reported in figures 2 and 3.

Cell turnover

The cell turnover was tested by the Scrub technique on the forearms according to the Nicholls and Marks method (23), which had been already used by our research group in a previous study (24).

This method uses of a haemocytometer to count the number of desquamating horny cells taken from the skin with a 0.06 M phosphate solution of X-100 Triton by cutaneous scarification of a known surface and for a given time.

Results are reported in figure 4.

Table I

**THIN WRINKLES DETECTED ON THE SKIN IN EYE AREAS
WITH PHOTO-INDUCED AGEING**

Following treatment with 8% AHAs creams (as compared to the cream vehicles).

WEEKS	QM-8% (ACTIVE)	QM BASE (VEHICLE)	% REDUCTION	p
0	390	392	---	n.s.
4	298	335	11	< 0.001
8	273	307	11	< 0.001
12	250	283	11.7	< 0.001
16	246	280	12.1	< 0.001

Thin wrinkles detected around the eyes in 60 women treated with two AHAs-based creams on one side of the face (morning and night) and with the cream vehicles on the other.
Analogic scale (0-10) x 100.

Table II

**WRINKLES DETECTED ON THE SKIN IN BACK HAND AREAS
WITH PHOTO-INDUCED AGEING**

Following treatment with 8% AHAs creams (as compared to the cream vehicles).

WEEKS	QM-8% (ACTIVE)	QM BASE (VEHICLE)	% REDUCTION	p
0	344	349	---	n.s.
4	315	322	2	n.s.
8	303	313	3.2	n.s.
12	281	304	7.6	< 0.05
16	274	296	7.4	< 0.05

Thin wrinkles detected on the back of the hands in 60 women treated with two AHAs-based creams on one hand (morning and night) and with the cream vehicles on the other.
Analogic scale (0-10) x 100.

Table III

THIN WRINKLES AROUND THE MOUTH AND ON THE CHEEKS
Following treatment with 8% AHAs creams (as compared to the cream vehicles).

WEEKS	QM-8% (ACTIVE)	QM BASE (VEHICLE)	% REDUCTION	p
0	424	430	----	ns.
4	402	411	2.2	ns.
8	385	403	4.5	< 0.05
12	366	386	5.2	< 0.05
16	354	378	6.3	< 0.05

Thin wrinkles detected around the mouth and on the cheeks in 60 women treated with two AHAs-based creams on one side of the face (morning and night) and with the cream vehicles on the other.

Analogic scale (0-10) x 100.



Fig. 1

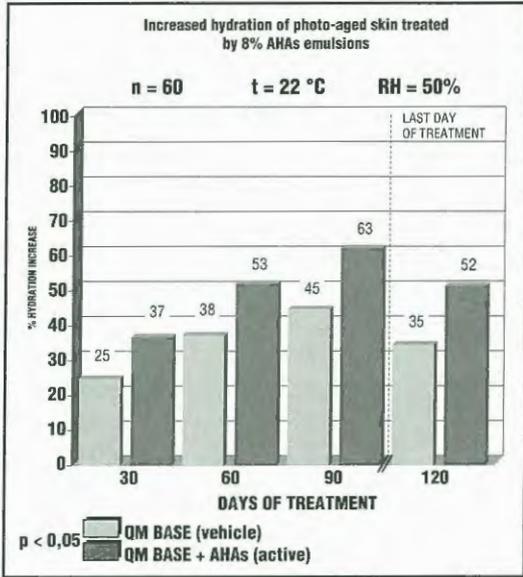


Figure 2

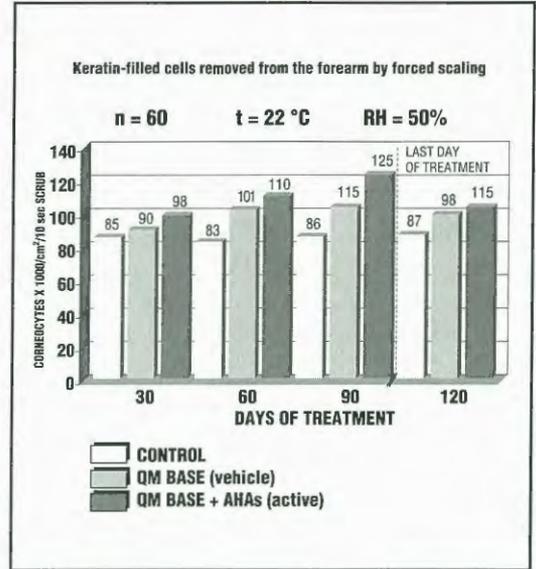


Figure 4

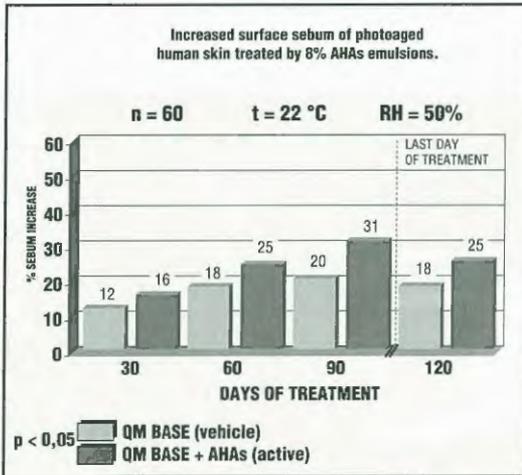


Figure 3

RESULTS AND REMARKS

As clearly reported in Tables I to III and as already shown by our research group (18), the vehicle by itself reduced the number of thin wrinkles which were detected on the face and hands between the 4th and 8th week of treatment. During the whole 12-week treatment, a significant decrease in thin wrinkles was detected,

which ranged from 16% (mouth and cheeks) to 20% (back of the hands) and 40% (eye area).

Adding AHAs to the vehicle reduced the number of thin wrinkles by a further 12%, 20% and 30% respectively. However, it should be underlined that the vehicle we used was added with Gelatin-glycine, which itself is active as an anti-aging agent, almost like AHAs (18).

Only a slight depigmentation of actinic keratosis and hyperpigmentations on the back of the hands occurred, while the number of these age-spots remained nearly unchanged.

The same applies to telangiectasis of the face. The skin moisture level increased by 45% after 3 months of treatment and by a further 40% when the vehicle was added with AHAs.

The same applies to the surface sebum, which increased by 20% with the vehicle alone and by 30% approx. with the active cream (Figures 2 and 3).

Interestingly, at the 16th week, that is 4 weeks after discontinuance of the cosmetic treatment, the tested values were still markedly better than the baseline values.

Thus, the effectiveness of the cosmetic treat-

ment tends to be steady over time at least of extra 30 days approx.

Similar improvements were obtained by forced scaling. By treating the skin with both the gelatin-glycine base and the active component (addition of AHAs), a marked increase in the cell turnover was shown (Fig. 4).

The aged skin behaves as the young skin.

In fact, through further tests still under way by the Dansil fluorescence method, fluorescence was shown to disappear by 22 days (25), and not by 34 days, as detected before the cosmetic treatment.

Again, both AHAs and the gelatin-glycine appear to be active substances stimulating and speeding up the cell turnover which photo-induced ageing usually reduces. As a result, the appearance of the skin is improved.

References

- 1) Gilchrest B.A. (1984) Skin and aging processes, CRC Press, Boca Raton, Florida
- 2) Montagna W. (1986) Common structure changes in aging skin. *J. Appl. Cosmetol.* **4**: 21
- 3) Balin A.K., Kligman A.M. (1989) Aging in the skin, Raven Press, N.Y.
- 4) Urbach F., Gange R.W. (1984) The biological effects of UVA radiations. Praeger ED, Australia
- 5) Kligman A.M. (1979) Perspectives and problems in cutaneous gerontology. *J. Invest Dermatol.* **75**: 39
- 6) Grove G.L. et al (1983) Age - associated changes in human epidermal cell renewal. *J. Gerontol.* **38**: 2, 37
- 7) Leger D.S., Francois A.M., Leveque J.L. Stoudmajer T.J., Grove G.L., Kligman A.M. (1988) Age-associated changes in stratum corneum lipids and their relation to dryness, *Dermatologica* **177**:159
- 8) Marks R (1993) Influence of age on stratum corneum cohesion, desquamation, and epidermal turnover. In: *Aging skin* (Leveque and Agache ED), M. Dekker, N.Y.
- 9) Saint-leger D., Agache P.G. (1993) Variations in skin surface lipids during life. In: *Aging skin* (Leveque and Agache ED), M. Dekker, N.Y.
- 10) Middleton J.D. (1978) Development of a skin cream designed to reduce dry and flacky skin. *J. Soc. Cosmet. Chem.* **25**: 519
- 11) Middleton J.D. (1978) Sodium lactate as a moisturizer. *Cosmet. Toiletries* **93**: 85
- 12) Idson B. (1982) Cosmetic dry skin, moisturizers, emollients and emulsions. *Cosmetic Tech.* **4** (5): 49
- 13) Tasumi S. (1972) Pyrollidone carboxilate acid. *Amer Cosmet. Perfum* **22**: 119
- 14) Kligman A.M. (1986) Topical tretinoin for photoaged skin. *J. Am. Acad. Dermatol.* **15**: 4
- 15) Smith W.P. and Smith W. (1993) Hydroxy Acids and skin aging. *Soap Cosmet. Chem. Spec.* **69**: 54 (n9)
- 16) Morganti P., Randazzo S.D. (1990) Skin hydration control and treatment: recent update. *J. Appl. Cosmetol.* **8**: 13
- 17) Walter P. Smith and W. Smith (1994) Hydroxy Acids and skin aging. *Cosmet. Toilet.* **109**: (n9) 41
- 18) Morganti P., Randazzo S.D., Palombo P. and Bruno C. (1994) Topical gelatin-glycine and alpha-hydroxy acids for photoaged skin. *J. Appl. Cosmetol.* **12**: 1
- 19) Lever L., Kumar P. and Marks R. (1990) Topical retinoic acid for treatment of solar damage. *Br. J. Dermatol.* **122**: 91
- 20) Cardillo A. and Morganti P. (1994) Fast and non invasive method for assessing skin hydration *J. Appl. Cosmetol.* **12**: 11
- 21) Roberts D. and Marks R. (1980) The determination of regional and age variations in the rate of desquamation: a comparison of four techniques. *J. Invest Dermatol.* **74**: 13
- 22) James B. and Morganti P. (1994) Oral administration of Gelatin-glycine for aged skin. *J. Appl. Cosmetol.* **12**: 17
- 23) Nicholls S. and Marks R. (1977) Novel technique for the estimation of intracorneal cohesion in vivo *Br. J. Dermatol.* **96**: 595
- 24) Muscardin L., Morganti P., Tartarin S., Valenzano L. (1976) Valutazione clinica dell'azione antiforforale e sebotatica di tensidi cationici associati allo zinco peritone. *Chron. Dermatol.* **7**: 659
- 25) 18) Morganti P., Randazzo S.D., Palombo P. and Bruno C. (1996) Stratum corneum "Turnover time" in aged skin: The effect of topical 14% ammonium lactate. *J. Appl. Cosmetol.* (in print)