

ENHANCING THE GLYCOLIC ACID EFFICACY BY PIEZOELECTRIC VIBRATIONS

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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 beginning 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 transmitted 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 et 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.

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'ispessimento 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 detera 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 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 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).

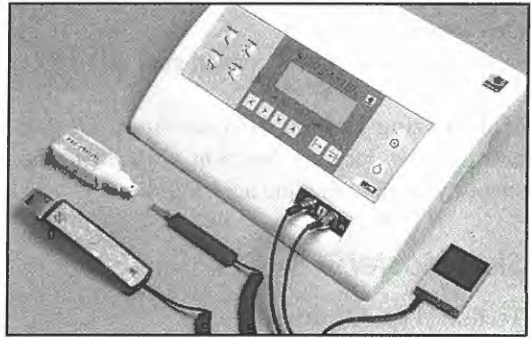
These side effects are linked to its own irritant properties as acid, but are also based on the following factors: concentration, pH, percentage and type of neutralizers used to adjust acidity, vehicle formulation, cleaning and/or degreasing treatment used, period of time the acid remains on the skin, 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 for 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®.

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 (*).

(*) Trade name: Keratotal® Peel

Cleansing Lotion:

(pH 4.5) Aqua, Cetareth-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 piezoelectric 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 capacitive 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).

(* Trade name: TS Gentle Cleansing

TEST PROCEDURE ON THE FACE

Patients

Fourthly 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 third 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.

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

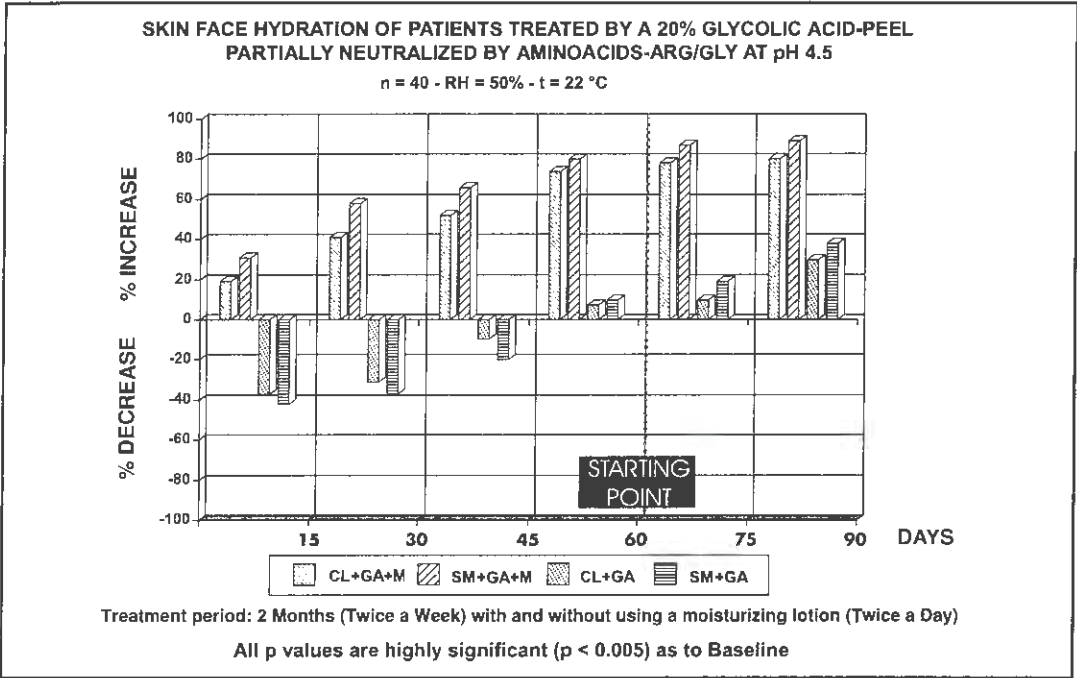


Fig. 1 Abbreviations: CL=Cleansing Lotion, GA=Glycolic Acid, M=Moisturizing Lotion, SM=Skin Master

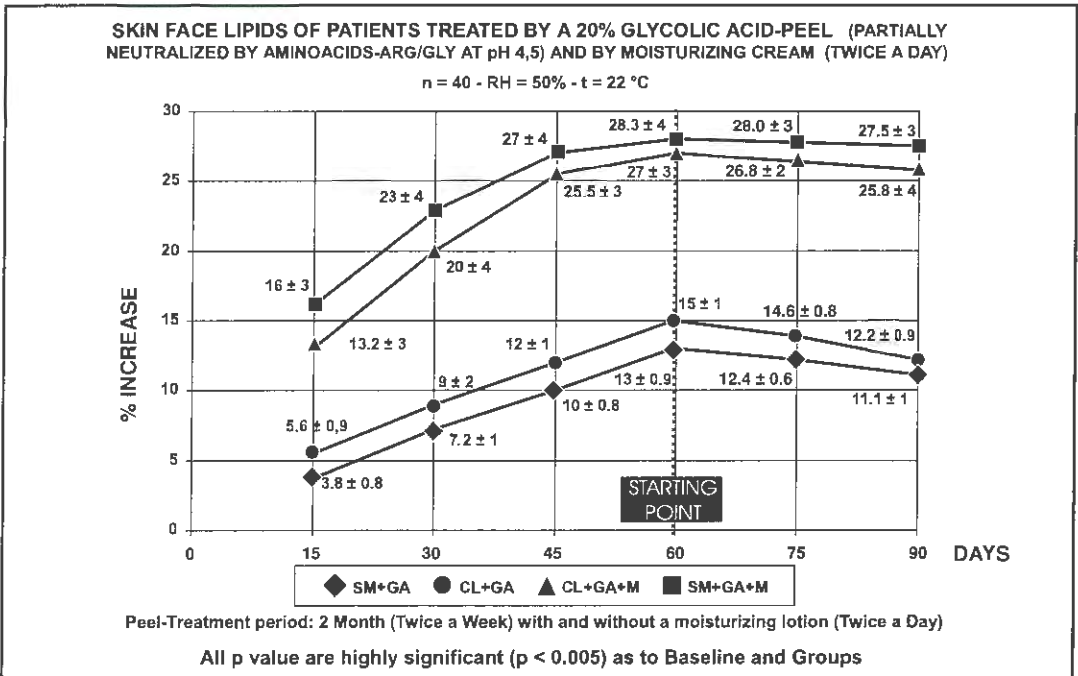


Fig. 2 Abbreviations: CL=Cleansing Lotion, GA=Glycolic Acid, M=Moisturizing Lotion, SM=Skin Master

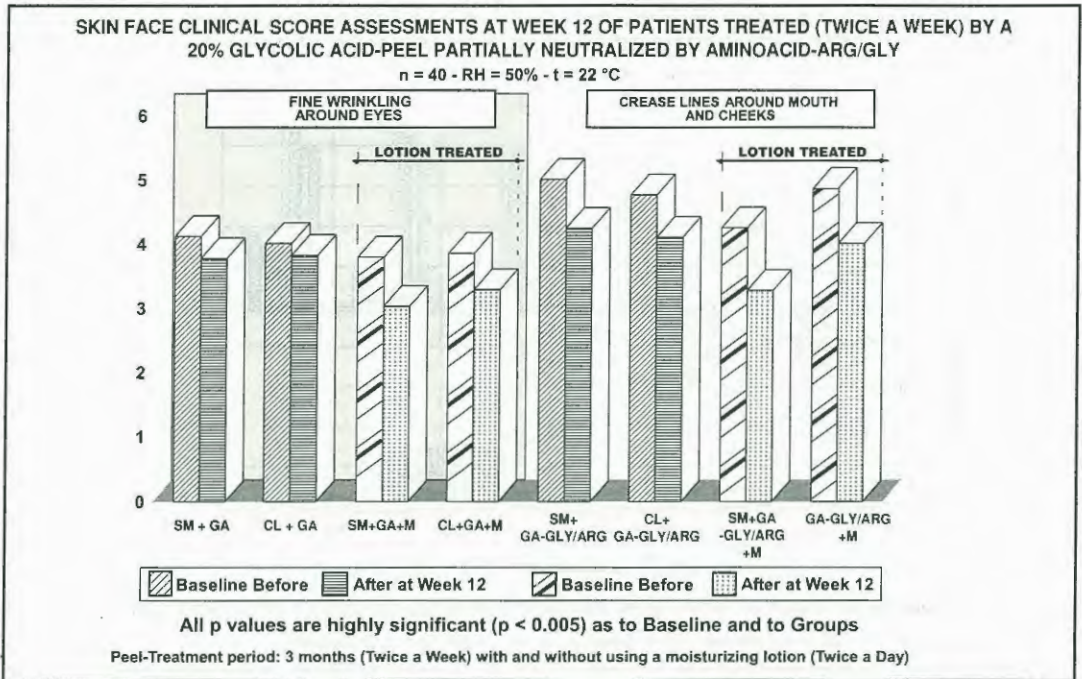


Fig. 3 Abbreviations: CL=Cleansing Lotion, GA=Glycolic Acid, M=Moisturizing Lotion, SM=Skin Master

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

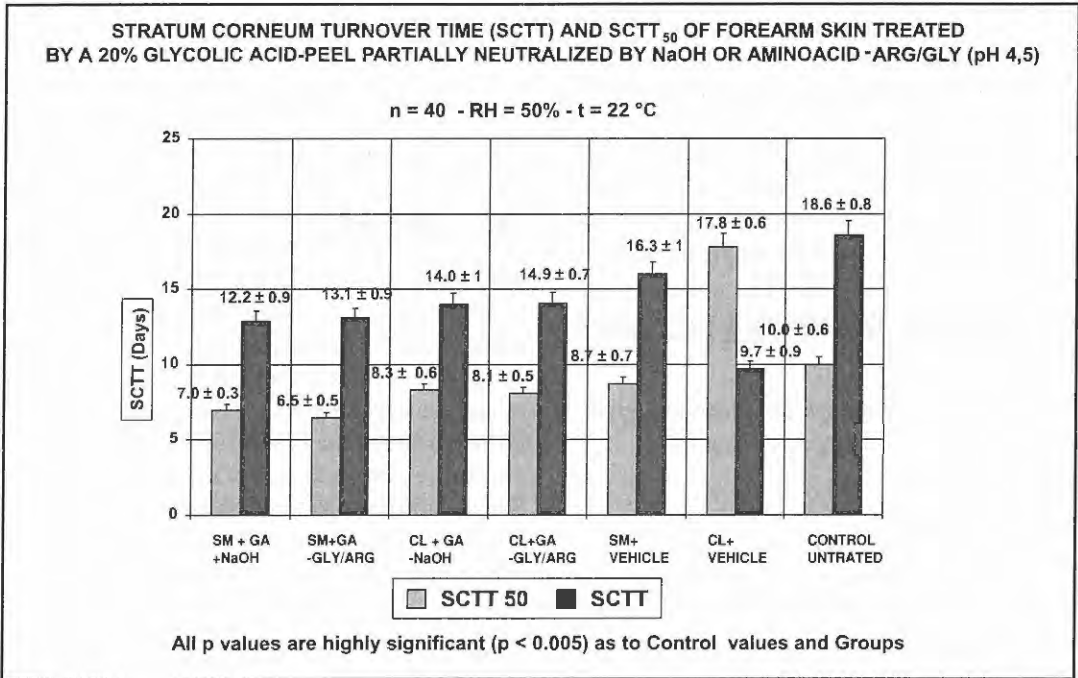


Fig. 4 Abbreviations: CL=Cleansing Lotion, GA=Glycolic Acid, M=Moisturizing Lotion, SM=Skin Master

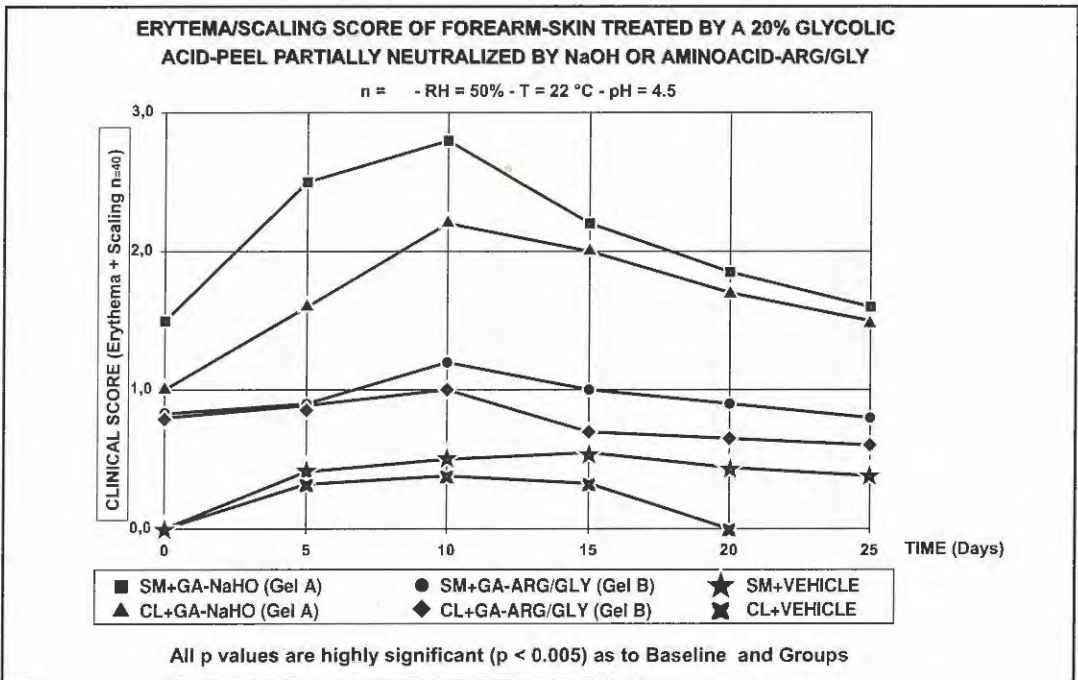


Fig. 5 Abbreviations: CL=Cleansing Lotion, GA=Glycolic Acid, M=Moisturizing Lotion, SM=Skin Master

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.

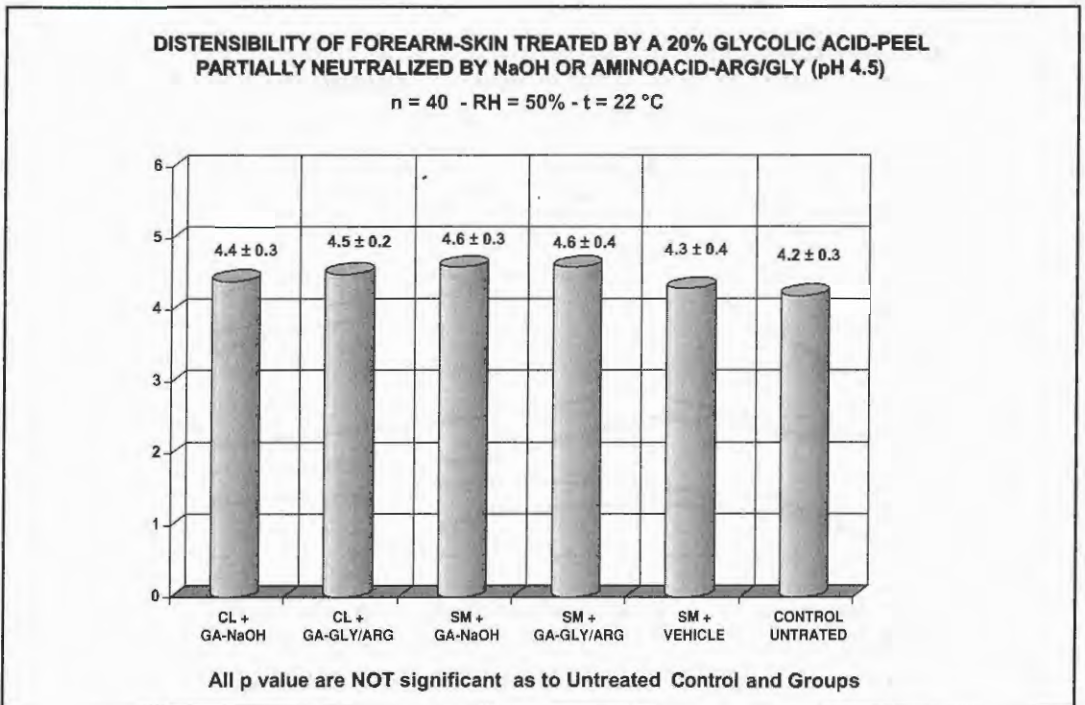


Fig. 6 Abbreviations: CL=Cleansing Lotion, GA=Glycolic Acid, M=Moisturizing Lotion, SM=Skin Master

RELATIVE ELASTIC RETRACTION (RER) OF FOREARM-SKIN TREATED BY A 20% GLYCOLIC ACID-PEEL PARTIALLY NEUTRALIZED BY NaOH OR AMINOACID ARG/GLY (pH 4,5)

n = 40 - RH = 50% - t = 22 °C

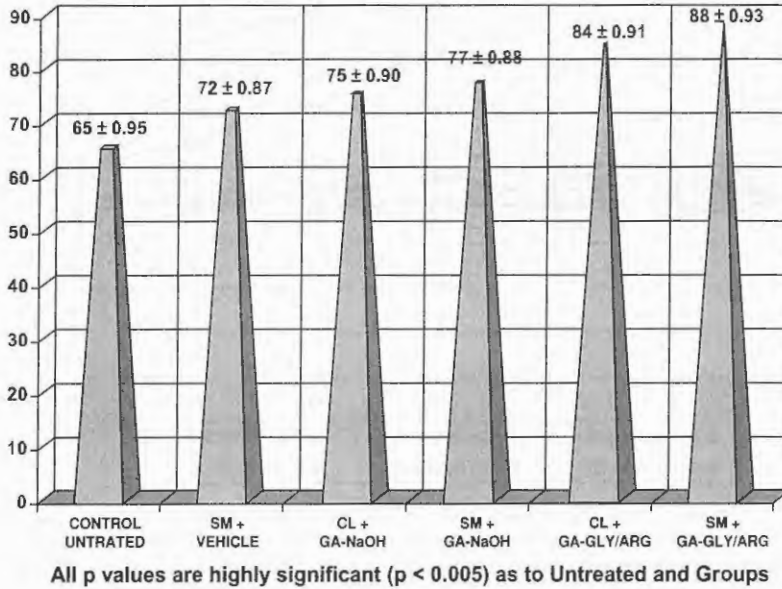


Fig. 7 Abbreviations: CL=Cleansing Lotion, GA=Glycolic Acid, M=Moisturizing Lotion, SM=Skin Master

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

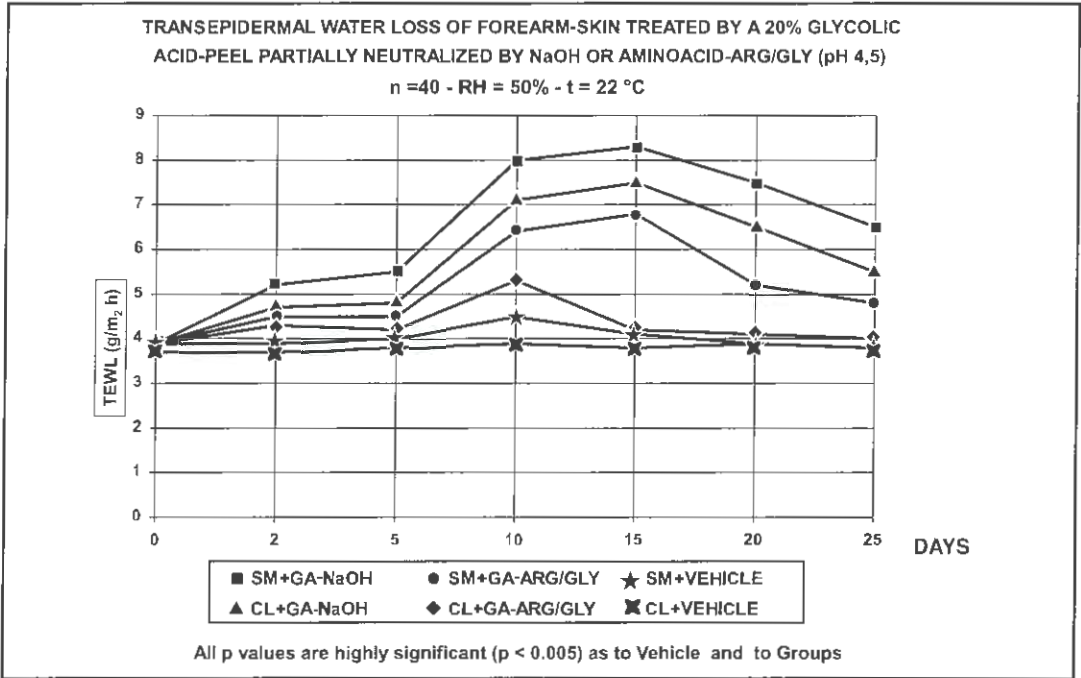


Fig. 8 Abbreviations: CL=Cleansing Lotion, GA=Glycolic Acid, M=Moisturizing Lotion, SM=Skin Master

($p < 0.005$), 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 erythemogenic 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.

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