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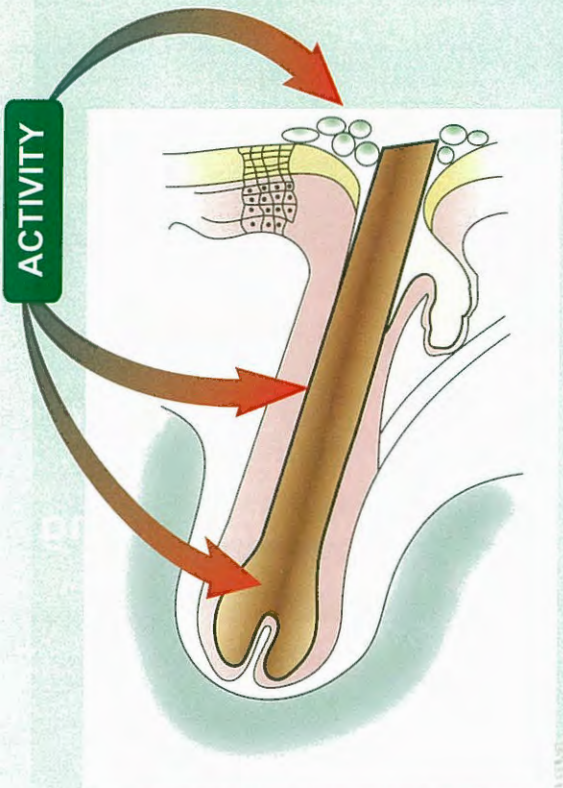

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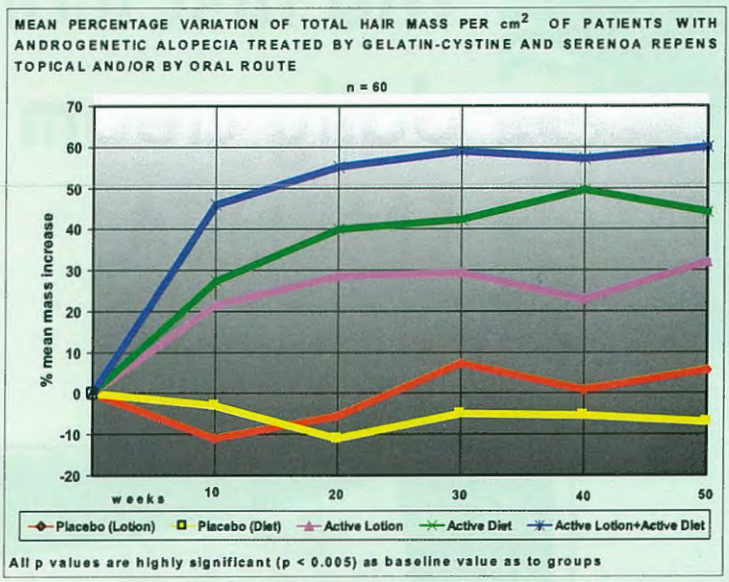

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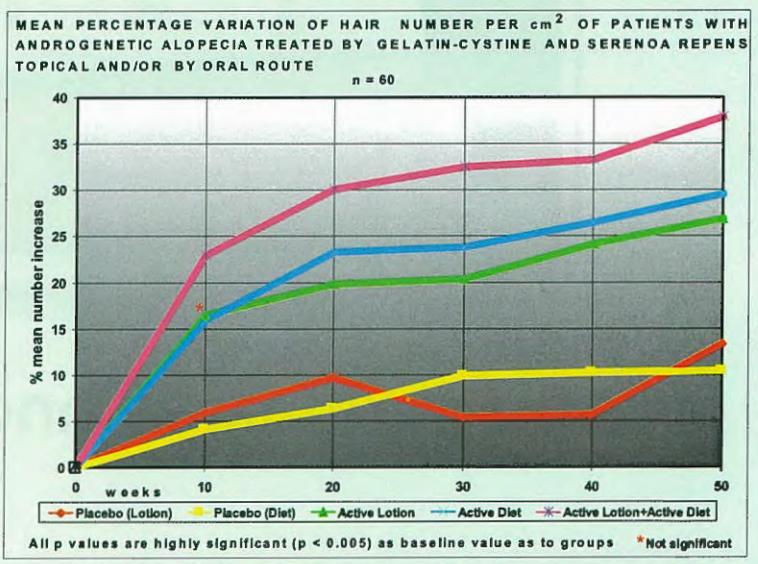

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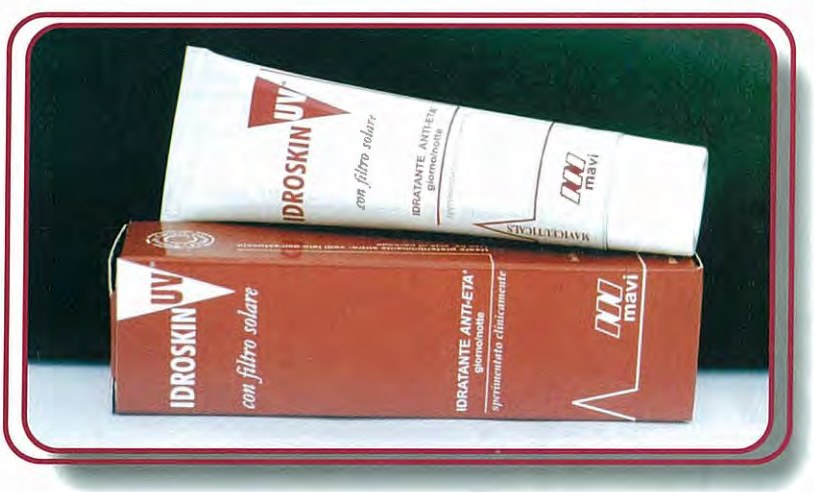

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Trimestrale di Dermatologia Cosmetologica
Quarterly Review of Cosmetic Dermatology

J. Appl. Cosmetol. **25,** 85-92 (July/September 2007)

SKIN CARE IN ATOPIC DERMATITIS

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Received: *February, 2007. Presented at Personal Care & Homecare Ingredients Conference, Warsaw, 25-26 October, 2006.*

Key words: *Atopic dermatitis; Epidermal barrier; Emollients;*

Summary

Atopic dermatitis (syn.: atopic eczema, AD) is the commonest childhood inflammatory skin disease. Many factors can influence the condition of the skin barrier in AD. They are linked with external environment as well as the general body condition. In earlier publications concerning AD pathogenesis, changes in barrier functioning were considered nearly solely as a consequence of inflammatory state. Now, alternative approach to this subject is postulated perceiving changes in epidermal lipids composition and disorders in epidermal cells differentiation as a group of crucial factors in pathogenesis of the disease.
The proper skin care, including omitting the factors responsible for barrier's damage (i.e. cleansing preparations based on aggressive surfactants, not containing refatting agents) as well as regular use of emollients, provide significant improvement in life quality of patients suffering from AD. It seems that emollient preparations for people with AD will be in the future based mainly on physicochemical forms that do not contribute to forming water-impermeable occlusive layer (o/w emulsions, lipid nanoparticles, w/o emulsions containing "light" emollients).

Riassunto

La dermatite atopica (DA) è la più comune affezione a carattere infiammatorio che colpisce i bambini. Legata ad una alterazione della barriera cutanea è influenzata sia dalle condizioni ambientali che dalle condizioni generali dell'organismo.
Mentre anni fa si pensava che il processo infiammatorio fosse esclusiva conseguenza dei cambiamenti verificatisi a livello del cattivo funzionamento della barriera, ora è stato dimostrato come la

composizione dei lipidi delle lamelle e la differenziazione cellulare rappresentano fattori cruciali di questa forma patologica. Così l'uso corretto di prodotti emollienti e l'eliminazione di detergenti aggressivi sono considerati molto utili a migliorare la qualità di vita delle persone affette da DA. Soprattutto tra gli emollienti si utilizzeranno nuove forme cosmetiche nanostrutturate risultate più adatte allo scopo.

INTRODUCTION

Atopic dermatitis (syn.: atopic eczema, AD) is the commonest inflammatory skin disease of childhood, affecting 15-20% of children in industrialized communities at any one time. Adults make up about one-third of all community cases. Moderate-to-severe atopic eczema can have a profound effect on the quality of life for both sufferers and their families.

Major milestone in describing the main clinical features of AD was the Hanifin and Rajka diagnostic criteria published in 1980. According these criteria, in order to qualify as a case of atopic dermatitis, the person must have:

- an itchy skin condition plus three or more of:
- past involvement of the skin creases, such as the bends of elbows or behind the knees
- personal or immediate family history of asthma or hay fever
- tendency towards a generally dry skin
- onset under the age of 2 years
- visible flexural dermatitis as defined by a photographic protocol.

EPIDERMAL BARRIER IN AD

Atopic dermatitis is apart from psoriasis one of the most frequently occurring dermatological disease that is accompanied by serious epidermal barrier disorders.

Many factors can influence the state of the skin barrier. They are linked with external environment (UV, decrease in humidity, etc.) as well as the general body condition (changes in barrier lipids composition at elderly, stress, pathological states). In many cases it is difficult to separate unequivocally the extent of the influence, which particular factors have on skin barrier condition and functioning. In case of atopic dermatitis the fact of occurrence the disease itself (excepting inflammatory state development, disorders in synthesis of barrier lipids, etc) generates a number of factors that additionally deteriorate barrier condition (stress, itching and *stratum corneum* damage related to it).

In earlier publications concerning AD pathogenesis, changes in barrier functioning were considered nearly solely as a consequence of inflammatory state. Now, alternative approach to this subject is postulated perceiving changes in epidermal lipids composition and disorders in epidermal cells differentiation as a group of crucial factors in pathogenesis of the disease [39]. In spite of this, there is still no theory that explains unambiguously the mechanism of arising changes in epidermal barrier structure in atopic dermatitis. The basic dysfunctions in the structure of epidermal barrier and homeostasis of epidermis are presented in Table I.

The result of disorders in epidermal barrier structure and homeostasis is a number of changes typical for AD. The main symptom is obviously skin dryness (increase in TEWL, decrease in values of electrical parameters measurements) [13, 16 - 20, 37, 40] related directly to the increase in water permeability of the barrier and disorders in mechanisms restoring the correct structures of the barrier. An increase in TEWL value is positively correlated to AD exacerbation [45]. Water deficiency in *stratum corneum* leads to disturbances in desmosomes degradation, abnormalities in desquamation and the decrease in epidermis elasticity [19]. Dysfunctions of skin barrier functioning result also in obviously higher susceptibility to irritations [36] related to more effective penetration of xenobiotics through the *stratum corneum*.

Table I

The basic dysfunctions in the structure of epidermal barrier and homeostasis of epidermis in AD

Type of change		Source
Increase in epidermis thickness		[Nassif 1994]
Decrease in stratum corneum thickness		[Al-Jaberi 1994]
Barrier damage may occur not only in atopic lesions but also beyond them (in the stage of acute changes)		[Seidenari 1995], [Melnik 1989]
Decrease in surface lipids amount		[Jakobza 1981], [Barth 1989], [Sator 2002]
Increase in proliferation area, disturbances in differentiation. Faster turnover, smaller corneocytes.		[Van Neste 1979], [Ekanayake-Mudiyanselage1998], [Watanabe 1991]
Disturbances in epidermal lipids metabolism, excessive phospholipase A2 activity		[Schafer 1991],
Changes in barrier lipids composition	decrease in the amount of ceramides, especially ceramide 1 and ceramide 3. Decrease in the amount of omega-hydroxyceramides bound to the corneocyte envelope. Disorders in proportions between individual classes of barrier lipids, increase in FFA and free sterols	[Melnik 1988], [Melnik 1990], [Imokawa 1991] [Macheleidt 2002] [Mustakiallo 1967]
Increase in the share of gel phase (hexagonal) with relation to crystalline phase (orthorhombic) in the intercellular cement		[Pilgram 2001]

COSMETICS IN AD THERAPY

For decades, topical corticosteroids were used in AD therapy. They brought good therapeutical effects, but sometimes they also gave a number of side effects such as: suppression of the pituitary-adrenal axis, Cushing syndrome (systemically), spread of untreated fungal infection, irreversible stretch marks and prominent fine blood vessels, contact dermatitis, perioral dermatitis and worsening of acne and mild loss of pigmentation (locally) as well as skin thinning considered as the most serious local side-effect [11].

Nowadays, as the basic medicines for external use immunosuppressive macrolide lactones isolated from the Streptomyces spp. – tacrolimus and pimecrolimus are used the most often [11].

The external use of preparations of emollient activity is commonly considered as essential supplementation for both types of therapies. The proper skin care, including omitting the factors responsible for barrier's damage (i.e. cleansing preparations based on aggressive surfactants, not containing refatting agents) as well as regular use of emollients, provide significant improvement in life quality of patients suffering from AD. One of the factors influencing the improvement is soothing of itching and limitation of scratching (and its consequences: excoriation, etc) [43] linked with an increase in the amount of water in epidermis and *stratum corneum*. Moreover, improvement in life quality (stress reduction) may result in benefits in the skin barrier homeostasis.

Cleansing procedures is of great importance in AD skin care. Negative influence on skin condition in AD may exhibit hard water and water from water-supply system containing big amounts of chlorine [30]. Some authors suggest that chlorine in water from water-supply system may be one of the factors inducing exacerbation of skin changes [34]. Tendency to use (in case of

hard water) surfactants excess (to obtain "better" cleansing acting, better foaming, etc.) can lead to significant deterioration of epidermal barrier as well as exacerbation or prolongation of skin lesions [30]. For that reason, cleaning cosmetics for atopic skin should not contain typical, irritating and damaging skin surfactants (SLES), and they should contain additives in the form of refatting ingredients. Good effects were obtained if during atopic skin cleaning the addition of rice starch to a bath was used. It was noted that starch molecules exhibit high affinity to horny layer structures and remain on the skin surface after bathing, providing moisturizing and reducing TEWL. A similar effect was not observed for healthy skin [7].

PUFA and their derivatives are a group of emollients in which faith has been put for several years. The interest of this group of compounds results from good effects of PUFA in therapy of other skin barrier damages as well as good effects of oral supplementation in AD [47].

Clinical trials carried out up to now, were based mainly on application of plant oils rich in linoleic acid (LA) and gamma-linolenic acid (GLA); in most cases satisfactory results were obtained.[11, 47]. It was also observed that systematic application of typical cosmetic emulsions containing 12% evening primrose oil allows to reduce risk of skin changes exacerbation after contact with an allergen [5].

In AD therapy, emollients of no biological activity are also used (Table II). They allow to improve barrier condition through replenishment with *stratum corneum* lipids and linoleic acid or on the way of simple occlusive activity (mostly based on petrolatum). Most probably in this case, the normalization of water content in *stratum corneum* is of the greatest importance for therapeutic effect. It is confirmed by the fact of good therapeutical effects obtained also in case of formulations containing especially hydrophilic moisturizing compounds. A small number of research studies comparing long-term effects of using creams of strong emollient activity as well as the creams based on hydrophilic substances revealed the lack of significant differences in TEWL reduction in atopic lesions for both types of cosmetics [28].

For the sake of disadvantageous influence of full (continuous) occlusion on epidermal homeostasis and the state of skin in AD [15, 29], it seems that emollient preparations for people with AD will be in the future based mainly on o/w emulsions, lipid nanoparticles or w/o emulsions containing "light" emollients, that do not contribute to forming water-impermeable occlusive layer. However, the mechanism underlying the "light" emollient efficacy in the treatment of dry, atopic skin have not been well elucidated.

Table II

Cosmetic preparations evaluated in clinical and laboratory trials

Cosmetic preparations evaluated in clinical and laboratory trials	Source
Moisturizing, urea based emulsions	[Loden 2001], [Loden 2002]
Moisturizing, glycerine based emulsions	[Loden 2001], [Loden 2002] [Matsumoto 2005]
Moisturizing emulsions	[Tabata 2000], [Loden 2003]
w/o emulsions	[Lucky 1997]
Emollient-type, petrolatum based emulsion	[Matsumoto 2005]
Nanolipid preparations	[Berardesca 2001]
Emollient preparations containing "physiological lipids"	[Mao-Quiang 1995], [Chamlin 2001]
Emollient-type emulsions containing GLA-rich oils	[Anstey 1990], [Ferreira 1998], [Gehring 1999]

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FLAVONOIDS: A REVIEW FOR COSMETIC APPLICATION. PART I

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Key words: *Bio-active substances; Biological extracts; Enzyme manipulation; Enzyme cofactor;*

Summary

Flavonoids are now recognised as essential dietary components, although their functions are just on the brink of understanding. Dietary requirements have been established. Their significance is probably equal to vitamins. Approximately 5000 flavonoids have been identified, and the list is quickly expanding. The functionality of flavonoids is frequently "multi-purpose", contrary to vitamins, enzymes and (to a lesser extent) hormones.

Riassunto

I flavonoidi sono riconosciuti come componenti essenziali delle diete, anche se non sono state ancora comprese appieno le loro funzioni. Comunque ne è stato riconosciuto il loro ruolo dietetico che dovrebbe essere simile a quello delle vitamine.

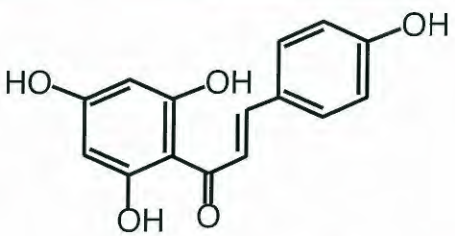
Circa 5000 sono i flavonoidi già identificati ed il loro numero si incrementa di continuo. Al contrario delle vitamine, degli enzimi e degli ormoni, l'attività di questi composti naturali è più complessa e serve a molteplici scopi.

INTRODUCTION

The Greek word "flava" means yellow. Flavonoids represent a broad variation of aromatic compounds occurring in higher plants, frequently with a yellow colour. Approximately 5000 flavonoids have been reported in the literature. The collective name flavonoids was introduced in 1952 by Geissman.

Many flavonoids are easily recognised as flower pigments in angiosperm families (flowering plants). However, their occurrence is not restricted to flowers only but may be found in all parts of the plant, in the roots, leaves and bark.

Flavonoids comprise a number of groups of structurally related products, also frequently identified as polyphenols. The majority of those have a similar skeleton containing 15 carbon atoms, subdivided in {6+9} carbon atoms. One part of the molecule, with 6 carbon atoms, is made up from a phenolic moiety. The second part, with 9 carbon atoms, has the cinnamic acid molecule as the building block. These building blocks are most visible in the group of chalcones, products that can be considered as the Friedel-Crafts condensation product of a (substituted) cinnamic acid and a phenol.



NARIGENIN CHALCONE
2,4,4',6-tetrahydroxychalcone

In naringenin chalcone the right part of the molecule is easily recognised as coumaric acid (4-hydroxycinnamic acid), condensed on resorcinol. The corresponding flavonoids may be formed from the chalcones via oxidative ring closure. Also flavonoids are known that are formed by reduction of the carbonyl group on the 4-position. In the laboratory this can be done via the Wolff-Kishner reduction.

A wide variety of chalcones occur naturally, and are considered to be precursors for condensed flavonoids. Plants use chalcone synthases (CHS) to make chalcones, enzymes that are highly specific for the synthesis of particular chalcones. Chalcones are, among others, used in the defense mechanism of plants against pathogenic organisms (fungi). Chalcones exist in several forms such the (trans)-chalcones (e.g.naringenin chalcone, lanceoletin & okanin), cis-chalcones (e.g. isookanin), but also dihydrochalcones (e.g. phloretin, asebogenin) where the Δ(2-3) double bond is hydrogenated and quinochalcones (2-cinnamoylquinone, pedicinin). In the last case two hydroxy groups in the ortho or para-position have been oxidised to the corresponding quinone.

Quinoid flavonoids have quite extensively been reported in the literature. Pedicinin occurs in Didymocarpus pedicellata (pathar-phori), next to isopedicin and pedicillin (Siddiqui) and is the active substance of Cystone (Subramaniam, 1961), an Ayurvedic preparation locally used as a non-toxic diuretic. The Ayurvedic medicine is truly a breeding place for physiologically active substances.

Flavonoids may occur as their glycosides, products that are substituted on one or more of the hydroxy groups with a sugar such as glucose, rhamnose, galactose, mannose, etc., or their aglycons, products that do not carry a sugar moiety.

In the identification and structure elucidation of flavonoids the first step is always full hydrolysis of the glycoside, to obtain the corresponding aglycon. This is subsequently fused with potassium hydroxide or barium hydroxide (Willstätter, Karrer) whereby always a polyhy-

droxybenzene is formed (e.g. catechol, phloroglucinol) and a phenolic acid (e.g. 4-hydroxybenzoic acid, protocatechuic acid [3,4-dihydroxybenzoic acid]), eventually as the (poly)-methyl ether. This is a relatively straight forward analytical procedure.

The determination of the identity and the position of the sugar moieties is more complex. In all cases total synthesis, combined with chromatography and spectroscopic techniques (especially FTIR, NMR and mass spectroscopy), must confirm the absolute structure of a particular flavonoid. The analytical problems encountered are frequently tough, tedious and laborious. It is like a jigsaw puzzle, reason why many chemists traditionally carefully have walked around this product group.

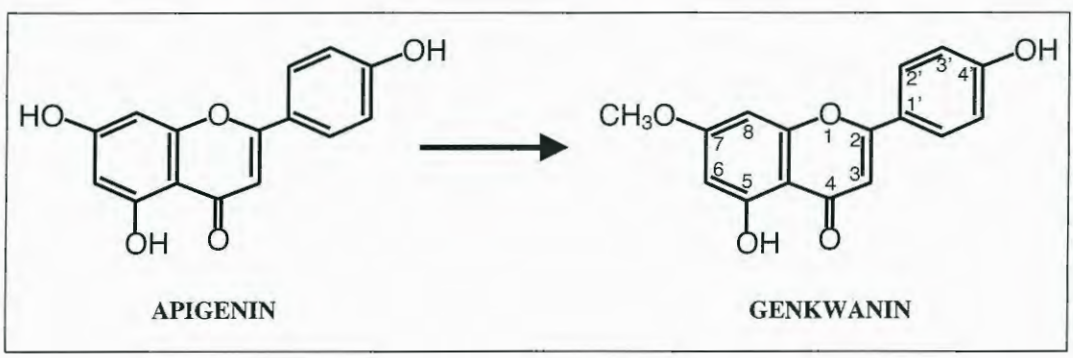
Reductive ring closure of chalcones results in the formation of flavones. Naringenin chalcone is enzymatically made from coumaroyl-CoA and malonyl-CoA using the enzyme naringenin CHS, and this is converted to naringenin, from which apigenin (4',5,7-trihydroxyflavone) is formed by ring closure. Enzymatic methylation using the enzyme flavonoid-7-O-methyltransferase results in the formation of genkwanin (4,5'-dihydroxy-7-methoxyflavone). The numbering system is included in the genkwamin molecule. The formation of genkwanin is only one possible pathway. There are a large number of permutations possible for the formation of flavonoids, depending on the enzymes that the plants make use of or that are made available by micro-organisms with which plants live in symbiosis (mostly fungi).

Many of these reactions, and the micro-organisms/enzymes involved, on the biosynthesis and metabolism of flavonoids (as well as styrene and lignin synthesis) are found in extensive databases such as from the Institute for Chemical Research of Kyoto University, found on www.genome.ad.jp. The ICR database also covers all other product groups such as carbohydrates, lipids, etc.

Flavones

The simplest representative of the group of flavones is "flavone", which does not carry any hydroxy, methoxy or glycosidic groups. It naturally occurs as "dust" on flowers and leaves. The laboratory synthesis of flavone is easy, and many different synthetic routes have been reported in the literature, using 2-hydroxyacetophenon and benzaldehyde. In table I some flavones have been collected that are frequently encountered in botanical extracts.

Most flavones are yellow solids. A bathochromic shift is observed when flavones are dissolved in concentrated sulphuric acid and a further shift of λ_{max} to bright orange/red is observed in a solution of magnesium chloride/hydrochloric acid, while also the value of e at λ_{max} is also increased. The photochemical stability is high.



Many flavones are soluble in (hot) water and ethanol, as well as in diluted alkali and acid, including α-hydroxycarboxylic acids (e.g. glycolic acid). It is interesting to note that a significant synergism has been reported in cosmetic preparations whereby the flavones were dissolved in medium concentrated α-hydroxycarboxylic acids such as lactic acid and/or glycolic acid. Also trimethylglycine (betaine; originating from sugar beets) is an excellent solubility enhancer for flavones.

Flavones are generally found in herbaceous families such as Labiatae, Umbelliferae and Compositae. Important flavones are apigenin (Apium graveolens [celery], Carum petroselinum [parsley]; 4,',5,7-trihydroxyflavone), luteolin (Equisetum arvense [horsetail] 3',4',5,7-tetrahydroxyflavone) and diosmetin (3',5,7-trihydroxy-4'-methoxyflavone).

Apigenin

Reported activities: anti-ageing, antidermatitic, antistress, antitumour, antiviral, COX-1/2 inhibitor, DNA protective, hyaluroniodase inhibitor, MAO inhibitor, ornithine decarboxylase inhibitor, topoisomerase I/II inhibitor, vasodilator, radioprotective.

Apigenin is a flavone found in parsley, artichoke, basil, Roman chamomile and celery.

Over the last five years, a large number of published studies have demonstrated the anti-cancer properties of apigenin. To study the effects of various plant constituents, an examination was made of 21 different flavonoids on the growth of human breast cancer cells.

Apigenin was shown to the most effective anti-proliferative flavonoid tested.

Table I

Frequently occurring flavones

Acacetin	5,7-dihydroxy-4'-methoxyflavone
Amentoflavon (Sciadopitysin)	4',4,7-trimethoxyflavone
Apigenin	4',5,7-trihydroxyflavone
Apigenin trimethyl ether	4',5,7-trimethoxyflavone
Baicalein	5,6,7-trihydroxyflavone
Baicalein-7-methyl ether	5,6-dihydroxy-7-methoxyflavone
Chrysin	5,7-dihydroxyflavone
Chrysin dimethylether	5,7-dimethoxyflavone
Chrysoeriol	4',5,7-trihydroxy-3'-methoxyflavone
Diosmetin	3',5,7-trihydroxy-4'methoxyflavone
Eucalyptin	5-hydroxy-4',7'-dimethoxy-6,8-dimethylflavone
Eupatorin	3',5-dihydroxy-4',6,7-trimethoxyflavone
Eupatorin-5-methyl ether	3'-hydroxy-4',5,6,7-tetramethoxyflavone
Gardenin	5-hydroxy-3',4',5',6,7,8,-hexamethoxyflavone
Genkwanin (Gerardol)	4',5-dihydroxy-7-methoxyflavone
Hinokiflavone	4',6"-O-biapigenin
Luteolin	3',4',5,7-tetrahydroxyflavone
Luteolin tetramethyl ether	3',4',5,7-tetramethoxyflavone
Morin	2',3,4'5,7,8-hexahydroxyflavone
Pratol	7-hydroxy-4'-methoxyflavone
Primuletin	5-hydroxyflavone
Scutellarein	4',5,6,7-tetrahydroxyflavone
Scutellarein tetramethyl ether	5,6,7,4'-tetramethoxyflavone
Sinensetin	3',4',5,6,7-pentamethoxyflavone

A related study showed that flavonoids such as apigenin bind to estrogen receptor sites on cell membranes in order to prevent over-proliferation of these cells in response to estrogens.
One particular study assessed the antioxidant potencies of several dietary flavonoids compared with vitamin C. Pre-treatment with all flavonoids and vitamin C produced dose-dependent reductions in oxidative DNA damage. When ranked in order of potency, only apigenin, rutin and quercetin were more effective than vitamin C in reducing DNA oxidative damage.
Apigenin was tested to ascertain its effect on human leukaemia cells. Apigenin was shown to induce apoptosis more effectively than quercetin and other flavonoids tested. The researchers attributed a unique mechanism of inducing apoptosis to the cancer preventive activity of apigenin. Another study showed that apigenin and the flavonoid luteolin strongly inhibited the growth of human leukaemia cells and induced these cells to differentiate. Topoisomerases are involved in many aspects of leukaemia cell DNA metabolism such as replication and transcription reactions. In one study, quercetin and apigenin were shown to inhibit topoisomerase-catalysed DNA irregularities. In a study of various agents used to induce differentiation of human promyelocytic leukaemia cells, apigenin and luteolin were among the flavonoids shown to cause these leukaemia cells to mature into healthy monocytes and macrophages.
In studies against thyroid cancer cell lines, apigenin and luteolin were the most effective inhibitors found. Apigenin was demonstrated to inhibit cancer cell signal transduction and induce apoptosis. It was concluded that apigenin may provide a new approach for the treatment of human anaplastic thyroid carcinoma for which no effective therapy is presently available. Another study compared the effects of genistein, apigenin, luteolin, chrysin and other flavonoids on human thyroid carcinoma cell lines. Among the flavonoids tested, apigenin and luteolin were, again, shown to be the most potent inhibitors of these cancer cell lines. The scientists noted that because these thyroid cancer cells lacked an anti-estrogen receptor binding site and an estrogen receptor, that apigenin and luteolin are inhibiting these cancer cells via previously unknown mechanisms. The scientists concluded that apigenin and luteolin may represent a new class of therapeutic agents in the management of thyroid cancer.
Caltagirone et.al. (1) recently showed tumour growth inhibition using apigenin in their research to investigate the effects of particular flavonoids on the growth and metastatic potential of B16-BL6 melanoma cells in vivo. A significant, dose-dependent delay of tumour growth, without toxicity, was observed in relative descending order of potency of apigenin > quercetin > tamoxifen > resveratrol > control. Furthermore, polyphenols significantly potentiated the inhibitory effect of a non-toxic dose of cisplatin.
Apigenin can inhibit skin cancer induced by UV radiation (UV-A & B) and is therefore a highly valuable ingredient for sun care products. As it becomes more and more obvious that UV-filters are coming to the end of their lifetime cycle, new mechanisms become applicable such as to avoid excessive water loss and the development of genetic damage due to [2+2] photoadditions, apigenin is one of the newborn stars.

Baicalein / Baicalin

Reported activities: lipoxygenase inhibitor, anti-acne, reverse transcriptase inhibitor (HIV), antidote (strychnine), apoptotic, COX-1/2 inhibitor, triglycerolitic, xanthine oxidase inhibitor.
Baicalein is a flavon found in Scutellaria Baicalensis (Baikal skullcap), largely as its glycoside with glucuronic acid (coupled on the 7-postion; baicalin). Baikal skullcap is member of the mint family, ornamentally used in many gardens because of the beautiful flowers; despite its relationship with the mint family the flowers and leaves are virtually odour-free.

Baicalein/baicalin have been described as the most significant non-nucleoside reverse transcriptase inhibitors (NNRTI's). Reverse transcriptase, a specific enzyme for viruses enabling a virus to invade healthy cells and duplicate themselves, can be inhibited by some nucleotide analogues (NRTI's; FDA approved since 1985). Baicalein & baicalin have been shown to also effectively inhibit reverse transcriptases, such as in the case of HIV-1, without side reactions. Integration of the viral DNA in the host chromosome is carried out by a second viral enzyme, an integrase, which unexpectedly is also vulnerable to enzyme inhibition (2).

3,5-Dicaffeoyl-quinic acid (a precursor for a number of flavonoids), found in Carqueja (Baccharis trimera) was reported to be a potent inhibitor of HIV-1 integrase *in vitro* at dosages as low as only 1 mcg/ml (3).

The applicable part of Baikal skullcap is the root. The pharmacological activity has been attributed to baicalin, baicalein, and to a lesser extent to the lesser investigated flavonoids wogonin and scutellarein. These flavonoids all appear to bind to particular receptors with benzodiazepine-like effects (4). Baicalein has weak antipyretic properties and there are indications that it also has anti-mutagenic alpha-glucosidase activity.

Baicalin has potent anti-inflammatory and anti-tumour properties. Some evidence suggests it can inhibit tumour growth and suppresses carcinoma cell proliferation. Baicalein and baicalin are reported to be far more active as free-radical scavengers than e.g. d,l-α-tocopherol.

Baikal skullcap has antibacterial and antiviral properties, as well as antifungal activity, particularly against Candida albicans. It has been suggested that Scutellaria extract can be used as preservative, although broad spectrum activity is subject to discussion.

Baikal skullcap, usually addressed a Scutellaria, has been listed in the Chinese Pharmacopoeia for centuries. Its dried roots are better known under the name "Oughon" were valued for their anti-inflammatory action. Oughon was much sought after by noblewomen, as it helped to give them a radiant, porcelain complexion. Today, it is still utilized in cosmetology for this reason (citation: Clarins).

Many flavones occur as glycosides. In table II some frequently occurring glycosides. Flavones also occur in nature in association with tannins (polyesters of gallic acid; 3,4,5-trihydroxybenzoic acid). Gallic acid and its esters (e.g. propyl gallate, dodecyl gallate) are well-known as powerful anti-oxidants, and probably these products fulfil a similar role in higher plants.

Next to the O-glycosides flavones also occur as C-glycosides. This has not been reported for other flavonoids. Examples of O-glycosides are vitexin (3,4',5-trihydroxy-2-glucosylflavone) and isovitexin (3,4',5-trihydroxy-4-glucosylflavone).

An interesting synthesis of flavones is by ring expansion of 2-benzylidenecoumaran-3-ones (Wheeler). These substances are known as aurones, and several have been reported to occur naturally. In aurones the 6-membered heterocyclic ring is replaced by a 5-membered ring. Coreopsis grandiflora (tickseed), a nice ornamental flower, contains various aurones: hispidol, sulfuretin, maritimetin, leptosidin. Sulfuretin is identified as 6,3',4'-trihydroxyaurone.

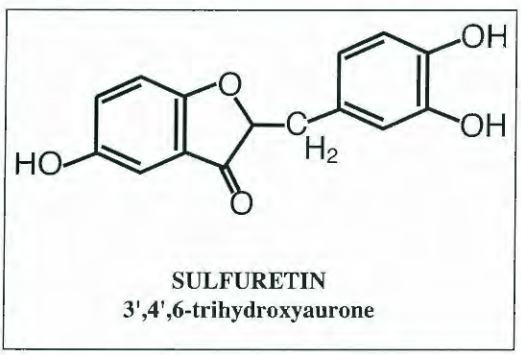
Flavonols

Flavones with a hydroxy group on the 3-position (3-hydroxyflavones) are usually considered as a separate group, and are named flavonols. To this group belongs the most important product quercetin (3,3',4',5,7-pentahydroxyflavone).

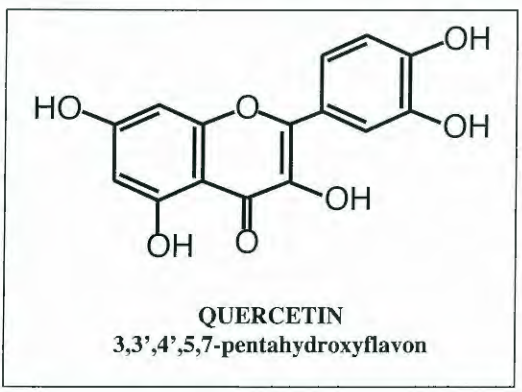
An important commercial source for quercetin is the glycoside quercitrin, which is present in large amounts in the bark of Quercus tinctoria. Quercetin is also present in significant concentration in Ruta graveolens [rue], Fagopyrum esculentum and Sambucus nigra [elder flower].

Table II
Frequently occurring flavone glycosides

Acacetin-7-neohesperidoside	Fortunellin
Acacetin-7-rutinoside	Linarin
Apigenin-7-apioglucoside	Apiin
Apigenin-7-glucoside	Apigetrin; Cosmetin; Cosmiin
Apigenin-7-rhamnoglucoside/neohesperoside	Rhoifolin
Apigenin-7-rutinoside	Isorhoifolin
Baicalein-7-O-glucuronide	Baicalin
Diosmetin-7-neohesperidoside	Neodiosmin
Diosmetin-7-rutinoside	Diosmin, Barosmin
Luteolin-8-C-glucoside	Orientin



SULFURETIN
3',4',6-trihydroxyaurone



QUERCETIN
3,3',4',5,7-pentahydroxyflavon

Quercetin is a very potent phosphodiesterase inhibitor with significant application potential. Quercetin is probably the most frequently occurring botanical pigment, and many glycosides of quercetin have been isolated and identified.

The flavonols kaempferol (3,5,7,4'-tetrahydroxyflavone; present in Sambucus nigra, Cassia senna, Equisetum arvense, Lamium album [white nettle] and Polygonum bistorta) and Myricetin (3,5,7-trihydroxy-3',4',5'-trimethoxyflavon; occurs in Glycyrrhiza glabra [licorice]) occur in many botanical extracts to which they give a significant value-added.
Other interesting flavonols are galangin (3,5,7-trihydroxyflavone; galanga root) and gossypetin (gossypol; 3,5,7,8,3',4'-hexamethylflavone; occurs in Gossypium herbaceum [cotton]). Gossypetin has anti-carcinogenic, antiviral and anti-allergic activity, and is active against infections with Trypanosomes, next to fisetin and rhamnetin. In table III the most important flavonols are collected, while in table IV some of their glycosides are listed.

Kaempferol

The consumer product market offers a multitude of products that claim to have anti-ageing properties. However, ageing is unavoidable, but the signs of ageing can be significantly delayed. The signs of ageing are biologically not at all significant. Ageing starts on the very moment of conception.

Table III
Frequently occurring flavonols

Fisetin	3,3',4',7-tetrahydroxyflavone
Fisetin-3',4'-dimethyl ether	3,7-dihydroxy-3',4'-dimethoxyflavone
Galangin	3,5,7-trihydroxyflavone
Gossypetin	3,3',4',5,7,8-hexahydroxyflavone
Kaempferide	3,5,7-trihydroxy-4'-methoxyflavone
Kaempferol	3,4',5,7-tetrahydroxyflavone
Myricetin (Cannabiscetin)	3,5,7,3',4',5'-Hexahydroxyflavone
Quercetin	3,3',4',5,7-pentahydroxyflavone
Quercetin-3,5,7,3',4'-pentamethylether	3,3',4',5,7-pentamethoxyflavone
Quercetin tetramethyl ether	5-hydroxy-3,7,3',4'-tetramethoxyflavone
Retusin	3,3,'4',7-tetramethoxyflavone
Rhamnetin	3,5,3',4'-tetrahydroxy-7-methoxyflavone
Robinetin (5-Hydroxyfisetin)	3,3',4',5',7-pentahydroxyflavone
Robinetin trimethyl ether	3,7-dihydroxy-3',4',5'-trimethoxyflavone
Syringetin	3,5,7,4'-tetrahydroxy-3',5'-dimethoxyflavone
Tamarixetin	4'-methoxy-3,3',5,7-tetrahydroxyflavone

The present points of view of gerontology is that the level of telomers is determining for the statistical age (2).

The signs of skin ageing originate from a biologically driven enzyme disbalance, whereby a wide variety of enzymes are involved (up to present more than 160 have been reported). This involves enzymes such as collagenases (collagen degrading enzymes), elastases (elastin degrading enzymes), hyaluronidases (hyaluronic acid degrading enzymes; seven have been positvely identified), tyrosinases (enzymes that induce the formation of melanin), c-ATPases (enzymes that degrade cyclic ATP), kinases (enzymes that catalyse the transfer of phosphate groups from a high-energy phosphate containing group [as ATP or ADP] to a substrate; many have been identified), etc. These enzymes require co-factors to become active, frequently vitamins or metal ions such as Mg^{2+}. Flavonoids may act as a negative co-factor: the enzyme is satisfied, but is immediately in-active, after the interaction {enzyme-flavonoid} has been realised, and there is no need for further enzyme production. Consequently degradation of particular products is partially inhibited. Good examples are collagen and elastin (polymers that give structure to the skin), hyaluronic acid (which plays a role in the maintenance of the cellular water balance), etc.

Park & Ikegaki (5) demonstrated that propolis (bee glue) contains high levels of flavonoids (kaempferol, quercetin, pinocembrin, sakuratenin and isosakuratenin, next to smaller amounts of kaempferide [4' methylated kaempferol], acacetin and isorhamnetin). It was claimed that especially kaempferol was a potent hyaluronidase inhibitor. Independantly Uda et.al (2) showed that kaempferol (also occuring in large amounts in kale), as well as Zhang et.al (7), using broccoli sprouts may induce phase II enzymes to delay carcinogenesis leading to premature apoptosis.

In today's cosmetic chemistry some flavonoids act on enzyme inhibition using the estrogen properties. Well-known examples of flavonoids with estrogen properties are the isoflavones

genistein and daidzein. They are also named phenolic estrogens, to distinguish them from steroidal estrogens. Geometrically the structure of daidzein compares to 17-β-estradiol and is therefore able to mimic the spatial structure. Activity-wise phyto-estrogens are much weaker than steroidal estrogens, varying from 0,005-2%. Also formonometin and biochanin have phyto-estrogen properties.

The estrogen properties are by no means suitable to replace steroidal estrogens, but they do have significant interactions with the organism to enable to reduce the effects of ageing, including the improvement of the quality of skin and the delay osteoporosis. In traditional Indonesian and Chinese phytopharmacy and in the Ayurvedic approach various sorts of legumes have been employed to control osteoporosis.

Nonetheless, it shall be emphasised that the use of phyto-estrogens has a potential risk as to interfering the human hormone system has a price, although this price has not yet been determined. This is not well possible either, as the issue of bio-availability has not yet properly been addressed.

Flavonols also occur widespread in nature as their glycosides. Table IV summarises some of these glyosides.

The hydroxy groups may also be esterified with substituted cinnamic acids, such as coumaric acid (4-hydroxycinnamic acid), caffeic acid (3,4-dihydroxycinnamic acid), ferulic acid (4-hydroxy-3-methoxycinamic acid), umbellic acid (2,4-dihydroxycinnamic acid), sinapic acid (3,5-dimethoxy-4-hydroxycinnamic acid). Also esters of the glycosides and substituted cinnamic acids occur widespread. A good example is tiliroside (Tilia cordata; Linden), which can best be described as kaempferol-3-glucosylflavone-[1,3]-coumaric acid ester.

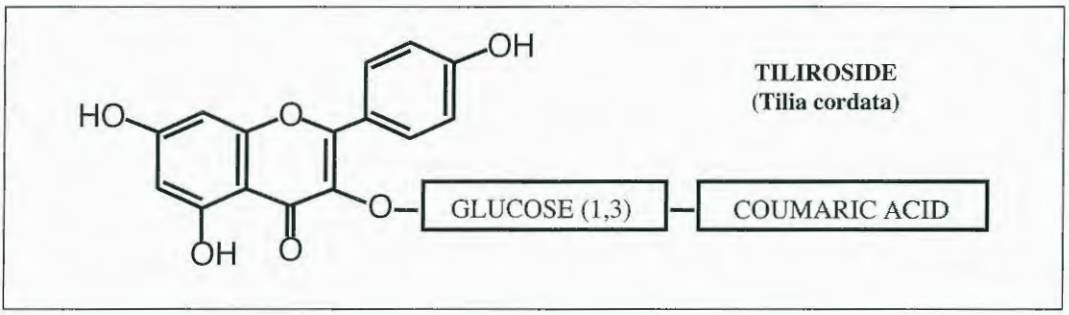
Isoflavones

Isoflavones differ from flavones from the fact that the phenyl group is attached to the 3-position, compared to flavones where the phenyl group is attached to the 2-position. The isoflavones also occur naturally, but have a rather limited taxonomic distribution, mainly within the Leguminosae (beans, soybeans, lentils, chick peas, etc). A very rich source of isoflavones is clover; soybeans are probably second best. Approximately 1000 different isoflavones have been isolated and identified; most of them are colourless solids.

Table IV

Frequently occurring flavonol glycosides

Isorhamnetin-3-rutinoside	Narcisin
Gossipetin-8-glucoside	Gossypin
Kaempferol-3-glucoside	Astragalin
Kaempferol-3-robinoside-7-rhamnoside	Robinin
Quercetin-3-arabinoglucoside	Peltatoside
Quercetin-3-arabinoside	Avicularin
Quercetin-3-galactoside	Hyperoside; Hyperin
Quercetin-3-glucoside	Isoquercetin
Quercetin-3-rhamnoside	Quercitrin
Quercetin-3-rutinose	Rutin
Myricetin-3-rhamnoside	Myricitrin



TILIROSIDE
(Tilia cordata)

Well-known examples of isoflavones are genistein (4',5,7-trihydroxyisoflavone) and daidzein (4',7-dihydroxyisoflavone). Daidzein and genistein are phyto-estrogens. They are also named phenolic estrogens, to distinguish them from steroidal estrogens.

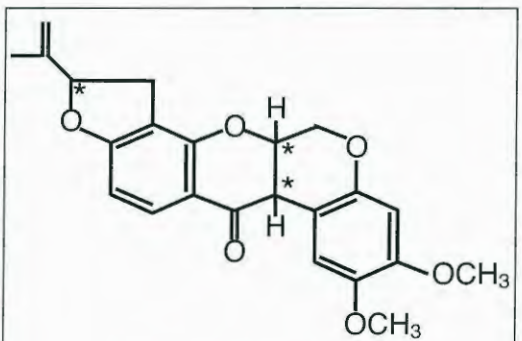
The interesting fact is that geometrically the structure of daidzein compares to 17-β-estradiol and is therefore able to mimic the spacial structure. Activity-wise phyto-estrogens are much weaker than steroidal estrogens, varying from 0,005-2%. Also formonometin and biochanin have phyto-estrogen properties.

The estrogen properties are by no means suitable to replace steroidal estrogens, but they do have significant interactions with the organism to enable to reduce the effects of ageing, including the improvement of the quality of skin and the delay osteoporosis. In traditional Indonesian & Chinese phytopharmacy and in the Ayurvedic approach various sorts of legumes have been employed to control osteoporosis.

Another interesting isoflavon is rotenone, which comes from derris root (Derris elliptica), Lonchocarpus utilis (Southeast Asia) and Lonchocarpus urucu (South America). It is a powerful insecticide and very toxic to fish, one of its main uses by native people over the centuries. The fish is paralysed enabling an easy catch.

It is remarkable that rotenone is toxic to guinea pigs and rats, but hardly toxic to rabbits. Human toxicity of rotenone is low; the LD_{50} is larger than 2g/kg body weight. Extracts with rotenone are traditionally used to fight ectoparasites such as head lice, having said that rotenone is a severe irritant to eyes, skin, mucous membranes and throat.

GENISTEIN
4',5,7-trihydroxyisoflavone



ROTENONE
(Rotenone has three chiral carbon atoms)

Table V
Some isoflavones, as their aglycons & glycosides

Biochanin-A	5,7-dihydroxy-4'-methoxyisoflavone
Daidzein	4',7-dihydroxyisoflavone
Formonometin	7-hydroxy-4'-methoxyisoflavone
Glycitein	4',7-dihydroxy-6-methoxyisoflavone
Genistein	4',5,7-trihydroxyisoflavone
Genistein-4',7-dimethylether	5-hydroxy-4',7-dimethoxyisoflavone
Prunetin	4',5-dihydroxy-7-methoxyisoflavone
Genistin	glucosyl-7-genistein
Glycitin	4',7-dihydroxy-6-methoxyisoflavone-7-d-glucoside
Ononin	formononetin-7-O-glucoside
Sissotrin	biochanin A-7-glucoside

Table VI
Some important flavanones, as their aglycons

Dihydrorobinetin	3,3',4',5',7-pentamethoxyflavanone
Pinocembrin	5,7-dihydroxyflavanone
Sakuranetin	4',5-dihydroxy-7-methoxyflavanone
Eriodictyol	3',4',5,7-tetrahydroxyflavanone
Hesperedin	3',5,7-trihydroxy-4'-methoxyflavanone
Pinostrobin	5-hydroxy-7-methoxyflavanone (pinocembrin-7-methylether)
Naringenin	5,7,4'-trihydroxyflavanone
Taxifolin	3,5,7,3',4'-pentahydroxyflavanone (2,3-dihydroquercetin)
Fustin	3,3',4',7-tetrahydroxyflavanone (2,3-dihydrofisetin)
Cyrtopterinetin; Farrerol	4',5,7-trihydroxy-6,8-dimethylflavanone
Poncirin	5-hydroxy-7-methoxyflavanone

Plants make rotenone starting with 4',5,7-trihydroxyisoflavone, which is hydroxylated to obtain 2',4',5,5',7-pentahydroxyisoflavone, followed by partial methylation with methionine and reaction with dimethylallyl pyrophosphate (the precursor for geraniol and farnesol) to introduce an isoprene unit on the 8-position. Ring closure finally leads to the formation of rotenone.

Flavanones

Flavanones are characterised by the absence of the D2-3 double bond. In this group some very important physiologically active products are found, which are summarised in table VI.

A typical representative is 2,5-dihydroxy-7-methoxyflavanone. This is found in black poplar buds (Populus nigra). Also hesperidin (3',5,7-trihydroxy-4'-methoxy-flavanone) and naringenin (4',5,7-trihydroxyflavanone) are frequently occurring products in botanical extracts.

Differentiation of products on the basis of the presence of a hydroxy group on the 3-position similar to flavones and flavonols is not applicable for flavanones. Due to the saturated Δ2-3 double bond there is at least one and frequently two asymmetric carbon atoms present. Frequently occurring flavanone glycosides are listed in table VII.

A very important flavanone is silymarine, obtained from Silybum marianum (Compositae; milk thistle, Maria thistle). Silymarin is a flavonolignan that is used because of its hepatoprotective properties. It is extracted from the seeds the milk thistle and comes together with three structurally related components: silibinin, silydianine and silychristine. What is commercially offered as silymarin is the mixture of these four substances. Silymarin was shown to provide cytoprotection and, above all, hepatoprotection.

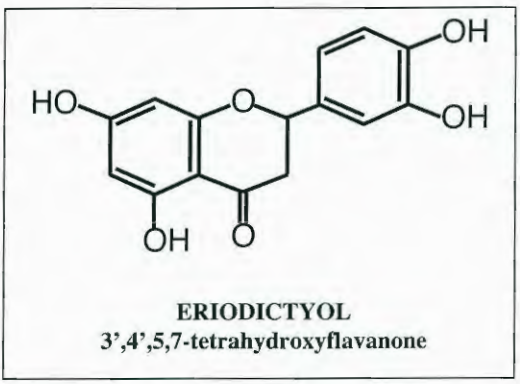
Silymarin is used for the treatment of numerous liver disorders characterised by degenerative necrosis and functional impairment.

Furthermore, it is able to antagonise the toxin of Amanita phalloides and provides hepatoprotection against poisoning by phalloidin, galactosamine, thioacetamide, halothane and CCl_4. It also protects hepatocytes from injury caused by ischemia, radiation, iron overload and viral hepatitis.

Also flavanones occur in Nature as glycosides, and some of those are collected in table VII.

Anthocyanins & Anthocyanidins

A lot of flowering plants obtain their colour from anthocyanins. The aglycons are named anthocyanidins. The products are derived from flavylium chloride. The colours are usually highly brilliant and may vary from orange, red blue to violet. Frequently the name of the plant can be deducted from the name of the dye (table VIII).



ERIODICTYOL
3',4',5,7-tetrahydroxyflavanone

Anthocyanins are water-soluble glycosides, ethers of polyhydroxy flavylium chloride and sugar moieties (e.g. glucose, rhamnose and galactose).

Pelargonidin is found in scarlet pelargonium and orange-red dahlia. Cyanidin is found in deep red dahlia, red roses and blue cornflower. Delphinidin is found in violet to blue flowers such as delphinium. Peonidin is also found in many flowers, such as red peony. Malvidin is found in e.g. Primula viscosa (less blue than delphinidin), while hirsutidin is found in e.g. Primula hirsute.

Table VII

Some important flavanones, as their glycosides

Eriocitrin	Eriodictyol-7-rutinoside
Neoeriocitrin	Eriodictyol-7-neohesperidoside
Flavanomarein	Isookanine-7-glucoside
Neohesperidin	Hesperetin-7-neohesperidoside
Hesperidin	Hesperetin-7-rutinoside
Naringin	Naringenin-7-neohesperidoside
Narirutin	Naringenin-7-rutinoside

Compared to flavones, flavonols, isoflavones, etc., the conjugated system of flavylium chloride has significantly been increased, resulting in a marked bathochro-mic shift of λ_{max}. A system of 8 conjugated double bonds is involved and many resonating structures are possible. Because of the positive charge on the oxygen atom these dyes are well soluble in water. Depending on their origin they may also be used in food products although the light fastness and the resistance to acid and alkali is rather limited.

The colour of anthocyanins not only depends on the substitution pattern of the (substituted) hydroxy groups, but also on the presence of polyvalent metal ions such as Ca^{2+}, Mg^{2+}, Fe^{2+}, Cu^{2+}, Mn^{2+} and other transition metal ions, as well as on the pH. In acid conditions the hydroxy groups are untouched and the dye will be red in colour. In alkaline condition the phenolic OH groups are neutralised and the dye will be blue.

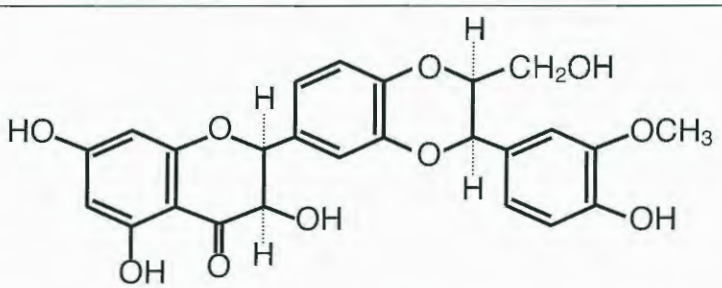
A further bathochromic shift will occur if the phenolate groups will sequester e.g. a Ca^{2+}-ion, resulting in a more intense, frequently very brilliant, blue colour.

They occur in the aqueous cell-sap and are responsible for the massive variation o colours in flowers. The colours may range from blue via violet to red. The basic structure is 2-phenylbenzopyrilium chloride.

Both the phenyl group on the 2-position and the benzopyrilium itself may contain hydroxy and methoxy groups, to such an extent that up to six hydroxy/methoxy groups may be present. The 2'- and the 6-position usually do not carry a hydroxy group.

Chromons & Coumarins

Also flavonoids exist that do not carry the phenyl group on the 2- or 3-position.

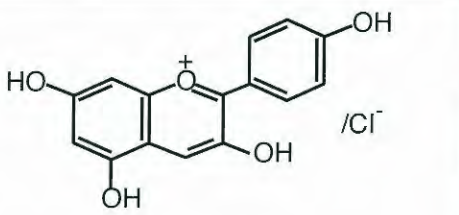


SILYMARINE

Table VIII

Some anthocyanidin flower dyes

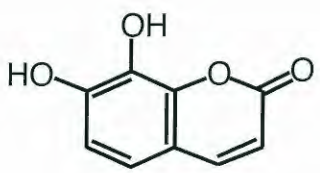
Pelargonidin	3,4',5,7-tetrahydroxyflavylium chloride
Cyanidin	3,3',4,5,7-pentahydroxyflavylium chloride
Delphinidin	3,3',4,5,5',7-hexahydroxyflavylium chloride
Peonidin	3,4',5,7-tetrahydroxy-3'methoxyflavylium chloride
Malvidin	3,4',5,7-tetrahydr oxy-3',5'-dimethoxyflavylium chloride
Hirsutidin	3,4',5-trihydroxy-3',5',7-trimethoxyflavyllium chloride



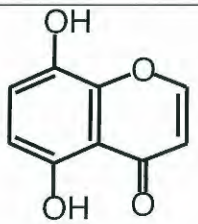
PELARGONIDIN
3,4',5,7-tetrahydroxyflaviylium chloride

These are chromones that do not very frequently occur in botanical extracts. This is contrary to coumarins found widespread in nature. Coumarins can be considered as intra-molecular esters of cis-2-hydroxycinnamic acid (cis-o-coumaric acid) which is not stable in free form and immediately forms the intra-molecular ester (see table IX).

The corresponding furo-compounds occur widespread in nature: furochromones and furocoumarins. Psoralens like 5-methoxypsoralen (bergapten), 8-methoxypsoralen (xanthoxantine) and imperatorin are examples of furocoumarins, while khelline is an example of a furochromone. Many representatives of this group of products are notorious because of there phototoxic effects. In a {2+2} photo-addition according to Woodward-Hoffmann these products react with the nucleic acids to such an extent that irreversible genetic damage occurs (see table X).



DAPHNETIN



5,8-DIHYDROXY

Table IX
Some frequently occurring coumarins.

Daphnetin	7,8-Dihydroxycoumarin
Daphnetin-7-methylether	8-Hydroxy-7-methoxycoumarin
4-Methyldaphnetin	7,8-Dihydroxy-4-methylcoumarin
Dicoumarol	3,3'-Methylene-bis-(4-hydroxycoumarin)
Dimethylfraxetin	6,7,8-Trimethoxycoumarin
Esculetin (Cichorigenin)	6,7-Dihydroxycoumarin
4-Methylesculetin	6,7-Dihydroxy-4-methylcoumarin
Citropten (Limettin)	5,7-Dimethoxycoumarin
Fraxetin	7,8-Dihydroxy-6-methoxycoumarin
Fraxin	Fraxetin-8-glucoside
Herniarin	7-Methoxycoumarin
Isoscopoletin	6-Hydroxy-7-methoxycoumarin
Scoparone	6,7-Dimethoxycoumarin
Scopoletin	7-Hydroxy-6-methoxycoumarin
Umbelliferone	7-Hydroxycoumarin
β-Methylumbelliferone	7-Hydroxy-4-methylcoumarin

Table X
Some frequently occurring psoralens.

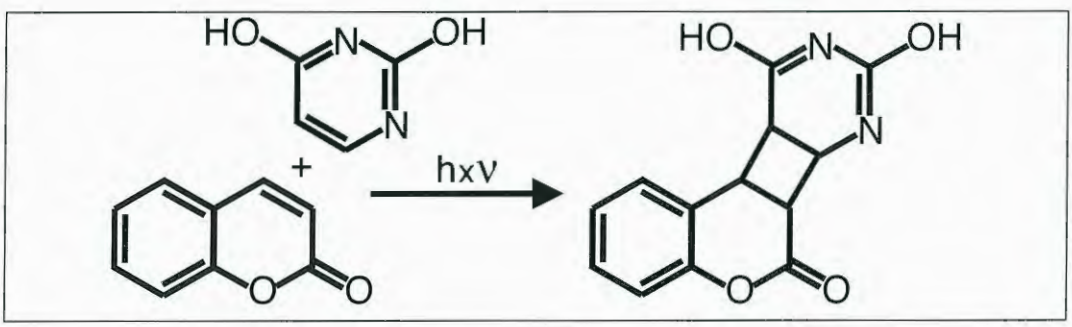
Angelicin (Isopsoralen)	furo-(2,3-h)-coumarin
Bergapten	5-methoxypsoralen
Bergaptol	5-hydroxypsoralen
Imperatorin (Ammidin, Marmelosin)	8-isoprenylpsoralen
Isopimpinellin	5,8-dimethoxypsoralen
Psoralen	psoralen
Trioxsalen (Trisoralen)	4,5',8-trimethylpsoralen
Xanthotoxin (Methoxsalen)	8-methoxypsoralen
Xanthotoxol	8-hydroxypsoralen

Imperatorin

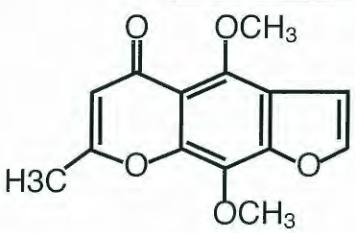
Imperatorin, 8-isoprenylpsoralen, is one of the examples being subject to {2+2} photo-additions according to the Woodward-Hoffmann rules. Imperatorin reacts with the nucleic acids, mainly thymine, to such an extent that irreversible genetic damage occurs. The genetic damage that eventually could be caused can be made reversible as on the skin so-called "repair enzymes" (thymidylate synthetase) occur that are able to cut out the damaged part of the DNA and replace it by healthy material.

The phototoxic effects of psoralens can be quite severe. In 1999 it was observed that agricultural workers in the north of The Netherlands harvesting celery had a 60% increased chance of developing skin cancer because of the presence of psoralens in celery oil. Similar observations were done in 2000 for St.John's wort (Hypericum perforatum).

Angelicin and its methoxy derivatives have been tested clinically in combination with ultraviolet A radiation for use in the treatment of psoriasis. Angelicin, 5-methylangelicin and 4,5'-dimethylangelicin, with and without UVA radiation, were also tested for skin carcinogenicity in mice by skin application. All compounds pro-duced skin cancer when administered with UVA radiation but not when given alone.



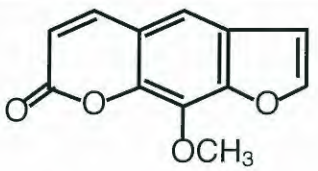
Angelicin and 5-methylangelicin form photoadducts with DNA upon illumination with 360 nm radiation. These are excised rapidly (within 24 hours) from normal cells: 80-90% of the initial angelicin adducts and 65% of the initial 5-methylangelicin adducts. There are mechanisms for the repair of damaged DNA, although this is not applicable for Xeroderma Pigmentosum patients.



KHELLINE
Khelline occurs in Visnaga vera (Khella extract)

Many of the psoralen-containing botanicals are beneficially used in skin care products. However, the interaction with light shall be avoided at any time. Psoralens are often highly functional to the skin and the body, and many of those products are pharmaceutically interesting or are already used in practice. Oral or intravenous toxicity of psoralens is usually not existent or negligible. Many vegetables contain psoralens, but the vegetables are on a day-to-day basis part of the menu.

The genetic damage that eventually is caused can be made reversible as on the skin so-called "repair enzymes" (thymidylate synthetase; folic acid is used as the co-factor) occur that are able to cut out the damaged part of the DNA and replace it by healthy material.



BERGAPTEN
8-methoxypsoralen

Neoflavonoids

Neoflavonoids have a totally different chemical structure. The carbonyl group is located on the 2-position (it is therefore a cyclic ester) and the phenyl group on the 4-position (4-phenylcoumarins). They could be considered as 3-phenyl substituted cinnamic acids. There are not many representatives known of the group of neoflavonoids, and frequently they are frequently identified as "abnormal flavonoids"

To be continued on vol. 25 issue no. 4

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Fig. 2 A view of Supply Side East.

Fig. 3 A view of Vitafoods.

Taste as indicator in the USA market

According with Jennifer Cooper from Lead Point Solutions "U.S data trends noted over the last ten years show a significant shift in the factors driving us consumer purchases and their perceptions of value". Ten years ago, the drivers were brand, efficacy and price meanwhile today the most important indicator is *taste*. In fact, statistically it is the over whelming winner over price, and even efficacy. Thus understanding the market dynamics of the nutraceutical industry is critical in determining the market growth opportunities. This was the topic discussed from Alexander Merolli from Life Sciences Alliance who has reported interesting data on the trends, drivers and restraints of the Nutraceutical market in USA.

Quality and safety both in USA and EU

Quality and Safety issues of special food are of fundamental importance also. In fact, some manufacturing and distribution of *fraudulent* is too common in the products dietary supplement industry and this unethical practice often times puts the entire industry at risk. This was the interesting topic reported from Alexandra Schauss from the Nation College of Naturopathic Medicine in US Conference and Normal Temple from Athabasca University (Canada) has underlined in his Vitafoods-Conference (EU) how, differently from Europe, there is very little regulation of the supplements marketing in USA and the commercialization of non-ethical products is more frequent. Also because around half of American and Canadian adults take dietary supplements and this represents a multi-billion dollar industry!

As a consequence while some supplements are of value, many others are grossly over –priced and of unproven value.

However , the government of Canada has passed a low to regulate these products including herbs. There are now new classed as natural health products and they must be shown to be safe, effective, and high quality, just as in the EU directive.

However it has to be remembered how the Dietary Supplements, if well selected, should have a potential health impact, saving health care cost, when used by a broader proportion of public. This was the topic presented by Joan E. Davanzo, vice President at the Lewin' Group, in California. The power nutrition appears, in fact, to lie in its ability to promote health and reduce the risk of many chronic diseases; thus preventive nutritiou should serve to increase the quality of life, decreasing the cost of health care.

The gold standard in USA market

But the efficacy of food supplements has to be demonstrated by well-done studies. The randomized, controlled clinical trial is now the *gold standard* for establishing the efficacy and safety of pharmacologic or biologic interventions and for recommending changes in diet and use of dietary supplements. However, the long latency and multifactorial causation of chronic disease, the impossibility of a zero exposure to a nutrient, and the multiple thresh olds for different actions of a simple nutrient in various tissues limit the value and the application of randomized, controlled trials to test nutrition hypothesis. This is the interesting topic discussed from Jeffrey Blumberg, senior scientist and director of the Antioxidants research Laboratory at Tufts University.

The Lutein intake

Going on with these guidelines, Richard Roberts from Kemin Health (USA) presented an interesting paper both in Supply Side East (USA)and in Vitafoods (EU) conferences on the activity that Lutein has on the skin when supplemented by oral route and applied topically. This double blind Italian clinical study has showed as the oral supplementation of 10 mg. of FloraGLO® Lutein daily may significantly increase skin hydration, elasticity and superficial skin lipids, while simultaneously decreasing skin lipid oxidation (Fig.4). Additionally, the simultaneous topical application of FloraGLO® Lutein may provide further benefits to the skin.

This interesting study has also showed how it is important to control the diet of involved people before starting to take a carotenoid diet supplement and during all the study, for obtaining objective results. The study suggests the antioxidant Lutein may be particularly beneficial to the skin. Since our body cannot manufacture this oxycarotenoid compound, the only way to get its antioxidant benefits in the skin is by consuming foods rich in lutein as, for example, green leafy vegetables such as spinach and kale. Given the fact that the outermost layers of the skin are more prone to the potentially damaging effects of light, including sun exposure, it make sense to maximize lutein's antioxidant benefits through a combination of topical and oral administration of diet supplements. This is with the high purity of Lutein can help to increase the its daily intake also.

The mystery of pleasure

However diet supplements and cosmetics not only have to be efficacious and safe, but should deliver an emotional experience exploring the mysteries of pleasure and desire.

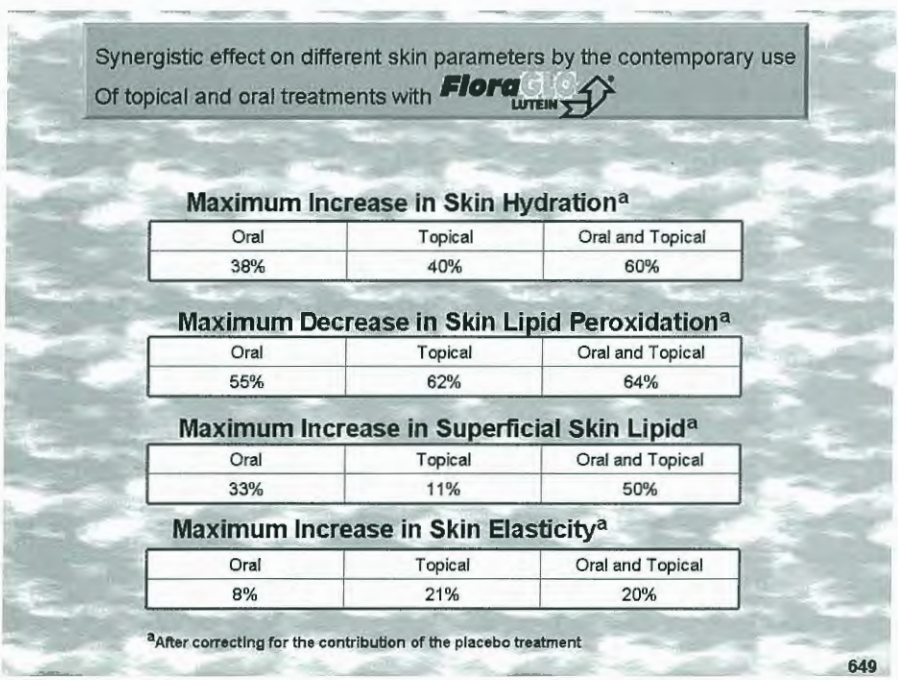

Fig. 4 The Lutein's activity.

Integrating the healthy and sensual components in cosmetic and diet supplement formulations should allow us to explore a much broader picture of the meaning of beauty and wellness.
And these perceptions may be controlled by modern brain structure. In fact, the different sensations perceived by our five senses, collected by specific receptors are transmitted by electricals signals and interpreted on different zones of the brain.
According to the combinations and intensity these messages are translated into pain or pleasure. This was the interesting topic reported from Basant Puri, Imperial College London (UK) in Vitafoods Conferences.
Moreover applying techniques such as rigid monomodal registration, Prof. Puri has shown that taking a completely natural supplement is associated with brain growth in children and adults. This brain growth is accompanied by significant improvements in cognition function.
But we know also how the sense of touch may stimulate our imagination and create emotions directly connected to our seductive instincts.
This is why the mystery of emotional reactions are traveling between the brain and the skin and the mucous membranes.
People want to feel beauty and in an healthy state through its body and mind. They desire a harmonious curves for a gorgeous body. Thus during the conferences it was also compared food trends with their beauty counterparts for trying to understand to what extent people transfer credibility between sectors as far as consumer is concerned.

Beauty from inside

Therefore functional cosmetics and beauty from inside are the fastest growing segments in cosmetics and nutraceuticals according with the presentation of Georg Gruenwald, President Analyze & Realizy (Germany) during the Vitafoods Conference.
Functional food improve beauty from the inside and cosmeceuticals from outside. And anti-aging anti-wrinkle, and anti-cellulite are the top claims made for many products containing a variety of mostly natural substances. Thus it was reported as the presence of the satiety factor CCK (cholestokins) increases at level of various target organs, by the release of the enzyme P12 (Proteinase Inhibitor II), naturally occurring in potato protein. Eleven clinical studies, with over 500 partecipants have demonstrated the efficacy and safety of P12, according with the paper presented by the scientist Debbie Dapena.
When taken as directed, Sledesta® (registered name of the potato protein) has resulted in statistically significant weight loss and reductions in waist and hip measurements (Fig. 5)

The feeling of satiety

This active potato protein extract enhances the release of CCK, the natural satiety signaling within our own body. Once released, CCK acts on various target organs, where it induces a feeling of fullness and satisfaction, known as satiety.
Sledesta" works differently from other weight loss ingredients on the market. It sends the signal to the brain "I'm full! Stop eating" and has no side effects. This potato extract helps dieters feel satisfied sooner and longer, and therefore dieters can manage their hunger, reduce their calorie intake with smaller portions, and control snaking between meals. Reducing calorie intake without hunger helps dieters meet their weight loss goals. This was another interesting innovative compound presented in Secaucus (New Jersey- USA) this year. In fact, according with the European Association for the study of Obesity about one third of all people living both in the European Union and in USA

are overweight, with more than one in then in the obese category. One new approach for the next generation of slimming food is the use of special food ingredients that increase satiation on (feeling full within the same meal) and/or satiety (reducing energy intake at the following meal) and ultimately decrease energy intake (food) over the day. However, the mechanisms of appetite regulation are complex and involve the interaction of many orexigenic and anorexigenic hormones that are released by the body (gastrointestinal tract and peripheral tissues) in response to the diet and which send messages to the brain (primary the hypothalamus) sensing the feeling of human and/or being full. Higher blood levels of these appetite-suppressing peptides such as the previously reported CCK, PP-fold peptide (PYY) and glucanon-like peptide 1 (GLPL1), are associated with lower subjective hunger ratings and lower food intake. On the contrary high circulating levels of the hormone ghrelin induce hunger and subsequently initiate food intake.

The problem of obesity

However obesity is a complex medical problem with multiple causative factors impacting some of the biggest killers in modern society, such as coronary heart disease, type 2 diabetes, stroke and many site specific cancers. Therefore it should be necessary to educate the public about the fundamental ways in which the environment of modern society, its economy & culture, can threat our health and wellbeing. It is necessary that governments take measure to involve family, school and neighbourhood /environment by a food politicy that promote an healthier life-styles, while people have to take some responsibility for maintaining an Health Society.

Fig. 5 The potatoes activity on weight loss as jokingly presented in the Kemin booth (USA).

Finally being a conflict between those who try to treat and prevent obesity and the vested interests of thus who profit from our current obesogenic environment, it is the responsibility of governments to alter the balance in favor of those who seek to improve the nation's health.
These where the conclusion of the interesting paper presented by Prof. Colin Waine of the National Obesity Forum (UK) during the Vitafoods Conferences.
At this purpose the Diogenes EU project, presented by Prof. Wim Saris from University of Maastricht (Netherlands) has focused the necessity to reduce the calorie load, increasing the satiating effect of food without compromising its taste. The first obtained results on 145,000 European adults seems to be promising. It seems possible to modify our obesogenic environment deeply changing our way of eating and our lifestyle of living. Numerous epidemiology studies support, in fact, the concept that diets rich in plant foods are associated with a reduced risk of cardiovascular disease. This is why tomatoes present in the Mediterranean diet, inhibit platelet aggregation in vitro and in vivo according with new studies, and it is considered an interesting food, being rich of the antioxidant lycopene.

Tomatoes and the Mediterranean diet

Tomato extract rich in lycopene inhibits thromboxane pathway, but may be beneficial in diseases such as cancer and coronary heart disease as well as other chronic conditions. However a look at the synergy between carotenoids and xantophylls has demonstrated that they do not act as a magic bullet. Effectiveness and safety of these compounds are married together in the whole fruits and vegetables of the Mediterranean diet
These the interesting results discussed from Prof. Asim K Duttarox dept of Nutrition University of Oslo (Norway).
Many other were the studies reported during the Supply Side East in USA and Vitafoods in Europe. What is important to underline is the continuous grow of Functional Food Market worldwide (Fig.6), arriving to a value of 36.2 bn of USD by a broad or 16.1 bn by a strict definition (Fig.7and 8).

Future prospects

Segmenting by health benefit the market remains dominated by gut health, ahead of heart and health products which are growing strongly, and other products to boost the immune function according with the data presented in Vitafoods by Fiona Angus, Business Manager Nutrition Sensory and Consumer Science LFI (UK). In the last years new health sectors are emerging, in particular, anti-aging nutriceuticals and weight control lines sold together with beauty cosmetic products.
However area of functional foods is evolving with consumers' growing interest in intrinsically healthy products.
The functional foods market, as we know today is growing at around 10% per annum and by 2010 with a provisional increase ranging from +47% (broad definition) to 56 bn USD (strict definition). The major activity will be centered around 6 major areas.
- Risk reducers
- Age of antioxidants
- Lifestage and gender nutrition
- Slimming solution
- Getting through the day
- Beauty from the inside out (antiaging)

What the real difference from Supply Side East in USA and the European Vitafoods?
Exibition companies over 400 booths in USA and in Europe with about 5.500 visitors for the two interesting manifestation .

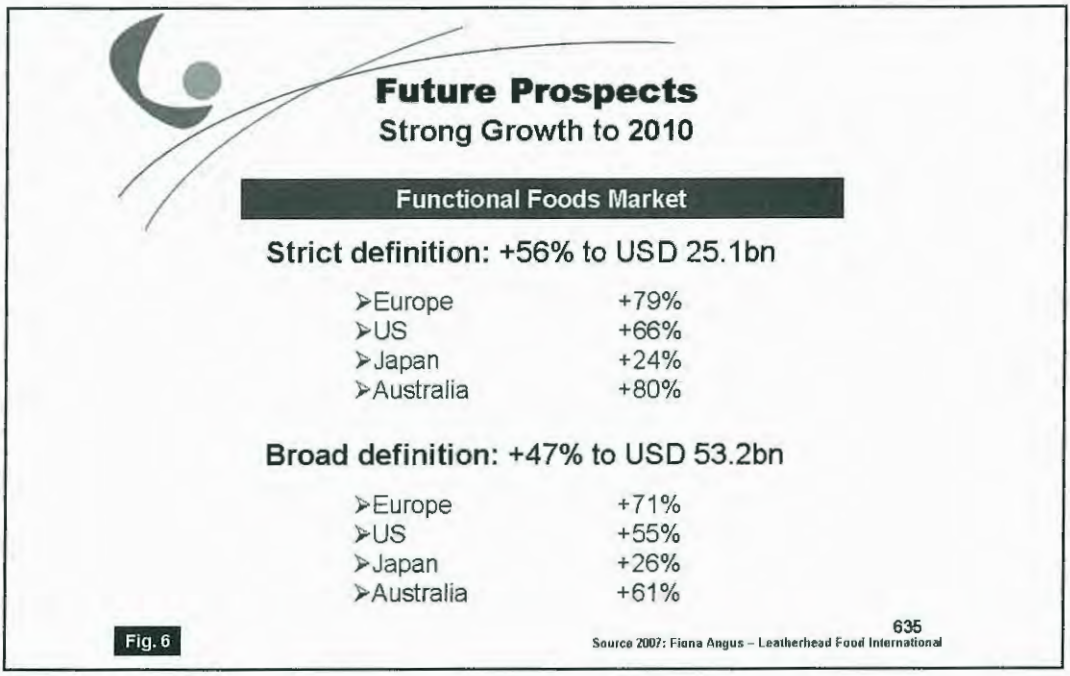

Fig. 6 Future prospects.

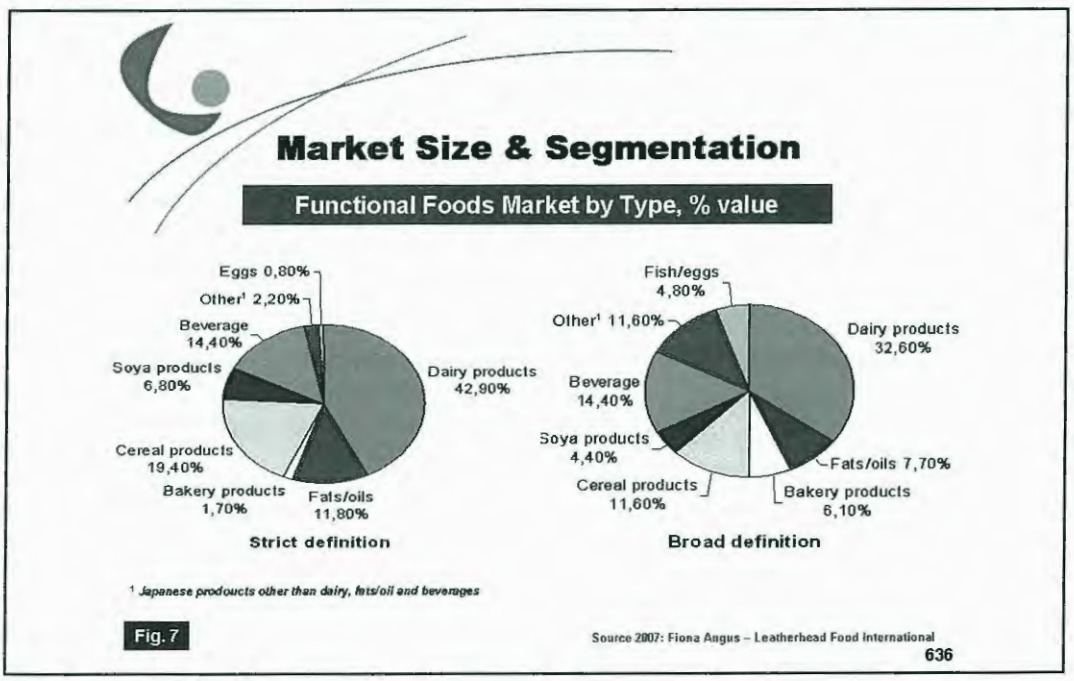

Fig. 7 Market size & segmentation.

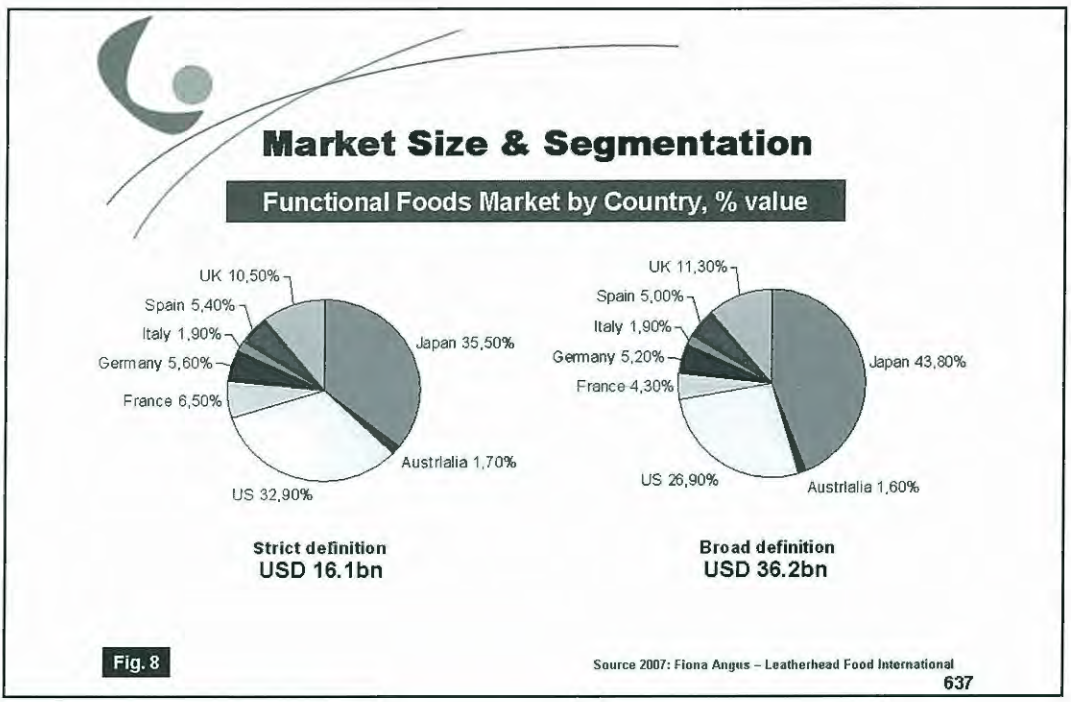

Fig. 8 Market size & segmentation.

What is surprising is that about 10% of all the manufacturers and companies present with pavilions, both in Secaucus and in Geneve (Fig. 9 and 10) are coming from the mainland China. However all the topics were interesting: Vitafoods, gave more room to topics covered by Academic experts meanwhile in Supply Side East in USA, the scientific presentations came in majority from industry and were more marketing oriented.

Conclusive notes

In conclusion a wide range of companies participated to these two international events, including suppliers of ingredients, equipment and packaging materials, as well as contract manufacturers and finished products in Europe.

The latest products and innovation from the leading suppliers were presented and discussed from experts from Academia and University during the numerous seminars. The links between aroma taste and health was also explored for trying to understand the relation between beauty and desire, considered the stimulating drive for innovation, both in cosmetics and nutraceuticals.

The frontier between Wellbeing, Beauty and Health is diminishing. What's good for health is good for the skin too, and vice versa. Thus has born the concept of health-food and Beauty-Food giving rise to nutri-cosme-ceutical products.

The new ingredients suitable to formulate cosmetics are useful for nutraceuticals also. All both have to be excellent aesthetics and sensory characteristics, to trigger emotions, stimulate all five senses, thus entering in the Chemistry of Seduction and maintaining their efficacy and safeness.

To go on with these fascinating topics participate to next international event: **COSMETIC DERMATOLOGY FROM WEST TO EAST: THE COMBINED REPLY FOR A GLOBAL WELLNESS** (http://www.chinamed.com.cn/iscd2007) to be held in Beijing (China) next October 20-23. For further information write to: morganti@iscd.it or ronmeng@cma.org.cn.

Working in connection with the scientist-leaders both from Dermatological and Chemical Schools and from Academia and Industry you will have the possibility to better understand the real meaning of wellness, focusing your interest on new ideas and incoming cosmetic and nutriceutical products.

Fig. 9 Chinese pavillons in Geneve -EU.

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Enhancement In Drug Delivery

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The main aim of the pharmaceutical and cosmetic preparations is to achieve a desired effect. Pharmaceutical preparations have to be effective because of a pharmacologically active compound delivered to the target area with the aid of a vehicle, whereas cosmetic products are not allowed to have a curative efficacy, but a preventive effect only.

However in contrast to pharmaceutics, in cosmetics the vehicle is of greater importance, because of itself topical efficacy. In fact, pharmaceutical vehicles, being inert, serve to deliver active substances to the target organ, meanwhile cosmetic vehicles show also a positive effect on the skin status when applied. However delivering active substances to the targets requires the right concentration of actives in the formulation to achieve the optimal release rate and desired distribution of active substances between the vehicle and the target site.

Thus enhancement in drug and cosmetic delivery and absorption via a specific route of administration often becomes essential in the design of novel pharmaceutical or cosmetic products. In any case the active principle is embedded into a matrix, the vehicle, has to be effective and to be delivered to the designed target.

This book, divided in VIII parts and 28 chapters, presents a comprehensive review of the theory and methods used today to enhance drug absorption through various routes of the human bodies.

Because of a great demand by consumers for innovative cosmetic products with a biological action, and because of the declared activity of cosmetics "to keep the skin, mucous membranes and hair in good condition", it seems fundamental that not only chemists involved in pharmaceuticals but also cosmetic chemists know and understand in a better way the different delivery systems and chemical permeation enhancers, necessary to formulate right and innovative products.

Part I, by 6 chapters, is entirely dedicated to the *Gastrointestinal Drug Absorption*.

The oral absorption of biological macromolecules is one of the most challenging topics in drug delivery research and the oral route is the most common means for ingesting drugs into the body. It is also the preferred route due to the low cost of drug treatment management and patient compliance resulting from the convenience of oral drug administration.

Thus a profound understanding of the biology and physiology of the gastrointestinal tract (GI) is crucial for optimizing the bioavailability of orally administered drugs. In fact, the main obstacles associated with oral administration and absorption of therapeutic macromolecules are the GI membrane impermeability to the large hydrophilic molecules and their susceptibility to inactivation by GI enzymes. Moreover the differences between the dimensions of the GI tract in small and large animal

models and even in humans could cause problems when scaling up the biological evaluation analysis.

Thus on one side a careful design, physiologically oriented should be employed when efficient absorption enhancement is desired. On the other side, it is to remember that drugs across the GI membrane is highly affected by the intrinsic properties of the molecule such as ionic charge, secondary structure, 3D conformation, molecular weight and lipophilicity. Therefore, various approaches have been tested to promote the absorption of high molecular weight drugs. One approach is the use of surfactants, with their potential toxicity, the other approach are the use of enzyme intestinal inhibitors, chemical derivatization, prodrugs, site-specific drug delivery, encapsulation of the drug in nano- and microparticulate carriers, selective opening of tight junctions, and the use of specially designed molecular carriers. Some of these approaches seem to be promising for the development of future pharmaceutical products.

These and other are the topics reported and discussed on **chapters 1** and **2**.

The administration of drugs to the GI tract normally involves an immediate or extended release formulation, by tablets or capsules, addressing specific issues. Addressing these different needs optimally requires a targeted delivery system to bring the drug to the correct site and at a controlled dissolution rate. For instance, some drugs are absorbed relatively rapidly in the upper small intestine. But delivering drugs to the large intestine to treat a local inflammatory disease, represents often a necessity. Thus targeting of drugs in GI tract remains a challenging goal and progress has been made using delayed release preparations.

Thus chitosan and some of its derivatives, capable to enhance drug absorption, has been used. Chitosan is, in fact, a polysaccharide produced by alkaline hydrolysis of chitin, natural sugar-polymer abundantly distributed among living organisms. It is a safe polymer for oral administration biocompatible biodegradable, muco-adhesive, and useful as excipient for controlled drug release as a tablet, film, or granule formulation. As a matter of fact, to achieve improvement or enhancement of drug action, it is essential to make dosage forms by taking into account the drug absorption site, gastrointestinal transition rate, interaction with GI site, drug stability, and the bio-adhesive characteristics of chitosan are ready available for the enhancement of intestinal absorptions in combination with micro-and nano particulate dosage forms. In addition, chitosan lowers the resistance of the intestinal cell layer membrane.

It is shown that the intercellular tight junction is reversible loosened by the interaction of chitosan with the cell membrane.

Targeted and improvement in oral drug absorption are the topics of **chapter 3** and **4**.

Efflux systems and pre-systemic metabolism are, beside poor water solubility, responsible for low bioavailability of orally administered drugs.

Presystemic metabolism can be divided into *luminal* and *first pass* individual and hepatic metabolism. *Luminal* is caused mainly by enzymes secreted from pancreas (chymotrypsin, esterase and miscellaneous nucleases); *first-pass intestinal metabolism* is caused by membrane-bound and intercellular enzymes (amino peptidase, carboxypeptidase and esterase).

First-pass hepatic metabolism biotrasforms absorbed drugs through the portal circulation before they reach the systemic circulation. Therefore these enzymatic proteins play a crucial role in the transfer of drugs across the intestinal membrane. On one hand these transport systems can positively influence drug uptake by acting as absorptive systems, on the other hand, they can build a barrier to

transport by causing drug secretion back across the intestinal membrane.
Attempts to reduce this enzymatic degradation include the use of analogous prodrugs, and formulations such as nanoparticles, microparticles, and liposomes that shield therapeutic agents from luminal enzymatic attack. Moreover, the co-administration of enzyme inhibitors has become of increasing interest, because of, by such excipients, a significantly improved bioavailability of drugs after oral dosing could be achieved. Nevertheless, the co-administration of enzyme inhibitors remains questionable because of side effects caused by these agents. Although several studies clearly indicate the efficacy of inhibitors to overcome the enzymatic barrier and therefore the feasibility to improve oral drug bioavailability by co-administrating enzyme inhibitors, the practical use of such inhibitors in formulations still remains questionable.
Another important factor is the diluition during the gastrointestinal passage, which makes high concentrations of inhibitors necessary to guarantee sufficient inhibitor concentrations at the absorption site. Very promising in this context are mucoadhesive multifunctional polymers, which offer many advantages. By the use of these polymers, diluition effects are negligible comparable to formulations with simply co-administered enzyme inhibitors.
Thus to improve oral drug bioavailability the most promising way seems to be connected to delivery systems based on unabsorbable, multifunctional polymers. Moreover, looking into the future, more lipophilic drugs are likely to be produced, and the delivery of these molecules through the oral route is expected to be a most important and relevant issue. For these new classes of drugs, also, logical selection of excipients and rational design of lipid-based formulations or prodrug synthesis tailored for drug candidates are key factors for the success of these delivery systems. All these topics are reported and discussed on **chapters 5** and **6**.
Part II is dedicated to the *Rectal Absorption*. The rectal route of administration is considered a practical alternative to oral administration when patients are prone to nausea, vomiting, convulsion, and, in particular, disturbances of consciousness. Therefore, rectal administration is used to deliver many kinds of drugs such as anticonvulsants, analgesic, antiemetics, antibacterial agents, anesthetics for children, and some anticancer agents. However, rectal bioavailability tend to be lower than the corresponding values of oral administration. Thus the development of novel absorption enhances with potential efficacy without mucosal irritation is very important. Generally, the aim is to evaluate the ability to achieve relatively constant drug concentrations for longer periods by using new carrier systems able to rate-controlling its delivery. Actually, various drug delivery systems in the rectal route have been developed e.g., products liposomes, micro-and-nanocapsules, chemical or biotechnological enhancer, prodrug, carriers, and enzymatic inhibitors. Among them cyclodextrins (CyDs) are known to alter various properties of drugs, pharmaceutical formulations, and biomembranes, resulting in enhancement and modulation of rectal drug absorption. CysDs, cyclic oligosaccharides consisting of several glucopyranose units, are host molecules, which form inclusion complexes. Their effects on the rectal delivery of drugs depend markedly on vehicle type, physiochemical properties of the complexes, and an existence of tertiary excipients such as viscous polymers. These topic are discussed on **chapters 7** and **8**.
Buccal and Sublingual Absorption is the topic of **chapters 9** and **10** contained in **Part III**.
The main difference between the oral mucosa and skin as compared to the GI tract lies in the organization of the different epitelia. While the latter has a single layer of cells forming the single epithelium, the skin and oral cavity have several layers of cells with various degrees of differentiation

within the oral cavity, the masticatory mucosa has a keratinized or cornified epithelium, and covers the stress-ending regions such as the gingival and the hard palate, providing chemical resistance and mechanical strength. As in the skin it is divided into four layers: keratinized, granular, prikle-cell, and basal layer. The lining mucosa, which provides elasticity, in contrast, is comprising of non cornified surface epithelium covering the rest of the regions including the lips, cheeks, floor of the mouth, and soft palate.

The third type of mucosa is the specialized mucosa consisting of both keratinized and non-keratinized layers, and is restricted to the dorsal surface of the tongue.

The intercellular spaces contain water, lipids, and proteins. The mucosal tissues are further covered with mucous, which is negatively charged, and contains large glycoproteins termed mucins. These are thought to contribute significantly to the viscoelastic natura of saliva, and maintain a pH of 5.8-7.4.

The mucus plays an important role during the mucoadhesive process by buccal drug delivery systems. In comparison to the skin, the buccal mucosa offers higher permeability and faster onset of drug delivery, whereas the key features which help it score over the other mucosal route, the nasal delivery system, include robustness, ease to use, and avoidance of drug metabolism and degradation. The main resistance to drug permeation is caused by the variant patterns of differentiation exhibited by the keratinized and non keratinized epithelia. However, despite various disadvantages, the oral mucosa route might be the potential for drug delivery and for macro-and-micromolecular deliveries. Oral mucosal route are more permeable than skin, although less permeable than most other mucosal routes. But it is also formidable barrier to drug absorption, especially for larger molecules. For this reason, chemical permeation enhancers have been developed and their physiochemical properties appear to provide challenges to the pharmaceutical scientist in their formulation. This discussion is focused on **chapters 9** and **10**.

Part IV describes by 8 chapters, the role and all the problems associated with circumventing barrier of the skin during *Transdermal Drug Delivery*. Dermal and transdermal delivery requires, in fact, efficient penetration of compounds through the skin barrier, the bilayer domains of intercellular lipid matrices, and keratin bundles in the stratum corneum (SC). Among the myriad strategies employed to increase both the amount of therapeutic or a cosmetic agent traversing the skin and the range of drugs that can be effectively delivered through this route, the best one lies in the application of chemical penetration enhancers. These agents interact with SC constituents to promote drug flux. The lipid organization in SC and the more investigated chemical penetration enhancers are widely reported in **chapters 11** and **12**, and the main physicochemical characteristics, and mechanism of action of prominent vesicular carriers are focused on **chapter 13**.

The high tolerability and efficiency of the reported vesicular systems open vast potential therapeutic uses, offering advanced local and systemic new therapies with agents that are unable to efficiently penetrate the SC via passive diffusion.

Moreover the employment of electrically assisted methods such as iontophoresis, electroporation, and ultrasound, reported on **chapters 14,15** and **16** are physical methods used to enhance the skin' permeation to different drugs.

Transdermal iontophoresis involves the application of an electric field across the skin to facilitate ionic transport across the membrane. Iontophoresis is differentiated from electroporation by the low fields employed.

Electroporation, in fact, involves the application of high-voltage pulses for a very short duration. The pulses are thought to produce transient aqueous pores in the lipid bilayers of the SC. These apertures provide pathway for drug penetration through the horny layer. On the other side ultrasound interact with the structural lipid lamellae of corneocytes enhancing the drug penetration through the SC. Combination of electroporation and chemical enhancement is the topic of **chapter 17** attempting to deliver challenging molecules from large hydrophilic molecules to simple electrolytes and keratolytic agents. According with the author it is likely that any future combination of the strategies will face challenges, not least of which are potential safety and economic considerations, particularly as the techniques involve prolongation of an electrically compromised skin barrier with all the safety issues that involve.

Despite these advanced strategies to deliver macromolecules, effective transdermal delivery is still generally restricted to a small number of low molecular weight, weakly lipophilic, and powerful therapeutic molecules. Thus the administration of biotechnology-derived macromolecular, particulate- and DNA-based medicines requires the development of further delivery strategies and devices that circumnavigate the SC barrier to promote delivery of a wide range of the therapeutics to the underlying epidermis, dermis, and possibly the systemic circulation. Therefore more radical methods of disrupting skin barrier function are required. New technologies at the interface of engineering and biological sciences are reported and discussed on **chapter 18**, at the end of part IV.

Nasal Absorption and optimization is the topic of **Part V** described by **chapters 19** and **20**. The nose is equipped with a unique cellular architecture to perform several functions, including filtration of inspired particles, humidification of inspired aria, olfaction, and some immunological functions.

Thus the nasal route of drug delivery is used for the direct administration of medicines to the nose for treatment of local conditions or for the systemic delivery of compounds that are not easily delivered by the oral route.

It is also suggested that there may be a direct route for drug absorption to the central nervous system (CNS) from the olfactory region of nose. And this possibility are currently being investigated for the delivery of polar drugs to treat chronic CNS conditions, such as Parkinson's or Alzheimer's disease. However it is not to forget that the nasal epithelium has defensive enzymatic barrier including the presence of phase I and phase II enzymes, plus proteolytic enzymes that provide a formidable barrier to the nasal delivery of drugs.

The influence of enzymatic degradation is obviously dependent on the susceptibility of the drug itself. Therefore to take full advantage of these opportunities offered by nasal delivery, innovative approaches to overcome the biological barriers to delivery are being developed. And absorption-enhancing agents are developed to delivering peptide-drugs through the nasal route to produce effects elsewhere in the body. Currently, in fact, the vast majority of administered nasally drugs are non-peptide therapeutic drugs for local effects rather than systemic effects. But nasal delivery is likely to achieve a prominent role in a large nnmber of therapeutic regimens that currently utilize peptide drugs delivered by injection. These fascinating topics are well focused on **chapters 19** and **20**.

Part VI is dedicated to the *Drug Absorption from Vagina and Uterus*.

Although anatomy and physiology, microflora, and secretions of the vagina are well understood, the scientific knowledge of drug delivery via vaginal route is still limited and relatively unexplored despite its potentiality as a non-invasive route of drug administration. The presence of a thick

network of blood vessels renders the vagina an excellent route for drug delivery to achieve both systemic and local effects. This is because of drug delivery to the uterus and, particularly, to the vagina is of increasing importance in women's health issues. Delivery systems of these routes can broadly be subdivided into those that are adaptations of technologies used for other applications such as semisolids or vaginal tablets that may incorporate mucoadhesive polymers or particulate carriers, and those systems specifically designed for vaginal or uterine application. Thus the great challenge in drug delivery remains the ability to delivery biomolecules by a nonparenteral route.

The increasing knowledge of physiology, histology, and immunology of vagina suggests, therefore, new challenging uses of this route for local and also systemic administration of drugs. Vaginal administration allows, in fact, lower doses, avoidance of first-pass metabolism, less frequent administration, ease of access and self-medication and, depending on drug physiochemical properties, good absorption potential. All these items are reported and discussed on **chapters 21** and **22**.

Part VII is dedicated to *Ocular Absorption of Drugs*. Preservation of sight as the mean age of the population increases, and thus as blindness becomes more prevalent will remain a key health care objective. The eye is, in fact, *prima facie* evidence of divine intervention, subject to all the vicissitudes of time and disease. And eyesight is so central to our way of life that irrational fear of losing vision is totally incapaciting for many individuals.

The eye is a biological embodiment organ of a familiar physical object-a camera, with the ability to control the focus, light, intensity, and depth of field of an image through movement of the external and internal musculature under intentional and autonomic nervous control.

The film of this camera is the brain itself, the stimuli being carried by the afferent pathways from the photoreceptors to the optic nerve that hands on the information to the visual cortex at the back of the through the optic tracts. Together with the nasolacrimal apparatus, the conjunctival, the cornea and sclera of the external features of the eye, and the internal structures such as the uveal tract, the lens, the internal humors the retina, it is to underline, however, the importance of the macula as the center of the field of vision. Thus for the visual loss during old age and macular degeneration, significant causes of blindness in the Western world, there is great expectation for new therapeutics.

To date, nearly all ocular therapeutics have been administered to the eye as single aqueous solution eye drops by instillation to the lower conjunctival sac. The main draw backs of these solutions are their inability to deliver lipophilic and insoluble molecules, their low retention time, and their limited ability to resist the washout effect of blinking and tears turnover. Thus, it is estimated that only 1% or less of the administered dose can penetrate the ocular surface. In contrast, lipophilic molecules can penetrate through cell membranes of the ocular epithelium but their formulation for topical ocular administration is complex because they are insoluble in single aqueous solutions. To overcome the penetration obstacles, the spreading on ocular surface as well as the adhesion properties to this surface must first be improved.

On one hand, knowledge of the anatomy and physiology of the eye should contribute to the identification on an appropriate drug delivery strategy that will enhance the penetration of active molecules through ocular tissues without eliciting any adverse effect and to the understanding of the mechanism of entry, which may lead to a better tuning of the formulation parameters of an ocular drug delivery system. On the other hand pharmaceutical investigators and pharmacologists are trying to develop delivery systems that allow the fate of a drug to be controlled and the optimal drug dosage to arrive at the site of action in the eye by means of novel micro-or nanoparticulate, insert dosage forms,

by the use of penetration enhancers and/or by the technology of ocular iontophoresis. However meanwhile the penetration enhancers should be introduced for clinical use after considering the balance of risks and benefits, it is only a matter of time until iontophoresis will be routinely used in the ophthalmic field.

All these interesting topics are reported from **chapter 23** to **26**.

Part VIII, the last part of the book, **chapters 27** and **28**, is dedicated to *Drug Delivery of Central Nervous System*.

The blood-brain barrier (BBB) needs to maintain an extremely stable internal fluid environment surrounding the neurons. In fact the quantal chemical communication that takes place at synapses, and the highly complex spatial-and temporal summation and integration signals that continually occur between neurons cannot take place efficiently if brains extracellular fluid were allowed to fluctuate in its composition as markedly as does the somatic central nervous system (CNS). Thus BBB prevents many macromolecules from entering the brain functioning as a protective barrier that shields the CNS from neurotoxic substances that circulate in the blood. Moreover it has the consequence of scaling off in the brain from many essential water-soluble nutrients and metabolities that are required by the nervous tissue. Therefore the BBBs together have a dual function, they firstly provide the especially stable fluid environment that is necessary for complex neural function, and secondly, they protect the CNS from chemical insult and damage. This protective function, however, becomes a major obstacle to the treatment of many devastating diseases of the CNS by restricting drug delivery. Disorders such as depression, severe pain, fungal infections, obesity, and lysosomal diseases require drug transport across the BBB as well.

Efficient delivery of imaging agents across the BBB is also necessary for accurate diagnosis of neuropathology, monitoring of disease progression, localization for surgical intervention and introduction of therapeutic agents. Thus, there remains a need to develop delivery technologies that are capable of transporting drugs across BBB. All the more innovative adopted strategies for overcoming the blood-brain barrier are reported and discussed on this ending part of the book.

In conclusion this interesting and exhaustive book represents an up-to-date authoritative reference test for cosmetic and pharmaceutical chemists, dermatologists, toxicologists, researchers and students who want to know better all the problems inherent to the enhancement in Drug and Cosmetic Delivery.

P. Morganti
Editor-in-Chief

Skin Protection

by S. Schliemann and P. Elsner
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This publication, organized in four sections and 16 chapters, provides a comprehensive update of all the products and programs used and to be used in the specific field of Occupational Dermatology, essentially based on prevention and protection.

Occupational skin diseases are provoked by exposure to irritants in the workplace due also to individual susceptibility. Therefore the prevention of chronic or cumulative irritant is the decisive and more important factor.

Occupational skin diseases encompass a wide array of conditions, including acne, cancer, connective tissue disorder, contact dermatitis, infections diseases, pigment changes, urticaria and aggravation of pre-existing skin diseases. Among all, *contact dermatitis* is surely the most frequent and epidemiologically relevant skin disease. Its economic impact is very high, having also a high effect on the quality of life.

The development of occupational contact dermatitis depends on a combination of exogenous factors (exposure) and individual ones, such as age, genetic background, anatomical regions exposed and pre-existing skin diseases. Of course the chemical manifestation of irritant contact dermatitis is also influenced by type and concentration of irritant solubility, vehicle, and duration of the exposure, as well as temperature and mechanical stress.

Therefore educational measures of the workers for workplace hazards and skin protection by the right materials may have an important role. Thus specific products has to be designed for each specific environmental condition or threat.

We need to better understand the *metamorphosis* of the vehicle after application to the skin, as well as the delivery of the active compounds used. In fact, in skin protection strategies, the topical vehicle often occupies a position of even greater importance in terms of the protective effect it must give to the skin.

However the complexity of topical dosage forms and of desired skin protection properties makes it difficult to formulate general guidelines for the development of protective dermatological formulations.

All these considerations and the basic necessity to understand the mechanisms of the protective effects of pre-work creams to be used in different workplaces are, therefore, reported on **chapters 1 and 2.**

Chapter 3 is dedicated to discuss an *in vitro* skin model suitable for studying barrier repair mechanisms and to gain insights into the protective and regenerative effects of cosmetic formulations.

What is important to underline is that all the products applied to the skin should be clinically tested in order to verify their propensity for causing cutaneous reactions, as well as evaluated in their whole safety testing the *hazard identification, the risk characterization, the risk evaluation,* and the *safety assessment*, prior to enter to the market as reported on **chapter 4.**

Contact dermatitis is a common disease caused by exposure to substances in the environment. Those substances act as irritants or allergens and may cause acute, sub-acute, or chronic eczematous inflammation. The theorically optimal way to minimize this problem is to use skin protection products such as barrier creams and moisturizers. These products help people to reduce the intensity of skin irritations caused by irritants at home and at the workplace. The ideal skin protection formulations should be non-toxic, non-comedogenic, non irritating, non-greasy foam and colorless. They should keep high efficacy but not interfere with the user's manual dexterity or sensitivity.

They should be easy to apply and remove, cosmetically acceptable and economical as reported in the conclusion remarks on **chapter 5.**

Protection from *Occupational Allergens and Toxicants* are discussed respectively on **chapters 6** and **7**, where concepts such as elimination of harmful exposures and allergen and toxicant identification are considered. Thus, personal protective equipment is an important component of prevention, including barrier creams, gloves and protective clothing. But, apart from the physical protective countermeasures, there is a need for pharmacological preparations for the topical treatment of the exposed skin to prevent, for example, the development of burns.

Protecting the worker from initial sensitization is the primary goal in allergy-prevention, as well as the earlier application of the specific ointment should be the better therapeutic treatment for toxicants.

On one side prevention of allergic skin disease in the worker continues to be a challenge, good basic skin care and prevention of irritant dermatitis may also reduce the decrease in barrier function of the skin and subsequent sensitization.

On the other side, there are no topical preparations for the pharmacological treatment of early stages of chemical-induced burns. Nevertheless, there are newly discovered topical formulations that seems to show a protective effect against skin irritants .

Chapter 8 is entirely focused on the biological activity and efficacy of sunscreen products. Several studies have shown that sunscreens are able not only to protect against ultraviolet-induced erythema in human and animal but also to inhibit photocarcinogenesis in animal skins.

In fact, on one hand, the cumulative lifetime dose of UVB radiation seems to be the most important factor for the carcinogenetic potential and an acute overdose of UVB results in a solar erythema. On the other hand, photoaging is attributed to chronic UVA radiation. Furthermore UVB and especially UVA2 have been associated with the exacerbation of autoimmune dermatosis. Thus, apart from erythema, sunlight triggers many biological processes such as photoaging, mutation of skin cells.

However, although the short-term efficacy of a sunscreen in the prevention of sunburn is undisputed, there is also some evidence that long-term use of sunscreens prevent the appearance of nonmelanotic skin cancer as solar keratoses and squamous-cell carcinoma.

Barrier disruption is one of the major pathogenic mechanisms of physical irritant contact dermatitis (PICD) characterized by a local inflammatory reaction (erythema, scaling and **induration**). Because the viable skin is more vulnerable to environmental conditions than the stratum corneum (SC), most of the SC abnormalities develop after environmental insults have induced an underlying inflamma-

tion. For example, when the relative humidity is less than 50%, the water content of the SC remains below 10%.

With a water content less than 10%, the stratum corneum dries and becomes brittle. The combination of low humidity, high temperature and rapid air movement (conditioned air or windy time) dehydrates the outer SC. This leads to pruritus and, finally, to low-grade eczema. Dry irritated skins occurs frequently in occupational settings, where different types of irritants (physical, chemical and mechanical) disturb the epidermal barrier. Changes in environmental humidity may contribute to the exacerbation of cutaneous disorders. This interesting topic is discussed on **chapter 9** where new insights into the pathogenic mechanism of PICD and its prevention are reported.

On **chapter 10** it is described a new test for evaluating the skin care's protective activity by the use of several combinations of irritants. In fact, in the workplace, repaired skin exposure simultaneously or one after the other is frequent. Therefore the necessity to evaluate the interaction of irritants in a tandem repeated irritation test.

Chapters from **11** to **14** are all dedicated to the practical application of skin protection respectively in the *Healthcare setting, Hairdressers, Food Industry and Metal Industry.*

Professions of Healthcare setting are at high risk for occupational diseases and irritant and allergic contact dermatitis of the hands frequently occurs.

Since the use of occlusive protection gloves has adversary effects on the skin barrier, use times have to be limited. Thus, a 3-step concept consisting of (a) *skin protection before* work, (b) *cleaning* and, (c) *skin care after* work are some of the generally recommended measures to prevent occupational contact dermatitis.

The application of protection creams in the *hairdressing* trade forms part of a complex concept for the prevention of occupational skin disorders. The regular application of adequate skin protection is always recommended.

In food occupations, like in many other skin risk occupations, the regular use of personal protection equipment is recommended as well as regular skin care for the prevention of occupational hand dermatitis.

However, the effectiveness of skin care programs is always based on 3 factors: (a) the *effectiveness* of the products used, (b) the *frequency* of the application and (c) finally the effectiveness of the *education*.

The metal industry as it is today is characterized by the increasing quality of products, accurately organized processes and generally well-designed workplaces.

Thus, in contrast to many other occupational disease, occupational skin diseases are not hidden. Therefore, teaching the company management and the workers about existing dermatological risk at the workplace and their consequences is reasonable. *Skin Protection Training* is the topic of **chapter 15.**

In fact, various studies have shown that success in the primary, secondary and tertiary prevention of occupational skin disease is possible with intervention measures which include skin protection training. However, knowledge alone does not automatically lead to a change of attitudes, and this in turn may not automatically lead to a change of behavior. The generation of health protection behavior is in fact a very complex process. The goal have to be, the contents and method of skin protection training, as well as the selection of the trainer.

The book ends with **chapter 16**, focused on *Limitation of Skin Protection*.

Skin protection products and gloves are essential constituents of personal protective equipment at workplaces which can be used in a complementary way, each offering particular benefits and disadvantages. Gloves can contribute to skin irritation when used over long periods without intermission. Therefore, protection from skin damage caused by potential noxae has always to be balanced against untoward glove effects.

Thus skin protection creams can be used to reduce unnecessary long glove usage in order to reduce occlusion-related effects on the skin barrier.

Usage of moisturizers, in contrast to special barrier products together or even under gloves is judged critically, although selected products showed beneficial effects.

Another future option is the implementation of *active gloves* that are intended to gradually release ingredients that help to strengthen and preserve skin barrier integrity.

Finally another recent study suggests a benefit from usage of gloves with an inside pH of 5.5 in order to maintain a tight control over the skin surface pH under and after occlusion, based on the concept that a more alkaline skin surface pH might contribute to irritation and dryness.

This interesting book gives a comprehensive update of all the products to be used and the possible practical application in the occupational setting. Moreover it has also explores some useful protection programs, remarking the limitations of currently available protection measures.

Written by a group of well-known experts, the book could be useful for all the specialists involved in the fields of occupational dermatology as well as for dermatologists, allergists, occupational physicians, industrial hygienists, plastic surgeons, toxicologists pharmacists and, of course, cosmetic scientists, and also for people involved in marketing, industrial and university research.

P. Morganti
Editor-in-Chief

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General Information

Basic Information

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8th International Congress of International Society of Cosmetic Dermatology

Program at a Glance

	Saturday	October 21 Sunday		October 22 Monday	October 23 Tuesday
09:00-12:00	Registration	PL1: Plenary Session 1		PL2: Plenary Session 2 (Hall 103)	Plenary Session 3 (Hall 103) Closing Ceremony
12:30-13:30		P&G (Hall 103)		Shiseido (Hall 113)	
13:30-15:30		S04: Beauty Ouside In 1 (Hall87)	S01: Basic Science & Cosmetic Techniques (Hall87)	S10: Cosmetic Surgery (Hall87)	S07: TCM & Botanics in Cosmetic Dermatology (Hall87)
		S05: Hair and Hair Care (Hall88)	S02: Cosmetics and Skin Care (Hall88)	S11: Laser and Photo Therapy2 (Hall88)	S08: Laser and Photo Therapy 1 (Hall88)
		J&J (Hall 113)		S12: Acne and Rosacea (Hall90)	S09: Beauty Outside In 2 (Hall90)
15:30-17:30		S06: Pigmented Disorders (Hall90)	S03: Photobiology and Sun Protection (Hall90)	CS4: Chinese Session (Hall92)	CS3: Chinese Session (Hall92)
		CS2: Chinese Session (Hall92)	CS1: Chinese Session (Hall92)		
17:40-18:40		L'Oreal (Hall 103)	Lumenis (Hall 113)		
18:45-20:00		Welcome Reception (Banquet Hall)			

Hall 113 Hall 87 Hall 88 Hall 90 Hall92

Secretariat: Hall 89

October 21

09:00-09:30 ***Opening Ceremony*** **October 21, Hall 103**

Scientific Sessions

PL1

October 21, Hall 103

Chairs: Hong-Duo Chen, P. Morganti

09:30-10:00 **PL1-1** **Nanostructured Products: Technology and Future**
P. Morganti

10:00-10:30 **PL1-2** **Mechanisms of Skin Aging**
Philippe G. Humbert

10:30-10:50 **PL1-3** **待定 Anti-Aging**
Tzuen-Yann Wang

Chairs: Xuejun Zhang, Xinzhong Feng

10:50-11:20 **PL1-4** **Vitamin Therapy for Various Skin Troubles and Burn Injury from the Aesthetic Point of View**
Tetsuo Shu

11:20-11:40 **PL1-5** **Cosmeceuticals and Traditional Chinese Medicine**
Xiran Lin

S01: Basic Science & Cosmetic Techniques

October 21, Hall 87

Chairs: Xuemin Wang, Philippe G Humbert

13:30-13:50 **S01-01** **Videocapillanoscopic Assessment of Rosacea (Erythrosis)**
Philippe G Humbert

13:50-14:10 **S01-02** **Proliferative and Contractile Activities of Fibroblasts from Wrinkle Skin and Normal Skin**
Li Li

14:10-14:20 **S01-03** **Study on Noninvasive Skin Examination Techniques at the Subclinical Irritation within the Difference Causes**
Yanyu Wu

14:20-14:30 **S01-04** **Regulation of Tyrosinase mRNA in B16F10 Murine Melanoma Cells by Retinoic Acid**
Quanzhong Liu

14:30-14:40	**S01-05**	**Effects of Heat Shock on the Expression of Matrix Metallopproteinase-1 and Matrix Metalloproteinase-9 in HaCat cells** Wenhai Li
14:40-14:50	**S01-06**	**Effects of heat shock on the secretion of IL-6 in HaCat cells** Wenhai Li
14:50-15:00	**S01-07**	**Specific Action on Cutaneous Nervous Sysytem: a major issue for innovative skin care** Xiang Ye
15:00-15:10	**S01-08**	**Effec of N-acetlglucosamine on Hyalnronic Acid Synthesis and its related enzyme genes in human epidermal keratinocytes** Cai-xia Tu
15:10-15:20	**S01-09**	**Effects of IPL on the content of collagens and the mRNA expression of procollagen in Balb/c mouse skin** Yan Cao
15:20-15:30	**S01-10**	**Enhanced production of extracellular dermal matrix by plant derived extracts for skin antiaging benefits** Brian Jones

S02: Cosmetics and Skin Care

Octoher 21, Hall 88

Chairs: Li Li, Wei Lai

13:30-13:50	**S02-01**	**Non-invasive biophysical assessments of the efficacy of a moisturizing cosmetic cream base for atopic dry skin** H. Tagami
13:50-14:10	**S02-02**	**Skin diseases induced by cosmetics in China:data from the monitoring network of MOH** Lingping Zhang
14:10-14:25	**S02-03**	**Characerization of Chinese Eye Bag** Xinzhen Ma
14:25-14:40	**S02-04**	**The efficacy and tolerance of Diroseal in the treatment of Rosacea** **Wei Lai**
14:40-14:55	**S02-05**	**Management of Skin Tone - Whitening Session Objective: Review of Whitening Technologies & Clinical Data** Claude Saliou
14:55-15:10	**S02-06**	**Effect of Collagen Implant for reduction of the Wrinkle** Li Li
15:10-15:20	**S02-07**	**Effects of APP17-mer peptide on oxidative damage and expression of MMP-1mRNA in cultured human skin fibroblasts irradiated with ultraviolet rays** Hui Chen

15:20-15:30	S02-08	Analysis of 118 cases of facial dermatitis Yan Le

S03: Photobiology and Sun Protection

October 21, Hall 90

Chairs: Dan Luo, Huachen Wei

13:30-13:50	**S03-01**	**Molecular Mechanisms of Ultraviolet Radiatiou-Induced Dehydration and Skin Aging** Yinsheng Wan
13:50-14:10	**S03-02**	**Strategies for Sunscreeu Technology and Produet Development** Tianxiang Wang
14:10-14:30	**S03-03**	**The Biological Effect of k-Elastin on Human Dermal Fibroblasts in vitro, Potential Implications for Photoaging** Zhou Chen
14:30-14:40	**S03-04**	**The effect of artemether on the expression of Fas and Bcl-2 in HaCaT cells after exposure to UV** Danqi Deng
14:40-14:50	**S03-05**	**Study on Ultraviolet-induced Production of Inflammatory Cytokine in Human Keratinocytes** Xian Jiang
14:50-15:00	**S03-06**	**Effective Summary and Analyze of Topical 5-aminolaevulinic Acid-photodynamic Therapy in The Cosmetic Treatment of Cephalic and Facial Skin Tumor** Qiang Li
15:00-15:10	**S03-07**	**Effect of P38 mitogen-activated protein kinase(MAPK) on UVB-Induced Apoptosis of Human Keratinocyte HaCaT Cells** Xiaoe Chen
15:10-15:20	**S03-08**	**Effect of hesperidin on B16 and HaCat cell lines irradiated by Narrowband-UVB light** Ruzhi Zhang
15:20-15:30	**S03-09**	**Modulation of EGCG on the intrinsic senescence and gene mutation frequency from UVA irradiation in human fibroblasts** Jie Zhu

S04: Beauty Outside In 1

October 21, Hall 87

Chairs: Xinghua Gao, P. Morganti

15:30-15:50	**S04-01**	**Importance of dietary lipids for internal skin care** Baoru Yang

15:50-16:10	**S04-02**	**Blu light and skin protection** P. Morganti
16:10-16:20	**S04-03**	**Natural chemistry: oxymoron or pleonasm** K. Lintner
16:20-16:30	**S04-04**	**Skin on skin: Italian natural leader improve health and wellness** L. Celleno
16:30-16:40	**S04-05**	**Dietary strategies for better health: the key role of redox ingredients** M. Serafini
16:40-16:50	**S04-06**	**A New compound for advanced photoprotection** M.C. Pasi
16:50-17:00	**S04-07**	**Bioactive natural products from Chinese tropical marine invertebrates and plants for human wellness** Yuewei Guo
17:00-17:10	**S04-08**	**Wine Therapy: from grapes to healthy skin and beauty** G. Galderini
17:10-17:20	**S04-09**	**Perfluoropolyether phosphate: a safe skin exfoliating agent for sensitive skin** Rossella Ingoglia

S05: Hair and Hair Care

October 21, Hall 88

Chairs: Weixin Fan, Chaogang Wang

15:30-15:50	**S05-01**	**Basic and clinical aspects of androgenetic alopecia** Shigeki Inui, Department of regenerative Dermatolo
15:50-16:10	**S05-02**	**Classification of AGA** Jianzhong Zhang
16:10-16:20	**S05-03**	**Serum level of testosterone, free testosterone and dehydroepiandrosterone in patients with androgenetic alopecia** Xiaoyan Wang
16:20-16:30	**S05-04**	**The relationship of androgen receptor CAG polymorogusn abd nake oatterb bakdbess** Yuping Zhao
16:30-16:40	**S05-05**	**Angiogenin derived from hair dermal papilla cells stimulates human hair growth in vitro** Nahui Zhou
16:40-16:50	**S05-06**	**Effets of EGCG on the growth of human hair follicles and cell proliferation of human dermal papilla cells (DPCs) in vitro** Meiyun Li
16:50-17:00	**S05-07**	**调控毛乳头生长新的相关蛋白的研究** Fei Hao

17:00-17:10	**S05-08**	**A Comprehensive Guide for the Accurate Recognization of Murine Hair Follicles Cycle Stages** Zhongfa Lv
17:10-17:20	**S05-09**	**The Effect of Hair Loss on Life Quality** Lei Wang
17:20-17:30	**S05-10**	**The Damage of Perm and Dyeing towards Hair & the Repair Effect of Shampoo and Hair Tonic on Hair** Lei Cao

S06: Pigmented Disorders

October 21, Hall 90

Chairs: Huilan Yang, Yaping E

15:30-15:50	**S06-01**	**Approaches to identify inhibitors of melanin biosynthesis via quality control of tyrosinase** H. Ando
15:50-16:10	**S06-02**	**New skin whiten agent for treating facial hyperpigmentation in Asians** 邱品齐
16:10-16:30	**S06-03**	**Current review of in vitro study of skin whitening method development** Yaping E
16:30-16:45	**S06-04**	**Combination of 308-nm excimer laser with topical pimecrolimus for the treatment of childhood vitiligo** Huilan Yang
16:45-17:00	**S06-05**	**Clinical study of Glycolic Acids in treatment of Melasma** Leihong Xiang
17:00-17:10	**S06-06**	**Functional polymorphisms of the FAS gene associated with rick of vitiligo in Chinese population: a case-control analysis** Miao Li
17:10-17:20	**S06-07**	**The Evaluation of Skin Whitening Efficacy of Cosmetic Products Using a Human Skin Pigmentation Model** Yan Tian
17:20-17:30	**S06-08**	**Epidemiologic Study of Vitiligo in Northeastern China** Uwesu Omari Mchepange

October 22

PL2

October 22, Hall 103

Chairs: Xiran Lin, Jiabi Wang

09:00-09:30	**PL2-1**	**Instrumental Characterization of the Skin Surface Properties and Evaluation of the Efficaey of Skin Care** Hachiro Tagami
09:00-10:00	**PL2-2**	**Melasma: In Search for an Ideal Depigmenting Agent** Evangeline B. Handog
10:00-10:20	**PL2-3**	**Seven Truths Chinese Women Should Know About Their Skin....But Don't** Greg G. Hillebrand
10:20-10:50	**PL2-4**	**Surgical Treatment of Skin Cancers in Darker Racial Ethnic Groups** Kim Phillips

Chairs: Shengqing Ma, Mary Matsui

10:50-11:10	**PL2-5**	**A Worldwide Classification of Human Hair** Didier Saint-Leger
11:10-11:40	**PL2-6**	**New Ideas in Non-sunscreen Photoprotection** Mary Matsui
11:40-12:00	**PL2-7**	**The Study on Some Growth Factors Stimulating Hair Growth in vitro** Weixin Fan

S07: TCM and Botanics in Cosmetic Dermatology

October 22, Hall 87

Chairs: Yan Wu, Yongming Li

13:30-13:50	**S07-01**	**Historical contributions to cosmetic Dermatology by Chinese physicians in the past twenty centnries** Yongming Li
13:50-14:05	**S07-02**	**The effect of green tea extracts in protecting the skin from photoaging and photo immune suppression** Yuanhong Li
14:05-14:20	**S07-03**	**Photoprotective Effect of Two Chinese Herbs on the Damage of Human Keratinocytes Induced by Ultraviolet-B Irradiation and its Mechanism** Shaomin Zhong

14:20-14:30	**S07-04**	**Revisiting Researches on Natrual Botanical Extracts as Whitening Agents** Jie Gao
14:30-14:40	**S07-05**	**The Use of Traditional Chinese Medicine in Cosmetology** Ping Song
14:40-14:50	**S07-06**	**The Protective Effects of Sodium Selenite and Aloin Against UV-Induced Damage of Dermal Fibroblasts** Ran Ji
14:50-15:00	**S07-07**	**Influence of EGCG on the cellular functions of dendritic dells after UVB irradiation** Bingrong Zhou
15:00-15:15	**S07-08**	**The Relationship Between Decoloration and Effectiveness of Cosmetics with Chinese Herb** Shinryo Yabe
15:15-15:30	**S07-09**	**Application of Chinese herbal medicines in cosmetic products – A brief introduction** Nuan Chen

S08: Laser and Photo Therapy 1

October 22, Hall 88

Chairs: Min Zheng, Yuanhong Li,

13:30-13:50	**S08-01**	**Minimally Invasive Aesthetic Procedures for the Aging Face** Youwen Zhou
13:50-14:10	**S08-02**	**New and Emerging Non-Invasice Cosmetic Laser Treatments and Devices in Dermatology** John Chen
14:10-14:30	**S08-03**	**Laser and Photo Therapy in Cosmetic Dermatology in China** Zhanchao Zhou
14:30-14:50	**S08-04**	**Impacts of Intense Pnlsed Light on micronucleus production, Cell Proliferation and Collagen Synthesis of fibroblasters** H. Jun
14:50-15:05	**S08-05**	**Resluts of Functional Photothermolysis in 105 pations with Diverse Skin Problems** Won-Suk Han
15:05-15:15	**S08-06**	**Effects of intense pulse light on the content of collagens and the mRNA expression of procollagen in Balb/c mouse skin** Di Wu
15:15-15:30	**S08-07**	**Treatment of wrinkles and skin laxity using Aluma Skin Renewal System: Review of 24 cases** Zhanchao Zhou

S09: Beauty Outside In 2

October 22, Hall 90

Chairs: Hong-Duo Chen, Wei Liu

13:30-13:50	**S09-01**	**Chitin nanofibrils: an innovative pluri-performance antiage compound** P. Mezzana
13:50-14:10	**S09-02**	**Cosmetics, a winning player for "Made in Italy"** Maurizio Crippa
14:10-14:20	**S09-03**	**The role of lutein in human health** K. Oshida
14:20-14:30	**S09-04**	**Lipid Vesicles for Topical Application** G. Blume
14:30-14:40	**S09-05**	**Oral Intake of Hydrolyzed Collagen may stimulate collagen production by human cells themselves – literature review and results** Pierre-Albert Thomas
14:40-14:50	**S09-06**	**Specific action on cutaneous nervous system: a major issue for innovative skin-care** Xiang Ye
14:50-15:00	**S09-07**	**Teprenone (geranylgeranylacetone=GGA), a novel isoprene analog of geranylgeranylphosphate prolongs cell survival and improves skin condition** K. Lintner
15:00-15:10	**S09-08**	**Live Healthier, Look Better and Feel Happier (A wonderful package)** Chaolin Lee

S10: Cosmetic Surgery

October 22, Hall 87

Chairs: Hang Li

15:30-15:40	**S10-01**	**The History and Evolution: Dermatologic surgery of Cosmetology in China** Hang Li
15:40-15:55	**S10-02**	**Epidemiology and Treatment of Skin Cancers in Korea** Seung-Chul Lee
15:55-16:05	**S10-03**	**Reconstruction of Nasal Defect after Tumor Excision** Yongjing Tian
16:05-16:20	**S10-04**	**Non-cosmetic uses of liposuction surgery** Chang-Hun Huh
16:20-16:30	**S10-05**	**Chemical peeling together with PHA cosmetics in the treatment of mild to moderate acne** Wu Yan

16:30-16:40	**S10-06**	**Autologous fat transplantation without social downtime; Small-volumed Multi-step Approach Technique (SMAT)** Kyle Seo
16:40-16:50	**S10-07**	**The Method of Hair Removal Laser to Create the Fine Hairs after Follicular Unit Transplantation in Females with Thick Hairs** Kyle Seo
16:50-17:00	**S10-08**	**Experience in wound repairof 312 cases operation of dermatologic surgery** Ting-min Gu
17:00-17:10	**S10-09**	**Treatment of Facial Explosive powder thesaurismosis with ultra-high frequency skin plastic operation apparatus** Hui Chen
17:10-17:20	**S10-10**	**Treatment of Giant Keloid with Core Excision£ƒA Clinic Stndy** Yan Wang

S11: Laser and Photo Therapy 2

October 22, Hall 88

Chairs: Ping Tu, Zhanchao Zhou

15:30-15:45	**S11-01**	**Efficacy and Therapy of Intense Pulsed Light Therapy in the Treatment of Melasma in Chinese** Yuanhong Li
15:45-16:00	**S11-02**	**Clinical Observation on Treatment of Melasma with Q-switched Nd:YAG 1064nm Laser** Jun Fu
16:00-16:15	**S11-03**	**Clinical Observation on Treatment of Freckle in Combination of IPL with Q-Swiched Nd:YAG 532nm Laser** Y. Xiao
16:15-16:30	**S11-04**	**Quantitative Assessment of Facial Pigmentation after Laser Therapy Using Angel Software** Xiangdong Qi
16:30-16:45	**S11-05**	**595 nm Tunable Palsed Dye Laser Treatment of Vascular Skin Lesions: long-term efficacy and complication in Chinese patients** Chunjun Yang
16:45-17:00	**S11-06**	**Adverse Effects and Complications of 595 nm Pulsed Dye Laser in Treatment of Skin Vascular Abnormalities** Shengxiu Liu
17:00-17:15	**S11-07**	**Clinical Efficacy of a 308nm Excimer Laser for Treatment of Psoriasis Vulgaris** Yanling He

S12: Acne and Rosacea

October 23, Hall 90

Chairs: Leihong Xiang, Li He

15:30-15:45	**S12-01**	**Study on Heredity Pattern of Acne and its Correlated Genes** Li He
15:45-16:00	**S12-02**	**Pathogenesis of Comedo Formation** Longqing Xia
16:00-16:15	**S12-03**	**The Physical Therapies in the Treatment of Acne** Leihong Xiang
16:15-16:30	**S12-04**	**The Principle of Antibiotics Application in the Treatment of Acne** Fei Hao
16:30-16:45	**S12-05**	**The Chinese Herbs in the Treatment of Acne** Ping Song
16:45-17:00	**S12-06**	**The Treatment of Adult Acne** Chenxin Li
17:00-17:15	**S12-07**	**The Theory and Practice of the Latest Cosmetic Treatment for Acne in Japan** Yasuo Asada

October 23

PL3

October 23, Hall 103

Chairs: Wei Liu, Tian Huang

09:00-09:30	**PL3-1**	**Chemoprevention of Photocarcinogenesis & Photoaging: Models, Mechanisms and Approaches** Huachen Wei
09:30-09:50	**PL3-2**	**The World and the Development of Chinese Aesthetic Medicine Discipline** Wei Liu
09:50-10:10	**PL3-3**	**A New Understanding of Sensitive Skin: A neurological perspective** Olivier de Lacharriere

Chairs: Bian Zhao, Xinghua Gao

10:10-10:30	**PL3-4**	**Behind an Aging Face and the Sharing of Clinical Experiences of Injectable Hyaluronic Acid** Serina, Yuanli Liao
10:30-10:50	**PL3-5**	**The Aspect of Skin Aging and in vitro Studies on Their Molecular Basis of Collagen I Synthesis and Fibroblast Telemere Progressive Changes with UV Radiation** Yaping E
10:50-11:10	**PL3-6**	**Photoprotections of the Extract from Green tea on Human Skin Cells and Mouse Skin Damaged from UV Irradiation** Dan Luo

*CS01: Chinese Session 1**中文会场 1***

October 21, Hall 92

主持人： 张学军　彭庆星

13:30-13:50	**CS01-01**	**遗传性色素性皮肤病研究进展**　张学军
13:50-14:10	**CS01-02**	Patient-oriented Thermage could be more friendly　Chen-Yeu Soong
14:10-14:30	**CS01-03**	**外伤后细菌性致死性肉芽肿—— 一个需要美容医生关注的新疾病** 高天文
14:30-14:50	**CS01-04**	服装与皮肤　高兴华

14:50-15:10 **CS01-05** **高原紫外线防护考察报告** 张怀亮

15:10-15:30 **CS01-06** **化妆品皮炎研究治疗进展** 赖 维

CS02: Chinese Session 2 ***中文会场*** *2*

October 21, Hall 92

主持人：张建中 高天文

15:30-15:50 **CS02-01** 中国男性脱发的分型与治疗 张建中

15:50-16:10 **CS02-02** 男性型秃发流行病学调查 王婷玲

16:10-16:30 **CS02-03** 脱发对生活质量的影响 王雷

16:30-16:50 **CS02-04** 毛发移植 范卫新

16:50-17:10 **CS02-05** 黄褐斑治疗体会 赵 广

17:10-17:30 **CS02-06** 羟基乙酸治疗黄褐斑的临床研究 项蕾红

CS03: Chinese Session 3 ***中文会场*** *3*

October 22, Hall 92

主持人：李莉 李航

13:30-13:50 **CS03-01** 皮肤外科的美容技术 李航

13:50-14:10 **CS03-02** 胶原植入对皱纹的疗效 李莉

14:10-14:30 **CS03-03** 血管瘤的分型与激光治疗 孙林潮

14:30-14:50 **CS03-04** 芦荟胶治疗激光后皮肤损伤研究 张大为

14:50-15:10 **CS03-05** 红景天甙对紫外线辐射后纤维细胞增生长干预作用的形态学研究 史飞

15:10-15:30 **CS03-06** 中胚层疗法（Mesotherapy）研究进展 付俊

CS04: Chinese Session 4 中文会场 4

October 22, Hall 92

主持人：杨慧兰 杜娟

15:30-15:50	**CS04-01**	白癜风治疗体会　刘仲荣
15:50-16:10	**CS04-02**	白癜风患者焦虑、抑郁情绪与皮损相关性研究　路永红
16:10-16:30	**CS04-03**	普特彼治疗白癜风疗效观察　杜娟
16:30-16:50	**CS04-04**	理肤泉抗红舒敏霜治疗脂溢性皮炎临床观察　杨慧兰
16:50-17:10	**CS04-05**	中药化妆品研究现状　翁玉萍
17:10-17:20	**CS04-06**	多发性黑子综合征 1 例报告　李晓东
17:20-17:30	**CS04-07**	Leser-Trelet 综合征　陈楠

Università degli Studi di Pavia
Facoltà di Medicina e Chirurgia

Master biennale di II livello in Medicina Estetica e del Benessere

Anni accademici
2007-08, 2008-09

Che cos'è

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.

Requisiti fondamentali per l'ammissione

Laurea in Medicina e Chirurgia
Abilitazione all'esercizio della professione di Medico Chirurgo
Iscrizione all'Ordine dei Medici Chirurghi

Numero massimo iscritti: 30
L'ammissione è determinata da una selezione secondo graduatoria di merito.
Per i criteri di ammissione consulta il sito www.plasticaticinensis.it

Obiettivi e Durata

Conseguimento del Diploma Universitario di Master in Medicina Estetica e del Benessere.
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

Percorso Didattico

Il percorso didattico si articola in 9 moduli di insegnamento ed in attività di tirocinio pratico:

- Aspetti generali della Medicina Estetica e del Benessere e discipline propedeutiche
- Dermatologia e Cosmetologia
- Termalismo
- Flebolinfologia
- Cura della silohuette
- Tecniche e metodiche in Medicina Estetica e del Benessere
- Apparecchiature e tecnologie di specifico impiego in Medicina Estetica e del Benessere
- Attività motorie
- Terapie complementari e non convenzionali
- Tirocinio-Stage

Costo di iscrizione

Il costo di iscrizione al Master in Medicina Estetica e del Benessere è di 6000€/anno **formula all-inclusive.**
Il costo di iscrizione comprende:
- Frequenza di tutti i corsi teorici e delle attività pratiche.
- Materiale didattico.
- Transfer e soggiorno all-inclusive nelle località di stage fuori sede.
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Master Universitario biennale di II livello in MEDICINA ESTETICA E DEL BENESSERE dell'Università di Pavia per gli anni 2008-2009: un prodotto formativo aggiornato e completo, una formula organizzativa d'avanguardia, nella lunga tradizione di un grande Ateneo.

IL MASTER biennale DI II LIVELLO IN MEDICINA ESTETICA E DEL BENESSERE dell'Università di Pavia viene riproposto per gli anni accademici 2007-2008, 2008-2009, in considerazione dei lusinghieri risultati formativi della precedente edizione, ora in via di conclusione.
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Lamine di chitosano (Hydagen HCMF) per tissue engineering al microscopio elettronico a scansione (SEM). *Su gentile concessione* della Prof.ssa Graziella Biagini, Istituto di Morfologia Umana Normale, Università Politecnica delle Marche, Ancona, Italia

Scanning electron microscopy (SEM) immage of **chitosan structures** (Hydagen HCMF) for tissue engineering applications *On kind permission of* Prof. Graziella Biagini, Istituto di Morfologia Umana Normale, Università Politecnica delle Marche, Ancona- Italy

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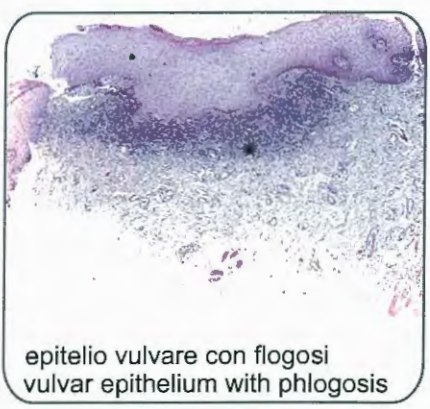

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