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2

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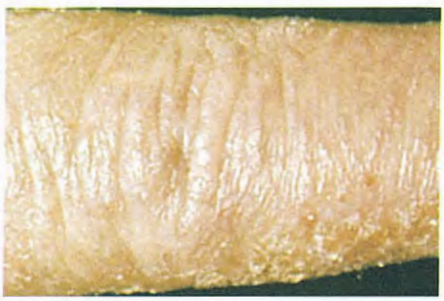

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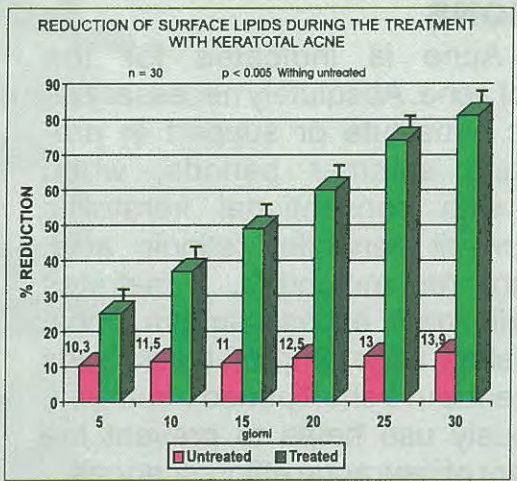

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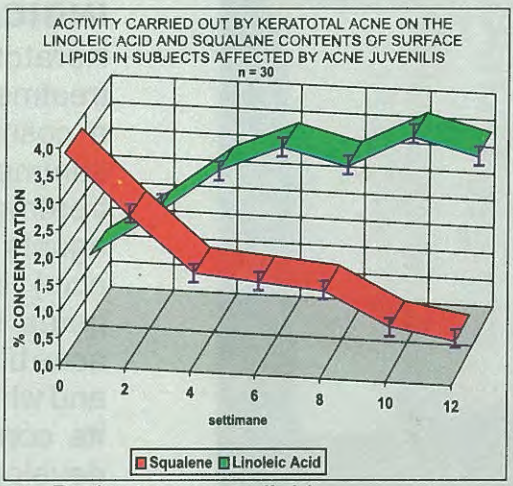

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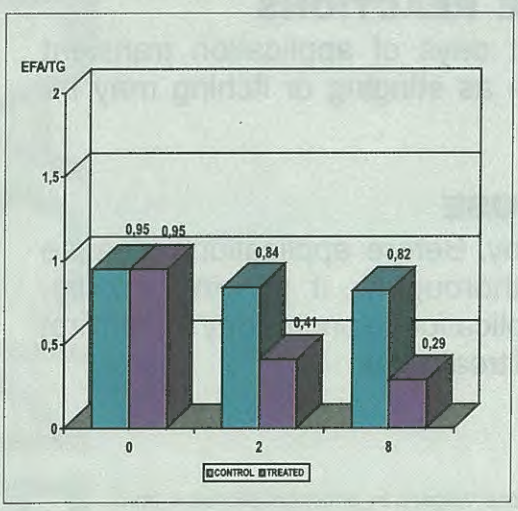

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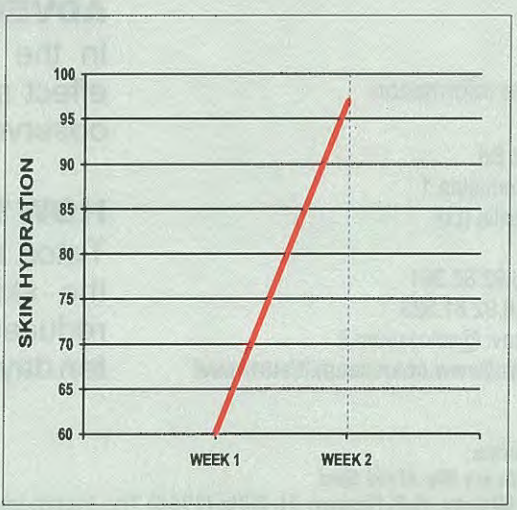

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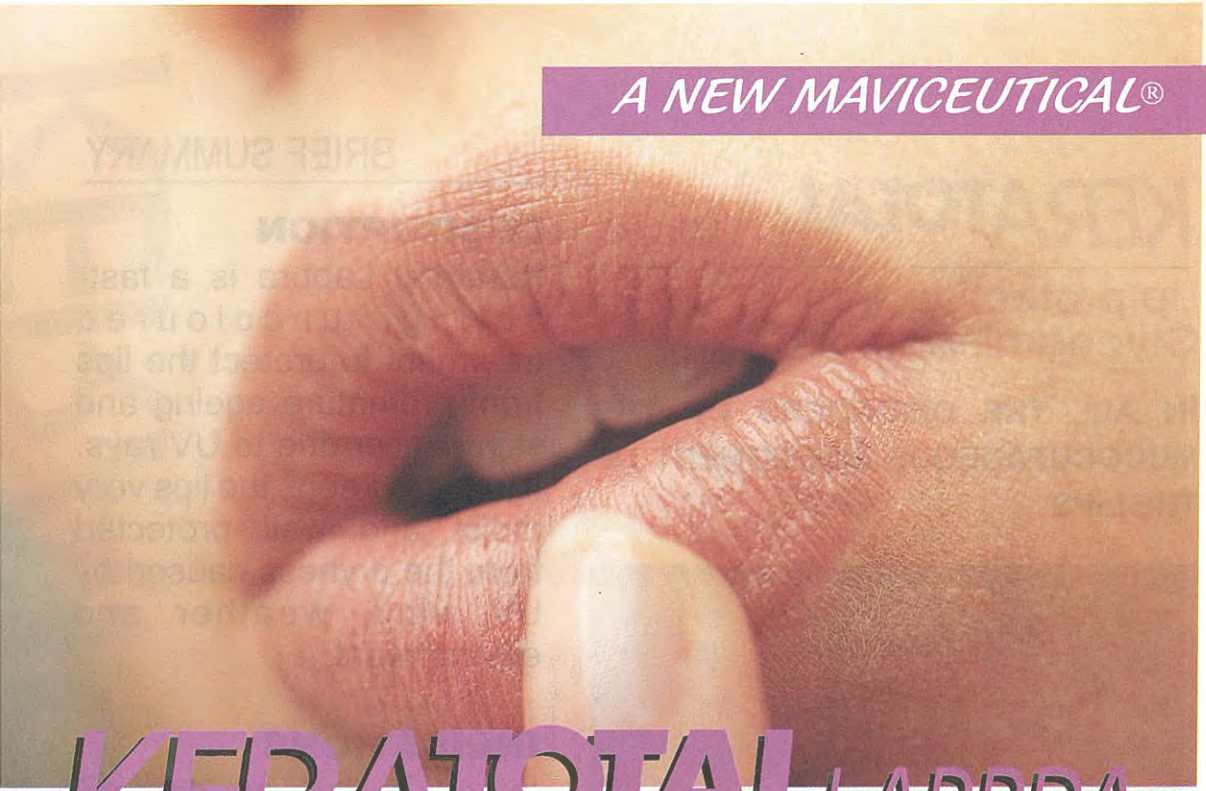
HOW TO USE

Twice a day. Before applications cleanse the skin thoroughly; if stinging occurs, reduce application to once a day for the first ten days of treatment

REFERENCES:

*1,2 - **Data on file Mavi Sud***

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



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• Weather	Exfoliative cheilitis
• Environmental pollutants	Angular cheilitis

HOW TO USE

Use day and night as a regular lipstick

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

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DESCRIPTION

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HOW TO USE

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what?
when?
where?
why?

why not?

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what?

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when?

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where?

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- controls erythropoiesis;
- optimizes membrane formation by protecting the internal structures of cells;
- acts within the synthesis of proteins, particularly keratins, thanks to its optimum, balanced content of folic acid, magnesium, omega-6 and omega-3 (DHA) in 1:4 ratio.

why?

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and to reduce the risk of

- functional neurologic disorders in the fetus;
- spina bifida;
- gestational hypertension;
- uterine hypercontractility;
- skin diseases (psoriasis, atopic eczema, alopecia, etc.);
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How to use

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General Articles

Original Laboratory Studies

J. Appl. Cosmetol. **15**, 43-47 (April-June 1997)

SKIN CARE PRODUCTS AND EVALUATION OF FEW SKIN PARAMETERS: IS THE FUTURE ALREADY HERE?

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[5] Istituto di Morfologia Umana Normale, Università degli Studi di Ancona - Italy

Received: *February 7, 1997*

Key words: stratum corneum, skin parameters, new techniques.

Synopsis

In recent years several sophisticated non-invasive methods for the evaluation of skin physiology and pathology have been developed. The interest increasingly attracted by cosmetics has prompted several studies on such methods, all aiming at assessing the effects of various skin care products on different properties of the skin. The Authors describe the latest and most significant techniques introduced in the study of some important cutaneous parameters.

Riassunto

In anni recenti sono stati sviluppati diversi sofisticati metodi non invasivi per la valutazione della fisiologia e della patologia della pelle. Il crescente interesse destato dai cosmetici ha stimolato vari studi su questi metodi, tutti tendenti alla valutazione degli effetti sulle proprietà della pelle di diversi prodotti. Gli Autori descrivono le ultime e più significative tecniche introdotte nello studio di alcuni importanti parametri dello strato corneo.

INTRODUCTION

In recent years several sophisticated non-invasive methods for the evaluation of skin physiology and pathology have been developed. The interest increasingly attracted by cosmetics has prompted several studies on such methods, all aiming at assessing the effects of various skin care products on different properties of the skin. Skin topography, for instance, has been measured on skin replicas by profilometry; friction with a newly-developed friction instrument; capacitance with a computerised apparatus - the 3C System; the barrier function in normal conditions with an Evaporimeter to assess transepidermal water loss (TEWL), and in pathological conditions by the application of an irritant followed by the measurement of the irritative reaction (1,2).

Some of these techniques were initially employed to characterise the differences between dry atopic and normal skin. More recently, however, researchers have begun to accept the idea that skin care products do not merely form an inert epicutaneous layer, but penetrate and influence the structure and function of the skin. For instance, a scrub cream removes the outermost part of the stratum corneum (SC) resulting in smoother skin. The application of moisturises modifies the skin's frictional response. Since the new friction instrument has given results comparable to those of skin friction can predict the degree of penetration of moisturisers (1). Moisturisers augment skin hydration, supplying water directly from their water phase. Skin hydration is also increased by a higher degree of occlusion, as measured by lower TEWL values. In dry skin, roughness parameters are higher and topographical peaks lower; TEWL is higher, indicating impaired barrier function. Friction and capacitance levels are lower and correlate significantly with each other, whereas TEWL does not appear to correlate with either of these parameters. Moisturisers can also alter the diffusional resistance of SC and reduce the skin's susceptibility to the surfactant sodium lauryl sulphate (SLS). Lipids in moisturiers can influence already developed SLS-induced irritatio (1).

In the light of these data, it is interesting to describe some of the latest and most advanced techniques introduced in the study of some important cutaneous parameters.

CORNEOSURFAMETRY

The stratum corneum is the outermost layer of the epidermis. The flattened keratinocytes of the granular layer lose visible evidence of the keratohyalin granules and, as they die, lose their nuclei: these dead keratinocytes form the SC (Fig. 1).

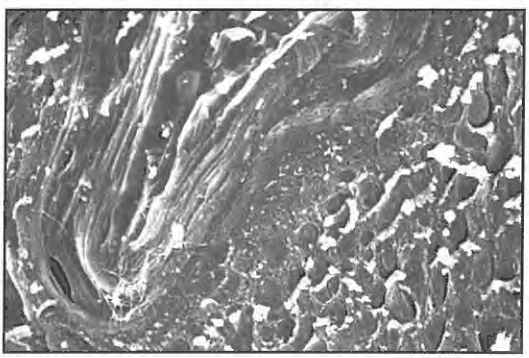

Fig. 1 Epidermis is the outermost part of the skin, note the stratum corneum layer (SEM x 906).

Corneosurfametry allows to study SC samples by measuring the variations in staining of samples obtained in different skin (3), however, it presents less interindividual variability than in-vivo testing, and allows for better discrimination among mild products. More exhaustive morphological information about surfactant induced loosening of corneocytes may be increased by testing surfactants on human skin equivalent. Results are similar to those provided by specimens used for corneosurfametry. The corneosurfametric prediction of surfactant irritancy seems to correlate well with in-vivo testing and in-vivo and in-vitro evaluation on human skin equivalent (3).

SKIN EQUIVALENT

Nonetheless, the legal procedure for evaluating the toxicity of household, cosmetic, chemical and pharmaceutical products is still the irritancy Draize

test on rabbits. Several irritation tests are currently being developed as alternatives to in-vivo animal testing. An interesting in-vitro model system is 24 equivalent dermis (ED) consisting in a chitosan-cross-linked collagen glycosaminoglycan matrix populated by foreskin fibroblasts (Fig.2) (4).

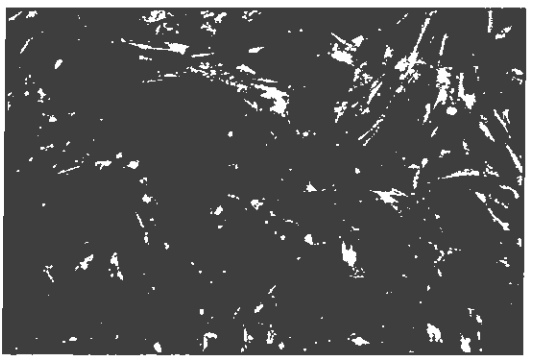

Fig. 2 Scanning electron micrograph of skin fibroblasts (SEM x 500).

Three main parameters of toxicity - MTT (dimethylthiazol diphenyltetrazolium bromide) reduction, lactate dehydrogenase and interleukin-6 can be used to determine the usefulness and the predictive value of this system compared with methods employing chemical products (cadmium chloride, lauryl sulphate, benzalkonium chloride). Preliminary results confirm the efficacy of ED as an in-vitro model for the prediction of cutaneous and ocular toxicity.
This and other in-vitro models are all the more significant in view of the European Union's directive banning the utilisation of animal models to test the safety of cosmetic products as of 1st January 1998. Devising effective alternative models is therefore an issue of outstanding interest to cosmetological research (5).

CONFOCAL LASER SCANNING

Confocal laser scanning microscopy allows the direct visualisation in unfixed material of diffusion pathways and of the cellular distribution of fluorescent markers following topical applications. Optically sectioned tissue specimens are analysed for the changes occurring in the distribution patterns of topically applied compounds depending on vehicle penetration time and depth, without the interference of the chemical alterations induced by most of the usual fixation techniques. With confocal laser scanning the permeability properties of in-vitro-reconstructed epidermis can be compared with those of the native or aged counterpart. The epidermis is reconstructed by culturing human adult keratinocytes at the air-liquid interface either on fibroblast populated collagen or on de-epidermised dermis. A fluorescent probe, Nile red, is applied in association with one of three different vehicles - polyethylene glycol with a molecule mass of 400 da, propylene glycol and dimethyl sulphoxide - which perturb the SC barrier function to different extents (6). These methods allow a better evaluation of permeability in different structural conditions.

FREEZE FRACTURE AND SMALL-ANGLE X-RAY SCATTERING

The interactions between three liposomal formulations and human SC can be visualised by freeze-fracture electron microscopy. Human SC is immersed for 48 h in liposome suspensions that can be prepared from commercially available phospholipid mixtures. The main difference between formulations may be the hydrophilicity of the headgroups. This technique investigates the composition dependence of the interactions between these vesicles and human SC. Different types of interaction can be observed: adsorption of the liposomes onto the outer surface of SC, and/or ultrastructural alterations in the deeper layers of SC caused by mixing of the liposomal constituents and SC lipids (7). The electron microscopical observations are verified with small-angle X-ray scattering. It is possible that liposomes composed of phospholipids containing relatively small hydrophilic headgroups showed a marked interaction with the skin lipids of human SC in vitro (7). These results are very promising for future applications of small-angle X-ray scattering in cosmetology, which is expacted to provide

essential information on the molecular structure and organisation of intercellular lipids of SC.

MAGNETIC RESONANCE

To gain a more datailed knowledge of the precise mechanism underlying SC elasticity, the molecular dynamics of chemical residues within the keratin fibres of human plantar SC can be investigated in various conditions by polarisation-image angle spinning 13C nuclear magnetic resonance (NMR) (8). In a recent study (8), the intensities of NMR spectra responsible for amide carbonyl, C alpha methine, and side-chain aliphatic carbons in the intact SC decreased markedly with increasing water content of up to 30% in dry SC, and remained consant over 30%. Lipid extraction of intact SC with acetone-ether (1:1) did not induce significant changes in the NMR spectrum, whereas additional treatment with water, which released natural moisturising factors (mainly amino acids), caused SC to lose elasticity (8). Elasticity recovered after treatment with basic and natural, but not acidic, amino acids. With the latter treatment, the movement of amino acid molecules was significantly disturbed, suggesting a strong interaction with keratin fibres. Parallel studies of the complex alastic modulus of a pig SC sheet with a rheovibron have also demonstrated that removal of natural moisturising factors reduce SC elasticity. This effect is also reversed by the application of basic and neutral, but not acidic, amino acids. These findings suggest that the structural keratin proteins, mainly consisting of 10 nm filaments, acquire elasticity with the help of hydrated natural moisturising factors via the reduction of intermolecular bindings, probably through nonhelical regions between keratin fibres (8).
The future seems indeed to be already here.

Correspondence:
M.G. Tucci, MD
Dipartimento Ricerche, I.N.R.C.A.
Via Angelini n.14
Ancona - Italy

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CONTACT ALLERGY TO PRESERVATIVES AND PERFUMED COMPOUNDS USED IN SKIN CARE PRODUCTS

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Key words: *contact allergy, preservatives, fragrances, parabens, Kathon CG.*

Synopsis

Contact allergy and irritation to cosmetic constituents, in particular perfumed compounds and preservatives, are a major problem, which is exacerbated because such substances are also greatly spread in the environment.
This report records data on contact dermatitis from cosmetic products among 19,546 unselected patients affected by eczematous dermatitis. The most common forms of this affection are caused by perfumed compounds (4%), eye cosmetics (2.1%), lip products (1.6%), and hair preparations (0.5%). Data on allergy to fragrances refers to the same individuals who have been tested with fragrance mix and its single components; 78.4% of the cases concern women; the main constituents are oak moss and cinnamaldehyde.
The highest rate of positive reactions was observed with parabens (1.9%) and Kathon CG (1.6%), some of the most common preservatives. Other preservatives are formaldehyde-releasers, butylhydroxyanisole and sodium metabisulfite.

Riassunto

Le allergie da contatto e le irritazioni verso gli ingredienti dei cosmetici, in particolare verso i profumi ed i conservanti, sono un grosso problema, che è ulteriormente esacerbato dalla diffusa presenza di queste sostanze nell'ambiente.
Questo lavoro registra i dati sulle dermatiti da contatto causate da prodotti cosmetici in 19.546 pazienti consecutivamente osservati ed affetti da eczema. Le forme più comuni di questa affezione sono causate dai profumi (4%), dai cosmetici per gli occhi (2,1%), dai prodotti per labbra (1,6%) e dai prodotti per capelli (0,5%). I dati sulle allergie ai profumi fanno riferimento agli stessi soggetti che sono stati testati con una miscela di fragranze e con i suoi singoli componenti. Il 78,4% dei casi riguarda donne; gli ingredienti principali sono il muschio di quercia e la cinnammaldeide.
Il più alto tasso di reazioni positive è stato registrato con i parabeni (1,9%) ed il Kathon CG (1,6%), che sono fra i conservanti più comuni. Altri conservanti sono quelli che liberano la formaldeide, il butilidrossianisolo ed il metabisolfito di sodio.

INTRODUCTION

Cosmetic products do not induce large-scale undesired effects, though they are used daily by a great number of people. Intolerance to cosmetic products ranges from 2 to 8% (1-4), allergic reactions acconnting for 80% and irritation for 16% (5-11). Irritation is thus much less frequent than contact allergy. This is true, however, only in respect of a studied and tested population. If we consider the general population, irritation is actually much more frequent, since contact dermatitis disappears fairly rapidly when the contact ceases, and it is often unreported. The greatest part of patients suffering from both allergy or contact irritation are women. The major allergens are perfumed compounds and preservatives.

This work presents some of our data on contact allergy to cosmetic products and their constituents. It concerns 19,546 patients with various kinds of dermatitis, who have been consecutively observed and tested.

FRAGRANCES

Table 1 shows the major groups of contact dermatitis due to cosmetic products. Most commonly, this affection is caused by perfumed compounds (4%), eyelid cosmetic products (2.1%) (5,12), and cheilitis due to lipsticks and toothpastes (1.6%) (5,13). Contact dermatitis due to hair preparations is not very frequent (0.5%). This may be accounted for by the fact that the cosmetic product is in contact with the cutis only for a short time, and that, when used, it is diluted with water (10).

Natural and synthetic fragrances are the most frequent allergens causing contact dermatitis due to cosmetic products (10,14,18). They can also occasionally cause irritant contact dermatitis, photodermatitis (berloque dermatitis), contact urticaria and depigmentation. The high rate of allergy to fragrances is due to their large presence in cosmetics as well as in a greater variety of other products, such as detergents, toiletries, toothpastes, local treatments, food and beverages (16).

Women comprise 78.4% of the patients affected by this kind of allergy. Eczematous dermatitis affects various areas.

Table 2 shows cases of allergy following ulcerative vascular dermatitis of the legs due to the use of local remedies containing perfumed componnds.

Table 3 shows contact allergy to the various compounds (single mix constituents) as observed in our 19,546 eczematous patients, where oak moss and cinnamaldehyde prevail.

In addition to traditional direct cutaneous contact, contact with perfumed compounds may also occur through the air (airborne contact dermatitis) (19). We have observed two young women with armpit contact dermatitis and high sensitivity to fragrances (cinnamic aldehyde). After visiting some perfumery where samples of perfume had been sprayed, the two women suffered from facial and, mainly eyelid erythemato-edematous rashes. In one of the two cases, in a test carried out in our Allergology Department, spraying resulted in eyelid erythema and edema after some hours (19).

Finally, we have observed that fragrances can often induce two different clinical pictures in the same person at the same time: contact allergy (cell-mediated pathogenesis) and contact urticaria (immediate mechanism).

Table I

INCIDENCE OF SOME GROUPS OF CONTACT DERMATITIS (CD) DUE TO COSMETICS IN 19,546 ECZEMATOUS PATIENTS.

CD to fragrances	4.0%
CD of the eyelids	2.1%
Contact cheilitis	1.6%
CD to hair cosmetics	0.5%

Table II

SITES OF ALLERGIC CONTACT DERMATITIS TO FRAGRANCES IN 19,546 SUBJECTS WITH DERMATITIS.

Face and/or axillae and/or neck	57.0%
Hands	16.7%
Legs (ulcerative dermatitis)	15.5%
Other sites	10.8%

Table III

PERFUME MIXTURE RESULTS.

Substance	Patients tested	Positive reactions (%)
Perfume mixture	19.546	4.0
Oak moss		1.2
Cinnamaldehyde		1.0
Eugenol		0.6
Cinnamic alcohol		0.4
Hydroxycitronellal		0.3
Geraniol		0.3
Isoeugenol		0.2
Alfa-amyl cinnamaldehyde		0.1

Table IV

POSITIVE REACTIONS TO SOME PRESERVATIVES IN PATIENTS WITH DERMATITIS.

Substance (conc.)	Patients tested	Positive reactions (%)
Parabens (15% pet.)	19,546	1.9
Kathon CG (100 ppm, aq.)	10,795	1.6
Sodium metabisulfite (1% pet.)	980	1.4
Chloracetamide (0.2% pet.)	1250	0.6
Formaldehyde (1% aq.)	19,546	0.3
Triclosan (2% pet.)	1250	0.3
Butylhydroxyanisole (2% pet.)	980	0.3
Imidazolidinyl urea (2% pet.)	13,647	0.2
Bronopol (0.5 pet.)	2852	0.2
Quaternium 15 (1% pet.)	14,897	0.1
Butylhydroxytoluene (2% pet.)	980	0

PRESERVATIVES

Preservatives are the second class of cosmetic compounds, after fragrances, which are the most frequent causes of contact allergy.

Table 4 shows the results of tests in eczematous patients. The highest numbers of positive reactions were obtained with parabens (1.9%) and Kathon CG (1.6%). Almost all the other preservatives induced a low rate of responses (below 1%), consistent with the relevant literature (11, 20, 22). Preservatives such as parabens and formaldehyde are known to cause contact allergy. However, it is necessary also to monitor sensitization to other less known preservatives, such as some formaldehyde-releasers (Quaternium 15, Bronopol, Germall 115 or imidazolidinyl urea), butylhydroxyanisole and sodium metabisulfite. The latter is present in cosmetic products and local remedies, and may cross-react with other sulfites.

Parabens

Para-hydroxybenzoic acid esters (parabens) are the most widely used preservatives throughout the world. They are included in cosmetic products and local remedies in a concentration of 0.1-0.3%. The sensitization power of parabens is low, according to maximization and Draize tests in man (23, 24). In literature, contact allergy to parabens, ranges from 0.3 to 6%. Our results from a series of 19,546 patients show an incidence of 1.9% which is comparable with the incidence reported by most authors (25-27).

Figure 1 shows the incidence of contact allergy to parabens observed between January 1968 and May 1991. In 1983 it decreased and has remained around 1% ever since. It is important to note that reduction in 1983 seems to have coincided with replacement of parabens by other preservatives in most of local remedies.

Table 5 gives important data on the incidence of contact allergy to parabens in various groups of patients tested for different forms of eczematous dermatitis. The highest incidence of allergy is found with leg ulcers (11%), and traumas (8.5%), followed by perianal contact dermatitis (3%) and hand contact dermatitis (2.2%). Incidence is lower for face contact dermatitis (1%) or atopic dermatitis (0.2%). This data leads to the following analysis. First of all, contact allergy to parabens was induced by local remedies applied directly over the dermis

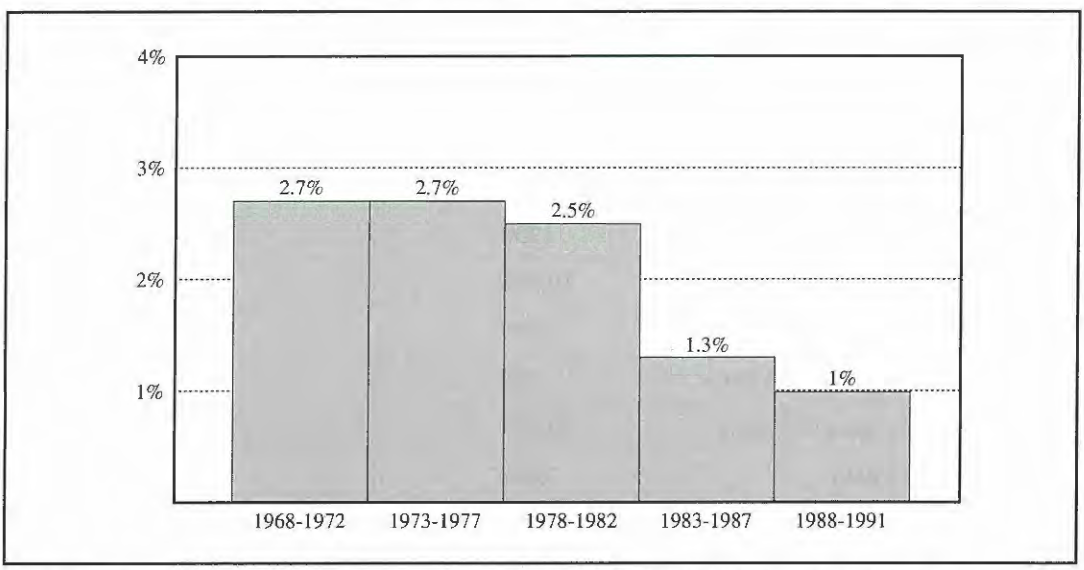

Fig. 1 - Incidence of contact allergy to parabens from 1968 to May 1991 in 19,546 patients with dermatitis.

Table V

INCIDENCE OF POSITIVE REACTIONS TO PARABENS IN 19,546 PATIENTS WITH DIFFERENT DERMATITIS (1968-1991).

Dermatitis	%
Leg ulcers	11.0
Traumatic injury	8.5
Perianal dermatitis	3.0
Occupational contact dermatitis	2.2
Jewellery and apparel dermatitis	2.2
Pompholyx	1.9
Contact dermatitis of face	1.0
Atopic dermatitis	0.2
Others	0.1

Table VI

CUTANEOUS SITES AND RISK OF SENSITIZATION TO PARABENS.

Group	Notes
Leg ulcers/traumatic lesions	very high risk area
Anoperianal eczema	high risk area
Hands	moderate risk area
Face	low risk area
Atopic dermatitis	low risk area

wounded skin (dermatitis due to other causes), as Table 5 shows (28). This means that parabens are easily absorbed when the skin filter is lacking (ulcers and traumas) or in case of dermatitis.
Our data reveal that allergy to parabens is due to the use of local remedies. On the other hand the literature indicates that the allergy to parabens can exceptionally be caused by the use of the cosmetic products which contain them (29). Parabens can thus be safely used on sound skin. This is the so-called "paradox effect" which is typical of these substances. Individuals with allergy to parabens contained in topical medicaments may tolerate the same substance when contained in cosmetic products on sound skin (30).
On the basis of this analysis, we may state that the risk of allergy to parabens varies according to the region of the body, in reference with particular cutaneous lesions and, obviously, with different degrees of absorption (Table 6).
Leg ulcers, traumas and the ano-perianal region present a high sensitization risk, as stated by other authors (31-35). Our data also show that allergy to parabens more often affects people around 50 and 60 , in relation with the greater incidence of leg ulcers due to vascular diseases at this age (32).
The absence of systemic contact dermatitis has been observed in patients affected by contact allergy to parabens, after introducing parabens through oral or injected remedies. This is most likely to be another "paradox effect" linked to these substances. Only one case exists in literature (36). We have carried out the oral challenge on 35 and 20 cases of contact allergy to methyl and propylparabens respectively. We have not observed any secondary reaction, at least in the concentrations used (37) (Table 7).
We have tested the single constituents of the mix on 45 patients with positive reactions to parabens, and we have obtained a greater incidence of positive responses to methylparaben (Table 8).
Simultaneous responses to two or more constituents have been often observed. This may be linked to cross or concomitant sensitization, since these constituents are found together in the various remedies (27).
Benzylparaben induced a low incidence of positive reactions, probably because of its molecular weight which is more or less twice that of methylparaben. The different reactivity, however, may be also due to a different bioavailability of vaseline esters. In this regard, the single esters should be tested using the same molar concentrations in order to make a real comparison (27).

Kathon CG

Kathon CG, a widely used preservative in cosmetic products, was introduced into our standard series in 1983. Since then, it has been tested (100 ppm in water: 0.01%) in 10,795 eczematous patients consecutively observed. Some data on this substance has formed the object of our previous studies (38-40).

Table VII

PERORAL TESTS IN SUBJECTS WITH CONTACT ALLERGY DUE TO PARABENS.

Substance	Peroral test	Cases No	Positive test
Methylparaben	20 mg	35	0
Propylparaben	5 mg	20	0

Table VIII

PATCH RETESTING WITH INDIVIDUAL ESTERS (ALL IN PET.) IN 45 SUBJECTS WITH A POSITIVE REACTION TO PARABEN MIXTURE.

Substance	Positive reactions (%)
Methylparaben	93.3
Ethylparaben	46.6
Propylparaben	45.0
Butylparaben	45.0
Benzylparaben	20.0

Table IX

SITES AND INCIDENCE OF CONTACT ALLERGY TO KATHON CG IN 10,795 SUBJECTS WITH DERMATITIS.

Site	Positive reactions (%)
Hands	52.4
Face	38.5
Forearms	9.7
Neck	8.9
Trunk	4.8
Legs	2.4

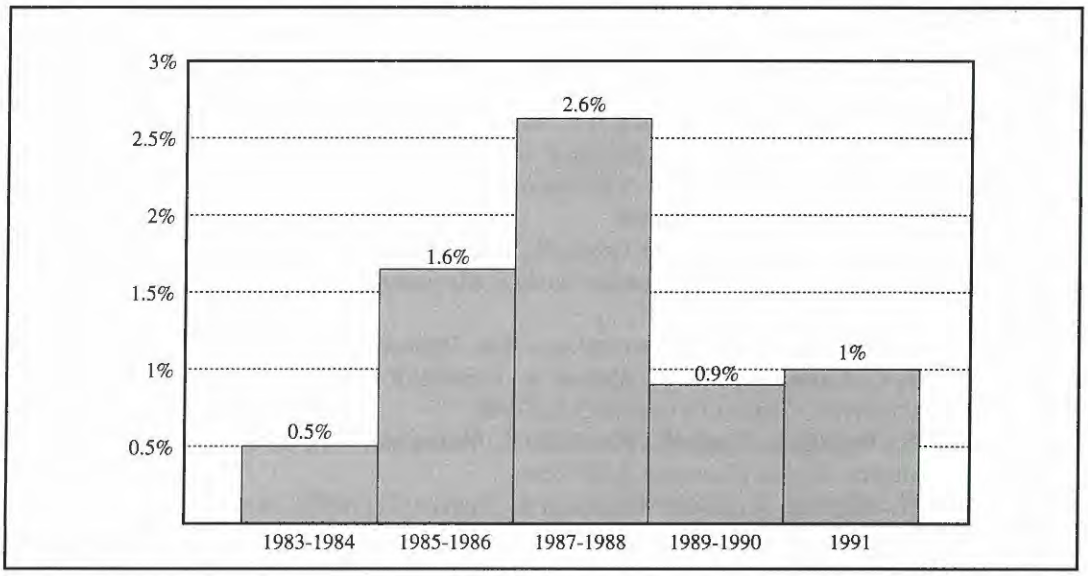

Fig. 2 - Incidence of contact allergy to Kathon CG from 1983 to May 1991 in 10,795 patients with dermatitis.

The overall incidence of contact allergy in our patients is 1.6%. This rose progressively from 1983 (0.5%) to 1988 (2.6%). The elimination of this substance from many cosmetic products, also for preventive purposes, resulted in a decreased incidence of 1% (Figure 2).

Contact allergy to Kathon CG is more frequently found in women (82%) than in men (18%). Most of the positive reactions were relevant, since the anamnesis revealed the use of cosmetic products containing isothiazolinones. In our opinion, it is important to highlight the morphologic features of the positive patch test. This test is regularly erythemato-edematovesicular, but has always given well defined roundish limits, without erythema propagation.

Table 9 shows that, unlike parabens, allergy to Kathon CG affects mainly the face and the hands.

Another important finding which is also confirmed in literature (40) was that retesting of the substance after 10-15 days following the first positive patch test, gave positive results in 88% of the cases. This good reproducibility suggests that the reactions observed in the first test are to be considered as true allergic reactions.

A multi-centre work on Kathon CG in which we participated (40), revealed the highest incidence of contact allergy (11%) to be recorded in Italy. This was probably due to the use of Kathon CG in concentrations highly exceeding the recommended values.

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HIRSUTISM. *PROFILE ON EGYPTIAN FEMALES*

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Synopsis

Hirsutism is excessive growth of coarse terminal hair in women on androgen dependent areas of the body . The most common causes of hirsutism are familial, idiopathic or polycystic ovaries. It is relatively common after menopause, especially in women of Mediterranean strains. The exact cause of this increased hair growth is not known. Lately dermatologists found that hirsutism became a noticeable complaint among Egyptian females. In this study we attempted to cover the various possible aspects playing a role in hirsutism in 244 hirsute females of different age groups. Furthermore, sonography on the ovaries was done and the level of free testosterone was estimated. Polycystic ovarian syndrome was evident in 20.5%. Free testosterone was abnormally high in 7%. They were treated with electrolysis using insulated needles. Complete cure could be achieved in 90%. We concluded that blend electrolysis using insulated needles seems to be the best permanent hair removal method with least side effects.

Riassunto

L'irsutismo si manifesta nelle donne con una crescita eccessiva di peli terminali in aree cutanee androgeno-dipendenti. Le cause più comuni di irsutismo sono di origine genetica, idiopatica o per la presenza di ovaie policistiche. È un fenomeno relativamente comune dopo la menopausa, soprattutto nelle donne della razza mediterranea. La causa esatta della crescita di questa peluria è sconosciuta. Recentemente i dermatologi hanno scoperto che l'irsutismo è diventata una patologia notevolmente diffusa fra le donne egiziane. In questo studio noi abbiamo cercato di analizzare le possibili cause dell'irsutismo di 244 donne di differenti gruppi di età; è stata eseguita anche la sonografia sulle ovaie ed è stato valutato il livello di testosterone libero. La sindrome delle ovaie policistiche è risultata evidente nel 20,5% dei casi. Il testosterone libero era abnormemente alto nel 7%. Le donne sono state trattate con elettrolisi usando aghi isolati ed il 90% delle pazienti ha completato il trattamento. Abbiamo quindi concluso che l'elettrolisi, tramite l'uso di aghi isolati, sembra essere il migliore metodo di rimozione della peluria con i minori effetti collaterali.

INTRODUCTION

Hirsutism is excessive growth of coarse terminal hair in women on androgen dependent areas of the body e.g. the upper lip, chin, cheeks, chest, lower abdomen and inner aspects of the thighs. The most common causes of hirsutism are familial, idiopathic and polycystic ovaries. It is relatively common after menopause, especially in women of Mediterranean strains. The exact cause of this increased hair growth is not known (1).

There are various available methods for removal of unwanted hairs either by epilation or depilation. Epilation refers to the removal of hair by extraction from its root. This occurs with plucking by tweezers, waxing and threading. Depilation refers to the removal of hair by means other than action upon the root i.e. upon the hair shaft above the skin surface. Examples include shaving, depilatories and abrasives (2). Every method has its advantages and disadvantages and several precautions should be observed irrespective of which is used.

Waxing is one of the oldest methods of hair removal. It is good and effective method for removing hair of upper lip, legs and arms but it has several drawbacks. It needs the hair to be long enough to be gripped by the wax. Furthermore the wax must not be too hot or it can burn or irritate the skin (3).

Plucking by tweezing is the preferred method for temporary hair removal of scattered hair on the face. However it is painful especially on sensitive areas such as upper lip. Regrowth sufficient to require repeated plucking may occur by 2 to 12 weeks later, depending on the density and speed of hair growth in a given area. However, poor technique or poor skin tolerance can lead to distorted follicles, folliculitis, pigmentation and tinny pitted scars (4).

Threading is used with remarkable effectiveness by many women, especially those of the Middle East and East Indian origin. Side effects are the same as plucking and waxing.

Shaving is easy, quick and effective method but most women consider shaving of the facial hair is too masculine. The distinct disadvantage of shaving is that it must be repeated everyday to avoid bristly filling. Also the skin may feel irritated if a fresh blade is not used (3).

The only practically applicable method for permenant removal of excessive hair growth is electroepilation. However this method is very time consuming, often painfull and may result in scarring (5).

In this study we attempted to cover the various possible aspects playing a role in hirsutism. We have studied 244 hirsute women of different age groups. The patients were helped to attain a better cosmetic appearance by removing the hairs of the face using electrolysis. Thereafter, any residual pigmentation was also treated.

PATIENTS AND METHODS

This study included 244 hirsute females aging between 13 and 50 years attending the out-patient clinics and department of dermatology of Ain-Shams university hospitals.

All patients were subjected to the following:

1.Detailed history taking with special emphasis on;

I. Family history of a similar condition.
II. Date and rate of onset as sudden onsets merit consideration of a more serious androgen problem.
III. Menstrual history as hyperandrogenaemia often results in oligomenorrhea or menstrual irregularities.
IV. Infertility
V. Medications known to induce hair growth e.g. androgenic and estrogenic hormones, phenytoin, minoxidil, cyclosporin, danazol and cortisone.
VI. Methods of hair removal used before and after onset of hirsutism.
VII. Breast discharge which is an indication for prolactin testing.

2.Complete physical examination; to determine if the hair is physiological or abnormal, or if there are any other clinical expressions of hyperandrogenism. The following sites were thoroughly examined;

I. Facial hair, especially noting hair on chin, mustache, angles of the jaw, cheeks and anterior neck. The density, coarseness and color and whether the hair is vellus, intermediate or terminal was noted.

Quantitative grading of hirutism using a new system was used in our patients taking into consideration any previous method of hair removal.

II. Body hair in the different parts of the body e.g. "V" central chest and central abdomen.

III. Body weight and contour.

IV. Acne and its severity.

3. Pelvic ultrasonography.

4. Serum free testesterone was estimated using the immunoenzymatic assay (ELISA)

The patients were helped to attain a better cosmetic appearance by removing the thick black hairs of the chin and angles of the jaw.

For electrolysis we used the individual prepackaged presterilised needles. We stored them in an individual envelop with the patient's name on it to avoid transmission of infection. We prefer the more flexible two-piece needles because it demands a more precise insertion. We also prefer the insulated needles as they have the capacity to deliver energy more precisely to the base of the hair follicle and this protects the upper follicle and skin surface from the destructive effects of electrolysis.

We used the blend method which combines galvanic electrolysis and thermolysis. The patients were informed to shave the affected area 2-5 days before electrolysis to ensure that the only growing anagen hair is epilated. Electrolysis was performed without local anesthesia in all the patients. It was performed in 30 minutes sessions twice weekly. Proper introduction of the fine needle into the pilo-sebaceous orifice was helped by wearing a 2+ magnifying loop. The black terminal and intermediate hairs were removed.

RESULTS

The patients age ranged from 13 to 50 years with a mean of 26 ± 6.53 years. Ninety four were single and one hundred fifty were married (61.5%). Forty patients of them had children (16.3%). One hundred and eight cases (44.3%) had a family history of hirsutism with different degrees of severity. Thirty cases (12.3%) gave a history of menstrual irregularity. The duration varied from 3 months to 20 years. Age of menarche varied from 9 years to 20 years. There was history of medication prior to onset of hirsutism in 38 cases (17%).They include clomid, cortisone, contraceptive pills and cyprotrone acetate (Diane). Ultrasonography revealed polycystic ovaries (PCO) in 50 cases (20.5%) but menstrual irregularities was only evident in 30 cases. Seventeen patients (7%) had elevated free testesterone. (Table I).

The excess hair involved mainly the chin in all the cases (100%), the mustache in 30 cases (12.3%), the angles of jaw in 130 cases (53.2%), anterior neck in 80 cases (32.7%) and the upper arms and "V" of the central chest in 8 cases (3.3%). (Table II).

Table I

RELATIVE CLINICO-PATHOLOGICAL FIGURES (M= MARRIED)

Age	13-50	(mean of 26 ± 6.53)
Marital Status	150 M	(61.5%)
Children	40 + ve	(16.3%)
Family History	108 + ve	(44.3%)
Medications	38 + ve	(17%)
Menstrual irregularities	30 + ve	(12.3%)
Acne	12 + ve	(4.9%)
PCO	50 + ve	(20.5%)
Free Testosterone	17 cases	(7%)

Table II

DISTRIBUTION OF HAIR GROWTH SITES.

	Chin	Mustache	Side angles of jaw	Anterior neck	Arms and Chest
No. of cases	244	30	130	80	8
Percentage	100%	12.3%	53.2%	32.7%	3.3%

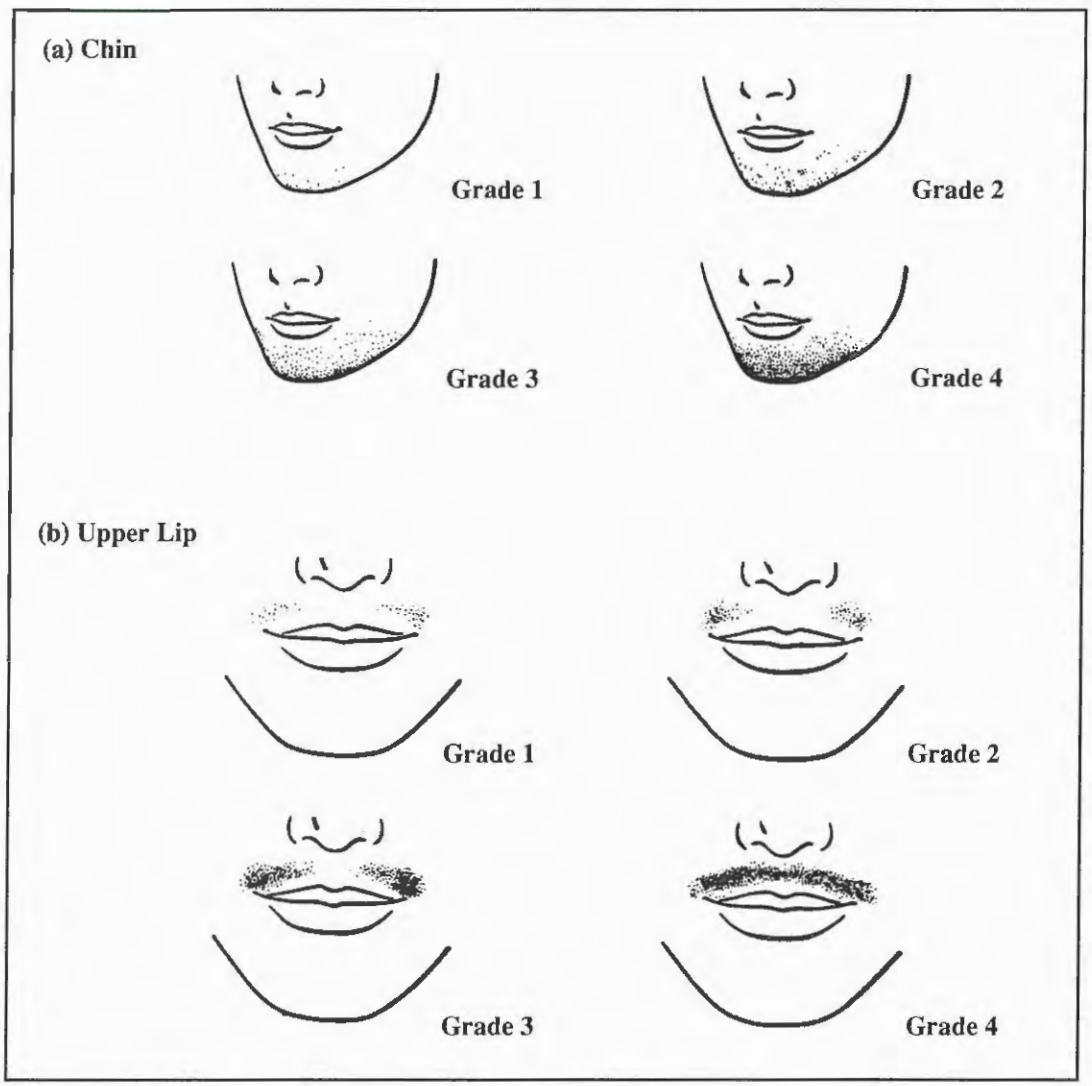

Fig. 1. Grading method of hirsutism Ferriman D.M. and Gallwey J.D. (1961)

Grading of hirsutism

The patients were graded according to a new objective method taking into consideration the previous method of hair removal. The patients weren't wearing any cosmetic cover-up. As regards the chin we used a ring 1/2 cm in diameter put it on the chin 1 cm lateral to the mid lon each

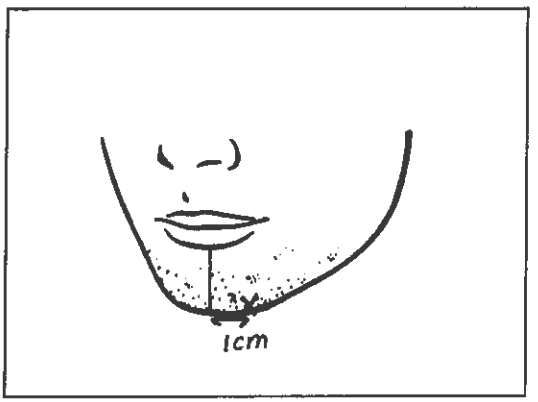

Fig. 2. Grading method of hirsutism on the chin.

side (Fig.2). The number of the thick and intermediate hairs were counted. According to the mean number of hairs 4 grades of hirsutism were postulated.

* 0 - 5 hairs grade 1,
* 6 - 10 grade 2,
* 11 - 20 grade 3,
* Above 20 grade 4

The same method was applied to the side angles of the jaw using the same ring. We applied it in the middle of a straight line drawn from the ear tragus to the symphsis menti on each side as shown in the figure (Fig.3).

The patients were graded according to our modified grading system. (Table III).

As regards the temporary hair removal method used before, 83 cases (33.7%) were using the plucking method by tweezers, 20 cases (12.3%) by waxing and 15 cases (5.9%) by threading. While 7 cases (2.4%)% were using depilatories either shaving or chemical depilatories. Ninety cases were removing hair with tweezer and threading while 39 didn't remove hair with any

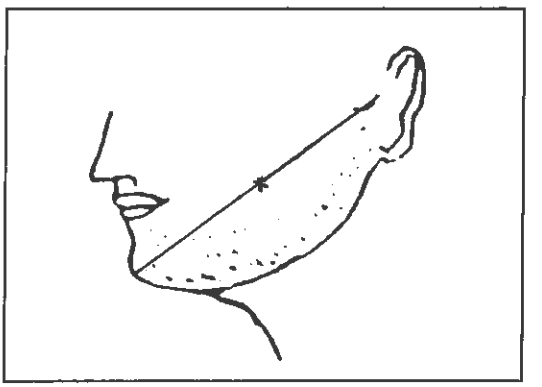

Fig. 3. Grading method of hirsutism on the side angles of the jaw.

method before. (Table IV).

Electrolysis was performed to all the patients as a permanent hair removal method. We didn't give the patients any concomitant hormonal therapy during the period of treatment.

DISCUSSION

Hair grows on every portion of the skin except the palms, soles and a few other small areas. Everyone is born with a fixed number of hairs on his or her body which is genetically determined. Most these hairs are vellus hairs. Excess hair does not mean an increase in the number of hairs (2). Hirsutism is the transformation of fine vellus hair to thickened terminal hair under androgenic stimulus in women.

Elevated androgens often produce oily skin and acne. In this series 4.9% were having acne ,however none of them had severe unusual acne but they had mild papulopustular acne. Also, free testesterone was above normal in only 7% of cases which means that the idiopathic hirsutism is still the major cause of hirsutism. However, we believe that the hormonal analysis must be estimated in every case of hirsutism regardless any obvious causes present as it may indicate a serious underlying medical problem such as tumors of ovaries or adrenals, PCO or cushing disease.

The commonest areas involved are the chin, central chest, abdomen and the pubic thigh areas (2). This agrees with our results because 96% of our cases

Table III

GRADING OF THE HIRSUTE PATIENTS

Grading	Chin	Side angles of the jaw
Grade 1	44 cases	50 cases
Grade 2	100 cases	75 cases
Grade 3	50 cases	5 cases
Grade 4	50 cases	0 cases

Table IV

METHODS OF TEMPORARY HAIR REMOVAL USED.

Method of hair removal	No. of cases
Plucking by tweezer	83 cases (33.7%)
Waxing	20 cases (12.3%)
Threading	15 cases (5.9%)
Shaving and chemical depilatories	7 cases (2.4%)
Tweezer and threading	90 cases (36.88%)

were presented with excess hairs on the face only. The chin is the most commonly affected area in the face as shown by our figures. (Table II).

Precise grading of hirsutism is difficult, due to previous hair removal by temporary methods or by electrolysis. Cosmetic cover-ups may mask hair and even stubble. The color, shape and texture of hair will affect the appearance of its density. Furthermore, perception is altered by lighting conditions and the presence or absence of magnification. In spite of these difficulties, the modified grading system is useful. (Fig. 1). However, their study was performed in Norway so we suggest a higher or modified grading suitable for the Mediterranean population as they are more hairy. Furthermore, we suppose that their grading system although it is useful yet it is not objective and they didn't apply it on the side angles of the jaw. (Fig. 2). In this work we introduced a new and objective grading method for the chin and the side angles of the jaw. We counted the hair in a circle 1/2 cm in diameter on each side. According to the mean number of hairs we graded our cases. Hirsute patients are always inquiring about the number of sessions they will need. We can use this grading system to tell every patient approximately the number of sessions she will need for electrolysis.

There are many known methods of temporary hair removal either by epilation or depilation. Epilation refers to the removal of hair by extraction from its root. In Egypt waxing and threading are the most common methods as shown by our figures i.e. waxing 12.3% and threading 5.7%. However as 96% of our cases were presented with hairs on the face for which the most practical method of removal is plucking. The highest incidence of hair removal method was plucking with tweezers (33.7%). Repeated plucking commonly resulted in side effects. It is also related to individual tolerance and technique. So some women are able to pluck facial hair for 30 minutes daily without side effects, while others not. We believe that repeated plucking in ad-

dition to its common side effects as hyperpigmentation, distorted follicles and scarring it may activate inactive follicles to produce new hair. Furthermore, we suggest that repeated epilation by any method either tweezer, waxing or threading might trigger transformation of the fine vellus hair into thick intermediate or terminal hair in susceptible women e.g. with family history of hirsutism. So, these factors must be considered in grading the hirsute females. This agrees with the results mentioned before by Speermen (7) who mentioned that hirsutism is considered a dynamic process and presently inactive follicles may be activated to produce new hairs. So, the body which approximately contains about 730 follicles /cm various factors may enable these follicles to emerge from dormancy.

Removal of hair by shaving was the least used method in our series. This might be due to the wrong concept among women regardless their culture that shaving thicken individual hairs. This is because short hair is less flexible than a long hair and therefore feels more bristly (3). Patients should be informed that shaving is an ideal temporary method of hair removal, particularly if combined with appropriate cosmetic cover-ups. If they prefer one of the methods of epilation they should be informed that plucking is more preferable as it removes individual terminal hairs only, in contrast to waxing which removes hair from the whole affected area, the vellus in conjunction to the terminal hair.

Electrolysis have been available for very long time (8), and for many hirsute women electrolysis seems the logical accepted solution since they are fed up with all non-permanent methods of management and their side effects as well (9). They are willing to accept complications as pigmentation or even scarring over the tedious and psychologically hurting frequent shaving or epilation which are not also free of almost the same complications (10).

Electrolysis satisfactorily removes hair from 90% of our patients without any concomitant hormonal therapy. The rest of them still require more sessions of electrolysis.

Some postinflammatory erythema is normal after electrolysis. Usually it disappears in 30 minutes to few hours. Small white swelling around the hair follicle is more common after galvanic electrolysis or the blend. This swelling vanishes within 1/4 to 1/2 hour. Poor insertion may result in bruises around the hair follicle openings. They are caused by minute bleeding known as microheamorrhages. Immediate pressure with a clean cotton for 2 minutes helps to minimize the size of the bruise.

Crusting may occur when tissue destruction reaches the skin surface. It resolves in a few days, however it may be followed by hyperpigmentation and even scarring.

Hyperpigmentation occurs most frequently in dark-skinned races (especially under the chin). (11). Pigmentation in susceptible individual can occur from any inflammation to the skin such as ingrown hairs, folliculitis or repeated plucking. Hyperpigmentation was the most common side effect seen in our patients after electrolysis. However, most of them were presented to our department with hyperpigmentation as a result of repeated plucking and threading in this area. This usually fades during the next weeks or months. In some patients we used topical tretinoin in association with hydroqiunone 2% for 2-4 weeks after end of electrolysis. The results were very much appreciated by our patients.

Scarring does not occur with properly performed electrolysis. However, tiny pitted scar may occur in some cases. Furthermore, if electrolysis currents are applied at too high a level e.g. telogen hair or because of operator error or defective short or broken needle, scarring occur. In most instances it takes several months to determine whether ornot scarring had occurred.

Shaving 1 to 5 days before electrolysis greatly increase efficacy. It ensures that only growing anagen hairs are epilated. This is very important because as many as 60% of the hairs may be in telogen. Telogen hairs are very difficult to eradicate because of the short telogen follicle which may predispose to more side effects.

Until the 1960s the same needle was repeatedly used in different persons. Electrologists thought that the heat of the process would produce sterili-

zation. Hepatitis was a danger in tattooing, ear piercing, accidental punctures and dental instruments. (12). He didn't mention electrolysis. Also AIDS virus is theoretically not likely to be transmitted by electrolysis. However, the public perceives this to be a hazard.

Recommendations for electrolysis

1. Blend method combines galvanic direct current and thermolysis high-frequency alternating current. This method requires 1/4 of the time needed for galvanic electrolysis alone.
2. The use of disposable, individual, prepackaged, presterilised electrolysis needles. These can be reused after sterilization but only for the same patient. They were kept in an individual envelop attached to each patient's file.
3. Using insulated needles as they have the capacity to deliver energy more precisely to the base of the hair follicle and this also heilps to protect the upper follicle and skin surface from the destructive effects of electrolysis.
4. Wearing gloves during electrolysis, although some electrologists found it to be unnecessary.

In conclusion we suggest that every case of hirsutism should be thoroughly investigated. The patient should be informed about different methods of hair removal and about the advantages and disadvantages of every method. The wrong believes about shaving should be corrected. If the patient will perform electrolysis precise grading of hirsutism should be done and accordingly the number of sessions she will need.

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CLINICAL AND INSTRUMENTAL EVALUATION OF THE ACTIVITY OF AN ANTI-WRINKLE COSMETIC PRODUCT ON CUTANEOUS RELIEF AND PHOTOAGED SKIN.

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Key words: wrinkles, replica, image analysis.

Synopsis

The aim of this trial is to evaluate the efficacy of an anti-wrinkle cosmetic product on the cutaneous relief and condition of photoaged skin using a method of clinical scores together with an instrumental technique, namely image analysis of imprints taken from the crow's feet area of the eye. Thirty women presenting with cutaneous photoaging of the face applied the product twice daily for two months. Skin condition was evaluated before treatment (D0) and after 15, 30 and 60 days of treatment (D15, D30 and D60). Safety was verified at each visit. Progressive and significant improvement in cutaneous relief and the state of the skin was found, which was identical by both methods of measurement, thereby confirming the value of the clinical score method.

Riassunto

Lo scopo di questo lavoro è di valutare l'efficacia di un prodotto cosmetico anti-rughe sul rilievo cutaneo e lo stato della pelle foto-invecchiata, usando un metodo di valutazione clinica insieme ad una tecnica strumentale, ovvero l'analisi per immagini di impressioni prese dall'area delle "zampe di gallina" degli occhi. Trenta donne con segni di foto-invecchiamento cutaneo sul volto hanno applicato il prodotto due volte al giorno per due mesi. Lo stato della pelle è stato valutato prima del trattamento (D0) e dopo 15,30 e 60 giorni di trattamento (D15, D30 e D60). La sicurezza è stata controllata durante ogni visita. È stato riscontrato un progressivo e significativo miglioramento nel rilievo cutaneo e nello stato della pelle, identico per tutti e due i metodi di misurazione, confermando quindi il valore del metodo di valutazione clinica.

INTRODUCTION

Cutaneous aging, which is the result of chronological aging plus actinic aging (1), is characterized by visible cutaneous damage, particularly on the face, which is regularly exposed to UV irradiation: dehydration of the epidermis reflects the slowing down of keratinocyte growth (2); the appearance of wrinkles, loss of firmness and suppleness in the skin result from the disorganisation of elastic fibres (3) and degeneration of collagen (4), which are components of the extracellular matrix synthesised by fibroblasts.

An extract of *Vitreoscilla filiformis*, a bacteria obtained from thermal sources and cultivated *in vitro* by biotechnology (5) induces multiplication of human keratinocytes cultured *in vitro* (C.M. Lapière et al, unpublished observations) and also has interesting effects on human fibroblast cultures: stimulation of cell proliferation and IL1ß production (J.A. Grimaud et al, unpublished observations). Furthermore, this bacterial extract induces cellular activation and the production of IL1ß in human macrophage cultures (V. Bayer et al, unpublished observations). IL1ß is involved in the regulation of elastin synthesis and in the mechanisms of dermal repair (6;7) and also acts on keratinocyte proliferation in the epidermis (8). In addition to its properties which have been demonstrated in vitro, *Vitreoscilla filiformis* probably induces, *in vivo*, restructuration of cutaneous tissues and thus improvement in the relief and appearance of the skin.

In this trial we have verified this hypothesis: the efficacy of a care product containing 1% *Vitreoscilla filiformis* extract has been studied over two months of treatment in a group of 30 women presenting with cutaneous photoaging of the face. The change in cutaneous relief and the state of the skin was followed using two distinct methods: clinical scores and image analysis of imprints taken from the crow's feet area of the eye; the correlation between the results obtained for cutaneous relief by the two methods has also been analysed.

METHODOLOGY

Volunteers

The trial was carried out in an open non-randomised fashion on 30 healthy Caucasian females, aged 38 to 60 years (mean age: 46 years). The volunteers had a normal skin and the state of their skin corresponded to degrees 3 to 5 on the photodigital scale described by Larnier and all (9).All the subjects gave their written informed consent in accordance with the ethics of cosmetic experimentation.

Product

The care product' was an oil/water cream containing 1% of the *Vitreoscilla filiformis* extract in association with traditional cosmetic active ingredients.

Treatment and monitoring of patients

The product was applied to the whole of the face, morning and evening, for 60 days. No other cosmetic product was allowed throughout the treatment period with the exception of cleansing products. This trial, carried out over a period of 2 months, included four control visits: before the beginning of treatment (D0), after 15 days (D15), 30 days (D30) and 60 days of treatment (D60). Evaluation of the state of the skin and cutaneous relief as well as verification of cutaneous safety were carried out by the investigator at each examination.

Evaluation methods

Clinical evaluations: scoring method (10)

The investigator carried out an analysis of skin condition (on the forehead, crow's feet, cheeks and medio-facial area) using a clinical score method. The following criteria were studied: cutaneous relief, suppleness, firmness, hydration, complexion. Each criterion, scored from 0 (negative value for the criterion) to 10 (positive value for the criterion) was evaluated individually. The means of the scores obtained on the four zones of the face were calculated for each criterion.

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Instrumental methods: taking imprints and image analysis

Silflo replicas of cutaneous relief (11) were taken from a precisely delineated zone including the crow's feet area. These imprints were quantitatively analysed by image analysis (12), using a video camera (Cohu) coupled to a microcomputer and using image analysis software (Quantrides, Monaderm). This technique enabled the number of wrinkles per unit surface area (u.s.) to be quantified as well as their depth (µm).

Subjective evaluation

After 4 and 8 weeks of treatment, the subjects evaluated the activity of the product on their wrinkles (satisfactory or unsatisfactory with respect to the results obtained), scoring the firmness, softness and hydration of the skin, using a scale of 0 to 4 for each criterion (0: unsatisfactory; 4: satisfactory).

Statistical analysis

A two-tailed Student's t test for paired series was used to analyse the differences between the values obtained before treatment and after 15, 30 and 60 days of treatment (clinical scores and image analysis). The differences were considered significant when $p < 0.05$. The correlation coefficient r and its threshold of significance p were calculated by linear regression analysis using the means of the values obtained for all the subjects at each control visit (D0, D15, D30, D60), in order to determine the correlation between the results recorded by the scoring method and those obtained by image analysis.

RESULTS

Clinical change

The mean of the scores obtained for all the subjects (+/- standard deviation from the mean), at each control visit and for each criterion, is given in Figure 1. A progressive and significant improvement in cutaneous relief can be observed during treatment. In comparison to D0 (before treatment), the cutaneous relief improves by 13, 34, and 57% after 15, 30 and 60 days of treatment (see Table 1).

The treatment also induces a significant increase in the firmness of the skin and an improvement in suppleness, hydration and complexion.

Quantitative change in cutaneous relief

The effect of treatment on the number and depth of wrinkles was determined by image analysis of the imprints. Figure 2 gives the means of the measurements made for all the subjects. The number of wrinkles is reduced in a significant fa-

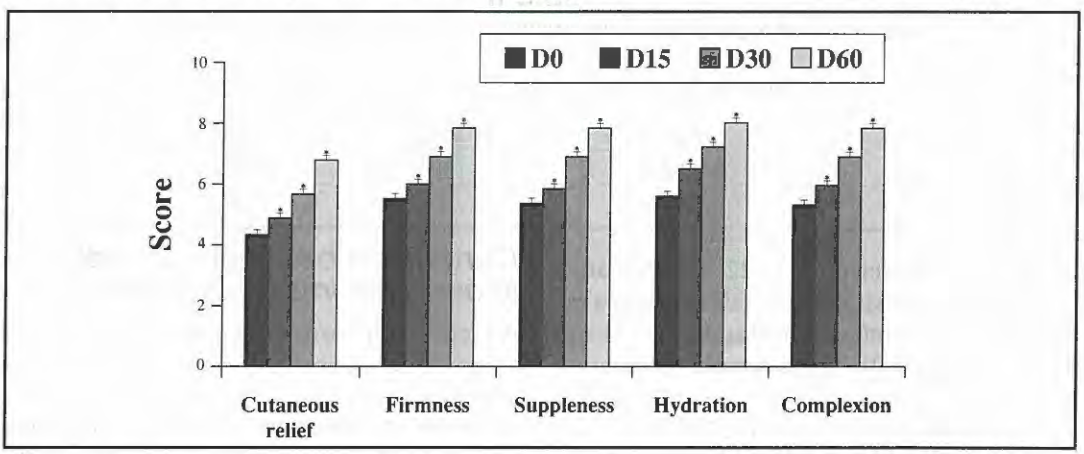

Fig 1: ***Clinical scores*** *(mean +/- standard deviation from the mean).*
D0: Before treatment; D15: After 15 days of treatment; D30: After 30 days of treatment; D60: After 60 days of treatment.
** significant difference with respect to D0 ($p < 0.05$).*

Subjective evaluation

Figure 4 gives the evaluation made by the subjects which confirms the activity of the product in terms of wrinkle improvement (90% of subjects were satisfied at D30). Good activity of the product on firmness, softness and hydration of the skin was also recorded.

Product safety

The use of the product did not lead to any unwanted cutaneous reaction, demonstrating its complete local safety.

DISCUSSION

The results of this trial demonstrate the efficacy of the studied product in terms of improvement in relief and the characteristic signs of photoaged skin, which are seen beginning from the 15th day of treatment onwards. This improvement continues to the end of treatment. The change in the clinical scores for cutaneous relief is correlated to a reduction in the number and depth of wrinkles measured by image analysis. This correlation shows the reliability and value of clinical scores for evaluation of cutaneous relief.

It therefore seems that the activity of *Vitreoscilla filiformis* measured *in vitro* on cutaneous cells has also been verified in vivo: activation of cutaneous cells by the bacterial extract may lead to an increase in keratinocyte cohesion as well as an increase in connective tissue density, leading to an improvement in cutaneous relief and the state of the skin.

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- **PHOTOSTABLE TANNING LINE**
- **NO CHEMICAL SUNSCREENS ADDED**
- **WATER-PROOF**

• LINEA SOLARE FOTOSTABILE • TOTALMENTE PRIVA DI FILTRI CHIMICI • RESISTENTE ALL'ACQUA

SPF 4	MAVISOLE WATER
SPF 6	MAVISOLE 6
SPF 9	MAVISOLE 9
SPF 15	MAVISOLE 15
SPF 18	MAVISOLE 18
SPF 20	MAVISOLE VISO
SPF 15	MAVISOLE GEL
	MAVISOLE DOPO

INDICATIONS
INDICAZIONI

- **Sun-sensitive skin.** *Pelli intolleranti al sole.*
- **Drug photosensitization.** *Fotosensibilizzazioni da medicamento.*
- **Photoageing prevention.** *Prevenzione fotoinvecchiamento.*
- **Chloasma.** *Cloasma.*
- **External exposure conditions.** *Condizioni esterne di esposizione.*
- **Scar and stretch-mark protection.** *Protezione delle cicatrici e delle smagliature.*
- **Protection from photodermatosis.** *Protezione dalle fotodermatosi.*
- **Protection from photoallergies.** *Proteziane dalle fataallergie.*
- **Prevention of sun-exacerbated dermatosis.** *Prevenzione delle dermatosi aggravate dal sole.*

mavi **SCIENCE SUN SERVING** • *LA SCIENZA AL SERVIZIO DEL SOLE*

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