

Journal of Applied Cosmetology

2

OFFICIAL JOURNAL OF

International Society of Cosmetic Dermatology


INTERNATIONAL
EDIEMME



Volume 18 - Number 2
April/June 2000

ISSN 0392-8543 Spediz. Abb. Postale 70% Filiale di Roma

ACROMOS PLUS

with vitamin C

The **scientific approach** to **[AGE-SPOTS]** (1-4)

UNA SOLUZIONE [chiara] per le iperpigmentazioni (1-4)

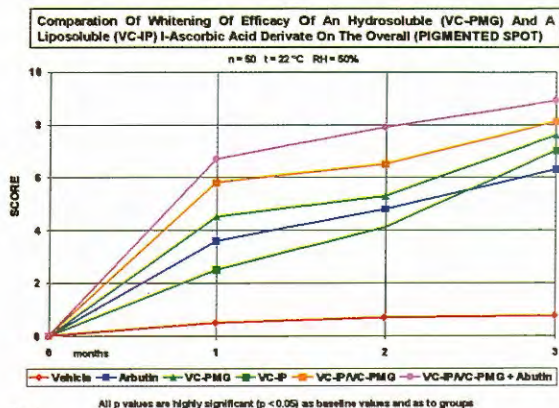


Fig. 1

MODO D'USO

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aree da trattare 1 o più
volte al di proteggendo la
cute durante il giorno con
MAVISAN BLOCK

To be applied on AGE-SPOTS
1 / 2 times a day, protecting
the skin by MAVISAN
BLOCK in the morning

HOW TO USE

REFERENCES - BIBLIOGRAFIA

- 1) MATOBA O., HASC, MOTOS, KOHATA Y., et al (1999), A new lipophilic L-ascorbic acid derivative, the synthesis, physical property and dermatological efficacy. Proceedings of 4th scientific Conference of the Asian Societies of Cosmetic Scientists, Bali, Indonesia, 7-8 April, 1999.
- 2) KEMEYAMA K., SAKAKI, KONDOH S., et al (1996), Inhibitory effect of magnesium L-ascorbyl-2 phosphate (VC-PMG) on melanogenesis in vitro and in vivo, J. Am. Acad. Dermatol., 34, 29-33.
- 3) P. MORGANTI, FABRIZI G., MORGANTI G. (1999), an innovative cosmeceutical with a skin whitening activity, Presented at the 4th International symposium on Cosmetic Efficacy, New York, May 10-12. In print on J. Appl. Cosmetol.
- 4) MORGANTI P., FABRIZI G., MORGANTI G., (1999) A new cosmeceutical with a skin lightening activity: Second note, The combining whitening activity of hydrosoluble and liposoluble vitamin C derivatives. Presented at the E.A.D.V.-Congress, September 29-October 3, 1999 (Fig.1)

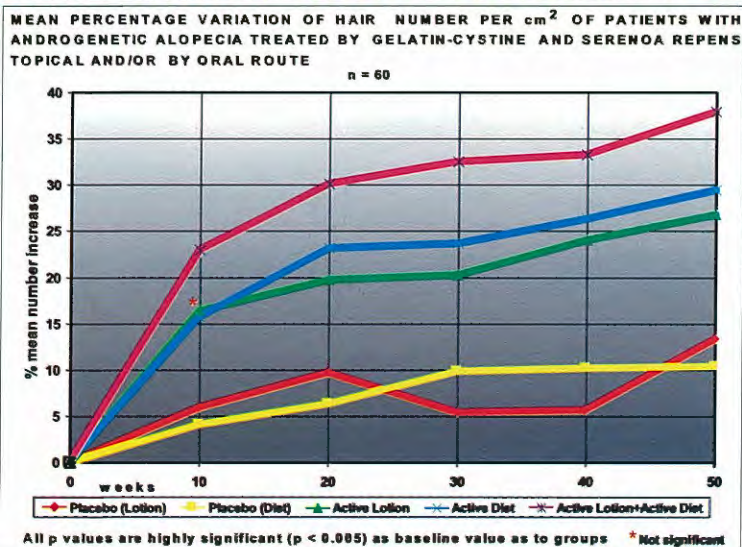
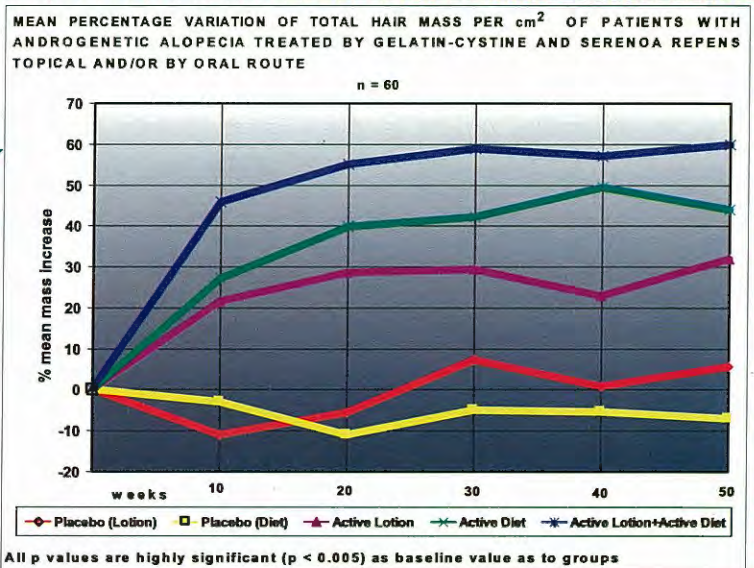


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hair mass



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increase in
hair number

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⁽¹⁾ Morganti P., Fabrizi G., James B., Bruno C. J. *Appl. Cosmetol.* 16,57,1998

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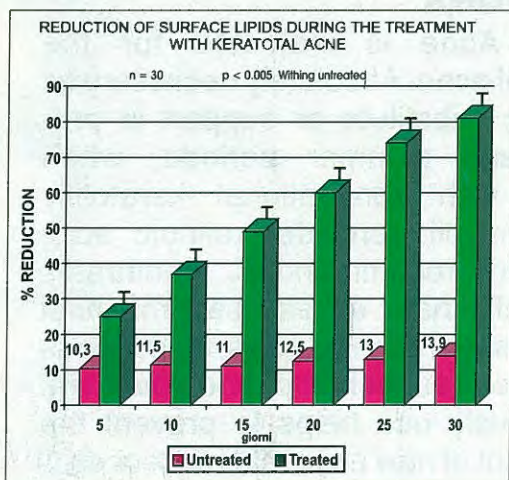
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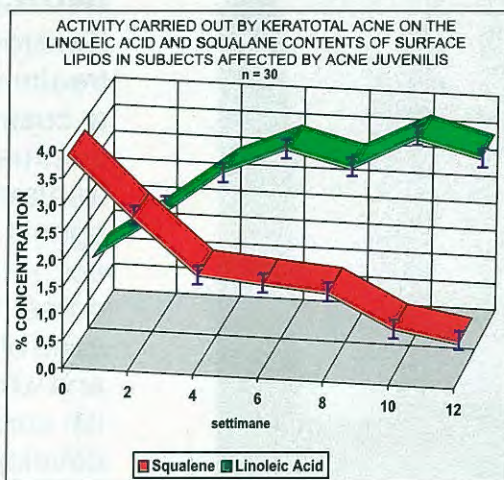
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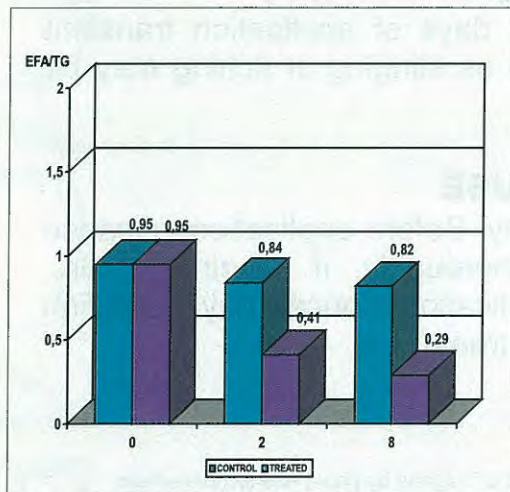
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⇒ Significantly reduces EFA/TG ratio



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In the first days of application transient effect such as stinging or itching may be observed

HOW TO USE

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

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REFERENCES:

1,2 - Data on file Mavi Sud

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

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ENVIRONMENT FRIENDLY GREEN CHEMICALS

P. Morganti¹, G. Fabrizi², F. Guarneri³ and C. Bruno⁴

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Received: June, 1999, Presented at the Personal Care Ingredients Asia Conference, Thailand, 8-10 March 2000.

Key words: gelatin, glycine, PCA, chitosan, polysaccharides, biomaterials, glycolic acid, skin roughness, skin dryness, skin hydration.

Summary

Polysaccharides are the main source of green biomolecules used as biomaterials in pharmacology and cosmetic dermatology.

The industrial interest about these molecules is continuously increasing and that's due to the different characteristics they proved to have: absence or near-absence of antigenicity, inability to cause an inflammatory reaction and high ability to enhance stromal-cell colonization and glycoprotein synthesis when employed in skin tissue repair and high environment compatibility.

The aim of this study was to evaluate the property of innovative and patented glyco-chitosan and PCA chitosan gels to increase skin hydration and elasticity, and to evaluate its protective and anti-irritation potential efficacy.

The two-month trial was a randomized double-blind-placebo-controlled study carried out on 60 dry skinned female volunteers, aged 32-43 with a moderate xerosis of grade 5 according to Dahl. Surface lipids, skin hydration and TEWL were detected by the 3C System® (Dermotech, Italy). Skin elasticity and softness were evaluated by the Dermaflex® A (Cortex Technology, Denmark). Irritation potential was detected by SDS Challenge test and Pyrexal Erythema test evaluating the intensity of skin redness by Chromameter® C 200.

The treatment by this green gels induced a significant and progressive improvement in skin hydration (from +30% to +80%, $p < 0.005$), skin surface lipids (from +10% to +60%, $p < 0.005$) and skin elasticity (+14%, $p < 0.005$) and a contemporary decrease of TEWL (from -50% to -70%, $p < 0.005$) and free radicals (-25%, $p < 0.005$) compared to the baseline values.

The most and unexpected property was the high anti-inflammatory activity recorded.

The improvement, that starts to be evident from the first week of treatment, shows how these gels could be considered as useful means to improve skin hydration and elasticity of subjects affected by skin xerosis due to environmental or pathological reasons.

No side effects were observed during the study period.

Riassunto

I polisaccaridi rappresentano la maggiore sorgente di molecole "verdi" utili come biomateriali di

uso farmacologico e cosmetico.

L'interesse industriale nei confronti di queste molecole è in continuo aumento date le loro particolari caratteristiche: assenza quasi totale nel provocare effetti antigenici, o processi infiammatori, capacità elevata di incrementare la colonizzazione delle cellule stromali e la sintesi delle glicoproteine, se utilizzate per la riparazione tissutale, ed alta compatibilità con l'ambiente .

Scopo di questo studio è di valutare le proprietà innovative quali idratanti ed elasticizzanti cutanei ad attività antinfiammatoria di diversi gel chitosanici trattati con miscele di gelatina-glicina o PCA gelatina.

E' stato condotto uno studio a doppio ceco su 60 pazienti volontari di sesso femminile di età tra i 32 ed i 43 anni con cute particolarmente secca e disidratata di grado 5 secondo la classificazione Dahl. I lipidi di superficie, l'idratazione cutanea e la TEWL sono state controllate utilizzando il 3C System® (Dermotech, Italia)

L'elasticità cutanea è stata controllata mediante l'utilizzazione del Dermaflex® A, mentre effetto antiirritante è stato determinato con la metodica dell'SDS e del Pirexal e controllato anche con l'utilizzazione del Chromameter® C200.

Il trattamento con questi gel "verdi" ha indotto un incremento statisticamente significativo dell'idratazione cutanea (dal + 30 all' + 80%, $p < 0,005$) dei lipidi di superficie (dal + 10 al + 60%, $p < 0,005$), della elasticità cutanea (+ 14% $p < 0,005$) ed una contemporanea diminuzione della TEWL (dal - 50 al - 70%, $p < 0,005$) e dei radicali liberi (-25%, $p < 0,005$) rispetto ai valori iniziali. Il risultato più sorprendente ed inaspettato è stata l'attività antiinfiammatoria riscontrata dei prodotti controllati. I miglioramenti, evidenti fin dalla prima settimana di trattamento dimostrano come questi gel possano essere utilizzati per migliorare l'idratazione e l'elasticità della cute di persone affette da xerosi cutanea provocata anche da cause patologiche in atto.

Non sono stati osservati effetti secondari di alcun genere dopo il periodo di trattamento.

INTRODUCTION

Polysaccharides are the main source of green bio-molecules for use as biomaterials in pharmacology and cosmetic dermatology. (1-11)

The industrial interest about these molecules is continuously increasing because of the interesting characteristics they proved to have: absence or near-absence of antigenicity, inability to cause an inflammatory reaction and high ability to enhance stromal-cell colonization and glycoprotein synthesis, when employed in skin tissue repair and high environment compatibility.

These characteristics have been highlighted particularly in the naturally occurring chitosan and chitosan derivatives (4-11). These green compounds because of their biocompatibility with the human body have been employed extensively in the development of anionic/cationic polysaccharide matrices for microparticulate drug delivery (12-15).

They seem also to be immuno-potentiating, considering their similarities with hyaluronic acid through the common N-acetylglucosamine sugar, and showed to be mucoadhesive.

As matter of fact, chitosans provide an attractive muco-adhesiveness because of their polycationic complementarity to the polyanionic mucins, which constitute the key macromolecular component of mucus (16,17).

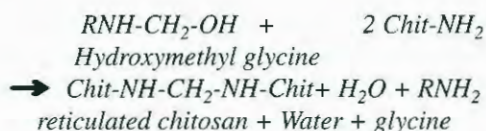
Moreover their topical application seems also to minimize scarring and improve skin healing process (18-22).

AIM

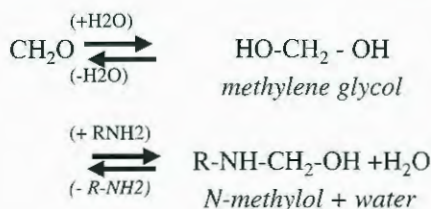
The aim of this study was to evaluate the property of an innovative glyco-chitosan and/or PCA-chitosan gel to increase hydration, elasticity and antioxidant potential of the skin, to restore the skin lipid content and eventually to decrease inflammation and skin irritation potential alleviating symptoms of dry skin during a 8 weeks treatment course.

The formulation of this gel is based on the exclusive usage of a new chitosan derivative solubilized with glycolic acid and/or with PCA (pyrrolidon carboxylic acid), and subsequently treated with a patented mixture of gelatin-glycine additivated with sodium methyl hydroxylglycinate (30).

The exclusive use of raw materials of natural origin, allows to define "green" the gel obtained, also because completely and of proved eco-compatibility. In fact the presence of this preservative compound, as methylene glycol, in this chitosan-based formulation does not provoke liberation of free formaldehyde at skin level because of the strong presence of groups NH_2 of chitosan. Therefore from two moles of chitosan and one of hydroxymethyl glycinate and one of water we obtain:



Where the reaction goes only versus the formation of reticulated chitosan. Differently it happens in most of methylols where it seems to establish an equilibrium between the methylol and methylene glycol in solution:



MATERIALS AND METHODS

MATERIALS

For this study was used a glycochitosan gel as base (glycolic acid and chitosan), and/or a PCA chitosan (pyrrolidone carboxylic acid and chitosan) preserved by a derivative of glycine, fundamental aminoacid in cutaneous biology. These three products, being of natural origin, could be surely classified as "green compounds" (21-23)

METHOD

SUBJECTS IN THE STUDY

The two-month trial was a randomized double-blind-placebo-controlled study carried out for 8 weeks on 60 dry skinned female volunteers, aged 32-43 with a moderate xerosis of grade 5 according to Dahl (24). Surface lipids, skin hydration and TEWL (25,26) were detected by the 3C System® (Dermotech, Italy). Skin elasticity and softness were evaluated by the Dermaflex® A (Cortex Technology, Denmark). (27) Antioxidant potential was evaluated by measurement of skin hydroperoxides (28) meanwhile irritation potential and the anti-inflammatory activity were investigated both by the SDS challenge tests and the Pyrexal Erythema test (29), using also the Chromameter® C 200.

EXPERIMENTAL DESIGN

PRE - TEST

Before starting the experiment, the erythema test was done in a dermatological office in order to check if the gel would perform also an eventual anti-inflammatory activity. This experimentation was tested on the volunteers' back of 20 people only, a week before starting the study, according to the methods reported.

No volunteers used other topical treatments within the two weeks or systemic drug or diet supplements within the 4 weeks before starting the study. All the subjects gave their written informed consent in accordance with the ethics of cosmetics experimentation.

The quantity of sodium-hydroxymethyl glycinate was always constant for each sample and was previously mixed with the chitosan solution.

Neither the operator nor the subjects were able to identify the assigned product.

The gel was applied twice daily all over the face and on both the forearms. The treated areas were always cleaned with the supplied cleansing emulsion (Mavigen® latte). Fifteen days before starting the study all other cosmetics were discontinued.

Measurements were performed at the 1st day

TEST

The subjects were randomly divided into six groups of 10 people each and received respectively:

I	GEL	A	glyco-chitosan neutralized with gelatin-glycine at pH 4.8
II	GEL	B	glyco-chitosan neutralized with glycine/sodium glycinate at pH 4.8
III	GEL	C	glyco-chitosan neutralized with gelatin at pH 4.8
IV	GEL	D	PCA-chitosan neutralized with gelatin-glycine at pH 4.8
V	GEL	E	PCA-chitosan neutralized with glycine/sodium-glycinate at pH 4.8
VI	GEL	F	PCA-chitosan neutralized with gelatin at pH 4.8

(baseline) and at days 10th, 20,30,40,50,60th (end of treatment), and day 90th always in the morning between 8 and 11 a.m.

3C SYSTEM METHODOLOGY

Quantitative measurements of skin hydration, surface lipids and TEWL were performed according to Cardillo and Morganti method (25) before the 1st day (baseline) and after days 10,20,30,40,50,60 (end of treatment) and 90 days of treatment, always in the morning from 8 and 11 a.m. on skin cleaned the night before.

This computerized methodology collects up to 10/15 measurements over 25 second sampling period and records the mean values, automatically standardizing the environmental conditions (RH = 50% $t = 22^{\circ}\text{C}$).

To alleviate the possibility of the patient physiologic state, the other major factor-influencing rate of water loss, it was asked to rest in the testing room for 30 minutes before measurements.

Possible site-to-site variation was eliminated by random selection of treated sites.

Skin hydration was assessed by measuring total capacitance of the horny layer and the values are expressed in 3C arbitrary units; *skin lipids*, observed by a special frosted plastic foil (1 cm²), are measured photometrically and expressed as $\mu\text{g}/\text{cm}^2$; TEWL was measured by a special 3C probe. It consists of a cylindrical open chamber measuring system, diameter 14 mm., height 10 mm. and two sensor units, containing a thin capacitance film transducer placed at 3 and 7 mm. distance from the skin.

TEWL is calculated digitally as $\text{g}/\text{m}^2 \text{ h}$.

The instrument probe was always held perpendicular to the skin surface and allowed to equilibrate for 20 sec.

All the obtained results are expressed as mean values of the measurements performed on four different right or left skin sites (cheek, forehead, chin and nose).

The obtained results are reported on fig. 1,2 and 3.

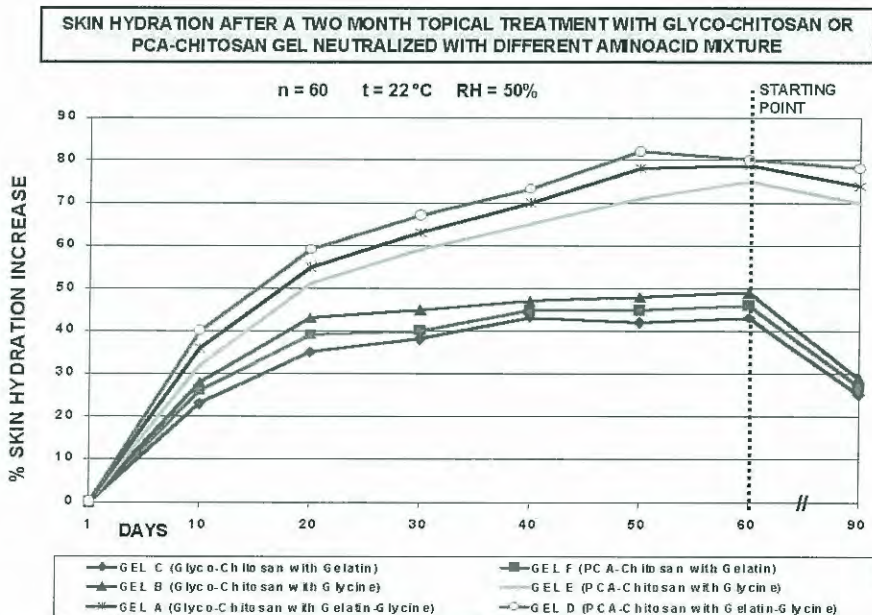


FIG. 1

All p values are highly significant ($p < 0.005$) as baseline values and as to groups

238

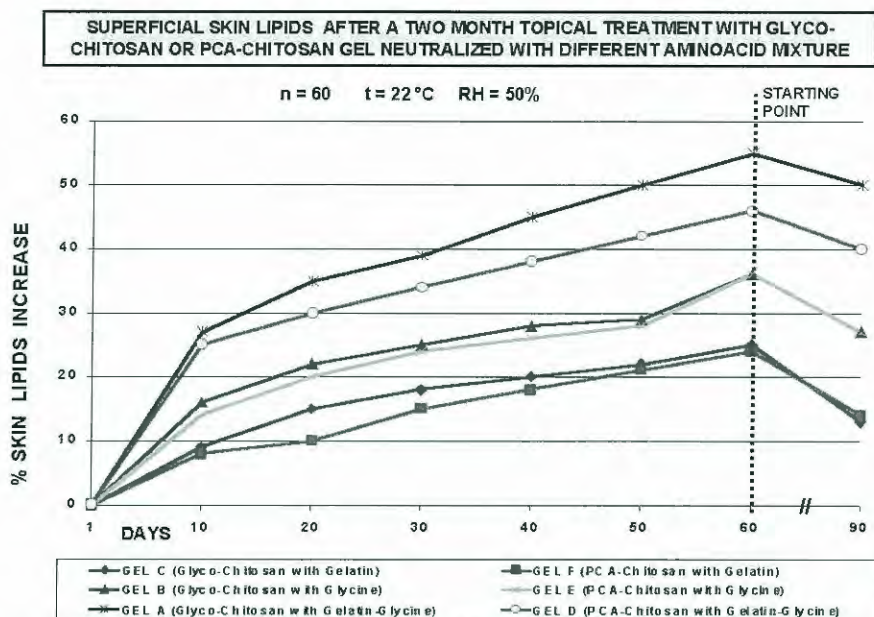


FIG. 2 All p values are highly significant ($p < 0.005$) as baseline values and as to groups

TEWL after repeated SDS application on the forearm skin pre-treated with Glyco-Chitosan or PCA-Chitosan neutralized with a different aminoacid mixture.
Comparison between sites untreated

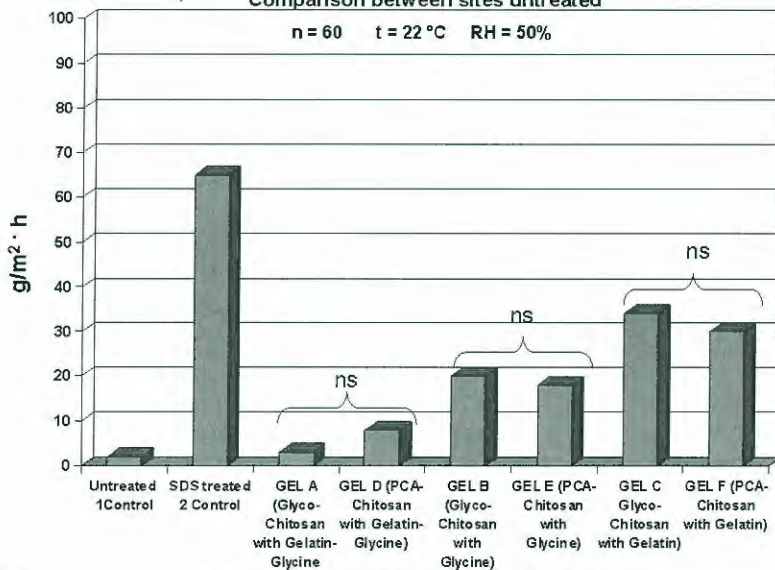


FIG. 3 All p values are highly significant ($p < 0.005$) as baseline

SDS CHALLENGE TEST

This test is generally assessed to evaluate protective and anti-irritation potential efficacy of the studied products. Thereafter, one occlusive patch with 20% sodium dodecyl sulfate (SDS) solution were applied in a randomized way to left or right forearm of each subject for 3 days and different hours before and after 8 weeks of twice daily treatment with the different kind of gels used.

Two SDS treated and untreated sites were left as control.

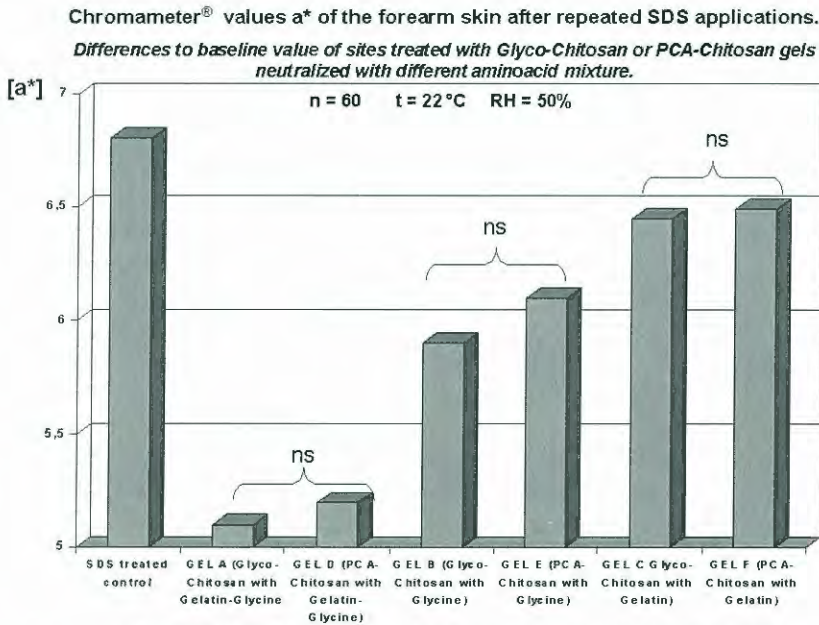
There was no further application of the studied gels after removal of the last patch. Patches were applied to the pre-marked forearm areas, re-

moved after 4 hours and reapplied to the same sites for two consecutive days for 4 hours each. After 1 hour and 24 hours of removal of the last set of patches, the skin reaction was graded and evaluated by TEWL and Chromameter® measurements.

The intensity of the irritation was assessed by visual scoring chromametry and TEWL measurements 5 hours and 24 hours after application of the patches.

(0 = no-erythema; 0.5 = equivocal reaction; 1 = slight erythema; 2 = moderate, uniform erythema; 3 = intense; 4 = fiery redness with edema.)

The obtained results are reported on fig. 3 and 4.



A and D are highly significant vs B and E or C and F ($p < 0.005$) and as control

FIG. 4

SKIN ELASTICITY

Skin elevation (elasticity) was evaluated electronically (according to G.Gniadeck and Serup 27) by measuring electric capacitance between skin surface and the electrode placed on the top of the suction chamber on the left or right forearms of the treated volunteers (suction 300 mbar, suction period 20 s, number of cycles 5). Measurements were performed on 1st day (baseline) and at 10th, 20, 30, 40, 50, 60th days (end of treatment) and at 90th days always in the morning between 8 and 11 a.m.

The obtained results are reported on Fig.5

SKIN HYDROPEROXIDES

Free radicals were evaluated according to Pu-gliese (28).

A glass cylinder measuring 5ml. in diameter was placed on the skin and held snugly, extracting the lipids by two different aliquots of 5ml. portion of acetone. The lipid residue, dried under nitrogen stream, was emulsified with sodium dodecyl sulfate, acetic acid and thiobarbituric acid. The supernatant extracted, read at 531 nm by a spectrophotometer, gave the concentration of lipid peroxides as MBA precursors.

Measurements were performed on 1st day (baseline) and at 20, 40, 60th day (end of treatment) and at 90th day always in the morning between 8 and 11 a.m.

The obtained results are reported on Fig.6

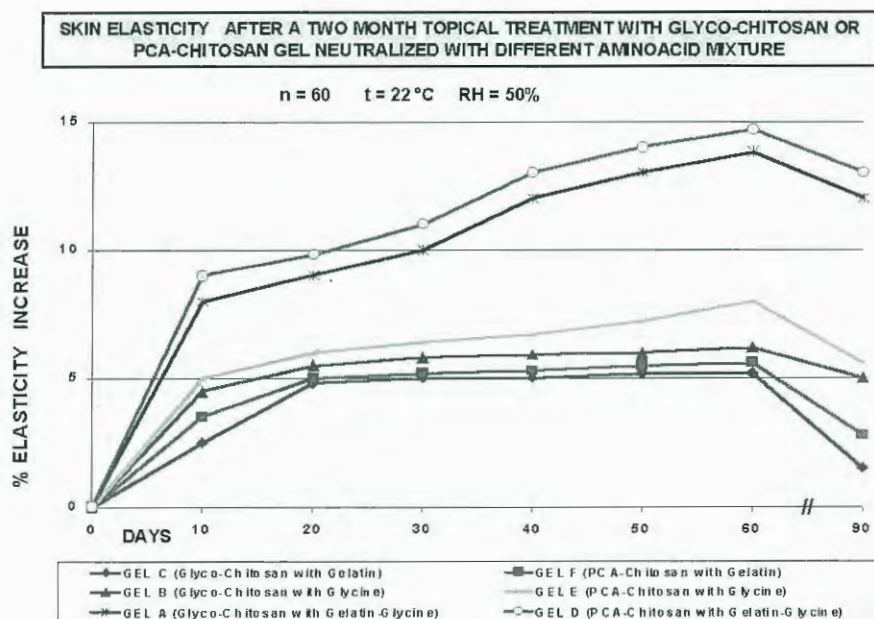


FIG. 5

All p values are highly significant ($p < 0.005$) as baseline values and as to groups

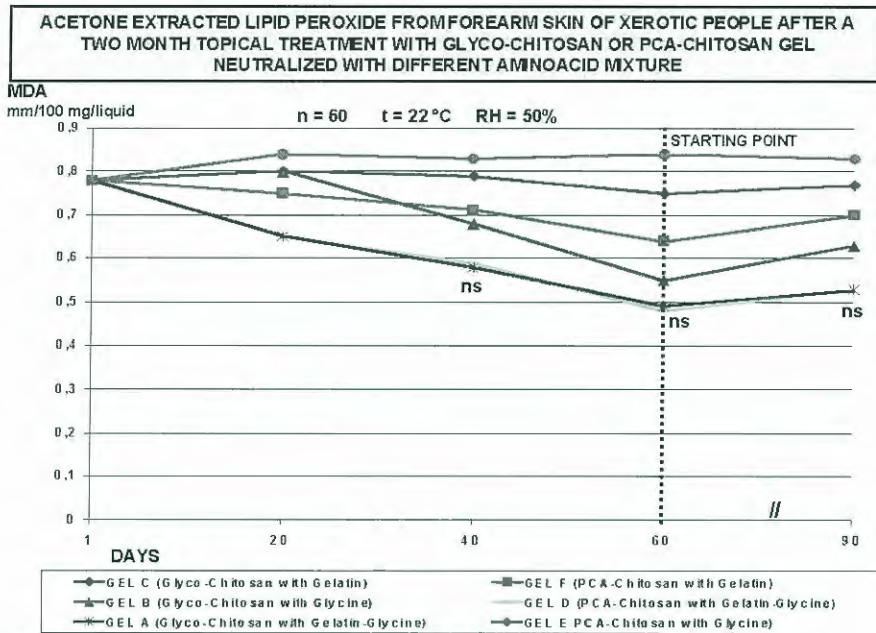


FIG. 6 All p values are highly significant ($p < 0.005$) as baseline values and as to groups

ERYTHEMA TEST

This inflammation is obtained injecting intracutaneously 0.1 ml. Pyrexal (lipo-polysaccharide from salmonella abortus equii) into dorsal skin of the volunteer subjects, according to Heilmeyer and Hiemejer (29)

These bacterial pyrogens induce an inflammation. The morphologic signs take the form of a sharply defined erythema whose surface area is measured over time. Simultaneous application of an anti-inflammatory cream inhibits its spread. By this injection 8 vials were induced in each subject. These were then topically treated in randomized succession with 0.2 ml. of the 6 different preparations and covered with transparent film.

One of these areas remained untreated to serve as a control and another was treated by 0.2 ml.

of betamethasone valerate 0.1% and covered also with transparent film.

In this way the erythema is visible at all times and can be measured through the film. The extent of the erythema was determined 6,8,10 and 12 hours after application, the maximum (a) and minimum (b) diameter being measured and the surface area calculated by the elliptic formula:

$$F = \frac{a \times b \times \pi}{4}$$

The efficacy was classified by determining the sum of the erythema surface areas from the 4th to the 12th hour. A small area means that the preparation is highly effective. The comparative evaluation was performed with the aid of bifactorial analysis of variance

The obtained results are reported on Fig. 7

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PHOTOAGING AND FREE RADICALS: CORRELATIONS BETWEEN SKIN BIOMECHANICAL PROPERTIES AND PLASMATIC LEVELS OF SKIN OXIDATIVE SPECIES AND ANTIOXIDANT COMPOUNDS

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Received: November 99

Key words: skin elasticity, skin aging, antioxidant, vitamin E.

Summary

Literature data suggest that human skin elasticity decreases with age on both face and forearm. Because it is well known that free radicals are involved in cutaneous aging and skin cancers, we investigate: correlation between bio-mechanical properties of human skin and blood levels of an oxidant product malondialdehyde (MDA) and antioxidants: vitamin E, superoxide dismutase (SOD) and glutathione peroxidase (GPx-SE); blood levels of SOD, vitamin E, GPx-SE, and MDA during aging.

Sixty-seven healthy subjects (44 women aged from 21 to 86 years and 23 men from 21 to 74 years) entered the study after giving written, informed consent. All the volunteers had no vitamins or antioxidants supplementation in the diet before six months. The measurements of the bio-mechanical properties were performed with a Cutometer Sem 474 on three different anatomic locations: forehead, cheek and volar forearms, then 7cc of blood were drawn for High-Performance Liquid Chromatography measurement of vitamin E (mg/ml), Standard Spectrophotometric Methods evaluation of SOD (U/ml) and MDA (nmol/ml) and ELISA investigation of GPx-SE (mg/ml).

RESULTS. We found no correlation between bio-mechanical properties of the skin and aging, sex, skin photo-types and plasma levels of MDA and antioxidants. About biochemical data, we found that vitamin E and SOD levels increase progressively during aging in women population while in men population the increase is not statistically significant. GpxSE levels also increase during aging but only in men population. MDA levels showed no correlation with any of the previous parameters.

Riassunto

Secondo i dati della letteratura sembrerebbe che l'elasticità della cute si riduca con l'età sia sul viso che sulle braccia. Dato che, come è noto, esiste un coinvolgimento dei radicali liberi sia nei processi di invecchiamento che nella formazione dei tumori, sono state controllate le correlazioni esistenti tra

le proprietà meccaniche della cute umana ed il livello di ossidazione dei lipidi circolanti, legata alla minore o maggiore presenza di antiossidanti quali la vitamina E, la superossidismutasi (SOD) e la glutatione perossidasi (GPx-SE).

67 soggetti sani (44 donne di età compresa tra 21 e 86 anni, e 23 uomini tra 21 e 74 anni) sono stati inseriti nello studio dopo aver dato il loro consenso scritto. Tutti hanno interrotto l'eventuale uso di vitamine e/o antiossidanti sei mesi prima dell'inizio dello studio. Le proprietà bio-meccaniche della cute sono state controllate mediante l'uso del Cutometer Sem 474 su tre diverse aree cutanee: fronte, guance e avambraccio. La concentrazione di vitamina E, di SOD e di MDA è stata controllata sul siero di 7 cc di sangue mediante l'utilizzazione dell'HLPC.

Non è stata riscontrata alcuna correlazione tra le proprietà biomeccaniche della cute, l'invecchiamento, il sesso, il fototipo cutaneo ed i livelli di MDA e di antiossidanti nel sangue. La vitamina E ed i livelli di SOD aumentano progressivamente con l'età nella donna mentre nell'uomo tale incremento non è statisticamente significativo. Anche i livelli di GpxSE aumentano con l'aumentare dell'età non soltanto nell'uomo. I livelli di MDA non sembrano correlati a nessuno dei parametri controllati.

INTRODUCTION

Skin aging is represented by the amount of the progressive clinical, functional and structural modifications of the main cutaneous strata which depends on aging itself and on many environmental external factors (environmental pollution, ionizing radiations, cigarettes' smoke, carcinogens, drugs, sunlight) [PHOTOAGING] (1); in both cases is to be considered the alterations of two particular genes (*c-fos* proto-oncogene, *SPR2*, *IL-1ra*, *c-myc*, *GADD*, *IL-1 beta*) involved in the regulation of the cellular immuno-modulation, growing, differentiation and UV reaction (2).

From these short premises, that partly explain the predisposition to photo-induced carcinogenesis, especially for the aged skins, comes the growing interest for the molecular events aging responsible, for its prevention and for an appropriate photo-protection.

The theory of Harman (3), considering the modern knowledge and the most accurate methodologies in determining free radicals and the relevant antioxidant enzymes, nowadays assumes an ongoing interest and actuality: aging seems to be the result of the progressive accumulation of free radicals and/or cutaneous lesions they caused.

As it is known, free radical is any molecule or atom able to live by itself and containing one or more unpaired electrons in the outer orbital (anion superoxide O_2^- , peroxide of hydrogen H_2O_2 , radical hydroxyl OH^- , singlet oxygen O_2 , nitric oxide NO). It should be remembered that they are produced separately by multiple exogen stimulation even in presence of: a) physiological reactions catalyzed by cytochrome P-450, cyclo-oxygenase, xantinaoxidase; b) oxidation of endogenous substances; c) mitochondrial chain of electron (mitochondrial leaking). Free radicals activity is characterized by: inactivation of enzymatic activities containing groups SH, interaction with DNA and consequent mutations and aberrations, destruction of cellular membranes by a direct damage and per-oxidation of un-

saturated lipids. The organism defends itself against these attacks by efficacious mechanisms of protection both enzymatic and not enzymatic (free radicals scavengers): the first ones act at cytoplasmatic level (SOD, catalase, glutathione peroxidase) the second ones act at cellular membranes level (tocopherol, carotenoids, ubiquinol, ascorbic acid, pantothenate calcium, nicotinic acid, pyridoxine, biotin, glutathione).

Furthermore, from the literature results examined, during skin aging free radicals not always show a real and constant increase (5-6), even if augmented in many physio-pathological conditions (inflammation, cancers, autoimmune diseases, photosensitivity and photo-toxicity, immunoallergic reaction) (4). By the way these data do not exclude their importance since a reduction with age of the antioxidative capabilities together with a contemporaneous increase of phenomena of lipidic peroxidation, could make pathological the physiologic concentration of free radicals produced (7).

Moreover, we have poor news about the correlation existing between cutaneous damage induced by free radicals, istopathological alterations and consequent modifications of the skin biomechanical properties.

At this regard, we carried out a study aimed to correlate the skin biomechanical properties to age, sex and plasmatic levels of SOD, vit. E, Se-GPx and products of lipoperoxidation, and to verify eventual tissue variations of oxidant and antioxidant substances in the global idea of aging.

MATERIALS AND METHODS

We enrolled 67 subjects, 44 men (aged between 21 and 86) and 23 women (aged between 21 and 74), healthy, with negative anamnesis for systemic and metabolic diseases and assumption of vitamins supplementation and/or antioxidants for at least six months.

Working anamnesis, food habits, life style, and photo-type were evaluated.

Skin biomechanical properties were evaluated

by CUTOMETER SEM 474 on three different areas: forehead, cheek and volar armpit area. After measuring in an environment at temperature and humidity controlled, were drawn 7 cc of blood in order to evaluate vit. E in HPLC, SOD and MDA in spectro-photometry and Se-GPx in ELISA*.

Skin Mechanical Properties

Were evaluated by Cutometer Sem 474 equipped with a 2mm-diameter probe. The measurements consisted in three cycles of 5 second's suction each at negative pressure of 400 mbar every 5 seconds pause. The values reported represent the average of the three measurements.

****Evaluation of the vitamin E ematic levels***

The analytic determination was done in HPLC. 0,2 ml of plasma treated with 200 micro-liters of tocopherol acetate (20 microg/ml in ethanol) [inner standard] and with 400 micro-liters of butanol-ethyl-acetate (1:1; V:V). After shaking for 20 seconds were added 20 mg of sodium sulfate followed by a 60 seconds shaking.

Further to a centrifugation at 15.000 xg for 5 minutes at 4°C was recuperated the organic stratum and 50 micro-liters of the same were injected in the HPLC column (ultratecfere C18, 250x4,6mm, 5 micron). The mobile phase was represented by a mixture of methanol-water (97:5; V:V) with a flux of 1ml/min at environment temperature. The detector was at wavelength of 280 nano-meters. The plasmatic concentrations of vitamin E are expressed as µg/ml

****Measurement of the MDA ematic levels***

The plasmatic levels of malondialdehyde were evaluated by spectrophotometry using a kit colorimetric Lipid peroxidation assay (n° 437634 -

Calbiochem-Novabiochem Corporation, San Diego, and USA). The plasmatic concentrations of MDA are in n/ml.

****Determination of the SOD ematic levels***

The activity of super-oxide dismutase was evaluated in spectro-photometry at 525 nm using a kit colorimetric Superoxide Dismutase Assay (n° 574600 - Calbiochem-Novabiochem Corporation, San Diego, USA). The plasmatic activity of SOD is in ml.

****Analysis of the SeGPx ematic levels***

Plasmatic levels of glutathione peroxidase selenium were evaluated by ELISA using a kit SP1-GPX EIA (Calbiochem-Novabiochem Corporation, San Diego, USA). The plasmatic concentrations of Se GPx are in µg/ml.

RESULTS AND CONCLUSION

The results obtained can be summarized as follows:

- Decrease of the elasticity (tab.I) and increased of the extensibility (tab. II) with aging;
- vit. E (tab. III) and SOD (tab. IV) showed a progressive increase and statistically significant in the female subjects only;
- Se-GPx (tab. V) increases in men only;
- MDA (tab. VI), constantly increasing in strong smokers, it did not showed significant correlation with the former parameters;
- Tissue levels of vit. E , in all the samples tested, were always less of one mcg/g (weight not sufficient of the material?); data concerning SOD and MDA presented wide variability even if at high levels of SOD corresponded high levels of MDA.

To conclude, on a general level at least, abstracting from the preliminary data in our experience, which did not allowed to highlight any

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correlation between the mechanical skin bioproperties, age, sex and plasmatic levels of oxidants and antioxidants, we would like to underline the following aspects:

- Free radicals play an important role in skin aging particularly in photo-aging, through mechanisms not yet clearly known;
- other systems, at least at cutaneous level, beside SOD, contribute in an efficacious way to defend the skin against free radicals (tioredoxine-reductase -TR-, system Glutathione reductase- Glutathione peroxidase -GR-GP) (8);
- the protective action of the diet supplementation, even if encouraging, still represents an open and controversial problem: the studies done did not demonstrated in uncontestable and definitive way a clear correlation between the assumption of antioxidant sub-

stances, aging and cancers growing:

- the great antioxidant capability of the skin, relative to a major alpha-tocopherol concentration in the skin (90%) compared to derma (9), together with the recent demonstration that keratinocytes of the more differentiate strata have antioxidant properties higher than germinal ones (10), underlining the importance of the topical application of antioxidants able to reduce in a significant way the production of free radicals induced by UV (11).

If the topical application of these substances gives certainly a further real protection against photo-damaging, we hope that, together with a possible dietary supplementation, the future studies will be devoted to this research exploiting at the best the peculiar and natural characteristics anatomic-functional of the skin.

Tab. 1

WOMEN					
ELASTICITY					
Age	N.	Cheek	Forehead	Forearm	
20-39	20	0.52 ± 0.25	0.49 ± 0.08	0.82 ± 0.18	
40-59	12	0.55 ± 0.23	0.46 ± 0.14	0.70 ± 0.17	
> 60	12	0.67 ± 0.42	0.41 ± 0.14	0.59 ± 0.14	

1a

MEN					
ELASTICITY					
Age	N.	Cheek	Forehead	Forearm	
20-39	7	0.55 ± 0.28	0.66 ± 0.16	0.73 ± 0.12	
40-59	10	0.50 ± 0.11	0.55 ± 0.19	0.70 ± 0.14	
> 60	7	0.61 ± 0.32	0.64 ± 0.20	0.62 ± 0.18	

1b

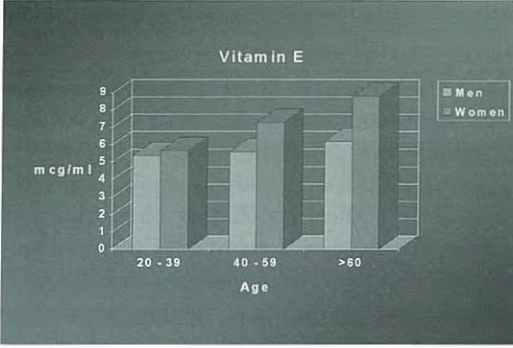
Tab. 2

WOMEN					
ESTENSIBILITY					
Age	N.	Cheek	Forehead	Forearm	
20-39	20	0.17 ± 0.06	0.29 ± 0.06	0.21 ± 0.07	
40-59	12	0.18 ± 0.09	0.26 ± 0.09	0.21 ± 0.07	
> 60	12	0.19 ± 0.07	0.24 ± 0.08	0.27 ± 0.08	

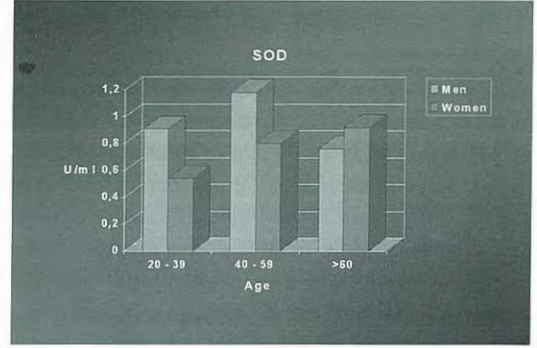
2a

MEN					
ESTENSIBILITY					
Age	N.	Cheek	Forehead	Forearm	
20-39	7	0.21 ± 0.08	0.28 ± 0.05	0.23 ± 0.05	
40-59	10	0.23 ± 0.08	0.26 ± 0.08	0.22 ± 0.09	
> 60	7	0.25 ± 0.12	0.27 ± 0.13	0.20 ± 0.08	

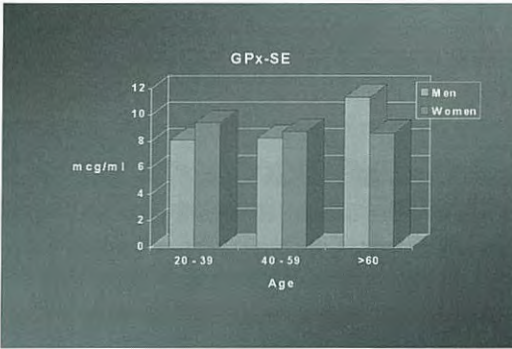
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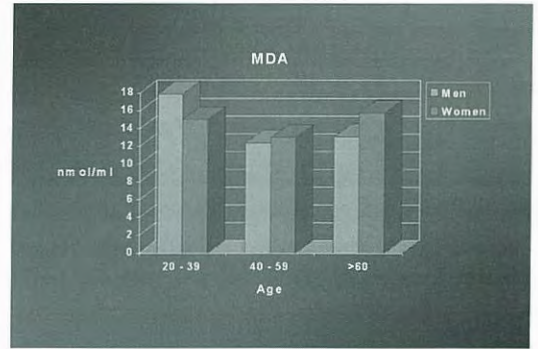
Tab. III



Tab. IV



Tab. V



Tab. VI

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LASER SKIN RESURFACING AFTER DERMABRASION OF ACNE SCARS

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Received: April, 2000

Key words: acne scars, laser skin resurfacing, CO2 laser

Summary

Acne scars show a great variety in their clinical appearance and therefore very often cannot be effectively corrected by a single treatment modality alone. Traditionally chemical peeling is continued with punch excision and also by dermabrasion. Laser skin resurfacing has been added to the numerous treatment options for acne scars. Whereas laser resurfacing showed good results in mild acne scarring, severe atrophic acne scars achieved only moderate results. Therefore, in the modern post-acne treatment the whole spectrum of adapted methods should be available. We would like to present as an example one patient with severe deep scarring who has been firstly flattened by dermabrasion following a more exact modelling of the scar borders by laser skin resurfacing resulting in a much better result than dermabrasion alone.

Riassunto

Le cicatrici da acne si manifestano clinicamente con modalità diverse ed è perciò difficile correggerle utilizzando un'unica metodologia. Tradizionalmente si utilizzano peeling e dermoabrasione; ora a questi trattamenti si è aggiunto l'uso del laser.

La metodologia del laser applicato alla cute dà sicuramente buoni risultati in tutte le forme di acne leggera, mentre limitati sono i risultati che si ottengono in caso di cicatrice profonda da acne. Per questi motivi nei trattamenti post-acne è necessario utilizzare insieme metodologie differenti.

Con questo lavoro desideriamo presentare come esempio il trattamento effettuato su di un paziente affetto da cicatrici profonde che è stato trattato prima con dermoabrasione seguita successivamente dal trattamento dei bordi cicatriziali mediante l'utilizzo del laser. Sono stati ottenuti così risultati interessanti, sicuramente superiori al solo uso della dermoabrasione.

INTRODUCTION

Traditionally acne scars are treated by punch excision and grafting or direct closure, often followed by dermabrasion with a diamant mill. For milder acne scars also diverse chemical peeling methods with various substances are performed.

In the last ten years laser skin resurfacing became a favoured method in the therapy of photoaged skin. Meanwhile it is used for the treatment of scars, especially acne scars. In contrast to elderly CO₂ lasers nowadays pulsed and ultrapulsed CO₂ lasers but also CO₂ lasers with scanning devices enable a more exact superficial dermabrasion with reduced or without thermal damage of the skin(1,2). The long lasting good results are due to the shrinking of collagen fibres besides the reepithelization.

In contrast, ER:YAG lasers are characterized by a high absorption in water and so their application resulted solely in reepithelization but not in damage, and change in the collagen structure.

Therefore, therapy studies of deeper wrinkles and scars CO₂ lasers showed better results than ER:YAG lasers (3).

Whereas laser skin resurfacing improves mild acne scars excellently, in severe acne scars this procedure achieved only moderate results (4). Also, combinations of laser skin resurfacing and punch excision have then been used (5), and recently a three-staged operation was proposed: first focal chemical peeling followed by CO₂ laser skin resurfacing, scar excision and punch grafts, and finally dermabrasion to treat the remaining scars (6).

MATERIAL AND METHODS

In the past we treated a 35 years old female with deep scars resulting from acne vulgaris and an overlying acne excoriée des jeunes filles. In an interval of several years we have done punch-grafting and dermabrasio for three times. Although the results were good some discrete

remaining scars provoked artefacts by the patient herself with deeper scarring.

Because of the strong psychological complaints we finally initiated a laser skin resurfacing using a CO₂ laser with scanner (Silk touch, Fa. Limmer). In endotracheal anesthesia 1-3 skin layers have been removed depending on the depth of the scars (power: 5 watt, pulse extent: 0,2 sec., pulse frequency: 0,1 sec.). To protect the patient from herpes virus reactivation we gave orally valaciclovir 3x 1000 mg/day one day before operation until six days after laser therapy. The local treatment was for two days a corticosteroid ointment followed by an unspecific wound dressing for 14 days.

RESULTS

The patient was very satisfied by the impressive scar flattening. The postoperative erythema diminished in about four weeks without hyperpigmentation.

CONCLUSIONS

Because of the clearly better result of laser skin resurfacing after dermabrasion in comparison to dermabrasion alone, we propose a two-staged procedure for the treatment of deep acne scars.

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NATURAL RAW MATERIALS OF INDIAN ORIGIN FOR PERSONAL SOPHISTICATION

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Received: November, 1999, Presented at the Cosmoprof Asia, Hong Kong, 12 November, 1999.

Key words: natural cosmetics, herbal cosmetics, medicinal plants, Indian plants, cosmeceuticals.

Summary

Recent years have witnessed phenomenal increase in utilization of plant products for development of new natural cosmetics. This is partly due to plausible deleterious effects of synthetic chemicals and partly due to increasing consumer consciousness about benefits of traditionally used herbs or natural products. Stress and strain of modern living and paucity of time to use natural products in a traditional manner induce the alert customer to look for alternative products that interweave herbal and cosmetic effects for a greater personal sophistication. Though some of the available products pass scientific scrutiny, others need to be researched and evaluated.

A large number of medicinal plants are said to possess cosmeceutical value and some of them pass antiaging effects. Scientific basic of some cosmeceutically useful Indian plants with special reference to their antiaging attributes and a few practical formulations involving natural products for cosmetic use have been discussed.

Riassunto

In questi ultimi anni è stato notevolmente incrementato l'uso di prodotti ed estratti di origine vegetale per la produzione di cosmetici naturali. Ciò è dovuto sia ad un "rigetto" delle persone verso tutti i prodotti chimici in genere, che ad una nuova presa di coscienza dei benefici che si possono ottenere con l'uso di prodotti naturali di origine vegetale.

Lo stress provocato dalla vita moderna ed il poco tempo a disposizione inducono il consumatore attento a cercare prodotti alternativi che combinano gli effetti ottenuti con l'uso di erbe che con l'uso dei cosmetici per una maggiore resa personale.

Anche se i prodotti disponibili sono sempre sottoposti ad uno "screening" scientifico, molti di essi richiedono ancora una più attenta valutazione.

Si ritiene che un gran numero di piante medicinali abbiano un valore cosmeceutico ed alcune di esse si ritiene svolgano un effetto anti-invecchiamento. A tal riguardo viene affrontata una discussione su basi scientifiche sull'attività anti-età svolta da alcune piante indiane e sul loro uso cosmetico.

Though the original meaning of cosmetics to describe a preparation or adornment designed to increase the beauty of face is still valid, the term has often been used to describe all such preparations or formulations which intensify the existing qualities and appearances. The preparations having pharmaceutical effects are called cosmeceuticals. Such substances also include materials which pass qualities that may or may not be inherent in the subject. Today, cosmetics are no longer restricted to the body, hair care and bath products and formulations. The science and technology of cosmeceuticals cut across various serious disciplines of sciences, medical sciences and social sciences. Cosmetic science in fact also crosses the bodily adornment barrier. The term *supracosmetology* was introduced last year to embrace all subdisciplines related to cosmetics be they belong to medicine, psychology, physics, chemistry or biological sciences.¹ In view of this, the present paper has been titled Natural Raw Materials of Indian Origin for Personal Sophistication rather than as Natural Indian Raw Materials for Cosmetics.

Personal sophistication embraces personal care but it is not restricted to body shopping only. It relates to supracosmetology and includes preparations required to reverse biomarks of natural aging, i.e., how one looks, how one feels and how one performs.² Whereas cosmetic preparations and formulations have traditionally been taking care of how one looks, it has by and large been neglecting the evaluation of performance and feeling components by experts. With the advent of sophisticated analytical instruments and specialised products for special markets during the last couple of years and World economies crossing transnational barriers, supracosmetologists are bound to transgress all boundaries. New millennium cosmetic products will combine scientific evaluation of performance and feeling component as well as their quality component. The emphatic change will become clearer during 21st century when greater competition between

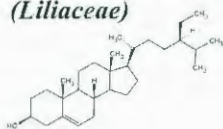
the sexes, young and the old will not only force cosmetic companies to invest in the development of products which will not only enhance the inherent attributes of target population but will also impart some of the genetically uncommon properties in a particular ethnic group. The interest of present day black to become less black and white to become tanned and urge of naturally tanned to use sunscreens to appear white, the middle aged to look young and the young to look sophisticated and wise, all reflect futuristic trends in cosmetic markets.³

Asia has been very rich in bio-resource technologies since ancient times. For example both China and India had very useful alternative medical systems which are practised even today with ease and significant success. Many of the diseases having no cure in the Western medicine have been reported to be cured by these traditional or folk remedies prepared from herbs that were known to the wise men⁴. There are documents which describe several preparations from herbs and medicinal plants that have extraordinary applications in the field of cosmetic science and technology. For example, Ayurveda describes several preparations from natural raw materials which are promotive in nature, i.e., by using which the person attains longevity, memory, intelligence, freedom from diseases, youthful age, excellence of lustre, complexion and voice, optimum strength of physique and sense organs, successful words, respectability and brilliance.⁴ Caraka Samhita describes the existence of preparations which promote strength and lineage of progeny, quick sexual stimulation and the medication which enables one to perform sexual act with women uninterruptedly and vigorously like a horse, makes one charming for the woman, provides infallible and indestructible semen even in old persons, renders one great through a number of offspring like a sacred tree branched profusely and commanding respect and popularity of society.⁵

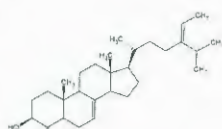
A large volume of data is available on several beneficial natural plant products that are being used in cosmetic preparations as practised today. However, many natural products/extracts are yet to be identified and studied scientifically for their cosmetic worth. Since it is not possible to describe all naturally occurring raw materials of value to supracosmetology in one paper, only those materials of Indian origin have been taken up here which have proved their usefulness to cosmetic science and technology. The raw materials described herein after have withstood the test of time and evaluation by modern research tools. It would have been better if a series of articles on natural cosmetics and cosmeceuticals could be combined in a volume but pending availability of such a situation. I have divided natural raw materials of Indian Origin under the following section for the sake of convenience. It should be kept in mind that many plant materials described and used in ancient literature have not been included here for the sake of brevity.

1. RAW MATERIALS THAT REVITALISE AND REJUVENATE SKIN
2. RAW MATERIALS THAT PROMOTE GROWTH AND BRILLIANCE OF HAIR
3. RAW MATERIALS THAT PROMOTE SEXUAL AND SENSE PERFORMANCE
4. RAW MATERIALS THAT PROMOTE LONGEVITY
5. RAW MATERIALS THAT PROMOTE INTELLECT, MEMORY AND VISION

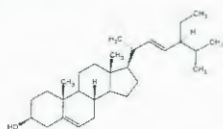
SMILAX SPECIES (Liliaceae)



β - Sitosterol



α - Sitosterol



Stigmasterol

RAW MATERIALS THAT REVITALISE AND REJUVENATE SKIN

A large number of plant materials are used for alleviating skin diseases and revitalizing and rejuvenating human skin. Some of these plants are discussed below:

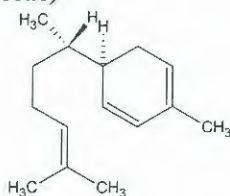
AMARANTHUS SPECIES (Amaranthaceae)

It is a common weed occurring throughout India and is used as a pot herb in the sub-mountainous districts of India. It is called *chulai* in Hindi. Two species of the genus that find use in cosmetics and skin ailments are *Amaranthus spinosus* Linn and *A. viridis* Linn. The roots of *A. spinosus* Linn are used for eczema, gonorrhoea and for relieving colic pain and in *menorrhage*.⁶ Its leaves are used in abscesses, boils and burns when employed in the form of emollient poultice. The roots and leaves when boiled in water are given as laxative to children. *A. viridis* and *A. spinosus* leaves and herbs are also used in scorpion sting and snake-bite.^{7,8} Good results have been obtained in cases of rashes and psoriasis.⁸

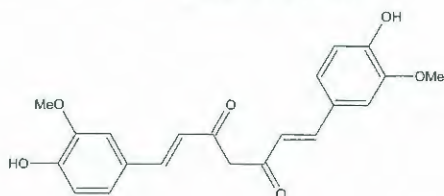
There are eight species of *Smilax* genus that occur in India. In Hindi, this plant is called *chobchini*. Two common species are *S. regelii* and *S. ornata* which contain saponins, sarsaponin and parrillin and potassium nitrate. The extract of root is diuretic due to the presence of potassium nitrate.⁷ The extract of fresh roots is used in chronic rheumatism,⁹ syphilis and other skin and venereal diseases. *Sarsaparilla* contains isomeric sapogenins called sarsapogenin and smilogenin and sitosterol and stigmasterol which are present in their free and glycosidic forms. *S. lanceifolia* and *S. ovalifolia* or *S. zeylanica* Linn. are used in rheumatism in the form of a refuse for applying to the affected parts after extraction

of the juice.

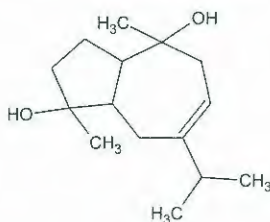
CURCUMA SPECIES (Zingiberaceae)



Zingiberine
(constituent of Ginger Oil)



Curcumin (Orange Prisms)



Curcumadiol

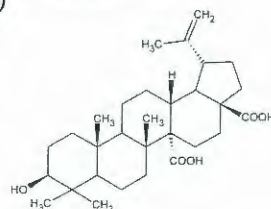
There are several species of *Curcuma* of which eight are of special significance from cosmetic point of view. The most important specie is called *Curcuma longa* or *C. domestica* Valetton. In Hindi it is called *haldi*. Its rhizomes are aromatic, stimulant, tonic and carminic. It is a potent blood purifier and an anti-perspiratory plant and is externally applied to sprains and wounds. Its fresh juice is used for many skin afflictions. It is cultivated in all States particularly Tamilnadu, Maharashtra and Bengal. About 80% of World production of *Curcuma longa* is produced in India.¹⁰ The plant has been in use since ancient times. Turmeric (as it is commonly called) has a

warm, bitter taste and it acts as a primary ingredient in curry powder and mustard. Its oleoresins are used as important flavouring agents. It is also used as a poultice, as an analgesic and for the treatment of ringworm.¹¹ Both Ayurvedic and Unani practitioners use different concoctions of turmeric (*Curcuma longa*) for treatment of leprosy and cobra bites. It is specially useful for ulcers on the surface of skin and gangrene in the flesh. When mixed with lime and made into a paste, powdered rhizomes make an important remedy for inflamed joints.¹²

It is also used by women to slow hair growth on body.^{13,14} It is used for curing cuts, burns and scalds. Powdered rhizomes are used in certain tribes for curing umbilical wounds of newly born babies and to treat skin ulcers. It heals extensive skin eruptions and inflammation associated with psoriasis.¹⁵ A paste made from sandalwood and turmeric is usually applied to the bride to be for achieving brilliance and glow on the face and body.

C. longa contains an alkaloid called curcumin and about 5.8% of essential oil. Fresh rhizomes contain about 0.24% of zingiberine. Essential Oil is antiseptic, antacid and carminic. It has been established that antioxidant properties of *C. longa* colouring matter are due to the phenolic character of curcumin.⁷ Several peptides have also been isolated from *Curcuma longa* which have been found to have immunological effects.

MELALEUCA SPECIES (Myricaceae)

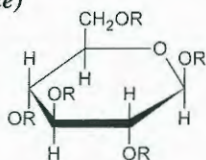


Melaleucic acid

Melaleuca leucadandron is also called *Cajuputte* in Bengali and *kayaputi* in Hindi. The oil when extracted from fresh leaves and twigs is used in-

ternally and externally for rheumatism, as a stimulant and antispasmodic in choleraic diarrhoea. It is used in psoriasis, acne and eczema and as a mosquito repellent. The active ingredient of essential oil is eucalyptol while its bark contains melaleucin. This plant can treat sores and dermatoses such as acne and psoriasis.¹⁶

HYDROCOTYL SPECIES (*Umbelliferae*)



Asiaticoside (contains tannin)

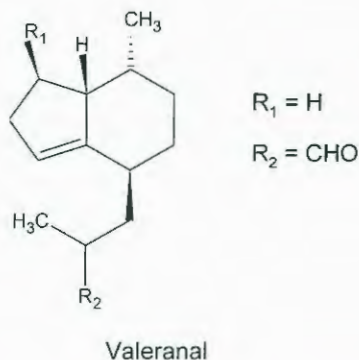
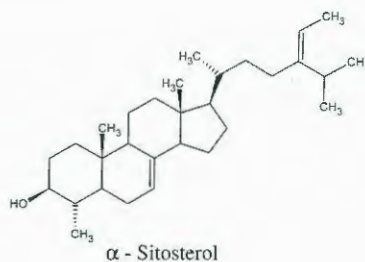
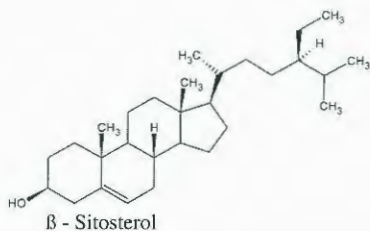
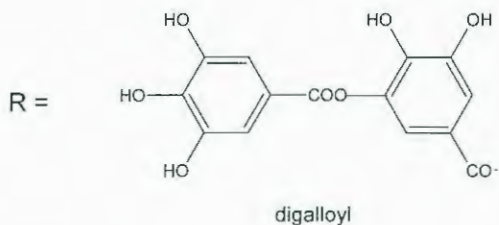
(approximate composition)

Tannic acid

Gallotanic acid

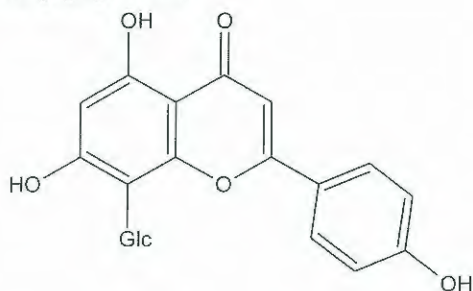
Gallotannin

Chinese tannin.



Hydrocotyl asiatica is the most important species of this genus which finds important uses. It is identical with *Centella asiatica* Linn. In Hindi it is called *Braham mundki* or simply *Brahmi*. It is used as a tonic in diseases of skin, leprosy, nerves and blood. Its leaves are used for improving memory and are useful in syphilitic skin diseases and is used both internally and externally. It contains asiaticoside to the extent of 0.07-0.12%. Its essential oil contains sitosterol, tannin and a resinous substance. Dried plant contains alkaloid hydrocotylin to the extent of 0.0016%. The active component useful in the treatment of leprosy is asiaticoside and oxyasiaticoside which are also used in the treatment of specific types of tuberculosis. The bitter principle is vallarine. Pectic acid and resin are present in leaves and roots and the plant also contains ascorbic acid. It has been found that when creams containing the oil and water extract of leaves is applied to patients of psoriasis for seven days, they show very significant improvement and skin lesions get cleared in most of the cases tried.¹⁸

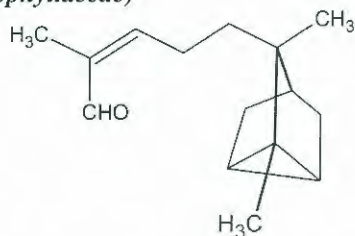
SAPONARIA SPECIES (Caryophyllaceae)



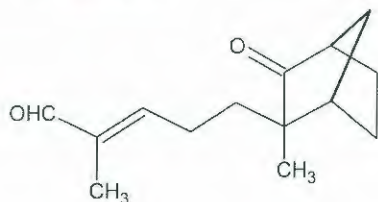
Vitexin

Saponaria officinalis also known as *soapwort* contains saponins, flavonoids ascorbic acid and a flavonoid C-glucoside, vitexin. It has been used for skin diseases like acne, psoriasis and eczema. Its root juice is a popular remedy for ivy rash.¹⁹

SAPONARIA SPECIES (Caryophyllaceae)



α - Santalol



β - Santalol

Santalum album is called *safed chandan* or simply *chandan* or *chandanam*. Its wood when ground up with water is used for headache, fevers and skin diseases to allay heat and *pruritus*.

Its oil from heartwood is used for symptomatic treatment of dysuria in *gonorrheal urethritis* and *cystitis*. Its essential oil content is 1.5-6.0% from heartwood and contains santalol. Several parts of plant are used as deodorants, disinfectants, stimulants and as tonics. *S. album* is useful in cutaneous inflammation and for allviating itching and invigourating blood circulation. It is helpful in softening of skin. It is also prophylactic against skin diseases and allergic conditions and removes skin blemishes. It is used in religious ceremonies and for making incense and cosmetics.^{20,21}

PTEROCARPUS SPECIES (Leguminosae)

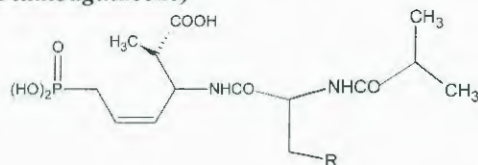
All the three species of *Pterocarpus*, i.e., *santalinus*, *marsupium* and *indicus* find use in cosmetic industry. For example, *P. marsupium* is used for external application to cure boils, sores and skin diseases.²¹ Its bark is astringent. *P. santalinus* is called *lalchandani* and is used as a tonic as well as for external applications for inflammation, headache, bilious affliction and skin diseases, boils, and to strengthen sight. It is also used for post acne and other facial scars.

OCIMUM SPECIES (Labiatae)

There are eight species of *Ocimum* that occur in India. *O. americanum* is called *kali tulsi*, *O. basilicum* is called *Babuitulsi* while *O. gratissimum* is called *Variddhatulsi* or *Ramtulsi*. It is considered as a sacred tree and is worshipped in homes and temples throughout the subcontinent. Lot of research work has been reported on this plant and its medicinal effects.²²⁻²⁸ It has antibacterial and anti-immuno-suppressant effects.^{28,29} Its infusion and decoctions are useful in gonorrheal and other skin diseases. Its essential oil contains a large number of terpenoids, acids and esters. The exact percentage and composition of

essential oil of *Ocimum* species varies with the nature of species and age of leaves and seeds.^{29,30} Pure and chemically transformed basil oil components are used in perfumery and flavours and fragrance industry.³⁰

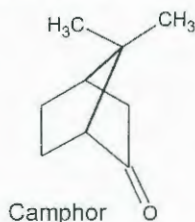
PLUMBAGO SPECIES (Plumbaginaceae)



Plumberrycin

Plumbago indica and *P. zeylenica* are two important species which find use in personal sophistication. Its roots find use in leprosy, acne vulgaris, surface sores and secondary syphilis. Its milky juice is useful in scabies, unhealthy ulcers and ophthalmic. It contains a sitosterol glucoside and a yellow naphthoquinone called plumbagin which is responsible for its antibiotic properties. The tincture of its root bark is a powerful sudorific and antiperspirant. Plumbagin is a strongly irritant and powerful germicide when applied externally. It stimulates muscular tissues in smaller doses and has a stimulating action on the nervous system with several side effects. Its very dilute solution (say 1ppm) is a lethal poison to a number of bacteria and pathogenic fungi.³¹

CINNAMOMUM SPECIES (Lauraceae)



Camphor

Chief species of this genera which is used in cosmetics common camphor or *Cinnamomum camphora* which is obtained from wood of this long living tree. Its action on skin is cooling and

it is therefore recommended for inflammatory conditions.⁷ It has been used in acne, burns and ulcers. Cold compresses containing *Cinnamomum camphora* for bruises and sprains are usually effective.⁷

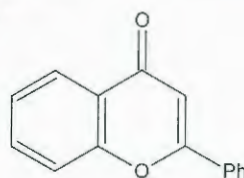
TARAXACUM SPECIES (Compositae)

Taraxacum officinale Weber is vernacularly called *Karanphul* or *Dandelion*. It is used in acne, biliousness, boils, cystitis, dyspepsia, and rheumatism. It is also useful in the treatment of pimples, acne and black heads. Leaves when eaten in salads are believed to clear the skin.³²

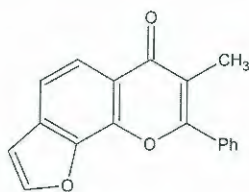
LAWSONIA SPECIES (Lathyraceae)

Lawsonia alba Lam or *Lawsonia intermis* Linn is one of the most important colouring plant whose bark is normally used for curing skin diseases and leprosy and in jaundice. The leaves are used for external application for headache and are rubbed over soles of feet to cure burning of feet. Decoction of leaves is used as an astringent for garle in relaxed sore throat. Its oil and essence is rubbed over body to keep it cool. The leaves of *L. alba* have been reported to contain a glucoside of 2-hydroxynaphthoquinone. The crushed leaves provide a reddish green powder that is applied to hands of a newly wed bride or by young girls for decorative and religious symbols. It is also used in some hair preparations.

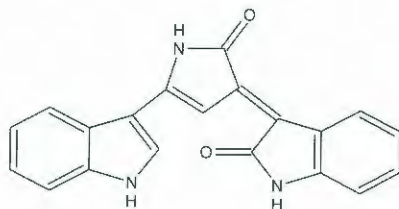
VIOLA SPECIES (Violaceae)



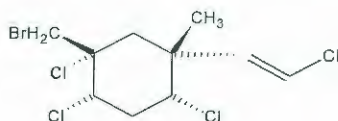
Simple flavone



Karanjanol



Violacein



Violacene

Viola tricolor is useful in rheumatism and its decoction is taken internally for skin eruptions. Its stems, leaves and flowers are applied to wounds and foul sores. The whole plant is used for its antipyretic, antidote for snake bite and antiphlogistic properties. The juice of fresh root is applied externally for abscesses. The active ingredients are sapogenious gaultherine, tannins and flavonoids. It is useful for acne and pruitis and eczema.⁷

JUGLANS SPECIES (Juglanaceae)

Juglans regia Linn. also called *Akhrot*, has antihelmentic and detergent properties. Its fruit is useful in rheumatism, while decoction of its leaves is useful in strumous sores. Its oil is used as a bath additive for rheumatism, gout, glandular swelling, gum problems, scrofula, sweaty feet,

acne, dandruff and other skin problems. It contains a red naphthoquinone pigment called juglone. Efforts are being spent to use this plant to prepare active ingredients for natural lipsticks. The species is rich in quinones, flavonoids, tannins, gallic, caffeic and neochlorogenic acid.^{33,34}

AZADIRACHTA SPECIES (Meliaceae)

Azadirachta indica or *Melia azadirachta* Linn is commonly called *neem*. It has a large number of useful properties. For example, its oil is astringent, insecticidal and antiseptic which finds use in rheumatic diseases.¹⁰ It is also used in making insecticidal and spermicidal preparations and for application in skin diseases. It is used as poultices and ointments for leprosy, burns, gangrene and scabies, herpes lesions, eczema and skin ulcers.¹⁰ Its oil is an anti-inflammatory and antibacterial agent. Neem oil is now being investigated as a safe natural pesticide for cotton and tomatoes and for the development of antifertility vaccine for the male.³⁵

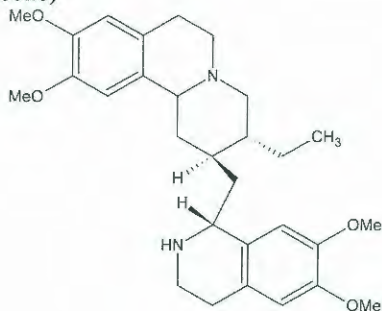
ECHINACEAE SPECIES (Echinaceae)

The purple cone flower or *Echinaceae. angustifolia* is important for treatment of acne, boils and for mastitis because of potent antiseptic properties of this plant. It is a native plant of USA which has been determined to increase immunity to infections and to cleanse the body when resistance to infection is low. It is also useful to lessen pain due to inflammation and is helpful in the treatment of gonorrhoea and syphilis, tonsillitis, impotency, eczema, psoriasis, acne, poison ivy and irritation problems.¹⁰ Its vasodilator and antiseptic properties have been indicated in folk medicine.¹⁰

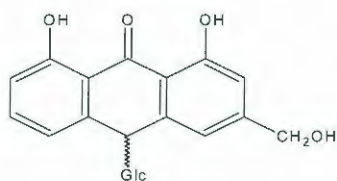
CASSIA SPECIES (Leguminosae)

Several *Cassia* species find use in the treatment skin infections. For example *Cassia fistula* leaves are useful for ringworm, rheumatism and in cases of snake bite while their juice is used in skin ailments. Its root bark contains anthraquinone pigments and tannins. *Cassia tora* leaves are used for skin itching and ringworm *Cassia* pods are useful in eczema. Some *Cassia* species are useful in perspiration and curing severe cases of skin conditions deteriorated due to contact of perspiration with bacteria.⁷

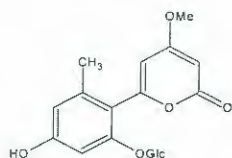
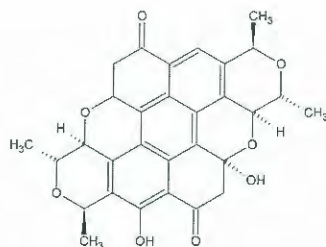
ALOE VERA (Liliaceae)



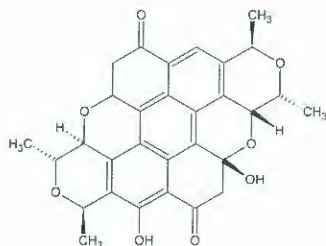
Emetine



Barbaloin

Aloenin
(consistuent of Aloe spp.)

Chrysoaphin fp



Chrysoaphin sl

Aloe vera has many uses and contains anthraquinone derivatives like emodin and chrysophanic acid as chemical constituents. It also contains a crystalline glycoside barbaloin, isobarbaloin and aloin. Its pulp contains uronic acid, catalase, oxidase and sugars. Its juice is cooling and is given internally in fevers and its gel is used for external applications. It has amazing wound healing properties and is useful in ulcers, sunburns, scalds, and scrapes. The gel can give a healthy glow when used fresh. It is also useful in urticaria and intense itching.³⁶

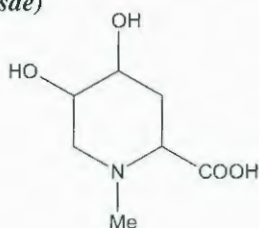
CEDRUS SPECIES (Pinaceae)

Cedrus deodara Roxb. oil is useful in skin diseases and ulcer. Its wood is known to possess insect repellent properties. It is an excellent treatment for dandruff and is a soothing tonic for skin. It is often used in men's perfumes, toiletries and after shave lotions and as a rub for sore joints and muscles.³⁶

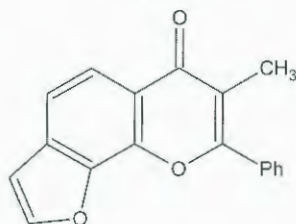
CORIANDRUM SPECIES (*Umbelliferae*)

Coriandrum sativum leaves alleviate urinary infections, rashes, cystitis, hives and burns and is useful for the digestive system.³⁶

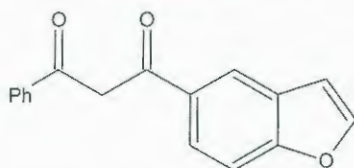
PONGAMIA SPECIES (*Leguminosae*)



Glabrin



Karanjanol



Pongamol

Pongamia pinnata or *Pongamia glabra* is locally called *Karanja* and is externally used in skin ailments. Oil from seeds is useful in cutaneous afflictions, herpes, scabies and rheumatism. Its leaves in the form of poultice are applied to ulcers infested with worms. Juice of roots is used for closing fistulous sores and for cleaning foul ulcerous wounds. Root juice is given internally with equal quantities of coconut milk and lime water for gonorrhoea. Its chemical investigation

has led to the isolation of karanjin, pongamol and glabrin. Karanjnin is believed to be the active principle of cure in *Pongamia* Species. *Pongamia* extract can be used for developing natural sunscreens and provide additional help to broaden UV protection. Internally it is used for bronchitis and whooping cough. Its seed extract has also been evaluated for herpes and *Smilex virus Type 1* and *Type 2* at concentrations of 1 and 20 mg/ml respectively and it has been found to inhibit the virus without any observable cytopathic effect.^{37,38,10}

SAPINDUS SPECIES (*Sapindaceae*)

The most important species of this genus, which finds use in supracosmetology, is *Sapindus mukorossi*. The fruit shell of the plant contains saponins and it is cultivated throughout the northern. It has beneficial properties which promote healthy hair growth and removes dandruff.³⁸ It has excellent properties to dissolve a number of dyes and hence can be used to make excellent detergents. Many new varieties of shampoos have been made from the fruit of this plant when mixed with medicinal components of turmeric and coconut pulp.³⁸

TERMINALIA SPECIES (*Combretaceae*)

Terminalia arjuna, *T. balerica* and *T. chebula* are three *Terminalia* species that have found extensive use in skin care and bath preparations. *T. Balerica* is useful in leprosy, biliousness, dyspepsia and headache. It is an important component of *triphalla*, used by early Ayurvedic physicians for curing a variety of diseases particularly for hair and rheumatic problems. *T. chebula* is used as a dentifrice for carious teeth, bleeding and ulceration of gums. Regular use of the fruit powder when mixed with coconut milk is believed to improve complexion.³⁹

CELOSIA SPECIES (Amaranthaceae)

Celosia argentea Linn., commonly called *cock-scomb* or *quail grass*⁴⁰ is used in bath preparations. Its leaves are used to treat itching sensation, sores, wounds and skin eruptions. When mixed with honey, its leaves are applied to inflamed areas and painful afflictions of abscesses. The whole plant is used as a snake bite antidote and for colic pains, gonorrhoea and eczema. The aerial parts of the flowers contain 5-methoxy-6,7-methylenedioxy-2'-hydroxyisoflavone and 2',5-dimethoxy-6,7-methylenedioxyisoflavone. The leaves and shoots of *C. argentea* are edible.

NELUMBO SPECIES (Nymphaeaceae)

It is commonly called *kamal* or *kanwal*. The flowers of *Nelumbo nuciferae* are used as astringent in diarrhoea, cholera, diseases of the liver and it is a cardiac tonic. Its roots are used as a paste in skin afflictions and ringworm. It has a vitalizing effect when used in bath preparations.

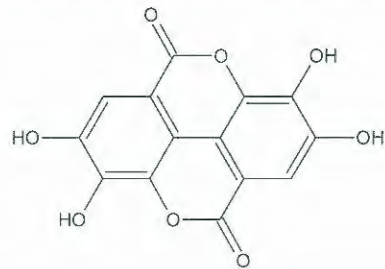
Besides these there are many other plant products of Indian origin that are valued for skin diseases. It is not possible to mention or even enlist them here. Some of these plants that are worth investigating further are given below:

Terminalia tomentosa (Combretaceae) (for increasing the glow on face, used as a paste), *Citrullus colosynthis* (Cucurbitaceae: fruit, for acne, black heads), *Trifolium pratense* (Leguminosae; leaf, to improve complexion), *Luffa amara* (Cucurbitaceae; for boils), *Astragalus strobiliferus* (Leguminosae; root, to remove blemishes), *Hedychium spicatum* (Zingiberaceae; root, skin), *Nigella sativa* (Renunculaceae; acne, seeds), *Cyperus rotundus* (Cyperaceae; skin diseases, itching, rashes), *Litsea glutinosa* (Lauraceae; poultice), *Astragalus strobiliferus* (Legu-

minosae; root, facial blemishes), *Sauropus lappa* (Compositae; eczema, skin diseases, facial complexion and glow), *Thespesia populnea* (Malvaceae; skin diseases, fruit and flowers), *Sphaeranthus indicus* (Compositae; skin ailments), *Symplocos racemosa* (Symplocaceae; skin diseases), *Berberis aristata* (Berberidaceae; boils, sores), and *Psoralea corylifolia* (Leguminosae; diseases of skin, psoriasis).

Some of the ingredients used to prepare cosmetics of commercial importance use *Acorus calamus* (vacha), *Anoropogan muricatus* (Usheeram), *Balsamodendron mukul* (guggulu), *Berberis aristata* (Dharu Haridra), *Cedrus deodara* (Devadaru), *Celastrus paniculata* (Jyothishmathi), *Coriandrium sativum* (Dhanyaka), *Cuminum cyminum* (Jeeraka), *Embelia ribes* (Vidangam), *Glycyrrhiza glabra* (Yashtimadhu), *Hemidesmus indicus* (Sariba), *Holarrhena antidysentrica* (Kutaja), *Melia azadirachta* (Nimb twak), *Nigella sativa* (Krishna Jeeraka), *Plumbago rosea* (Chitraka), *Psoralea corylofolia* (Bakuchi), *Smilax china* (Chobchini), *Zingiber zerumbet* (Vanandraka) to get beneficial effects in cases of prickly heat, pimples, dandruff and to provide potent natural antiseptic and deodorising action to remove bad smell due to perspiration disorders.

RAW MATERIALS THAT PROMOTE GROWTH AND BRILLIANCE OF HAIR



Ellagic acid

There are a number of plants that are used for promoting the growth of hair and to have vitalizing effects on their appearance and brilliance.

Cinnamomum cassia oil is used to keep the hair dark and to prevent baldness in men.⁴¹ *Eugenia jambos* (Myriaceae) or *Syzygium jambos* or *Rose apple* is used as a ritual post natal facial wash. Its seeds contain ellagic acid. Jambu is believed to have properties which stimulate the scalp and regenerate the damaged hair.⁴²

Shellac or Lac obtained from the resin secreted by insect *Laccifera lacca* is perhaps the only resin from the animal origin which is used commercially. Shellac can be used as a hair lacquer resin. Its thin film forming properties and non toxic nature make it the ideal raw material for a variety of applications for development of hair care products like aerosprays, fixatives or even mascaras. Many new applications of shellac compounds have been recently reviewed and projected.⁴³ New fruit coatings, leafshine, lac gloss for lipstick applications and anti aging and anti-wrinkle cream formulations are being investigated. Ambrettolide grade aleuritic acid isolated from lac has been found to be a good substitute for alpha hydroxy acids. It passes several beneficial effects to cosmetic formulations. Several hair setting cosmetics have been obtained from components obtained from Shellac. Lac also contains a red dye that can be employed for dyeing silk, meat and for making natural lipsticks.⁴³

Indigofera tinctoria is another plant cultivated extensively in India before the advent of synthetic indigo but its cultivation has been substantially reduced now. Leaves of the plant when mixed with henna and made into a paste are very beneficial to provide darker and beautiful look to the hair⁴⁴. *Indigofera tinctoria* contains glycosides, alkaloids and oleoresins that are useful in the treatment of infections as they have been found to be anti-microbial in nature.

Anagallis arvensis has bright scarlet flowers and is used for the treatment of eye diseases.^{45,46} The herb is used in cases of jaundice, dropsy and in-

flammation. When given in the form of a lotion, the herb regulates pigmentation and removes freckles and other blemishes. The tincture prepared from fresh leaves is useful in the treatment of itches, ivy rash and swelling. Its leaves are used to colour hair and to give them a fresh look.^{45,46}

Eclipta alba of the *Compositae* family is extremely useful for natural formulations for hair care.⁴⁷ Its leaves and roots are used for making ointments or creams that promote hair growth. Juice of fresh leaves is applied to scalp to promote hair growth and is taken internally to blacken the hair and beard.^{48,49} The elderly women use decoction of the plant to avoid greying of hair. When mixed with *Centella asiatica* and *Phyllanthus embelica*, the plant is valued for its anti inflammation effects, and as a cure against insect bites, stings and swellings.

Withania somnifera or simply *Withania* or *Aswagandha* or *Ashwagandha* is used for varied physiological effects. The plant is considered as an aphrodisiac and an Indian equivalent of Chinese ginseng.⁵² A leaf infusion is given in fevers, and is applied to boils and swelling with good efficacy and results. The fruit is diuretic while its seeds are considered to be hypnotic. The plant is good for circulation of the scalp and improves the structure of hair and is used in preparations intended for greasy hair and dandruff. It contains a number of steroids and plant is anabolic and provides a safe alternative to steroids for building muscle mass. It has been observed that massage of the scalp with infused oil of ginger or fenugreek helps to cure sudden loss of partial or total hair loss (alopecia).^{50,36,51}

RAW MATERIALS THAT PROMOTE SEXUAL AND SENSE PERFORMANCE

There are many plants that are recommended for

improving sexual performance and alleviating sexual problems of both males and females. Since this paper is primarily concerned with description of personal sophistication, we will list only those plants which are directly used in cosmetics or cosmeceuticals and enhance the performance and self esteem of the person. Details of these plants have been omitted for the sake of brevity.

It has been observed that garlic pearls, almonds, black eyed beans, hazel nuts, pumpkin seeds, kidney beans and yoghurt are useful for curing disorders of the male reproductive system. Ayurveda mentions the use of saffron for infertility. Coriander leaves, clove, ginger, cinnamon, vetiver, cardamom and sandalwood and rose essential oil are believed to act as aphrodisiacs and may help in impotence. Gotu kola, cedar and celery seeds are natural diuretics and help in prostrate problems. Coriander leaves also help address the low libido problem. Sandalwood is known to alleviate anxiety and hence may be useful in premature ejaculation. Black pepper increases blood circulation and feeds the nervous system and therefore will help in priapism. Calamus oil massage provides relief for the same disorder. Local massage with rosemary or peppermint or tea oil is helpful. Angelica species are also used for sexual ailments.

Many cures for disorders of the female reproductive system have also been derived from Ayurveda. For example cumin and fenugreek seeds can increase milk production in females. Most breast problems can be treated with calamus oil massage while swellings can be treated with celery seed decoction. Aloe vera and basil leaves promote menstruation. Caraway relaxes uterine tissues and therefore reduces menstrual cramps. Cedar stimulates the menstruation cycle and celery seeds can treat irregular menstruation. Angelica and Calamus root are useful for premenstrual syndrome (PMS). Cloves can tone up the uterous and garlic has a rejuvenating effect. Saffron can help when infertility is associated

with sexual problems. Rose oil is said to increase sperm count and its quality and is known to act as a mild aphrodisiac. Basil oil is helpful in inducing labour and in migraine associated with sexual problems. Calamus and celery are also useful in post menopausal problems while cinnamon is especially powerful during menopause and in cases of low libido and edema. Aloe vera, gotu kola and Angelica are helpful in pelvic inflammatory disease (PID). Preparations involving plants and herbs like *Cupressus sempervirens* Linn. (*Cupressaceae*), *Asparagus recemosa* (*Liliaceae*), *Solanum verbascifolium* (*Solanaceae*), *Saccharum officinarum* Linn roots (*Gramineae*), *Desmotrichum fimbriatum* (*Orchidaceae*), *Dichrostachys cinera* (*Leguminosae*), *Berberis aristata* (*Berberidaceae*), *Hibiscus tillaceus* (*Malvaceae*), *Sida acuta* Burma. (*Malvaceae*), *Tribulus terrestris* Linn. (*Zygophyllaceae*), *Phoenix dactylifera* (*Palmae*), etc are considered to stimulate individuals for sexual union.³⁶

RAW MATERIALS THAT PROMOTE LONGEVITY

There are several plant materials that are supposed to promote longevity of human beings. Though factors that promote successful aging without debility are numerous, some biomarks have been identified in literature. Modern research has established that, yoga, meditation, diet, breathing exercise, low caloric diet, fasting interspersed with fibre food and sprouts reverse the visible effects of ageing. Himalayan herbs, asparagus, ginkgo fruit, fennel and other secret ingredients have also been used by individuals for a long life in the past. Ancient Chinese used to follow the Tao way of life by regulation of respiration, diet, sexual urges and selected gymnastics for the same purpose. Ancient Greeks used to inhale the breath of virgins to regenerate their selves. Modern researchers advocate the use of under nutrition without malnutrition for

antiaging effects.²

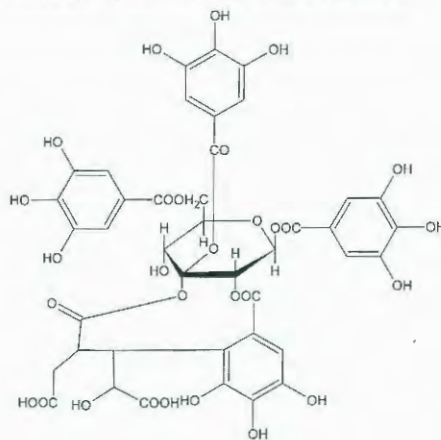
Several organic compounds and plant species have been mentioned in patented literature that have been determined to have beneficial antiaging effects when mixed with OTC(over the counter) products. Though enlistment of all these plants and organic compounds is beyond the scope of this article, following plant extracts have been found to pass antiaging benefits when examined by modern researchers.

- (a) Tangerine peel extract
- (b) Ginkgo leave extract
- (c) Swertia japonica extract
- (d) Panax ginseng
- (e) Shaddock extracts
- (f) Proanthocyanidin containing extracts
- (g) Kiwi oil
- (h) Coleus forskohlii root extract
- (i) Jojoba oil
- (j) Olive oil

Carak Samhita and Ayurveda mention thousands of plant species that can contribute to the development of new antiaging products. For example different parts of the following plants when used alone or in conjunction with other natural materials are said to promote longevity and vital strength.³ *Pippalli*, *Aguru*, *Dhava*, *Tinisa*, *Khadi- ra*, *Simsapa*, *Vaca*, *Cavya*, *Citraka*, *Vidanga*, *Sankhapuspi* and *Palas* have been mentioned in the literature. Some plants identified through Ethnobotanical techniques are *Ougeinia dalbergioides* (*Leguminosae*), *Dalbergia sissoo* Roxb. (*Leguminosae*), *Carissa carandas* (*Apocynaceae*), *Styrax officinalis* Linn. (*Styraceae*), *Garcima cowa* Roxb. (*Guttiferae*), *Embelia ribes* (*Myrsinaceae*), *Butea frondosa* (*Leguminosae*), *Embllica officinalis* (*Euphorbaceae*), *Evolvulus alsinoides* (*Convolvulaceae*), *Anethum sowa* (*Umbelliferae*), *Anogeissus latifolia* (*Combretaceae*), *Aquilaria agaliocha* Roxb. (*Thymelaceae*), *Piper longum* Linn. (*Piperaceae*), *Bacopa mannieri* Linn (*Scrophulariaceae*) have been

mentioned in the *Samhita*. Some of these plants have not been examined for their chemical constituents while others have been critically examined and many new chemical constituents have been isolated and identified. However their effects on the aging processes have yet to be studied and it is too early to state which type (s) of chemical constituent (s) are helpful in reversing the aging process despite the fact that several processes like involvement of free radicals, antioxidants etc have been studied extensively. Decoction of one or a combination of some of these herbs and plants are believed to provide strength, vitality and longevity without debility, senility and diseases.

RAW MATERIALS THAT PROMOTE INTELLECT, MEMORY AND VISION



Chebulinic acid

The potions of *Terminalia chebula* (*Combretaceae*) (*Haritaki*), *Embelia officinalis* (*Euphorbaceae*) (*Amalaki*), *Terminalia arjuna* (*arjuna*) and *Terminalia belerica* (*Bahira*) when mixed with honey have been recommended for promoting intellect, memory and vision. Chemical examination of *Terminalia* has yielded many chemical components which include arjunine, arjunetin, chebulinic acid and anthraquinone pigments. The fruits of the species seem to be very rich in

tannins (which are present to the extent of about 40%). *Embelia officinalis* is also very rich in vitamin C and tannins. Fruits of this tree have been successfully used for the treatment of human scurvy. Seeds are used for asthma, bronchitis and biliousness. Fermented liquor prepared from its juice can be used in haemorrhage, diarrhoea, dysentery and is beneficial to patients of jaundice, dyspepsia and anaemia when used in combination with iron. *Centella* species (*Umbelliferae*) have very important properties that are useful in diseases of skin, leprosy, nerves and blood. For example leaves of *Centella* are taken as tonic and for improving memory. It has been determined that they are also useful in syphilitic skin ailments when taken internally and externally. Fresh leaves of *Centella asiatica* contains a glycoside asiaticoside to the extent of 0.07-0.12% besides essential oil, sitosterol, tannin and an alkaloid hydrocotylin in 0.0016% yield., vallerine, pectic acid and resinous material. Similarly roots of *Acorus calamus* (*vacha*) is a brain tonic and increase endurance and stamina. The plant is anticonvulsive, bronchodilator and increases blood circulation to brain and hence reduces brain toxins.^{3,37} Some components of lac have also been mentioned to pass anti-aging effects in cosmetic preparations.⁴³

Rosemary leaves (*Rosmarinus officinalis*) enhance memory by improving circulation to head. It strengthens brain and improves quality and strength of hair and consequently prevents hair loss due to stress. Tea prepared from *Rosemary leaves* is good for glossy and shining hair.. Black ginger seed, fleece flower, ginseng and gotu kola are considered very good for memory, for reversing depression, anxiety and for curing lack of memory due to injury to brain or to memory functions in the brain owing to diseases of the brain. Lecithin containing fruits, vegetables (e.g., cauliflower) are considered beneficial for curing memory loss due to stress, nervousness and are useful in amnesia and Alzheimers disease.³⁶

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Establishment of the Korean Society of Cosmetic Dermatology

-Emerging new society of new millenium-

Prof. Seung Hun Lee

We, civilized citizens, are now confronted by new turning point at the beginning of new era which ask new thoughts to us. In cosmetic dermatologic field also, we as scientists need to adapt new paradigm about cosmetic demands of people on the scientific basis. According to these academic pressure, the needs for organizing new academic society, which can possibly join all the scholars related to cosmetology including dermatologists, pharmacists, chemists, chemical engineers, and researchers of cosmetic industry, were growing.

A meeting of thirty nine promoters to set up new organization were held on December 16, 1999 on Seoul, Korea. As consequences, a preparatory committee for establishment were held with fourteen active members on January 31, 2000 and Dr. Yoon-Kee Park from Yonsei University was elected as the president of the preparatory committee for establishment. After first preparatory committee, four more committee were held and made the regulations of the society and prepared the inaugural meeting and academic meeting.

At last, the historical inaugural meeting of the Korean Society of Cosmetic Dermatology(KSCD) and the first academic meeting were held on July 9, 2000 on Seoul. There was a great turnout of people at the meeting. There were more than seven hundred crowd beyond the capacity of the venue. At the inaugural meeting, Dr. Yoon-Kee Park was elected as the first President of the society, Dr. Seung Hun Lee was elected as the Chairman of the board of director and Dr. Chil Hwan Oh as secretary general of KSCD. In the academic meeting, there were fifteen invited presentations divided into five sessions such as research session for cosmetic dermatology, cosmetics session, skin care product session, medical skin care session, and cosmetic treatment session. Before general presentations, Dr. Yoon-Kee Park, President of KSCD delivered the lecture titled "Present and future of cosmetic dermatology" and Dr. P. Morganti, general secretary of the International Society of Cosmetic Dermatology delivered guest lecture titled "Botanicals in acne therapy".

This new emerging society will join the various specialties relating cosmetic dermatology and conduct all the activities regarding whatever subjects promoting the health and the beauty of the skin. Also, this society hope to share the experience and the friendship with the other related societies abroad such as the International Society of Cosmetic Dermatology. Through these activities, we believe that we can meet the needs of new millenium in the cosmetic dermatologic field.

대한코스메틱피부과학회 창립총회 및 학술대회

일시: 2000년 7월 9일(일요일) 장소: 전경련회관 국제회의장



VITAMIN D IN DERMATOLOGY

By Knud Kranfalle

2000. 360 pages. Hardbound

US\$ 165.00

ISBN 0-8247-7704-2

Marcel Dekker, Inc.

New York USA

Fax: +212-685-4540

<http://www.dekker.com>

This interesting book provides the basic science of vitamin D research in investigative and chemical dermatology. As matter of fact, vitamin D activities include important function on cellular proliferation, differentiation and apoptosis in addition to immune suppressive effects; and are not only limited to calcium metabolism and bone homeostasis.

Vitamin D has little biological activity per se but must be metabolized first in the liver to 25.OH.D and then in the kidney to a number of metabolites, the most important of which is 1,25 (OH)2D. However, the keratinocyte is fully capable of producing its own 1,25 (OH)2D.

The book is divided in four big sections respectively on: the mechanism of action and metabolism, the first, its cell target in the skin, the second, and its therapeutic use in psoriasis or in other skin diseases, the third and the fourth sections.

The biologically active form of vitamin D, 1a, 25-dihydroxyvitamin D3(VD) is a lipophilic molecule that easily passes cellular membrane and enters the nucleus, where it binds to specific receptors.

The vitamin D receptor (VDR) is however a member of the nuclear receptor superfamily and appears to arise from a single ancestral gene with a DNA binding domain close to the N-vitamins and ligand-binding domain at the carboxyl terminal. Moreover, VDR appears also to have indirect effects on gene regulation through other nuclear receptors and general transcription factors. These "nongenomic" actions seem to be mediated via membrane receptors. What it is to underline is, however, that VD, the active form of vitamin D, is an important nuclear hormone with pleiotropic physiological function, such as maintenance of calcium and phosphate homeostasis, bone formation, and cellular growth. Moreover vitamin D is lighter taken up systemically directly through diet or can be synthesized in the skin from 7-dehydrocholesterol, requiring energy from UV radiation at an approximate wavelength of 300 nm and, of course, during day light hours.

With regard to the damaging effects of excessive exposure to sun light, it was demonstrated that suberythral exposure of hands, face, and arms from two to three times a week is more than adequate to satisfy the vitamin D body requirement. Moreover a sunscreen application after the initial exposure will prevent the damaging effects of excessive sunlight.

For all these reasons the recommended daily allowance (RDA) for vitamin D is 200 IU (5 µg) per day for adults, and 400 IU (10 µg) per day for children and the elderly, even if the RDA for elderly and other risk groups seems to be augmented.

The first section of the book ends with the suggestion to avoid an excessive oral intake of vitamin D, considering that the maximum tolerated dose should vary from one individual to another, and that some granulomatous diseases make patients hypersensitive to vitamin D treatment.

Keratinocytes are met only capable of producing vitamin D3 from endogenous sources of 7-dehydrocholesterol, (7-DAC) but are also capable of producing a variety of D metabolites, including

1,25 (OH)₂D; 24,25 (OH)₂D and 1,24,25 (OH)₃D.

Both the formation and catabolism of 1,25 (OH)₂D are under hormonal control and calcium is the best-studied pro-differentiating agent for keratinocytes. In presence of calcium adequate levels, keratinocytes progress from rapidly proliferating cells to cells capable of making cornified envelopes. Cytokines such as tumor necrosis factor- α (TNF), interferon- γ (IFN- γ), epidermal growth factor (EGF) and transforming growth factor- α (TGF- α) stimulate proliferation of keratinocytes via the EGF receptor.

Notwithstanding the regulatory mechanism governing hair cycling are still obscure, several studies suggest that 1,25 (OH)₂D₃ (calcitriol) and/or vitamin D analogs, endogenously produced or therapeutically applied may be interesting candidate as a hair growth-regulatory factor. Of course their potential clinical applications have to be adequately evaluated in hair follicle targeting to control, for example, their topical activity on androgenetic alopecia or on other distinct variants of scarring alopecia. However, new vitamin D analog exerting less systemic side effects, may represent promising new drugs for the modulation of hair growth and the treatment of various hair diseases.

Vitamin D seems also to have a role in melanogenesis also because of evidence of interactions between keratinocytes fibroblast and melanocytes. As matter of fact, some studies in rodents provided evidence that vitamin D deficiency or supplementation may affect some parameters relating to pigmentation in skin, especially after UV exposure. However the question of whether vitamin D compounds can be shown to influence melanogenesis or melanocyte numbers rests on very limited and conflicting scientific studies. On balance it could be argued that there is evidence that vitamin D receptors are present in pigment cells, along with most other nucleated cells, and that vitamin D compounds may modulate melanogenesis under some conditions.

Concerning the immunological activity until now almost none of the studies support the hypothesis that the primary mechanism of action of the available vitamin D₃ analogs in vivo is on the immunocytes in the skin. As matter of fact, these compounds have not demonstrated any effects in the treatment of diseases where the immune system is known to play an important role, such as, atopic dermatitis and allergic contact dermatitis.

How it is known the immune system plays a critical role in the pathogenesis of psoriasis. Otherwise vitamin D₃ seems to have strong immunomodulatory effect in vitro and inhibits some autoimmune diseases in animal model in vivo.

By the way it is still unclear whether vitamin D₃ achieves its effect in psoriasis via direct effect on the keratinocytes, immunocytes, or both.

The latest studies show that the primary mechanism of vitamin D analogs in psoriasis has to be due to a direct effect on the hyperproliferative keratinocytes.

However calcipotriol (vit. D₃) at doses used clinically changes the morphology of langerhans cells (LC) as well as and suppresses the number of LC suppression by vitamin D₃, together with the change in secretion of proinflammatory cytokines by epidermal cells and lymphocytes, should serve to inhibit the immunological component of psoriasis. Calcipotriol, as synthetic vitamin D analogs, differs from calcitriol only in the structure of the side chain characterized of a cyclopropane ring. For the presence of the ring this vitamin D analog is only slowly metabolized in keratinocytes. Consequently, the effect of calcipotriol in the target tissue is maximal and the systemic side effects are minimal. From the long-term studies for topical treatment of chronic plaque psoriasis, by this drug there was no evidence of skin atrophy.

Furthermore, it is important to subline that calcipotriol treatment can be stopped without a resulting exacerbation of psoriasis.

Moreover both UVB and PUVA phototherapy can be enhanced by the use of this drug. Finally the combination treatment of calcipotriol/cyclosporine can enhance the response to treatment. In particular, this combination-therapy permits the use of a lower dose of cyclosporine and hence improves the risk /benefit ratio beyond ciclosporine monotherapy.

Calcipotriol-acitretin is also a highly effective and safe combination indicated in patients with severe psoriasis.

In conclusion calcipotriol seems to be as effective in the treatment of psoriasis in children as it is in adults and it is well tolerated as an adjunctive therapy with other antipsoriatic treatments.

It should be remembered that patients receiving ultraviolet light should not apply it before phototherapy and dermatologists should be aware of the possibility of photosensitivity.

Oral calcitriol for treating psoriatic arthritis is also a relatively safe and effective new approach for treating this difficult disorder.

Many other news are reported in this interesting book dedicated to the therapeutic use of vitamin D. Furthermore, are described the European and Japanese way to use the new Tacalcitrol (1,24-dihydroxycholecalciferol) and of the vitamin D analogs in ichthyosis and other disorders of keratinization.

The activities of the vitamin D derivatives are well described and well documented are the news about their mechanism of action and their therapeutic use.

This interesting and exhaustive book represents an up-to-date text of the most recent findings on the biochemistry and therapeutic benefits of vitamin D and its synthetic analogs.

Therefore Vitamin D in dermatology represents an authoritative and reference text for chemical dermatologists, cosmetic scientists and technologists, pharmaceutical scientists, pharmacists, and for all medical school students in these disciplines.

P. MORGANTI
Editor-in-Chief

Vitamin A and Retinoids

An Update of Biological Aspects and Clinical Applications

By Livrea M.A.

2000. 312 pages Hardcover

sFr. 228.- / DM. 268.- / öS. 1957.-

ISBN 3-7643-5882-3

Birkhäuser Verlag

P.O. Box 133 CH-4010 BASEL -SWITZERLAND

Fax. + 41.612050799

<http://www.birkäuser.ch>.

This book presents in a very detailed way the state-of-the art knowledge on the role of vitamin A and retinoids from basic chemical, biochemical and cell biology research, to nutritional aspects and clinical applications.

The book is divided in 22 chapters all very interesting and so well linked in order to give the reader a complete and exhaustive idea of the mechanisms regulating metabolism and functioning of retinoids at cell level.

Retinol is the predominant retinoid in the fasting circulation, even if other retinoids are also present such as all trans and 13-cis retinoic acid, as well as retinyl esters and soluble glucuronides of both retinol and retinoic acid, and carotenoids like b-carotene. Retinol is always bound to its specific plasma transport protein, retinol-binding protein (RBP), and in the fasting circulation it has a half-life of approximately 12-h. Moreover nutritional and health status are the most important factors which influence circulating retinoid levels.

We know that retinol and retinoids delivery to cells occurs through many different pathways and it is influenced by a number of physiological factors, but we have limited understanding of how circulating levels are regulated and interact within the intact organism.

For all these reasons we need to better understand how retinoids are generated and transported in the body.

With this quotation the first chapter ends.

Meanwhile retinyl palmitate is the major storage form, b-carotene represents the major provitamin A carotenoid. As matter of fact, in a nutritional sense, the vitamin A family includes all naturally occurring compounds with the biological activity of retinol and common dietary sources as carrots, yellow squash, dark-green leaf vegetables, corn, tomatoes, papaya and orange.

The best known biological action of carotenoids is the ability of some of these compounds to be metabolized in human to form retinol. The major pathway of enzymatic b-carotene, metabolism involves cleavage by a 15,15'-central dioxigenase that results in the formation of retinol, which can either be reduced to retinol or oxidized to retinoic acid. This process occurs in the cytoplasm of many cell types. In addition, there is a minor pathway associated with mitochondrial oxidation of b-carotene breakdown products and produces retinoic acid without requiring the intermediacy of retinol.

b-Carotene and carotenoids are also interesting quenchers of singlet excited oxygen, (102) which, as it is well known, is a highly reactive specie, capable of oxidizing nucleic acid, various aminoacids in proteins, and unsaturated fatty acids.

As matter of fact each carotenoid molecule can quench 1000 102 molecules before it reacts clinically, and form products, thus serving as very effective antioxidants. Therefore it is apparent that people who consume higher levels of carotenoids are at lower risk for a number of chronic diseases including a variety of different cancers.

Even if carotenoids and therefore food provides the major portion of dietary vitamin A, vitamin A inadequacy, together with those of iron and iodine are major micronutrient problems in the world, especially for those populations socio-economically disadvantaged. For these reasons different public institutions recommended daily dietary intakes of vitamin A, estimated to maintain the body in well being conditions. Supplements are not needed by healthy persons ingesting a balanced diet, but are necessary, for example, for pregnant women to prevent deficiency-induced fetal abnormalities, especially in that regions of the world where vitamin A deficiency is common. Therefore it is essential to remember that vitamin A is an essential nutrient for humans.

The dietetic and clinical role played by vitamin A and by carotenoids is largely and perfectly described from the 2nd to the 4th chapter.

Vitamin A as aldehyde has also an essential role in the visual process and the maintenance of the structural integrity of the photoreceptors, even if the transport and metabolism of vitamin A within the retina is far from being fully understood.

What seems to be sure is that retinal is a key factor in the control of the visual pigments meanwhile the process by which 11-cisretinal is formed and pigment regenerated are not yet understood. However there is strong evidence that the regeneration of pigment in rods and cones may involve different mechanisms. The knowledge of this process will be relevant to understand in future many clinical disorders.

All these problems are described in the 6th and 7th chapters.

Retinoids can enhance immune responses. Vitamin A appears to play a role in modulating a wide spectrum of immune responses, including T and B lymphocyte function of other immune effector cells such as monocytes, neutrophils, and Langerhans cells, and maintenance of mucosal immunity. Moreover all retinoids are likely to be directly involved in regulating the production of some of the cytokines, cytokine receptors, and transcription factors involved in cytokine signaling.

Another important therapeutic application of vitamin A is its use in reducing the morbidity and mortality of the infection diseases. Therefore it has been shown that vitamin A supplementation can reduce child mortality in the developing country by 30-50%.

Vitamin A is also currently under investigation as an "anti-infective" therapy for different infection diseases, such as HIV infection and malaria.

Some dermatological conditions, ranging from acne to photoaged skin have proven to be responsive to topical and/or systemic retinoid treatment. They exhibit significant effects on cell proliferation and for severe hyperkeratotic inflammatory diseases and genodermatoses.

Moreover the sebosuppressive effect of retinoids is being increasingly used for treatment of mild to moderate acne also because they are able also to decrease the abnormal desquamation of the sebaceous follicle and to diminish the proliferation of *P. acnes*, improving the inflammatory acne lesions. Topical retinoic acid is effective in reducing fine wrinkling and roughness in-patients with photodamaged skin. This damage involves an accumulation of disorganized elastin-containing fibers and reduced content of types I and type III procollagens in extra-cellular matrix, involving matrix-degrading metallo-proteinases (MMPs).

Recent data suggest that retinoic acid may also work at the molecular level through inhibition of these matrix metalloproteinases, by blocking induction of the UV-induced activator protein-1 (AP-

1) transcription factor that regulates these enzymes.

From a careful reading of all the 22 chapter of this book, we understand that retinoids are remarkable drugs with multiple pharmacological effects. They act in different ways on a broad spectrum of different disorders and the known mechanism of action of retinoids does not explain all their diverse biological effects. Many studies were done on hundreds of retinoids, but further studies are needed in order to test all their possible biological activities.

This interesting volume will be certainly stimulating for all the specialists and chemists who wants to enlarge their knowledge on retinoids, but it has to be considered also a book indispensable for the medical class, and especially physiologists, pharmacologists, biologists, dermatologists, cosmetic chemists and who are involved and interested in the study of the activities performed by the vitamin A and its derivatives.

P. MORGANTI
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COSMECEUTICALS

Drugs Vs. Cosmetics

By P. Elsner and H. Maibach

2000. 368 pages illustrated - Hardcover

ISBN: 0-8247-0305-7 / \$175.00

Marcel Dekker Inc.

250 Madison Avenue New York, NY, 10016

Fax: +212-685-4540

<http://www.dekker.com>

With this very interesting twenty-chapter book, the authors intend to give a concrete meaning to the term cosmeceutical coined twenty years ago in USA by Prof. A.M. Kligman in a meeting of the Society of Cosmetic Chemistry.

A long and never-ending international dispute seems to have raised on the use and meaning of such term.

What Kligman affirms in his first chapter, anyway, must be underlined. He says, "whether one is pro or con, the thermal cosmeceutical has permanently entered the vocabulary of skin care science".

As a matter of fact, though, "cosmeceuticals" meet the consumer demand for high efficacy products it is surely in the interest of manufacturers to prove the efficacy of active cosmetics, efficacy and proof that, according to the European rules, must be scientifically documented.

According to the present rules, then, in Europe, but also in Japan, cosmeceutical can be regarded as a subclass of cosmetics, while in the USA they can only be regarded as a subclass of drugs. This is what chapter two deals with.

Advocacy of the term cosmeceutical, as an attempt to compromise and bridge the gap between cosmetic and pharmaceutical greatly enlivened the debate.

Photoaging, is the ideal skin condition to focus the debate. In fact, people wish "turn back the clock" that is, they do not want to get old.

It is therefore necessary to use cosmetics with a proved efficacy and therefore "with an activity of at least a mild pharmacological or pharmaceutical, nature". What active principles to use, how to vehicle them and thus demonstrate their efficacy as antiaging products is well described in both in chapter three and nine, dedicated to topical retinoids.

As a matter of fact retinoids are a diverse class of pharmacological compounds consisting of retinol (vitamin A/ROL) and its naturally occurring synthetic derivatives which possess biological vitamin A activity, such as retinal (RAL) and all-trans-retinoic acid (RA).

The main focus of retinoid in cosmeceuticals has been its role as the mythical "fountain of youth".

And that even because many studies demonstrated a metabolic capacity for topical ROL, RAL and RA to penetrate the skin in a gradient manner from the epidermis to the dermis. Moreover topical RA has been found effective in the treatment of photoaging, stimulating enzymatically the growth of keratinocytes fibroblasts and extracellular matrix. Whether the enzyme markers in the skin reflects the ability of retinoids to produce a pharmacological effect is not clear. However, cosmetic-type preparations mandate sufficient retinoid concentrations to allow adequate penetration for a pharmacological effect. An insufficient concentration in the cosmetic or inadequate application by the consumer, may render the formulation relatively ineffective.

A wide scientific literature demonstrates a definite cosmeceutical effect of alpha-hydroxy-acids (AHA). Hydroxy acids are organic-carboxylic-acids classified into the a- and b- types (AHA and BHA) according to their molecular structure.

According to the last studies AHAs seem to stimulate HA production in cultured dermal fibroblasts. Moreover some of mildly acidic AHA preparations involve increased skin smoothness with the disappearance of lines and fine wrinkles. Long-term use results in thickening of the skin, in both the epidermal and papillary dermal layers because of the mild fibrous reaction typical of diffuse wound healing. In fact the increased collagen deposition, the consequent increased thickness and firmness of both dermis and epidermis, documented in skin after prolonged use of AHAs, is consistent with a wound-healing effect.

Both AHAs and BHAs are used worldwide as active dermatological drugs and cosmetic ingredients. Many aspects concerning the mechanisms of action of hydroxy acids still remain unknown and little information is available about the general toxicity and secondary biological effects of AHAs.

In contrast, the toxic effect of the BHA salicylic acid is well known when the percutaneous absorption is high. Therefore, the various beneficial effects of hydroxy acids should be better explored. This is what chapter four deals with.

Sebum and hair growth enhances are extensively treated in chapters six and seven. The positive correlation between the occurrence and severity of acne and sebum secretion rate is now well known as sebum surely contributes a degree of lubrication of the skin surface. Therefore dry skin results from insufficient sebum production. The most widely used methods for studying sebum are reported together with the main skin lipids class composition. The new understanding of hair growth regulation both biochemically and genetically are discussed and the new studies on type I and type II of the enzyme 5 α reductase and on aromatase are reported clearly and extensively.

Dry and chapped skin is a common problem both in healthy individuals and in patients with skin diseases. This condition may also occur in response to an environment with low humidity and/or low temperature. Application of moisturizers to the skin are expected to increase skin hydration and to modify its physical and chemical nature, inducing tactile and visual changes of the skin surface. At this purpose products used for treatment or prevention of dry skin are called emollients or moisturizers. These low-molecular-weight substances have water-attracting properties and seem able to affect the structure of barrier function.

The interesting findings that moisturizers also can effect barrier homeostasis clearly indicate that the used ingredients are not as inert to the skin as previously considered.

What is important to underline is that the increased understanding of the interactions between topically applied substances and the epidermis biochemistry will improve the formulation of future skin care products. Chapter seven, that is completely dedicated to moisturizers, ends with these considerations.

Moreover the key molecule involved in skin moisture is the sugar polymer hyaluronic acid (HA) with its associated water-of-hydration. HA in the skin has a protective, shock-absorbing, and structural stabilizing role in the extracellular matrix (ECM) of the skin. As matter of fact this unbranched polyamionic molecule fills the space between collagen fibrils and moisturizers the separation between collagen and elastin fibers. Moreover HA is also a signaling molecule, and its fragments has major influences on angiogenesis and inflammation. Tissues that contain high molecular weight HA are unusually resistant to invasion and penetration. This is probably linked to the extraordinary characteristics of this polysaccharide, which can take on a vast number of shapes and configurations dependent on polymer size, pH, salt concentration, and associated cations.

The large volume that HA occupies including its cloud of solvent, the water of hydration under physiological conditions underlies its ability to distend and maintain the extracellular space, and preserving tissue hydration. Its ability to organize ECM and its voluminous water of hydration, and its interactions with other molecules explain only a portion of the remarkable fractions with which it is associated.

All the characteristics and activities performed by HA are reported in chapter twenty.

How is well known radical species ROS (Radical Oxygen Species) and RNS (Radical Nitrogen Species) deplete the skin of its antioxidant defense, damaging biomolecules such as lipids, proteins and nucleic acid. At this purpose natural mammalian antioxidative network intervene at different levels: scavenging free radicals and lipid peroxy radicals, binding metal ions; or removing oxidatively damaged biomolecules. However, the antioxidant defense in cutaneous tissues can be overwhelmed either by an increased exposure to exogenous (UV rays) or endogenous (e.g. inflammatory compounds) sources of ROS or by a depleting of antioxidant defenses.

Therefore, preventing ROS activity by strengthening the skin's antioxidative capacity is an emerging approach in limiting UVR-induced skin damage.

Topical administration of appropriate combinations of antioxidants in combination with sunscreens or/and anti-inflammatory agents seems to be particularly promising.

The role of antioxidants in the photoprotection of skin and its antioxidant defense system is well documented and described in chapter 11th.

All pigmentary disorders get worse with the influence of UV rays even if the real cause of melasma, for example, is considered to be an increase in progesterone in the women serum at luteal phases.

The problem of hyper-pigmentation affects a wide area of female population and it requires the usage of de-pigmenting substances, among which there are hydroquinone, kojic-acid, arbutin, ellagic acid and rucinol. These compounds distributed as cosmeceuticals are described and treated in chapter ten.

How to treat the contact dermatitis and seborrheic dermatitis using cosmeceutical products is dealt with in chapters twelve and thirteen. Both pathologies, in fact, can be prevented with the use of protective topic moisturizers, like in the irritant contact dermatitis (ICD) and allergic contact dermatitis (ACD). They can also give good results for the treatment of dandruff and seborrheic dermatitis.

Chapters fifteen and sixteen are entirely dedicated to the legal distinction in the United States between a cosmetic and drug and to the meaning that Japanese give to the cosmeceuticals.

The juridical aspect and the difference between drug and cosmetics is well depicted, and the meaning that drug has in the Japanese law is very clear.

What lacks is an attentive study of the new European legislation, that is often mentioned by the co-authors of the book.

Problems regarding dermatotoxicology are widely examined, as this is one of the main problems that Prof. Maibach has dealt with in other books as well.

Even if the authors should give a greater importance to cosmetic industry, especially the European one, to try enrich the debate on cosmetics, the term cosmeceutical (and Prof. Kligman agrees with it), has already acquired "political economical, and legal connotations" and "has permanently entered the vocabulary of skin care science".

That is why this subject represents an interesting specification on the theme.

It is therefore important that the whole medical and the chemical class that deals with topic products, both drug and cosmetic, has this book in the personal library.

This easily readable book will for sure be printed over and over.

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Editor-in-Chief

Chiuso in tipografia: Ottobre 2000

Journal of Applied Cosmetology published quarterly by INTERNATIONAL EDIEMME. Via Innocenzo XI, 41 00165 Roma, Italy. Direttore responsabile: P. Morganti. Direzione, Redazione ed Amministrazione: Via Innocenzo XI, 41 - 00165 Roma, Italy. Impaginazione e Stampa: Grafica Flaminia, Roma. Copertina: Dr P. Morganti - Roma Italy - Sped. abb. Postale Comma 34 art. 2 Legge 549/95 Roma. Aut. del Trib. di Roma n. 3173/83 del 8-7-83.

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