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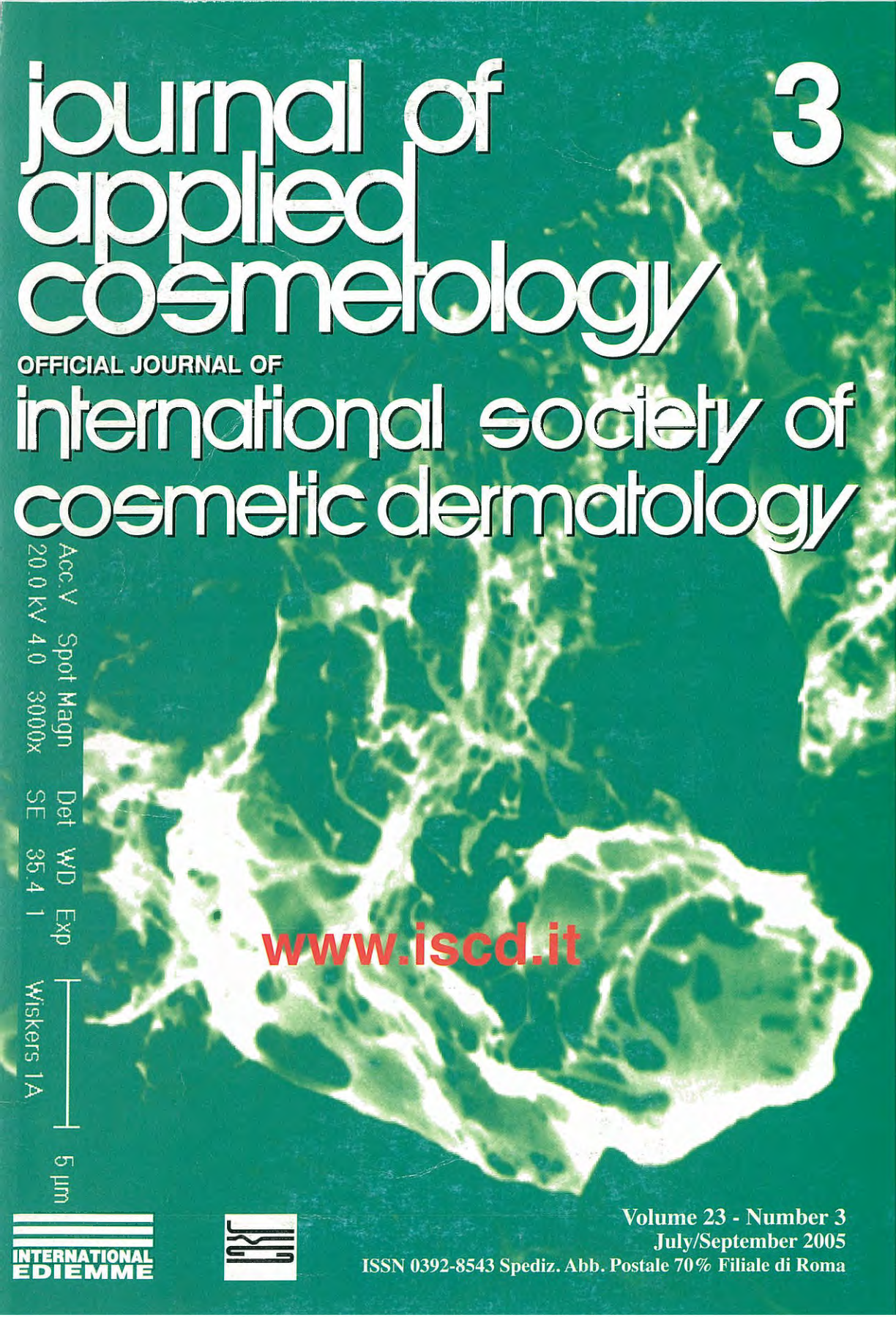

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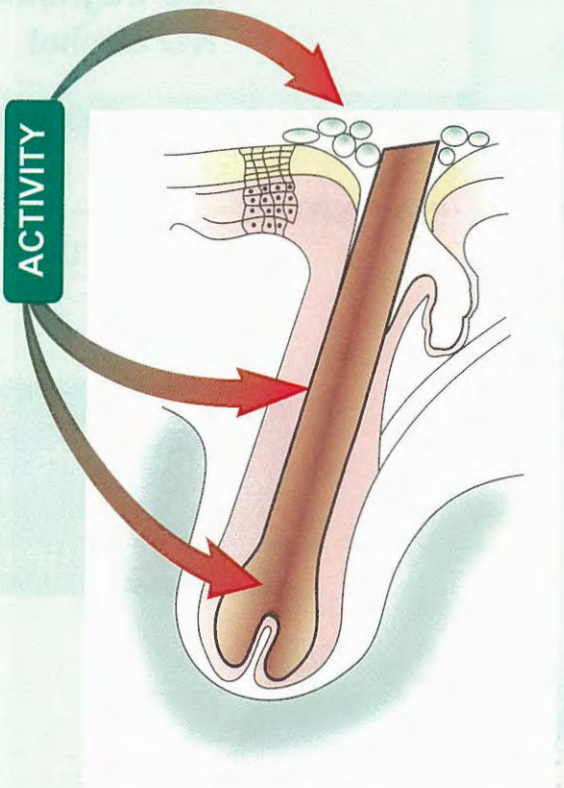

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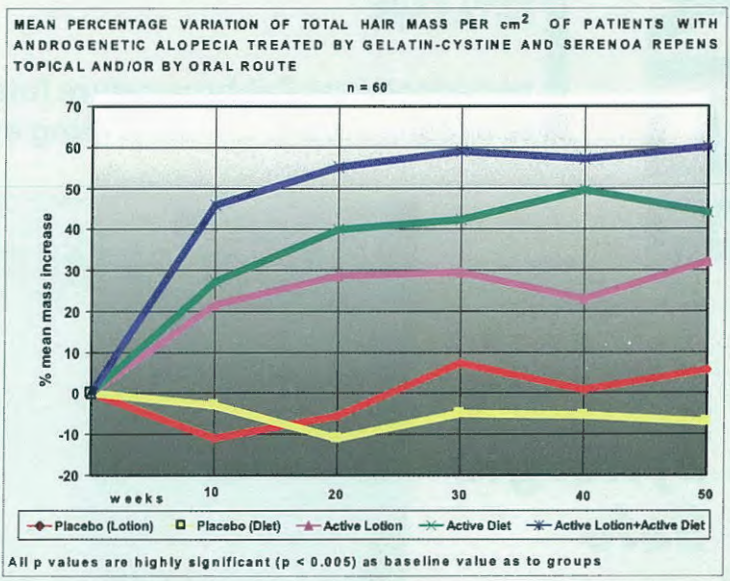

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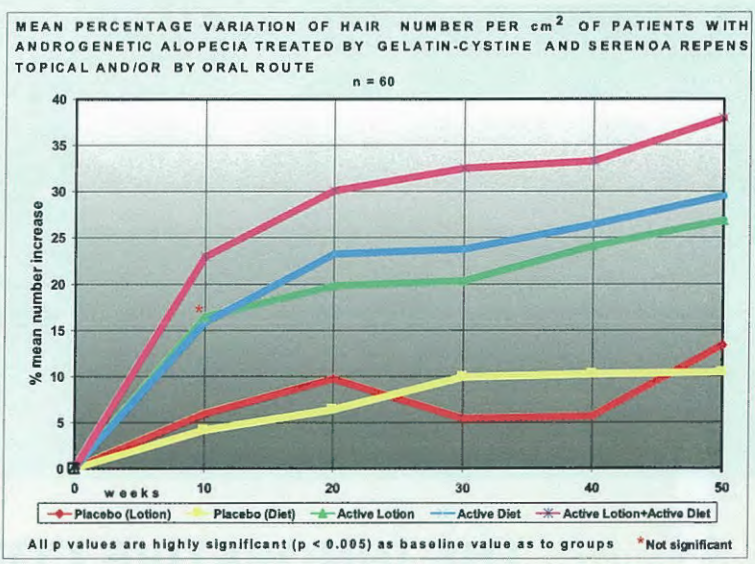

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Trimestrale di Dermatologia Cosmetologica
Quarterly Review of Cosmetic Dermatology

We wish to dedicate this issue of the Journal of Applied Cosmetology to the memory of two well known dermatologists: professor Damiano Randazzo and Dr. Brodie James

Unfortunately Damiano Randazzo is not among us anymore but he will live forever in the memories of all his friends and admirers for his versatile personality.
We will remember him as a man of wide scientific knowledge in the field of Dermatology, Cosmetology, and Humanities.
As a professor and researcher, Damiano has been not only an eminent representative of the experimental dermatology, but also the co-founder with me of the International Society of Cosmetic Dermatology and of this Journal.
He's been, above all, a great poet full of humanity.
A typical trait of his character was the huge feeling and the desire to share all his knowledge both with his near friends, and with the numerous students of his School.
He's been a great teacher of Experimental Dermatology and, most of all, of Cosmetic Dermatology that he considered as the most important scientific branch of Dermatology.
With his death we've lost not only a valid collaborator and promoter of this Journal, but a Man of worthy Culture, a real Gentleman, and a big Friend.

This month we had another unexpected loss.
Our friend Brodie James gently passed away.
His inborn kindness, courtesy and distinction left an inextinguishable mark in all his old friends who shared with him the passion for Cosmetic Dermatology and for research in Cosmetics.
Brodie has always been an attentive expert of Dermocosmetology and followed carefully the progress had in the latest 20 years in Cutaneous Biology.
With him, the lamented Luciano Muscardin and Damiano Randazzo, in 1982 I founded the initial nucleus of the International Society of Cosmetic Dermatology (ISCD) and of this Journal
Brodie represented the American side of the Association that has the American office in Boston and the European one in Roma.
The idea of founding the ISCD born precisely some years before in California in the splendid location of the Golf Club of Carmel in Monterey, where the beauty of the place let our memories go to the ancient Greece.
In fact, as the Greek artists developed and interpreted the beauty of human body in a unique and so ideal way to reach perfection, so we were driven to found a non profit Scientific Association.
Founding the ISCD, our intent was to join dermatologists, plastic surgeons, chemists, biologists and experts interested in develop health and beauty of the skin. Just as the ancient Greeks, our desire was to dedicate our studies and the forthcoming Congresses of the Association to achieve beauty, perfection, and general human wellbeing.
Joining and working out the ideas of the experts of different but analogous sciences, we aimed at expanding the bases of a Dermatology, solely oriented to skin pathologies, and of a Cosmetology, too much oriented to technical notions of chemistry, towards a new field "the Dermocosmetology" that unifying the various knowledge on skin and cutaneous biochemistry, was devoted completely to human wellbeing.
Brodie, a gentleman with his quite behaviour, has been for years the Friend able to settle the controversies on the topics to be discussed during the Congresses and on the selection of the speakers to invite.
With his unforgettable smile when facing discussions, he was always able to find the solution to every single problem.
Together we carried out some scientific studies demonstrating in vivo the hydrating activity of natural products taken by oral route. Those studies represented the origin of the present and so claimed Nutraceutical Science.
Brodie demonstrated his successfully research ability in many other fields of applied biomedicine and he did much to promote the enlargement of the ISCD and of this Journal.
With Brodie disappear not only the Friend but also the American brother.

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Trimestrale di Dermatologia Cosmetologica
Quarterly Review of Cosmetic Dermatology

Contents

J. Appl. Cosmetol. 23, 83-91 (July/September 2005)

DRY SKIN: SPECIFIC FEATURES IN CHINESE WOMEN

Yuan-Hong Li [1], Fazhi Yang [2], Yizhi Zhang [3], Wei Zhu [4], Ziliang Yang [5], Stéphanie Nouveau [6], Boyuan Qian [5], Shi Lian [4], Yuping Ran [3], Claude Bouillon [6], Olivier de Lacharrière [6], Hong-Duo Chen [1]

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Received: *March 2005*

Key words: *Non-invasive measurement; Climate; Skin capacitance;*

Summary

Dry skin, a very common complaint in China, has not been extensively investigated in Asia. Thus we conducted a multicentric study, involving 1800 Chinese women from 5 cities with a view to determine the prevalence and specific factors related to dry skin.

Skin type self-assessment, environmental factors and cosmetic use were recorded using a questionnaire. In addition a clinical evaluation and measurement of skin capacitance and sebaceous follicles activity were performed by trained dermatologists. The skin typology as defined by a multiple correspondence analysis of the self –assessed skin type resulted in a prevalence of dry skin of 30.8%. Women with self-assessed dry skin were clinically characterized by presence of skin scales on forehead, cheeks and lips and by a lower sebum excretion level (Sebumeter®) but no lower hydration level (Corneometer®). Self-assessed dry skin was found to be associated with: non-seborrheic skin, facial tightness discomfort and dry lips. Two factors appear to be linked with the pathogenesis of dry skin condition: (i) climate, as demonstrated by a higher prevalence of dry skin in Harbin, a northern Chinese city; (ii) use of water or soap only as face cleansing product.

Riassunto

La cute secca, che rappresenta un problema comune in Cina, non è stata ancora esaustivamente analizzata in Asia.

A tal proposito, abbiamo condotto uno studio multicentrico su 1800 donne cinesi provenienti da 5 città con l'intento di determinare la prevalenza dei fattori specifici collegati alla cute secca.

Sono stati riportati in un questionario alcuni dati quali: l'autovalutazione di cute secca, i fattori ambientali e le abitudini cosmetiche dei soggetti. In più esperti dermatologi hanno condotto una valutazione con relativa misurazione clinica della capacitanza e dell'attività sebacea dei follicoli dei soggetti in studio.

La tipologia cutanea, definita attraverso un'analisi di corrispondenza multipla con l'autovalutazione del proprio biotipo, ha messo in evidenza una prevalenza di cute secca del 30.8%. Le donne che hanno definito la propria cute secca, clinicamente mostravano la presenza di squame sulla fronte, guance e labbra ed un minore livello di secrezione sebacea (Sebumeter r) ma non presentavano alcun livello inferiore di idratazione (Corneometer r).
E' stato riscontrato inoltre che la cute autodefinita secca viene associata con: cute non seborroica, spiacevole senso di stiramento facciale e labbra secche.
2 sono i fattori che sembrano essere legati alla patogenesi relativa alla condizione di cute secca: (i) il clima, come dimostrato dell'alta prevalenza di cute secca ad Harbin, una città della Cina del nord; (ii) l'uso di acqua o sapone come unici prodotti per la pulizia del viso.

INTRODUCTION

Dry skin is a major problem which dermatologists and cosmeticians are often faced with.
It is frequently a sign of epidermal dysfunction, especially involving the stratum corneum (1). Dry skin is sensitive to a variety of exogenous influences, such as climate, detergents and air conditioning (2-3). It is mainly clinically characterized by scaling, tightness, and redness. In Western countries it is a very common complaint that has been extensively investigated (4-6). However, few relevant data are available on this condition in China. We therefore undertook a multicentric clinical study to determine the prevalence of dry skin in China at different latitudes. Moreover, the statistical typology was based on the self-assessment of skin type in order to take into account the specificities linked to the different regions of the country. This self-assessed dry skin was statistically characterized by looking at the parameters (clinical, instrumental, environmental,) which are discriminating in this group (women with dry skin) as compared to the whole studied population.

MATERIALS AND METHODS

Population sample

After approval by local ethical committees, 1800 healthy women (Northern cities: Harbin n=360, Shenyang n=360, Beijing n=360; Southern cities: Chengdu n=360, Suzhou n=360) were involved in the study after signing an informed consent. They were distributed in five age-balanced sub-groups in each center (18-25 yr., 26-35 yr., 36-45 yr., 46-55 yr., 56-65 yr.; mean age=40±13 yr.).

Evaluation criteria

Each volunteer underwent 3-step procedure: clinical interview, clinical skin assessment and non-invasive measurements. In order to limit investigator related bias as much as possible, we chose and trained only one investigator in each center. Furthermore, all the centers carried out the study simultaneously from November to December, 2001. On the morning of examination, all the volunteers were recommended to wash their face with water only and not to use any cosmetic.
The clinical interview was composed of 4 main parts: 1) Self-assessment of global skin type, dry or greasy skin intensity (with a three point-scale) on forehead and cheek, and frequency of lip scaliness. 2) Cosmetic habits for face cleansing and skin care. 3) Skin sensitivity to the sun (sunburn frequency and sun exposure habits), skin reactivity to different environmental factors and the related symptoms. 4) History of atopy (family and personal atopy).
Clinical skin examination assessed skin dryness as roughness and degree of scaling on the forehead and cheeks; and scaling intensity and chapping intensity on the lips. Skin greasiness was assessed based on the shiny intensity appearance and seborrheic condition was estimated by touch on forehead, nose and cheek and also by the presence of open skin pores on these areas. All the clinical evaluations were performed using a four-point scale (none, mild, moderate or severe).
Corneometer® (CM825 Corneometer®, Courage & Khazaka, Electronic GmbH, Cologne, Germany) measurement was performed on the cheekbone. It measures changes of the capacitance with increasing or decreasing hydration level of the skin (7-8). The results are also related to skin roughness as the capacitance value depends on tight contact between the probe and the skin surface. Ten measurements were recorded and averaged for each volunteer. Sebum excretion rate was measured with a Sebumeter® (SM810 Sebumeter®, Courage & Khazaka,

Electronic GmbH, Cologne, Germany) on the forehead. In this photometric method, the transmitted light is related to the sebum content on the measured surface.

Statistical analysis

A multiple correspondence analysis (MCA) was performed on self-assessed skin type parameters on the different facial sites (i.e. active variable) to identify skin types and define a skin typology. A hierarchical clusters analysis (HCA) was carried out on the factorial components determined by the MCA. The cluster characterisation was carried out on the Value-Test (V-test). Variables with V-tests of more than 2.0 are judged statistically significant at the 5% level (non-adjusted) and are potentially discriminatory between items of the variable to be characterised. Statistical analysis was carried out using SPAD (version 4.00; CISIA, Montreuil, France). In order to identify some links between the facial cleansing habits (i.e. active variables = water, soap, or milk/lotion) according to the other variables (i.e. skin types and Corneometer® and Sebumeter®), the same method was applied.

RESULTS

Multiple correspondence analysis led to identify 4 skin types: women with self-assessed dry skin represented 30.8% of the total population involved in the study and were characterized by self-assessed dry skin on the cheeks and forehead. Women with self-assessed greasy skin represented 25.6% of the population, women with self-assessed combination skin represented 27.4%, while women with neither dry nor greasy skin amount to 16.2 %.

When compared to overall population sample (mean age: 39.9 yr.), women with self-assessed dry skin (mean age: 44yr.) were relatively older ($p<0.001$), with a greater number of them used to spend more than 4 hours a day outdoors (5.6% in women with dry skin vs 3.9% in the whole population, $p=0.01$). They were more numerous in Harbin (Fig. 1a) (23.5% of the women with dry skin live in Harbin and 19.9% of the whole population live in Harbin, $p=0.002$). These women are more frequently menopausal women (28.9% of women with dry skin are menopausal versus 22.9% in the whole population, $p<0.001$) but this is probably linked to the age.

Thirty percent of women in this group experienced tightness and discomfort on their skin versus 20% in the whole population ($p<0.001$). They were also more numerous to be affected with dry lips (43.7% vs 33.9% in the overall population sample, $p<0.001$).

Clinical parameters, as assessed by the investigator, showed that self-assessed dry skin women more frequently exhibited some scales on the forehead (Fig 1b) (20.4% vs 14.4%, $p<0.001$), on the cheeks (23.5% vs 18.1%, $p<0.001$), and on the lips (45% vs 39.6%, $p<0.001$) as compared to the whole population. They also had a lower level incidence of seborrhoeic skin (69% vs 39.4%, $p<0.001$), and for a larger part no open skin pores when compared to the overall population sample (77.1% vs 64.6%, $p<0.001$).

Non-invasive instrumental methods did not evidence statistically significant differences in the skin capacitance mean values between women with dry skin and the whole population (Fig. 1c), whereas the women with dry skin had a significantly lower sebum excretion ($p<0.001$) (Fig. 1d).

Regarding the cosmetic uses are concerned, the analysis evidenced that a greater number of women in the dry skin group used water or soap to wash their face (49.3 % of women with dry skin vs 39.4% for the whole population, $p<0.001$) and a greater number did not wear

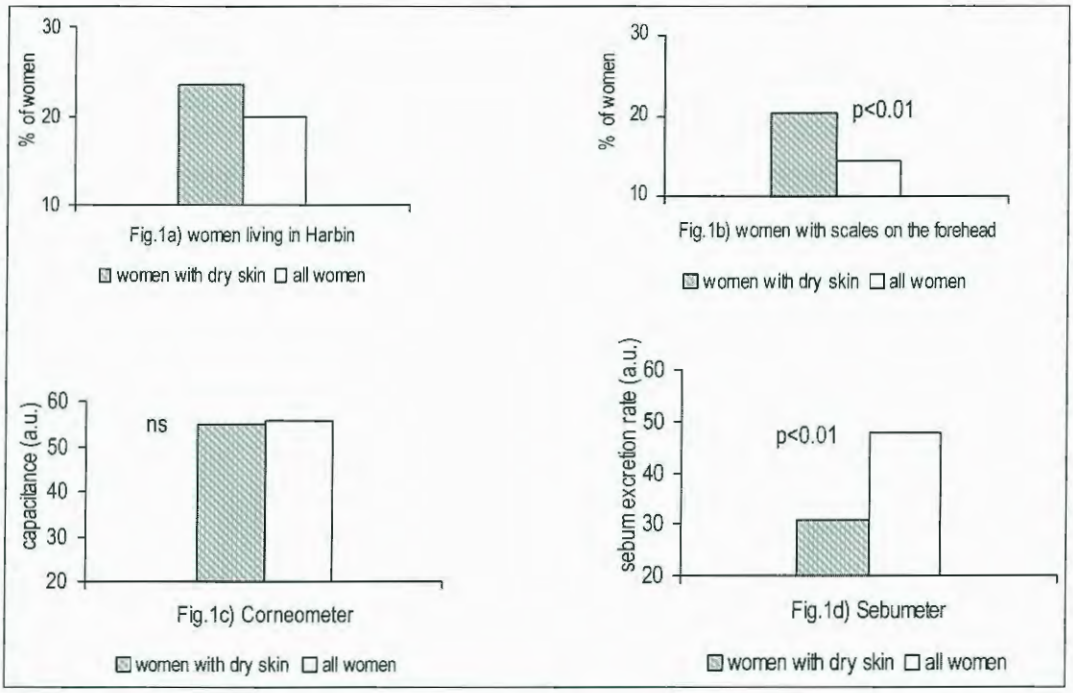

Fig. 1 *Characterization of skin type (dry skin) according to other variables 1a) more women with dry skin live in Harbin; 1b) women with dry skin have more scales on the forhead; 1c) Corneometer® and 1d) Sebumeter® mean values for women with dry skin and for the overall study population..*

make up frequently (78.6 % of women with dry skin vs 75.3% of the overall population studied, $p<0.05$).

However the prevalence of women using water or soap only to wash their face was shown to be age-related: a larger number of women using water rather than soap or milk/lotion were found in the 46-55 yr. sub-group (Table I). Thus the link between facial cleansing habits and dry skin condition could be biased by age factor, as the mean age is older in women with dry skin than in the whole population.

Specific analysis was therefore carried out on facial cleansing habits. Multiple correspondence analysis focussed on women who used water only as daily facial cleansing routine showed that they were found for a larger part in the group of women with self-assessed dry skin and low seborrhoeic skin.

Although Corneometer® measurements did not show any significant difference in the group of women with dry skin, lower skin capacitance values were obtained in the group of women who used water only as their daily cleansing routine when compared to the aggregate population (Fig. 2). In contrast, women who used milk or lotion to cleanse their face had significantly higher skin conductance values than the overall population sample (59.9 versus 56.2, $p<0.001$) (Fig. 2)

Table I

Facial cleansing habits in different groups of age. Percent of women within the age group is written in italic, percent of women within face cleansing habits group is written in bold character.

n= women number **% row** *% column*	Only water	Soap	Milk or lotion	All
18-25 yr.	n= 62 **18.8%** *8.8%*	n= 43 **13.1%** *11.4%*	n= 224 **68.1%** *31.5%*	n= 329 **100.0%** *18.3%*
26-35 yr.	n= 117 **30.9%** *16.5%*	n= 73 **19.3%** *19.4%*	n= 189 **49.9%** *26.6%*	n= 379 **100.0%** *21.1%*
36-45 yr.	n= 176 **45.8%** *24.9%*	n= 76 **19.8%** *20.2%*	n= 132 **34.4%** *18.6%*	n= 384 **100.0%** *21.4%*
46-55 yr.	n= 210 **49.2%** *29.7%*	n= 105 **24.6%** *27.9%*	n= 112 **26.2%** *15.8%*	n= 427 **100.0%** *23.8%*
56-65 yr.	n= 143 **52.0%** *20.2%*	n= 79 **28.7%** *21.0%*	n= 53 **19.3%** *7.5%*	n= 275 **100.0%** *15.3%*
All	n= 708 **39.5%** *100.0%*	n= 376 **21.0%** *100.0%*	n= 710 **39.6%** *100.0%*	n= 1794 **100.0%** *100.0%*

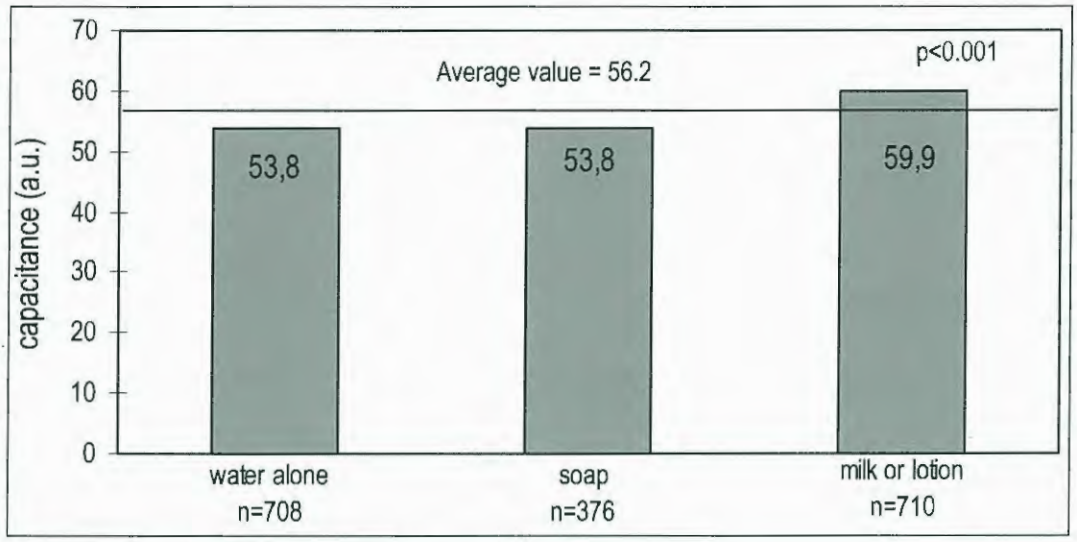

Fig. 3 *Corneometer® values according to facial cleansing use.*

DISCUSSION

To date there is no standardised objective methods available for classifying facial skin type (9-10). In this study a statistical method was used to establish a classification based on self assessed parameters. According to the typology obtained from these parameters, women with self-assessed dry skin represented 30.8% of the population involved in the study.

On clinical examination, women with self-assessed dry skin showed significant differences in skin scaling on the forehead, cheeks and lips. They had non seborrhoeic skin and more frequently experienced facial tightness and discomfort. They also reported dry lips with more scales and more chapping. This indicates that the presence of scales is an important clinical sign in the diagnosis of dry skin. Moreover there is a good agreement of self-assessment of this parameter with clinical examination of dry skin. Sebumeter® values in women with dry skin were significantly lower than those observed for the overall population sample. This result was in accordance with both the self-assessment and the clinical exam of greasy aspect of the skin. However Corneometer® values did not confirm the clinical examination as no statistical differences were evidenced between the group of women with dry skin and the aggregate population. Corneometer® values tended to decrease with age but not significantly, as it had been frequently published, even recently (11). It would mean that Corneometer® measurement alone is not sufficient to assess dry skin typology.

Climatic factors also contributed to this condition (12-14). The prevalence of dry skin was higher in Harbin, where there was a Siberian like weather. Furthermore in this study, women who spent more time outdoors were most likely to have dry skin.

The use of water or soap for facial cleansing also increased the prevalence of skin dryness. In this study more than 50% of women who used water

or soap only to wash their face had dry skin and a significantly lower skin capacitance than women who used cosmetic cleansing products. In cleansing milks and lotions, there are moisturizing ingredients, which improve skin mildness and help maintain proper hydration level of the stratum corneum.

CONCLUSION

In conclusion, self-assessment of dry skin in Chinese women was well correlated to clinical assessments but poorly concurred with instrumental measurement of skin capacitance. It was shown that the overall prevalence of dry skin was around 31% in China, which represented a mean value encompassing different latitudes involved in the multicentric study. The presence of scales was an important clinical sign for dry skin, which was also associated with facial tightness discomfort and dry lips. Specific features related to dry skin in China were similar to what was known in Western countries. However two factors increased dry skin prevalence: siberian-like climate and face cleansing habits.

ACKNOWLEDGEMENTS

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BOSWELLIC ACID BASED CREAM IS EFFECTIVE AND WELL TOLERATED TREATMENT FOR STRIAE DISTENSAE

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Summary

Problem: Striae distensae are a common disfiguring skin disorder for which few effective therapeutic alternatives are available. The main topical agent, retinoic acid, is often associated with irritation.
Method of study: 118 healthy subjects (102 women) aged 22±8.0 years with striae distensae of recent onset (<2years) applied a boswellic acid based cream twice daily onto the striae and randomly on the left or right volar forearm for 3 months. Global severity score and the severity of erythema, atrophy and edema were assessed using a 4-item semiquantitative scale, and extensibility of the volar forearm skin using the Dermeter device at baseline and after 45 and 90 days. Opinions on efficacy and tolerability were also collected. Subjects evaluated the cosmetic acceptability of the cream by expressing their opinion on its color, odor, consistency, ease of application, freshness, absorption, its effect and its residues on the skin.
Results: Global severity score diminished from 2.3±0.9 to 2.1±0.9 (-10% p=0.05) after 45 days and to 1.9± 0.8 after 90 days (-17.4% p<0.001). Also erythema, edema and atrophy improved significantly (all p<0.001, -46.1%, -35.3% and -29.6% after 90 days, respectively). Skin extensibility improved 15 minutes after the first application of the cream from 8.31±0.97 mm up to 8.72±0.71mm (p<0.001). At the end of treatment a substantial improvement was achieved in 60% of subjects and slight improvement in 25%. Erythema improved in 80% of patients and edema in 48%. No subjects worsened. Cosmetic acceptability was good or excellent in 66-93% according to the parameter taken into consideration. Subjects particularly appreciated the consistency and ease of application of the cream. No important adverse events were reported.
Conclusions: The study suggests that the boswellic acid based cream is effective and well tolerated treatment for striae distensae of recent onset. It is also well accepted as a cosmetic.

Riassunto

Causa: Le strie distensae rappresentano un diffuso inestetismo della pelle per il quale sono attualmente disponibili poche terapie alternative efficaci. Il principale agente topico, l'acido retinico, è spesso associato ad irritazione.

Metodi: 118 volontari sani (102 donne) la cui età era di 22±8 anni con strie distensae di recente formazione (< 2 anni) hanno applicato una crema a base di acido boswelico 2 volte al giorno sulle strie distensae e, in maniera randomizzata, sulla faccia volare dell'avambraccio sinistro o destro per 3 mesi. Mediante una scala semiquantitativa a 4-punti, sono stati valutati il punteggio totale relativo alla gravità e la gravità dell'eritema, atrofia ed edema, inoltre, è stata valutata al basale e dopo 45 e 90 giorni l'estensibilità della cute dell'avambraccio utilizzando lo strumento Dermeter. Sono state quindi raccolte le valutazioni sull'efficacia e tollerabilità. I soggetti hanno valutato l'accettabilità cosmetica della crema esprimendo la loro opinione sul colore, odore, consistenza, facilità di applicazione, sensazione di freschezza, assorbimento, effetti e residui sulla pelle.

Risultati: Il punteggio relativo alla gravità diminuisce da 2.3±0.9 a 2.1±0.9 (-10%, p=0.05) dopo 45 giorni e a 1.9±0.8 dopo 90 giorni (-17.4%, p<0.001). Anche l'eritema, l'edema e l'atrofia migliorano in misura significativa (tutti p<0.001), rispettivamente -46.1%, -35% e –29.6% dopo 90 giorni). 15 minuti dopo la prima applicazione della crema si aveva un miglioramento dell'estensibilità cutanea da 8.31±0.97 mm fino a 8.72±0.71 mm (p<0.001). Alla fine del trattamento è stato ottenuto un sostanziale miglioramento nel 60% dei soggetti e un lieve miglioramento nel 25%. L'eritema migliorava nell'80% dei pazienti e l'edema nel 48%. Nessun soggetto peggiorava. L'accettabilità cosmetica e' stata giudicata buona o eccellente nel 66% - 93%, in relazione al parametro preso in considerazione. I soggetti hanno particolarmente apprezzato la consistenza e la facilità di applicazione della crema. Non sono stati riportati in nessun caso eventi avversi indesiderati.

Conclusioni: Lo studio suggerisce che la crema a base di acido boswelico è un trattamento efficace e ben tollerato per le strie distensae di recente formazione. Risulta inoltre ben accettata come cosmetico.

INTRODUCTION

Striae distensae, more commonly called stretch marks, are a frequent skin disorder that is not associated with any major medical complication, but that can cause distressing disfigurement. Initially they appear as pink-purplish elongated marks (striae rubrae) that in time turn into whitish, depressed and irregularly shaped bands (striae albae).

They are the result of continuous and progressive stress exerted on the connective tissue, which generally are due to changes in body size. They frequently occur on the abdomen and breasts of pregnant women, on the thighs, buttocks, hips, abdomen and upper arms of subjects who repeatedly lose and regain a considerable part of their body weight, on the shoulders of body builders and in various parts of the body in adolescents during the growth spurt (1, 2, 3).

According to a recent survey in 505 Italian women, they are present in approximately 80% of women aged up to 45 years and in 70% of women aged over 45 years. The main risk factor, besides positive family history (49%), is changes in body weight, either weight loss (59%) or weight gain (39%) (4). Indeed, striae distensae are included among the common complications obesity and its management (2).

Several risk factors have been identified, such as a genetic predisposition, inadequate diet (low intake of milk, meat, citrus fruit and vitamins) and hormonal factors, which make the skin particularly vulnerable to stress during pregnancy and adolescence. An example of hormonal effects are the striae that frequently appear in Cushing's syndrome (5).

The pathogenesis of striae distensae has not been elucidated. It is believed that the skin reacts to undue stress with an inflammatory process that ultimately damages the framework of collagen and elastin fibers, which is responsible for the tensile strength and elasticity of the skin i.e. its ""plastoelasticity" (6).

Currently available treatment consists of the topical application of trans-retinoic acid, which is able to improve the clinical appearance of striae of recent onset, but is often associated with irritation that leads to discontinuation of application, and surgical treatment, such as chemexfoliation and laser therapy, which produces satisfactory results (7, 8) .

A cream containing boswellic acids and other active ingredients is now available for topical treatment of striae distensae.

Boswellic acids are extracted from the bark of *Boswellia serrata*, a tree found in India, Northern Africa and the Middle East. The extract is a gummy oleoresin containing essential oils, gum and terpenoids, including four pentacyclic triterpenoids, called boswellic acids (9). These compounds exert anti-inflammatory activity by inhibiting the production of leukotrienes and free radicals via 5-lipoxygenase acid selectively and dose-dependently; they do not block cyclooxygenase and are therefore devoid of the typical undesired effects of NSAIDs (10-13). The inhibition of leukotriene synthesis, in turn, inhibits leukocyte migration towards the area of inflammation, thus preventing the activation of enzymes, such as human leukocyte elastase, a serine protease that catalyses the rupture of cell membranes, beta-glucuronidase, beta-N-acetylglucosoaminidase, collagenase and various cathepsins. This puts fibroblasts, the most important cells responsible for the production of collagen and elastin fibers, in favorable conditions that enhance their function. Such fibers are crucial for the degree of firmness and suppleness of the skin i.e. for the plastoelasticity of skin. Thus, boswellic acids are able to act on all the main factors that contribute towards to formation of striae (14-16).

The cream also contains other active ingredients: centella asiatica, soia phospholipids and

polyunsaturated fatty acids. Centella asiatica (Indian pennywort) is a medicinal plant that grows in Sri Lanka and Southern Africa (17). It contains pentacyclic triterpenic derivatives that promote re-epithelization and restoration of the microcirculation during wound repair, by stimulating fibroblasts and collagen metabolism; they have also been shown to increase the levels of enzymatic and non-enzymatic antioxidants, such as superoxide dismutase, catalase, glutathione peroxidase, vitamin E and ascorbic acid in newly formed tissues (18-19). Clinical investigations have shown that it is effective in the treatment of striae distensae, wound healing disorders and in preventing stretch marks during pregnancy (18-20).

Soia phospholipids resemble the physiological constituents of cell membranes and contribute towards the prevention of skin dehydration. The polyunsaturated fatty acids are extracts from mosqueta rose seeds, rice bran and karitè butter, which moisturize and soften the external layer of the skin.

The objective of this study was to assess the efficacy, tolerability and cosmetic acceptability of this new cream in the treatment of striae distensae of recent onset.

METHODS

This multicenter study was carried out by dermatologists in a total of 118 subjects at 13 centres throughout Italy. Each centre recruited up to 10 subjects of both sexes who met the following eligibility criteria:

- from 14 to 40 years old
- presence of striae distensae of recent onset (< 2 years)
- body mass index (BMI) from 19 to 25 (Quetelet's formula body weight in kg / height2 in cm)
- in good health
- written informed consent (if < 18 years, authorization from parents was requested)
- no specific therapy for striae, except for normal cleansing, in the last 3 months

Also pregnant women were eligible.

Women who were breast-feeding, and/or were taking part or had taken part in a similar study in the last month, had other dermatological lesions involving the skin areas to be treated or were affected by diabetes, other hormonal disorders, progressive cancer, debilitating diseases and/or were receiving systemic corticosteroids or local medical or surgical treatment in the skin areas to be treated were excluded. Also women who did not appear to be reliable i.e. were at risk of low compliance, were excluded, as well as those who had changed their lifestyle in the last 3 months in terms of diet, physical activity and medication. Subjects were not to change their lifestyle also during the study.

The investigational cream was provided by the Sponsor in its usual marketed packaging.

Subjects applied the cream onto the striae and onto a specified area of the left or right volar forearm massaging slightly until it had been completely absorbed, twice daily, preferably always at the same time of day, for 3 months. The forearm was selected following a randomization list.

Subjects were given a diary to fill-in, specifying date and hour of each application.

The parameters of efficacy were:

- Global severity score related to the striae according to the following 4-item semiquantitative scale:
  Grade 1: less than 10 lesions, less than 3 cm long and less than 5 mm thick
  Grade 2: more than 10 lesions, less than 3 cm long and less than 5 mm thick
  Grade 3: more than 10 lesions, more than 3 cm long and less than 5 mm thick
  Grade 4: more than 10 lesions, more than 3 cm long and more than 5 mm thick
- Severity of signs of erythema, atrophy and

edema of the striae according to a 4-item semi-quantitative scale
1 = absent 2= mild 3=moderate 4=severe
- Skin extensibility on the volar forearm in the treated area by means of a metal device called "Dermeter®" that has already been described (21) (Figure 1).

Fig. 1

In brief, the device resembles a caliper with fins. The body of the caliper contains a spring connected to the fins, a battery and the connections to an external digital display with control buttons. The fins are fixed onto the skin with specifically shaped, biocompatible tape and the device exerts a predefined traction force that produces extension of the skin. The extension, measured in up to hundredths of a millimeter, can be read on the display and expresses the extensibility of the skin.

In order to reduce the risk of mistakes, the measurement was always performed twice. Moreover, at baseline it was repeated 15 minutes after the first application of the cream.
- overall evaluation of efficacy by both the dermatologist and the patient

Dermatologists also expressed their opinion on tolerability, specifying whether they had observed any redness or other signs of intolerance, and whether the patient had reported itching and/or burning or any other complaint.

Patients evaluated the cosmetic acceptability of the cream by expressing their opinion on its color, odor before and after application, consistency, ease of application, freshness, absorption, its effect and its residues on the skin after application.

The subjects attended the centre three times, at baseline and after 45 and 90 days. Demographic data, medical history information, a detailed description of the striae and an extensibility measurement were obtained at baseline. Efficacy, tolerability and cosmetic acceptability data were collected at the subsequent visits.

The statistical analysis of the data was performed by Derming Srl Monza (MI) under the supervision of a biomedical engineer. Scores were analyzed using the test of Wilcoxon, whereas extensibility data were analyzed using Student's t test for paired samples and the judgements on efficacy and tolerability using Friedman's test.

The study was performed according to the principles of the Declaration of Helsinki and subsequent amendments. All subjects gave their informed consent in writing before entering the trial.

RESULTS

The main characteristics of the recruited subjects are summarized in Table I. Most of the patients were young women, in whom striae had developed for the first time at puberty. The striae to be treated had appeared 10-12 months earlier in nearly half of the subjects and were located mainly on the thighs, hips, buttocks and breasts. The most common risk factors were a positive family history and changes in body weight.

Five patients dropped out of the study, so the final evaluation included 113 patients (95.8%).

All parameters of severity of the striae improved significantly after 45 days of treatment and even further after 90 days of treatment.

Table I

Main characteristics of the study population at baseline

Characteristic	Unit	value
Sex - Female Male Not specified	N (%)	102 (86) 2 (2) 14 (12)
Age (years)	Mean ± SD	22 ± 8.0
BMI	Mean ± SD	21.4 ± 2.9
Onset at puberty as an adult during pregnancy not specified	N pat (%)	67 (57%) 34 (29%) 12 (10%) 5 (4%)
Months since onset - 1-3 4-6 7-9 10-12 >12 missing	N pat (%)	17 (14%) 19 (16%) 22 (19%) 52 (44%) 1 (1%) 7 (6%)
Risk factors - Positive family history Body weight gain Body weight loss Muscle hypertrophy Hypertension	N pat (%)	58 (49%) 45 (38%) 33 (28%) 2 (2%) 0
Previous topical therapy for striae	N pat (%)	21 (17.8%)
Location of striae - Thighs Hips Buttocks Breasts Abdomen Arms	N pat (%)	71 (60%) 55 (47%) 52 (44%) 50 (42%) 20 (17%) 9%
Overall clinical severity score	Mean ± SD	2.3 ± 0.9
Erythema severity score	Mean ± SD	2.6 ± 0.8
Edema severity score	Mean ± SD	1.7 ± 0.8
Atrophy severity score	Mean ± SD	2.1 ± 0.7
Skin extensibility (mm)	Mean ± SD	8.31 ± 0.97

The mean global severity score related to the striae diminished significantly from 2.3 ± 0.9 down to 2.1 ± 0.9 (-10% p=0.05) after 45 days and to 1.9 ± 0.8 after 90 days (-17.4% p<0.001) (Figure 2A). Both the signs of inflammation, namely erythema and edema, and of atrophy improved significantly (all p<0.001), but the regression of erythema was more pronounced than the regression of the other two signs: the mean erythema severity score diminished from 2.6 ± 0.8 down to 1.9 ± 0.7 after 45 days and down to 1.4 ± 0.5 after 90 days (-46.1%) (Figure 2B); the mean edema severity score improved from 1.7 ± 0.8 down to 1.3 ± 0.5 after 45 days and to 1.1 ± 0.3 (-35.3%) (Figure 2C); the mean atrophy severity score improved from 2.1 ± 0.7 down to 1.8 ± 0.6 after 45 days and to 1.5 ± 0.5 after 90 days (-29.6%) (Figure 2D). An improvement in erythema by 1 degree or more was achieved in 80% of patients, whereas edema improved by 1 degree of more in 48% of patients and atrophy did so in 52%.

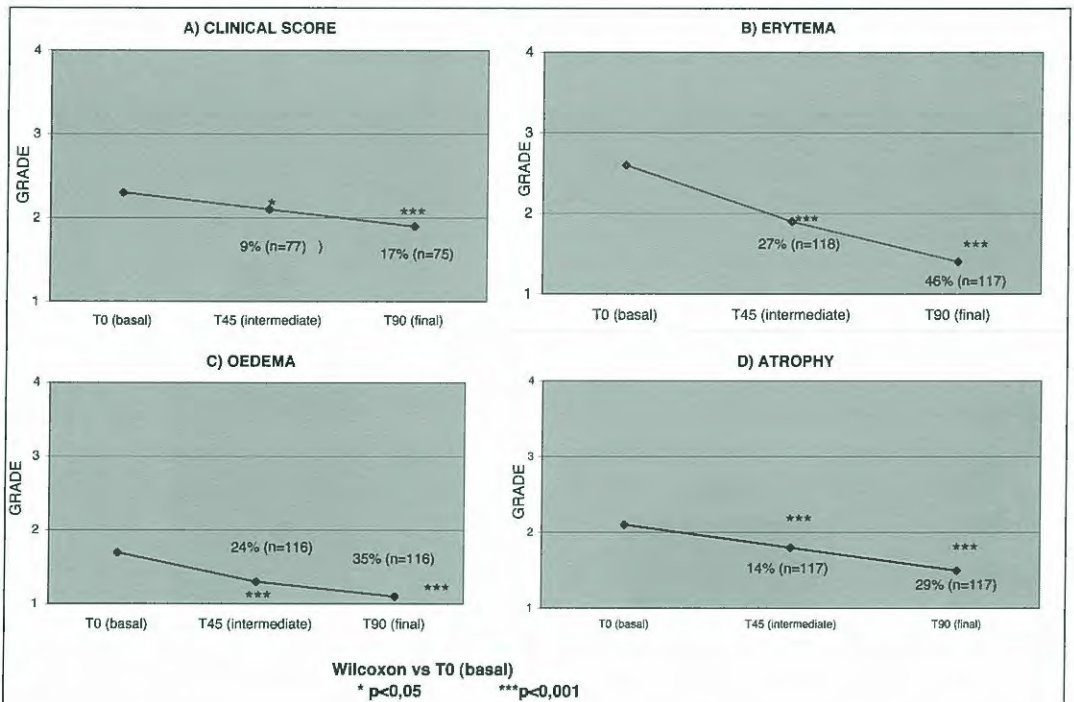

Fig. 2: *Clinical evaluation of striae and evolution of symptoms:A) global severity score; B) erythema; C) oedema; D) atrophy*

The assessment of skin extensibility 15 minutes after the first application of the cream revealed a significant immediate improvement from 8.31 ± 0.97 mm up to 8.72 ± 0.71 mm (+4.9% - $p<0.001$) (Figure 3). Subsequent measurements carried out after weeks of treatment, but performed hours after the application of the cream, also documented significant improvements, but to a smaller extent: 8.53 ± 0.95 mm (+2.6% $p<0.001$) after 45 days and 8.56 ± 1.03 mm after 90 days (+3.0% $p<0.001$)

The overall efficacy judgement of the investigators coincided with the judgement of the patients. They both considered that substantial improvement had been achieved in 40% of cases (investigators: 39%, subjects: 41%) and that slight improvement, namely slight attenuation of redness, had been achieved in another 38% of cases after 45 days. They also agreed on the final results after 90 days of treatment: substantial improvement in 60% of cases (63% according to the subjects) and slight improvement in redness in another 25% (26% according to the investigators). Investigators and subjects disagreed on other miscellaneous signs of improvement in a small proportion of patients (up to 10%). The striae did not worsen in any cases. No improvement was recorded in approximately 14% of subjects after 45 days (investigators: 13%, subjects: 15%), and in 4 cases according to the investigators (3%) and in 5 according to the subjects (4%) after 90 days.

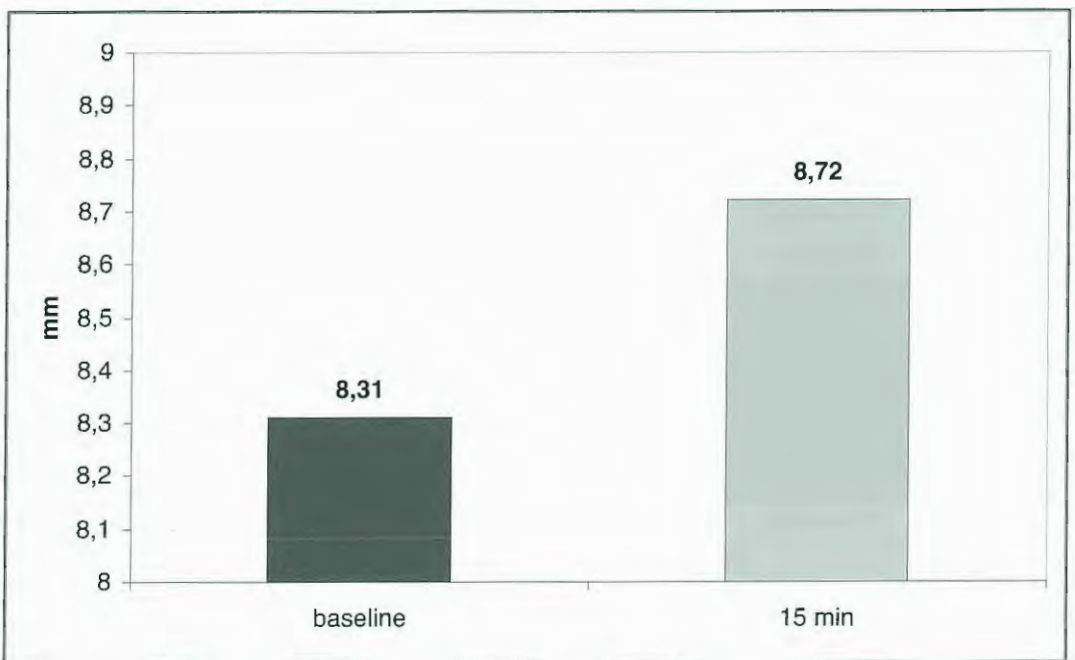

Fig. 3: *Skin extensibility before (baseline) and 15 minutes after the application of the boswellic acid based cream (mm)*

Cosmetic acceptability was good or excellent in 66-93% according to the parameter taken into consideration. Subjects particularly appreciated its consistency, ease of application (positive opinion in 93-94% of cases and no negative opinions). The worst judgements regarded its odor after application (positive opinion 63%, negative opinion 11%) (Table II).

No important adverse events were reported. Tolerability was good in 80% subjects after 45 days and in 94% of subjects after 90 days. Transient itching was reported in 8 subjects, which persisted up to the end of treatment in 3; transient redness was reported in 8 subjects, which persisted in only 1 case; another 2 subjects reported persistent burning.

DISCUSSION

This study suggests that the boswellic acid based cream is effective, well tolerated and well accepted as a cosmetic in the treatment of striae distensae of recent onset.

The efficacy data suggest that the cream can produce an improvement in up to 85% of subjects both according to objective (investigator's opinion) and subjective (subject's opinon) criteria. Its efficacy appears to consist in the improvement of plastoelasticity of the skin, as shown by the highly significant improvement in skin extensibility and the 30% mean improvement in the signs of atrophy in 48% of patients, and in the amelioration of the inflammatory component, as shown by the 46% mean improvement in erythema in 80% of patients.

Table II

Cosmetic acceptability of the boswellic acid based cream used for striae distensae

Parameter	% Subjects (n)				
	Negative	Mediocre	Good	Excellent	Not specified
Appearance					
Color	3 (4)	15 (17)	55 (62)	25 (28)	2 (2)
Odor	10 (11)	15 (17)	50 (57)	23 (26)	2 (2)
Tactile sensations during application					
Consistency	0	4 (5)	65 (73)	28 (32)	3 (3)
Ease of applic.	0	5 (6)	62 (70)	32 (36)	1 (1)
Freshness	1 (1)	15 (17)	52 (59)	30 (34)	2 (2)
Absorption	2 (2)	14 (16)	51 (58)	31 (35)	2 (2)
After application					
Odor	11 (12)	22 (25)	43 (49)	23 (26)	1 (1)
Effect on skin	1 (1)	6 (7)	57 (65)	33 (37)	3 (3)
Residues	8 (9)	12 (14)	43 (49)	33 (37)	4 (4)

The improvement in the extension of the striae and the severity of signs was assessed using classical semiquantitative rating scales, whereas skin extensibility was measured by a novel device, the Dermeter®, which has been properly validated (21).

The cream was also well tolerated. None of the subjects discontinued treatment because of intolerance and persistent local symptoms were recorded in only 6 subjects (5%).

Cosmetic acceptance was also very good. However, there were differences in the various parameters. Its consistency and ease of application were particularly appreciated, whereas opinions on its odor after application were mixed, being positive in 66% of cases and clearly negative in 10%. This is a difficult feature to correct as it does not depend only on the product, but also on the individual conditions of the skin of the subject, making it impossible to achieve a positive result in all subjects.

A limitation of the study is that practically only women were included, so the data apply to female skin only. Another limitation is that this was an open-label study. It is not possible to establish how much of the improvement was due to the greater attention given to the striae during the trial, which involved massaging the striae regularly. Moreover, the subjective opinion of both investigators and subjects may have been influenced by the knowledge that the cream had been regularly applied, making them expect some improvement.

The results of this study provide modern evidence supporting the efficacy of a therapeutic principle that has been used empirically by ancient cultures for hundreds of years. Boswellia serrata i.e. Indian frankincense bark extracts containing boswellic acid have been recommended for a number of inflammatory disorders in ayurvedic medicine for centuries. Two thousand year-old papyri describe the use of incense bark extracts for cosmetic purposes in Egypt and provide recipes for incense extract preparations to be used as disinfectants, sedatives and as cosmetics. It appears that these recipes were the secret of the women of the Egyptian region of Nubia, who were famous for their exceptionally beautiful skin.

Nowadays boswellic acid preparations, such as the tested formulation, are recommended for the prevention of striae distensae and for the treatment of striae of recent onset in weight lifters and during pregnancy, puberty and slimming dietary regimens. Prevention is particularly important for subjects who have a positive family history for striae distensae. They may also be used as co-adjuvant therapy together with other surgical and medical therapies, such as dermo-peeling and retinoic acid, which benefit from its anti-inflammatory and soothing properties. Treatment should be instituted as early as possible and continued regularly for at least 3-6 months.

CONCLUSIONS

In conclusion, the efficacy results of this study are consistent and pronounced, strongly suggesting that the boswellic acid based cream is effective in striae distensae. The next step should be a double-blind, placebo-controlled study with the objective of assessing the efficacy of the cream in striae distensae.

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Riassunto

L'articolo descrive le potenzialità dei sistemi di rilascio nanoparticellari nel settore dermo-cosmetologico.
In particolare vengono presentati sistemi di trasporto innovativi alternativi ai liposomi quali nanoparticelle solide lipidiche (SLN), etosomi e cubosomi.
Studi dermo-cosmetologici effettuati applicando SLN sulla pelle indicano un aumento dell'idratazione cutanea ed una riduzione di profondità delle rughe, inoltre è stato dimostrato che le SLN sono in grado di controllare il rilascio degli agenti cosmetici.
La struttura malleabile degli etosomi facilita l'interazione degli agenti attivi in essi incorporati con il doppio strato lipidico dello strato corneo. In particolare la maggior capacità degli etosomi rispetto ai liposomi nel promuovere la penetrazione attraverso la pelle è da attribuire ad una interazione tra etosomi e lipidi cutanei.
I materiali cristallini lipidici cubici rappresentano un interessante argomento di ricerca in quanto la loro struttura unica permette notevoli applicazioni dermocosmetologiche nel settore del rilascio controllato. I cubosomi vengono generalmente prodotti grazie a metodi che richiedono tempo e dispendio di energie. In alternativa abbiamo recentemente sviluppato tecniche di produzione più convenzionali. In particolare abbiamo dimostrato che l'emulsionamento di miscele monogliceridi/tensioattivi in acqua porta alla formazione di dispersioni acquose composte da particelle lipidiche grossolane (28% p/p) e cubosomi di forma sferica, pochi aggregati, diametro medio di 193.5 nm e un'elevata percentuale di recupero (88% p/p). Le caratteristiche organolettiche e morfologiche dei cubosomi non cambiano nel tempo, essendo privi da fenomeni di separazione di fase per almeno un anno dalla preparazione. Studi di Spettroscopia di Correlazione Fotonica hanno evidenziato che i cubosomi subiscono un iniziale aumento di diametro durante il primo mese dalla produzione; quindi mantengono le dimensioni per i 6 mesi successivi.

INTRODUCTION

Research efforts in pharmaceutical and cosmetic field are currently aimed to develop new nanoparticulate systems able to control release and to improve tatgeting to skin. Among nanoparticles, liposomes are of course the best known systems. In the last decades, a number of studies has demonstrated their efficacy as drug delivery systems both for parenteral and topical administration ways. The well characterized liposome vesicles can host different molecules in the bilayer, on the surface or in the inner of their structure. Since liposome composition and structure strictly resemble to the stratum corneum, percutaneous administration of this vehicle leads to deposition of lipidic components from which liposome load can be slowly release. Until now the major liposome drawbach is their limited physical stability (1).

As an alternative to liposome, solid lipid nanoparticles (SLN) represent innovative drug carrier systems firstly designed for i.v. administration and recently investigated for peroral and transdermal application. The solid matrix of SLN should be able to protect chemically labile agents from degradation and to modulate drug release profiles (2).

SLN are an alternative to polymer nanoparticles, liposomes and nanoemulsions. Chemically labile agents should be protected from degradation and the release profile of drugs can be modulated (3).

Ethosomes could be decribed as lipid vesicular systems embodying ethanol in relatively high concentrations (4). These "soft vesicles", represent novel vesicular carrier for enhanced delivery to/through skin (5). Ethosomes have a particle size that can be modulated from tens of nanometers to microns. One main feature of this new type of vesicle is its soft structure which carries the incorporated active agent into the skin lipid bilayers, enabling facilitated delivery (6).

Bicontinuous cubic liquid crystalline materials are an active research topic because their unique structure lends itself well to controlled release applications (7). Cubosomes are discrete, submicron, nanostructured particles of bicontinuous cubic liquid crystalline phase (8). Cubosomes possess the same microstructure as the parent cubic phase but have much larger specific surface area and their dispersions have much lower viscosity than the bulk cubic phase (9). After formation of the cubosomes, the dispersion is formulated into a product and then applied to a substrate of interest, usually bodily tissue. Thereafter materials are either absorbed or released via diffusion.

SOLID LIPID NANOPARTICLES

Solid lipid nanoparticles (SLN) offer a number of potential advantages as delivery systems, such as better availability for poorly water-insoluble molecules, the use of physiological lipids and a wide application range (dermal, per os, intravenous) (1).

SLN for the topical application to the skin are made up from lipids such as glyceryl behenate (Compritol 888 ATO), glyceryl monostearate (Imwitor 900), glyceryl palmitostearate (Precirol ATO 5), triglycerides (trimyristin, tripalmitin, tristearin) or the wax cetyl palmitate. Nanodispersions contain 5 to 40% lipid, the higher concentrated preparations are of a semisolid appearance. These are cosmetically acceptable as they are while the fluid nanodispersions with lower lipid content should be incorporated into a e.g. cream which facilitates the application.

Mean particle size ranges from 50 to 1000 nm. Depending on the type and concentration of the lipid, 0.5 to 5% emulsifier (surfactant) have to be added for physical stabilisation. For dermal use these are very often poloxamer 188, polysor-

bate 80, lecithine, tyloxapol, polyglycerol methylglucose distearate (TegoCare 450), sodium cocoamphoacetate (Miranol Ultra C32) or saccharose fatty acid ester.

SLN can be obtained by different methods, based on solvent emulsification/evaporation or on high pressure homogenization. The latest is an estabilished production method which prevents the need of organic solvents and allows large scale production (2).

SLN dispersions possess interesting features for topical use. Firstly SLN are able to improve chemical stability since their solid matrix protects the molecule from hydrolysis and oxidation. For instance the chemical stability of tocopherol and retinol improves considerably as compared to an aqueous dispersion (1).

Moreover cutaneous application of SLN can exert occlusive properties. In fact, after application of the lipid nanodispersion to the skin surface, the evaporation of water induce the lipid particles to form an adhesive layer applying occlusion to the surface. As a consequence, an increase in the hydration of the stratum corneum occurs.

The occlusive effects depends to the particle size, in particular it has heen demonstrated that nanoparticles are 15fold more occlusive than microparticles (1).

The generally low lipid content and the poor viscosity of lipid nanodispersions make these preparations as they are less suitable for dermal drug application. The handling of the preparation by the patient is improved by SLN incorporation into ointments, creams and gels. If SLN are incorporated into vehicles, interactions with the vehicle constituents may induce physical instabilities such as dissolution or aggregation of lipid particles. Therefore, during storage particle sizes and the solid character of the particles have to be followed (3).

Retinol incorporated into Compritol-based SLN has been released more rapidly and to a higher extent as compared to conventional vebicles and a nanoemulsion. This effect appears to result from a burst release from tbe solid particles following water evaporation on the skin surface and the change of lipid modification.

Non-loaded and loaded SLN were already investigated with respect to use in

cosmetics. Although adequate controls are difficult to prepare, first experiments indicate an increase in skin hydration and a reduction in wrinkle depth following SLN application . Moreover, cetyl palmitate-nanodispersions act both as particulate UV blockers themselves and as carriers for UV absorbing agents (e.g. 2-hydroxy-4-methoxy benzophenone; Eusolex 4360) (2). This results in a threefold increase in UV protection which allows reducing the concentration of the UV absorber. This is particularly important since UV absorbers are currently in discussion because of possible estrogenic activity and long-term effects in the environment. SLN may also be suitable for long-lasting perfume and insect repellent formulations(2). As with drugs, an improved uptake of cosmetic agents (Q 10, tocopherole) into the horny layer has been described. The relation of cutaneous penetration to particle size indicates that the increase is due to an occlusive effect.

Recently nanoparticulate lipid carriers (NLC) have been developed composed of oily droplets embedded in a solid lipid matrix. Since liquid lipids solubilize lipophilic molecules to a much higher extent than solid lipids, the NLC particles would provide a high incorporation capacity and control of release (1).

ETHOSOMES

The use of ethosomal carriers results in delivery of high concentrations of active to/through the skin regulated by system composition and their physical characteristics.

Touitou and colleagues have demonstrated the

major potential of ethosomes to promote drug penetration through skin with respect to liposomes (4).

In vivo experiments and clinical trials have demonstrated that a range of molecules such as testosterone, acyclovir (Zovirax; Glaxo Wellcome plc) and insulin can be delivered effectively through the cell membranes of animal and human skin. An alteration of the ethosome formulation can modulate the level of penetration (restricting drug delivery to the skin only, as required for herpes labialis treatment with Zovirax, or allowing full dermal penetration as required for insulin therapy) (4). Another molecule, trihexyphenidyl hydrochloride, incorporated in ethosomes is proposed for transdermal administration in Parkinson patients, from which the geriatric population may greatly benefit (5). Transdermal absorption of polypeptides is currently under investigation. The high interest of ethosomes in the design of new therapies has been investigated with other drugs such as propranolol; in this respect ethosomes showed their potential as transdermal dosage forms for prophylaxis of migraine. Moreover the ability of ethosomes to deliver compounds to cells in culture was investigated (6).

The enhanced delivery of actives using ethosomes over liposomes can be ascribed to an interaction between ethosomes and skin lipids. A possible mechanism for this interaction has been proposed. It is thought that the first part of the mechanism is due to the 'ethanol effect', whereby intercalation of the ethanol into intercellular lipids enhances lipid fluidity and decreases the density of the lipid multilayer. This is followed by the 'ethosome effect', which includes interlipid penetration and permeation by the opening of new pathways due to the malleability and fusion of ethosomes with skin lipids, resulting in the release of the drug in deep layers of the skin (4).

The basic properties and the in vitro release rate kinetics of azelaic acid (AA) alternatively vehiculated in different phospholipid based vesicles, such as ethosomes or liposomes, were investigated (6). Ethosomes were produced by a simple method based on addition of an aqueous phase to an ethanol solution (comprised between 20 and 45 % v/v) of soy phosphatidyl choline (5 % w/w) and AA (0.2 % w/w) under mechanical stirring. Liposomes were obtained by the same composition in the absence of ethanol with the reverse-phase evaporation method. Vesicle size was measured by Photon Correlation Spetroscopy (PCS) evidencing smaller mean diameters and narrower dimensional distributions in the case of ethosomes with respect to liposomes (Table I) . In order to obtain homogeneously sized vesicles, both ethosomal and liposomal dispersions were extruded through polycarbonate membranes with pores of calibrated diameter (400 and 200 nm). Vesicles morphology was characterized by freeze-fracture Scanning Electron Microscopy (SEM) showing the presence of unilamellar vesicles both in liposome and in ethosome based dispersions (Fig.1).

AA diffusion from ethosomal or liposomal dispersions and from ethosomes and liposomes incorporated in a viscous gel was investigated by a Franz cell assembled with synthetic membranes. Release rate was more rapid from ethosomal with respect to liposomal systems, in particular ethosomes produced by the highest ethanol concentration released AA more rapidly, the same trend was found using viscous forms (Table II).

This behavior can be attributed to the presence of ethanol that makes the lipidic membrane packed less tighly than liposomes and confers a softer, more malleable structure to the ethosomes, possibly promoting azelaic acid diffusion through the vehicle (6).

Table I

Vesicles mean diameter and polydispersity acid containing liposomes and ethosomes before and after extrusion through 200 nm pore size membranes, as determined by PCS

Vesicles	Z Average (nm)	Polydispersity	Intensity (nm)
LIPO	817.8	1.00	814.9
LIPO *ex 200*	165.1	0.14	162.3
ETHO 20	440.8	0.28	428.8
ETHO 20 *ex 200*	179.5	0.09	177.2
ETHO 40	527.5	0.22	531.0
ETHO 40 *ex 200*	173.9	0.02	174.9

LIPO: liposomal suspension
ETHO 20: ethosomal suspension produced by the use of ethanol 20%
ETHO 40: ethosomal suspension produced by the use of ethanol 40 %
ex 200: vesicles extruded through 400 nm pore size polycarbonate membranes and through 200 nm pore size polycarbonate membranes
Data were the mean of four determinations on different dispersions, SD were always comprised between ± 5%.

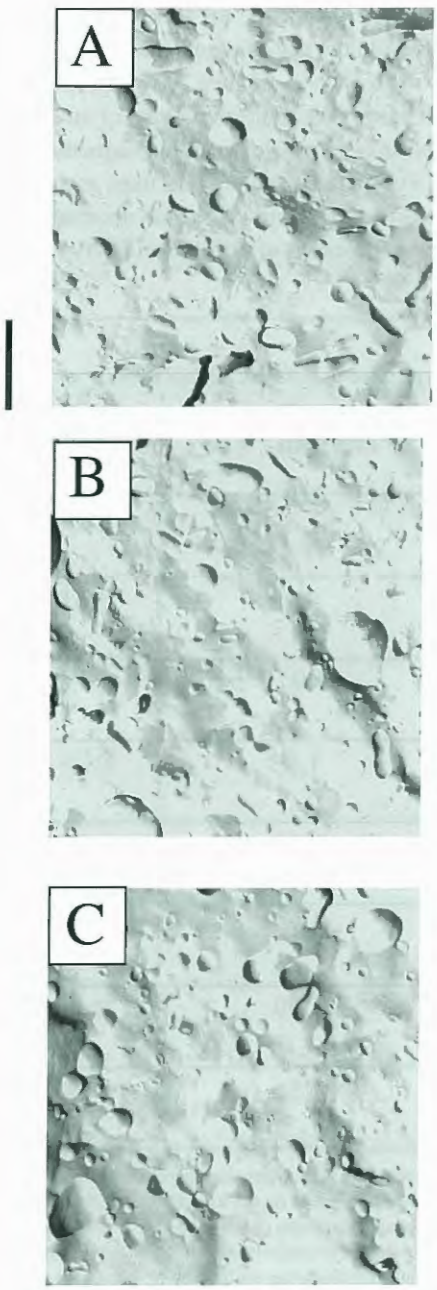

Fig. 1 *Freeze-fracture electron micrographs of liposome (panel A) and ethosome 20 (panel B) or 40 % (panel C). Liposome and ethosome dispersions were subjected to extrusion through 200 nm pore size membranes. The bar equals 510 nm.*

CUBOSOMES

Unsaturated long-chain monoglycerides such as monoolein are able to form a variety of structures in aqueous media by self-association, depending on water content and temperature. The addition of small amounts of water to the lipids at 37°C results in the initial formation of a reverse micellar solution. As the water content and/or temperature increase, different mesophases such as lamellar, reversed hexagonal, bicontinuous cubic, and isotropic sponge phase are formed (7). In particular cubic liquid crystals are transparent, isotropic viscous phases and physically stable in excess water (8). Cubic phase represents a unique system for the production of pharmaceutical dosage forms (9).

Aqueous dispersions of cubic lipid phases can be used for the development of nanoparticulate drug delivery systems characterized by high biocompatibility, bioadhesivity, and easy production protocol (10). Because of their properties, these versatile delivery systems can be administered orally, parenterally, or percutaneously.

Landh and Larsson have patented the preparation of colloidal dispersions of nonlamellar lyotropic crystalline phases and have termed the particles "cubosomes" (11). Cubosomes usually have been produced by means of time-consuming methods involving high energy input. For instance Gustafsson et al. have investigated the production and structure of aqueous dispersions of lipid-based lyotropic liquid crystalline phases (12). The dispersions were based either on glycerylmonooleate/sunflower oil or glycerylmonooleate/retynilpalmitate mixtures plus a nonionic triblock polymer (Poloxamer 407) in water. Dispersions were produced by dropwise addition of a melt of lipids and poloxamer in water, followed by reduction of size by homogenization under high pressures at 80°C. Recently Seikmann et al. have reported the preparation and characterisation of dispersions constituted

of monoolein-rich monoglycerides with or without purified soya phospholipids (13). Dispersions were prepared by equilibration of the monoglyceride/phospholipid/ water cubic phase, subsequent fragmentation by a solution of Poloxamer 407, predispersing by probe sonication and finally high pressure homogenization. Moreover some authors have developed experimental protocols for cubosome production based on the use of organic solvents. In particular Spicer and Hyden have proposed a method based on a dilution process of an ethanolic solution of monooleine with an aqueous solution of Poloxamer. Ethanol was used as a hydrotrope to create a liquid precursor, spontaneously forming cubosomes after dilution (14).

Table II

"In vitro" release rate coefficients of azelaic acid incorporated in different topical forms.

Formulation	F_0 $\mu g/cm^2 * min^{0.5}$	D $cm/min^{0.5} * 10^3$	log D
EtOH solution	186.6	15.55	1.19
EtOH / Carbomer gel	49.31	4.1	0.61
LIPO	59.63	4.97	0.70
LIPO gel	13.88	1.9	0.28
ETHO 20	87.79	7.31	0.86
ETHO 20 gel	38.62	3.22	0.51
ETHO 40	119.96	9.99	0.10
ETHO 40 gel	54.77	4.56	0.66

EtOH / Carbomer gel: ethanol solution incorporated in Carbomer based gel; LIPO: liposome suspension; LIPO gel: LIPO incorporated in Carbomer based gel; ETHO 20: ethosomal suspension produced by the use of ethanol 20%; THO 20 gel: ETHO 20 incorporated in Carbomer based gel; ETHO 40: ethosomal suspension produced by the use of ethanol 40 %; ETHO 40 gel: ETHO 40 incorporated in Carbomer based gel; °Azelaic acid concentration was always 12 mg/ml
Experiments were performed by a Franz release rate cell assembled with a cellulose ester membrane (0.6 μm pore size) and IPB / ethanol 70:30 v/v as receptor phase.
Data were the mean of six determinations, SD were always comprised between ± 8%.

Finally Nakano et al. have suggested a method for the production of cubosomes based on hydration of a dry film of monooleine/poloxamer with an aqueous buffer (15). The authors proposed to mix monooleine and poloxamer in chloroform and to dry the mixture by solvent evaporation. After hydration, cubosome were formed by homogenization at 80°C, structure of cubosomes was investigated by small-angle X-ray scattering and 13C NMR.

A recent investigation by Esposito et al. has demonstrated the chance to produce cubosome dispersions by a simple processing technique, avoiding time consuming procedures, multiple equilibration steps, intermediate formation of viscous bulk cubic gel, high energy input and use of organic solvents (16). In particular the use of a stirring speed 1500 r.p.m., monooleine 5% w/w (with respect to weight of dispersion) and Poloxamer 407 10% w/w (with respect to the disperse phase) enabled to produce dispersions presenting 28% of larger irregular particles and cubosomes characterized by spheroidal shape, few aggregates, mean diameter of 193.5 nm and high percentage of recovery (88% w/w).

Figure 2 shows two cryo-TEM micrographs evidencing the heterogeneous morphology of the disperse phase. In particular one can observe the coexistence of spherical vesicles and few faceted particles together with well shaped cubosomes exhibiting the typical ordered cubic texture (16). Vesicular structures appear also attached on the surface of cubosomes, as found by other authors, suggesting that by time a transformation may take place from conglomerates of partially fused vesicles to well ordered particles (7,8,12). These results were in agreement with X-ray diffraction data, revealing the coexistence of two different cubic phases, the first being a bicontinuous cubic phase of spatial simmetry Im3m (Q229) and the second belonging to the P4(3)32 (Q212) spatial symmetry.

Stability studies were performed demonstrating that the organoleptic and morphological aspects of cubsome dispersions do not change by time, cubosomes in fact are free from phase separation phenomena for almost one year from production (16).

Moreover PCS studies were conducted at different time intervals (from 0 to 5 months from production) in order to evidence possible variation of mean diameter of cubosomes by time.

Cubosomes undergo an increase in their mean diameters after 30 days from production. and generally maintain their dimensions in the successive 4 months, not exceeding 595 nm after 5 months from their production (16).

L'Oreal has patented the use of cubosome particles as oil-in-water emulsion stabilizers and pollutant absorbents in cosmetics. More recently Nivea has introduced cubosome use in personal care product as skin care, hair care, cosmetics, and antiperspirants (17).

A recent cryo-TEM study evidenced that the global cryo-electron density pattern of the stratum corneum keratin intermediate filament network resembles "inverted" cryo-transmission electron micrographs of cubic lipid/water phases with a "cubic-like rod-packing simmetry"(18). The observation that biological interface itself possesses a cubic architecture appears particular important in the development of cubosome based cosmetic as well as dermal products.

18) **Norlén Al-Amoudi (2004)** Stratum Corneum Keratin Structure, Function, and Formation: The Cubic Rod-Packing and Membrane Templating Model. *J. Invest. Dermatol.* **123** (4): 715

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VITILIGO: Problems and Solutions

by Torello Lotti and Jana Hercogovà
2004. 528 pages Hardcover
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The book comprehends 48 chapters but it can be ideally divided in two parts.
The first part provides many updated information from basic science to appropriate therapeutic choices, the second part is dedicated to other clinically relevant hypomelanotic disorders and their possible treatments.
A special mention goes to the interesting novel 34th chapter, that is entirely dedicated to the most important media source of information published on *internet*.
But what is vitiligo?
Vitiligo is an acquired loss of pigmentation histologically characterized by the absence of melanocytes, that represent the melanin's factory.
The etiology and pathogenesis is not yet known, but the cause may be an autoimmune disease associated with antibodies. The made of inheritance is thought to be autosomal dominant with variable penetrance.
There is a positive family history in at least 30% of cases and both sexes are affected equally. What is to consider is that approximately 1-4% of the world population is affected: 50% of cases begin before age 20 and the pigment loss may be localized or generalized. However, although the clinical picture should be quite similar, the etiology and pathogenesis mechanisms vary individual by individual. This is the opinion of the book's authors.
Moreover according to the recent investigations, the authors agree and support the hypothesis that melanocytes are *never completely absent in the depigmented epidermis* and capable of recovering their functionality. This and other interesting news are reported on **chapter 1.**
The importance of psychic factors and social behaviour in the etiopathogenesis of vitiligo and its epidermiology are discussed in **chapters 2** and **3**.
As a matter of fact, social behaviour can be devastatingly affected by pigmentation disorders and vitiligo, particularly in deeply pigmented peoples, can be a terrible psychosocial disease. However it is necessary to remember that the patient's life situation provides emotional warmth and support, as well as practical help, as it happens with child care or financial assistance. Thus the attitude of intimates, is one of the most important factors that determine the impact of any skin disease, including vitiligo.
Moreover epidemiological research may contribute to a better understanding of all the etiological, but also the psychological and prognostic factors improving its management.
Biology of *hypopigmentation*, together with family's history and the auto*immune hypothesis* of viti-

ligo are the topics of **chapters 4-8.**

The substance responsible for skin colour is melanin, a pigment produced by melanocytes and transferred to surrounding keratinocytes.

Melanin in the melasome, the specialized epidermal melanin-bearing organelle, is responsible for the colour variation of human skin.

The functional unit responsible for this process is called the *epidermal melanin unit*, which is composed of a melanocyte and an associated cluster of keratinocytes. Thus, visible skin colour arises from constitutive skin' colour plus the effects of light, hormones, and depends on the genetic factors and facultative skin colour.

Absence or loss of pigmentation of the skin is therefore, due to three main etiological factors: an absence/loss of melanocytes, a deficit of melanin formation, and no melanocytes etiology. In addition to the loss of functioning melanocytes, the keratinocytes and Langerhans cells are distributed in vitiligo.

However both cellular and humoural immunity are probably involved in the pathogenesis of vitiligo, even if the former is considered the most important by the majority of experts in the world, and clinical ultrastructural, and biochemical data seem to involve all the immunoneuroendocrine system.

Thus clinical and experimental data seem to demonstrate the role of an autoimmune reaction in this particular skin pathogenesis, but many are the hypothesis suggested to really understand and explain the loss of melanocytes and the really causative factors implicated in the depigmentation process.

The most important of these seem to be (a) the suggested autoimmune theory, (b) the intrinsic/genetic theory, (c) the antocytoxic theory, and (d) the neural theory.

However, the recent data seem to provide evidence of our important change in the expression of epidermal cytokines in vitiligo as skin, which can lead to peroxidant effects. The persistent alteration of the pro-oxidant ratio could be the first pathogenetic event in melanocyte degeneration, occurring even after external stimuli. The subsequent release of melanocyte antigens could lead to an autoimmune response, which can maintain and propagate the disease.

As a result a programmed melanocyte death or destruction, coming from toxic intermediates of melanin or from other sources. In any case, in vitiligo the inadequate response to nitric oxide represents an event sufficient to induce depigmentation.

These topics are discussed from **chapter 9** to **19.**

What about treatment of vitiligo?

There is no standard treatment. Treatment of this pathology can be divided into non-surgical repigmentation therapies, autologous transplantation methods, and depigmentation therapies. All these different therapies are reported from **chapter 20** to **33.**

The efficacy and safety of classical and new therapies are well presented and discussed on **chapter 20,** where guidelines of available repigmentation and depigmentation therapies are reported.

As a matter of fact, "a treatment" is regarded as being successful when more than 75% repigmentation is observed.

Based on the results of the literature-studies, treatment with a patent local corticosteroid is advised for patients with localized vitiligo (50-62% of mean success).

When patients exhibit generalized vitiligo, UV-B therapy is recommended (50-76% of mean success). However, it seems there are no statistical differences in the success rates of oral PUVA, nar-

rowband UV-B and broadband UV-B.
With regard to the autologous transplantation methods, splitth kness skin grafting and epidermal blister grafting can be recommended as the most effective and safest techniques with in respective mean success of 88-91% and 83-90%.
Minigrafting seems to have the highest rates of adverse effects, but it was shown to be the easiest, fastest, and least expansive method.
Because of the small patients treated, no definite conclusions can be drawn with regard to the effectiveness of culturing techniques.
However, most of these therapies require treatment periods lasting months or years before repigmentation occurs. In the meantime the apparent disfigurations of vitiligo may lead to emotional distress and loss of self-image, impairing the patient's private and professional life. Therefore an adjunctive cosmetic therapy may be necessary by the use of cosmetic temporary or permanent camouflage. About temporary camouflage cover creams, including conventional compact and liquid foundations, stick and pressed powders are normally and easily used as make-up. With regard the permanent camouflage obtainable by tattoos, the cosmetic result are strongly on the doctor's or technician's experience in matching the colours.
With **chapter 35** begins the discussion on other clinically relevant hypomelanotic disorders.
The *Halonevus* is the topic of the chapter that gives a clinical picture of this benign melanocytic nevus sometime difficult to differentiate from rare halo malignant melanoma. The *Alessandrini's Syndrome*, an oculo-cutaneous hypomelanotic disease associated with retinic degeneration and with auditory involvement, is treated on **chapter 36.** Acquired and idiopathic *Hypomelanoses* are the topics of **chapter 37** and **38**, the nail *Leukoychia* is described on **chapter 39.**
Soon after the description of other hypomelanotic disorders, this interesting book dedicated to vitiligo, ends with other 9 chapters dedicated to other hypomelatonic disorders which *Vogt-Koyanagi-Herada syndrome and Nevus Depigmentosus.*
In conclusion abnormalities of pigmentation may be acquired, or congenital, localized or generalized, circumscribed or universal, familiar or non-familiar, of known or unknown etiology, and associated with either cutaneous or systemic findings or isolated events.
For the exhaustive information given on vitiligo, this book will be surely of great interest not only for dermatologists but also for all clinicians and scientists belonging to medical and chemical community who wish to know more deeply what is and how to treat the *white* spot by the world defined *vitiligo.*

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BIODEGRADABLE SYSTEMS IN TISSUE ENGINEERING AND REGENERATIVE MEDICINE

By R.L. Reis and J. San Roman
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The search for better methods of producing porous scaffolds with the right mechanical properties is still an important and challenging issue in regenerative medicine.

As a matter of fact, besides the obvious demands of biocompatibility and biodegradability, an ideal engineering scaffold should exhibit appropriate mechanical properties and a suitable degradation rate.

Furthermore the scaffold must possess adequate porosity interconnectivity, and permeability to allow the ingress cell and nutrients, as well as the appropriate surface chemistry for enhancing cell attachment and proliferation.

Taking into account the aforementioned requisites, the processing technology used to produce the scaffolds is mainly expected to provide maximum control over macro-and-microstructural scaffold - cell interactions such as toxicity and surface chemistry or topography, and, of course, accuracy and reproducibility.

The main scope of this book is to give all these information to the readers.

Divided in 5 parts and organized in 29 chapters, it tries to address a range of relevant topics in an integrated and *looking forward perspective* with the scope to improve the quality of life of thousand of patients.

Part I is dedicated to *Processing and Applications of Biodegradable Systems* from injectable systems and scaffolds to partially degradable polymers and composite .materials useful first of all for orthopaedics and dentistry. These topics are reported and discussed thorough twelve chapters.

Until now it is by no means clear what defines ideal scaffold-cell or scaffold-neo tissue constructs, even for a specific tissue type.

This field is still young and the considerations are complex and include architecture, structural mechanics, surface properties, degradation products, and composition of biological components along with the changes in all of these factors with time.

Scaffold-based tissue engineering concepts, in fact, involve the use of combinations of viable cell, bio molecules and structural matrix combined into a *constrict* to promote the repair and regeneration of tissues. For all these reasons this *constrict* has to support cell migration, growth, and differentiation, but in parallel, its components has to undergo degradation or resorption via production of biocompatible, excretable, or metabolizable by-products.

Of course the factor governing scaffold properties are complex and include considerations about architecture, mechanics, surface properties, degradation products, composition of biological components, and the change in these factors with time.
Up today scaffolds might be categorized from a physical point of view into three groups: cellnlar solids, textiles, and injectable systems. However engineering strategies require the design of materials that reflect the understanding of all the possible biological interactions as much as possible allowing the development of increasingly intelligent devices that can combine different functions.
Injectable systems offer a great potential for applications, for example, in interactive bone tissues engineering approaches, as they can be designed with a wide range of properties and configurations and can incorporate cells and a number of different biological agents capable of different combined functions.
Of course these specific biomaterials, that are intended to use as tissue engineering templates, must also exhibit several general requirements, such as degradability, biocompatibility high surface area/volume ratio, osteoconductivity, and mechanical integrity, in order to efficiently perform the function for which they are designed. All and other interesting considerations on these topics are reported from chapter 1 to chapter 6.
In chapters 7 to 18 are discussed some of the raw bio- materials developed for a different range of biomedical applications and all the efforts and studies being made to optimize their use .
When we compare, in fact, biological material with synthetic or man-modified materials one finds that nature developed adaptive materials with hierarchical structure based in building blocks of the same type.
Living tissues, in fact, are based in molecules composed of a few basic elements of the periodic table and interwined with living cell communities.
For all these reasons it is difficult to build hierarchical structures capable to mimic the essential attributes of biological tissues, giving adaptive condition for the living cells.
Thus the high quantity of studies on biomaterials suitable for all the required needs, provided the development of non-degradable and degradable polymers, such polymethylmethacrylate (PMMA), polysulfure (PSU) or collagen/chitin/chitosan and hyaluronate-based composites.
The incorporation of chitosan to bone cements, in fact, intends to improve or modulate properties such as injectability, degradation rate, or mechanical performance.
Another use of biodegradable or non-biodegradable polymeric materials is to produce the so-called biotextiles that have numerous applications in medicine, including sutures, vascular grafts, artificial skin substitute ligaments, wound dressing and cartilage scaffolds, etc.
However the development of biomaterials requires an extensive evaluation in terms of biocompatibility mechanical properties, and degradation behaviour in order to determine whether a certain material is suitable for a particular application.
Understanding the factors that control the systems and a greater comprehension of these mechanisms is indispensable to optimize their current usage.
This interesting topic represents the closure of the Part I book, where the new strategies developed to achieve biomaterials with controlled degradation rates are also reported.
Production of *Biomimetic Coatings on the Surface of Degradable Polymers* is the topic of **Part II** focused on two chapters, (the 13th and the14th), designing bonelike apatite coatings on biodegradable polymers by means of biomimetic coating technologies. In bonelike calcium phosphate coatings

have great potential when applied to biodegradable polymers since they can stimulate the tissue regeneration at the bone-implant interface while the material is being reabsorbed. These coatings, in fact, facilitate the cell attachment and proliferation in the interior of the scaffold, followed by the process of vascularization.

As a matter of fact, bone consists of an organic framework (mostly collagen) in which mineral (carbonated apatite) plate-shaped crystals are dispersed. It is a complex living tissue in which the extracellular mineralized matrix confers rigidity and strength to the skeleton while still maintaining some grade of elasticity.

Thus the bone tissue can be viewed as a two-component composite material, composed primarily of collagen and mineral hydroxyl-apatite in the form of needle like crystallites precipitated along the collagen fibrils.

Therefore, when considering an ideal material to replace and mimic bone, synthetic calcium phosphates is an obvious answer, since they can replicate the structure and composition of bone mineral in a reproducible way. And starch-based polymers are particularly interesting for bone-related application because of their easily convertion into complex geometries, exhibiting interesting mechanical properties that match those of human bone.

Moreover they are associated with degradation kinetics adequate to the healing of the tissues to be replaced or fixed. However we have to remember that no implant has biomechanical properties equivalent to the tissue it replaces. Therefore, every implant is a compromise, a balance between biochemical compatibility and biomechanical compatibility.

Thus design strategies for creating a biomimetic coating that has a dual beneficial effect (on one side its osteoconductive properties and on the other side its ability to act as a drug carrier delivering therapeutic agents directly to the interface) might have a very promising future.

Part III, focused on *Systems for Controlled Release of Bioactive Agents*, is treated into four chapters, from the 15th to the 18th.

They provide a detailed description of different application of biodegradable polymers in the controlled release of bioactive agents, including their possible release mechanisms and the relative biomedical applications.

As a matter of fact, there is a growing interest and significant progress in the research and development of innovative biomaterials because of the increase in the lifetime and the search to bettering the general quality of life.

Thus of great importance is the assurance that the delivery system biological activity is preserved throughout manufacturing, storage, delivery, and release, otherwise its use would be worthless. And, of course, it has to be safe.

But what controlled release means in the field of pharmaceutical science?

It is a term that represents an increasing number of techniques by which active chemicals are made available to a specified target at a rate and duration designed to accomplish a specific therapeutic effect. Therefore the preparation of controlled –delivery systems regulated by the functional groups of chain segments of polymer-polymer macromolecule components is now the base for the development of *intelligent systems*.

At this purpose strong ionic interactions between functional groups with apposite charge are well established.

And this is the basis for the development of several bioadhesive controlled-delivery systems.
According to this principle, there are two large categories of design and preparation of controlled-delivery systems considering the structure and functions of the polymeric supports.
These are classified as *physically controlled delivery systems,* based on the physical interactions of the bioactive components with the support and polymeric drugs based on the chemical link of the bioactive component to the polymeric support.
However the main objective in the design and preparation of a controlled drug delivery system is the possibility to release a bioactive compound in a predetermined, predictable, and reproducible fashion.
The development of controlled-release systems will surely offer more interesting strategies for the effective pharmacological application of active compounds, growth factors, proteins, hormones, etc, and will contribute to the development of new emerging technologies such as tissue engineering, gene therapy and to the success of diagnosis and enzyme therapy approaches by the use of the immobilization methods.
Part IV, *Biocompatibility and Immunobiological Responses to Degradable Biomaterials* (chapters 19 to 23) includes all the special requirements necessary for the best biological performance of biodegradable systems and reviews the problem related to testing the biodegradable polymers, giving also a great attention to the immune response obtainable from the implanted systems of natural-origin.
As we reported previously the most important requirement for a biodegradable polymer to be used in medical applications is its compatibility not only in terms of physical and chemical properties but also in those that define their behaviour at the time they contact the body.
Therefore the evaluation of the biological response to the materials should follow procedures that allow for the objective evaluation of the devices safety and biocompatibility.
Thus collecting information from several types of tests-morphological, biochemical, and gene-level-will allow for a full-range characterization of the biogradable system before further *in vivo* tests are carried out.
Only a combination of tests, giving different answers, can give an accnrate final answer the posed question: is this material harmless for it to be tested in *vivo?*
Thus we must have an overall picture of the biomaterial/host interface or biomaterial/cell interface, especially in the case of *in vitro* studies. Great attention is also to be given to the immune response to implant natural-origin degradable systems and to several disposable methodologies to tailor the cell adhesion and proliferation on the surface of biodegradable polymers.
The last part of the book, Part V, (chapters 24 to 29), provides the reader with a description on the different use of biodegradable polymers in tissue engineering, such as bone, articular cartilage, liver, skin, etc.
The application of microfabrication techniques, which allow the design and fabrication of so-called biomimetic surfaces, offer interesting tools to overcome the poor surface properties of bionatural polymers in respect to promote for example, attachment proliferation, and differentiation of epidermal cells.
The last conclusive chapter of the book is dedicated to the problem related to design a nerve guide able to provide nerve cell attachment and growth, and that has the desired mechanical, geometrical, and permeability properties for guided nerve regeneration.

With this new and interesting topic ends this interesting book entirely dedicated to the tissue engineering for the *regenerative medicine*.
Written from well-known experts, the book gives a comprehensive overview of all the open and solved problems related to the role played from polymer-based systems in tissue engineering replacement, and regeneration. For the complete overview of all the subjects reported and for the interesting discussion opened, it has to be in the library of all the chemical and medical community that has interest or should like to know in a deeper way all the problems linked to this relevant and fascinating topic.
In my opinion, especially dermatologists and plastic surgeons have to consider this book as mean for explaining and teaching their students and not as a tool to show off in their own in-office libraries.

P. Morganti
Editor-in-Chief

HAIR CARE

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Organized in 8 chapters this interesting book ends with an extensive description of *Hair Care Formulary.*

Hair is an appendage of the epidermis, the outer layer of skin.

Hairs are derived from specialized epidermal cells that form the hair follicles. Hair follicles develop before birth. The average scalp contains from 80,000 to 120,000 hair follicles. This number is determined genetically, and no new hair follicles form after birth.

The only growing, or live, portion of the hair is the hair root (papilla), found at the base of the follicle. As soon as the cells that make up hair are produced, they die and become cornified (hardened) to form the hair shaft.

The hair shaft, like the epidermis, is composed of cells filled with keratin, and it is gradually pushed up the follicle tube toward the surface of the scalp at a rate of about 1/3 to ½ inch per month.

The hair shaft is lubricated with an oily substance (sebum) secreted by the sebaceous glands that open into the follicle. There's also a muscle attached to each hair follicle (the arrector pili) that can cause hair to *stand on end* or produce "gooseflesh."

The nourishment, which enables hair's cells to grow and multiply, is ensured by the blood vessels reaching the bulb through the dermal papilla.

Thus, these cells should be well-nourished, mainly during the anagen stage, and receive a continuous flow of several substances absolutely necessary for their life. Among them, a major role is played by sulphurated aminoacids, such as cystine and methionine (which make the hair strong and thick), carbohydrates (which supply the energy necessary for cell longevity) and vitamins, such as vitamin B6 and panthotenic acid (which are fundamental to enzyme-induced reactions of oxydation). Finally, minerals, such as copper, zinc and iron, act as indispensable co-enzymes.

Like the skin, the hair need specific treatments, depending on both individual characteristics and the season.

In summer, the hair need softening oils and packing masks; protective, nourishing, gelatin-rich screens to prevent excess loss of mineral salts and proteins, due to prolonged exposures to the sun or frequent bathing.

In winter, precautionary measures must be redoubled if fog, smog, widespread humidity and cold weather occur: mild-acting shampoos and products should be used to cleanse and nourish the hair in a balanced, *tailor-made way.*

Like the skin, which, in order to control the effects of the sun when sun-bathing, requires a variable protection factor (SPF Skin Protection Factor) depending on its sensitiveness, also the hair requires

personalized protection (HPF Hair Protection Factor) and nourishment factors.
Depending on whether the hair is weak, dehydrated or healthy, so different intakes of active components are recommended. A light but complete diet is recommended to keep healthy hair; a rich and nourishing one is indicated for sensitized hair; a strong-acting and intense one is to be adopted in case of damaged hair which need to be revitalized.
The above treatments, both topical and systemic, ensure a thorough cleansing and nourishing action and completely remove impurities, always protecting the hair and the scalp.
For all these reasons, several shampoos, hair conditioners and masks, have been developed to be topically applied and specific dietary supplements set up to be taken by oral route.
All these products are based on sulphured aminoacids, vitamins and minerals useful to hair bulbs, to bring the moisture level back to normal in dull hair or to protect the hair against damage due to free radicals, induced by UV rays and environmental pollutants. Thanks to their special nutrients, such as essential fatty acids, these products are able to restore strength, thickness and shine to the hair, improve microcirculation and regulate sebum secretion.
This is the topic of **chapter 1** dedicated to *Structure and Physiology of Hair.* Ethnic and Asian hair characteristics are reported also.
Hair Cleansing and Conditioning is discussed on **chapter 2.**
Beautiful hair is a question of texture.
Healthy hair should be manageable and beautifully silky and soft, just like skin. But hair texture can deteriorate. The main problems are dryness or oilness. They are caused by internal physiological factors or ageing or by external ones such as dry atmosphere, wind, sun, or pollution.
Whatever the cause, the result is the same: rough, dry or excessively oily and lifeless hair.
Hair is also subject to physical and chemical treatments which can sometimes be quite rough. Damage can be caused by constant styling, hair-dryers which are too hot, colourants which are too harsh, too many perms or a wrong way of eating. As a result, it may appear a deterioration of the cuticle, the outer covering of the hair.
Examining a damaged hair through a microscope, it is possible to see some changes in its surface shaft: the normally smooth scales deteriorate, making the hair's surface extremely rough. As a result, the scales engage those of other hairs causing tangling. The hair loses its shine and softness and the ends split easily. Delicate and lifeless, the hair becomes difficult to style.
At this stage it is necessary to treat the dry or oily hair just as it is generally done for the skin.
Cleansing the hair: Lipidic surface film
It is known that sebum, produced by the sebaceous glands, reaches the surface of the epidermis via the pilo-sebaceous duct. Once it reaches its destination it emulsifies with sweat forming a thin coating known as the hydrolipidic surface film.
The equilibrium between sebum and the surface is of basic importance for the protection of the skin from aggressive external agents, be these chemical-physical, bacterial or mycotic, and for the maintenance of normal acidity, an optimum state of hydration and the elasticity and plasticity of the skin.
The surface skin lipids film, which is naturally present on the scalp, covers the hair shaft, making it soft, shiny and combable. The excessive presence of this hydrolipidic film on the scalp, but especially on the hair shaft, makes the hair difficult to comb and causes opacity and a *feeling of dirtiness,* which significantly reduces the basic function which hair play as an important factor in sexual attraction.

Function of shampoos

The main function of the shampoo is to remove the surface grease, the skin debris, the dirt accumulated from the environment and the residue of hair-grooming, cosmetics from hair shaft and scalp, leaving the hair soft, lustrous and manageable. Of course this cleaning activity has to have no side effects for the health of the user.

The removing of lipid soil from the hair is controlled by the same processes as those that have been identified in wool detergency, in spite of the differences in respect of time and temperature. The principal agency is generally considered to be the *roll-up* mechanism i.e. the displacement of surface soil by the detergent solution.

The detergent micelles make contact with the lipid surface, form lipid-detergent co-micelles which detach and *float away* into the bulk acqueous solution. The *signal* to which the user responds when applying a shampoo is how quickly it builds up lather and how copious that lather is. This tends to colour the user's later impressions of the other characteristics of the shampoo.

Scientifically speaking, foaming properties play not a fundamental role in the cleaning of hair. Certainly it is more important the kind of cleaning agent (surfactant) used and the active compounds selected for the scalp health, including antidandruff or anti-oilness additives.

Society's obsession with hair and hair colour is an ancient one. This obsession is further heightened today as the cult of youthfulness becomes, even more extreme. *Colouring hair and Reactive Treatments for Hair* are the respective topics of **chapters 3** to **5.** Three are in fact the ways to modify hair colour, by oxidation, semipermanent or temporary dyes.

Permanent or Oxidation Dyes are commercially the most important. They consist of dye precursors, e.g. p-phenylenediamine, which are oxidized by hydrogen peroxide. The active intermediate condenses in the hair fibre with an electron-rich dye coupler, e.g. resorcinol, and possibly with electron-rich side chain groups of the hair, forming a bi-, tri or polynuclear product that is oxidized to an into dye.

Semipermanent Dyes. The term semipermanent hair dyes dye the hair without the use of hydrogen peroxide, with a colour that persists after four to six shampooings. The semipermanent dye formulations contain 10 to 12 admitted cosmetic dyes, mixed together to get the desired shade. Other ingredients are solvents (water, glycols or their derivatives), surfactant(s), amides, fragrance, acid or alkali for pH adjustment.

The dyes are mono, di or trinuclear and consist of neutral aromatic amines, nitro aromatic amines or anthraquinone derivatives. These dyes diffuse into hair and are retained by weak polar and van der Waals attraction forces; the affinity of the dyestuff for the fibre increases with increasing molecular weight.

Temporary Hair Dyes or Color Rinses. The objective of temporary dyes is to provide colour that can be shampooed out of the hair with a single shampooing. Each colour-rinse product consists of a mixture of anionic or acid dyes.

On **chapters 4** *(Stiling Hair)* **5** *(Styling Hair)* **6** *(Formulating Hair Care Products)* are described how to treat and styling the hairs.

New hair styling technology is reported topically based on acrylate, acetate, methyl vynil ether maleic anhydride, PVP, and other traditional copolymers technology.

To optionizing the hair physical properties, a new concept of *dynamic style* is based on a first truly durable hold.

The *dynamic style* is designed to meet the needs of today's consumer who is active, on the go, and pressed for time, but who still wants to look as good as possible all day. Thus acrylate copolymers have been *engineered* to make formulations and manifacture easier and more pleasing to the consumer. A lot interesting hair formulations are reported on the final chapter after having previously discussed all the technical problems involved in formulating and fragrancing hair care products.
Combination of science and art is in fact, necessary in giving consumers products that are pleasing to use, enhancing also their appearance and their self-esteem. **Chapter 7** is totally dedicated on *Testing and Evaluating Hair and Hair Care Products*.
Testing on hair tresses readily provides data that match consumer perception of the combing properties of hair. However the success of such testing is dependent upon the reliability of the equipment and the methodology used to evaluate the tresses.
The final judge on the hair care product is generally given by a consumer-use study that tell the formulator how well the consumers will like the product.
Many are the damaging effects imparted to hair due for example, to environmental causes such as UV rays, or to cosmetic treatments such as permanent waves or hair bleaches.
Thus to understand the basic mechanism of these aggressive assaults may allow development of safer and more effective hair formulations.
The Hair Care Formulary ends this interesting book giving to the formulator many ideas necessary to realize interesting hair care products.
This book is a good source of information on how to formulate the right products for hair care for all cosmetic chemists, dermatologists, and for medicine and chemistry students.

P. Morganti
Editor-in-Chief


Note

NEL TURNOVER CELLULARE ALTERATO
IN ABNORMAL CELLULAR TURNOVER

MAVICEUTICALS

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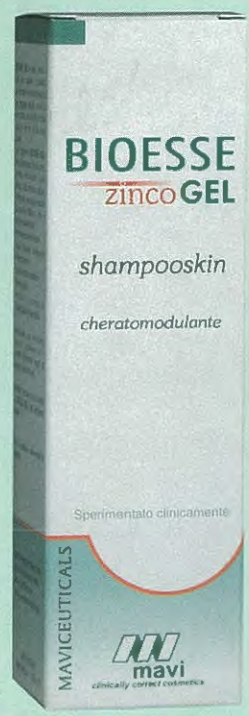
zinco GEL
shampooskin



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