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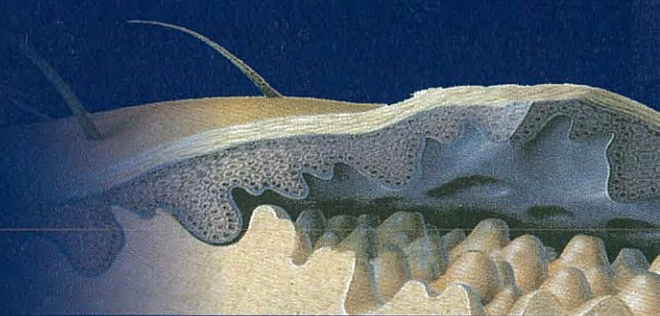

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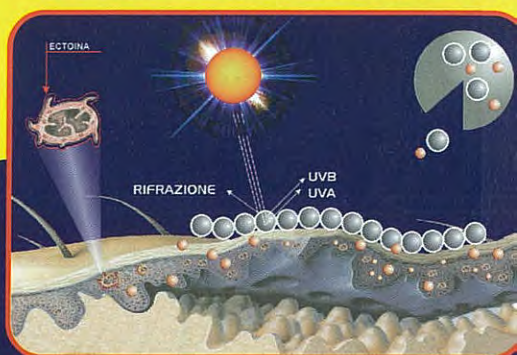

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Quarterly Review of Cosmetic Dermatology

Contents

J. Appl. Cosmetol. **27**, 41-48 (April/June 2009)

SIX KEY CRITERIA TO CHALLENGE TITANIUM DIOXIDE MATERIALS FOR HIGH PERFORMANCE AND COMPATIBILITY

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Received: *February, 2009.*

Key words: *Avobenzone; Butyl Methoxydibenzoyl Methane; Photo stable sunscreens; UVA; Coated Titanium Dioxide;*

Summary

We developed a collection of six assessment methods to reliably predict stability and integrity of coated TiO_2 materials. Five of the six tests can easily be run in a normal equipped cosmetic application laboratory.
We ran nine commercial TiO_2 materials through the test battery. Surprisingly, most materials showed issues in one or several challenge tests. Only one material did fulfil all requirements. It is a double-coated rutile variant with silica and dimethicone.

Riassunto

Sono stati messi a punto sei diversi metodi per studiare la stabilità e l'integrità del biossido di titanio (TiO_2) utilizzato per le formulazioni cosmetiche.
Cinque di queste metodologie possono essere usate utilizzate facilmente con le attrezzature presenti in un normale laboratorio cosmetico.
Perciò sono state controllate nove diverse tipologie di TiO_2 presenti in commercio.
Con grande sorpresa si è visto che di questi campioni, soltanto quello ricoperto con un doppio strato di silicio e dimeticone rimaneva invariato a tutte le prove di stabilità a cui è stato sottoposto.

INTRODUCTION

Titanium Dioxide is widely used in cosmetic products and is well accepted by the consumer due to its outstanding safety profile. It has become a standard building block of high performance sun screen products. Numerous qualities of Titanium Dioxide are available. In particular, Aluminum Oxide coated materials are preferred due to the tightness of the coating, which gives them good photo stability. The current trend for modern sunscreens requires both a high SPF as well as significant UV A protection. Butyl Methoxydibenzoylmethane (BMDBM), due to its top performance and global regulatory approval, is the material of choice; and particularly since several suitable solutions have been developed for its photo stabilization. The compatibility of Titanium Dioxide with this powerful UV A filter is therefore a must. Although it has already been reported that there is an incompatibility between Aluminium Oxide coated Titanium Oxide and BMDBM, the impact of this interaction on the UV A performance was not studied in depth.

STABILITY AGAINST DISCOLORATION

BMDBM is well known to give color reactions with certain metal ions, e.g. with iron. The formed iron complex is deep red and is visible when present at a level of even a few ppm. The same discoloration will occur with TiO_2 qualities that bear a high level of impurities. Such discoloration can not be tolerated in consumer products. Here we describe a simple test that can be performed in an application lab and which will assess this quality. We compared different grades of Titanium Dioxide and their compatibility with BMDBM. The test setup is rigid, but gives a good indication as to what will happen under real usage conditions in a consumer formulation. The test is independent of the coating method of the TiO_2.

Description of the BMDBM compatibility test

Raw materials:

Caprylic/capric triglyceride	85%
Titanium Dioxide	10%
BMDBM	5%

Preparation

Disperse Titanium Dioxide in Caprylic/ capric triglyceride thoroughly. Add BMDBM and wait for 1hour at ambient temperature, then check for discoloration. Most likely you will need to look for two types of discoloration: yellow and red.
A yellow hue may be attributed to an incomplete coating which is caused by an excessively small primary crystal size below 17nm.
The red discoloration most likely originates from the presence of some residual iron coming from the crude TiO_2 source. If the iron impurity is present at too high a level in the TiO_2 crystal structure, there is no way to prevent the discoloration of the final product; not even by adding complexing agents like EDTA. If you observe a discoloration, most likely your final formulations will not be stable as well.

FORMULATION AND PERFORMANCE STABILITY

While iron forms colorful complexes with BMDBM, other complexes, such as those with Aluminium or Magnesium, are colorless. Nevertheless, there are other techniques to detect their presence. Certain aluminium complexes are marginally soluble in an emulsion system and can lead to crystal formation upon storage (figure 1). The crystals that form are large enough to

be detected easily by the consumer through the resulting gritty feel of the emulsion. We also found that the formation of the crystals can be accelerated through higher temperature storage (43° C), and the beginning of crystal formation can be seen with a microscope already after 2-3 weeks storage. Additionally, we followed the crystal formation by HPLC measurements (figure 1).

We further assessed the solubility of the BMDBM-Al complex in Alkyl benzoate and found it to be below 2 %.

The complex formation and resulting crystal formation not only destroys the sensory properties of a formulation, but also affects its performance. The efficacy decreases due to uneven UV filter distribution. Nowadays, as UV A protection is more in the focus of both consumers and authorities, it is recommended and in some cases required to demonstrate that the UV A protective properties of a product are stable also after a period of storage.

To elaborate the effect on performance, we investigated the incompatibility between the two components in regards to UV A in vitro performance measurements. We employed the MUT System and discovered a very significant performance loss in UV A protection after storage.

Figure 2 shows a dramatic decrease in the UV A region of an aluminium coated TiO_2 material vs. a silica/ dimethicone coated variant after storage. Each data point was assessed 5 times.

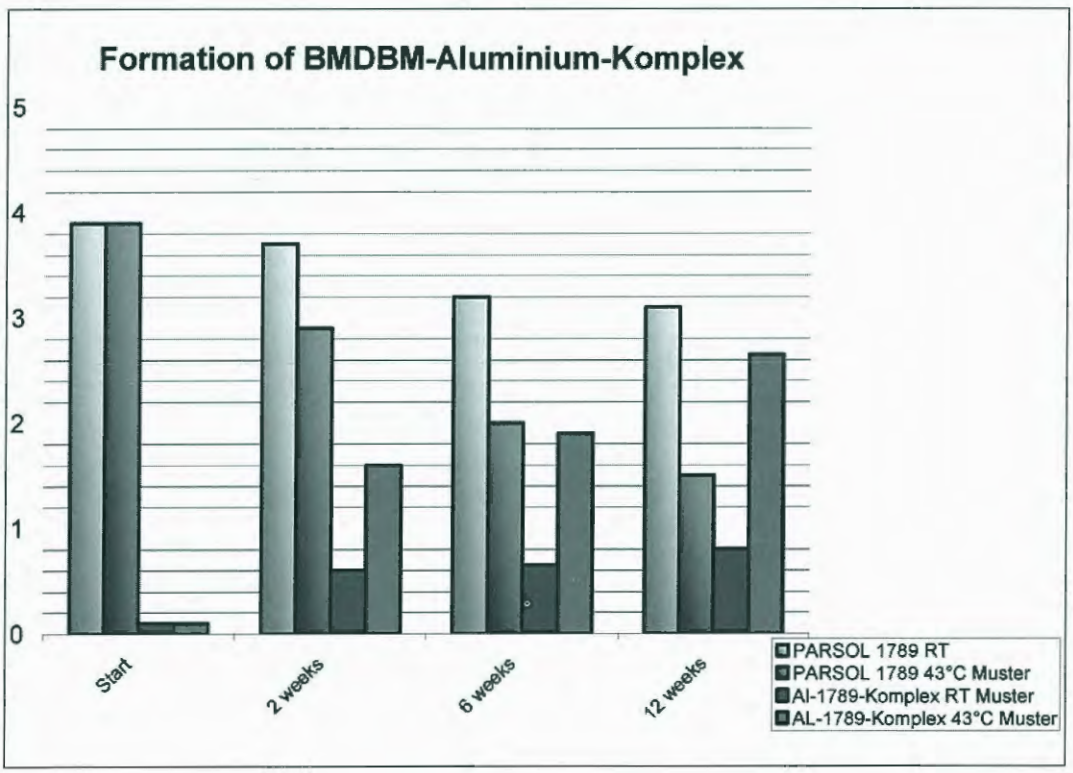


Fig. 1

PERFECTION OF COATING (APPLICATION LABORATORY METHOD)

Today all cosmetic TiO_2 qualities are coated to avoid catalytic reactions leading for example to oxidative stress. However, the degree of coating varies. Sometimes there is a residual activity left, which may lead to discoloration of the formulation and bears an unwanted risk for oxidative stress on the skin. It is therefore crucial that the TiO_2 used has a highly complete coating. The aluminium hydroxide treated TiO_2 often has a fairly good coating, however, as demonstrated earlier is incompatible with BMDBM. Silica/ and or Stearic Acid coatings are compatible; however it is difficult to achieve a perfect coating with these components. Through careful consideration of the product parameters and advanced methods, we have improved the quality of the silica coating and also added a second layer to reach a complete and non-reactive coating on the TiO_2. With an easy test, a bench chemist can check the integrity of the coated TiO_2 material. It simply requires the use of Ascorbylpalmitate and the visualization of the reactivity with this ingredient.

Description of the Vitamin C reactivity test

Composition of the test formulation:

Caprylic/capric triglyceride	88%
Titanium Dioxide	10%
Ascorbylpalmitate	2%

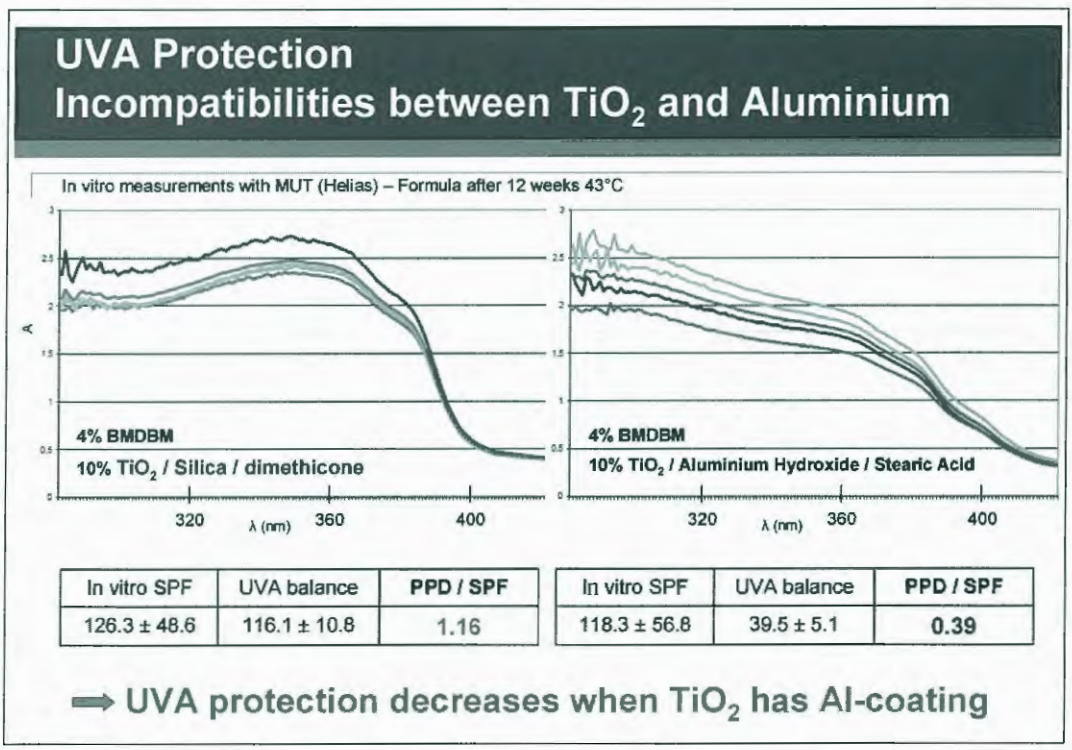


Fig. 2

Preparation

Disperse Titanium Dioxide in Caprylic/ capric triglyceride or in any other solvent of your choice; add Ascorbylpalmitate, shake well and wait for 2 hours. After the two hours, check for discoloration.
If TiO_2 is not well coated, you will see a beige discoloration initially, which intensifies over time. We have seen color formation up to dark brown. The test result is independent of the type of coating.
We made a comparison of 9 different commercial TiO_2 qualities incorporated into the test formulation and stored for 2 hours. In particular, materials with a primary particle size smaller than 20 nm exhibit increased reactivity and discoloration.

LIGHT STABILITY TEST WITH GAS PHASE PHOTO REACTOR

To perform this test specific equipment is necessary.
The principle of this test is to determine the decomposition of Propanol-2 into acetone and carbon dioxide.
To check the sample, 20 gr of TiO_2 is placed onto a Petri dish in this photo reactor. After preparation 1ml of 2-propanol is injected into the reactor. After a while UV light is switched on. The degradation processes of 2-propanol and the formation of acetone and CO_2 are monitored by using FTIR, as a function of time. After the photoreaction, the reactor is flushed with synthetic air to obtain information about the amount of substance of the remaining reactants and the products formed in the photo catalytic reaction (figures 3 and 4).
Under the influence of UV light, TiO_2 can become photoreactive and discolor. The anatase form of the TiO_2 crystal is particularly sensitive to UV exposure. A proper coating will also work to prevent this reactivity.
To perform this assessment a sun tester is required. We used the Suntest XL+ from Atlas. The minimum radiation dose is 40 MED. This test has been performed in cosmetic oil with and without additional UV filters; however, our recommendation is to use a simple dispersion of TiO_2 in Alkyl benzoate or Caprylic/Capric Triglyceride. Incorporating additional sun filters can lead to a false positive discoloration reaction.

PHOTOSTABILITY OF TiO2

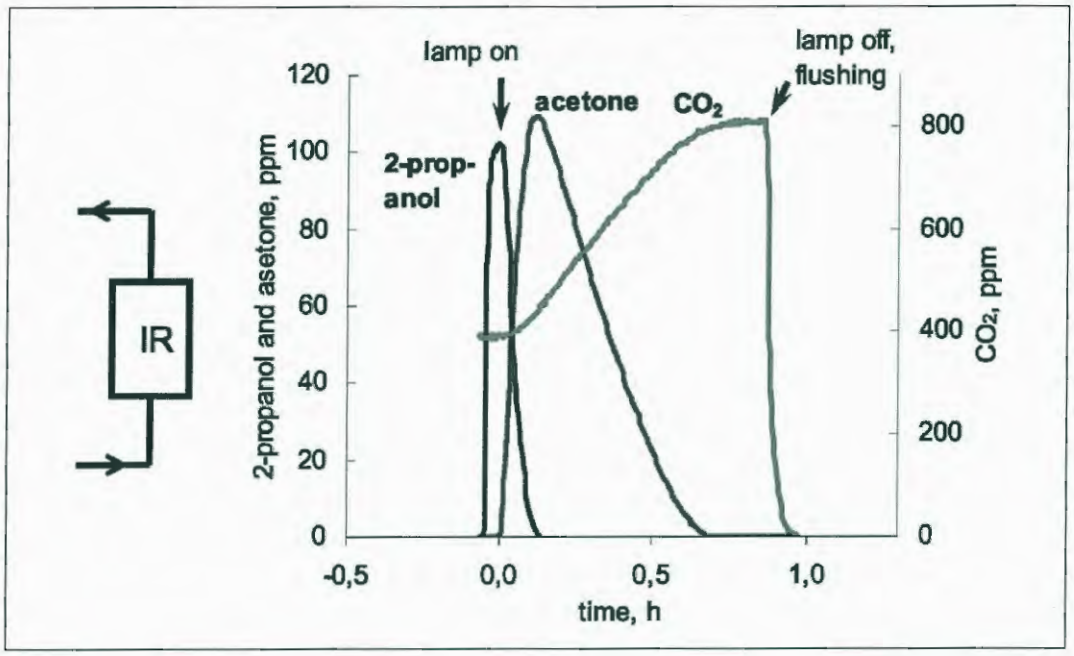
Description of the UV challenge Test

Test formulation:

Finsolv TN	90%
Titanium Dioxide microfine	10%

Preparation

Disperse Titanium Dioxide completely in Alkyl benzoate. Apply this dispersion with a 20 micron film applicator on to normal microscope slides. Cover it with another slide and put it into the Sun Tester. Radiate with 40 MED and check the color after radiation. After the radiation you may see a greyish/bluish discoloration which is indicative of photo reactive behavior.


lamp on
lamp off, flushing
acetone
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2-propanol and asetone, ppm
CO_2, ppm
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Fig. 3

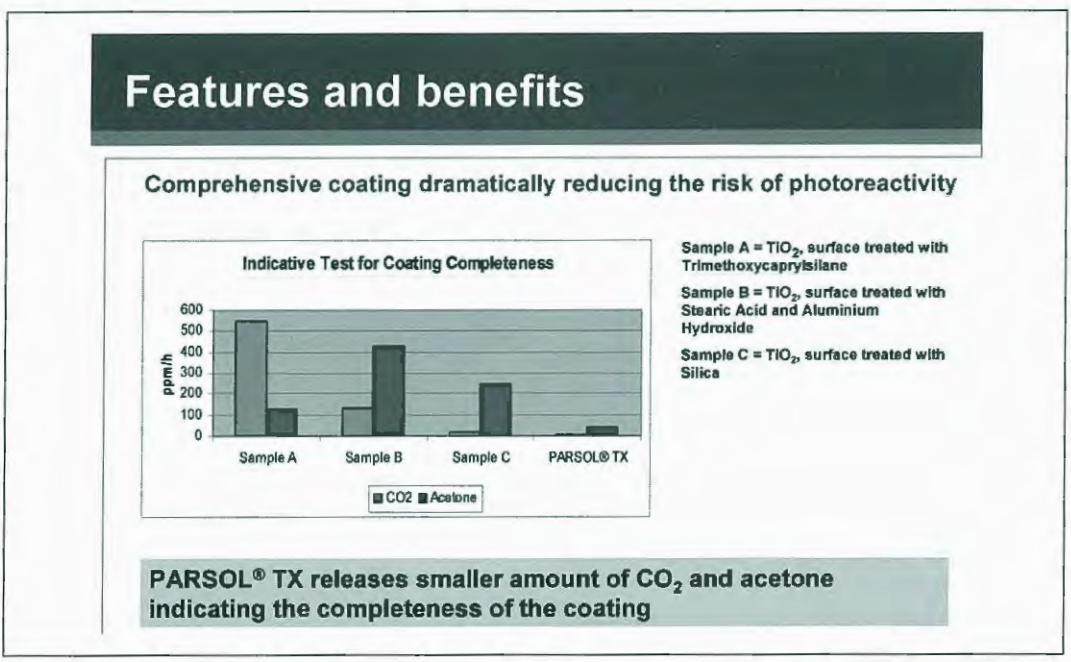
Features and benefits
Comprehensive coating dramatically reducing the risk of photoreactivity
Indicative Test for Coating Completeness
ppm/h
600
500
400
300
200
100
0
Sample A
Sample B
Sample C
PARSOL® TX
CO2
Acetone
Sample A = TiO_2, surface treated with Trimethoxycaprylsilane
Sample B = TiO_2, surface treated with Stearic Acid and Aluminium Hydroxide
Sample C = TiO_2, surface treated with Silica
PARSOL® TX releases smaller amount of CO_2 and acetone indicating the completeness of the coating

Fig. 4

DAY LIGHT PHOTO STABILITY OF TiO2 IN FORMULATIONS

All described tests above are challenge tests that can help to find the most appropriate TiO_2 grade in a relative early stage of the development work. But as we have learned in the past, not every challenge test gives you all the information you need to bring a product onto the market. In addition to indicative short term challenge tests, also long term testing should be performed to ensure that your product is stable and ready for launch. One particularly important feature is stability under ambient light conditions. It is recommended to perform this test even if all prior tests were passed without issues. Instability will be demonstrated by a discoloration of the formulation.

Description of the day light photo stability test

Test formulation:
Launch product formulation
Store the samples near the window, preferentially the north side of the building with minimal direct radiation.

Preparation

The products, filled in glass jars or in the finished packaging, are simply stored for 2 to 3 months near the window. In addition to color change caused by TiO_2 reactivity, oxidation of unstable ingredients and fragrances can be assessed.

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J. Appl. Cosmetol. **27**, 49-61 (April/June 2009)

PROTEIN MEMBRANES AS MODELS OF COSMETIC INGREDIENTS PENETRATION THROUGH BIOLOGICAL STRUCTURES

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Academy of Cosmetics and Health Care, Warsaw, Poland

Received: *November, 2008.*

Key words: *Nail plate; Stratum corneum; Keratin; Hair fibre; Cuticle; Hair dyes; Penetration; Model membrane;*

Summary

Interactions with proteins may influence on penetration through such biological structures as *stratum corneum*, nail plate, and hair fibre cuticle.
Current paper presents interactions affecting diffusion processes through *stratum corneum* (effects of keratin intermediate filaments), hair fibre cuticle, and through nail plate. There are presented artificial models imitating mentioned barriers.
Authors carried out studies concerning protein hair structure-like membrane. One can find results comparing penetration of oxidative hair dyes ingredients in artificial membrane and penetration into hair fibres.

Riassunto

La penetrazione attraverso lo *strato corneo*, il letto dell'unghia e le tegole cheratiniche del capello è influenzata dalle proteine presenti nelle relative strutture.
Questo studio pone in rilievo le interazioni che si verificano evidenziando gli effetti provocati dalle fibre di cheratina. Esistono modelli artificiali in grado di imitare l'effetto barriera provocato dalle proteine. Così è stato condotto uno studio utilizzando una membrana artificiale simile alle cheratine dei capelli per verificare la penetrazione di coloranti per capelli attraverso questa struttura.

INTRODUCTION

Interactions with proteins influence on penetration through such biological structures as *stratum corneum*, nail plate, hair fibre cuticle.

Although a major pathway for penetration through *stratum corneum* is intercellular lipid matrix route, there are examples of compounds that may have affinity to keratin filaments. Thus interaction with corneocytes may influence on penetration rates.

Another example of biological protein membrane is nail plate, indicated by most to have similar properties in penetration like concentrated hydrogel. One can find data concerning use of model (hoof bovine keratin) of nail plate in permeation studies.

Hair shaft is mainly built of keratin. Key factor in penetration process is a structure of hair shaft cuticle, more precisely: structure of cell membrane complex (CMC).

Studies on penetration tbrough all mentioned membranes may create difficulties. Sample preparation of skin *stratum corneum* may be costly, need special equipment. Because of that keratin hoof membrane are used for prediction of skin penetration (influence of keratin filaments). Sample preparation for nail plate penetration experiments also may be hard. Thus keratin obtained from bovine hoof is applied for such studies as a model. Penetration of chemicals into hair fibre can be assessed by many methods that are hardly accessible. Hair shafts obtained from one source (person) may be different comparing to those obtained from other. Because of that at the Academy of Cosmetics and Health Care studies concerning cross-linked protein membrane are carried out. We examined penetration into, and through model membrane. Parallel we have examined diffusion into yak hair.

STRATUM CORNEUM

Skin is the main layer which protects the body against exogenous substances. The main barrier is located in the outer layer of the skin: *stratum corneum* (1). It has a biphasic structure consisting of keratinized cells – the corneocytes – that are embedded in an ordered lipid matrix.

There are many papers dealing with structure of the *stratum corneum* (2-4). Most of them indicate that lipid lamellae are responsible for the main barrier function of the skin. Although lipids are seen to be main factor, organization of keratin filaments, major component of the corneocyte matrix, is also important.

Precise description of the structure of both lipid and non-lipid filaments in the *s.c.* is difficult.

The major lipid components of the *s.c.* are: ceramides, free fatty acids, cholesterol, cholesterol sulfate and sterol/wax esters.

The organization of the lipids is an issue of discussion. There are few models of structure and function of the skin barrier proposed, including the "brick and mortar" model (2), "domain mosaic model" (3). Another proposed model: the single gel phase was presented by Norlén (4). Current paper does not descript in details mentioned models, one can find those descriptions in the references (2-4).

The architecture of the keratin filaments also remains speculative (5,6). The three dimensional high-order organization of keratin has been discussed over the last 50 years. There are comprehensive reviews concerning structure of keratin filaments (5,6).

Transport of molecules through the *stratum corneum* is similar as diffusion of solutes across a composite membrane.

Penetration through stratum corneum

Skin penetration is an essential parameter in efficacy of active cosmetic ingredients activity.
Compounds can penetrate through skin by three potential pathways: through the sweet glands, hair follicles, sebaceous glands (called appendageal route), or directly across the *stratum corneum*. Diffusion through appendageal route is minimal, exceptions are iontophoretic drug delivery which uses electrical charge to drive molecules into the skin (7,8). For almost every compounds transport across *stratum corneum* is preferred one (Fig. 1).
Taking in consideration character of the penetrant, it can be conclude that hydrophilic chemicals diffuse within the aqueous regions near the outer intracellular keratin filaments, and lipophilic compounds diffuse through lipid matrix between the filaments. Of course situation like that is oversimplification. Molecules penetration via transcellular route must penetrate through lipid cement and diffuse through keratinocytes. Partitioning into and diffusing across multiple hydrophilic and lipophilic domains is unfavorable for most compounds. Because of that the intercellular pathway is considered as preferred one.
There are plenty of papers pointing lipid matrix as preferred pathway, especially for a lipophilic compounds, however there are some suggesting that binding to the protein filaments may also play a significant role (10).

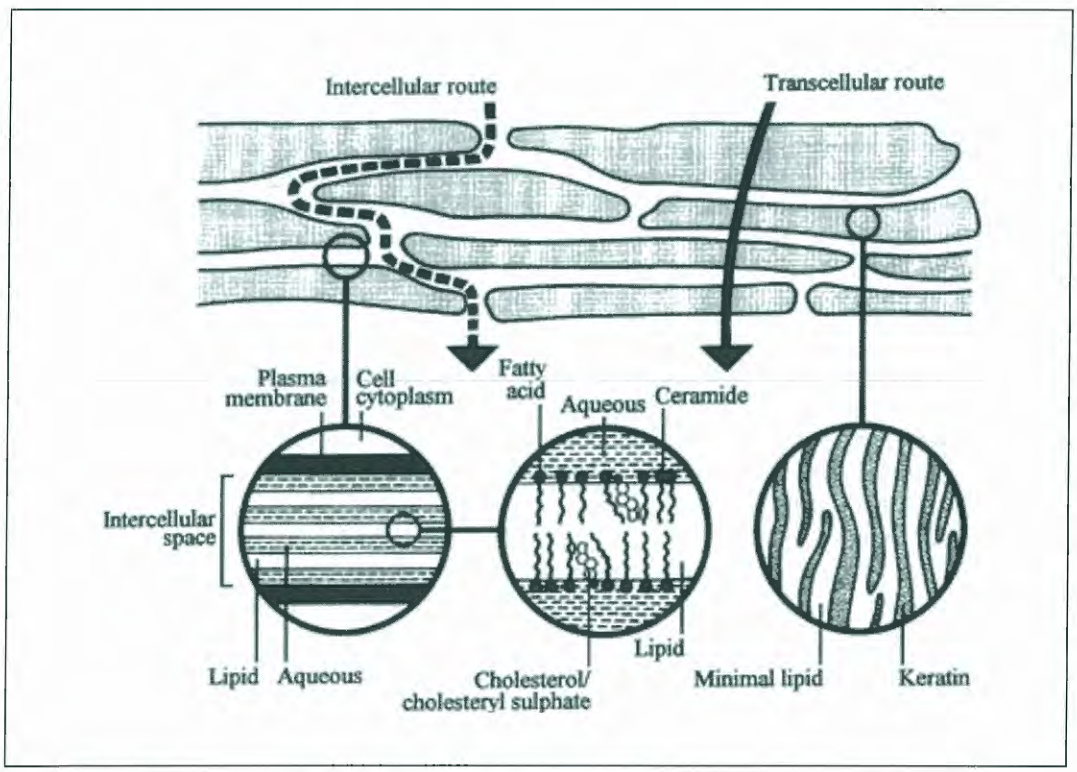

Fig. 1 *Schematic representation of stratum corneum and its intercellular and transcellular pathways of drug permeation, adapted from (9).*

Skin penetration studies are carried out on few models, including phospholipids vesicles model (11), as well as models based on pig, snake and human skin samples for *in vitro* experiments (12,13).

Banning and Heard (14) investigated binding of doxycycline, a licensed drug for prophylaxis of malaria, to keratin structures. They used as a model keratin from bovine horn. Data obtained suggests that during permeation process doxycycline may bind to epidermal keratin. That may involve a mixture of electrostatic and non-electrostatic interaction between oxygen atoms in the doxycycline and the hydroxyl groups present in the keratin aminoacids. The interaction with keratin filaments is not only factor that may influence on permeation process, as indicated in experiments carried out on human epidermal, both native and delipidised samples. They showed that more drug molecules bounded to native skin than delipidised samples, what suggests that doxycycline is able to interact with both keratin filaments and lipid matrix in the *s.c.*

Bovine keratin powder was also used as a model of human keratin filaments in the *stratum corneum* in studies of Heard et al. (15). They examined binding properties o primaquine, an antimalaria drug, to skin samples and as well as mentioned, to bovine keratin. Experiments carried out on delipidised samples showed that primaquine bound to the corneocyte. Experiments on bovine keratin showed that primaquine has affinity to the keratin. Authors claimed that bovine horn keratin does provide an indicative model for such experiments.

Another example of model of skin penetration, less frequently used, but worth noting is a keratin immobilized on silica, as stationary phase for chromatographic modeling of skin permeation (16). Modeling of skin permeation with use of chromatography was also performed with so-called immobilized artificial membranes (IAM), which are synthesized by covalent binding of tbe phospholipids to solid silica surface (17). In that model lipophilicity of penetrant is main factor. To model skin permeability one should take into account also possible interactions with keratin filaments. Turowski and Kaliszan (16) examined interaction of phenolic derivatives with prepared stationary phase. They observed that affinity to keratin may decrease permeability of skin, even though the lipophilicity of examined compounds increases. Taken together, retention parameters determined on the keratin column along with the retention parameters determined on the IAM column, can be useful for the skin permeability (16).

Skin penetration is an essential parameter in efficacy of active cosmetic ingredients activity. Penetration depends on the structure of penetrant and on structure of skin outer layer *stratum corneum*. *Stratum corneum* is a biphasic structure consisting of keratinized cells – the corneocytes – that are embedded in an ordered lipid matrix. Although the intercellular – through lipid matrix pathway is seen to be the major route of diffusion, interaction with keratin filaments may play role for some of the compounds. Experiments in that field are carried out *in vivo*, and *in vitro*. *In vitro* studies are more cost effective. There are skins samples derived from human and animals applied as models, as well as artificial models including phospholipids vesicles or immobilized on silica surface phospholipids, keratin obtained from bovine horn and immobilized on silica keratin as stationary phases for HPLC.

NAIL PLATE

Nail plate protects delicate tips of fingers and toes against trauma (18).

Topical application of drug to the nail plate is used in treatment of nail disorder like onychomycosis (infection of nail caused by fungi specie). When one considers nail permeability nail plate structure is a key factor.

The nail apparatus is built of the nail fold, nail matrix, nail bed, and the hyponchium, forming together the nail plate (Fig. 2) (19).

Nail plate is a thin elastic and hard translucent structure. Nail plate consists of approximately 25 layers of dead, keratinized, flattened, bound one to another. Each layer is linked via intercellular links, desmosomes and membrane-coating granules. Cells at the dorsal surface form smooth surface of the plate. Palmar surface of the nail plate is irregular (18). On the cross-section of the nail plate one can find three macroscopic stratas: dorsal, intermediate and ventral. The dorsal layer is thick for a few cells. Intermediate plate is a softer, is indicate as more flexible, and as a major layer when nail thickness is considered. The ventral layer is very thin, consists of a few layers of cells. That layer is responsible to connect the nail plate to the nail bed.

From chemical point of view plate is mainly built of fibrous proteins, keratins including hair-type hard keratin, as well as soft skin-type keratin (21). The hair-like keratin filaments can be found in the intermediate nail layer. Such filaments are oriented perpendicular to the growth axis. Skin type keratins are present in the ventral layers and are oriented in two directions transverse and perpendicular to the growth axis (22). Keratin fibres are held together by cysteine rich proteins – making possible disulphide bridges formation. S-S links act as glue. Among proteins, plate contains also water (10-30%), humidity of the plate is important for nail flexibility and elasticity. The nail plate contains as well small amounts of lipid. They are oriented into bilayers, and can be found in the ventral and dorsal nail layers (22).

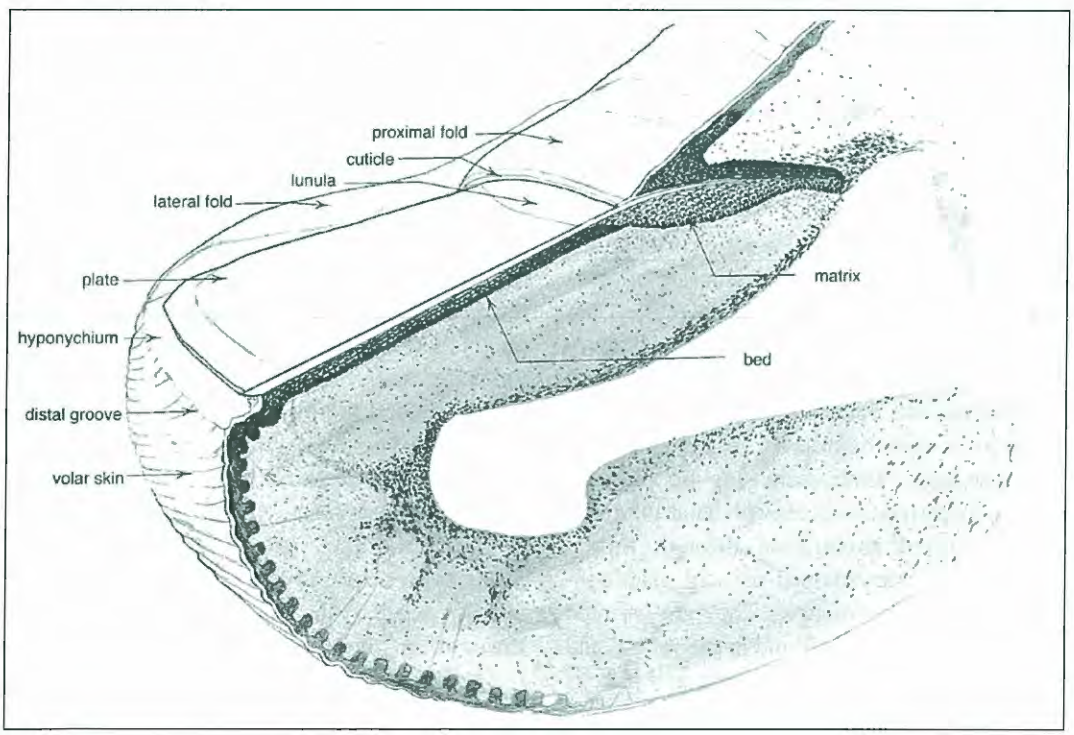

Fig. 2 *Nail apparatus, adapted from (20).*

As was mentioned above topical application onto nail plate is used for treatment of nail apparatus disorders. Being applied, drug molecules have to enter nail plate and diffuse into deeper layers, into nail bed. Penetration of different chemicals through human nail plate was widely investigated (23,24). Walters et al. (25) suggested that nail plate behave rather like hydrogel than lipophilic membrane. Interesting studies were carried out by Mertin and Lipold (23). They compared penetration through nail plate, and diffusion through polymers, and they concluded that keratin fibres may create holes ('pores') that are formed because of the thermal movement of the keratin fibres. Transport through plate may occur due to the partition mechanism. Penetration of drug through nail plate is thus influenced by physico-chemical properties of permeant such as: size, shape of the chemical structure, charge, lipophilicity.

Influence of permeant properties

As was pointed above, human nail plate is similar in the properties to hydrogel, rather then lipophilic membrane. Such dependency is presented in several published studies. Walters et al. (26) examined the permeation of a series of homologous alcohols (C_1-C_{12}). Penetration rate of alcohols from methanol to octanol decreased, the more lipophilic penetrant, the less of such penetrant permeated. Authors concluded that nail plate behaved like concentrated hydrogel.

Interesting is analysis of the C10 and C12 alcohols permeation. With increasing lipophilicity pentration rate increased as well. That is probably due to the penetration through lipidic pathway. As was mentioned the nail plate contains small amounts of lipid. They are oriented into bilayers, and can be found in the ventral and dorsal nail layers. Lipid level in the nail plate is very low (up to 1% w/w), however for very lipophilic compound it seems to be preferred route of penetration.

On the contrary, Martin and Lippold (27) found that the permeation coefficients of alkyl nicotinates are not caused by lipophilicity of penetrating compounds. There was no influence of increasing lipophilicty on decrease of penetration rate. Authors suggested that such results were an effect of properties of nail plate.

Kobayashi et al. (28) developed a modified side-by-side diffusion cell using nail tip pieces from healthy volunteers to investigate the nail penetration mechanism. They were carrying out experiments on p-hydroxybenzoic acid ester penetration. Drug diffusion in the upper layer of human nail plate is the limiting stage of the transport phenomena. That layer is the main barrier to nail permeation.

Like elsewhere (23,25) Kobayashi et al. (28) indicated that nail plate is similar in "penetration properties" to hydrogel. They did not found lipidic pathway in the nail plate. Penetration depended on penetrant molecular weight, i.e. on the drug diffusivity.

Another factor which may influence on penetration is charge of the drug, what was shown in the studies performed by Martin and Lippold (27) concerning penetration of benzoic acid and pyridine. It seems that dissociation of benozic acid (in pH higher than 2.0) (27) and pyridine (in pH lower than 7,4) leads to reduction in penetration rate (18). It may be caused by Donnan effect i.e. the electrostatic repulsion between the charged membrane and the like-charged diffusing molecule (23). The isoelectric point of keratin is thought to be around 5 (29). Thus, keratin is negatively charged at pH 7.4 and has positive charge at pH 2.0. At pH 7.4, the benzoic acid is in the form of negatively charged benzoate ion and is repelled by the negatively charged keratin, lower affinity between the nail plate and the diffusing ion at pH 7.4, results in decreased diffusion of solute through the plate. In an acidic medium at pH 2.0, the pyridine is found to be in

the form of pyridinium cation that is repelled by the positively charged keratin, and as well diffusion is retard (18).

Difficulty in evaluation of products for nail apparatus diseases is mainly caused by the lack in proper *in vitro* model for penetration through nail plate. Because of that many studies have been caring out to simulate penetration through nail plate as well as nail bed which nail plate is glue to. Kim et al. (30) developed such a model based on porcine hoof membrane. Precise instruction for the model membrane preparation one can find elsewhere (30). In Kim et al. experiment ciclopirox was used as a model drug. It was applied in the commercial lacquer on the dorsal side of the porcine hooves. Each porcine hoof was placed into the plastic chamber on a poloxamer gel. Poloxamer was chosen as the receptor because in the condition of the described penetration experiment it is in the gel form and that makes possible intimate contact with hoof membrane.

Authors compared the nail penetration *in vivo*, with nail penetration model. When comparing with other results obtained by Ceschin et al. (31) they found good correlation between *in vitro* results (from experiments carried out on hoof membrane and poloxamer gel) and *in vivo* human nail plate penetration studies. They concluded that such a membrane can be an adequate model for prediction of penetration through the nail.

HUMAN HAIR SHAFT

Hair fibres, among keratin filaments of the *stratum corneum*, and human nail plate are another example of protein complex membrane material. Description of factors, pathways in which chemicals may diffuse into hair shaft may give interesting data useful in hair conditioning, hair regenerating, as well in hair dyes molecules transport and as a consequence color effect on hair.

Penetration into hair shaft may be evaluated using many methods including microspectrophotometry, scanning near-filed optical microscopy, confocal laser scanning microscopy, or scanning electron microscopy (32), however all these methods need specialist analytic equipment. Because of that we have been carrying out experiments concerning model of hair fibre structures.

Morphologically hair fibre contains different unit. First, the outer layer contains flat cover lapping scale-like structures and is called cuticle. Cuticle covers the inner part of hair fibre – the cortex. This region contains macro fibrils, each fibril contains micro fibrils, and each micro fibril is build of α-keratin chains. Cortex consists of spindle–shaped cells that are aligned along the fibre axis. Cortical cells contain tbe fibrous proteins (33). Near the centre of hair fibre lays loosely packed porous region – the medulla.

The cuticle is the major part of hair fibre that influence on diffusion processes. Because of that the structure of cuticle is described in details.

The scales are formed in ratchet-like structure. This part of the fibre is built in high percentage of cysteine (34). The cuticle has a lay, scale structure. Thin outer part is epicuticle, than A-layer (high cysteine coutent (up to 30%). The exocuticle - also known as the B-layer, and beneath lays the endocuticle. The most inner part of the cuticle is under membrane (epicuticle of underlying cells).

Between endocuticle and epicuticle of underlying cells, cell membrane complex (CMC) is situated.

What is important the CMC is the major pathway for diffusion into hair structure, this feature is connected to the chemical composition of intercellular matter. It consists of cell membrane and adhesive material. Intercellular matter has scalping structures. Most important of which is the central delta layer, its proteins contains low level of cytseine aud high level of polar ami-

noacids, as Robbins claimed 12% are represent by basic amino acids, 17% by acidic amino acids (33). δ-layer is coated from both sides by inert β-layers, these layers are built of lipid components, such as squalene, fatty acids, i.e. palmitic, stearic, oleic acids (35).

Cell membrane complex together with endocuticle layer are called "nonkeratinous regions". They are soft and characterized by a large potential for swelling in aqueous solutions. Because of that these two parts of hair structure are believed to be the major path of diffusion processes into the hair fibres (36) (Fig. 3).

Diffusion into hair shaft

There are two theoretical pathways into human hair (37). Transcellular penetration route is connected with diffusion through the cuticle cells. Transport by this pathway means diffusion across both high and low cross-linked proteins. Second possible way of flux into hair fibre is an intercellular pathway (Fig. 3). It involves penetration between cuticle cells, through intercellular cement, region with low cross-link density.

Although transport by both pathways is possible, intercellular route is preferred for large molecules, like large cationic dye – rhodamine, because the low-sulphur, non-keratinous proteins are more easily swollen than the highly cross-linked regions.

Diffusion of chemical substances into hair depends on their condition. Penetration is faster into damaged, than unaltered, untreated hair. In some conditions transcellular route is preferred. When highly cross-linked A-layer and exocuticle in the cuticle are damaged, small molecules would diffuse through the cells (33).

As in the case of nail plate, and human *stratum corneum*, preparation of human hair sample for penetration studies may be difficult. Hair fibres from one source (person) are different than fibres taken from other. Standardization of sample may be problematic; because of that, simple model, making possible obtaining quick, repeatable results may be good alternative for experiments carried out on hair samples.

We have been caring out experiments on cross-linked protein membrane. Such protein film would be good tool for studies concerning penetration into hair structures, e.g. penetration of hair dyes ingredients. It can be useful for assessment of interactions occurring between hair shaft structure and penetrating compounds.

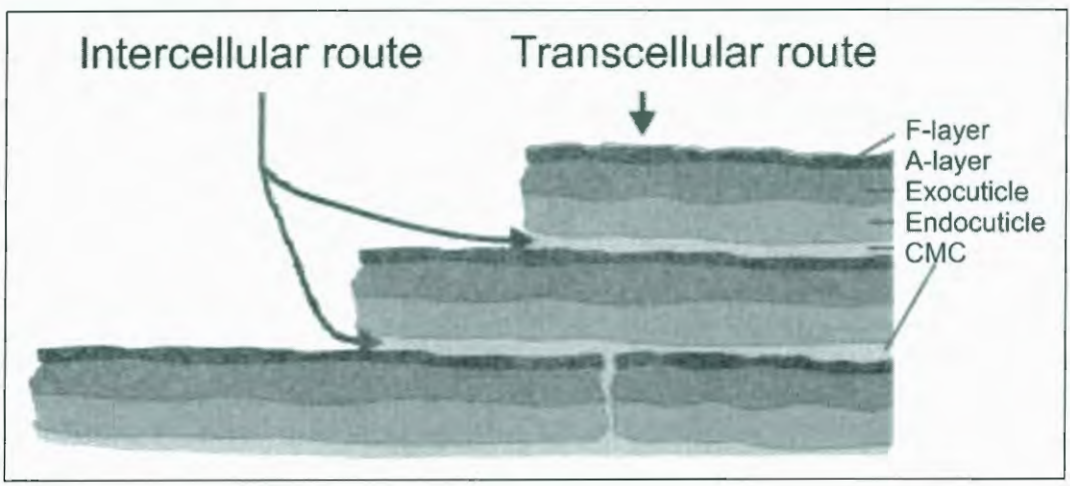

***Fig. 3** Penetration pathways into hair fibre, adapted from (36).*

Model membrane was formed by crosslinking of collagen with formaldehyde. As it was described above, main route for penetration into hair fibre is cell membrane complex in the cuticle. CMC consist of two layers made of lipid structures, and delta layer built of protein with low content in cysteine and high in polar amino acids. Crosslinked hydrolyzed collagen seems to be similar in properties as unordered proteins in delta layer of CMC in hair cuticle.

Another reason for choosing collagen is simplicity in membrane preparing. Crosslinking hydrolyzed collagen with formaldehyde is simple, quick method for protein film preparation. Furhermore that method is highly repeatable, what makes possible using such film as a model for hair shaft penetration studies.

Efficacy of hair dyeing, when oxidative hair dyes are used, depends on penetration of precursor and couplers into hair shaft. Precursors and couplers are the substrates in the oxidative polycondensation reaction that yield to colorful product that change the color of hair shaft. To obtain permanent effect, precursor and couplers must penetrate into hair shaft and there undergo reaction with oxidizing agent (such as solution of hydrogen peroxide).

We have examined diffusion across protein cross-linked film of two precursors: p-phenylenediamine and 2,5 toluenediamine, and three couplers: resorcinol, 2-methylresorcinol and 4-chlororesorcinol (Fig. 4).

Our results suggest that penetration through membrane cannot be described as penetration through concentrated hydrogel (like it is in the case of nail plate). Penetration depends on many parameters, including lipophilicity of penetrating compound, molecular size (described by molar volume), as well as ability for interactions with membrane material (including ability for H-bonds formation).

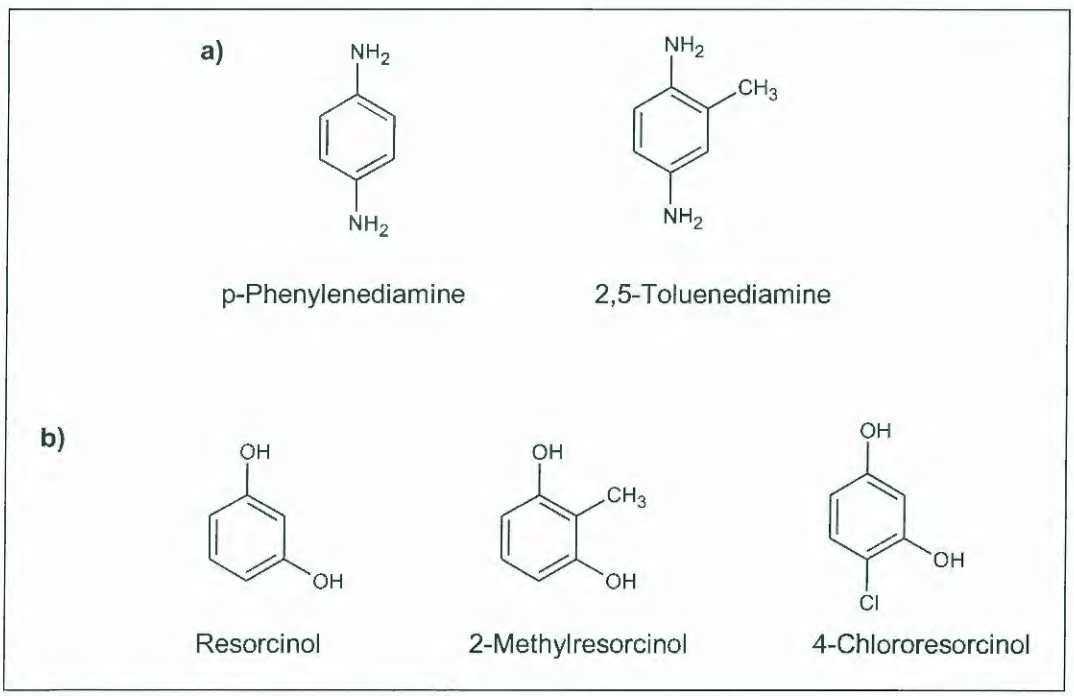

Fig. 4 *Examined oxidative hair dyes ingredients: a) precursors; b) couplers.*

Interaction occurring between molecules of the penetrants and model membrane, i.e. possibility of hydrogen bonds formation between amino, and hydroxyl groups in precursors and couplers molecules and side groups of aminoacids of the model protein membrane seem to be one of the major parameter that affects penetration process. Parallel we investigated penetration into yak hair, to check if our model membrane is similar in properties as the cuticle of hair fibre. Characteristic of precursors and couplers penetration into membrane is similar to those obtained after study with hair yak fibres. It can be concluded that similar properties affected penetration into both protein model membrane and hair fibres.

Full data concerning mentioned above studies will be published soon.

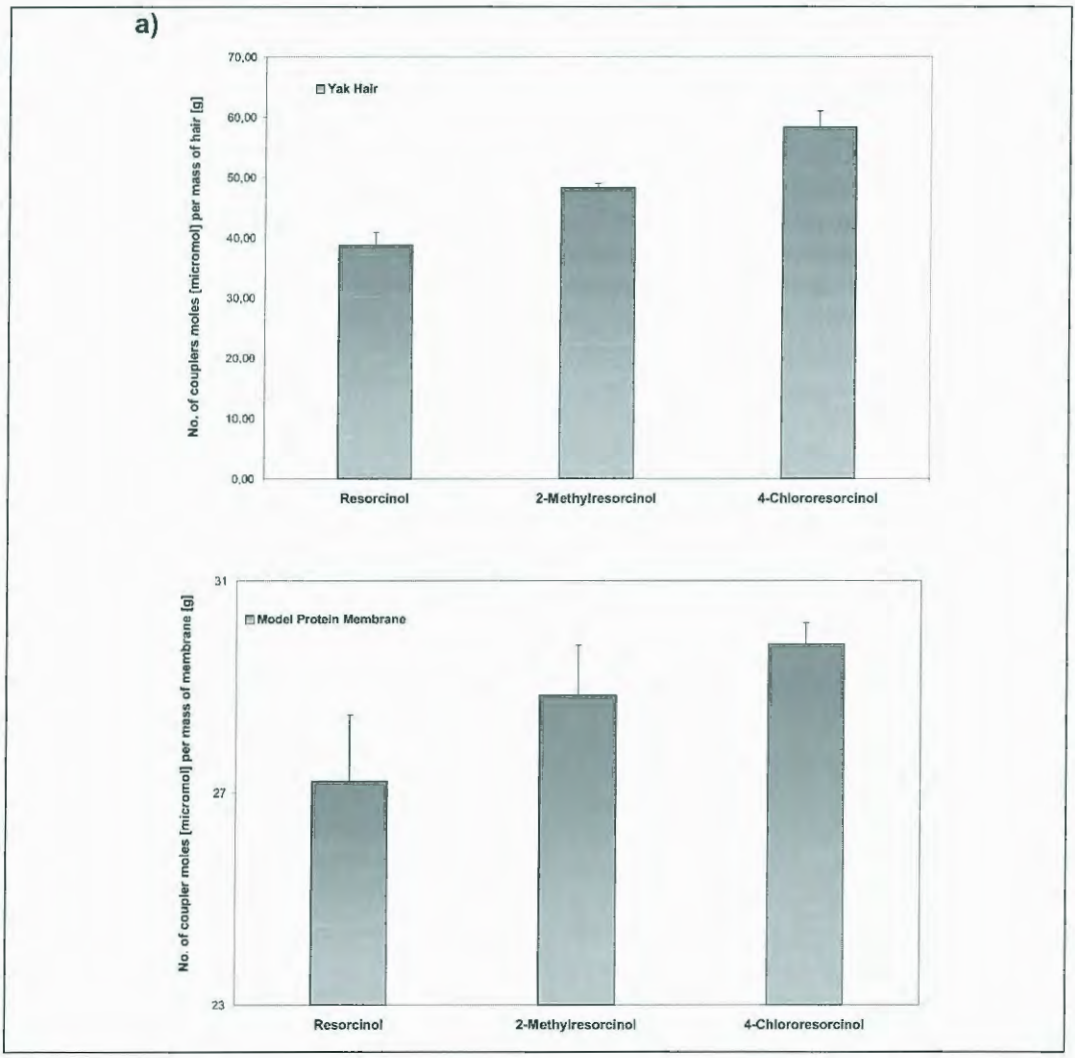

Fig. 5a Amount of oxidative dyes: couplers.

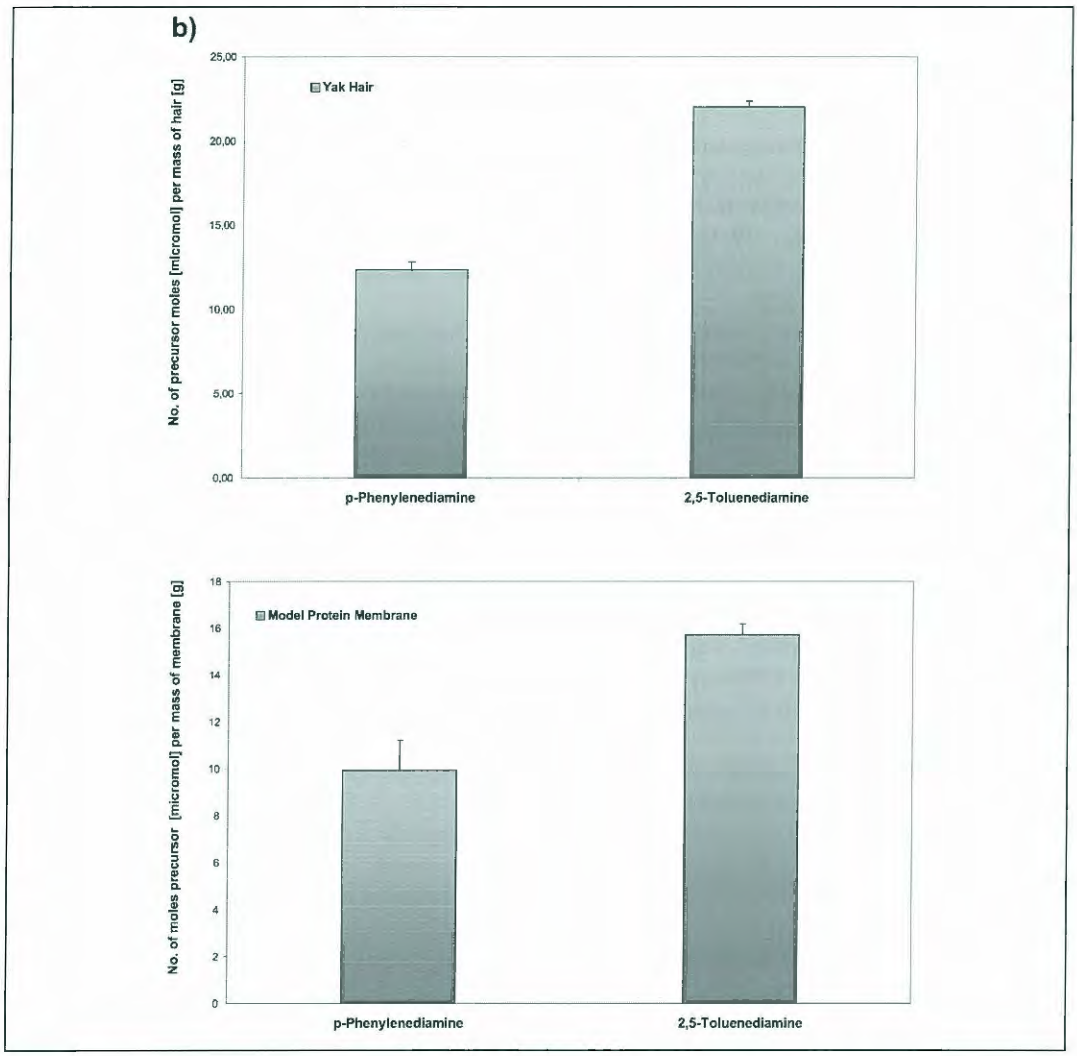

Fig. 5b Amount of oxidative dyes: precursors that diffused respectively into hair fibre and protein membrane.

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COUNTERACTING AGING PHENOMENA BY NEW PURE TETRAPEPTIDES WITH TARGETED EFFICACY

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Summary

In the skin, proteoglycans are present both in the epidermis and the dermis. In the latter layer, a group of small proteoglycans (< 60 kDa) plays an important role in fibrillogenesis, growth factors modulation and dermal homeostasis. The epidermis also synthesizes several small proteoglycans, involved in keratinocyte functionality.

The knowledge about the alteration of the synthesis and the structure of such small proteoglycans during skin aging used to be rather limited in the past. In fundamental studies, Laboratoires Sérobiologiques could recently identify two small proteoglycans whose influence in skin proper functioning is significant, and whose synthesis decreases with aging. Lumican is located in the dermis, where it is involved in the formation of the collagen fibers and consequently in the skin firmness and thickness. Syndecan-1 occurs preferentially in the supra-basal layers of the epidermis; it is jointly implicated in the epidermal cohesion.

The dermo-epidermal junction assures the connection between dermis and epidermis. With certain anchor molecules like collagen XVII, hemidesmosomes attach the basal cells to the basal membrane.

The stimulation of the synthesis of lumican in dermal cells, of syndecan-1 in epidermal cells and of collagen XVII in the basal layer counteracts the aging process on three different levels in the skin. In order to identify ingredients with a corresponding activity, skin specific DNA-arrays were used, allowing to selectively analyze the expression of genes highly implicated in the skin physiology. Two efficient acetylated tetrapeptides (respectively AcTP1 and AcTP2) were selected.

The efficacy of both peptides was further demonstrated on cell cultures, skin models and finally in clinical studies.

Riassunto

I proteoglicani sono presenti sia a livello dell'epidermide che del derma. Nel derma un gruppo di proteoglicani a basso peso molecolare (p.m) (<60k Da) gioca un ruolo importante nella fibrillo genesi, nella modulazione dei fattori di crescita e nell'omeostasi di questo strato cellulare. Comunque, anche l'epidermide sintetizza diversi piccoli proteoglicani, coinvolti nella funzionalità dei cheratinociti.
Negli anni passati l'alterazione che si verifica durante l'invecchiamento nella sintesi di strutture quali i proteoglicani a basso p.m era poco conosciuta. Recentemente i laboratori della Seròbiologique hanno identificato due piccoli proteoglicani che influenzano in modo significativo le funzioni cutanee, la cui sintesi viene a ridursi durante l'invecchiamento.
Così il proteoglicano denominato Lumican è localizzato nel derma dove è coinvolto nella formazione delle fibre di collageno e quindi nello spessore e nella compattezza della cute.
Il proteoglicano Syntecam-1 si riscontra normalmente negli strati soprabasali dell'epidermide ed è implicato nella coesione delle cellule epidermiche.
La giunzione dermo-epidermica rappresenta il punto di congiunzione tra epidermide e derma attraverso l'attività di legame svolta da alcune molecole quali il collagene XVII e gli emodesmosomi.
La stimolazione esercitata rispettivamente da Lumican a livello delle cellule dermiche e del collagene XVII esercita un effetto positivo sul processo dell'invecchiamento cutaneo a tre diversi livelli.
Per verificare l'effettiva attività svolta dagli ingredienti in studio, ne è stata verificata l'efficacia con una serie di DNA specifici analizzando selettivamente l'espressione dei geni implicati a livello fisiologico. Sono stati così selezionati due specifici tetrapeptidi acetilati (AcTP1 e AcTP2). L'efficacia di entrambi i peptidi è stata dimostrata su culture cellulari, su modelli di cute ed infine a livello clinico.

INTRODUCTION

Cosmeceuticals or so-called 'doctor' brands have recently enjoyed increasing appeal to consumers because they offer anti-ageing benefits without the need to undergo invasive procedures. To achieve this, a growing number of active ingredients is being incorporated into skincare products.

This trend holds out the possibility of sustainable growth for cosmeceutical products but also poses challenges to suppliers of active ingredients. Cosmetics manufacturers are seeking ever more effective and innovative cosmetic ingredients, such as enzymes, amino acids and peptides, with identified and specific mechanisms of action and demonstrable benefits that perfectly fit into the growing cosmeceutical trend.

The phenomenon of skin ageing and the identification of its biological pathways remain a constant focus of many research programmes. Laboratoires Sérobiologiques (LS), the active ingredient business of Cognis Care Chemicals, has recently undertaken a fundamental research study targeting one specific family of molecules, small proteoglycans.

Small proteoglycans are characterised by glycosaminoglycan chains fixed to a linear core protein by covalent bounds. They are present both in the epidermis and the dermis and act as biomechanical supports, tissue organisers and biological filters, thereby playing an important role in skin homeostasis. However, knowledge of their synthesis and structure during skin ageing has always been rather limited.

Our research programme has identified two specific proteoglycans – lumican1 and syndecan-1 - whose synthesis counteracts the ageing process in the skin and has been demonstrated to decrease with ageing.

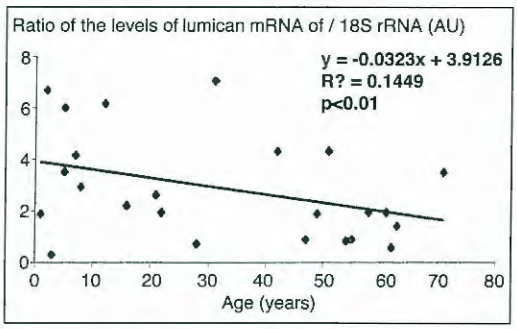

Fig. 1 Lumican during skin aging – Variation in dermal fibroblasts with age (Northern-blot).

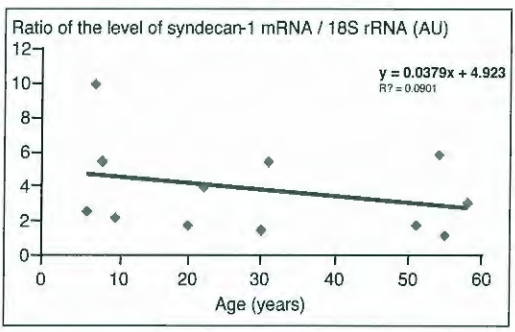

Fig. 2 Syndecan-1 during skin aging – Variation in keratinocytes with age (Northern-blot).

Lumican is located in the dermis, where it is involved in the formation of collagen fibres and consequently in skin resistance to traction. Syndecan-1 occurs preferentially in the suprabasal layers of the epidermis and is involved in epidermal cohesion.

In order to identify ingredients with corresponding activity, skin-specific DNA arrays[2] were used. This allowed us to screen selectively potential actives that would influence the expression of genes coding for the two identified proteoglycans but also growth factors and structural proteins involved in skin structure and homeostasis.

Based on these findings, LS has developed two new pure tetrapeptides, **ACTP1** (INCI name: Glycerin (and) Acetyl Tetrapeptide-9) and ACTP2 (INCI name: Glycerin (and) Acetyl

Tetrapeptide-11), which are designed to fight the skin ageing process. The efficacy of both was further demonstrated on cell cultures, skin models and finally in clinical studies.

At the dermis level: to optimize collagen fibers functionality

ACTP1 has been singled out for its unique biological anti-age action, which is targeted at increased collagen network functionality via lumican synthesis. DNA array tests[2] made it possible to evaluate ACTP1's influence on the general gene expression profile of dermal fibroblasts including lumican and the structural protein COL1A1 coding for collagen I.

Stimulation of lumican synthesis by aged human dermal fibroblasts showed that ACTP1 achieved increases of 66% and 115% over a control in the expression index, as measured in terms of the number of stained pixels by fluorescence intensity of the green channel in arbitrary unit, when used at 0.74 and 2.2 µg/ml respectively. IL-4 at 0.1 µg/ml scored a 73.6% increase over the control

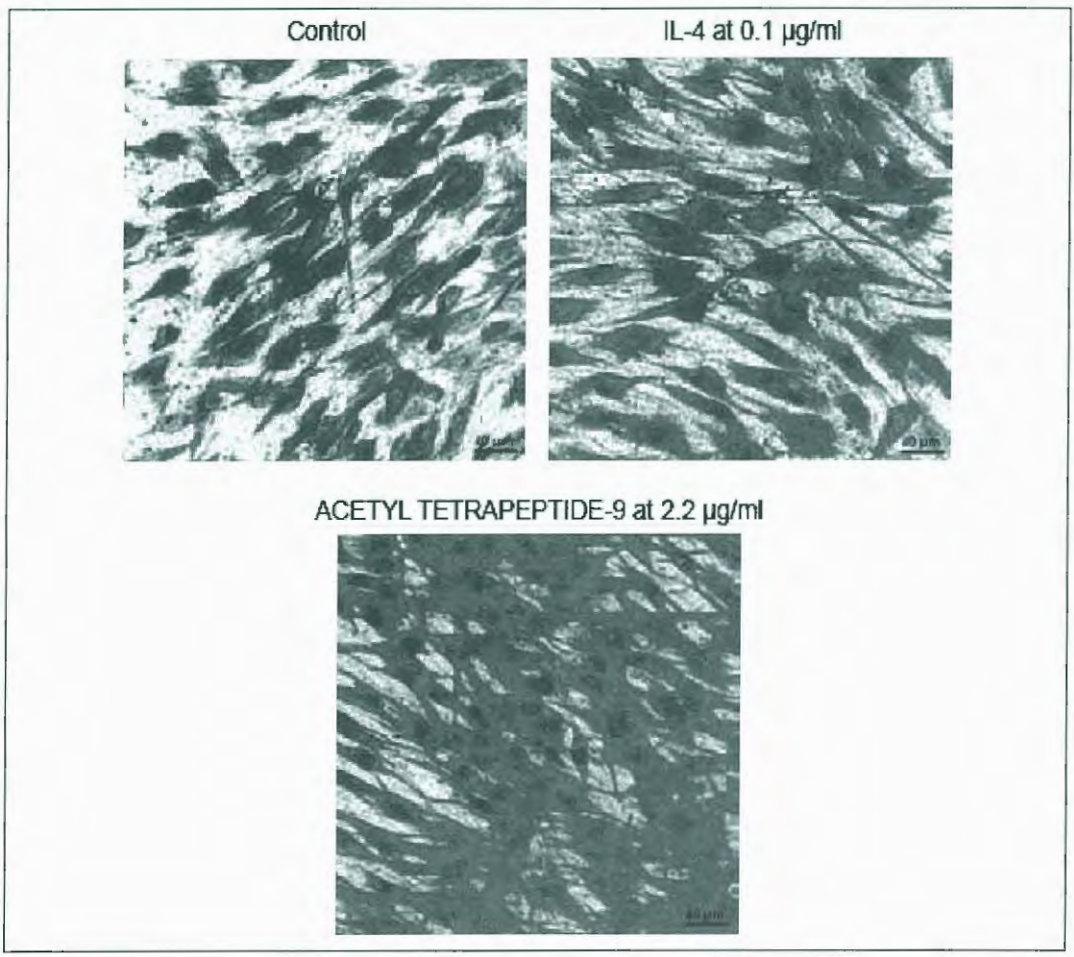

Fig. 2 Stimulation of lumican synthesis by aged human dermal Fibroblasts: vizualisation (lumican in green).

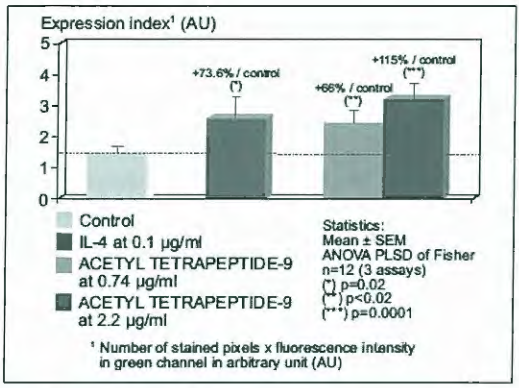

Fig. 3 Stimulation of lumican synthesis by aged human dermal Fibroblasts: quantification.

Likewise, in the expression of COL1A1 gene, 2.2 µg/ml ACTP1 showed a 22% increase over the control, while TGF-β1(the reference substance)[3] at 10 ng/ml showed a 125% increase. In the stimulation of collagen I synthesis, ACTP1 showed increases of 49% and 112% at 2.2 and 7.4 µg/ml respectively; TGF-β1 at 3 ng/ml showed a 65% increase. For proteins in the same test, the increases were 4%, 5% and 20% respectively.

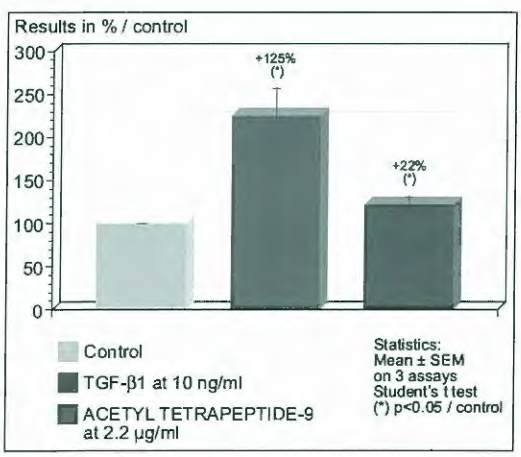

Fig. 4 Stimulation of the expression of collagen I COL1A1 gene by human dermal fibroblasts.

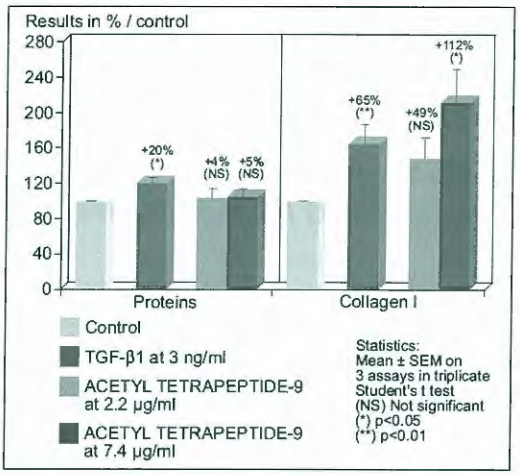

Fig. 5 Stimulation of collagen I synthesis by human dermal fibroblasts using DOT-BLOT technique[4].

Thus, lumican is directly involved in the synthesis of the collagen fibers (fibrillogenesis) and consequently in the organisation of the collagen bundles, resulting in tighter and firmer skin. Several in vitro tests have demonstrated ACTP1's capacity to boost the synthesis of lumican and collagen I.

ACTP1's efficacy and tolerability were demonstrated in a clinical study with 17 female volunteers aged between 45 and 55. After four months of treatment, it induced an increase in skin thickness (evaluated on the forearm by echography/ultrasound[5,6] using the 2D DermaScan C® equipment with a 20MHz probe) and an improvement of skin firmness (the evaluation of variations in the extensibility and elasticity of superficial cutaneous layers was performed using a SEM 575 CUTOMETER®[7]).

By acting both on the structure and mechanical properties of skin, it confirmed its anti-ageing efficacy, leading to a firmer and plumper skin. With ACTP1, we are moving to the next generation of anti-aging products. Beyond collagen synthesis, we also ensure that newly synthesized fibers are fully functional.

Based on its mechanism of action, this active

ingredient is also suitable for other applications related to firmer skin, and it is thus distinctly possible that ACTP1 may improve stretch marks as well.

At epidermis level: to restore the radiance and firmness of mature skin

With age, the epidermis loses its resistance and radiance, mainly due to reduced cohesion of the epidermal cells. As a result, skin becomes dry and slack and is easily damaged with even the lightest friction or shock. To prevent this, manufacturers of personal care products must design products to meet the specific needs of mature skin.

ACTP2 specifically targets the two constituents of the epidermis that are primarily responsible for its cohesion: syndecan-1 and collagen XVII. The latter is a protein that occurs in the hemidesmosomes, a microscopic, rivet-like structure that affects the strength of the bond between the epidermis and the dermo-epidermal junction[8].

The overall effects of ACTP2 were established by DNA array[2] technology. This test made it possible to evaluate ACTP2's influence on the general gene expression profile[9,10] of human primary epidermal keratinocytes.

Several in vitro tests on keratinocytes demonstrated ACTP2's ability to boost the synthesis of syndecan-1, reinforcing epidermal cohesion, and the production of collagen XVII protein, leading to an improvement of the adhesion between the epidermis the and dermo-epidermal junction.

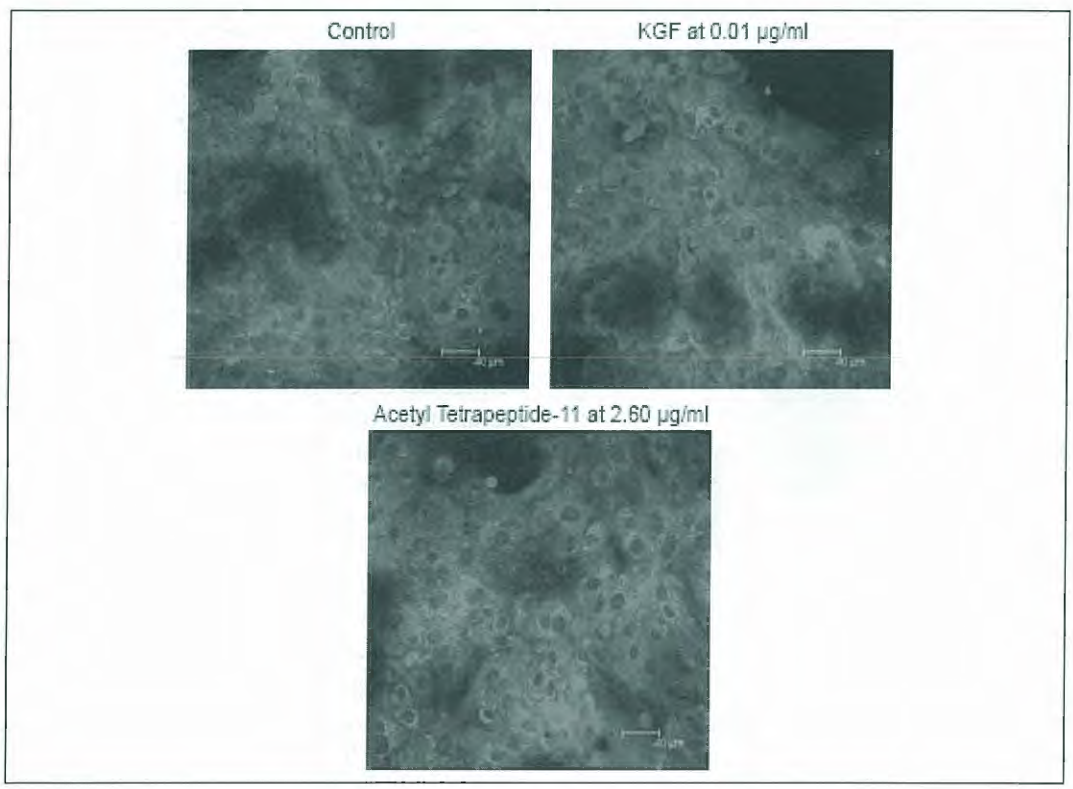

Fig. 6 *Stimulation of syndecan-1 synthesis by human keratinocytes: visualization at 5 days (syndecan-1 in green).*

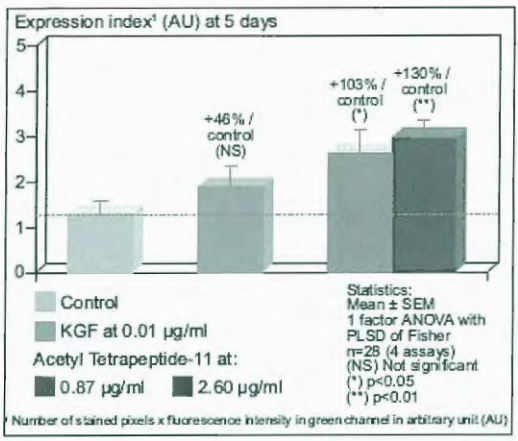

Fig. 7 *Stimulation of syndecan-1 synthesis by human keratinocytes: quantification.*

Over five days, ACTP2 achieved increases of 103% and 130% in the synthesis of human keratinocytes by comparison with a control, as measured by the number of stained pixels by fluorescence intensity of the green channel in arbitrary unit, when used at 0.87 and 2.6 µg/ml respectively. KGF (the reference substance[11]) at 0.01 µg/ml, meanwhile, scored a 66% increase over the control.

In the expression of the collagen XVII COL17A1 gene over three days, meanwhile, ACTP2 achieved increases of 13% and 18% over a control when used 0.87 and 2.6 µg/ml respectively.

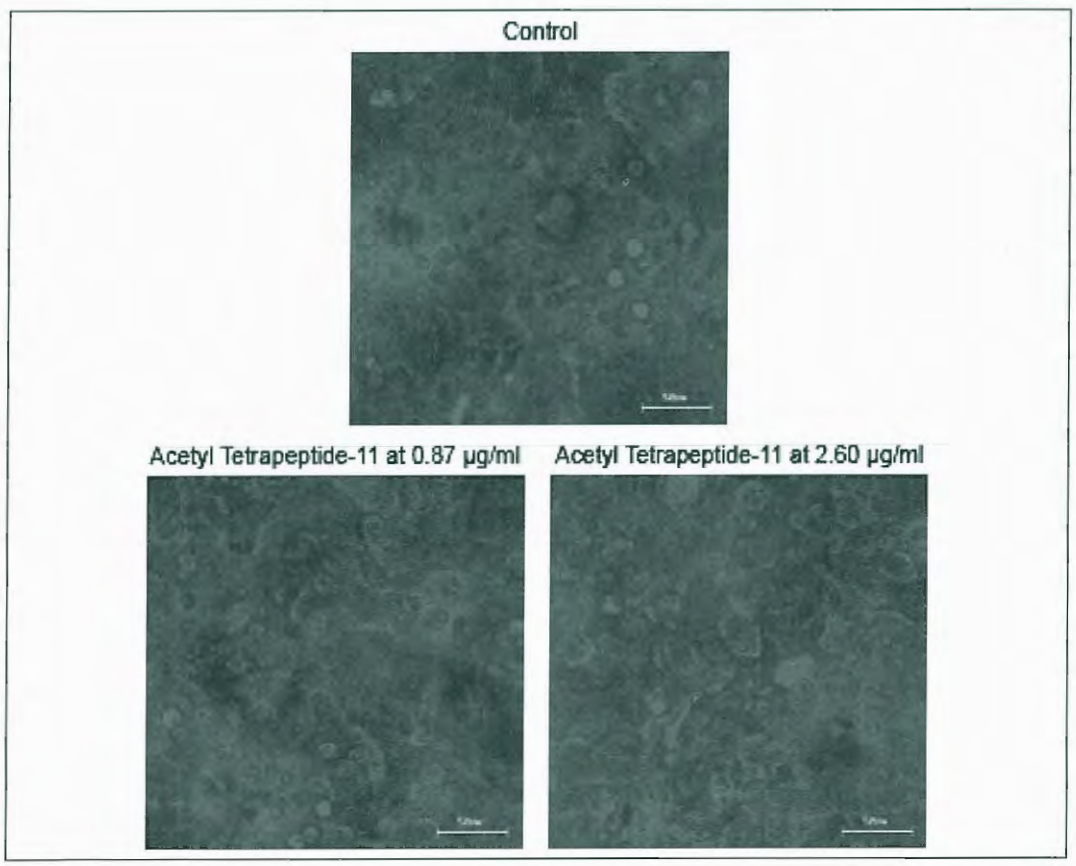

Fig. 8 *Stimulation of the synthesis of collagen XVII protein by human epidermal keratinocytes: visualization at 3 days.*

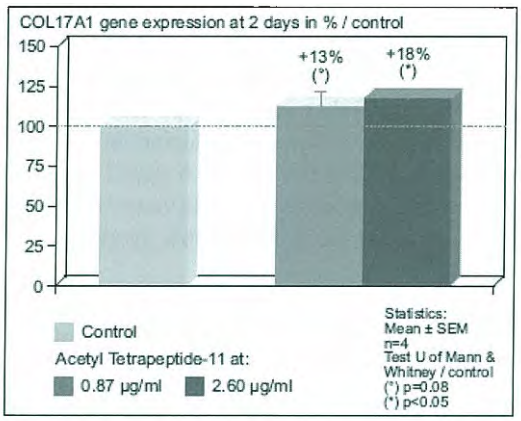

Fig. 9 *Stimulation of the expression of collagen XVII COL17A1 gene by human epidermal keratinocytes: visualization at 3 days.*

The efficacy and tolerability of ACTP2 was proven in a clinical test on 19 female volunteers aged between 60 and 70. After a two-month course of treatment, the biomechanical firmness and elasticity of the superficial epidermal layers had increased significantly and the skin texture was refined, so that the subjects looked visibly younger.

For a comprehensive anti-age approach, the combination of ACTP2, specific for the epidermis, with ACTP1, which specifically targets aging of the dermis is an optimal choice of ingredients for various easy-to-use products in the growing market for cosmeceutical skin care products.

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Environmental Factors in Skin Diseases

by Ethel Tur

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The major function of the skin is to protect the human organism from the external environment. And the major challenge for dermatologists, pharmacologists and toxicologists is understanding the role of toxic agents in modulating the growth and differentiation of skin cells, continuously exposed to UV radiation, industrial pollution, and climatic determinants.

Interactions between genetic risk factors and environmental triggers are, in fact, involved in skin aging and skin carcinogenesis, as well as in many autoimmune diseases. Thus, to understand the pharmacology of skin, it is necessary to identify the agents that regulate skin cell function and those cells in the skin that possess receptors corresponding to each hormonal and chemical agent investigating the interplay among environmental and genomic elements in skin biology.

At this purpose, the book provides the state-of-the art of research in this fascinating topic covering five different subjects: *Genetic Predisposition, Genetic Modifiers and Extrinsic Factors in Aging of the Skin and in UV Carcinogenesis* by 3 Chapters; *External Factors, Other than UV, in Skin Carcinogenesis* by 2 chapters; *External Factors, in Skin diseases with Genetic and Intrinsic Predisposition* by 4 chapters; *Skin and the Nervous System: Stress, Itch and More* by 3 chapters; *and Work-Related Skin Diseases* by 1 chapter.

The aging of human skin, area of increasing concern for medical and cosmetic reasons, is a consequence of both genetic program and cumulative environmental effects. Among harmful environmental factors that contribute to extrinsic aging of the skin, exposure to UV light (photoaging) is considered to be the most significant and well recognized.

UV irradiation is a cumulative process of photoaging which depends primarily to the degree of sun exposure and smoking. It creates, in fact, photoproducts and irritations clinically relevant to premalignant cutaneous tumors. Wrinkling increases with increased pack years of smoking, and heavy smokers are more likely to be wrinkled than non-smokers. However, numerous endogenous mechanisms protect the skin from these endogenous damages but, over a lifetime the defence mechanisms decline leading to accelerated skin damage.

This is the topic discussed on **chapter 1**: *Exogenous skin Factors in Skin Aging*. Primary prevention of UVR exposure is the most effective means of reducing UVR carcinogenesis. And limiting UVR exposure can be achieved in various ways, including avoidance of outdoor activities during noon hours when the amount of solar UVR is maximal, the use of protective clothing and sunscreen application.

UVR has, in fact, a wide range of acute and chronic effects on normal skin, as erythema, immuno-

suppression, photoaging and carcinogenesis also. Microarray analyses show that following UVR exposure of human skin there is a wide range of activation and silencing of genes. Thus, both UVA and UVB induce DNA damage, which is inherently repaired by cellular mechanisms, many times only partially. The typical UV DNA damage is the generation of dimeric photoproducts between adjacent pyramidine bases, namely cyclobutane pyrimidine and pyrimidine pyrimidone photoproducts. The immunesuppressive effect of UVR contributes to its carcinogenetic activity. *Nonmelanoma* skin cancer is the most common type of human cancer, meanwhile the mechanism by which UVR leads to cutaneous *malignant melanoma* is less clear.

Ultraviolet Radiation and Cutaneous Carcinogenesis is focused on **chapter 2**.

The genetic variations play a pivotal role to the oncogenic effects of UV light widely varying between individuals. Both acquired and genetic factors account for this variability. Thus, a number of genetically defined pathways are reported on **chapter 3**: *Genetic Factors in the Pathogenesis of UV-induced Skin (Cancer)* were preventive and therapeutic modalities are discussed.

Apart UV irradiation, viral proteins may directly transform keratinocytes by activation of cancer-promoting genes. They drive cells to proliferate or generate inflammatory responses and relative injures leading to their malignant transformation.

The immune suppression, caused by UV irradiation also, gathers to support viral tumorgenesis. Thus, the interest in oncogenic viruses is twofold: clinical and mechanistic. Their clinical manifestation shed light on the important role of host defense, genotoxic exposures and new options of therapy. The growing understanding of molecular mechanisms utilized by viruses for tumor formation reveals new pathways of carcinogenesis and points at critical genes which in the future may be the basis of new therapies.

These are the insights reported on **chapter 4**: *Viral Carcinogenesis in Skin Cancer.*

Environmental Risk Factors for Mycosis Fungoides (MF) is the topic of **chapter 5**.

MF is an epidermotropic malignancy of T/lymphocyte origin, almost always of memory T-helper cells which have the propensity to home to the skin, to function in an activated state, and to achieve clonal dominance. It is a low-grade lymphoma, more frequent in men, that usually starts late in life and has an indolent course. Its etiology is unknown. However, despite much effort to identify a unifying environmental factor in the development of MF and related disorders, epidemiological data indicate that this prolonged carcinogenic process is probably multifactorial and multistep. Further studies are important as substantiating the etiology will make it possible to decrease its incidence through preventive interventions and appropriate health policies and methods of surveillance.

chapter 6, Exogenous Factors in Connective Tissue Diseases, reviews all the probable exogenous factors implicated in or suspected of precipitating connective tissue diseases. It is not known why benign autoimmunity sometimes progresses to pathological autoimmunity, which may be organ-specific or systemic, cell –mediated or tumoral. Nevertheless, the actual development of an autoimmune disease in genetically susceptible individuals requires an interaction with certain environmental factors, reported all in this interesting chapter.

However, occupational exposure can influence the development and course of the autoimmune diseases. Moreover there is also evidence that the developing immune system, especially the hypothalamic-pituitary-adrenal axis, can be permanently altered or *programmed* by the early environment during key stages of development.

Vitiligo, which is the topic of **chapter 7**, is an acquired disorder characterized by progressive skin

depigmentation resulting from an autoimmune response targeting epidermal melanocytes.
Its etiology is poorly understood and additional factors are probably involved, as vaccination, radiotherapy, and sun exposure, drugs, psychological factors, etc. However, there appears to be a certain genetic predisposition and a number of potential precipitating causes. Thus, several candidate genes and genetic linkages have been identified that appear to mediate susceptibility to both generalized vitiligo and to a specific group of other autoimmune inflammatory disorders with which vitiligo is epidemiologically associated. Since there is no curative treatment for vitiligo, it is important to recognize the etiology in order to prevent progression of the skin changes, especially in patients with previous vitiligo.
According to Prof. Jean Civatte: "Dermatology and Cosmetology are no longer alien to each other's: on the contrary, each reaches out into the other's territory". Thus the cosmetologist focuses his interest on hygiene, beauty enhancement, and care from outside in; whereas the dermatologist is concerned with therapy for preventing and curing the skin diseases. At this purpose, hair plays a role of such importance in social life to become a full-fledged science based on many research studies of both Dermatologists and Cosmetologists.
Thus, *Environmental and Cosmetic Factors in Hair Loss and Destruction* is focused on **chapter 8**. As a matter of fact, there are many exogenous factors that may cause hair loss or otherwise impaired cosmetic appearance. The various physical and chemical procedures that the hair is exposed to, either deliberately or not, often act synergistically with one another and inflict increasing damage upon the hair fiber. Hair loss may be temporary and followed by complete recovery or permanent immediate or delayed. However, it is usually categorized into five pathogenetic mechanisms: hair shaft defects, telogen effluvium, anagen arrest, destruction of hair follicles or miniaturization of the follicle. In this chapter the different mechanisms promoting hair loss are reported together with the downgrade hair's physical properties such as strength, shine, and tactile characteristics.
On one side, psychological stress plays an important role in the pathophysiology of numerous skin disorders. On the other side, the life spent at work, and thus environmental factors are of great importance also. Work occupies, in fact, a large proportions of the modern daily routine. However, the mechanisms underlying stress and environment–induced dermopathologies are not fully understood. Thus, in the last five chapters, the relative mechanisms known are reported for different pathologies, such Psoriasis, Itch Response, Atopic Dermatitis and some Occupational Skin Diseases, where the skin barrier function is disrupted.
All these reported diseases may be modulated by both endogenous and exogenous factors including stress lifestyle, excessive use of drugs together with environmental triggers.
Moreover, a comprehensive overview on recent findings and novel technologies used to investigate the skin cell biology are reported and discussed in this interesting book.
In this way, by the fascinating research studies reported, the biochemical steps played among environmental and genomic elements may be better understood.
For the wide range of news reported and for the simplicity of the discussion on the different topics, the book will be a useful tool for Dermatologists and Cosmetic Chemists wanting to enlarge their horizons on the influence the environment has on different skin diseases.

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Sun Science: Formulation For Protection

by Angela C. Kozlowski

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Exposure of skin to solar radiation leads to acute inflammation, followed by tanning and thickening of the skin, associated with vitamin D synthesis and immune suppression. Depending on UV dose and skin type, inflammation (erythema) becomes visible, reaching maximal intensity by 18-24 h., and fading in about three days. Excessive exposure to sunlight can led to increased risk of basal and squamous cell carcinomas as well as decreasing the elasticity of the skin and consequently skin aging. However, the intensity and duration of exposure to visible light plays an important role for mental wellbeing and regulation of circadian rhythms. Being a link between sun exposure and skin cancer, it is necessary to protect the skin by the use of sunscreens limiting sun exposure also.
This book in VIII sections and 39 chapters provides a complete overview on formulating and testing the cosmetic products.
Formulating – Basic Review is reported on **chapters 1** to **12**.
Topical sunscreens available as consumer products, act by absorbing or scattering UV radiation. They contain organic or inorganic filters which absorb mainly UVB although the majority of sun-care products offer protection from UVA also. Moreover, the ideal formulation strategy removes ingredients known to be deleterious to UV filter photostability and includes ingredients that are known to improve photostability also. The uniqueness of UV filters depends, in fact, on their ability to reach an excited state after absorbing UV energy and then to return to ground state by dissipating the energy. Thus, their functionality depends on their ability to do that process over and over again, dissipating the energy without self-destruction.
According to the up-to-date insights the sunscreens products have to protect not only against UVB, the radiation primarily responsible for sunburn, but also against UVA responsible of skin ageing. Over time a better education of consumers to use the sunscreens in the right way should be necessary.
A higher and uniform distribution of the product on the whole skin surface is also necessary to obtain the best protective activity. Homogeneity of UV filters in the sunscreen formulation and on the skin has, in fact, important consequences for sun protection. However, today's consumers worldwide are looking for personal care products that supply multiple benefits with minimal effort. They also expect the latest technology advances to be incorporated into innovative formulations.
Thus, the use of phosphatydylcholine and azelaic acid to formulate sunscreen products capable to protecting against UV rays while, at the same time, improving the acne condition. On the other side

it is advisable to formulate sunscreen products having a moisturizing activity or an anti-aging efficacy.

At this purpose, prevention of sun damage on the skin by the use of sunscreens can be reinforced by some antioxidant and immunoprotectant agents such as lutein, lipoic acid, tocopherols, ectoin and beta-glucan. Treatment of sun damages with repair or anti-inflammatory actives during or immediately after sun exposure may be also justified. However, formulating the sunscreen products in the right way, and teaching the consumer how to manage the sunlight has become part of the marketer's obligation.

How Formulating New Ingredients is reported from **chapters 13** to **22**.

As a biology clock, the skin is affected by innate aging in a manner similar to other organs of the body. Superimposed on the innate chronological aging process are the effects of a lifetime of exposure, the environment elements, the most damaging being UV radiation. Thus, we cannot efface or ignore the cumulative effects of sunlight that are manifested as skin cancer and aging of the exposed skin. This overexposure, in fact, is linked to cutaneous aging through the production of reactive oxygen and nitrogen species (ROS and RNS) that can activate matrix metalloproteinases, enzymes involved in the breakdown of the dermal protein, such as collagen and elastin.

The degradation of these proteins is a primary contributor to wrinkle formation and loss of the skin elasticity.

Moreover stress connected with our way of living induces changes in the ceramide content of the skin, leading to its compromised barrier function. The goal of a sunscreen is to deliver the UV filter to the skin surface as evenly as possible, protecting the skin barrier also.

At this purpose silicone compounds, combined with organic or inorganic sunscreens can improve their stability at the skin surface, boosting the SPF (Sun Protection Factor) also. In this way it is possible to set up products with greater protection and enhanced claims without added cost.

Another significant formulation challenge is to protect from the UV oxidation the skin lipids.

Twenty-five percent of the lipid in the skin's surface are, in fact, unsaturated and therefore prone to be attacked by free radicals produced from UVA radiation. It is to remember how the deteriorative oxidative changes triggered by free radicals include wrinkling, hyperpigmentation and inflammation. And at this purpose cosmetic *bio-protectants* may be considered, for example, stable tocopherol derivatives or many botanical extracts rich of curcumin, curcuminoid compounds and other protective ingredients.

Section III of the book is focused on *Formulating-Future innovation* from **chapters 23** to **30**.

Nanotechnology, as understanding, characterization, producing, controlling and utilizing structures measured on a nanometric scale, has become a new must for marketing-oriented chemical companies.

The seduction of raw material at a nanoscale dimension, in fact, may not only reduce the cost but enhance its efficacy. Thus the metal oxides ZnO and TiO_2 reduced to less than 200 nanometers (nm) have a higher UVA/UVB filtering capacity being aesthetically more acceptable.

These two metal oxides block UVR by both physically scattering and reflecting the incoming radiation and by chemically absorbing it.

The wavelength range in which these scattering/reflection occur is crucial for the effectiveness of solar protection. The particle size determines, in fact, these mechanisms and the incoming radiation is bounced from the particle when the particle diameter is about twice the wavelength or larger.

Moreover TiO_2 and ZnO nanoparticles are coated by hydrophobic polymeric material to allow their dispersion in oils, avoid the direct contact with the skin and give them much more photostability.
As we have previously seen, UVB rays cause sunburn, the UVA cause long-term damage such as wrinkling and some types skin cancer. Moreover, UVA accounts for more than 80% of the damage that occurs to the skin in terms of aging, DNA damage and skin cancer. Therefore, the ability of the ingredients to protect against UVA rays while remaining photostable gives them the potential to provide products with full-spectrum protection.
In combination with Terephthalylidene dicamphor sulforic acid, ZnO and TiO_2 may give the best results as broad-spectrum UV protection for the skin.
UVA is the main cause of oxidative stress, damaging protein via cross-linking and denaturation, and lipids through peroxidation. To reduce this damages we may reinforce the anti-oxidant skin's defence mechanism by the use of the dimeric cysteyl-glycin dipeptide obtained either by synthesis or extracted from plants. It seems to provide a high protection against oxidative stress.
By another mechanism of action, some Chinese medicinal plant materials, as *Herba Menthae* and *Lignum Dalbergiae Odoriferae* seem able to increase the melanin production at level of the skin or hair. The melanin in the epidermis can absorb most UV light and diminish the penetrability of UVA and UVB rays.
Moreover, a *Phyllantus emblica* extract composed of low molecular weight tannins, has been shown to reduce UV-induced erythema, having an excellent free-radical quenching ability also. It has, in fact, a chelating activity to iron and copper and inhibitory activity against MMP-1 and MM-3 (metalloproteins). Possibly, this extract modulates UV/ROS-initiated signal transduction pathways of matrix metalloprotease induction, thereby protecting the extracellular matrix proteins from degradation. Finally the combination of acetyl-tyrosine and proline, seems to promote an increase of the natural skin repairing mechanism at level of DNA. As known, prominent among UV-induced lesions on DNA are cyclobutane pyrimidine dimers (CPDs) formed between adjacent pyrimidines on the same DNA strand exposed to UB irradiation. These dimers alter the biological function of DNA and are the major cause of lethal transformational and tumorigenic events induced by UV exposure.
This proline-tyrosine complex, named TRC, seems to reduced CPDs, dramatically reducing the UV-light-induced erythema also.
Testing-Research, Efficacy and Claims are the topics reported on Section IV – VIII by the last **9 chapters**.
There are t least 10 major organizations that regulate sunscreens globally.
Permitted UV filter differ widely from one country to another making it practically impossible to formulate uniform sunscreens. Thus, the necessity to harmonize the different rules for uniform labels of SPF, water-resistance and UVA claims, so that they may be understood worldwide. This is surely the challenges of tomorrow.
However, when claims are made for marketed products, they are usually supported by appropriate professionally recognized studies. And today the sunscreen products have non only a photoprotective activity but also an antioxidant and vasculative protectant activity.
With the spiralling statistics in the proliferation of skin cancer, UV filters for protection are now of paramount importance more than ever. Thus, the control of the protective activity from the sun damages and the photostability in time of the sunscreens and antioxidant compounds used become more and more important, as well as the issue of harmonizing worldwide regulations also requires special

attention from all the practitioners in the field.
In the last years it has been shown that the response of human cells to UV is not limited to constitutive DNA repair and pigmentation, but also encompasses associated systems of detoxification and the expression of many defense proteins.
By the use of sunscreen products topically applied and/or taken by oral route also, it is now possible to reduce the environmental skin damages, to improve the rate of repair of DNA, to stimulate melanin production and to boost the immune response.
This interesting book, focused on what is today known on the topic of sun science, give the reader all the information necessary to better know how to prevent UVR-induced skin damage. Its careful reading is fundamental to learn more about the efficiency of sunscreens and the necessity to use them to protect the skin from the negative effect of the sun.
Therefore, *Sun Science: Formulating for Protection* represents an up-to-date and authoritative reference text for cosmetic Chemists and Dermatologists, Researchers and Students who desire to know the impact the sun have on our skin and how to formulate and use the sunscreen products.

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Dermatologic Immunity

by B.J. Nickoloff and F.O. Nestle

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Inflammation is a physiological, protective cellular response designed to repair or dilute noxious stimuli, injury or tissue destruction. Thus, as physiologically controlled self-limiting phenomenon, inflammation plays a central role in mediating immune mechanisms of host defence and wound healing. Disruption of the physiological control mechanisms of this defence system, however, forms the basis of the pathology of many diseases, such as autoimmune diseases, affecting many different organs.

This book, in 19 chapters, covers the autoimmune disease processes of and in skin, featuring disorders of humoral as well as cellular immunity also.

And *Allergic Contact Dermatitis* (ACD) focused in **chapter 1** is a classic example of a common inflammatory skin disease. It occurs as a result of xenobiotic chemicals penetrating into the skin, chemically reacting with self proteins, eventually resulting in an hapten-specific immune response. The interactions of T-lymphocytes with antigen or mitogen leads to the activation of metabolic processes of the cell, increased DNA synthesis, mitosis and the synthesis of small proteins or polypeptides, such as lymphokines, cytokines and many other proinflammatory factors.

The production of such factors is not exclusive to the immunomodulatory cell types including fibroblasts and endothelial cells. These products provide a system of communication between cells by means of molecular signals, and keratinocytes play a role in all phases of allergic contact dermatitis. However, as the molecular and cellular pathogenesis of ACD will be elucidated, new therapeutic targets will become available.

Immune Privilege and the Skin is the topic of **chapter 2**, where the evidence that defined compartments of the hair follicle (HF) and nail epithelium maintain an area of relative immune privilege (IP). This hair and nail immune privilege offer the development of innovative strategies for these and other autoimmune diseases, such as alopecia areata (AA). While, in fact, the pathogenesis of AA has still not been fully elucidated, recent consensus is building this pathology that reflects an organ-restricted T cell-mediated autoimmune disease. Therefore, rather than targeting the secondary autoimmune phenomena associated with AA, as most of our currently employed treatment regimens continue to do, the primary goal of effective AA management must be to restore the HF's lost of compromised IP-both for preventing the progression of AA lesions and for inducing hair regrowth.

Toxic Epidermal Necrolysis (TENS), linked to ingestion of various medications, is the most dramatic example of enhanced premature epidermal keratinocyte cell death in dermatology. TENS disease is, therefore, the topic of **chapter 3**: *Immunobiology of Acute Cytotoxic Drug Reactions*.

When patients experience this idiosyncratic drug reaction, their skin begins to slough and after several days following the onset of symptoms, the skin resembles that of individuals that have been scalded of suffered a superficial thermal injury. One important clue to suggest the involvement of the immune system and immunocytes in TENS patients comes from the recognition that the mortality for these patients is higher than that seen in burn patients, when the total body surface area of involvement is taken into consideration.

However the theories actually proposed for pathogenesis of TENS range from a direct toxic effect of the ingested drug by which keratinocytes are directly induced to undergo cell death, to an allergic-type theory by which the drug binds to major histocompatibility complex on antigen-presenting cells and thereby activates autologous cytotoxic T cells which attack the keratonocytes, producing indirect cytopathic reactions in the epidermis.

Chapter 4 is focused on *Psoriasis*.

Psoriasis is a spectrum of clinical syndromes with varying degrees of abnormal keratinisation, hyperproliferation, vasodilation, and abnormal leukocytes chemotaxis. However, it is an inflammatory disorder based on the combined influence of predisposing gene variants, genetic modifiers and environmental factors. Meanwhile 19 genetic susceptibility loci have been identified, replication of single has been only provided for few of those.

Moreover, there is some suggestive evidence in the literature pointing to the existence of a potential (auto-)antigen, but no direct functional evidence has been provided for any of the candidate antigens. However, therapeutic success of anti-TNF-α therapy in the treatment of psoriasis has validated the cytokine network hypothesis and supports the search for key effect or cytokines as possible drug targets in psoriasis.

Future developments for research and therapy of the disease might include (1) a synergistic view between our genomic and immunologic understanding psoriasis, (2) a focus on very early initiating events in its pathogenesis, (3) a better understanding events of its systemic inflammatory compounds, (4) an in deep knowledge on the skin-resident immune effector cells and their interaction with the epithelium and surrounding connective tissue.

It is likely that skin barrier defect as well as other major factor such as allergens and immune disregulation play their respective roles in the development and maintenance of atopic dermatitis. This topic is discussed on **chapter 5**, *Atopic Dermatitis in 2008*.

This infantile eczema is a chronic itchy, inflammatory skin disease that, setting on at early childhood, is observed increasing in prevalence around the industrialized countries.

Investigations of atopic dermatitis in humans suggest that this disease is initiated, maintained and perpetuated by the actions of cytokines, chemiokines, T cells, antigen-presenting cells and other inflammatory cells. Nevertheless, the role of epidermal barrier defect should now be considered as a very important factor for the initiation and maintenance of this important disease. Thus, it is generally accepted that not only lesional skin, but also non-lesional skin, in atopic dermatitis patients suffers some degrees of skin barrier alteration at level of lamellar LIPID system. Therefore, this disease is targeted by focusing on 2 major pathways: (1) prevention by vigorously protecting and repairing the impaired skin barrier and (2) *improvement* of its development by the identification and neutralization of the responsible factors of its initiation or maintenance, such as T cells, antigen- presenting cells, cytokines, chemiokines, adhesion molecules, proangiogenic factors and IgE overproduction.

Chapter 6 is entirely dedicated to *Cutaneous Lupus Erythematosus*. (CLE). It is an heterogeneous autoimmune disease with well defined lesions produced by the use of drugs also. As matter of fact a drug or its metabolites (A) may have a direct pharmacological effect on the immune systems; (b) may binds to DNA or proteins producing CLE, pemphigus, or pemphisigoid-like skin disorders. Pemphigus-like skin reactions are primarely caused by drug bearing a free SH-group, while LE-like disorders develop frequently after treatment with isoniazid and procaine. Skin manifestations in CLE are extremely heterogeneous clinically and, therefore, it has been difficult to develop a unifying concept of the various cutaneous lesions of this disease. Several risk factors may influence the cause and, prognosis of this pathology: genetic predisposition, race, sex, clinical presentation, age at disease onset, and triggering factors, such as exposure to ultraviolet light and oral medications.
However, a complete understanding of the diverse pathophysiologic mechanisms and interactions in CLE does not exist, but no donors appears to be a promising target for therapeutic intervention in this disease.
Bullous Pemphigoid and Related Subepidermal Autoimmune Blistering Diseases is the topic of **chapter 7**.
The pemphigoid groups of autoimmune blistering diseases, including distinct entities characterized by relatively consistent clinical findings, are known for their substantial morbidity and in some instances mortality.
Although most cases of Bullous Pemphigoid (BP) occur without any obvious precipitating factors, several reports have suggested that UVB, PUVA or jonizing irradiation or the use of some drugs may induce or provoke this disease. For example, it has been proposed that the chemical thiol group may allow the molecule to combine with proteins in the lamina lucida, acting as a hapten and therefore, resulting in autoantibody formation to epidermal basement membrane proteins.
Drugs, such as *furosemide, phenacetin, enalapril, ibuprofen, amoxicillin, ampicillin, penicillin, β-blockers and influenza vaccinations* have also been implicated for inducing BP. Drug-induced BP can develop in 1-90 days following consumption of the offending agent. Moreover, a cohort of patients with antiepiligrin cicatricial premphigoid was reported to have an increased relative risk for solid cancer, appearing to be highest in the first year of disease.
Patient with BP of minimal severity and/or distribution can sometimes be controlled with topical and/or systemic glucocorticoids. Patients with extensive disease may require the addition of other immunosuppressive agents to a regimen of daily glucocorticoids.
However, advances in translational research will be the potential to better elucidate the pathophysiology of these disorders and identify new approaches for their treatment. Pemphigus, is a group of chronic blistering skin diseases in which autoantibodies are directed against the cell surface of keratinocytes, resulting in their loss of cell-cell adhesion through a process called acantholysis. This disease, divided into three major forms: pemphigus vulgaris (PV), pemphigus foliaceus (PF) and paraneoplastic pemphigus, has been reported on **chapters 8** and **9**.
In PV, all patients have mucosal membrane erosions and more than half of them have skin erosions and blisters, developed in the deeper part of the epidermis, just above the basal cell layer. PF and its endemic form fogo selvagem (FS), are characterized by transient cutaneous superficial blisters. These blisters tend to be fragile to the point that often only scaly, crusted erosions are appreciated on physical examination. The hallmark of pemphigus is the finding of IgG autoantibodies against the cell surface of keratinocytes. These antibodies play a primary pathogenic role in reducing the loss of

cell adhesion of keratinocytes with resultant blister formation.
PF and PV antigens are termed *desmoglein 1*: Dsg1 and Dsg3 respectively. Compelling lines of evidence support the theory that autoimmunity to Dsg is the principal cause of pemphigus pathogenesis.
Thus, characterizing the Dsg binding site of these autoantibodies is an essential step in understanding the pathophysiology of blister formation in pemphigus, as well as the basic molecular mechanism of Dsg-mediated cell-cell adhesion.
To investigate the related pathophysiological mechanisms and to develop therapeutic strategies, animal disease models have been playing important roles in the study of various conditions including autoimmune diseases. But, the major difficulty in the development of an autoimmune reaction, for example, is the animal self-tolerance, which prevents the immune system from reacting destructively against components of the living body. Thus, the molecular and cellular mechanisms for tolerance against peripheral antigens or tolerance break that leads to harmful autoimmune reaction, remain to be elucidated. For these reasons several studies are in progress on this line.
On **chapters 10** and **11** are reported respectively *Epidermolysis Bullosa Acquisita* (EBA), an acquired disease characterized by autoimmunity to type VII collagen, and Lichen planus, (LP) characterized by an autoimmune attack on the epidermis by skin-infiltrating T cells.
The autoimmune etiology of EBA is supported by several independent lines of evidence derived from clinical, histological and immunological studies. Passive transfer animal models of EBA provide direct proof of the pathogenicity of EBA autoantibodies. All EBA patients require supportive therapy, including instruction in wound care and strategies for avoiding trauma. In some patients, the use of sunscreens and avoidance of prolonged sun exposure may be helpful in preventing new lesions on the dorsal hands and knuckles.
About LP, although many different mechanisms have been invoked, it is still not-precisely clear how autoreactive T cells could be achieved in vivo to cause tissue destruction. One mechanism is that environmental factors are required to activate the preexisting, potentially autoaggressive T cells in the periphery before the onset of an autoimmune disease. Thus, contact allergy to a variety of metals has been shown to be important in the pathogenesis of oral LP; including amalgam (mercury), copper, palladium, beryllium and gold. However, for safer and more efficient treatments it will be necessary to have a better understanding of the physiological role T cells have in the initiation and amplification of LP.
Autoimmune Etiology of Generalized Vitiligo is the topic of **chapter 12**. Vitiligo that strikes approximately 1% of the global population is characterized by progressive skin depigmentation resulting from an autoimmune response targeting epidermal melanocytes. Several factors may contribute to the pathogenesis of vitiligo, including genetic predisposition, toxic metabolities interfering with melanin metabolism, neurochemical factors and specific autoimmunity against melanocytes.
However, melanocytes are particularly immunogenic by virtue of the contents of their melanosomes, generating the complex radical scavenging molecule melanin in a process that involves melanogenic enzymes and structural compounds, including tyrosinase and caderines. These molecules are also prime targets of the immune response in both vitiligo and melanoma. Thus trauma to the skin generating locally oxygen radicals and reduced ability of melanocytes of eliminating these reactive species may be another cause of vitiligo. Moreover, nitric oxide is toxic to melanocytes and nitric oxide synthase is inhibited by MSH, suggesting that abundant nitric oxide contribute to vitiligo pathoge-

nesis.
A definitive cure of vitiligo has yet to be found. Currently, successful therapeutic measure require a situation of stable disease to repopulate lesional vitiligo skin with melanocytes by a variety of skin grafting methods in combination with (narrow-band) UVB radiation. Effective measures are available to repopulate stable vitiligo lesions by surgical transplantation measures in combination with UVB treatment to stimulate melanocyte migration, proliferation and melanization.
However, for the *Genetics of Generalized Vitiligo* recent progress have been obtained by the Human Genomal Project. This project has led to efforts to map and identify specific genes involved in vitiligo susceptibility and pathogenesis. This is the topic of **chapter 13**.
As a result., there has been considerable recent progress towards the identification of vitiligo susceptibility genes, some of which may provide novel therapeutic and prophylactic targets for new international approaches to treat and even prevent vitiligo in the future.
Disease specific autoantibodies are also found in *Scleroderma*, the subject of **chapter 14**.
This disease is different from other cutaneous autoimmune diseases because epithelial injury does not occur. Immune system, vascular and extracellular matrix abnormalities are, in fact, the most likely triggers in an individual with a genetic predisposition to scleroderma. These lead to increased synthesis of normal collagen in skin, lungs and gut in the systemic form of scleroderma, systemic sclerosis. Systemic sclerosis/scleroderma has the highest morbidity and mortality and no definitive therapy is available to date.
Alopecia Areata, Dermatomyositis and other autoimmune diseases are reported and discussed from **chapters 15** to **19** with the aim of characterizing their mechanisms of action, to improve the currently available treatments and develop more effective therapies.
However, the evolution of anti-inflammatory and immunosuppressive drugs continuously progresses. The hope is that as drugs have more targeted mechanisms, efficacy in the treatment of immunologically mediated disease can be maintained and immune and non-immune side effects will be reduced. This is the fnture goal.
A wide range of autoimmune disease processes of and in the skin are reported and discussed in this book together with the up-to-date therapeutic strategies.
Thus its lecture is recommended for basic and clinical researchers as well as for dermatologists, plastic surgeons, immunologists, cosmetic chemists and internists but also for anymore working and being involved in Cosmetic Dermatology has interest and wish to better understand the role of immune system in the pathogenesis of the more known autoimmune diseases.

P. Morganti
Editor-in-Chief

INTERNATIONAL CONGRESS ON GLOBAL WELLNESS & BEAUTY

Title: Wellness and Beauty outside in: East & West working together
Location: CNR -Consiglio Nazionale delle Ricerche (National Research Council) - Piazza Aldo Moro 7 - ROMA
Date: 21 to 23 October 2009
Organized: International Society of Cosmetic Dermatology - (ISCD) In Collaboration with: UNIPRO - FEDERSALUS
Patronage: Ministero Del Lavoro, Della Salute e Delle Politiche Sociali - Ministero Della Sviluppo Economico S.I.C.C.

YOU HAVE FIVE IMPORTANT REASONS TO BE PRESENT

BECAUSE

Because
in this occasion you may know the latest innovations involving WELLNESS & BEAUTY at 360°.

Because
it is the first time the globality of WELLNESS & BEAUTY will be discussed from a multidisciplinary team of scientists.

Because
many scientists coming both from Academy & Industry from East and West will define the significance of WELLNESS & BEAUTY outside in.

Because
are coming scientists & expert in:

- Cosmetic Science
- Environment & Wellbeing
- Functional food,
- Bio-textiles & Leather
- Nanoscience
- Intellectual Properties & Counterfeiting

all involved in WELLNESS & BEAUTY.

Because
Rome is an hystorical wellknow city where you may live a wonderfull and exciting experience.

Look the program on our website www.congress2009.iscd.it and come as active participant

ISCD International Congress
Wellness and Beauty outside in: East & West working together
Rome - October 21-23, 2009

The Organizing Committee
congress2009@iscd.it

TARGET AUDIENCE

The Congress addresses both Clinical Physicians and Cosmetic Chemicals as well as policy makers and scientists with a background in Biology, Physiology, Pharmacology, Dietology, Toxicology, Intellectual Properties, physics and Chemistry involved in the development of Cosmetic Dermatology as a new science.

The meeting is also of interest to industrial and marketing experts directly and indirectly involved in the field of wellness.

DEBATE STYLE

The speakers will comment themselves to short presentations, making the outcome of their speech between 10 and 15 minutes.

Thus, several hours will be reserved for discussion to all conference participants.

This way a proficous exchange of knowledge and know-how between the chemical, medical community as well as and technical community will be possible.

CALL FOR PAPERS/ POSTER SESSIONS

Paper covering original research reports based on new ideas aimed at future clinical of wellness based on the use of cosmetics, functional food, bio-textiles and bio-leather should be submitted. Submitted papers will undergo peer reviewing and, if accepted, will be chosen for oral or poster presentation.

Submission should be made before July 15, 2009 at least

Enter www.congress2009.iscd.it and upload your proposal following the steps submission.

The submitted file should be in Word or RTF and must fit **on one single page, including tables and figures.** The text should be single-spaced with a 12-point font italics rather than underlined words should be used all illustrations, figures, and tables should be placed within the text at appropriate points rather than at the end.

Besides the uploaded documents, please also send your submission by e-mail to: congress2009@iscd.it

All authors whose papers are not accepted for a presentation may apply for a poster presentation. Poster sessions have **to be submitted by August 18, 2009.**

SLIDE & PROGRAM

Slides center

The Powerpoint presentations should be submitted to the slide speakers room located at the 1st floor in the Slide Meeting Center.

The Powerpoint presentations should be taken to the area preferably on the day before the session or at latest 4 hours before the starting time of the session.

Variations

The scientific secretariat and the organizing secretariat have the rights to change the scientific program for technical and scientific reasons.

	REGISTRATION FEE			
		up to 30.06.09	from july 1 up to sept.15	on site
☐	ISCD, Federsalus, Unipro, and SICC Members	€ 400	€ 450	€ 500
☐	Non Members	€ 500	€ 550	€ 600
☐	Accompanyng person	€ 90	€ 90	€ 90
☐	Exhibitor exceeding 2 badges	€ 130	€ 130	€ 130
☐	Beauticians	€ 80	€ 80	€ 150
☐	1 day registration	€ 200	€ 220	€ 250

Participants registration fee includes	Fee Accompanying person
• Welcome Reception and Admittance to Opening Ceremony • Admittance bag to all Sessions • Admittance to Exhibition • Conference Documentation and Abstract Book • Certificate of Attendance • Coffee - Refreshments - Brunches	• Welcome Reception and Admittance to Opening Ceremony • Admittance to Exhibition • Coffee break.

REGISTRATION PROCEDURE

All registrations must be made on the official registration form only (or a copy – 1 form per participant) No registration form is accepted unless accompanied by full payment (banker's draft or duplicate of the transfer order raised by the bank, in EURO only). The registration will be confirmed only after receipt of these required.

In order to avoid any confusion due to mail or bank delays, advance registrations by mail will close on.

After this date, registrations will be made on site at the Congress Welcome Desk, on October 21 2009 from 8:00 to 18:00

SATELLITE SYMPOSIUM

There will be satellite symposia planned by term in conjunction with the Congress organizing committee.

INFORMATION FOR AUTHORS

Abstracts may be presented and will be included in the abstract book, only if the registration fee for at least one of the authors have been remitted and if the abstract form as been approved.

PLACE AND DATE OF THE CONGRESS

The Congress will take place in:
CNR Consiglio Nazionale delle Ricerche (National Research Conncil)
P.za Aldo Moro 7 - ROMA - From 21 to 23 October 2009.

REFRESHMENT AND LUNCHES

Refreshments and lunches are included in the registration fee.

CLIMATE

Average temperature in Italy range from 10°C (minimum) to 20°C (maximum) in October/November.

DRESS

Dress will informal for all congress session.
The most suitable dress for each events will be suggested.

ENQUIRES

All scientific enquires about the Congress should be addressed to Scientific Secretariat Desk.

OFFICIAL LANGUAGE

The official language of the meeting will be English.

ATTENDANCE CERTIFICATE

The participants will collect their certificate directly from the Organizing Secretariat. congress2009@iscd.it

BADGES AND IDENTIFICATION

Registration badges will be used during the Congress. For identification purposed and admission to the session halls, participant are request to wear their badges, which will be given to them upon registration.

Admission to the Congress site will not be allowed badge identification.

DEADLINES

Submission for oral presentation:	**July 15, 2009.**
Submission for poster presentation:	**August 18, 2009.**
Hotel Accommodation Registration:	**September 1, 2009.**

Università degli Studi di Pavia
Facoltà di
Medicina e Chirurgia

Master biennale di II livello in Medicina Estetica e del Benessere

Anni accademici 2009-10, 2010-11

Un corso di alta formazione post-laurea istituito ai sensi del D.M. n. 270 del 22/10/2004 per il conseguimento del Diploma Universitario di Master in Medicina Estetica e del Benessere, titolo di studio accademico con valore legale.

Un percorso di studio intensivo teorico-pratico per formare il Medico Estetico, figura professionale destinata all'attività in studi autonomi, centri polispecialistici, centri-benessere, palestre, beauty farms e stazioni termali.

Due anni di lavoro full-time, armoniosamente articolato tra lezioni teoriche, attività pratiche e stages presso aziende di settore.
Monte ore di 1500/anno così ripartito:

- 480 h/anno di didattica frontale
- 300 h/anno di stage e tirocini pratici
- 720 h/anno di studio individuale

Scadenza domande di ammissione: 10 dicembre 2009

Università degli Studi di Pavia
Cattedra e Scuola di Specializzazione
in Chirurgia Plastica e Ricostruttiva

Dipartimento di Scienze Chirurgiche
Rianimatorie-Riabilitative
e dei Trapianti d'Organo
Via Aselli, 45 - 27100 Pavia

Segreteria del Master:
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+ 39 366 5091688
Fax + 39 0382 592220
+ 39 0382 423504

Le attività didattiche si svolgono presso
il Centro Studi della Fondazione
Salvatore Maugeri
Via Maugeri, 10 - 27100 Pavia

info@plasticaticinensis.it
www.plasticaticinensis.it

FSM Centro Studi
Fondazione Maugeri

Il Master Universitario biennale di II livello in MEDICINA ESTETICA E DEL BENESSERE dell'Università di Pavia: un prodotto formativo nuovo e completo, una formula organizzativa d'avanguardia, nella lunga tradizione di un grande Ateneo.

La Medicina Estetica consiste nell'applicazione di tutte le conoscenze del laureato in Medicina e Chirurgia finalizzate non al trattamento delle malattie ma al raggiungimento e mantenimento dello stato di salute e di benessere psicofisico. Tale obiettivo viene raggiunto sia educando il paziente/utente a gestire al meglio la propria persona sia intervenendo opportunamente con le giuste correzioni per minimizzare gli inestetismi che possono essere causa di disagio.

Per l'ormai indiscussa richiesta di mercato di tale professionalità e per il bisogno di stabilire percorsi formativi qualificati, esaurienti, seri, tali da costituire un riferimento e una garanzia per gli utenti e gli Ordini dei Medici, l'Università risponde con le competenze proprie, armoniosamente integrate con le migliori risorse provenienti dal mondo produttivo.
E' stato quindi istituito a partire dall'anno accademico 2005-2006, presso l'Università di Pavia, il MASTER BIENNALE DI II LIVELLO IN MEDICINA ESTETICA, ora giunto alla III edizione, corso di alta formazione post-laurea per il conseguimento del Diploma Universitario di Master in Medicina Estetica.
Si tratta di un percorso di studio intensivo teorico-pratico particolarmente pensato per il neolaureato in Medicina e Chirurgia, armoniosamente articolato in due anni di lavoro full-time tra lezioni teoriche, attività pratiche e stages presso aziende di settore, finalizzato alla formazione del Medico Estetico, figura professionale destinata all'attività in studi autonomi, centri polispecialistici, centri-benessere, palestre, beauty farms e stazioni termali. Una grande opportunità di formazione professionale qualificata e di rapido inserimento nel mondo del lavoro dopo la laurea in Medicina e Chirurgia.
Il monte ore è di 1500/anno articolato in 480h/anno di lezioni e seminari presso le strutture dell'Università di Pavia, 300h/anno per tirocinio pratico presso centri di Medicina Estetica, centri benessere, terme, palestre, aziende di settore appositamente convenzionati con l'Università di Pavia e 720h/anno dedicate alle attività di studio e preparazione individuale. La frequenza è obbligatoria per almeno il 75% del monte ore previsto.
Il percorso formativo è organizzato in 9 moduli principali di insegnamento che coprono tutti gli aspetti e le tematiche della Medicina Estetica e del benessere: aspetti generali della Medicina Estetica e discipline propedeutiche, dermatologia e cosmetologia, termalismo, flebolinfologia, cura della silohuette, tecniche e metodiche in Medicina Estetica, apparecchiature e tecnologie di specifico impiego in Medicina Estetica, attività motorie, terapie complementari e non convenzionali.
Per un prodotto formativo così complesso ed articolato è stato organizzato un nutrito corpo docente di ben 63 insegnanti di cui 27 docenti universitari, 18 docenti universitari di ruolo e 7 a contratto, dell'Università di Pavia, 2 di altre Università Italiane e straniere, 8 docenti provenienti da Istituti di

Ricovero e Cura a Carattere Scientifico Nazionali, 20 esperti esterni di chiara e riconosciuta fama nazionale ed internazionale nell'ambito della Medicina Estetica e 6 tutors provenienti dal mondo del lavoro e dai settori aziendale e produttivo.
E' stabilito un numero chiuso di massimo 30 iscritti, selezionati secondo una graduatoria di merito che privilegia il curriculum degli studi universitari, la giovane età ed il non possesso di alcuna specializzazione post-laurea.
Le iscrizioni sono aperte dal settembre e si chiudono alle ore 12.00 del 10 dicembre 2009. Requisiti essenziali per l'ammissione sono: la laurea in Medicina e Chirurgia, l'abilitazione all'esercizio della professione di Medico Chirurgo e l'iscrizione all'Ordine dei Medici Chirurghi.
Con il Master di Medicina Estetica l'Università di Pavia ha voluto studiare un prodotto formativo che soddisfi proprio ogni esigenza. Grazie alla rivoluzionaria formula all-inclusive, il costo di iscrizione di 6500?/anno comprende infatti la frequenza di tutti i corsi teorici e delle attività pratiche, il materiale didattico (testi scolastici, dispense, audio-video), il trasferimento alle sedi distaccate in Pavia, il lunch di lavoro giornaliero in Pavia, il trasferimento ed il soggiorno con pensione completa nelle località di tirocinio-stage fuori sede. Inoltre sono previste formule agevolate di soggiorno in Pavia per gli studenti fuori sede.
Nessun pensiero superfluo deve turbare l'apprendimento dell'arte della Medicina Estetica a Pavia.
La Banca Regionale Europea mette inoltre a disposizione un comodo finanziamento a 5 anni a tasso agevolato per coprire l'intero costo d'iscrizione. Una ragione in più per non avere preoccupazioni inutili e pensare con tranquillità al proprio futuro.

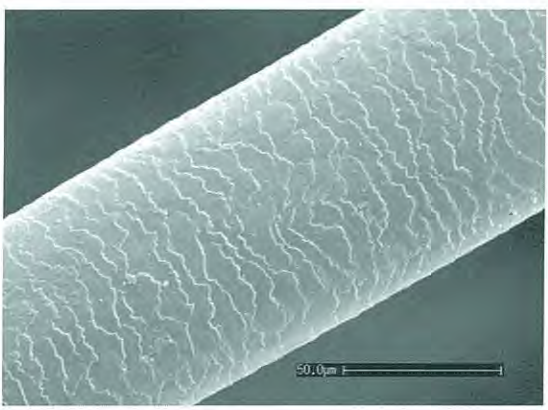
Apertura iscrizioni: settembre 2009
Scadenza domande di ammissione: 10 dicembre 2009
Per informazioni:
+39-0382-592225
+39-366-5091688
www.plasticaticinensis.it
Mail: info@plasticaticinensis.it
Bando di concorso: http://www.unipv.it/webesami/post.htm
Finanziamento a tasso agevolato: www.brebanca.it

DWI an der RWTH Aachen e.V.
ITMC Lehrstuhl für Textilchemie und Makromolekulare Chemie

16th International Hair-Science Symposium

HairS'09

Weimar / Germany
September 9-11, 2009



www.dwi.rwth-aachen.de/hairs09.html

Conference Scope

HairS'09 will follow the tradition of the DWI organized symposia which forged a unique platform for exchanging the newest and most appealing ideas of hair care science. Internationally renowned professionals from hair science, hair care science, technology and practice from all over the globe continue attend the series of hair symposia, to present their last research fi ndings and to keep up to date with latest achievements and developments in this very fast moving field.

11:15 **F.J. Wortmann**[1], G. Wortmann[1], J. Marsh[2], K. Meinert[3]
[1] University of Manchester, School of Materials, Manchester/UK
[2] Procter & Gamble Company, Cincinnati, OH/USA
[3] Procter & Gamble Service GmbH, Darmstadt/D
DSC of human hair: contrasting experimental techniques and theoretical approaches

11:40 **C. Popescu**, D. Demco; DWI an der RWTH Aachen e.V., Aachen/D
Details of human hair structure as revealed by multinuclear solid-state NMR

12:05 **Y. Kamath**[1], N. Sanjeeva Murthy[2], Ram K. Ramaprasad[3]
[1] Kamath Consulting/USA
[2] Center for Biomaterials, Rutgers University/USA
[3] TRI, Princeton/USA
Small angle neutron scattering studies of human hair: relevance to distribution of water

12:30 **M. Zimmerley**[1], C.-Y. Lin[1], D.C. Oertel[2], J.M. Marsh[2], J.L. Ward[2], E.O. Potma[1]
[1] Department of Chemistry, University of California, Irvine, CA /USA
[2] The Procter & Gamble Company, Cincinnati, OH/USA
Use of CARS (Coherent Anti-Stokes Raman Scattering) microscopy to measure molecular penetration in hair

12:55 End of Lectures

13:00 Lunch and Social Event

Friday, September 11

9:00 **E. Max**[1], C. Wood[2], F. Bartels[3], A. Sugiharto[3], A. Fery[1]
[1] Department of Physical Chemistry II, University of Bayreuth/D
[2] Care Chemicals & Formulators Europe, BASF SE, Ludwigshafen/D
[3] Polymer Physics, BASF SE, Ludwigshafen/D
Haptics on human hair: from automated touches to single hair interaction measurements

9:25 **J.M. Marsh**[1], A. Schwan-Jonczyk[2], M.G. Davis[3], S.W. Stofel[3]
[1] The Procter & Gamble Company, Cincinnati, OH/USA
[2] Procter&Gamble Service GmbH/WELLA, Darmstadt/D
[3] The Procter & Gamble Company, Cincinnati, OH/USA
Consumer perception vs single and bulk fiber technical measurements

9:50 **S. Breakspear**, T. Itou, M. Nojiri, M. Fukuhara, A. Kiyomine, S. Inoue
Kao Corporation, Tokyo/JP
Alignment control and softness creation in hair with glycylglycine

10:15 **J. Jachowicz**[1], M. Zielinski[2]
[1] Better Cosmetics, Bethel, CT/USA
[2] Zevax/USA
The effect of hair damage on surfactant and polymer deposition from shampoos and conditioners by dynamic electro-kinetic and permeability analysis

10:30 Coffee Break

11:30 **R.L. McMullen**, S. Chen, G. Lu, D.J. Moore
Materials Science, Corporate R&D, International Specialty Products, Wayne, NJ/USA
Spectrofluorescence of keratin tissues

11:55 **A.L. Schulze zur Wiesche**[1], F.-J. Wortmann[2]
[1] Fiantec GmbH, Hamburg/D
[2] Textiles & Paper School of Materials, University of Manchester/UK
Controlling hair shine by natural and synthetic lipid films

12:20 **S. Mhaskar**[1], V. Shirhatti[1], V. Gode[1], N. Bhalla[1], N. Agarwal[1], P. Augustin[2]
[1] Marico Research Centre, Mumbai/IND
[2] DWI an der RWTH Aachen e.V., Aachen/D
Coconut oil - a natural „Do good" hair conditioner

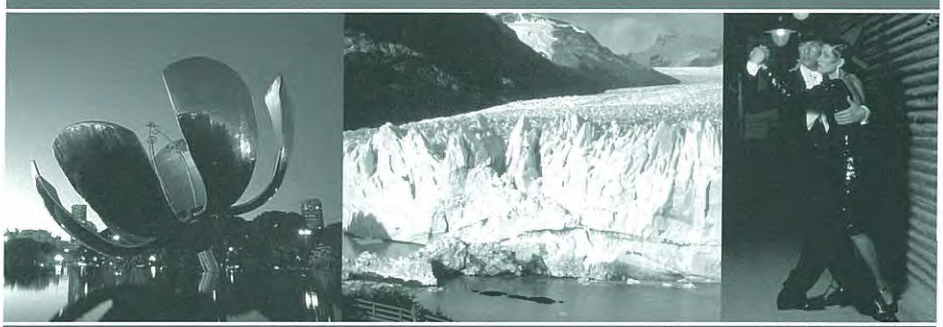
12:45 **R.K. Ramaprasad**, K. McAllister, S. Ruetsch, Y. Kamath
TRI, Princeton/USA
Impact of nanotechnology on hair attributes

13:10 Awarding of Best Presentations
Closing Remarks

13:30 Lunch and Farewell

26th Congress of the International Federation of Societies of Cosmetic Chemists

September 20-23, 2010
Buenos Aires, Argentina



DEADLINE FOR ABSTRACTS SUBMISSION
November 2, 2009

PRELIMINARY TOPICS

COSMETICS: Physical, chemical and biological aspects
a. Developments in Actives Research
b. New Materials and Formulations
c. Advances in Delivery Technology
d. Advances in Cosmetic Manufacture and Control. Equipment.
e. Assessment of Cosmetic Efficacy

WELL-BEING AND BEAUTY COSMETICS
a. Immune System and Cosmetics
b. Neurobiology to Improve Skin Wellness
c. Cosmetic Performance through Sensorial Appeal
d. Advances in bioavailability technology
e. Decorative Cosmetics

PROTECTIVE STRATEGIES
a. Special Cosmetics
b. Care of Hair, Nails and Skin
c. Anti-aging Research: What is New?
d. Sunscreens and Sun blockers.

SOCIETY AND COSMETICS
a. Environment-friendly Cosmetics
b. Consumer Health: Prevention, Care and Safety
c. Animal Testing Alternatives
d. Legislative Changes and Challenges

Organized by:
Asociación Argentina de Químicos Cosméticos

Developed under the auspices of:
IFSCC

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Note

In copertina / Front cover

Tessuto biofunzionale di acetato di cellulosa con nanofibrille di chitina e luteina.
Foto al microscopio elettronico a scansione (SEM). Su gentile concessione dell'Istituto di Morfologia Umana Normale, Università Politecnica delle Marche, Ancona, Italia.

Biofunctional tissue of cellulose acetate with chitin nanofibrils and lutein.
Scanning Electron Microscopy (SEM). On kind permission of the Institute of Human Normal Morphology, Università Politecnica delle Marche, Ancona - Italy.

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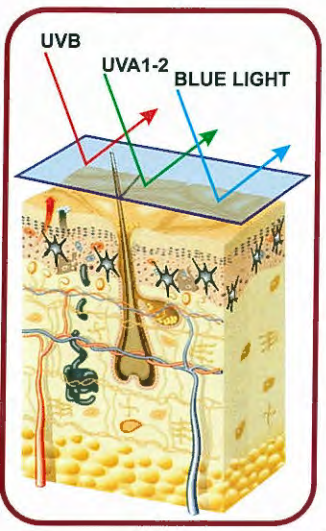

against

- UVB-UVA and blue light
- free radicals
- photoimmunosuppresion
- photoinduced dehydration

La fotoprotezione integrata

contro:

- UVB-UVA e luce blu
- danno radicalico
- fotoimmunosoppressione
- disidratazione fotoindotta

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