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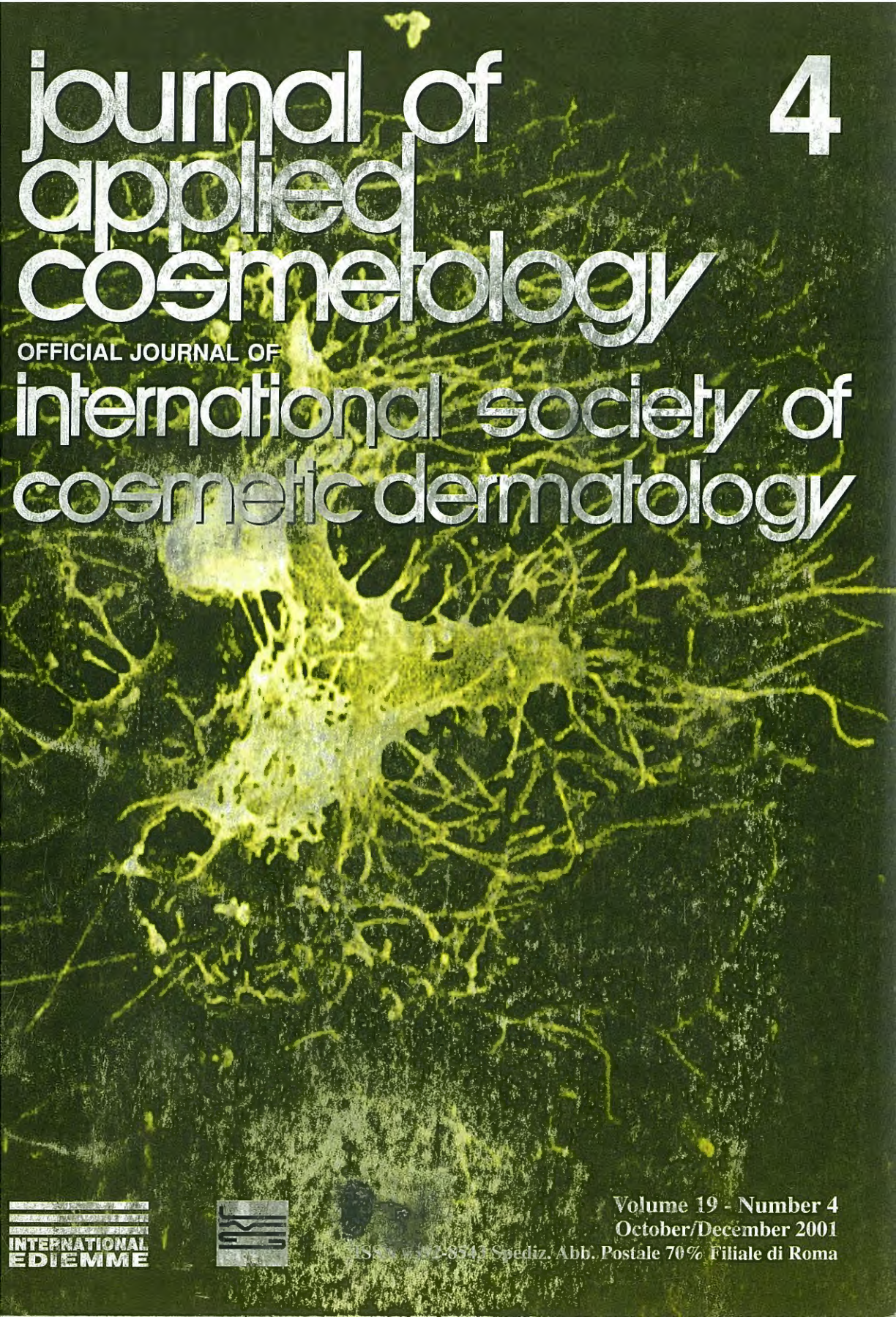

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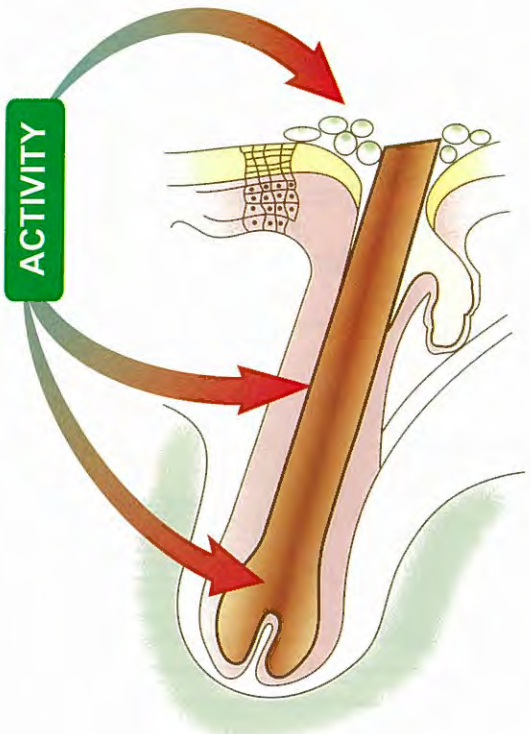

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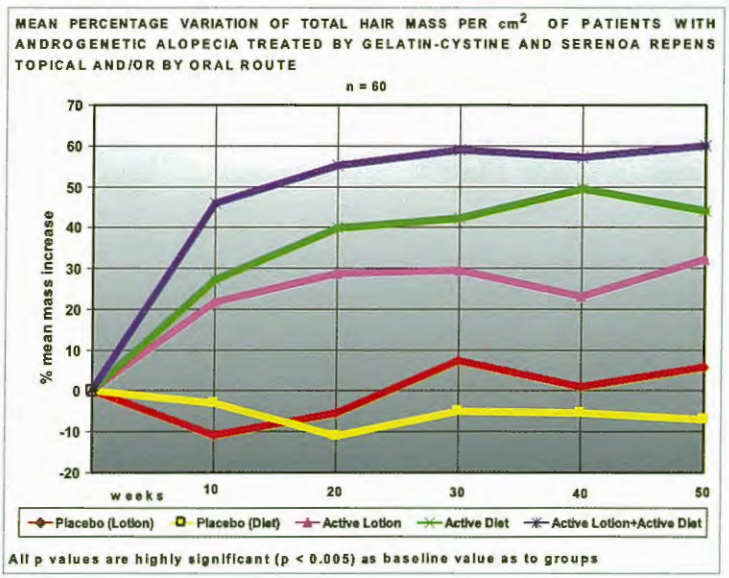

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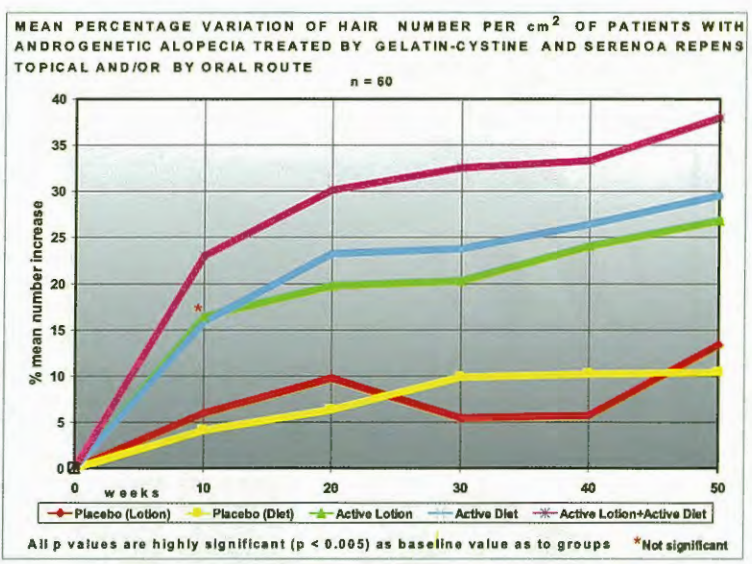

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BIWEEKLY IN-OFFICE INJECTABLE TREATMENT OF STRIAE DISTENSAE VS A LONG-TERM DAILY USE OF TOPICAL VITAMIN C

P. Morganti[1], P. Palombo[2], G. Fabrizi[3], M. Palombo[4], and S. Persechino[5]

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Received: *October 2001. Presented at The 10th EADV Congress, Munich, 10-14 October, 2001.*

Key words: *Striae distensae, Betaglucan, Vitamin C, Hyaluronan.*

Summary

The treatment of striae distensae (SD) is difficult, generally unsatisfactory, and no placebo-controlled study has been carried out to ascertain the effect of different topical treatments.

The aim of this study was to control the activity of both an office injectable treatment and a topical treatment of water solutions of vitamin C, betaglucan and hyaluronic acid (active A).

A single blind placebo-controlled randomized comparative clinical study was performed on 66 women aged between 18-24, with SD localized over the abdomen and buttocks. The subjects were divided into 3 study groups. Active B was applied at home twice a day for 16 weeks to 24 patients (group A). Twice a week they received also dermal injection of active A for the entire period. 22 patients in group B applied, twice a day, active B for 16 weeks. The remaining 20 patients in group C applied a placebo solution (distilled water) twice daily during the same period.

The differences between the results in the different groups were statistically significant at week 12 and 16 ($p<0.05$) both by visual score and by istological control performed. However, the combined use of injection and topical application (group A) provided superior results (+57%, $p<0.05$) compared with the group B (topical treatment only) (+32% $p<0.05$ vs. placebo). No side effects were observed during the treatment period, except a light burning at the moment of the injection. No results from placebo.

The combined topical and injectable use of vitamin C, betaglucan and hyaluronan seems to be effective to stimulate cell proliferation provided that the right concentration of the active with the right carrier is used.

Riassunto

Il trattamento delle striae distensae (SD) è difficile, scarso di risultati positivi e non è stato mai condotto uno studio di verifica confrontato con il placebo per controllare gli effetti di diversi trattamenti topici.

L'obiettivo di questo studio è stato quello di controllare per 16 settimane l'attività svolta da un trat-

tamento iniettivo e/o topico di una soluzione acquosa di vitamina C, betaglucano e acido ialuronico
E' stato eseguito uno studio clinico a doppio ceco randomizzato su 66 donne di età compresa tra 18-24 anni con presenza di SD localizzate su addome e glutei.
I soggetti sono stati suddivisi in 3 gruppi.
ACTIVE B è stato applicato localmente a casa due volte al giorno per sedici settimane su 24 soggetti del gruppo A che, due volte alla settimana, venivano anche trattati con applicazioni sottocutanee di un prodotto analogo sterile ed apirogeno (ACTIVE A).
22 pazienti del gruppo B venivano trattati due volte al dì con la sola soluzione topica (ACTIVE B).
Ai restanti 20 soggetti (gruppo C) veniva applicata localmente la soluzione placebo (acqua distillata).
I dati ottenuti alla 12° ed alla 16° settimana, controllati clinicamente ed istologicamente, sono risultati statisticamente significativi ($p< 0.05$) nei diversi gruppi.
Comunque l'uso congiunto delle applicazioni topiche e di quelle iniettive (gruppo A) è risultato superiore del 57% ($p< 0.05$) se paragonato con il solo uso topico (+32% $p<0.05$).
Non sono stati osservati effetti secondari .
L'uso congiunto topico ed iniettivo della vitamina C, del betaglucano e dell' acido ialuronico sembra possa considerarsi quale ottimo biostimolante cutaneo se utilizzato nei tempi e nei modi giusti.

INTRODUCTION

The treatment of striae distensae (SD) is difficult, generally unsatisfactory, and no placebo-controlled study has been carried out to ascertain the effect of different topical treatments (1-7).

AIM

The aim of this study was to control the activity on striae distensae of both an office injectable treatment (active A) and a topical one (active B) by the use of water solutions of vitamin C, beta-glucan and hyaluronic acid. As matter of fact it seems that this treatment increasing the secretion of growth factors and stimulating cell proliferation, may improve the appearance of SD (8).

MATERIAL AND METHODS

Material

1. *Active A:* hyaluronic acid, sodium salt 2 mg, sodium- carboxymethyl betaglucan 0,1 mg, ascorbic acid 0,5 mg, arginine 1 mg, sodium chloride 9 mg, sterile water for injectable solution q.b. at 1 ml, pH 7 [1];
2. *Active B:* aqua, sodium ascorbyl phosphate, 3-aminopropyl-L-ascorbyl phosphate, carboxybetaglucan, hyaluronic acid [2];
3. *Placebo:* distilled water solution;
4. *Cleansing foam:* Aqua, decyl glucoside, glycerin, chlorexidine digluconate, sodium hydroxymethylglycinate, methyl gluceth-20, lactic acid, triclosan, piroctone olamine, linseed acid, disodium EDTA, parfum[3];
5. *Scrub:* Aqua (Water), Decyl Glucoside, Glycerin, Hydrogenated Jojoba Oil, Trideceth-9, Potassium Azelaoyl Diglicinate, Peg-5 Octanoate, Glycine, Carbomer, Sodium Hydroxymethylglycinate, Polyethylene, Phosphatidylcholine, Propylene Glycol, Phenoxyethanol, Arginine, Aloe Barbadensis (Aloe Barbadensis Extract), Alcohol[4].

[1] *Trade name HCG 2000*
[2] *Trade name HCG 1000*

Clinical Methodology

A single 4 months blind placebo-controlled randomized comparative study was performed on 66 women aged between 18-24, with SD localized over the abdomen and buttocks.
The subjects were randomly divided into 3 groups:

1. *Group A:* composed of 24 patients, applied Active B at home twice a day for 16 weeks. Twice a week and for the entire period, they received also dermal injection of Active A. The product was applied directly on the SD area cleaned both by a supplied cleansing foam [3] and a scrub [4].
2. *Group B:* composed of 22 patients, applied Active B the same period and the same way.
3. *Group C:* composed of 20 patients, applied the Placebo solution.

In conclusion all the three groups applied at home on the skin ACTIVE B or PLACEBO and only 1 group (group A) was treated also by injection with ACTIVE A.

Patients

Each patient, supplied with identical vials containing ACTIVE B or PLACEBO, was instructed to apply them on the SD pre-cleansed area (cleansing foam + scrub) twice a day for all the study period. The patients were also instructed to not use any other skin care product.

Skin Biopsies

Biopsies specimen were taken from a SD area, sectioned into 1-mim wide strips, fixed in formalin at 4°C for 18 hours and transferred to ethanol for further fixation, and paraffin embedded. Three-micrometer sections were studied by means of SEM or normal histology.

[3] *Trade name ALFA 4 Micospuma*
[4] *Trade name KERATOTAL SCRUB*

Injection Methodology

ACTIVE A was injected by using a linear threading puncture technique with a 30-gauge needle. For each SD skin area was used from 1 to 4 ml of the product diluted with 3 percent carbocaine.

Prophilometry

Prophilometry of the SD areas was carried out by scanning the surface of its skin replica and quantitatively determining its microtopography according to Makky et al (9,10). The impression of the SD area was taken by using the SIFLO® rubber (Flexico Development Ltd., London, UK) and the quantitative topographic measurement of the surface microrelieves was determined by the Confocal Laser Scanning Microscope (CLSM) (11,12).
The obtained results are reported on Fig. 1.

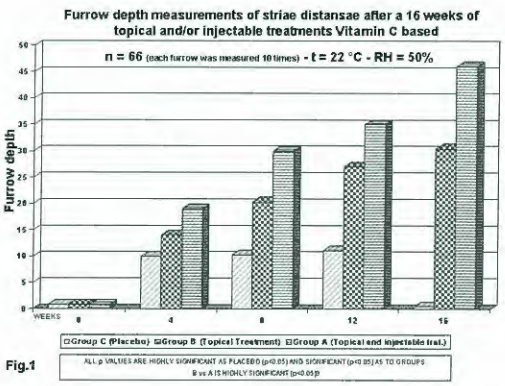

Fig.1

Clinical and Histological Evaluation

Obtained results, performed on the first day (baseline) and at week 4 8, 12 and 16 (end of treatment) were evaluated with a visual score-method, sequential photographs and biopsies in two patients.
Clinical evaluations included the efficacy for reduction of color and appearance of the STRIAE DISTENSAE as well as the skin tolerance after the application phase.
0 = normal color and dermatoglyphic pattern;
0.5 = white/pinky color and dermatoglific pattern less evident
1 = pink color, moderately flat skin
2 = intense pink color, flat skin
3 = violaceous color, flat skin
The obtained clinical results are reported on Figure 2.

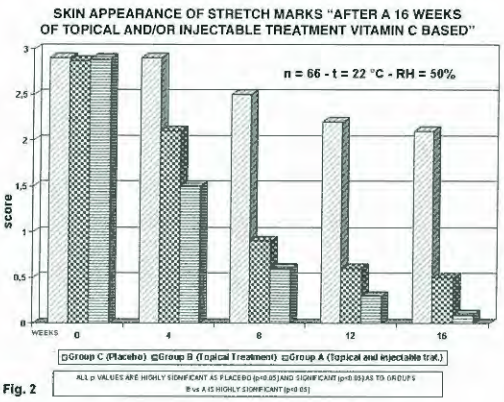

Fig. 2

STATISTICAL ANALYSIS

Mean and standard error of the mean were calculated for all data. The student *t* test was used for comparison between groups with a *p* value less than 0.05 considered significant.

RESULTS AND COMMENTS

As it is seen on Figure 1 and 2 the combined use of injection and topical application (GROUP A), both by the visual score and the prophilometry method showed that this treatment protocol improves the striae inducing the neoformation of the dermatoglyphic pattern of a bi-dimensional skin surface topography rich in micro and macrorelieves. Moreover the bioptic result showed also an increased production of elastin and normalization of histologic architecture of the cell component (Fig. 3 and 4).

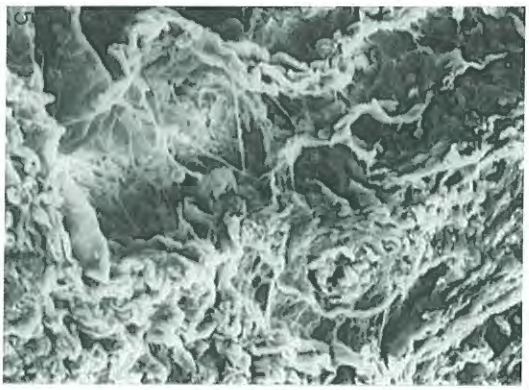

Fig. 3

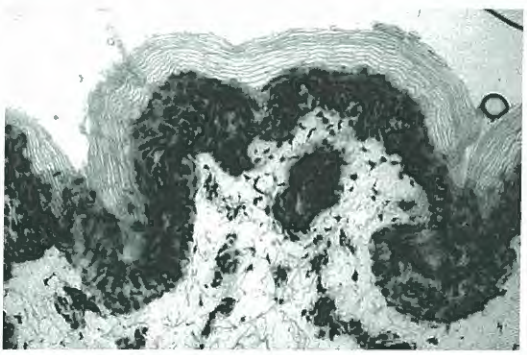

Fig. 4

What is interesting to underline is that the combined use of injection and topical application (GROUP A) provided superior results (+ 57%, $p< 0.05$) compared with the topical treatment only (GROUP B).
On the other side the topical treatment (GROUP B), compared to PLACEBO (GROUP C), showed to perform an interesting activity both on the deratoglyphic pattern and on the collagen bundles organization (+ 32%, $p<0.05$).
As matter of fact, both the treatments, topical and by injection, showed to ameliorate and to improve the striae that change in color appearing less evident. Moreover the combined solution used containing vitamin C, betaglucan and hyaluronic acid has been shown to normalize collagen bundles, to increase elastin production and stimulate both fibroblasts and cell proliferation (Fig. 3 and 4).
No side effects were observed during the treatment period, except a light burning at the moment of the injection.

CONCLUSIONS

From the obtained results from this first placebo-controlled study it seems realistic to state that this balanced solution of different active compounds, such as vitamin C, hyaluronic acid and betaglucan able to normalize the histologic architecture of the dermis and epidermis together with the dermatoglyphic skin pattern, may be successfully in the treatment of striae distensae and dermal scars.

Aknowledgements

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PREPARATION AND *IN VITRO* CHARACTERIZATION OF LIPOSPHERES AS A CARRIER FOR THE COSMETIC APPLICATION OF GLYCOLIC ACID

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Key words: *glycolic acid, liposphere, polymorphism, release, tristearin.*

Summary

Lipospheres for the cosmetic delivery of glycolic acid were prepared by the melt method using tristearin as the lipid phase and hydrogenated soybean phosphatidylcholine as the emulsifier. The most favourable conditions leading to the highest liposphere yield involved triglyceride/phospholipid ratios of 4:1 or 5:1 and a phospholipid concentration of at least 2%. The lipospheres, sized from 5 to 40 μm, contained a rather high glycolic acid loading level probably due to a partial polymorphic modification of the lipid and determined glycolic acid sustained release pattern.

Riassunto

Tramite la tecnica di fusione sono state preparate liposfere per il rilascio di acido glicolico ad uso cosmetico. A questo scopo è stata impiegata tristearina quale fase lipidica e fosfatidilcolina di soia idrogenata quale stabilizzante. Le condizioni operative migliori, in grado di determinare la resa più alta in liposfere, hanno previsto rapporti 4:1 o 5:1 tra trigliceride e fosfolipide e una concentrazione in fosfolipide di almeno il 2%. Le liposfere così ottenute, di dimensioni comprese tra i 5 e i 40 μm, presentavano elevati livelli di caricamento in acido glicolico, probabilmente attribuibili ad una parziale trasformazione polimorfa del lipide e profili di rilascio di tipo sostenuto.

INTRODUCTION

Lipospheres represent a recent fat-based microparticulate system developed for parenteral (1), oral (2) and topical (3) delivery of bioactive compounds. The recent focusing of the cosmetic technology on such a lipid carrier is due to its ability to modulate the cutaneous permeation by retaining or sustaining the release of active substances to the stratum corneum. This is an important feature, since an increase of the effectiveness of compounds involving or not skin absorption as well as a decrease of side local or systemic effects could be achieved. Moreover, lipospheres represent a microparticulate system utilizing naturally occurring lipids having chemical affinity with cutaneous components (triglycerides and phospholipids). Lipospheres consist of water dispersible, solid microparticles composed of a solid fat core, stabilized by one layer of phospholipid molecules at the surface. They have some advantages over other microparticulate systems, including liposomes and microspheres, for example, better physical stability, low cost of ingredients, ease of preparation and scale-up, high dispersibility in an aqueous medium, high entrapment of hydrophobic substances, controlled particle size and non-toxicity. Lipospheres having particular structure and names were developed for cosmetic companies, whereas lipid nanoparticles were registered under trade names as Lipopearls™ or SLN™ (4). A range of cosmetic ingredients like coenzyme Q10, vitamin E and its derivatives, retinol and sunscreen agents have been incorporated into lipid nanoparticles (5).

In this regard, the present study describes the preparation and the characterization of lipospheres for the cutaneous delivery of glycolic acid in order to reduce the skin damage and improve the effectiveness of this compound. In particular, lipospheres were obtained by the melt method using tristearin as the lipid phase and hydrogenated soybean phosphatidylcholine as the emulsifier. The formed lipospheres were evaluated for yield, morphology, size, thermal properties, entrapment capacity and glycolic acid release pattern.

MATERIALS AND METHODS

Materials

The following chemicals were obtained from commercial suppliers and used without further purification. Tristearin as the lipid phase and glycolic acid as the active substance were supplied by Fluka Chemie (Buchs, Switzerland), hydrogenated soybean phosphatidylcholine as the emulsifier was supplied by Lucas Meyer (Hamburg, Germany). All solvents and other products were analytical grade.

Methods

Unloaded liposphere preparation. Tristearin (1.6 g) was melted at 80°C and hot phosphate buffer solution at pH 7.4 containing hydrogenated soybean phosphatidylcholine was added in a ratio of lipid to phospholipid (lip/pho) ranging from 2:1 to 5:1. The ratio of lipidic phase to aqueous phase ranged from 1:25 to 1:10 (Method I) or it was kept constant at 1:25 (Method II) (Table I). The mixture was homogenized at 13,000 rpm by Ultra-Turrax (T25 Basic IKA-Werk, Labortechnik, Staufen, Germany). After 3 min the O/A emulsion was rapidly cooled under stirring to below 20°C. The formed lipospheres were washed with water, recovered by centrifugation at 4,000 rpm and freeze-dried.

Loaded liposphere preparation. A 4:1 lip/pho ratio according to the Method I was selected for the loaded lipospheres. Practically, glycolic acid (1.2 g) was mixed with tristearin (1.6 g), melted and homogenized in presence of 20 ml of 2 % hydrogenated phosphatidylcholine pH 7.4 phosphate buffer solution, as described above.

Table I

Liposphere formulation parameters

Lipidic/aqueous phase ratio	Lip/pho ratio	Phospholipid (%)
1:25	2:1	2
1:17	3:1	2
1:12	4:1	2
1:10	5:1	2
Method I		

Lipidic/aqueous phase ratio	Lip/pho ratio	Phospholipid (%)
1:25	2:1	2
1:25	3:1	1.3
1:25	4:1	1
1:25	5:1	0.8
Method II		

Liposphere yield. The yield in lipospheres was calculated on the weight of the supernatant fraction recovered by centrifugation compared with the whole sample.

Morphological and particle size analysis. Liposphere morphological structure was examined by both optical microscope and Scanning Electron Microscope (SEM, XL-40, Philips, Eindhoven, The Netherland). The particle size was determined by computerized image analysis (IMG-VIEW, CIGS, University of Modena and Reggio Emilia) of at least 200 lipospheres on SEM micrographs.

Determination of tristearin/water apparent partition coefficient of glycolic acid. A known volume of glycolic acid water solution was added to a known amount of melted tristearin. The mixture was maintained at 80°C under stirring until equilibrium was reached. Glycolic acid concentration was determined in the aqueous phase by spectrophotometrical analysis at a wavelength of 220 nm (model Lambda 3B, Perkin-Elmer, Norwalk, CT, USA).

Entrapment capacity. Glycolic acid content was determined by placing a weighted amount of loaded lipospheres in water. After 48 h glycolic acid concentrations in the filtered solutions were assayed by spectrophotometry.

Thermal analysis. Thermograms of commercial tristearin, commercial glycolic acid, (10:1) tristearin/glycolic acid physical mixture and loaded lipospheres were recorded on a differential scanning calorimeter (DSC-4, Perkin-Elmer, Norwalk, CT, USA) coupled with a computerized data station (Perkin-Elmer). Samples (about 10 mg) were heated in crimped aluminum pans at a scanning rate of 10°C/min using dry nitrogen flow (30 ml/min).

Glycolic acid dissolution and release. Drug dissolution and release from the loaded lipospheres were examined by using a column-type apparatus (Apparatus 4, USP XXIV) (Dissotest CE-1, Sotax, Basel, Switzerland) in 100 ml of pH 7.4 phosphate buffer at a flow rate of 25 ml/min and a temperature of 37±0.2°C. All experiments were carried out under sink conditions by determining the amount of glycolic acid released spectrophotometrically at fixed time intervals. All the data were averaged on three determinations.

RESULTS AND DISCUSSION

Lipospheres can be produced by melt or solvent technique. A melt process was preferred to avoid the risk of organic solvent residuals. Various lipid/phospholipid (lip/pho) ratios ranging from 2:1 to 6:1 were used by other authors and the formation of different phospholipid structures such as liposomes is described for higher phospholipid contents. Moreover, the determination of the surface phospholipid showed that 79-90% of the phospholipid polar heads were on the surface of the lipospheres prepared from lip/pho at a 2:1 to 4:1 w/w ratio (3).

To examine the effect of such a parameter on liposphere yield, morphology and size, lip/pho ratios ranging from 2:1 to 5:1 were obtained by keeping constant both the phospholipid concentration (2%, w/v) (Method I) and the internal/external phase ratio (1:25) (Method II). According to the Method I, lipospheres having spherical shape, smooth surface and without aggregates were recovered in the supernatant by centrifugation (Fig. n. 1). On the contrary, the lower fraction as well as the whole samples obtained by the Method II resulted in unshaped aggregates (Fig. n. 2).

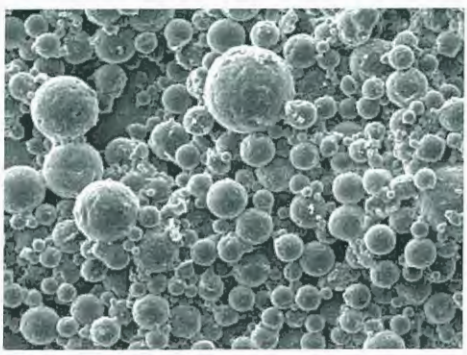

Fig. 1 SEM micrograph of lipospheres recovered in the supernatant by the Method I.

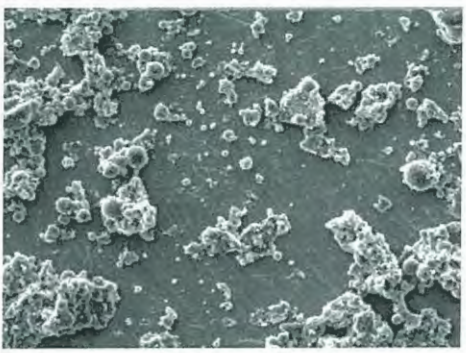

Fig. 2 SEM micrograph of lipospheres obtained by the Method II.

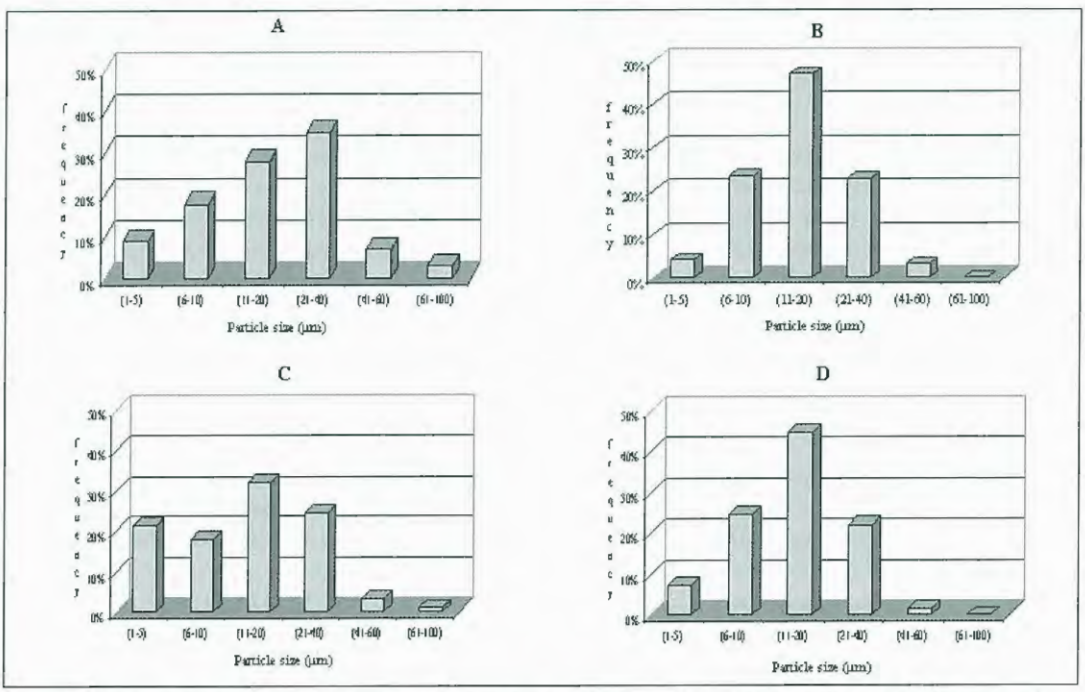

Fig. 3 Particle size distribution of lipospheres obtained by the Method I according to the lip/pho ratio: A) 2:1; B) 3:1; C) 4:1, D) 5:1.

The lip/pho ratio did not appear to affect significantly both average and distribution size of the lipospheres (Table II, Fig. n. 3). Lipospheres sized between 1 and 100 μm, the most population (80-90%) being in the size range of 5-40 μm, considered useful for topical applications (3).
The yield in lipospheres, calculated by considering the percentage of supernatant on the whole samples obtained by the Method I, increased with increasing the lip/pho ratio until 4:1 ratio (Table II). Therefore, the most favourable lip/pho ratios were found to be 4:1 or 5:1.

Table II

Yield and particle size lipospheres obtained according to the Method I

Lip/pho ratio	Particle size (μm)	Yield (%)
2:1	20.0±14.3	44.1±2.2
3:1	16.1±9.3	64.1±3.1
4:1	15.9±13.3	82.0±4.1
5:1	15.2±8.5	86.7±4.3

Therefore, 4:1 lip/pho ratio was selected to obtain lipospheres loaded with glycolic acid. The loaded lipospheres were examined for morphology, size distribution, water dispersibility, entrapment capacity, thermal behaviour and glycolic acid release pattern.
No significant differences in morphology and size were found in comparison with the unloaded microparticles. The loaded lipospheres showed a high dispersibility in water (Fig. n. 4). Since topical products don't support high amount of solid components owing to applicability and feel of use failure, a relatively high entrapment capacity should be required to achieve the necessary dose. Several factors can affect the entrapment capacity such as active substance partition coefficient and lipid polymorphic form and crystallinity degree (5-6). Though glycolic acid was characterized by a high solubility in melt tristearin (apparent partition coefficient between melt tristearin and water at 80°C resulted 0.08), the entrapment capacity of lipospheres was found rather high (34.06 ± 6.44 % w/w). This can be related to both the emulsification short period and the re-partitioning of the substance into the lipid phase with decreasing temperature of the water phase during the emulsion cooling. When recrystallization temperature of the lipid was reached, a solid lipid will entrap the substance which is present at this temperature (5). In addition, the crystallization of tristearin in lipospheres led to partial lipid polymorphic modifications. In fact, as thermograms show (Fig. n. 5), the stable ß-form (m.p. 57.55 ± 0.50°C, enthalpy of melting 91.92 ± 4.48 cal/g)

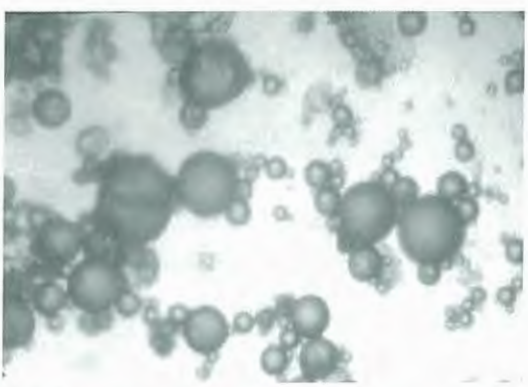

Fig. 4 Optical micrograph of an aqueous suspension of loaded lipospheres (X 400).

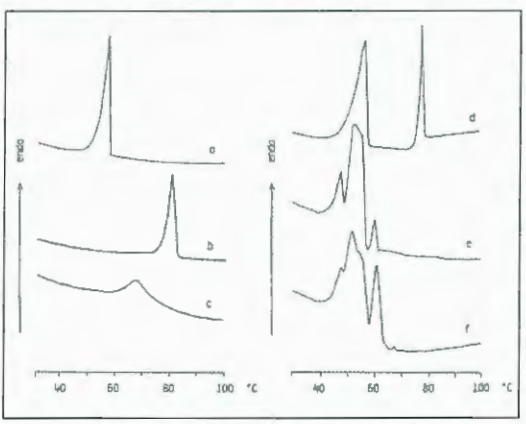

Fig. 5 DSC thermograms: A) tristearin; B) glycolic acid; C) hydrogenated phosphatidylcholine; D) (10:1) tristearin/glycolic acid physical mixture; E) loaded lipospheres.

transform partially in the unstable α (m.p. 48.92 ± 0.20°C, enthalpy of melting approximately between 6 and 30 cal/g) and ß' (m.p. 51.37 ± 1.59°C) forms. The unstable α–form is characterized by a lattice with disordered chains and imperfections that mean increased possibility to include and retain molecules (5). Moreover, the coexisting ß-form presents a decreased cristallinity degree (enthalpy of melting 22.41 ± 3.42 cal/g) with imperfections offering further space to accommodate the active substance.

Thermograms of lipospheres did not show the characteristic melting endotherm of glycolic acid, which is well evident in a 10:1 physical mixture, suggesting a complete molecular dispersion of the substance inside the lipospheres.

The lipid matrix so obtained provided prolonged release profiles (t_{50} = 30-90 min) compared with glycolic acid dissolution rate (t_{50} = 2 min) (Fig. n. 6). No "burst effect" was observed that could means the absence of glycolic acid at the liposphere surface.

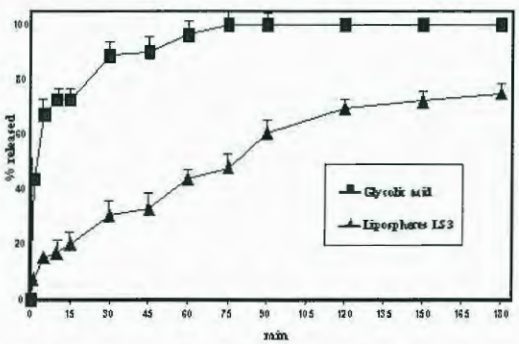

Fig. 6 Glycolic acid dissolution and release profile from lipospheres.

CONCLUSIONS

The present in vitro study involving the preparation and the characterization of lipospheres loaded with glycolic acid revealed lipid/phospholipid ratio and lipid crystalline structure as parameters to be considered in achieving appropriate liposphere yield and active substance incorporation, the latest being of particular interest for hydrophilic compound entrapment.

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AFTER-SUN CLAIMS SUBSTANTIATION: EXPERIMENTAL CRITERIA TO ASSESS THE IN VIVO EFFECTS OF SUN CARE PRODUCTS UNDER CONTROLLED-USING CONDITIONS

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Key words: *After-sun Products; Efficacy; Claim Substantiation; in vivo; Cosmetics*

Summary

Cosmetic claim substantiation is a new exciting reality although some complexities involving methodological guidance and technical sophistication justifies some reserve from the industry. Nevertheless, this can also be a beneficial opportunity for all the agents involved, as long as science-based demonstration of the above mentioned claims is achieved. The present study is a practical demonstration of this possibility regarding the claim substantiation of "after-sun" products. Ten healthy women 35 to 65 (44,5 ± 8,7) years old , following informed written consent, were selected after specific inclusion criteria. The procedure involved irradiation of both legs (antero-lateral) in laboratory for 6 sequential days using an indoor solarium-type as the UV source. Efficacy assessment endpoints were defined from the product's typical claims. Thus, methodological strategies included (a) sensorial (clinical) evaluation, by a trained observer, (b) biometrical measurements involving the assessment of Hydration (epidermal "capacitance") biomechanics (Ua and Uf descriptors obtained from the Cutometer suction method) and Erythema and Melanin indexes (Mexameter MX16) and, (c) a user's preference questionnaire. Results have shown that, regarding the clinical evaluation, discrete but, nevertheless positive appreciation was detected on the scored parameters. This was further confirmed by the biometrical assessment showing that both evaluation zones were significantly different, by the end of the study, in terms of hydration and biomechanical descriptors. The biometrical assessment of erythema and melanin served only to confirm the procedure's safety and efficiency regarding the irradiation phase. Finally, the "consumer's preference" questionnaire concluded on an absolute favourable opinion on the product's characterisation regarding the previewed claims. Thus, this study design and protocol illustrates how the predefined endpoints can meet claims under a scientifically based perspective, contributing to the definition of experimental criteria for "cosmetic efficacy" substantiation.

Riassunto

La pubblicizzazione dell'efficacia documentata di un determinato prodotto cosmetico rappresenta una stimolante novità anche se la difficoltà delle metodologie utilizzate, spesso molto sofisticate, giustifica alcune riserve da parte dell'industria. Questi studi documentati, rappresentano comunque una opportunità per tutti gli studiosi in grado di dimostrare tale efficacia con ricerche scientificamente ineccepibili.
Questo studio rappresenta una dimostrazione: il controllo che può essere effettuato su di un prodotto cosmetico "dopo sole".
Sono state sottoposte a sperimentazione controllata 10 donne volontarie di età variabile tra i 35 ed i 65 anni (44,5 ± 8,7), irradiando in laboratorio entrambe le loro gambe antero-lateralmente, e per 6 giorni consecutivi mediante l'uso di un solarium.
La metodologia di studio si è basata su (a) osservazioni chimiche soggettive, (b) misurazioni biometriche e biomeccaniche che hanno rilevato l'idratazione cutanea, l'elasticità (cuteometer), l'indice di eritema e di melanizzazione (Mexameter MX16) e (c) la stesura di un questionario di preferenze.
Sia le rilevazioni cliniche/soggettive che i controlli biomeccanici oggettivi, hanno rivelato una differenza significativa nei confronti dei controlli ed una sicurezza di impiego di tali metodologie. Infine, il parere dei consumatori si è rivelato positivo nei confronti dei messaggi pubblicitari utilizzati per il prodotto.
Il protocollo sperimentale utilizzato dimostra come sia possibile coniugare attività ed efficacia dei prodotti cosmetici definendola con criteri sperimentali corretti.

INTRODUCTION

The proof of the effect claimed for the cosmetic product is a known reality born from the progressive adoption of the Council Directive 93/35/CEE of June 1993[1] within the European Union.

From a practical point of view, although determined "by the nature of the effect or product"[1], the manufacturer (or his representative) is now strongly encouraged to avoid unnecessary claim disputes adopting a proactive posture and focusing the claims as a function of what can be defined as a sufficient proof of efficacy from experienced professionals[2-4].

Despite the obvious advantages implied, for the industry and regulatory authorities as well as for the consumer's information on the basis of which cosmetic expectation and satisfaction are built, several difficulties are apparent. Primarily because it is necessary to support any experimental demonstration on the basis of what may be called a "good scientific practice" and, simultaneously, to demonstrate the relevance of the claim substantiation procedure facing the product itself [2,5-7]. Detailed information and guidance on methodologies and other technical aspects to meet those purposes has not been produced by the European Union nor by the national authorities. The European scientific authority (SCCNFP, Scientific Committee for Cosmetic Products and Non-Food Products) published some notes regarding skin compatibility [8,9] and is expected to produce complementary opinion on the efficacy issue. Meanwhile, the Danish authority produced some notes on the subject[10] and COLIPA (the European Cosmetic Toiletry and Perfumery Association) formed a special task-force to face the efficacy-testing problem, publishing from 1997 a few guidelines and some general information for the cosmetic's efficacy evaluation[11,12]. Finally emphasis is due to the work produced by the EEMCO (the European Group for the Efficacy Measurement of Cosmetics and Other Topical Products), an independent European expert group formed to endorse many of the relevant issues implied[13,20]. Several reviews on technical assessment of efficacy-interesting variables have been published[14-23] which should be looked upon as being technical advisory keynotes meant to offer scientifically based assistance to meet the requirements of the Council Directive.

From a practical standing, several papers, specially addressing methodological aspects of the analysis, have been produced[5-7,24-28] definitely contributing to build up a scientific domain where the claim substantiation is the central motivation. Basically principles that are generally accepted include (a) clear and objectively defined test hypothesis, (b) adaptation of the level of experimental sophistication to the final endpoint in the trial, which in turn should be supported by (c)[5-7,29] an adequate study design and protocol. These are crucial aspects which should be permanently considered prior to any study and regarded as good scientific procedure.

In order to contribute to this new (conceptual) reality, the present protocol was designed to specifically address "after-sun" formulation claims, from the cosmetological properties referred on the product labelling and packaging analysis. This provides a good example to test the main principles which should be attended regarding study design of cosmetic claims substantiation, since obvious variability factors are present. Moreover it is clear that search for after-sun products is a fast growing market, mostly resulting from a poorly established sun-protection awareness. Official data is missing but practice reveals that exaggerated sun exposure is taking place probably as a consequence of over- expectation / misinformation regarding the use of sun-protection products [30,31].

Claims were assessed from the biological impact of the product in the normal human skin

and taking into account the user's appreciation (consumer's preference) regarding the product. This way, the authors aims to contribute to an objective definition of experimental criteria involving the efficacy assessment of this class of products, thus contributing to a better management of solar skin care.

MATERIAL AND METHODS

Pannel

Experimental data was obtained from healthy women selected after informed written consent, according with previously defined inclusion criteria. Volunteers (n=10) were aged from 35 to 65 years (44,5 ± 8,7), phototype II to III (Fitzpatrick classification) referring regular or occasional use of "after-sun" products, clearly expressing their availability to be exposed to the experimental procedure involving irradiation at laboratory for 6 sequential days.

Specific non-inclusion criteria included:

- cutaneous marks at the evaluation area which may influence or interfere with the effects appreciation (pigmentation disturbances, scars or scarring elements, hirsutism, ephélides and/or naevi high density distribution);
- allergy or special reactivity to body care products, including solar cosmetics;
- cutaneous sensitivity to sun exposure, including solar urticaria and idiopathic photodermatitis,
- treatment by any photosensitising medication within 1 month before the study
- treatment by acid Vitamin A or its derivatives within 3 months before the study;
- treatment by UVA or UVB within 1 month before the study

Irradiation Challenge

All experimental procedures were taken at laboratory, involving the permanent control of room temperature and humidity, in accordance with the usual recommendations regarding the application of this type of technologies[5-7, 24-28]. Prior to all measurements volunteers were left in the room for at least 20 minutes in order to allow skin's adaptation to room's temperature (21 ± 1° C) and humidity (40-60%) conditions .

The irradiation challenge was initiated with a reduced dose of radiation (Table I) in order to avoid any late form of erythema development. Following sessions took place 72H later, and proceeded for 5 sequential days (Table II).

In order to ensure full protection of the volunteers, the irradiation challenge was performed under permanent control involving the following measures:

(a) Irradiation was achieved through the system Sunny HB-406 Solarium, from Phillips; this system includes a 50Hz Carrying grip Compact UV lamp (type: Cleo HPA 400), corresponding to safety standard referred by the European CENELEC requirements (Insulation class II, UV-type III), and uses a specially shaped reflector of high-grade anodised aluminium and a UV-A filter glass

(b) The use of the Sunny system allowed to select the irradiation areas; in the present case only the evaluation and control anatomical areas (antero-lateral faces of both legs) were irradiated, always at a fixed distance (50cm).

(c) the irradiance was controlled through a radiation meter (Waldmann UV meter, France) which allows a detailed detection of UV-A and UV-B (long and short range) radiation

(d) all volunteers wore protective eye goggles (type: HB 072) while irradiated

(e) The mean UV radiation exposure dose or fluence (in the respective SI units – J/cm^2) achieved for the present study is shown in Table I

Table I

Mean UV radiation exposure dose or fluence (J/cm2) achieved during the irradiation procedure. The second session (Day 4) took place 72H after Day 1 session in order to detect any late form of cutaneous reactivity to UV radiation (see text)

	Day 1 session	Day 4 session	Day 5 session	Day 6 session	Day 7 session	Day 8 session	Day 11 (no session)
UV A	7,8	11,7	15,6	15,6	15,6	15,6	0
UV B	0,024	0,036	0,048	0,048	0,048	0,048	0

Table II

Schematic presentation of the sequential experimental calendar adopted according with the proposed study design. Clinical and biometrical evaluations preceded the irradiation sessions where indicated. Assessments at Day 11 were taken to evaluate the effect's persistence 72H after the last irradiation session (see text).

	Day 1 session	D 4 (D1+72H) session	D 5 session	D 6 session	D 7 session	Day 8 session	D11 (D8+72H) (no session)
Clinical evaluation:	X	-	-	-	-	X	X
Skin Biometrics :							
Mexametry	X	-	X	X	X	X	X
Capacitance	X	X	X	X	X	X	X
Cutometry	X	-	-	-	-	X	X
Self-perceptive evaluation (Questionnaire):	-	-	-	-	-	-	X

Evaluation Methodology

The evaluation methodology was defined to support the biological efficacy eventually claimed by the manufacturer. Under this perspective, the global evaluation of the product's properties and the respective in vivo efficacy were investigated through three complementary approaches as follows (Table II illustrates the sequential calendar of the experimental methodology):

The "Clinical" Assessment

This evaluation was performed by a trained evaluator and involved the sensorial (visual and tactile) investigation of each volunteer's skin characteristics at the application and control zones,. Considering the reference literature on the subject[14], sensorial parameters considered relevant for the study purposes were

- Desquamation (scaling)
- Roughness
- Cracks (fissures)

All these parameters were scored by the beginning and end of the study, and results expressed through semi-quantitative analogue scales (see ahead);

The Biometrical Evaluation

Skin properties were assessed by several variables obtained through non-invasive technologies considered specially relevant for the present study purposes. These were :

- Epidermal hydration obtained by the Corneometer CM825™ system (Courage±Khazaka GmbH, Koln, Germany); this system is actually the most frequently and referenced technological tool used to assess skin surface hydration 14-16 expressed in Arbitrary Units (AU's);

- Skin Biomechanics assessed through "cutometry" a well known method using the Cutometer SEM474™ system (Courage±Khazaka GmbH, Koln, Germany); this method allows to define several biomechanical descriptors from the skin deformation obtained after applying a negative (suction) pressure on skins surface through an appropriate probe[19, 22]. In the present case an 8mm aperture diameter probe was used in all measurements in order to ensure adequate signal resolution at the anatomical site chosen. Relevant descriptors for the study purposes were:

Uf – Total extensibility of the skin (expressed in mm), and

Ua– Total deformation recovery at the end of the stress-off period (expressed in mm);

The Melanin and the Erythema indexes obtained with the Mexameter MX16™ (Courage±Khazaka GmbH, Koln, Germany), used as a complementary assessment tool to follow up two biological expressions resulting from the experiment: the erythema and the melanogenic response following irradiation. These systems are based on the diffuse remittance spectrometry principle[17]; the absorbance of a volume of tissue at specific wavelengths is measured and the concentration of the absorbing pigment is estimated and given as a relative index (in Arbitrary Units, AU's);

The Self - Perceptive Cosmetic Evaluation Assessment (the "in use" Consumer's Preference Questionnaire)

The self-perceptive Cosmetic Evaluation Assessment corresponding to the volunteer's "in use" preference questionnaire, included the evaluation of the most important product – related aspects emerging from its regular use. These aspects were defined according to the product's "vocation", the manufacturer's claims (see ahead), and the foreseen consumer's expectation regarding the product's utilisation.

Tested aspects and respective options were :

(a) " Cutaneous comfort after application" - (A: Agreeable; W: Without any changes; D: Disagreeable)

(b) "The Calming Effect" - (V: Very satisfactory; S: Satisfactory; I: Insufficient; M: Very Insufficient)

(c) "The Refreshing Effect" - (V: Very satisfactory; S: Satisfactory; I: Insufficient; M: Very Insufficient)

(d) "The Moisturising (hydrating) Effect" - (V: Very satisfactory; S: Satisfactory; I: Insufficient; M: Very Insufficient)

Results were quantified and expressed in percentage referred to each qualitative scale adopted.

Methodological remarks

Other relevant aspects to consider were:

- the quali-quantitative composition of the after – sun formulation was irrelevant for the study purpose, chosen for being referred to present moisturising properties with soothing and revitalising benefits, helping to replace lost moisture and to feel cool.
- biometrical evaluation took place every day from the beginning of the study to the last day of essay (D11) 72H after the irradiation sessions (Table II); measurements were taken after the volunteer's adaptation to room condition, before irradiation
- application took place in one hemipart of the body, the contralateral hemipart serving as negative (intra-individual) control; performed by the volunteer, in both legs, after each session, there was no quantity restriction regarding daily application; additionally, each volunteer was allowed to take the formulation with you and to apply it, until a maximum of 3 applications /day
- each volunteer was also encouraged:

(a) not to apply similar products ("après soleil") in the tested zones;

(b) to strictly respect the application conditions specified by the protocol
(c) to maintain the regular hygiene and skin care (including make-up) habits

Statistics

Paired t student test or the non parametric Wilcoxon paired-test and Mann-Withney (for independent variables comparison) were chosen according with a normal or asymmetric data distribution. Data normality was tested, for both reference and application zones, through the Kolmogorov-Smirnov Test and through the distribution analysis (Normal Q-Q Plot and Detrented Q-Q Plot tests), and variance analysis performed through the Kruskall-Wallis test. A 95% confidence level was adopted ($p < 0.05$).

RESULTS AND DISCUSSION

The experimental criteria adopted intended to reduce the many different variability factors which are known to determine this type of studies, being recognised as the main source for experimental bias and inconclusive data. Therefore, these criteria involved the previous identification of experimental variability sources related with the evaluation methodology chosen.
Following the panel profile definition, assumed to represent the consumer's reference profile, it was crucial to define the "stimulus nature". In the present case this corresponded to the radiation source exposure in order to mimetise with adequate reproducibility, the "using" conditions justifying the use of this class of products. The variability introduced by the natural exposure to the sun (in the beach or at the sea-side) added to the risk involved in a whole-body solarium (tan-centres) were sufficient arguments to exclude them as alternatives. The UV stimulators used for solar testing and the phototherapy systems used for UVA/UVB therapy could also be regarded as alternatives but it is necessary to attend to the implied specificities and cost. Thus, the in-doors solarium alternative assured a suitable radiant light source providing:

1. control of the irradiation process, crucial for the study appreciation and validity, assuring that all individuals received the same UV radiation doses during the experiments;
2. selective irradiation of the chosen part of the body, contributing to measurement standardisation
3. full control of the experimental methodology including each individual safety conditions
4. low cost

Considering the study global objectives, evaluation analysis involved complementary approaches, meant to provide the maximum quantitative information about the product's biological impact on in vivo healthy human skin. These were defined having in mind several aspects regarding the most frequently referred claims found in this class of products[31-34] including:
- Hydration (replacement / reinforcement)
- Skin nutrition
- Calming effect
- Refreshing effect
- Fast "vapouring" effect
- Pleasant feeling (after application on the skin) / lubricating /
- Easy to handle and to apply
- Non - "gras" / non "tacky"

These determined the nature of the analysis involving the three complementary approaches as follows:

Sensorial (clinical) Assessment

Sensorial evaluation of both areas allowed to confirm that the same skin condition was present in both legs. Scaling (small scales only, surface lightly dull in colour) was present in 6 / 10 volunteers at the beginning of the study. By the end of the study, scaling was absent in 8 / 10 volunteers on application area while at the reference area this condition worsened in 4 volunteers.

Roughness, detected by tactile evaluation was also present, slightly irregular and scratchy on tangential tactile evaluation, in 4 / 10 volunteers at the beginning of the study. By the end, this condition still persisted in 3 volunteers, in the application area. In the control area, this condition worsened in 5 / 10 volunteers.

Single and superficial cracks were also presented in the skin evaluation area in 2 / 10 volunteers, disappearing in one of them only in the application area, by the end of the study.

Skin redness and pigmentation although not related with the product's efficacy, were also evaluated to follow the adequacy of the methodological procedure. At the beginning of the study, redness was detected in one volunteer who presented small areas of minimal / diffuse faint redness. The end of the study revealed no change on this parameter, thus not related with the product. Regarding the pigmentary reaction no changes were detected whatsoever.

Results obtained from the present approach stresses the relative usefulness of the sensorial evaluation even when normal (non-pathological) skin is involved. Taken as indicators of the product's impact on normal in vivo skin only slight but, nevertheless, clear changes can be observed between the first and the last day of the study. Although reflecting a positive evolution in all the hydration – related variables, there's no dramatic evidence of significant differences between these two evaluation moments. Some significant differences, regarding skin dryness could still be found from the independent variables analysis between reference and application zones ($p< 0.05$). However, considering that tbe scores itself, being non-continuous variables, may evoke major distribution changes around the mean, these results should be carefully interpreted and complemented with data from biometrical measurements.

Biometrical Assessments

Erythema and melanin indexes were determined by the need to ensure that the experimental procedure was adequately developed, meaning to avoid any acute response to the UV exposure and, at the same time, to confirm that the pigmentary reaction was effectively occurring. Therefore, these results are rather meant to confirm the efficacy of the experimental procedure than to support any other claim related to the product's properties.

As suggested in Figure 1 significant differences

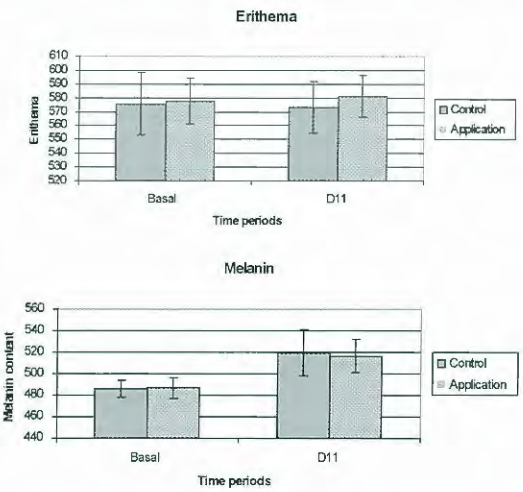


Figure 1. *Erythema and Melanin indexes evolution over the experimental protocol. Mean values and respective standard deviation are expressed in Arbitrary units (AU's) both for control and application zones. As shown there's no evidence of change for the erythema index, while at D11 the melanin index suggests that the melanogenic response took place, equivalently, at both evaluation areas.*

between control and application zones could not be found for the erythema index (575,7 ± 7,24 UA's in D0 and 573,5 ± 5,96 UA's in D11 for the control zone and 577,7 ± 5,19 UA's in D0 and 581,3 ± 4,76 UA's in D11 for the application zone) confirming that the experimental procedure prevented any risk of acute or delayed erythema.

Regarding the Melanin index at the end of the study (Figure 1) both zones were significantly different ($p< 0.05$, Wilcoxon paired test) from the respective values obtained at D0; no statistically significant differences were demonstrated between both zones at D0 and D11 (486,0 ± 2,57

UA's in D0 and 519,4 ± 6,78 UA's in D11 for the control zone and 486,7 ± 3,08 UA's in D0 and 516,5 ± 4,89 UA's in D11 for the application zone).These results suggested the efficacy of the pigmentary reaction induced through the chosen experimental procedure.

Regarding the skin's surface hydration, statistically significant differences were immediately found from D4 on, following the application procedure (Table III). These seems to result directly from the product's hydration capacity since a clear improvement of the epidermal "capacitance" is apparent in the application area, while in the control zone, no differences are detectable. Also noteworthy is that these differences are progressively marked form Day 6 on (Table IV). This is further confirmed by the variance analysis (Kruskall-Wallis test) which shows significant differences for D7 ($p < 0.05$), D8 ($p < 0.05$) and D11 ($p < 0.005$) as a consequence of the product's impact on the biological elements of human skin. Data from reference zone shows a distinct evolution including progressive dryness in the last days of the study.

Table III

Skin surface hydration changes, expressed in terms of epidermal "capacitance" (UA's) obtained in the different phases of the experimental protocol in both experimental areas.
Results from comparative statistics (Wilcoxon) are also shown, illustrating a clear significant difference at the application site when compared with reference (basal) values.

Application zone	**Basal**	**D4**	**D5**	**D6**	**D7**	**D8**	**D11**
Mean	44,4	49,7	49,6	52,2	54,6	53,8	54,7
St. deviation	8,81	7,56	7,09	8,35	8,71	7,05	7,07
p		*	*	**	**	**	**
Control zone	**Basal**	**D4**	**D5**	**D6**	**D7**	**D8**	**D11**
Mean	44,0	44,2	44,7	44,9	45,7	42,8	43,5
St. deviation	8,63	6,76	7,07	6,98	7,57	6,14	5,17
p		NS	NS	NS	NS	NS	NS

NS non significant differences found * $p < 0.05$; ** $p < 0.005$

Regarding tbe biomechanical assessment, a special careful analysis is recommended having in mind the many complexities involved in this present approach, specially for claim substantiation purposes[19, 22]. For the chosen method, data results from analysis of the curves obtained by applying a negative perpendicular pressure to the skin's surface (creep). Deformation of the analogue signals is an obvious factor to attend when choosing the appropriate parameters. Additionally, a clear-cut relationship between those variables provided by the system and the respective biophysical equivalents, is absent. Therefore, considering the various biomechanical descriptors available, those whose interpretation depend less from the curve deformation, should he chosen[22, 35]. This is the case for descriptors Uf corresponding to the total extensibility of the

skin, and Ua corresponding to the total deformation recovery at the end of the stress-off period.

Regarding the total extensibility of the skin descriptor (Uf), as shown in Table V, very significant differences are detected at the end of the essay (D8 and D11) in the application zone as opposed from the control zone. Failing to demonstrate significant differences between control and application zones (Man-Whithney test, Table VI) may result from some data dispersion around the mean. This may be justified by an eventual low sensitivity of the system to detect small changes (around the mean), evoking enough dispersion to transform the mean in a non-significant "p" for the present confidence interval. In any case, the border-line "p" value obtained should be noted (Table VI)

Table IV

Man-Whitney tests for independent data regarding the hydration changes obtained in the different phases of the experimental protocol in both experimental areas. Results clearly detect progressively marked differences between both zones, which can be attributed to the after-sun formulation impact on skin's surface.

Application v. Control zone	Basal	D4	D5	D6	D7	D8	D11
p	0,970	0,069	0,130	0,064	0,045	0,004	0,003
	NS	NS	NS	NS	*	**	**

*NS non significant differences found * $p < 0.05$; ** $p < 0.005$*

Biomechanical related improvement is further confirmed by the Ua descriptor, which shows again, at the application zone, very significant differences in D8 and D11; while, for the reference zone no differences are detected (Table V and Table VI).

Table V

Skin biomechanical changes, expressed in terms of the biomechanical descriptors Uf and Ua (mm) obtained in the beginning and in the end of the experimental phases (D8) in both experimental areas. Assessments at Day 11 were taken to evaluate the effect' s persistence 72H after the last irradiation session (see text). Results from comparative statistics (Wilcoxon) are also shown, illustrating a clear significant difference at the application site when compared with basal (see text)

Uf	Application			Control		
	Basal	**D8**	**D11**	**Basal**	**D8**	**D11**
Mean	1,22	1,42	1,42	1,21	1,22	1,21
St. Deviation	0,23	0,31	0,30	0,19	0,18	0,19
	**			NS		
p	**			NS		

Ua	Application			Control		
	Basal	**D8**	**D11**	**Basal**	**D8**	**D11**
Mean	1,00	1,14	1,14	0,89	0,87	0,86
St. Deviation	0,23	0,27	0,27	0,21	0,28	0,26
	**			NS		
p	**			NS		

NSnon significant differences found * $p < 0.05$; ** $p < 0.005$

Table VI

Analysis of independent data (Man-Whithney) perfomed for the chosen biomechanical descriptors in both experimental areas. A positive effect over the skin biomechanics is only shown from the Ua variable. The border line "p" detected for the Uf variable may indicate about some dispersion of results (see text).

Uf
Application v. Control zone

	Basal	*D8*	*D11*
p	0,940 NS	0,064 NS	0,059 NS

Ua
Application v. Control zone

	Basal	*D8*	*D11*
p	0,112 NS	0,008 *	0,013 *

NS non significant differences found

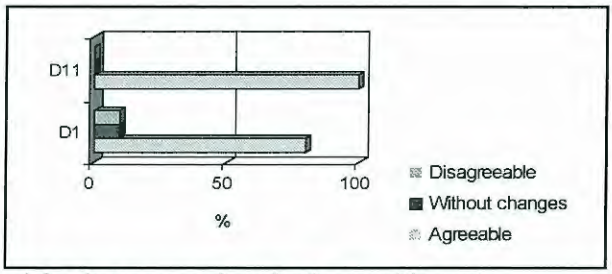
* $p < 0.05$; ** $p < 0.005$

No significance differences between basal values and values obtained by the end of the essay could be detected at the reference (control, non-treated) zone. So, the present assessment suggests that, under the present experimental condition, the positive evolution of both biomechanical descriptors Uf and Ua can be attributed to the regular "treatment" foreseen in the experimental methodology.

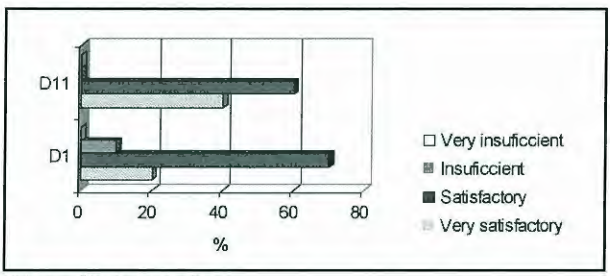
THE SELF-PERCEPTIVE COSMETIC EVALUATION

Finally, regarding the self-perceptive evaluation of the product, an important tool useful to assess the consumer's satisfaction (regarding the expectation generated by the product), a clearly positive appreciation of the product utilisation and characteristics resulted from the present evaluation. Again, it should be stressed that the self -perceptive evaluation questionnaire was constructed from the most frequently referred properties claims by the manufacturer for this special class of products. Excluding other aspects more related with the formulation characteristics, this assessments revealed an absolute positive appreciation (100%) regarding the " Cutaneous comfort after application", "The Calming Effect", "The Refreshing Effect", and "The Moisturising (hydrating) Effect" questions (Figure 2) .

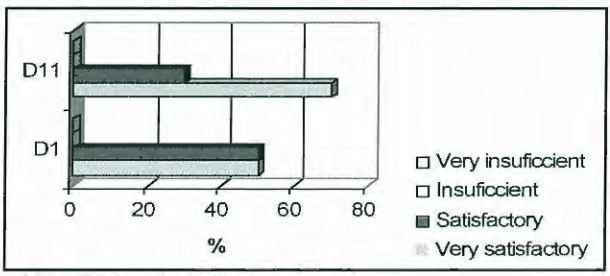
These results are in full agreement with data from the other assessments corroborating a global positive biological impact, under the present experimental conditions, on normal human skin.



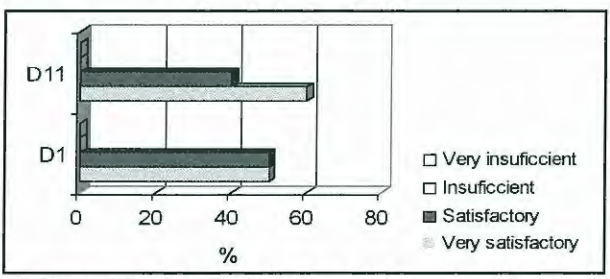
a) Comfort sensation following the use of the produ



b) The "Calming" effect



c) The "Refreshing" effect



d) The moisturising effect

Figure 2. *("a" to "d"). Results from the self-evaluation questionnaire on the volunteer's opinion about the product qualities (efficacy claims) and the consumer's satisfaction. Results, expressed as a percentage of the obtained responses, are referred to two different moments of product's use – D1 and D11. A clearly positive appreciation is obtained from the regular use of the product under study (see text).*

CONCLUSION

Previously defined endpoints and a clear definition of the study's rationale, are crucial elements for any scientifically based study.
Keeping in mind the multiple factors which supervise the validity of biomedical trials involving human subjects and the critical determinants of non-invasive methodologies used for efficacy assessments, the present proposal illustrates how to involve the most frequently used evaluation tools – clinical, biometrical and consumer's in-use assessments, to establish a relevant relationship with the claim and the parameter, in order to reveal the main effects of the product. In spite of recognising that several experimental aspects can be improved, as it happens in the present example with the irradiation source, this approach also demonstrates how to meet under acceptable compromise (main goals-level of sophistication-cost), the predefined endpoints with the respective claims, in a scientifically based perspective.

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LASER HAIR REMOVAL

By D. J. Goldberg
2001. 224 pages with about 400 colour illustration. Hardcover
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E-mail: info.dunitz@tandf.co.uk
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Nowadays total and partial laser hair removal is considered a real problem in modern Aesthetic Medicine, in Dermatology and in Plastic Surgery.
The laser/light sources to remove unwanted hair are fashionable even because their relevant techniques have been improved.
This book clearly reports in 10 chapters all the problems concerning this hair removal novel technique.
The first two chapters respectively review hair biology, laser physics and its application to hair removal. Long-term or permanent hair removal requires a laser or light source impact on one or more growth centers of hair, such as dermal papilla, that is also the major probable site of melanin production in terminal hairs. It is melanin itself that absorbs visible and laser light used to remove unwanted pigmented hair.
Is then realistic to discuss about permanent hair removal? Currently there is no agreement on a definition of treatment-induced permanent hair loss.
Thus hair may be considered permanently removed from its location if there is no recurrence after its complete growth cycle of 3-7 months. If no hair regrows after this time, it can be assumed that the growth centers have no capacity to recover from injury. Therefore, meanwhile the permanent hair loss, as an absolute lack of hair for the lifetime, is surely an unrealistic goal, it is now widely accepted that any laser can induce temporary hair loss for at least 1-3 months.
However the development of localized or diffuse unwanted excess hair induces many individuals to seek hair removal by chemicals, mechanical or laser. At this purpose the knowledge of the hair cycle and especially the length of telogen phase, because essential for determining whether laser or light-source treatment of unwanted hair, will be temporary or permanent.
As matter of fact long-term hair removal requires that a laser source impact on one or more growth centers of hair, such as the matrix.
Laser light emitted in the visible and near-infrared electromagnetic spectrum, is absorbed by melanin chromophores and converted into heat which can exploited to destroy hair. The impact of laser light on hair varies with energy fluence, wavelength, pulse width, and spot size. Therefore the optimal pulse duration for photothermolysis selective for hair removal seems to be less than or equal to its thermal relaxation time.
Thus for a typically treated hair follicle of 200-300 μm in diameter, the thermal relaxation time would be about 40-100 ms.
Chapter 3 is dedicated to electrolysis, that refers to the permanent removal of hair by the insertion of a fine wire needle into the hair follicle.
This needle acts as a conductor to carry the appropriate current to the base of the hair follicle and particularly to the controlling hair papilla.
The goal of this technology is to provide enough electrolysis energy to destroy the germinative ma-

trix cells and dermal papilla without allowing destructive energy to reach the skin surface.
At this purpose precise needle insertion is the cornerstone of electrolysis excellence, and attention must be paid to needle direction, angle and depths and, of course, to deliver sufficient current (intensity) for an adequate time (duration) necessary to destroy the growing portion of the hair follicle.
According to the author, although large areas of hair may be more efficient ly removed with lasers, non-pigmented hair appears to respond best to electrolysis.
In addition, it maybe more economical to treat small areas of undesirable hair with electrolysis than with lasers.
However the two techniques, laser and electrolysis, would complement each other.
Chapters 4, 5, 6 and 7 report studies on hair removal by four diverse technologies such as the ruby, the alexandrite, the diode and the Nd: YAG laser.
On these four lasers are reported the technical characteristics, the instruction and the clinical result obtained by different authors in treating diverse hypertrichosis. Many color photos showing the results obtained complete the four chapters.
The 8th chapter is entirely dedicated to a non-laser light source named Intense.
Such a light source, when used for hair removal, delivers non-coherent light in the 590-1200 μm range. Cut-off filters are utilized to tailor the spectrum of light to the skin type and hair color of the patient. The filter cuts off part of the emitted light, so that only wavelengths longer than the filter value pass to the treated hair and skin.
Cool gel and a bracketed cooling device have been used also to coal the skin.
This chapter also is enriched with many interesting pictures of the different treatments of photothermolysis for hair removal. The treatments illustrated before and after show also the eventual side effects occurred.
The 9th and the 10th chapters report respectively the complications occurring using laser, such as the post-laser perifollicolar erythema, hypertrophic scars or post inflammatory hyperpigmentation, and the marketing notes to acquire in order to introduce the therapeutic use of laser to the patients.
This book written by a plastic surgeon, expert in using laser for surgical purpose, represents undoubtedly an invaluable tool for all those working in laser area of medicine, such as dermatologists and plastic surgeons.
Enriched by the vast photographic section of about 400 color illustrations, and by the peculiar bibliography, the book will be useful also for the medical class interested in the modern techniques used in the field of hair laser removal.

P. MORGANTI
Editor-in-Chief

COSMETIC SURGERY
An Interdisciplinary Approach

By Rhoda S. Narins
2001. 986 pages Hardcover
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This interesting volume undoubtedly represents the most complete text reporting step-by-step all the new surgical techniques acquired in these years in the plastic and aesthetic surgery. On 41 chapters are reported the diverse techniques used covering topics from facelifts, filling substances, laser procedures and liposuction as well as handling the dissatisfied patient.

Each surgical procedure, particularly explained, give invaluable practical tips providing also pre-op information, instruction sheets, consent forms and post-op instruction useful for the novice as well as the experienced cosmetic surgeon.

The first chapter is entirely dedicated to the description of the best-organized ambulatory surgical center in relation to the treatment to be done and in accordance with the diverse country regulation.

It is possible to develop a high-quality office surgical facility (OSF) without the expense of an ambulatory surgical center, when light oral or local anesthesia is used.

On the contrary if general anesthesia or intravenous sedation is used, a more expensive recovery area should be available.

Big room is also dedicated to the organization of administration and staffing, to the space planning and to the equipment necessary to develop a high-quality office.

The second chapter approaches the analysis of the aging face classifying the photoaging in four types: type 1) no or minimal wrinkles and pigmentary changes, type 2) wrinkles in motion and early senile lentigines, type 3) wrinkles at rest and visible keratoses, type 4) only wrinkles and severe photoaging.

As matter of fact, younger patients, in their second or third decade, show only the earliest signs of photoaging, usually as a change in homogeneity of color (type 1).

As the patient ages wrinkles begin to appear only where the face is in motion (type 2). As the photoaging proceeds, the damage to the elastic fibers becomes more severe.

Eventually the wrinkles produced by dynamic movement of the face persist even when the face is at rest (type 3).

With continued photoaging the wrinkles gradually spread to cover the majority of the facial skin (type 4).

Chapters 3rd to 5th are dedicated to superficial, medium and deep chemical peelings defined as the application of a caustic agent to the skin resulting in partial thickness injury with subsequent re-epithelization by adnexae. This results in a skin surface that is more homogeneous and improved in both texture and appearance.

The chapters reported all the pre-surgical considerations, instructions and techniques necessary to use the different kind resurfacing agents, such as alpha and beta- hydroxy-acids, trichloroacetic acid

and Sessner's solution. Management of peel complications are reported on chapter 6 where the risk-to-benefit ratio is evaluated also.
Many chapters are dedicated to the effective use of skin remodeling by laser surgery technologies. The diverse techniques and types of laser to be used to obtain successful applications of the principles, which are fundamental for selecting photothermolysis, are described.
As matter of fact, the impact of laser and skin varies with energy fluence, wavelength, pulse width and spot size. Therefore the employment of the correct wavelength and pulse duration of laser light could effect selective destruction of a particular cutaneous target without unwanted thermal injury to normal surrounding skin.
Pre, intra, and postoperative considerations, protocol and technique to be used for laser removal of vascular lesions, scars, warts, and tattoos are reported and well described, recognizing also and treating the rate of side effects and complications.
All the chapters focused on laser therapies reports an appendix the consent form and postsurgical instructions to be filled and signed by the patient before the surgical operation.
The patient must understand that the cosmetic procedures useful to improve the appearance, cannot always achieve a perfect result and possible complications may occur.
Seven chapters are dedicated to the implantable substances and devices used to improve soft-tissue defects and deficiencies. These facial implants are used to create soft-tissue fill and thereby enhance the appearance of the soft-tissue of the face as well as to reduce the appearance of skin creases or wrinkles. In such a way, these procedures can improve facial balance and rejuvenate the early signs of facial aging.
All the chapters focus on the use of all the filling substances known to improve facial proportions, describing the composition of raw material used, the patient screening and skin-testing to be done before implantation, and the theory and technique to be used.
In order to use facial implants effectively, the surgeon has to understand the relationship between the body prominencies of the face, the principles of ideal facial proportion, and the effects of aging on the soft-tissues of the face.
The identification of norms of facial proportion associated with attractiveness may help the surgeon to identify facial imbalance and disproportion.
However, to obtain the best result often different cosmetic procedures also can be used simultaneously at the same time part of the body, or segmentally, at the same time on different parts of body. It is therefore necessary to remember the possibility of a bigger number of side effects. The first job of the physician is to do no harm. Although it is often convenient for the patient and the physician to combine multiple procedures, safety must be the primary guiding principle. Therefore the best surgeons have to offer their patients a variety of possible approaches for improving their appearance and use these in a skillful and thoughtful manner.
Different chapters are also dedicated to liposuction technique for the aesthetic removal of undesirable adipose tissue. In this case it is of great importance to approach body contouring from the standpoint of balance. In order to obtain an ideal silhouette, fat is removed from some areas and added to others.
Anesthesia topical or general is a fundamental choice to obtain the best results.
To evaluate the obtained results, good photographic records are an important necessity for a cosmetic surgery office.
This topic is widely treated in the 38 chapters.The different cameras, lens, and pose time ideal to obtain correct medical photography are widely described.

Slides or prints can be stored either in the patient's chart or in a separate file to retrieve them easily. As with the medical procedure, it is necessary to obtain consent to take photographs as well as a patient release to use them.

Finally an entire chapter has been dedicated to management of the difficult patient dissatisfied with a favorable or an unfavorable results.

Patients should be encouraged to express their feelings openly while the physician listens carefully and provides support and reassurance. As matter of fact, proper management is important in order to resolve difficulties, improve patient satisfaction, and avoid legal claims.

This interesting book answers to all these questions, giving to cosmetic surgeon and dermatologist the opportunity to comprehend all the problems connected to the Cosmetic Surgery, and to plan the best combination of skin treatment and maintenance for each patient.

This volume is also suitable as a course textbook for students of various biomedical and pharmaceutical sciences and as a supporting text for medical and postgraduate students who want to know better the innovative cutaneous surgical procedures such as dermoabrasion for scars, hair transplantation, chemoexfoliation, tumescent liposuction, soft tissue implant laser treatment of part-wine stains and tattoos and most of the new cutaneous procedures performed today to advancing skin surgery. This book undoubtedly represents an indispensable tool to enter in the fascinating world of the Cosmetic Surgery.

P. MORGANTI
Editor-in-Chief

Second Announcement and Call for Abstracts

The 2nd World Conference on Medical Esthetics and Cosmetology

Date & Venue:
July 19-22, 2002 Beijing

Official Language:
English

Scientific Topics:
- ✧ Medical Esthetics & Cosmetology
- ✧ Esthetic & Cosmetic Dentistry
- ✧ Esthetic & Cosmetic Surgery
- ✧ Esthetic & Cosmetic Dermatology
- ✧ Technology and the Art of Esthetic & Cosmetic Medicine and Dentistry
- ✧ Esthetic & Cosmetic Traditional Medicine

Registration Fees:

	Early Bird	Later Bird	On-site
Participate	US$250	US$300	US$350
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Accommodations:
There are hotels in Beijing ranging from deluxe to economy. Special room rates for this Conference will be negotiated.

Sponsorship/Exhibition:
Industry members are encouraged to sponsor, exhibit and also stage satellite symposia at the Conference.A separate industrial prospectus will be available from the Conference Secretariat.

Tours:
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Conference Secretariat:
The 2nd WCMEC
Dept. of Foreign Relations
Chinese Medical Association
42 Dongsi Xidajie
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Deadlines:
Abstracts Submission: Mar 1, 2002
Guaranteed Hotel Reservation: Jun. 1, 2002

Organized by:

Chinese Medical Association
Chinese Society of Medical Esthetics & Cosmetology

Index to Volume 19, 2001

Contents:

Book Reviews

Original Laboratory Studies

Short Communications

Author Index

Subject Index

Note

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