

Journal of applied cosmetology

4

OFFICIAL JOURNAL OF

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The New Frontiers of Dermo-Cosmetology

Efficacy, Stability and Safety

7° ISCD International Congress - Rome November 4-5-6- 2004

ISCD - International Society of Cosmetic Dermatology - Via Innocenzo XI, 41 - 00165 Rome

PROGRAMME and ABSTRACTS

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Trimestrale di Dermatologia Cosmetologica Quarterly Review of Cosmetic Dermatology

VII ISCD INTERNATIONAL MULTIDISCIPLINARY CONGRESS

The New Frontiers of Dermo-Cosmetology: Efficacy, Stability and Safety

Rome 4- 6 November 2004

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CARTA ECOLOGICA - ENVIRONMENTALLY PAPER - PAPIER ECOLOGIQUE - PAPEL ECOLÓGICO





The New Frontiers of Dermo-Cosmetology

Efficacy, Stability and Safety

7° ISCD International Congress - Rome November 4-5-6- 2004

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Welcome from the ISCD

Our over-all health, the harmony of our body development, the correctness with which its system regulates its internal and external environment are some of the biological factors that control one's life, hence, human longevity. Over the past decade, there has been a vast explosion in new information relating the art and science of cutaneous biology and cosmetic chemistry. Thus better nutritional regimes, better bodily care and regular controlled exercise have improved the physical quality of life. The idea of Cosmetic Dermatology is the recognition that cosmetics, skin fillers and functional food complements are more than a matter of chemistry. Therefore this multidisciplinary international meeting will be devoted to pharmacognosy and skin biology, to verify and control the safety and function of cosmetics and the dermatological and legal problems arising from the use of cosmetics, and surgical practices used for beautifying the skin.

Special sessions will be dedicated to the new frontiers of Cosmetic Thermalism, and/or Botanicals, SPA organization, and the innovative use of diet complements to ameliorate the general well-being. A new frontier was, in fact, personally broached from me, since to 1987 (2nd I.S.C.D. meeting), by the proposal that the skin might be cosmetically approved by oral therapy, also.

Thus Cosmetic Dermatology, as interdisciplinary science, borders on numerous related fields, and for each product specialists who cannot function in isolation from these fields are required.

To enhance not only the appearance but the general wellbeing, is central to the very idea of this congress.

I thank you in advance for contributing to its success.

*Pierfrancesco Morganti Ph.D.
ISCD Secretary General*

ISCD Congress Opening Lecture

The skin as a source of psycho-physical well-being

The human skin is a marvellous mantle that protects our body from harmful stimuli, performing many vital functions for the organism. However, it should not be considered as a simple barrier, an envelope that separates us from the external world, but as an interface that actively participates in exchanges between the internal organs and the environment. Through nerve endings, it sends signals to the central nervous system via afferent pathways and, in turn, is the site of stimulation via efferent pathways of the sympathetic and parasympathetic systems. It receives stimuli that it transforms into sensations and reacts with functional expressions appreciable by an observer. Since birth, it is the site of exchanges of sensory information with the exterior that can condition our psychological development.

The skin is modelled around the musculo-skeletal apparatus not in a random manner but conferring plasticity and an aesthetical sense to the body. Its physical and organoleptic aspect, expressed by attributes like colour, luminosity, elasticity, softness, heat, odour, etc., consists of a set of characters that can, to a variable degree, create attraction and what we define as beauty. This is not an absolute quality but is in the eye of the observer, since it is capable of stimulating an aesthetical feeling that pleases our eyes, a kind of visual pheromone.

The sensations transmitted by the skin, intimately perceived by everyone, do not represent only a means of communication with others but also a means of self-affirmation. Understood in this way, the appearance of our skin represents the perception of our body, the way of considering oneself within the self-image that everyone has. An image that is an expression of a person's general well-being and state of health, fundamental in the attainment of happiness, serenity and personal success in all fields: work, friendships and social relationships.

In recent years, many convincing scientific studies have tended to show that a debilitated psychological condition can upset a precarious equilibrium, favouring the onset of disease. However, if it is true that psychological debilitation, particularly a state of depression, is a risk factor for somatic illness, it is logical to imagine that the opposite can occur, that psychological well-being can help prevent and combat illness. Although the variables involved in this assumption are so numerous and distributed over a period of so many years that it becomes impossible, with current technologies, to define the random or chaotic sequences of this hypothetical relationship, experimental data and clinical observations tend to support this idea. In particular, it seems certain that various types of psychological-psychotherapeutic intervention can positively influence the quality of life, the course of disease and general survival.

We wonder how it is possible that a psychological condition stimulates a somatic response. Well, this probably occurs through complex conditionings that involve the nervous, endocrine and immune systems, a thesis supported by a large body of scientific research.

These concepts represent the basis of a correct methodological approach to the relationships between beauty and psycho-physical well-being. In particular, they allow us to ask the following question: can the aesthetical appearance of our body positively affect our psychological attitude and condition somatic responses? The answer is "yes", as there is reliable scientific evidence to believe that psycho-

logical well-being can not only prevent the development of disease but also positively affect its course.

It follows that if the beauty of the body, particularly of the skin, is fundamental for psychological and physical well-being, anything that contributes to improving the aesthetical appearance of our body will be an important element in the attainment and maintenance of good health. Obviously, cosmetics can play a very important role in this context.

In this regard, it is useful to remember that modern cosmetology largely proposes the use of functional products, containing substances that interact with the skin and induce structural and functional modifications that improve its appearance. Products with these characteristics seem to best satisfy the demands of a cosmetology whose main goal is to provide psycho-physical well-being.

Therefore, cosmetics take on the connotation of true "skin drugs" that provide charm and beauty, thus improving self-perception of the body and producing health and well-being. They are products capable of covering our body in an imperceptible and extraordinary manner, giving it extra value that improves the quality of life, increases self-assuredness and assuages the fear of non-acceptance of one's image.

Prof. Lucio Andreassi
ISCD Congress President

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The International Society of Cosmetic Dermatology, a non-profit association, was founded in 1982 to fulfill some very special needs. Its purpose is to encourage a more continuous and stable exchange among the medical community in general, dermatologists in particular and cosmetic chemist, pharmacologists, physiologists, toxicologists and experts of all other disciplines that may be related to Cosmetic Dermatology.

The ISCD organizes a meeting at varied locations around the world every two years.

Official languages is English.

The official publication of the ISCD is the "Journal of Applied Cosmetology" published in English.

PUBLISHED PROCEEDINGS

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Vol. 2 – Every Day Problems in Dermatology: the Cosmetic Connection (1987)

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“LANCISI” HALL

SESSION

I

COSMETIC DELIVERY TO THE SKIN

CHAIRMAN: *J. Arct (Poland)*

14.00	Introductory remarks: <i>L. Andreassi (I), P. Morganti (I), and C.Orfanos (D)</i>	
14.15	Biological factors which influence percutaneous absorption <i>B.Berra, S. Zava (I)</i>	<i>pag. 167</i>
14.30	Alopecia between Drugs and Cosmetics <i>G. Biagini, F. Giantomassi, G. Lucarini (I)</i>	<i>pag. 168</i>
14.45	Percutaneous absorption by <i>in vivo</i> techniques <i>E. Berardesca (I)</i>	<i>pag. 169</i>
15.00	Cosmetic delivery: are we passing the final barrier into dermatology? <i>J. Wiechers (The Netherlands)</i>	<i>pag. 170</i>
15.15	Lipid vesicles as carrier systems <i>G. Blume (D)</i>	<i>pag. 171</i>
15.30	DISCUSSION	
15.45	COFFEE BREAK	
	CHAIRMEN: <i>S. Calvieri (I), E. Touitou (Israel)</i>	
16.00	A New concept for prevention of sunscreens permeation across the skin <i>E. Touitou (Israel)</i>	<i>pag. 172</i>
16.15	Topical and systemic photoprotection for a better skin-umbrella <i>P.U. Giacomoni (USA)</i>	<i>pag. 173</i>
16.30	Skin care: the innovative nanotechnology to improve the performance of delivery systems <i>E. Esposito, R. Cortesi E. Menegatti (I)</i>	<i>pag. 174</i>
16.45	Skin Penetration – the Key Factor in Cosmetic Activity Firms <i>J. Arct (Poland)</i>	<i>pag. 176</i>
17.00	Percutaneous absorption by <i>in vitro</i> techniques <i>S. Majewski (Poland)</i>	<i>pag. 178</i>
17.15	Best Innovator: a European Award for High Technology Firms <i>A. Cannavacciuolo (I)</i>	<i>pag. 179</i>
17.30	Technological strategies to improve photostability of Parsol MCX. <i>P. Perugini, M. Vettor, R. Tursilli, S. Scalia, I. Genta, T. Modena, F. Pavanetto, B. Conti (I)</i>	<i>pag. 180</i>
17.45	DISCUSSION and Session Closure	

November 5, 2004

“LANCISI” HALL

SESSION	II
THERMALISM VS NATURAL COSMETICS	
CHAIRMEN: <i>A. Dweck (UK), G. Salvatore (I)</i>	
9.00	Understanding consumers' new expectation for health and well-being <i>G. Salvatore (I)</i> <i>pag. 183</i>
9.15	The role of Phytohormones, phytosterols and iso-flavones in the care and improvement of the skin. <i>A. Dweck (U.K.)</i> <i>pag. 185</i>
9.30	How to combine natural ingredients from thermal springs with good science <i>G. Agostini, P. Morganti, F. Russo, H. Vaziri (I)</i> <i>pag. 186</i>
9.45	Botanicals: no longer a niche market <i>A. Cristoni (I)</i> <i>pag. 187</i>
10.00	DISCUSSION
10.15	COFFEE BREAK
CHAIRMAN: <i>D. Raskovic (I)</i>	
10.30	What natural and /or thermal cosmetic means? <i>P. Morganti (I)</i> <i>pag. 188</i>
10.45	Cardiovascular prevention and psychophysical wellbeing <i>C. Di Veroli (I)</i> <i>pag. 189</i>
11.00	The correct advertising communication on cosmetic field: the Italian law approach <i>M. Caponeri (I)</i> <i>pag. 190</i>
11.15	Clear, truthful and fair claims: The role of Italian Competition Authority <i>A. Mancini (I)</i> <i>pag. 191</i>
11.30	Lutein and Skin Health <i>R. Roberts (Portugal)</i> <i>pag. 192</i>
11.45	Thermal tools: new cosmetics or old drugs <i>T. Lotti (I)</i> <i>pag. 193</i>
12.00/12.30	DISCUSSION, BRUNCH and POSTER VIEWING

November 5, 2004

“LANCISI” HALL

SESSION

III

**PLASTIC SURGERY AND MEDICAL
DEVICES FOR THE BODY WELLBEING**

CHAIRMEN: *L. Gramiccioni (I), R. Bracaglia (I)*

14.00	Medical devices, body appearance and wellbeing. The EU rules <i>L. Gramiccioni (I)</i>	<i>pag. 194</i>
14.15	Safe and innovative temporary dermal fillers <i>C. Muzzarelli and R.A.A. Muzzarelli (I)</i>	<i>pag. 195</i>
14.30	Temporary dermal fillers <i>R. Bracaglia, R. Fortunato, S. Gentileschi (I)</i>	<i>pag. 196</i>
14.45	Antiwrinkling activity of a medical device based on hyaluronic acid, betaglucan and vitamin C. <i>M. Palombo and F. Svolacchia (I)</i>	<i>pag. 197</i>
15.00	DISCUSSION	
15.30	COFFEE BREAK	

CHAIRMEN: *L. Rusciani (I), P. Palombo (I)*

15.45	Mini-aggressive facial remodeling and rejuvenation: combined techniques <i>L. Rusciani, A. Rusciani (I)</i>	<i>pag. 198</i>
16.00	Chitosan films for culture and transplantation of melanocytes and keratinocytes to vitiligo cases <i>M. Mojamdar and D. Gillet (India)</i>	<i>pag. 199</i>
16.15	Session Closure	
17/20.00	COCKTAIL CEREMONY <i>at The House of Parliament “Sala del Cenacolo and Sagrestia”</i> Speakers in alphabetical order: <i>Prof. Lucio Andreassi</i> <i>President - 7° Congresso ISCD (Italy)</i> <i>Prof. Angelo Capparoni</i> <i>President - Accademia di Storia dell'Arte Sanitaria (Italy)</i> <i>Prof. Hong Duo-Chen</i> <i>President - Ass. Dermatologi e Vice-Presidente Ass. Medici Cinesi (China)</i> <i>Prof. Pierfrancesco Morganti</i> <i>ISCD Secretary General (Italy)</i> <i>On. Giuseppe Palumbo</i> <i>President - 12° Commissione Affari Sociali della Camera (Italy)</i> <i>Sen. Riccardo Pedrizzi</i> <i>Pres. 6° Commissione Tesoro e Finanze del Senato (Italy)</i>	

November 5, 2004 "ALESSANDRINA" HALL

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ROUND TABLE "ALESSANDRINA" HALL

ROLE OF NATURAL COSMETICS AND DIET SUPPLEMENTS ON WELLBEING

11.00/13.00

CHAIRMEN: *O. Cozzoli (I), B. Berra (I)*

11.00	Introductory Remarks: <i>O. Cozzoli (Lab. SSOG Milano, Italy)</i>	
11.10	The international scenario of the so-called natural cosmetics and functional food <i>P. Morganti (II Univ. of Napoli - Italy)</i>	<i>pag. 207</i>

11.20	Thermal cosmetics: do they really exist? <i>G. Agostini (Univ. of Pisa- Italy)</i>	
11.30	How to control the bio-natural products <i>L. Nori (President of Consorzio per il Controllo dei Prodotti Biologici - Italy)</i>	
11.40	How to protect the consumers's expectations on natural products <i>M. Marletta (Ministry of Health, Rome Italy)</i>	
11.50	GLA and omega 3 oils: the future in cosmetic and nutraceutical applications <i>Parodi A&A F.lli Parodi (Campomorone – GE - Italy)</i>	
12.00	Omega 3 – fatty acids of botanical and marine sources: which are safer? <i>P. Morganti (R&D. Mavi Sud, Rome, Italy)</i>	pag. 208
12.10	Specialty oils: processing methods and there application in cosmetic and nutraceuticals <i>Parodi A&A F.lli Parodi (Campomorone - GE - Italy)</i>	
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ROUND TABLE “ALESSANDRINA” HALL

SKIN AGING: THE ART OF COMBINATION THERAPY IN AESTHETIC MEDICINE

14.00/16.00

CHAIRMEN: *A. Corbo (I), L. Rusciani (I)*

14.07	The art of collagen for special rejuvenation <i>A. Corbo (I)</i>
14.14	Combination chemical peels <i>G. Londei (I)</i>
14.21	Medical –surgical combine technique for facial rejuvenation <i>R. Eccellente (I)</i>
14.28	Botulinum toxin type A. How to avoid complications <i>M. Benci (I)</i>
14.35	Photo rejnvenation <i>M. Laurenza (I)</i>
14.42	Side effects and complications of chemical peeling <i>G. Labrini (I)</i>
14.49	A new peeling formula for damaged skin <i>C. Sciuto (I)</i>

14.56	Botulinum toxin. Technical of injection: how avoiding mistakes <i>P. Cirillo (I)</i>	pag. 209
15.03	Hair Transplant. From the punch-graft to the follicular unit, the evolution of a technique <i>G. Agostinacchio, M. Cioccolini and V. Mancini (I)</i>	pag. 210
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17/20.00	COCKTAIL CEREMONY <i>at The House of Parliament "Sala del Cenacolo and Sagrestia"</i> Speakers in alphabetical order: <i>Prof. Lucio Andreassi</i> <i>President - 7° Congresso ISCD (Italy)</i> <i>Prof. Angelo Capparoni</i> <i>President - Accademia di Storia dell'Arte Sanitaria (Italy)</i> <i>Prof. Hong Duo-Chen</i> <i>President - Ass. Dermatologi e Vice-Presidente Ass. Medici Cinesi (China)</i> <i>Prof. Pierfrancesco Morganti</i> <i>ISCD Secretary General (Italy)</i> <i>On. Giuseppe Palumbo</i> <i>President - 12° Commissione Affari Sociali della Camera (Italy)</i> <i>Sen. Riccardo Pedrizzi</i> <i>Pres. 6° Commissione Tesoro e Finanze del Senato (Italy)</i>	

SESSION

V

BIOLOGICAL FUNCTION AND EFFICACY OF COSMETIC INGREDIENTS

CHAIRMEN: *I.R. Scott (UK), C. Scesa (I)*

8.30	Anti-Stress Active Ingredients: A new Generation of Cosmetics <i>C. Dal Farra, K. Cucumel, JM. Botto, E. Bauza, and N. Domloge (France)</i>	pag. 213
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9.00	Cosmetological Education in Poland <i>K. Pytkowska, J. Arct (Poland)</i>	pag. 215
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9.30	Efficacy of new cosmetic compounds with a hotox-like activity <i>C. Scesa (I)</i>	pag. 217
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ABSTRACTS

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Biological factors which influence percutaneous absorption

B. Berra, S. Zava

Istituto di Fisiologia Generale e Chimica Biologica Facoltà di Farmacia - Università degli studi di Milano - Italy

The functions of the skin can be summarized as follows: · physical barrier against friction and shearing forces · protective barrier to infection · prevention of excessive water loss or absorption · ultra-violet induced synthesis of vitamin D · temperature regulation · sensation (pain, touch and temperature) · antigen presentation/immunological reaction/wound healing · protection from ultraviolet irradiation, and are made possible by the cells present in the epidermis, basement membrane, dermis which have a highly organized structure. As can be appreciated by this brief overview, describing the skin complexity, numerous causes may interact to determine the overall rate of skin permeation that will be the result of competitive, additive or synergistic action of different factors. Fortunately the problem is simplified because of the rate-limiting role of the stratum corneum. However even in these "simple" cases, extrinsic variables may influence stratum corneum permeability in-vivo and confound the ability to predict absorption in a specific individual. These variables are: · environment: temperature, humidity which condition hydration of the skin · cutaneous blood flow · diet and its nutritional components · coadministered compounds, in particular the use of penetration enhancer with their effects on the lipid pathways · cutaneous biotransformation. The problem has been circumvented in many transdermal drug delivery systems by making the drug delivery device, rather than the skin, the rate-limiting process.

Alopecia between Drugs and Cosmetics

Graziella Biagini, Federica Giantomassi, Guendalina Lucarini

Università Politecnica delle Marche, Facoltà di Medicina e Chirurgia, Istituto di Morfologia Umana Normale-Istologia, Torrette (AN) - Italy

Hair loss, although a benign medical condition, can provoke psycho-emotional impacts with several levels of implications as a) a primary inducer, b) an aggravating factor in hair loss disorder, c) a stress as secondary problem also contributing to the increase of hair loss as a vicious circle.

Among these different hair loss conditions we focused our interest onto Alopecia areata that is a relatively common inflammatory form of nonscarring hair loss of unknown pathogenesis, but possibly of autoimmune origin.

Our investigation evidences as a topical therapy with a contact allergen diphencyprone (DPC) may be considered an effective mode of treatment. After DPC therapy the CD4/CD8 ratio is restored closely to normal scalp skin. Moreover this therapy exerts an important role in angiogenesis, upregulating VEGF in human hair follicle keratinocytes and upregulating survivin to preserve endothelial cell viability.

Transfollicular drug delivery through microspheres is another method of current therapeutic interest mainly with regard to follicular targeting of essential structures containing stem cells.

Therefore more close ties among enhanced therapeutic modalities, clinical symptoms specific pro-adapting coping strategies and quality of life improvements are emerging.

Percutaneous absorption by *in vivo* techniques

E. Berardesca

S. Gallicano Dermatology Dpt - Rome - Italy

NOT RECEIVED

Cosmetic Delivery: Are We Passing the Final Barrier into Dermatology?

Johann W. Wiechers

Uniqema, Skin R&D, Gouda, The Netherlands

It is often claimed that drugs penetrate the skin and cosmetics do not, but it is the physicochemical structure of the penetrating molecule and the formulation in which it is formulated that decides whether a molecule really penetrates the stratum corneum, not its efficacy profile (i.e. drug or cosmetic). In this talk I will outline the ideal molecular requirements for chemicals to penetrate skin (polarity and size of the penetrating molecule) as well as the influence of the formulation on skin delivery. It will become clear that depending on its structure a molecule will or will not have the potential to penetrate skin, and that the formulation in which it is incorporated subsequently has to transfer this potential into a kinetic reality. Whether it then acts as a drug or a cosmetic depends on the intrinsic efficacy of the penetrating molecule as well as its concentration at the target site. The methodological implications of the similarities and differences in topical drug delivery and cosmetic delivery will also be discussed.

Lipid vesicles as carrier systems

Gabriele Blume

ROVI Cosmetics, Schlüchtern, Germany

To ensure effectiveness of cosmetic or pharmaceutical active ingredients in the deeper skin, the transport of these components to the target sites is the crucial point. The stratum corneum, the outermost skin layer with its "brick and mortar" architecture effectively prevents dermal drug permeation. Indeed, the interstices in the horny layer, which seldom exceed more than 20 nm in width, are extremely impermeable even for small molecules. Water actually trepasses the skin at the rate of 0.4 mg cm⁻² h⁻¹. To overcome the skin barrier, normally chemical enhancers are used which typically increase the fluidity of the lipids in the stratum corneum. Liposomes are commonly used in dermal applications as protective system for active ingredients and for their moisturising properties. But they also can have the property to penetrate into the skin, carrying actives to the target site, where these molecules will be released. This, however, can only be achieved if the form, size, flexibility, composition and number of the membranes of the liposomes meet certain criteria like our ROVISOMES. ROVISOMES are small sized liposomes (150-300 nm) with one to three bilayers surrounding an aqueous core. The lipids, ROVI is using for the preparation is in particular phosphatidylcholine obtained from soy bean, having a high content of essential polyunsaturated fatty acids (linoleic acid) [1]. Vesicles with this high content of stabilised linoleic themselves help to promote the skin care properties of cosmetic formulations. The effects on the skin's moisture balance and its surface profile were determined in the course of a 28-day study carried out on 22 female test persons. There were also significant differences in the unfilled liposomes, compared to the initial value. After 28 days, the moisture content of the skin had increased by 16.4 %, and its surface was 17.4 % smoother. In addition to this, the number of wrinkles was reduced by 6 % [2]. After the encapsulation of active ingredients in these liposomes we have shown that liposomal bound molecules are significantly carried into deeper skin layers to a larger extend and in shorter time in comparison to non-encapsulated ones, even into the hair follicles [3]. The enhanced penetration results in a better bioavailability of the actives at the target side, which could be observed in increased physiological effectiveness (Moisturisation, Skin Smoothness, Anti-Wrinkle [2], Anti-ageing [4], Depigmentation [5], Free radical scavenging properties in the epidermis [6]). In addition, stabilisation effects on the active ingredients by the carrier system could be observed [7].

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A New concept for prevention of sunscreens permeation across the skin

Elka Touitou

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Skin cancer is one of the most common diseases in the world and is highly related to the exposure of the skin to the sun. Sunscreens are prophylactic agents that absorb UV radiation. They are generally small organic molecules, which act on the surface of the skin. Due to their physico-chemical characteristics they possess a good potential to penetrate the deep strata of the skin and to have systemic absorption. Actually, for many years researchers have been aware of the possible toxicity caused by percutaneous absorption of chemical sunscreens topically applied to the skin. Some recent reports support this concern. For example, widely used sunscreens were reported to have an estrogenic effect in laboratory tests, caused cancer cells to grow more rapidly and triggered developmental abnormalities in rats. It is important to keep in mind that sunscreens are applied to a large skin area and for a long period of time. Thus there is an absolute need for skin non-penetrating photoprotectors.

In this work we investigated skin non-penetrating sunscreen (NPSUN) with high applicability for cosmetic and pharmaceutical formulations. The concept behind the design of NPSUN agents was to immobilize the sunscreen molecules within structure that do not penetrate the skin but preserves its UV absorption characteristics. NPSUN are derivatives of a natural compound with synthetic or natural UV sunscreens approved for human use.

UVA, UVB or UVA-UVB protective products could be designed.

NPSUNs were characterized for their MW, UV absorption spectra and structure by Mass Spectroscopy, UV Spectrophotometry, IR and NMR. The skin permeation behavior was studied. As an example, the permeation of a methoxycinnamate-NPSUN was tested against octylmethoxycinnamate (OMC) through model skin. The experiments were carried out for 24 hours at 37°C in Franz diffusion cells with the effective area of 1.77cm². At the end of the experiment the skin was cleaned and the compounds were extracted. The amounts of sunscreens that permeated across or remained into the skin were assayed by HPLC. It was found that almost 10% of the initial quantity of OMC permeated the skin.

No penetration of the new NPSUN across the skin was observed throughout 24 hours in vitro permeation experiment. Area and time are two main parameters directly contributing to the total percutaneous absorption of a penetrating molecule, thus relatively high systemic absorption of currently used sunscreens could be anticipated.

The non-penetrating characteristics of NPSUN new compounds are not only an important advantage over the currently used sunscreens but can be seen as meeting the future requirements of sunscreens. Their use will generate new improved cosmetic and pharmaceutical products as demanded by the market and health care needs.

Topical and systemic photoprotection for a better skin-umbrella

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Clinique Laboratories, Melville, NY - USA

In this review, the most frequent molecular damages inflicted by ultraviolet radiation on living tissues will be recalled, such as lipid peroxidation and protein carbonylation via singlet Oxygen, as well as direct and indirect DNA damages. The spectra of action of the production of these damages will be discussed. The current interpretation of the mechanisms involved in some of the clinical effects consequent to exposure of human skin to ultraviolet radiation will be discussed.

Protection offered by stratum corneum and pigmentation as well as individual differences in the capability to perform protein and DNA repair will be discussed. Emphasis will be brought on recent results relative to the parameters susceptible to affect the clinical effects of ultraviolet radiation, such as phototype and ethnicity, since data seem to indicate that ultraviolet radiation damages DNA in the decreasing order: Caucasians > Asians > African-Americans>Latinos.

The short-term clinical consequences of exposure to UV radiation will be discussed, with particular attention to the suppression of contact hypersensitivity and delayed type hypersensitivity and to the means to avoid the immune depression, or to restore the immune response.

Recent technologies to protect/restore the immune response, such as the topical application of polysaccharides, or of sunscreens with specific absorption spectrum, or of DNA repairing enzymes or the systemic administration of specific carotenes, will be discussed.

Skin care: the innovative nanotechnology to improve the performance of delivery systems

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Research efforts in pharmaceutical and cosmetic field are currently aimed to develop new nanoparticulate systems able to control release and to improve targeting to skin. Among nanoparticles, liposomes are of course the best known systems. In the last decades, a number of studies has demonstrated their efficacy as drug delivery systems for topical administration way. Until now the major liposome drawback is their limited physical stability. As alternative to liposomes, solid lipid nanoparticles (SLN), ethosomes and cubosomes represent innovative carrier systems. SLN have been firstly designed for i.v. administration and recently investigated for peroral and transdermal application. Their solid matrix should be able to protect chemically labile agents from degradation and to modulate drug release profiles. Skin care studies performed by the use of SLN indicate an increase in skin hydration and a reduction in wrinkle depth, moreover SLN can improve uptake of cosmetic agents. Ethosomes could be described as lipid vesicular systems embodying ethanol in relatively high concentrations. These "soft vesicles", represent novel vesicular carrier for enhanced delivery to/through skin. One main feature of this new type of vesicle is its soft structure which carries the incorporated active agent into the skin lipid bilayers, enabling facilitated delivery. The use of ethosomal carriers results in delivery of high concentrations of active to/through the skin regulated by system composition and their physical characteristics. The major potential of ethosomes in promoting penetration through skin with respect to liposomes is ascribed to an interaction between ethosomes and skin lipids. Polar lipids such as monoolein, commonly used as food emulsifiers, are known to form bicontinuous cubic phase liquid crystals. Cubic liquid crystalline materials are an active research topic because their unique structure lends itself well to controlled release and skin care applications. Aqueous dispersions of cubic lipid phases led to the development of new nanoparticulate delivery systems, the so-called "cubosomes", characterized by high biocompatibility and bioadhesivity. Because of their properties, these versatile delivery systems can be administered percutaneously. Cubic phase materials can be formed by simple combination of biologically compatible lipids and water and are thus well-suited for use in treatments of skin, hair or other body tissues. Cubosomes usually have been produced by means of time-consuming methods involving high energy input. Conversely we have recently tested more conventional dispersion techniques demonstrating that the emulsification of monoglyceride/surfactant mixtures in water results in the formation of aqueous dispersions composed of large lipid particles (28 % w/w) and cubosomes characterized by spheroidal shape, few aggregates, mean diameter of 193.5 nm, and high percentage of recovery (88% wt/wt)1. Moreover, to overcome the large particles presence, a method based on a dilution process of an ethanolic solution of monoolein with an aqueous solution of Poloxamer has been proposed. Ethanol was used as a hydrotrope to create a liquid precursor, spontaneously forming cubosomes after dilution. This is all done without the need for high shear, minimizing the risk of degrading the cubic liquid crystalline structure. Organoleptic and morphological features of cubosomes do not change by time,

appearing free from phase-separation phenomena for almost 1 year from production. Photon Correlation Spectroscopy studies showed that cubosomes undergo an initial increase in mean diameter within the first month following production; afterwards they generally maintain their dimensions for the next 6 months.

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Skin Penetration – the Key Factor in Cosmetic Activity

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The term of “biologically active” has a very broad meaning with regard to cosmetics and it is difficult to define it unequivocally. Not only substances that have an immediate effect on receptors of intracellular and intra-tissue homeostasis regulating systems, but non-specific impact factors also influence physiological processes within a skin. The most important are “typical” biologically active substances that bind to the particular receptors in viable layers of epidermis or in dermis. Such substances act within viable skin tissues, so their activity depends on ability of reaching an appropriate target site. Therefore the final cosmetic effect depends on two factors – the activity of a substance in relation to reception site and kinetics of penetration and distribution in the skin.

Penetration rate through the skin results from a number of physicochemical processes. The most important are phenomena that determine distribution of a component between occlusion layer and lipid structures of *stratum corneum* as well as a rate of diffusion inside this layer. Passing of an active from the cosmetic into epidermal barrier lipids depends on a concentration gradient and a rate of substance thermodynamic activity in both phases. High solubility of a substance in an occlusion layer decreases a partition coefficient. On the other hand higher affinity to the lipids of intercellular cement is conducive to penetration.

Until recently it was considered that the most important factor determining the rate of penetration through *stratum corneum* is polarity of a substance indicating its affinity to the lipids of intercellular cement. The influence of other components was taken under consideration only with regard to their influence on liquid crystalline structures of a barrier. Research conducted by us on systems modelling physicochemical phenomena appearing during penetration of various active substances through *stratum corneum* showed that in many cases the factor that determined permeation of actives could be an influence of cosmetic base components on a thermodynamic activity of substance in occlusive layer.

As a model compounds we used flavonoids, hair dyes components, amino acids, alfa-hydroxyacids and some metal salts. It appeared that typical penetration enhancers like propylene glycol could decrease penetration rate particularly if they were used in relatively low concentrations. The compounds of that type in lower concentrations decrease thermodynamic activity of actives in an occlusive layer and decrease a partition coefficient of a component between this layer and lipids of *stratum corneum*. In higher concentrations an influence on fluidity of liquid crystalline structures of intercellular cement becomes dominant and an increase of a permeation rate can be observed. Similar phenomena could be observed in a case of surface active agents. In this case a factor that hampers permeation is formation of stable micellar systems decreasing thermodynamic activity of a compound. In a case of some metals such as nickel and copper introduction of sequestering agents clearly hampers their permeation into *stratum corneum*.

The same time formation of lipophilic ion pairs in an occlusive layer increases a partition coefficient

and speed up permeation of more hydrophilic ionisable substances such as alfa-hydroxyacids and aminoacids as well as more hydrophilic metal ions like zinc.

The results obtained by us show that the problem of bioavailability of cosmetic actives is more complex than it has been thought so far. Lack of unequivocal rules concerning an influence of particular components can cause necessity of experimental optimisation of bioavailability of active substances for each cosmetic formulation in the future.

Percutaneous absorption by *in vitro* techniques

Ś. Majewski

Univ. of Warsaw - Poland

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Best Innovator: European Award for High Technology Firms

Alessandro Cannavacchiolo

Senior Manager A.T. Kearney - Milan - ITALY

Best Innovator Award has identified a set of European companies, whose success is primarily based on Innovation.

Starting from about 1,000 companies, identified from all manufacturing industries, A.T. Kearney developed a methodology to point out the 'strategic levers' that conducted these companies from managing innovation to business success.

Five dimensions have been explored to identify different levers of Innovation:

- Innovation Strategy
- Innovation Organization and Culture
- Lifecycle management
- Customers and Suppliers involvement
- Enabling factors

Then some common best practices for all business leaders have been identified.

A.T. Kearney presentation will focus on:

- the methodology used to identify these 'champions',
- the best practices identified for Innovation Management,
- the paths to follow to become an 'Innovation leader'.

Technological strategies to improve photostability of Parsol MCX

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Due to the reduction of the ozone layer, there is an increasing need of effective UV protection systems with simultaneously minimised side-effects. Trans-2-Ethylhexyl-p-methoxycinnamate (Parsol MCX) represents the most widely used sunscreen compound. Several studies have demonstrated that Parsol MCX is unstable following irradiation both in solution and in emulsion formulations. Moreover, various reports of photocontact sensitization induced by Parsol MCX have appeared in the literature. Consequently, in order to ensure adequate efficacy and safety for this sunscreen agent, there is a need for new carrier systems to enhance Parsol MCX photostability. In the present study, nanoparticles based on poly-D,L-lactide-co-glycolide (PLGA) as carrier for Parsol MCX are investigated. The influence of the nanoparticle matrix on the photochemical stability of the sunscreen agent is presented. In addition, the photostability of the filter in different formulation types (emulgel, gel and emulsion) with various ingredients, is also reported. The results obtained demonstrated that PLGA nanoparticles are effective in reducing the light-induced degradation of the sunscreen agent. Moreover, the choice of formulation type and the excipients used play an important role in order to obtain a stable cosmetic product containing Parsol MCX.

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Understanding consumer's new expectation for health and well being

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The words health and well-being occur frequently in common parlance, whether singly, together or in the reverse order, thus betraying a certain confusion as to their meanings and an overlapping of the concepts intended. Both terms are widely used to advertise and promote products of mass consumption by humans, as well as the SPAs and beauty farms popular with the growing numbers of people desirous of caring for their bodies, improving their looks and changing their lifestyles. How should we regard this seemingly consumeristic perception in a world in which the best intentions of governments and international organisations have so far failed to narrow the health gap between persons, communities and nations – especially the developing countries?

The World Health Organization (WHO) in its 1948 statute defined health as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”. The determinants of health for individuals and for populations are numerous and interconnected; they comprise the entire range of social, economic, health and environmental factors, as well as economic, ideological and military conflicts of interest. However the state of health and well-being of individuals or populations can be described and/or measured at any given moment using the relevant indicators.

None of the international or national documents consulted makes any reference to the possible role of cosmetics as one of the determinants or indicators of health or well-being. Another surprising finding was that personal hygiene and care are not considered part of a correct behaviour pattern or lifestyle, although other indicators recognise their important role in the primary prevention of certain diseases. This latter claim was upheld in a convention hosted in 1998 at the National Institute of Health, “Cosmetics, health and the quality of life”, motivated largely by the reaffirmation, at international level, of health as a fundamental good for the individual and for society at large. It thus seemed appropriate to include the ultimate purposes of cosmetics among the needs, behaviour and lifestyles of a society in which hygiene, personal care and disease prevention are considered part of the foundations for civilised living.

The same rationale underlies the present meeting, which restates the principal that cosmetic products are not luxury goods – as certain members of the scientific community and general government continue to maintain – but an important determinant of health and a means to well-being. This international congress will confirm how well-established is the use of cosmetics in the daily lives and customs of citizens of all age brackets.

Moreover, the quality, efficacy and safety of cosmetics are essential to consumers' health. The principles governing these are listed in the regulations currently in force, which are based on EU Directives and on the guidelines laid down by the Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP). The safety of each cosmetic product is attested by a safety assessor in a special dossier. For this purpose the producer takes into account the

general toxicological profile of the ingredients, the chemical structure and the level of exposure, based on data supplied by the producers of the raw materials.

Other matters connected with the use of cosmetics include substances such as hair dyes, natural products, aromas and perfumes, substances that affect the endocrine system or which may be classified as carcinogenic, mutagenic or toxic for reproduction, as well as waivers to the use of banned substances, the inventory of ingredients, human volunteers for skin tolerance and irritancy tests and for efficacy trials.

In conclusion it is hoped that this paper may provide a useful reference for understanding health and well-being in the true meaning of the terms and, within the resulting holistic framework, substantiate the claim of the science of cosmetics to claim its proper role.

The role of Phytohormones, phytosterols and iso-flavones in the care and improvement of the skin

Anthony C. Dweck

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The search for new actives from the world of botanicals has reached almost saturation point with a wealth of antioxidants and free radical scavengers. The search is now for a different perspective, for those materials that repair and reverse the signs of aging. The concept of protection will always remain, however, the need for wrinkle reduction and elimination of fine lines and visible demonstration of effect is essential.

The role of iso-flavones (the steroidal mimetics), phytosterols and phytohormones is an area that is attracting greater interest. This paper reviews the history of phytohormones from the discovery of diosgenin in the wild yam (*Dioscorea villosa*) and fenugreek (*Trigonella foenum-graecum*) through to modern day materials derived from the date palm (*Phoenix dactylifera*). We will examine the traditional Thai plant White Kwao Krua (*Pueraria mirifica*) for its use in breast development creams. The leguminosae or bean family has many sources of fascinating [UTF-8?]phytosterols which we propose to review – this family includes soy (one of the largest sources of phytosterols) and we will review the extensive data and derivatives that have recently been developed from this source.

How to combine natural ingredients from thermal springs with good science

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In our opinion it doesn't exist any difficulty in finding natural components of thermal origin and to treat them in a convenient way so as the correct technology praxis requests. From this point of view thermal means (mineral waters, muds, vegetable extracts, sea weeds etc.) can be treated accordingly by the standard of normal ingredients which are currently used for the preparation of dermo-cosmetic lines. Even the difficulties coming from the presence of high concentration of salt or of compounds not easily emulsiable are more theoretical than real.

Problems set when is it necessary to evaluate the interference between thermal or synthetic ingredients (stabilizers, emulsifiers, preservatives, colouring, perfumes, etc.) especially in comparison with the expected plusvalence "natural" share should carry to the finished product.

We have to remember, at this purpose, what thermal means for the Italian directives at thermal product should provide pharmacological properties in the treatment of precise pathologic diseases.

We wouldn't ask for the improbability question if these properties keep themselves in the finished cosmetic product. In these sessions we limited ourselves to refer of a Torba vegetal mud extract from the lake dwellings of Massaciuccoli, dear to M^o G. Puccini, starting point for a series of products characterized by a marked mechanism of action on different cutaneous conditions on the border line with the pathology or frankly pathological.

On these muds we tried to reconcile the nature with the exigency of a cosmetological chemistry.

Botanicals: no longer a niche market

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Indena SpA - Milan - Italy

In recent years, in USA, natural products have grown from a niche segment to one of the fastest-growing categories in personal care, according to marketing research companies. Natural personal care outperformed other natural product segments, such as functional foods, and supplements. In the opinion of some representative USA producers of botanical extracts, "growth in nutraceutical and alternative therapies has greatly increased consumer awareness about the benefits of naturals, and this can only help increase usage in cosmetics." Moreover, "recent scientific studies have validated the beneficial effects of botanicals for more than just pharmaceutical and nutraceutical products. As a result, we have witnessed greater interest and increased growth of botanicals for a variety of applications in the personal care and cosmetic categories". In Europe, the situation is quite different from a country to another. For instance, in France botanical ingredients have been always widely used, whereas only today German cosmetic producers are opening to botanicals. But even in Europe the consideration for the importance of botanicals in cosmetics has progressively changed. In the past the botanicals were considered a kind of additives, mainly to provide natural fragrances, or contribute to colour, or just as a marketing tool mainly based on the plant traditional use. Today, it is not casual the Inventory of Cosmetic Ingredients clearly distinguish between botanicals and additives. >From a regulatory point of view, an important change happened in 1993. Before, a cosmetic product was intended only for skin, skin annexes and oral cavity cleaning, perfuming, changing appearance, correcting odour. This time, the concept of protecting them or keeping them in good condition has been introduced. Or, better, officially accepted, because this route has been already runned trough by the more innovating companies. In other words, a cosmetic can contain physiologically active principles, being in the field of the so-called "functional cosmetics". And because drugs are not permitted in cosmetics, an important way to achieve this goal has been the utilization of the huge bulk of possibilities given by the plant kingdom.

What natural and / or thermal cosmetic means?

P. Morganti

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According to the latest worldwide market data, meanwhile the global market of the so-called natural cosmetics increases in an unexpected way, up today the real chemical and/or legal definition of this category of products does not exist.

All the cosmetics are, in fact, regulated by the same EU Directive 76/768 CEE.

Hence, which are the expectations on natural and thermal cosmetics?

Consumers are convinced that these two categories of products are deeply different from normal cosmetics because they are more active and effective in their functions, more compatible with the environment, purer, non allergenic and exclusively formulated with raw materials of botanical and thermal origin.

But this is not the reality.

There are limited and scientifically documented studies to demonstrate the real efficacy and the general toxicity or side effects associated with ingredients of botanical and thermal origin.

Moreover it is not well defined the meaning of a botanical/thermal cosmetic and the optimal percentage of botanical/thermal raw materials for defining it as "natural".

Therefore, first of all, it is necessary to characterise the natural cosmetic for the minimum /maximum percentage of compounds of thermal or botanical origin to be used as well as it is fundamental to define the marker to be recovered at level of the finished product.

Some opinions and new ideas on this subject will be reported and discussed.

Cardiovascular prevention and psychophysical wellbeing

C. Di Veroli

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The correct advertising communication on cosmetic field: the Italian law approach

M.Caponeri

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Specific laws and regulations don't exist, in matter of advertising communication, Italy has been one of the first industrialized countries to provide with an auto discipline code of regulation (from may the 12th 1968) that would involve all the protagonists of the delicate informative process such as productive factory/ distribute, professionalists of the advertising communication – mass media . Those all were to forced to adapt themselves to the rules for seen by the code regulation (that represents, the collegial expression of all the protagonists) and to accept all the discussions of the control committee in the dissuasive fase and of the jury in the coercive one.

We are so arrived at the constitution of the Istituto di Autodisciplina Pubblicitaria (IAP) that has provided with a deontologic code expression of a bound affirmation of the professional ethics to this jury all have to refer and it's judgment is required in presence of elsewhere contestation.

The IAP has been one of the founder of the European association called AEEP/EASA (Alleanza Europea per l'Etica in Pubblicità/ European Advertising Standard Alliance) born in 1992 and composed from all the EU representative together with Switzerland, Center/east Europe, Russia, Turkey, and most of all USA, Canada, New Zeland and South Africa.

All the adopted methodologies from the IAP control - committee together with some comminated sanctions will be reported and discussed.

Clear, truthful and fair claims: the role of Italian Competition Authority

A. Mancini

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Lutein and Skin Health

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Topically applied products exhibiting Sun Protection Factor (SPF) values have been the primary vehicle used by skincare formulators for more than 20 years to reduce the potential of premature aging of the skin as well as to protect the skin from sunlight exposure- induced skin damage. However, a recent scientific study demonstrated that although high SPF, broadspectrum sun care products provide significant protection against sunburn, they only provided about 50% protection against the induction of reactive oxygen species (ROS) and associated free radical damage to the skin caused by UVA wavelengths. Additionally, since most skincare products containing sunscreen agents also contain antioxidants, the available data can be interpreted to indicate that topically applied antioxidants may not be available at the site where ROS and free radicals are generated. This may not be surprising since it is well documented that the UVA wavelengths of sunlight have the potential to penetrate into the dermis of the skin. Furthermore, data demonstrating the ability of most topically applied antioxidants to penetrate to the deeper layers of the skin are scarce. Therefore, a new approach is needed capable of providing antioxidant activity against ROS and free radicals in the basal levels of the epidermis as well as in the dermis. Lutein, a carotenoid abundantly found in green leafy vegetables, may be capable of providing such protection when taken orally.

Skin sampling studies on the oral ingestion of lutein demonstrate that this molecule has the ability to accumulate in the skin of human subjects. Additionally, since orally ingested lutein is delivered to the skin from the blood vessels instead of topically, it may be present in the very layers of the skin where the UVA wavelengths induce damage. Furthermore, studies conducted in animals have demonstrated that the oral ingestion of lutein provides protective activity against the tissue damage caused by solar UV light and the thickening of the skin induced by these wavelengths. These studies have shown that lutein also has activity in modulating the suppression of the immune functionality of the skin and reducing the free radical induced damage caused by the wavelengths of solar ultra-violet light. These activities are further supplemented by the fact that lutein has the potential to absorb the most energetic wavelengths of visible light which can also penetrate the skin and induce the generation of ROS and free radicals. Therefore orally ingested lutein may provide a new approach helping to reduce premature aging of the skin.

Thermal tools: new cosmetics or old drugs

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Thermal treatments represents a traditional medicine which efficacy is always confirmed and, at the same time, always discussed. They are based on the utilization of natural means, being used as a drug: waters, mud-baths, inhalation etc. Thermal medicine is slowly passing by the times of empiric wizards' remedies, to reach the dignity of an evidence-based therapeutic option in treating many pathologies. Many studies have confirmed the biological effects of the various thermal waters, stating their different composition in mineral elements, about the activation and modulation of skin immune responses and about their influence on the neuro-endocrine system.

Thermal medicine is also demonstrated to be effective in treating free radical damage in skin ageing. Many works reported that some mineral waters, rich in oligoelements such as selenium and zinc, are particularly effective in reinforcing the antioxidative systems of the skin.

However, most of the works about mineral waters and thermal medicine are about the influence of these means in modulating the immune system, explaining in which way, and how much, certain chronic skin diseases, such as psoriasis, atopic dermatitis, seborrheic dermatitis, can be alleviated by the clinical effects of balneology and spa-treatments.

Last but not least, thermal treatments can be considered as a useful adjuvant to many "modern" therapies, such as phototherapy or specific drugs.

Medical devices, body appearance and wellbeing. The EU rules

Luciana Gramiccioni

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Medical devices are regulated at european level from a directives defined of the “new approach” or “global approach”.

This main lines, that have been recepit from the EU states, define the “essential qualifications” that meens the minimum qualification that medical device have to satisfy before the manufacturer lets it in the market.

The application of these regulations to a specific product are based on the definition that the same regulations give to the medical device: “...instrument, apparatus, installation, substance...destinated..to be used by the human for diagnosis, prevation, controll, therapy or attenuation of an illness...of a wound or of an handicap...”

From the above defination appears rather clear that the range of application appears being very wide and interesting all a series of products that are different between them for presentations and configurations.

This of couses gave problems in the classification of the products and to deal with the problematic of the so-called borderline products, that is to say of those products wich is not easy to individualize the applaid regulation : the product is a medical device, a medical speciality, a biocid or a cosmetic?

In these cases besides considering the use destination of the product it's important to individualize the principal action that the same product has in regard to the human body.

Some examples of borderline that can been considerd cosmentic products are rappresented by products for the body cleanness, like soaps with antibacteric compunts or shampoo against dandruff.

They can be considered cosmetic if ther primary funcionality is in agreement with the definition of cosmetic (product that dosen't have therapeutic effects) and don't act against the infections supported by micro-organisms.

Also for example a sun-screen cream containing an insect repellent compound having as principal effect a sun protective activity maybe considered a cosmetic and not, for example, a biocid.

Safe and innovative temporary dermal fillers

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It is known that the currently used dermal fillers based on hyaluronic acid are promptly degraded in vivo by hyaluronidases and other enzymes. As a consequence, the treatment has to be repeated frequently.

In order to avoid the drawbacks associated with the use of hyaluronic acid-based fillers, we have carried out an experimental investigation on the potential use of chitosan hyaluronate, a polyelectrolyte complex. The rationale of this approach is that chitosan possesses reparative capacities for human tissues and is slowly degraded by endogenous enzymes, mainly lysozyme and lipase; similar considerations can be made for chitin.

The resorption of chitosan hyaluronate can be further delayed by chemical and enzymatic cross-linking. Selected biocompatible cross-linkers were used such as dicyclohexylcarbodiimide, ascorbyl palmitate, and epichlorohydrin. The swelling degree of the resulting materials has been measured. Two chitin-based preparations have also been tested, namely dibutyl chitin and plain chitin. Injectable preparations have been formulated.

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Mini-aggressive facial remodeling and rejuvenation: combined techniques

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The facial remodelling is one of the treatment today widely utilized for the management of intrinsic and extrinsic skin ageing or for many inestetisms of the face. The criterion that inspire this protocol of treatment is mainly represented by the fact that when are present more slight blemishes the total improvement of face aspect make less evident the persistence or the partial correction of a single defect. Different are the technical possibilities, it depends on to the defects to treat.

Among the therapeutical possibilities more utilized today we find:

- Laser
- IPL
- Lipofilling
- Fillers
- Botulin Toxin
- Soft Lift
- Peeling

The right choice of the technique or a combination of two or more techniques in relationship with degree of the defects, with of course the operator experience, are the requirement indispensable for a good result.

All these technique are easy practicable in the outpatient, and if necessary, in local anesthesia.

Chitosan films for culture and transplantation of Melanocytes and Keratinocytes to Vitiligo cases

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Melanocyte and Keratinocyte culture and transplantation to stable vitiligo cases is becoming popular in India and abroad. However, transfer of the cultured cells to wound beds is a difficult procedure. Many biocompatible polymer films are being tested for growth of cells and ease of transfer from film to wound bed.

We have evaluated films made from chitosans, commercially available as well as those prepared in our lab, for the optimal culture of melanocytes and keratinocytes. Chitosan vary with respect to viscosity and degree of acetylation and show variable behavior towards growth of mammalian cells. Using keratinocytes and melanocytes cultures as test material, we have now isolated and purified Chitosan that permits optimum growth of these cells. Dopa staining reveals that melanocytes do makes melanin and transfer them to Keratinocytes. Histology reveled that the ratio of Melanocytes to Keratinocytes varied from 1:14 – 1:32 in these cultures.

In three cases of stable vitiligo, biopsies from normal skin were taken and the epidermal cell suspensions were seeded on these films. They were grown for 14 – 16 days when they become near confluent. The films were then washed repeatedly with PBS and grafted on to dermabraded vitiligo patches. Transfer of the cells from the film to wound bed was complete on day 7 post grafting. Repigmentation was seen within 30 days. We conclude from these results that specific graded of chitosan films can be made and used for cell culture therapeutics.

Cell integument from single-celled organism to mammals

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Integument is the “ideal line” which allows to distinguish the edge of an organism and the world outside its vital border. Within the tegument and protected by its structure all the physico-chemical phenomena are made possible. Integument is so a defence barrier, which however allows to communicate with the exterior and to receive and transmit vital information. In other world this defense barrier has several controlled “windows on the outside world”.

The tegument of the single cell organism has mainly a defense function, since the vital informations needed by the cell are very few; cell needs only to know “what happens” outside its borders in order to better adapt itself to the enviroment.

During the evolution this dual nature of the tegument is slowly but continuosly modified and a balance is more and more needed between the defending opportunity and the procedures for comunication. This last more physiological function needs of course a higher sophisticated organization, perhaps modifying its shape permanently or not. At this evolution phase there is the appearance of an ectodermic membrane .

All these schematically presented passages will be illustrated passing from Protozoa, Amoeba, Sponge, Polyp and Jellyfish, Artopoides, Mollusc, Echidorm, arriving to the presence of pluristratified epithelial epidermis of ectodermic origin connected with connective tissue of mesodermic origin, typical of mammalians.

The skin barrier: its architecture and function

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The concept of the skin as a barrier between the internal of the human body and the environment has been always present in medicine, but the definition of "skin barrier" had greatly varied across times, along with the increasing knowledge on constituents, architecture and functions of the skin, ranging from the ancient idea of an "impermeable cover", passive defense for internal organs, to the current, fascinating term of "smart system", used in 2002 by Gopinathan to point out the ability to interact with, and actively respond to, external and internal factors to maintain homeostasis.

In a modern view, skin is, in fact, a metabolically very active organ, providing passive and active defense against nocive factors (physical, chemical, biological), selectively regulating absorption and elimination of exogenous and endogenous molecules, processing environmental "signals" of different nature and feeding related "data" to the immune, endocrine and nervous systems, to which it is strictly connected.

All these features are a direct function of the constituents and of the peculiar structure of the so-called "skin barrier". Lipids are, also for historical reasons, its most studied components, and, in general, attention of researchers was always focused on the stratum corneum, but available data show that anatomical and functional integrity of the whole dermal-epidermal unit –including different cell types, extracellular matrix proteins, basement membrane, intercellular connections– is necessary for a correct skin barrier activity.

More recent studies, pointing out that other factors –like cutaneous pH, antimicrobial peptides of cutaneous surface, skin associated lymphoid tissue, "universal" mediators and effectors as nitric oxide, etc.– play a decisive role in the physiology and pathophysiology of the skin barrier, go even beyond this interpretation, suggesting that "skin barrier" should be considered a functional, not merely anatomical, concept. Thus, skin barrier is not made by cutaneous lipids alone, nor by stratum corneum alone, nor by the structured juxtaposition of different cutaneous cells, but it is the result of all complex interactions between cutaneous elements (cells and their products), endogenous (immune, nervous, endocrine) factors and environmental agents.

Together with a "panoramic" review of the above aspects, we present our experimental data about anatomical and functional alterations of non-lipid skin components in diseases characterized by skin barrier alterations: namely, we studied the modifications of cell-cell and cell-extracellular matrix interactions in psoriasis and the role of nitric oxide in the pathophysiology of psoriasis, atopic dermatitis and allergic contact dermatitis. In both studies, significant differences of the considered aspects were shown between skin of healthy subjects, uninvolved skin of patients and lesional skin. This remarks, in agreement with the general trend of the most advanced researches, the multifactorial nature of the skin barrier function and the need for further studies on its less investigated elements and for the definition of new, integrated models to be used for design and evaluation of cosmetics and cosmeceuticals.

Lipid Organization in The Stratum Corneum: metabolic and functional aspects

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Introduction. One of the major functions of the skin in land animals is to provide a barrier to water loss in order to prevent desiccation, and the specific site of this barrier is represented by the Stratum Corneum (SC). The cellular components, the corneocytes, are tightly opposed to each other, and the barrier function depends upon a unique mixture of lipids in the intercellular spaces of the SC.

Lipid organization. Lipids accumulate as epidermal cells move from the basement membrane toward the skin surface, being packaged in specialized organelles (lamellar granule, LG). At the end of differentiation, the LG discharges lipids and hydrolytic enzymes into the intercellular space. At the time of exocytosis this lipid mixture consists mainly of phospholipids (PL), glycolipids and cholesterol. Enzymatic processing of the lipids in the vicinity of the stratum granulosum-SC interface gives rise to a mixture of mainly ceramides (cer), fatty acids (FA) and cholesterol (Ch). The free FA (FFA) are straight chain saturates species. The monounsaturated FA are transferred from PL to Ch, and the essential fatty acid linoleic (LA, 18:2 n-6) is recycled within the viable epidermis. The unsaturated cholesterol ester containing oleic acid derived from PL separates from membrane lipids into the liquid phase, at the end of keratinization, thus isolating the potential permeability enhancer oleic acid. In lamellar granules there is also an unusual glycolipid (acyl glucosyl ceramide, AGC)), containing w-hydroxy acids and a LA-ester linked to the w-hydroxyl group and glucose b-glycosidically attached to the primary hydroxyl group of the base. AGC is involved in the formation of the lamellar granules.

Stratum corneum lipids.

The major lipid classes in the SC are ceramides, Ch and FA, making up approximately 50, 25 and 10 percent of the SC lipid mass. Small amounts of cholesterol sulfate and cholesterol esters are also present. There are several types of ceramide of increasing polarity, in human skin, including the previously mentioned AGC. They generally contain 24 to 28 C FA bound to 16 – 20 C bases, but they may contain also phytosphingosine as the base, and 24 to 28 C hydroxy FA. The FFA in the SC are straight-chain saturated species, in the range of 16 to 30 C, the most abundant species being however C24:0, C26:0 and 28:0. They may be required for the formation of a lamellar phase being the main ionizable lipid class in the SC. Ch is the most abundant (25 % of the lipid mass) individual lipid being present at a saturating level. Ceramides and FFA in SC are rod or cylindrical in shape and this physical attribute makes them suitable for the formation of highly ordered gel phase membrane domains.

Functional considerations. Compromise of the SC leads to decreased elasticity, cracking and scaling of the skin in addition to increased transepidermal water loss (TEWL). These symptoms are present in workers exposed to lipid-stripping chemicals (strong soaps and detergents), in susceptible persons in low humidity conditions (winters) and in patients with dermatologic conditions (atopic dermatitis, eczema). Treatments of these conditions can be based on the application of “non physiologic”

lipids, such as petroleatum and analogues, with subjective and objective (reduced TEWL) improvements. "Physiologic" lipids alone or in mixtures, e.g. cholesterol, ceramide and FA (palmitate + linoleate) increase the rate of skin repair and reduce TEWL. Only a cholesterol enhanced mixture, however, is able to increase barrier repair in aged skin. New approaches are in progress in the preparation of lipid preparations and in their formulation, for the promotion of healing after SC injury.

Lipid peroxidation and ceramide depletion in skin diseases

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The skin is constantly exposed to oxidative stress induced by reactive oxygen species (ROS), that are generated both from endogenous sources, such as enzyme activity or activated neutrophils, and external pro-oxidant stimuli, such as ultraviolet radiation (UV). ROS-mediated oxidative damage involves a vast number of biological molecules since it causes DNA modification, lipid peroxidation and secretion of inflammatory cytokines. To deal with the harmful effect of oxidative stress, mammalian skin is equipped with antioxidant defence mechanisms. They prevent oxidative injury of structural lipids and proteins contributing to barrier integrity, which is essential for healthy skin condition. Among skin lipids, ceramides, which are the main constituents of lamellar sheets present in the intercellular spaces of the stratum corneum, play an essential role in structuring and maintaining water permeability function of the skin. The link between skin disorders and change in barrier lipid composition, especially in ceramides, is suggested by the evidence that most skin diseases showed a diminished barrier function associated with a decrease in total ceramide content with some differences in the ceramide pattern. Moreover lipid peroxides and their break-down products, such as malonaldehyde and 4-hydroxy-2-nonenal, can directly or indirectly affect many functions integral to cellular and organ homeostasis. As result, the increased membrane lipid peroxidation may evoke immune and inflammatory response, activate gene expression and cell proliferation, or initiate apoptosis. Thus, a close relationship between ROS production, antioxidant defence impairment, peroxidative membrane damage and inflammatory or degenerative pathological processes could be postulated. Several innovative therapeutic approaches, including topical and/or systemic antioxidant supplementation, and utilization of formulations containing various lipid mixtures that can improve skin barrier functions, have been recently suggested. The major recent findings regard the relationship between oxidative stress and dermatological diseases, such as atopic dermatitis, psoriasis, or acne, focusing on the possible implications of antioxidant imbalance, lipid peroxidation and ceramide depletion in both pathogenesis and therapeutic strategies.

Biology of hair pigmentation: what's new

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Various selective evolutionary pressures within the context of our specific ethnic backgrounds have contributed to the bewildering array of natural shades of human hair color; yellows, reds, browns to black and that harbinger of lost youth, gray/white hair. Although ancient, our pre-occupation with hair, and particularly its color, is further heightened today as our increasing longevity inevitably fuels the desire to delay or loss of youthfulness. Growth and pigmentation of hair fibers is affected by numerous intrinsic factors including; hair-cycle dependent changes, body distribution, racial and gender differences, variable hormone-responsiveness, genetic defects and age-associated change. We are only now beginning to unravel differences between epidermal and hair follicle melanocytes. My presentation will discuss major advances in human hair pigmentation research over the last decade. We first published a methodology to establish in long-term culture melanocytes in 1995 from human scalp hair follicles and this breakthrough has enabled us to generate model systems for assessing differences between epidermal and hair follicle-derived melanocytes. Recently, we have examined a role for melanotropins derived from pro-opiomelanocortin (POMC) eg. α -MSH and ACTH and have further identified b-endorphin to be a potentially new POMC-derived melanotropin. All these POMC-derived peptides significantly stimulate melanocyte numbers, melanogenesis and dendricity in culture, and we have extended these studies to include an assessment of CRH, the most proximal element in the HPA axis. There has been much recent excitement about hair follicle epithelial stem cells and recently the anatomic location of the melanocyte stem cells (melanoblasts) niche has been determined. These cells facilitate the cyclical generation of melanocyte precursors for the hair bulb and, if needed, for the epidermis. The fate of melanoblasts during hair cycling involves complex signaling interactions including stem cell factor and its receptor c-kit. Researchers can de-pigment regrowing hair by blocking c-kit. Pigmentary change is clinically seen with altered hormonal status and we have recently suggested new roles for sex steroids, especially estrogens, in hair melanocyte biology. Furthermore, melanogenesis, an oxidatively stressful pathway, may involve nitric oxide and nitric oxide synthases, a system that may differentially regulate epidermal and hair follicle melanocyte biology. Noggin and BMP is another signaling pair that may regulate pigment type and amount. MCR-1 (receptor for α -MSH) is the only known gene to predict a human phenotype - particular MCR-1 variations result in red hair and poor tanning ability, a trait of particular interest to evolutionary biologists. Finally, new research is examining how hair goes gray/white and it was encouraging to note that some melanocytes can be detected even after advanced hair graying. We have shown that these residual cells can be induced to proliferate and pigment in culture. In summary, research into human hair pigmentation has finally awoken from its long sleep and promises to lead to many fascinating and hopefully therapeutically useful developments.

Cosmetovigilance pilot study

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Cosmetics are largely diffuse substances topically applied to wash, to perfume, to improve the look. Cosmetic industries use about 9.000 chemicals traded in 30.000 different commercial denomination. Although a large use of cosmetics, no high incidence of adverse reaction is reported. Therefore cosmetic adverse reactions might be underestimate because of not severity of event, diagnostic inability without any medical consultation. Skin disease are the most common cosmetic adverse reactions. They are generally not serious but widely various. The cosmetic intolerance is increased by the presence of toxic substances involuntary introduced in the formulation, originate by ingredients reaction, created by photo-induced reaction. Abuse/incorrect use or association of several products, pre-existent injuries and at last individual factors also play an important role in the appearance of cosmetic adverse reactions. Aims To evaluate the population cosmetic use behaviour through a questionnaire supplied by pharmacists To asses the prevalence and the features of cosmetic adverse reactions. Material and Methods Pharmacies involved agreed to submit a specific questionnaire to all customers. Two weeks, 7 hours/day, of data collection were made between 10am to 01pm and 04pm to 08pm. Customers were asked about the cosmetic use behaviour and the possible onset of any adverse reaction ascribed to their use. The typology of reaction and the substance probably involved were also investigated. The filled questionnaires were recorded in a database and data were analyzed. Results Actually about 4000 people were interviewed in 9 different pharmacies and the first 460 answers collected from one pharmacy were analyzed. 88 (19,1%) of costumers refused to fill the questionnaire. Female represent 78,2% of responders with 44.2 ± 15.6 mean age (no differences between gender). 99% of female and 88.9% of male customers declares cosmetic use. About an half of people goes to the pharmacy to take a drug and over one third to buy a cosmetic. 24,2% of cosmetic users experienced at list one adverse reaction and female at most (26.7% F; 13.9% M) Data entry is actually in course to increase the power of the study, necessary to analyse the impact of cosmetic use and the real prevalence of cosmetic adverse reactions. Preliminary results highlight the large use of cosmetics among pharmacies customers. The rate of people reporting adverse reaction, although preliminary, suggests that these products, often considered as completely safe, may pose people at risk of adverse events and need a higher level of attention in their use.

The international scenario of the so-called natural cosmetics and functional food

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There is increased interest in more natural-based products from both the consumers and the scientific community.

This alongside increased interest in: better quality of life, prevention of disease, self medication, role of nutrition, innovative medical devices and cosmetics.

For example, in 2003 the market value of nutrition industry in USA was US\$ 62 billion and the organic sales have now reached US\$ 10.8 billion/year, meanwhile the market value of licensed herbal preparation is approaching US\$ 500 million (FIG1).

About natural cosmeceutical cosmetics the value is of US\$ 39.9 with a 20% of annual growth rate since 1990.

Just as nutraceuticals!

Current top selling herbs include Ginkgo Biloba, St. John's Wart and garlic.

Many of these materials are now being developed as nutraceuticals and cosmeceuticals so US and EU nutrition and cosmetic industry is experiencing new growth from categories such as organic foods, calcium, magnesium and EFAs (replacements) while specialised cosmetic products based on new and old botanical extracts are being reviewed.

Thus plant-derived products account for a large proportion of dietary supplements and cosmetics.

Despite not holding the largest category of over the counter preparation, herbal vitamins, minerals and photoprotective cosmetic supplements demonstrated the strongest growth in this market.

This is consistent with the increased and expanding scope of interest in alternative therapies other than just for pain relief and treatment of coughs and colds.

Omega 3 – fatty acids of botanical and marine sources : which are safer?

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Omega-3 fatty acids may be extracted from either botanical or marine sources. Meanwhile marine fatty acids obtained from cold water fish include both eicosapentaenoic (EPA) and docosahexanoic acid (DHA), the botanical ones are generally available in the form of alpha-linoleic acid (ALA).

However DHA is also contained in the oil of micro alga *crypthecodium cohnii* grown under controlled fermentation processes, and in other different plant seeds such as blackcurrant, canola or soybean.

What the reason to prefer botanical omega-3 oil to the marine one? Because of contamination.

As a matter of fact, some species of fish contain high levels of mercury polychlorinated biphenols; dioxins and other environmental contamination while plants are free. Hence, from this point of view, omega-3 oil of botanical origin is safer than marine one. This interesting debate will be reported and discussed.

Botulinum toxin - Technical of injection: how avoiding mistakes

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The botulinum toxin, since from its advent in aesthetic medicine, has triggered controversies for the more problematic regarding tied to its authorization for such scope. Today we can say to know the toxin rather is well from the chemical point of view, than from the therapeutic point of view. The use of the botulinum toxin is at this point one truth in the treatment of the wrinkles from muscular hyperactivity of the face. To inject the toxin without some undesired effect sure has had one wide experience. The cautions, for that of it regards the use, consist essentially:

- taken care of attention in avoiding some anatomical districts
- taken care of instruction of the patient in the management of the period post-treatment.

The botulinum toxin, has been revealed extremely poured them in its uses in aesthetic medicine. The protocols are multiple that have been gradually proposals. The variable ones of the use of the toxin, are essentially two:

- the various formulas of dilution
- the different techniques of injection.

Authors propose dilutions beyond that they go from 1,2, 2,5, 4 cc and more.

The techniques of injection in the use of the toxin differ in many aspects:

- places of injection
- amount
- depths of injection
- other variable ones

In the relation come compared several dilutions, the variable ones to connected they and that one that the author prefers. We bring back some lines in detail guides on as to avoid errors in the use of the botulinum toxin in the wrinkles of the face.

Hair Transplant. From the punch-graft to the follicular unit, the evolution of a technique

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Hair transplanting is now universally adopted as a surgical technique to solve androgenic alopecia, as perfectly natural results can be obtained with this method, if carried out with care and by expert hands.

Who, like us, started in the 80s, or even earlier, can remember that initially, patients were doubtful that hair could be transplanted to different parts of the scalp, without risks of rejection or infection. Doubt was then expressed, more than anything else with regard to the aesthetic results of the operation: patients, in fact, by now realised that hair transplanting worked, but were worried about an unnatural end result.

The introduction of strip harvesting from the donor site, with multi-bladed knives, or with a single blade, has revolutionised hair transplanting, not only helping to save the donor area for further operations, but above all, grafts of any required size can be obtained with this method, from mini, micro-grafts, to the actual follicular units. The authors, in their video presentation, underline the importance of the evolution of this method over the years, and how the efficiency of a close dermatosurgical team is the most important factor to successfully carry out an operation which, on the surface may seem uncomplicated, but which requires the skills and dedication of the surgeons involved.

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Anti-Stress Active Ingredients: A New Generation of Cosmetics

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Developing cosmetics to fight against aging became the center of interest in cosmetics.

By aging, skin becomes fragile towards stress, in particular UV stress, and exhibits less defense against sun damage.

Today, it has become evident that stress is one of the major characteristics of our modern life, and much data has shown that stress has direct effect on skin health and appearance.

Through the long evolution, living cells have developed different ways to respond to stress. In this field, the family of "Heat Shock Proteins" (Hsp) represents one of the principal mechanisms of cell defense and protection from different kinds of aggression and stress.

Among stresses, UV stress is at the center of the human fight against photoaging and skin cancer.

Hsp are highly conserved and abundant in all Eukaryotes, they represent a very wide family of what are called "chaperon proteins".

In the absence of aggression, cells contain a constitutive rate of Hsp that play an important role in cell development and proliferation. Hsp also survey protein synthesis and assembly.

When the cell undergoes a stress, Hsp play a major role in stabilizing intracellular processes under the stress, acting as "molecular chaperones".

In the search in skin aging field, heat shock proteins represent an innovative and essential approach to modern cosmetics which aims at comprehensive skin care products that protect from and fight the aspects of skin aging.

Therefore, we were interested in these "chaperon molecules" as a new natural approach for cosmetics. And, we investigated the effect of two new Hsp-related active ingredients on increasing the immediate and long-term defense of the skin from stress. We used two different approaches for this investigation:

- inducing the Hsp70 molecule in human cells, in a stress-free manner, using Artemia extract (AE),
- or providing the cells with Hsp70 molecules by the administration of Hsp-rich yeast extract.

RonaCare® Ectoin – The Natural Cell Protection Factor

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The UVA-radiation inherent in sunlight can cause damage to the human skin and plays an important role in premature and accelerated skin aging. However, a new substance – from the group of compatible solutes – has become available as a protection against skin aging.

UVA-radiation initiates the gene-regulatory mechanisms in human keratinocytes that are responsible for the damage caused by such radiation. It has been shown that UVA-irradiated keratinocytes release ceramides which, as second messengers, initiate the UVA-induced activation of transcription factors AP2 and the expression of genes. In this particular case, the regulation of transcription factor AP2 for the UVA-induced gene expression, e.g. of pro-inflammatory genes, is of primary importance in photoaging. UVA-induced mutation of mitochondrial DNA is also of decisive importance in the premature aging of skin brought about by UVA-radiation. The spherical mitochondrial DNA is located near the inner mitochondrial membrane. However, this means that it is subject to UV-stress that can result in mutation of the mitochondrial DNA. This in turn is important in the development of degenerative disease and in the aging of cells and tissues. UVA-radiation could cause mutation of mitochondrial DNA. It has been shown that repetitive UVA-irradiation of human fibroblasts can lead to both time- and dose-dependent formation of mutations in mitochondrial DNA.

With the help of a new "UVA Stress Model", it was shown that Ectoin protects the skin from the effects of UVA-induced cell damage in a number of different ways. Using cell cultures, high performance thin layer chromatography (HPTLC), gel electrophoresis mobility shift assays (GEMSA), reversed transcript-polymerase chain reaction (RT-PCR), ion exchange chromatography (IC) and UV spectroscopy, it was demonstrated that the UVA-induced second messenger release, transcription factor AP-2 activation, intercellular adhesion molecule-1 (ICAM-1) expression and mitochondrial (mt)-DNA mutation could be prevented. The results obtained clearly demonstrate that Ectoin counteracts the effects of UVA-induced and accelerated skin aging at different cell levels.

In conclusion, ectoin protect human skin cells against the structural changes in the cell membrane brought about by UVA-radiation as well as AP-2 activation, ICAM-1 gene expression and the formation of mitochondrial DNA mutation.

Cosmetological Education in Poland

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Cosmetology as a scientific discipline has a long tradition in Poland. Modern and efficiently organised cosmetic industry that existed in Poland before the World War II has been transformed during post-war nationalisation into a network of big factories. Only at the end of the 80-ties small, private cosmetic companies started production. Those companies, after a political system transformation in 1990, built a foundation of current Polish cosmetic industry.

Today all market sectors in Poland connected with cosmetology face a period of dynamic development. Currently in Poland there are over 400 cosmetics producing companies and the number of spa and beauty salons is estimated at 25 – 30 thousands. Because of specific social structure a supply in cosmetic product and services market is still not sufficient. Until recently the main factor hampering development of cosmetic trade was lack of adequate scientific and educational basis. It resulted from the former political system and disrespectful attitude towards cosmetology within some scientific circles. Great quantitative development resulted in relatively low quality of services and products and poor functioning of controlling and concurrent mechanisms.

The first wind of change was an introduction of elements of cosmetology into specialised educational programmes for students of Warsaw University of Technology Faculty of Chemistry and post-diploma studies in cosmetic chemistry at Lodz University of Technology ten years ago. Shortly after that the cosmetological studies was opened. Since then the number of academic institutions that run BA studies in cosmetology increased dramatically and today they are organised by both state and private universities. The other significant factor of broad cosmetological education development was joining the EU by Poland. Change of legal regulations created many new working places as well as a demand for highly qualified specialists of broad general knowledge in cosmetology. There are still many vacancies for them and the job marked for cosmetologists is waiting for new employees.

The position of Polish cosmetology as a scientific discipline is also changing: common activities of state and private universities supported by The Polish Society of Cosmetic Chemists (The Lester Conrad Award in 2001) resulted in official recognition of this scientific discipline by Ministry of National Education in Poland.

Studies in cosmetology in Poland are interdisciplinary and include medical, chemical and general subjects that go beyond traditional education connected to a profession of beautician in the past. Currently the studies regarding cosmetic chemistry are organized by four academic centers in Poland –Universities of Technology in Warsaw, Lodz and Radom and private Academy of Cosmetics and Health Care in Warsaw. At the same time the studies in aesthetic cosmetology are organised by three state medical universities and six private universities. The fact that only at the Warsaw Academy of Cosmetics and Health Care itself study over 500 students proves the popularity of cosmetological specialisation in Poland.

High order synergy – A new route to highly biologically effective cosmetics

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The new science of systems biology seeks to understand the behavior and control of biological systems not one pathway at a time but as a complete and highly interacting network. While this science is in its infancy, it is already clear that there is huge potential to achieve potent and highly specific biological effects by combining active ingredients acting at several different points in the biological network. When properly chosen, these ingredients behave highly synergistically. Thus the correct combination of ingredients that individually are of low activity can act with the efficacy normally associated with a potent drug.

Finding these effective combinations is extremely difficult however due to the incredibly large number of possible combinations. An example will be presented where combinations of 5 cosmetic ingredients exceeds the potency of the prescription drug retinoic acid for skin antiageing. Only 1 in 1016 of possible combinations does this however and unique strategies are required to discover these very rare combinations. In the case described, the strategy relies on a combination of detailed mechanistic understanding of the mode of action of retinoids in the skin together with modern methods of high throughput screening.

Finally, the implications of this new paradigm for achieving potent biological effects will be discussed both in the context of the cosmetic industry and also in the wider medical field.

Efficacy of new cosmetic compounds with a botox-like activity

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Biological efficacy of cosmetics is a challenge the scientific community is facing well through the continuous improvement of knowledge and of technologies. By making use of increasingly sophisticated techniques, we are studying the biological mechanisms which basically give rise to the major cosmetic defects (aging, cellulitis, loss of hairs). Nevertheless, many skin parameters are still unknown, as well as the mechanisms through which the products effectively work and provide beneficial effects. We must not forget the large difference between drugs and cosmetics. Results not only depend on the mechanism of action, but also on the whole formulation program through which the product is developed..

In drugs, active principles are dosed and supported by an excipient. In cosmetics, the whole formulation often plays a fundamental role in the skin activity, according to the conception of "global functionality". A second important difference is related to the level of action. Drugs must act very deep inside, must reach the blood stream and be transported to all the organs of the body. On the contrary, cosmetics must act only on the skin, whose most superficial layers must not be passed. For this reason, precise international legislation sets down the limits of the role and the functionality of cosmetics, excluding any curative claim.

Nevertheless, cosmetology is becoming more and more active and efficient, and many problems are close to be effectively resolved. New active principles, extracted from natural sources through chemical or biological synthesis, effectively prevent and treat many aesthetic anomalies, achieving scientifically assessable results. As evidence of the aforesaid advances and improvements in the field, recent years have seen new cosmetic functions being developed, such as recently developed effects like "lifting", "filler", "firmness", "peeling" and many others, accompanied with an impressive improvement of the techniques for protection against the photoaging and free radicals.

This report describes a number of classes of active principles, such as: hydroxy acids, skin lighteners, sunscreens, aminoacids and their derivatives, polysaccharides, desensitizing molecules, antioxidants, plant extracts with hormone-like action and the more recent multifunctional blends, with a short reference to the technological advances of basic formulations, which improve the biological efficacy of the active molecules.

Natural protection of the Cell's DNA from oxidative stress and photoaging

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All the information allowing the cell to fulfill perfectly its function in living organism are issued from the DNA present in the nucleus and mitochondria.

The DNA is continuously submitted to noxious assaults from endogenous or environmental origin. Among environmental factors, the major origin of DNA damages in human skin is the oxidative stress generated by the sunlight radiations.

To face these assault, life has developed a sophisticated system for DNA repair, necessary for cells to maintain their integrity.

Due to increasing intensity of external aggressions, this endogenous system can be saturated. It then becomes necessary to support and boost it. With the aim of complete cellular protection, i.e prevention and repair of UV induced DNA damages, we have developed an new Active Ingredient based on the extract of the plant *Senna alata* (L.) Roxb whose main active component -a molecule spontaneously synthesized by the plant itself for sun protection- has been identified.

The DNA protection was demonstrated by measuring the reduction of release of cytoplasmic DNA fragments and by "comet assay". A quantification of UVB-induced thymine dimmers was carried out by ICC (ImmunoCytoChemistry) on human keratinocytes. The DNA protection was extended to mitochondria by evaluation of the rate of "common deletion" in UVA-stressed human dermal fibroblast

In order to investigate further the mechanism underlying the DNA protection and repair, the gene expression profile of human keratinocytes was screened by DNA -arrays technique and the observed activation of the gene expression of a gene involved in DNA repair was confirmed by real time RT-PCR (Reverse Transcriptase-Polymerase Chain Reaction).

Innovative sun filters for a safe photoprotection

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Consumers and patients are highly interested in sunscreens with a low potential for adverse effects such as skin irritation or allergies. Here we report the use of an innovative encapsulated UV filter (OMC). In combination with titanium dioxides (inorganic, mineral UV filter) it is highly effective in the UVA/B region. Encapsulation keeps organic UV filters mostly on the outermost skin layers while micronized TiO₂ does not penetrate into the skin.

Microcapsules were shown to effectively retain the encapsulated UV filters in release experiments, which demonstrate the stability of the capsules. Tape strips were taken after topical application and electron microscopy showed intact particles forming a homogeneous layer on the skin surface. Dermal absorption experiments show a tremendous reduction in dermal uptake of microcapsules (Eusolex UV Pearls OMC) compared to non-encapsulated material. Persistent Pigment Darkening is one of the most reliable methods to measure the UV-A protection factor of UV-filters. Using this biological endpoint TiO₂ (Eusolex T-2000, T-S) exhibit a very good UV-A protection factor e.g. at a 10% use level the UVA PF = 9, while a sun protection factor (SPF) of approx. SPF 20 can be reached.

In conclusion, encapsulated sunscreens reduce the contact of UV filters with the body tissue, leading to an increase in margin of safety. Non-penetrating TiO₂ offers real broad-spectrum protection (UVA and UVB). A combination of encapsulated UV filters and titanium dioxide lead to sunscreens that are more than safe especially if combined with cell protection substances such as Ectoin.

Future trends of Nutri- cosmeceuticals

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Intelligent products can help to make life easier. Thus by research and innovation industry may create new technologies and innovative products and services.

Growing health consciousness also constitutes a challenge and obligation for manufactory. In fact, the consumer wants an effective product, without health risks.

Have science and research come up with additional knowledge about old known or unknown new active ingredients?

Certainly yes. And new or reviewed old raw materials treated by new technologies, health and environment friendly, play now an important role in cosmetic toiletries and in functional food as in all the other market-focused business sectors of wellness.

Hence, for example, a specific polymerization of some sugar-like compounds may have a tensor activity, therefore absorbed and spread on the surface of the skin, these skin-friendly compounds form an elastic, cohesive and continuous film supporting the skin's smoothness.

New stable flaxseed ingredients have restored now their unique nutraceutical and cosmetic quality. Flaxseed's omega –3 and lignant phyto-oestrogens are the focus of mounting evidence documenting their benefits for a wide range of health conditions, such as autoimmune diseases and mental health. Proteins derived from pulses are specially used in regard to weight reduction products because of their high content, for example, of lysine which maintains lean body mass, and of arginine which increases muscle mass while reducing body fat.

Finally current evidence supports the hypothesis that the oxy-carotenoid, lutein, effectively increase macular pigment level protecting the eyes from free radicals insult.

These and other new and old reviewed raw materials useful for a better wellbeing will be reported and discussed.

New derivatives for magnifying skin pigmentation

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The application of cosmetic products containing Tyrosine, is based on the concept that L-Tyrosine is the primary substrate for tyrosinase, in order to induce melanogenesis. But it has been proved that pure tyrosine, per topic application, hasn't an acceptable bioavailability. Enhancing of cutaneous absorption could be reached by utilizing derivatives of Tyrosine in the perspective of magnifying tan. Aim of the present work was to obtain new functional derivatives from Tyrosine, with innovative and proved cosmetic efficacy.

In order to increase skin bioavailability CAPROYL TYROSINIC ACID has been obtained via the condensation of tyrosine with caprylic acid, a C10 saturated fatty acid, delivering the equivalent of about 10% pure tyrosine.

In particular two new cosmetic functional derivatives has been obtained

- Lipophilic

INCI Name: Caproyl Tyrosinic Acid and Glyceryl Oleate and Sorbitan Isostearate

- Idrophilic

INCI Name: Potassium Caproyl Tyrosine

They are easy-to-use N-acyl derivatives of tyrosine, clear liquids, completely water or oil soluble, and compatible with traditional cosmetic ingredients, similar to other lipoaminoacids, oligopeptides and water-soluble amino acids.

Furthermore it has been made the evaluation of the skin pigmenting properties of a cosmetic product after exposure to UV-radiation, on volunteers. The product (Potassium Caproyl Tyrosine), formulated at 5% concentration in a emulsion-gel, has been compared with a placebo and a control, untreated, area for three consecutive weeks, using a solar simulator.

Statistically significant differences among the set of values recorded at different times in the three areas have been evidenced:

- o the area treated with the sample of PCT at 5% showed a highly significant decrease in ITA° values (T0 versus T3 $p=0.002$ and T0 versus T14 $p=0.002$)

- o the area treated with the sample of Placebo did not show a significant decrease in ITA° values at any time

- o the control area untreated did not show a significant decrease in ITA° values at any time

In the results, it can be noted that the values recorded in the control area treated with the two products are lower than those recorded in the control area. That means a tendency to a pigmentation increase. The difference of values is nevertheless not significant ($p=0.005$)

Potassium Caproyl tyrosine is significantly effective in increasing the skin tanning in comparison to the start conditions, where a tan magnifying effect is requested, with significative efficacy, modulated in time. A similar level of significance could not be obtained in the comparison with the reference areas, probably because of the high standard deviation.

The cosmetic application as tanning magnifier has been developed in products for suncare during exposure, and for suntan maintenance after exposure and its stability over time has been confirmed in several formulations in the form of cleansers, gels and emulsions.

New trends in skin aging: the activities of innovative compounds

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Many functional principles are shown to be active in determining modifications of the cutaneous physiology and, from biological point of view we can refer these substances as pharmaceutical agents.

The skin aging is one of the most exiting field to verify the true capability of molecules to treat light-induced damages.

Today the possibility in using new technological approaches has permitted to create a new generation of scientifically-advanced skin care and cosmetic products.

These products promise to smooth wrinkles, strengthen skin, inhibit enzymes, trigger growth in elastin and collagen or manipulate skin color .

Most experts agree that alpha hydroxy acids started a new era for cosmeceuticals and after these the research has taken many steps forward.

For example a new generation of acids is creating interest in the personal care industry. One of them is a poly hydroxy acid, which contains gluconolactone and lactobionic acid.

Poly hydroxy acids also contain antioxidant benefits, a property not found in glycolic acid. Lactobionic acid acts as a powerful antioxidant and chelates excess iron in the skin, thereby reducing potential oxidative damage.

Other ingredients of big interest are some compounds that are said to mimic the action of botox.

Acetyl hexapeptide-3 is an anti-wrinkle peptide, which works through a unique mechanism that relaxes facial tension leading to a reduction in superficial facial lines and wrinkles with regular use

Great attention is exiting molecules that are nature - identical plant grow factor , like N-6 furfuriladenina, or new antioxidants. Some new compounds that we consider as skin whitening are being positioned in antiaging products because they give brightening, luminosity and act on age spot.

The Italian hot chili pepper from Calabria to save the Human Health

Giovanni Sindona

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Food safety and quality represent the main issues of national and international bodies appointed to health control and research funding. The production and transformation of foodstuff in developing countries and the introduction in the European markets of uncontrolled goods causes a deep concern. In April 2003, a French agency discovered the presence of substantial amounts of 1-(phenylazo)-2-naphthalenol, an azo dye (Sudan I), in dried and crushed or ground chili pepper imported from some Eastern countries. An European Commission directive was issued soon after [1] stipulating that in the absence of documentary evidence of purity, no hot chili or hot chili products from those countries would be allowed to enter the EU market.

Sudan I is an industrial dye used for coloring hydrocarbon solvents, oils, waxes of known carcinogenic action [2]. Its use in foodstuff is forbidden in any national and international food regulation act. Its potency as a carcinogen for humans was recently demonstrated [3].

We have developed an "absolute method" of analysis for determining without any ambiguity the presence of this contaminant in olive oil, salami, meat, "nduja" and many other typical foodstuff of the deeply appreciated Mediterranean diet [4].

The benefits of the active principles present in Calabria hot chili peppers have been widely documented. With our method we can discriminate between even low-contaminated foods and organic products for the presence of Sudan I. This is an opportunity for adding value to some typical and healthy southern products and to help improving the activity of the local SMEs active in the agrifood total food chain.

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Mass Spectrometry: A powerful Analytical Method in Safety and Quality Control of Commercial Virgin Olive Oils

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Within the many applications of mass spectrometry in the olive oil total chain, those oriented towards the determination of nutraceuticals and micro elements and to traceability of the product deserve particular attention. In this contest we have applied the metabolomic approach to the evaluation of vitamins, anti-oxidants, flavour, etc., in order to achieve a deep characterization of the foodstuff. Oleuropein, a secoiridoid glycoside, is a secondary metabolite present in olive leaves of known pharmacological properties. It is used in alternative medicine for a number of diseases and is available in the US market as tablets with different content of the active principle. The number of studies that report on the biological and pharmacological activity of oleuropein allow us to assume that its presence confers to olive oil, whose nutritional value is widely recognized, a preventive action toward a number of pathologies generated by free-radical action.

We have demonstrated that oleuropein is present in virgin olive oil [1] by means of an analytical procedure based on tandem mass spectrometry which has been further improved. A survey on oils produced in different Italian regions confirm that the amount of oleuropein is cultivar dependent and is in the range of 1 ppm.

A similar approach was devised to develop an analytical method able to discriminate among the different olive cultivars. It considers the metabolic cascade of olive oil lipids and is based on the evaluation and assay of five molecular markers present in the aroma [2]. The results obtained are very promising and the methodology is now applied in the survey of Italian and Tunisian olive oils.

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Developing an Antioxidants and Pro-antioxidants rational approach to an health supplementation

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Oxidative stress may led unbalanced body antioxidant defences, this is an important factor in the etio-pathogenesis of numerous diseases. On the other hand antioxidants overload may also led to unbalanced antioxidants pool, with not well elucidated consequences. The antioxidant defence system is composed by antioxidants and pro-antioxidants. Several components of this system are micronutrients (e.g. vitamins C and E), or dependent upon dietary micronutrients (e.g. CuZn and Mn superoxide dismutase) or produced by specific endogenous pathways. Leaving beings has evolved over the past two billion years through adaptation, to an increasing atmospheric oxygen concentration, by both taking advantage of oxygen activating function and developing a complex control network. The antioxidant defences act, to control levels of these species, as a coordinated system where deficiencies in one component may affect the efficiency of the others. In this network some of the components act as direct antioxidants whereas others act indirectly (proantioxidants) either by modulation of direct agents or by regulation of the biosynthesis of antioxidant proteins. Correct approach to healthy antioxidant supplementation should take into account all aspect related to the global efficiency of the network in order to avoid possible unbalanced effects related to antioxidants overload. In this contest, the needing of the monitoring of the integral antioxidant capacity of biological fluids, may be a useful tool to a rational approach aimed to a balanced antioxidants supplementation.

The Italian coffee as a classic component of the Mediterranean diet

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Coffee became a essential complementary in the all day life of people, so this small perfumed and ritual drink has become a ritual that gives not only a nice stimulated effect, but also matches together with peaceful moments, short rests in relaxing meetings between people and parents.

In fact its big success is principal given by for its tonic activity and anti-depressive psycho-logical and physical effects.

Coffee is a watering solution containing many substances that can be present in variable quantity according to the variety of the plants (arabic, robust), the roasting system and naturally by the way of preparing the drink. One of the principal chemicals besides the aromatic compounds is the trigonelline (which is transformed during the roasting in nicotil acid or PP vitamin),chlorogenic and caffeic acid, potassium, the essential oil of the coffee and most of all caffeine, a trimethyl-xantine on which supporters and detractor give normally have their particular attention.

Caffeine develops the effects on the cardiovascular , respiratory, renal , nervous apparatus through an inhibentic activity on adenosine receptors. With the correct doses Italian coffee determines only positive effects with an increment of the coronary flux, an anti-asthma and diuretic activity but especially it gives an incentive to the brain cortex developing attention in learning.

Concerning negative effects its necessary to drink big quantity , in fact all the studies indicate the lost of this negative effects with small quantity. In particular no risk has been noticed for athero – sclerosis, for iper-tension, for pregnancy and for malignancy tumors (and even showed protective effects for the cancer of the colon)

It has to be notice that the quantity of caffeine taken by a cup of espresso-coffee consumed by an Italian is inferior (40-70mg) in compare to a cup of coffee made at home (80-100mg) and most of all from a standard cup of American coffee (100-150mg).The extraction of caffeine is in fact proportional to the time of contact with water.

Of very important notice it appears the presense in the coffee of two phenolic compound, chlorogenic and caffeic acid that pursuing an anti-oxidant effect that protects against the deterioration of the free radicals that are responsible of aging and of many chronic degenerate diseases .About this, it has been attribute to the chlorocenic acid the antineoplastic activities of the of the coffee.

So, even if it has been found a contra-indication in some patients with neurological diseases, we can assert that this special italian drink, taken in a quantity of 4-5 cups a day gives only positive effects, such to consent in the morning a better passage from the sleeping stage to the awakening stage and during the day a better rendering of work besides giving also a moment of relax between friends.

Re-dox status and Prevention of Diseases: Recent Evidence from Literature

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Oxidative stress-related diseases have a complex etiology with multiple risk factors that involve the interplay between genetic and environmental influences. There is compelling evidence that dietary plant foods appear to be protective against these pathologies. Among a number of mechanistic hypotheses, diet-derived antioxidants have been proposed to explain these findings. The variegate composition of plant foods could represent a natural step of regulatory hierarchies that modulate the interaction between antioxidants to achieve the physiological red-ox balance in body fluids.

Total Antioxidant Capacity (TAC) considers the cumulative action of all the antioxidants present in complex matrixes thus providing an integrated parameter rather than the simple sum of measurable antioxidants (Serafini et al. 2004). The capacity of known and unknown antioxidants and their synergistic interaction is therefore assessed, thus giving an insight into the delicate *in vivo* redox balance. New evidences are mounting on the importance of understanding the mechanisms at the basis of the homeostatic control of plasma TAC and its modification during oxidative stress development (Serafini et al. 2003a; Serafini et al. 2003b). Moreover, the epidemiological application of TAC has been proposed as a new tool for investigating the relationship between dietary antioxidants and disease in population studies (Serafini et al. 2002).

Under a methodological point of view, the presence of a large number of assays for measuring TAC with their own characteristics and noticeable differences make extremely complex choosing the appropriate analytical method and deciphering the results. Special attention will be paid to describe the pros and cons of selected assays for measuring plasma TAC.

The feasibility of "TAC concept" to monitor red-ox status and to provides valuable information for understanding the dietary counteracting forces involved in the multi-factorial process toward oxidative stress-related pathologies and will be discussed.

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Blackcurrant seed oil: a unique source of essential fatty acids nutraceutical and cosmeceutical use

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Polyunsaturated fatty acids (PUFAs) play an indispensable role in human physiology. Theoretically only linoleic (18:2n-6, LA) and α -linolenic (18:3n-3, ALA) acids are essential fatty acids required in human diet. Other polyunsaturated fatty acids (PUFAs) can be synthesized from the two fatty acids in human body. However, it is often necessary to supplement the diet with PUFAs derived from LA and ALA to overcome deficiencies in the metabolism cascade. Conversion of LA to GLA and ALA to SDA are the rate-limiting steps in the cascade and are often deficient in people under stress, ageing and some other physiological and pathological conditions. Moreover, human epidermis is not able to synthesize GLA and SDA because of the absence of D6-desaturase. Incorporating GLA and SDA into diet and skin preparations helps maintain a normal pool of essential fatty acid metabolism. GLA and SDA also have their own biological functions. In vivo, GLA is converted to anti-inflammatory dihomo γ -linolenic acid (20:3n-6, DGLA). SDA reduces the production of inflammatory eicosanoids by inhibiting the release of arachidonic acid from phospholipids. GLA and SDA rarely exist in edible materials. Blackcurrant (*Ribes nigrum*) seed oil is the only food source that combines significant levels of GLA and SDA. Dietary supplementation with blackcurrant seed oil alleviates atopic skin symptoms, improves plasma lipid profile of hyperlipidemic patients and inhibits platelet aggregation. Blackcurrant seed oil also has potentials in lowering blood pressure and enhancing immune function. Topical application of blackcurrant seed oil improves skin lipid barrier, reduces chemically-induced skin irritation and improves dry, sensitive and inflammatory skin. In addition to fatty acids, blackcurrant seed oil is a rich source of natural α - and γ -tocopherols providing radical scavenging property and additional anti-inflammatory efficacy in skin. Combining oral and topical use of blackcurrant seed oil may bring synergistic effects of improved skin health.

Functional food: the EU rules

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NOT RECEIVED

Dietary supplements and functional food in Italy and the UE

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The area of dietary supplements is nowadays regulated in Italy by the legislative decree 21st of May 2004, n.169, in accomplishment of the community directives 46/2002/CE of June 10 2002, that proposed, at normative level, the progressive and deep evolution governing the role and the purpose of these products in the field of a new alimentary conception.

This regulation, in fact, considering at the moment specific dispositions only for vitamins and minerals, includes in dietary supplements also those products with ingredients different from the nourishment ones, such as substance able to produce the so called "physiological" effects. These last ones have to be considered as health effects helpful to the well-being of the organism even if not founded on nutritional and curative basis.

Among the substances with "physiological" effect, that can be obtained from all those available natural sources, there are plants and their derivatives. The condition for their employment is a convenient security level to the assumption quantity proposed, considering that the products which we are talking about, are of free choice and self administrated by the consumers themselves. Hence, the so called herboristic products, object in national ambit of different legislative regulations aimed at giving to them a specific and autonomous regulatory frame (this last one is still "in itinere"), represent a variant among the functional food.

In the Europe frame it's becoming to be delineate a regulatory system for health food covering all the products turned in the well-being, leaving out of consideration the contents, and including in the pharmaceutical area only the products with the express aim of cure.

After all, in the well-being arena more and more non medical products are available in capsule, tablets, vials and similar, and have to provide however adequate limits of safety. They are frequently based on nutritional components associated with non nutritive components and therefore, would be artificial as well as unproductive foreseeing a distinction between nourishing and not nourishing health food and with a nourishing "physiological" effects.

This distinction could fluctuate in permanence with the progression of the knowledge and would create other borderline areas, besides the already problematic one between the medicinal and non medicinal effect, without offering appreciable advantage.

Especially nowadays that, for various functional foods, benefits deriving by a larger assumption of the useful one to "nourish" appears possible. These health foods in fact would have physiological purpose. Scientific progress, brought a revaluation of the dietetic needs of nourishing for which it appear a positive effect in certain pathological conditions or because the level of quantification tends anyway to move from the simple prevention of the need to the exigency to assure a perfect health.

About dietary supplements, as it has been said, the actual European regulatory system represents the progressive evolution that brought to an amplification of the role and the purpose of the food. The regulatory floodgates are based on the incentive of the growing knowledge of a healthy alimentation

as fundamental way for health prevention and maintenance, in accordance with a dynamic and perfectible state.

Health food, in fact, not anymore considered like simple nourishment complement, have acquired additional purposes," functional" type, aimed in a well-being way already described for the dietary supplements, and deriving from the possible presence in the compositions of not recognizable substances like nourishments compounds.

"Functional" properties of food and "physiological" effect of the dietary supplements present narrow interconnections, so that the same compound presented as diet supplements ,can represent also the component of an active compound used as functional food (for example the probiotics).

As a further evolution stage, is underlined that concerning the communitarian project on the admitted claims for the health food on the labeling and in advertising, we arrive at the point to include, in determine conditions, declarations on the "reduction of a risk factor of illness". This in the consciousness that the right alimentary regimen and certain food can contribute in large measure to preserve health, developing a role in the management of some risk factors linked to the development of a human disease. Consequently, in this way it's possible to promote alimentary choices by the consumers influencing there own health and stylish way of life.

Sport and Integration

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In our lecture we make a revisal of the most important integrators used by the athletes during the sport performance. The concept we want to dissert about is that a nutritional integrator is a normal nutrient, commonly available in the food, selected and concentrated by factory, to satisfy the daily intake needs.

Nutritional integrators are usefull and in some case essential only when the food we eat is not sufficient to perform the daily work. If the sportman has a regular nutritional intake and if he has to perform not particulary stressfull excercises with an energetical need less than 3000 Kcal/day, he doesn't need any nutritional integration.

For instance, a person that performs fitness – body building, spinning, cardiofitness -, three times weekly for one hour each working schedule, does not have to follow particular nutritional care. Different behaviour is needed for people that perform sport as agonists every day.

Some of those need more than 4000 kcal to perform their activity and for them it is justified nutritional integration, as, their nutritional need cannot be covered by even a complete food intake.

In our lecture we'll talk about:

- Energetic integrators
- Hydrosaline integrators
- Plastic integrators
- Regulators and metabolic coadjuvants
- antioxidant

For every integrator class we explain the use and the utility, when and for whom they are indispensable, and furthermore in which moment of the performance they may be used to give to the organism the right effect.

We want to add alimentary suggestion to improve not only the result of the sport activity but to rationalize the dely diet of everyone of us.

Health-benefit of dietary and topical antioxidants: an update

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In the last 10 years the research on antioxidant has given a variety of conflicting clinical results, such that the activity of these compounds is still matter of discussion.

What is coming out from the available clinical data is that not all antioxidants have the same biological activity since some of them are located on membranes others are circulating or in the cytosol and finally some are part of the enzymatic and non enzymatic antioxidant systems. Furthermore, brain oxidation can not be compared with muscles or skin oxidation. In strict terms oxidation has to be divided into different compartments.

One of the major problem is related to the lack of reliable tests to determine oxidative stress, and consequently it is not possible to evaluate if an appropriate antioxidant therapy has been properly administered to a given patient. An antioxidant therapy has to be addressed according to the system or organ which is under oxidative stress and patients have to be treated accordingly. In this review general principles of oxidation will be reviewed and four compartments of oxidation will be analyzed: the endothelium, the brain, the intestine and the skin with the relevant antioxidant combination for each system and the clinical outcome in terms of oxidative stress.

New findings on sensitive skin

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Sensitive skin is largely agreed to be a lay term used by individuals who consider them-selves to have more reactive facial skin to applied products and/or environmental factors than the general population.

We conducted several epidemiological studies on women in Europe (n=1200=), USA (n=800) and China (n=2000). The prevalence of auto-assessed sensitive skin is 51% in Europe and USA, and 36% in China. Sensitive skin is clinically characterized by facial discomfort with burning, stinging and itching mainly provoked by climatic factors as wind or fast changes in temperature, or by topical application usually well-tolerated on skin. Comparing the skin reaction to known allergens on sensitive skin subjects versus non sensitive skin subjects, we have demonstrated that sensitive skin is not related to an allergic process.

We hypothesize in the 90's that sensitive skin could be related to a neurological origin based on the sensitive epidermal nerves: (i) Sensitive skin subjects demonstrate a significant higher skin hyper-reactivity to capsaicin which stimulate specifically the C-fibers; (ii) With age, as sensitive skin is decreasing, facial sensitive epidermal nerve density is also decreasing; (iii) Spicy food (rich in capsaicin) increase the prevalence of sensitive skin. More recently, by using functional MRI, we show that sensitive skin subjects demonstrate a specific pattern on cerebral activation with a higher brain activity for sensitive skin subjects on prefrontal and cingulated area.

These findings on PNS and CNS give a neurological perspective for the origin of sensitive skin.

Safety requirements for the development of innovative cosmetics

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Cosmetic products are getting more popular in daily life. These products, either botanical or chemical, are developed for the purposes of a variety of functions, such as cleansing, sun-protection, skin nutrition supplement, anti- photoaging, etc.

Although these products do far more good than harm, many unwanted adverse effects do occur in daily dermatological practice. Cosmetics related dermatoses include irritant cosmetic dermatitis, allergic dermatitis, contact urticaria, pigmentary (hyper- or hypo-pigmentation) dermatitis, photosensitivity, cosmetic acne, cosmetic intolerance, hair and nail abnormalities, and rarely skin tumors. Polluted cosmetics may cause skin infection. Biological composite in a cosmetic product might spread an infectious agent. Thus careful safety evaluation and application of cosmetic components remains to be the priority for the development of cosmetics.

On the other hand, unwanted responses to cosmetics might be influenced by different living environment and different ethnics. Clinical trials in different region on different people are needed before a cosmetic product is marketed.

Zinc and its derivatives: their applications in cosmetic

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Zinc is one of the most widespread cation present in human body and mainly in skeletal muscles, bones, teeth, hair, testes and skin (about 6% in stratum granulosum).

Zinc is involved in many metabolism processes and its deficiency results in different pathological conditions.

Zinc plays a major role in epidermis maturation and cutaneous integrity.

For all these reasons Zinc salts find several applications in personal care.

Combining skin cleansing with skin care is one of the main goal of cosmetics.

A new zinc salt, zinc coceth sulfate, is a surfactant provided with additional functional properties.

The work will illustrate the relationship between Zinc and skin and will quantify the total amount of residual Zinc in stratum corneum at different depths after cleansing with its aqueous solution. Functional properties of Zinc Coceth Sulfate will be demonstrated: underarm deodorant effect (sensorial and microbiological evaluation), dandruff control capacity (corneocytes count and dimension), skin renewal (dansyl chloride method). Dermatological properties (skin/eye irritation and sensitization) will be also shown.

From all these data we will show that skin cleansing with Zinc Coceth Sulfate involves some form of Zinc bond with stratum corneum in its outermost layers, providing so a base for its efficacy and safety.

Parabens and breast cancer: is there a health risk?

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A recent article "Concentrations of Parabens in Human Breast Tumours" reported trace amounts of several parabens in human breast tumour tissues and suggested that the presence of paraben residues in tumour tissue may be due to the use of parabens in underarm cosmetics. In addition, the authors gave the impression that parabens from consumer products may play a role in the aetiology of human breast cancer.

None of these allegations are supported by the study data, which demonstrated neither an association nor a correlation between an effect (mammary tumours) and a possible exposure (parabens). First of all, in the absence of control data from healthy human breast tissues, the presence of trace amounts of parabens in tumour tissues cannot be put into perspective. More important, the analytical results on blank samples reported in the study (analysis in absence of breast tumour tissue) showed an unacceptable degree of variation (up to 8-fold) and revealed considerable contamination. Taking into account that the analysis of blank samples was performed with pure chemicals and in the absence of tumour tissues, the presence of an unknown contamination source is troubling. Given that the blanks and the tumour tissues show the same qualitative and quantitative finger print of parabens, this suggests that the origin of parabens in the tumour tissues was due to laboratory contamination. In our view, the general contamination of all blank samples by parabens puts into question the overall validity and reliability of the analytical methods and results of the entire study. We strongly disagree with the author's suggestion that the observed paraben residues may be due to use of underarm cosmetics; this is highly implausible since no known mechanism would explain a selective transport of topically applied substances from the axilla into the breast. Further, given that the great majority of underarm products do not contain parabens (according to data of major cosmetic companies), this allegation becomes completely untenable. Moreover, the allusion that parabens may accumulate in breast tissue is contradicted by the study results, which revealed higher residue values for the less lipophilic parabens when compared with those of the more lipophilic long-chain parabens. Taking into account that a) development of malignant breast tumours requires many years or decades and b) the short half-lives of parabens in mammalian organisms, trace residues in tumours lack any temporal relation with tumour aetiology. Finally, although breast cancer patients are routinely treated with intravenous anti-cancer drugs, the study did not report the therapeutic history of the donors of tumour tissues, their drug exposure and the possible paraben content of the drug products. Given that anti-cancer drug products may contain paraben preservatives, their presence in tumour tissues may be due to cancer chemotherapy, rather than the cancer due to parabens. Application of the criteria for causality accepted by modern epidemiology, a) strength of association, b) consistency of association in different studies, c) specificity of a cause resulting in an effect, d) temporality of the effect, e) exposure-response relationship, f) biological plausibility, g) coherence and h) experimental analogy, would lead to the conclusion that the study data present no evidence of an association or a role of

parabens in human breast cancer or its aetiology. This view is supported by the results of an epidemiology study that showed no association between use of underarm cosmetics and breast cancer. A scientific journal is under the obligation to ensure that work published is based on sound science and that the conclusions are presented objectively. Overall, the report did not merit publication in a peer-reviewed scientific journal.

Solar UV simulator skin testing

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The most common cutaneous phenomenon resulting from an irritant stress is erythema, which can be evoked experimentally by several types of stimuli. UV radiation is particularly potent in inducing erythematous reactions varying in extension and intensity. These reactions can be quantified with great precision by instruments that measure the redness of skin surface. With this model, important information has recently been acquired concerning the skin sensitivity to UV radiation, the assessment of sun protection factor (SPF), the ability of some antioxidant agents to prevent photodamage, the effectiveness of antiinflammatory drugs.

The 601 Multiport Solar Simulator precisely reproduces the solar ultraviolet spectrum while eliminating the visible and infrared component. The light source is a 150 Watt xenon lamp, whose spectral output follows the distribution of sunlight from 290 to 400 nm. This results in UV levels 15-20 times stronger than tropical sun without causing thermal discomfort or damage. Its 6 independently adjustable outputs allow for 6 simultaneously conducted tests, thus saving time, reducing tedium and improving accuracy.

Erythema can be easily quantified by means of colorimetric evaluation. ChromameterTM, (Minolta, Japan) is a colorimetric instrument, which contains a xenon lamp as a light source, photodetectors, a microcomputer, and colored filters which closely match the CIE colorimetric Standard Observer curves.

Solar simulator and colorimetric evaluation has been largely used in our department for the assessment of SPF according to the COLIPA recommendation. Combining UV exposure to solar simulator and colorimetric evaluation we demonstrated that some antioxidants are able to protect the skin from UV radiation.

Efficacy and Safety of Cosmetics: the Evaluation Methodologies

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The efficacy of a cosmetic product is associated both with the capability to affect the cutaneous equilibrium and to improve the skin functions in an effective and specific way. At the same time, unwanted effects (both acute and delayed) are to be avoided. Many experimental techniques are used in order to predictively evaluate the functionality and the tolerability of a cosmetic. Most known evaluation methods use bioengineering techniques and special instruments which are considered suitable to assess many cutaneous parameters. Results of such complex procedures may be impaired by their inadequate application. As examples of the universe of evaluation methods, measurements involved with the integrity of the stratum corneum and the barrier function of the skin have been taken into account. These may be carried out in several ways. Indeed, predictive evaluations can be performed after a short or long usage period of the product or after occlusion. Mathematical significance of results require, among other factors, accurate standards of evaluation, controlled environmental conditions, regular calibration of instruments, selection of reference standards and adequate number of subjects. The issue concerning the relationship between instrumentally measured efficacy and results perceived by the consumer may be investigated by associating instrumental measurements with sensory analysis.

On-line raw material and finished cosmetic control with HPLC

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Any discussion of the present and future role of analytical chemistry in the cosmetic industry cannot fail to observe a growing need for chemical analysis. This demand is largely the result of a number of interdependent developments taking place both within and outside the industry. Especially the last decades pressure on the cosmetic industry to deliver demonstrably safe, good quality products has increased. It is difficult to designate which development is most important, but several may be expected to become more important with the approach of a bigger unified European market.

Over the last thirty years a great number of new analytical techniques have been developed, while familiar techniques have been refined to a high degree; On the other hand only analysis of the raw material and finished products can provide same kind of protection against potentially dangerous contaminant. HPLC is the main chromatographic technique that has pushed GC technique into more specialized analyses. The main reason for this is the fact that the analyte need not be volatile as with GC giving HPLC a wider scope.

Some means of detection must be available by HPLC and in this field the major developments are taking place. The most usual means of detection is still UV/VIS. This detection technique requires the analyte absorbs light. Many compounds of cosmetic interest may be determined, however, among which many preservatives, and all UV filters and colours. An important development in UV/VIS detection is the Diode Array Detector. This instruments allow real time acquisition of the spectra of the compounds passing the detector, giving additional information on the identity and purity of the peaks involved. For most applications in cosmetological analyses the sensitivity of UV/VIS is adequate, but it is not really baffling. Analyses may be possible in the ppm range and sometimes even lower, but this heavily depends on the compounds and matrix involved. For this purpose Fluorescence detection is far more sensitive and also more specific eminently suitable to detect low levels of fluorescing compounds in complex matrix. The recent improvements in LC/MS technology have been staggering. Ten years ago there was no competitor in the field of analytical chemistry that could satisfy the requirements of high-throughput, sensitivity and selectivity. Additionally, LC/MS instruments have become easy to use, cost effective and robust, and helped by the readiness of the instrument manufacturers to meet the requirements of their customers, the different techniques and instruments have been optimized. Consequently, MS is becoming step by step a kind of universal detector for HPLC. In parallel to this evolution in LC/MS instrumentation there has been tremendous growth in LC/MS methodologies for cosmetic analysis; so much so that LC/MS is now accepting as a routine tool within the major cosmetic industries. A number of alternative detection technique is also available for compounds that do not absorb light or fluorescence. Refractometric detection is useful when the analyte concentration is not too low. Electrochemical detection allows electroactive species to be determined with good sensitivity and specificity. In conclusion the increasing sensitivity of modern analytical methods allows the determination of tra-

ces of contaminants that could not be detected ten years ago, sometimes determining unnecessary alarm. On the other hand only analysis of the raw material and finished products can provide same kind of protection against potentially dangerous contaminant. It is in the common interest of both, industry and consumer, that the almost is done to guarantee the safety of cosmetic products. Analytical chemistry is crucial to this goal, both for the industry and the government control laboratory.

Acidic compositions with a perfluoropolyether phosphate: safety and potential in dermocosmetics

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The dermatologist, the microbiologist and the cosmetic chemist know the advantages (and the problems) of acidic compositions. Acidity is a physiological condition for the skin mantle, helps preservation, and increases the stability (and/or the effectiveness) of important actives. The use of lactic acid or citric acid is the most common means of adjusting the pH of various products, enhancing their antimicrobial performance; lactic acid is reported to work better than citric acid as moisturizer; among α -hydroxyacids (AHAs), glycolic acid is the most effective in the cell renewal. However, the use of acids to achieve low pH values (2.5-4), causes concerns, because of the risks of skin irritation.

The recent availability of a perfluoropolyether phosphate, simply PFPE phosphate, offers the cosmetic chemist a completely new way to develop safe and effective cosmetic formulations or to enhance the safety and the effectiveness of existing products. PFPE phosphate, chemically a perfluoropolyether phosphoric acid ester in the un-neutralized form, is a unique material combining emulsifying activity, a high dissociation constant (from which stronger acidity can be assumed in comparison with most common organic acids), and a rather good toxicity profile (according to testing on animals). These properties suggested us to use PFPE phosphate as a means for formulating acidic compositions containing actives with pH dependent stability (eg dihydroxyacetone, DHA) or with pH dependent effectiveness (eg AHAs). The safety of these compositions was evaluated by testing on volunteers.

In a first study, it was assessed the safety of various acidic compositions based on PFPE phosphate - an aqueous solution, a hydrogel, and an O/W emulsion. The study included the comparison of the hydrogel with a hydrogel where PFPE phosphate had been replaced by lactic acid, with a content to have the same pH. In a second study, self-tanning products containing DHA were evaluated, comparing acidic products (containing PFPE phosphate) with product at physiological pH (without PFPE phosphate) and with a product at the same acidic pH achieved with lactic acid. In a third study, the anti-irritant potential of PFPE phosphate was evaluated comparing two aqueous solutions containing glycolic acid, with/ without PFPE phosphate.

The results of this preliminary investigation were such that further research work has been already set out in three areas:

- synergistic properties of the combination AHAs and PFPE phosphate;
- long term stability of self tanning products containing DHA and PFPE phosphate;
- preservative-free compositions containing a polar solvent (alcohols, glycols) and PFPE phosphate.

Hair and Skin Evaluation by Image Analysis

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Image analysis has found numerous applications in cosmetic science for characterization of skin and hair and for quantification of the effectiveness of cosmetic treatments. In skin research, image analysis techniques are used in combination with profilometry, topography analysis, scanning electron microscopy (SEM), and stereomicroscopy, which are all used for cutaneous microrelief analysis as well as for quantification of the effects of moisturization, anti-aging, exfoliation, and "peeling" of various products [1,2]. These techniques can be employed to visualize and quantify the skin surface in various regions such as lips, aging spots, thinning cellulite, wrinkles, etc. Quantitative parameterization includes depth and peak distributions, hole analysis, Fourier analysis, power spectrum analysis, angle measurements, distance measurements, etc. [1-3]. Similarly, image analysis can also be employed for hair research in combination with photography, optical microscopy, SEM, scanning probe microscopy (SPM), and color analysis. Specific problems, which can be solved by using image analysis measurements, include quantification of hair luster on both idealized geometrically arranged straight hair as well as on free hanging frizzy or curly hair tresses [4,5]. By varying the illumination conditions one can obtain hair images for quantitative characterization of hair surface deposits such as styling polymer films (flakes), micronized and non- micronized inorganic sunscreens, pigments, etc. For idealized geometrical conditions of fiber arrangement and illumination, one can perform color analysis by quantitative measurements of image histograms, which can provide information about color shifts as a result of styling treatments, dye deposition, as well as color distribution in hair fiber assemblies. An important area of hair evaluation is the characterization of hair damage. Image analysis can be employed in visualization, and both qualitative and quantitative characterization of hair damage based on optical, SEM, and SPM micrographs. Finally, optical micrographs can be used for the characterization of fiber organization in hair fiber assemblies.

The paper will review both published and previously unpublished data.

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Cosmetic product claims in advertising

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One of the main ingredients in the composition of the marketing mix for cosmetics is advertising. This makes the cosmetics sector an important client both of the advertising industry and of institutions concerned with the repression of misleading advertising. In most of the economically developed countries there is a quite homogeneous situation as for what regards the repression of misleading advertising. The relevant regulation, according either to laws or to voluntary rules or both, enforced by either public institutions or national advertising industry self-regulatory bodies or both, has much in common among various countries, regarding both the general features of advertisements and the peculiar ones regarding the specific field of cosmetics advertising. In a few countries specific guidelines have been issued regarding what should be avoided in order to prevent advertisements to be misleading for consumers. In most of these cases particular guidelines for cosmetics advertisements have been devised, which are in fact very similar among various countries, and often coincide with the case law of the countries in which such guidelines have not been issued. This is no surprise considering the growing flow of information among institutions of different countries concerned with the repression of misleading advertising, which now cooperate constantly keeping regular contacts and operating common cooperation projects. This set of circumstances makes it increasingly important for the cosmetics industry to monitor the evolution of regulation for the repression of misleading advertising both in every single country and in the whole of the ones taking part to international cooperation on the subject.

Role in SPA of medical and beautician community in China

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Dermatologists worldwide feel that they should take a more active role in coordinating each patient's total skin care program not only in their own office but also in SPAs and Beauty Centers.

A good collaboration between well-qualified aestheticians and dermatologists may surely provide better skin care results for patients monitoring more frequently their eventual compliance.

Whether the skin care team is housed at a single facility or at a separate location, it provides an excellent support system for patients.

This is especially important for those being treated for chronic skin disorders such as acne, psoriasis, and atopic dermatitis, or for patients undergoing cosmetic surgery.

In fact for patients desiring facial cosmetic surgery, many skin surgeons recommend pre and post operative skin care by a well-qualified aesthetician.

This is what frequently happens not only in many hospitals, but also in private medical offices, SPAs and Beauty Centers in the main China.

Chinese dermatologists have in their staff one or more aestheticians in hospital also locally treating the patients. For example, for disease such as acne, there are aestheticians using appositely formulated herbal masks.

Aestheticians are viewed as important adjunct to medical professionals not only providing skin care but also helping them to some surgical procedures. As a matter of fact, Chinese aestheticians must undergo 3 years of training in massage therapy, electrology, magnetotherapy, and basic skin care. They must have also basic knowledge of cosmetic chemistry, electrical facial and body equipment, and techniques necessary for chemical exfoliation and hair removal.

Moreover they are trained by dermatologists to recognize basic skin diseases such as precancerous and cancerous lesions, allergic and inflammatory reactions, ipo and hyperpigmentations etc.

For all these reasons China dermatologists and aestheticians works always in connection in hospitals, SPAs, Beauty Centers and medical offices.

Role in SPA of medical and beautician community in USA

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The situation in the USA as regards the status and use of adjunct personelle is a very confused one. Not only are there varying types of nurses, medical assistants, and physician "extenders", there are various other licensed and non-licensed individuals who are involved in the delivery of aesthetic care.

The main thrust of this paper is to illustrate the various levels of cosmetologists and aestheticians as they exist in the many different regions of the United States. This discussion includes their types of education, the various procedures which they are permitted to do (such as lasers, pulsed light, microdermabrasion, chemical peels, and others), and the forms of supervision required. Also noted are the types of cosmetic procedures which are most popular, the settings in which they take place, and the financial ramifications of each of them to both the practioner and the client/patient. Unfortunately it is this latter issue which tends to drive the market for aesthetic medicine and surgery.

The SPA in Italy: State-of-Art

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Women and men are becoming more and more involved in total skin care in beauty salon and always more in specialized SPAs (*Salus Per Aquam*).

Researches also indicate that more than 30 million of adult women use facial moisture, and increasing numbers are using multiply product regimes and SPA facial and body services.

Men also seek saloon skin care services, although they still account for a small but increasing percentage of the total clients.

What is interesting to underline is that where patients may consult a dermatologist once every 6 months if they are involved in caring for their skin, they may consult a saloon skin care specialist every 4 to 6 weeks.

Thus it happens that a beautician or non licensed salon skin care technician will be discussing skin care with the individuals and recommending cosmetic products for use at home, whether or not the dermatologist has suggest it.

On the contrary working as a team, the dermatologist and the expert beautician can better understand the care that each provides thereby ensuring optional skin care results for the patient. Therefore it is necessary that a qualified beautician should be experienced with the use of basic electrical facial equipments and must have the knowledge to understand the basic cosmetic chemistry necessary to select products with ingredients that are appropriate for a particular skin biotype. Moreover she/he should also be able to recognize common skin disorders such as actinic keratoses and precancerous and cancerous skin lesions and refer to dermatologist for further evaluation.

In this way the patients compliance with both medical and non medical recommendations can be monitored and reinforced regularly.

The Biological Role of Water on Human Health

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Water is the essential element for human health. Are taken in consideration the biological-function aspect of the metabolism in general water and in particular in kids water. Are underlined the essential elements for the choice of water in babies alimentation.

A description of the existing Spa in Malaysia

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Impress Esteem, Melacca - Malaysia

Every spa in Malaysia is having 38C to 40C thermal facilities, customers first go to warm water then go to the heat water and there is no sea water facility. These spas generated approximately USD 138 million (MYR 524 million) in revenue during the 2002/2003 financial year including resort and day spa. Almost two thirds of the spas' development costs were than USD 220,00 (MYR 836,000). The average size of spa facilities was 426 square meters and offered private treatment rooms, having two rooms on average. The therapies practiced most often in spas were aromatherapy and reflexology having increased their visits by 20% over the last two years.

The relative used treatments have been influenced by China, European-Cosmetic company, Thai-Common Thai massage, Indonesia-Start import from Mandela spa and mandolin.

A reflection about what spa is today in Malaysia will be reported.

Wellness in Italy: Aesthetic Medicine, Beauty and Fitness Centers, and SPAs

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Skin is a complex entity consisting of cells and tissues that form the outer surface of the body.

As the first line of defence, it can suffer from a number of environmental insults, including temperature, humidity and solar energy.

All of them change our general appearance and changes on the skin are perceived as aging which is one the most powerful factors influencing social interactions in many situations.

Since in our culture, a physical attractiveness stereotype exists, those who are attractive gain advantages while the unattractive ones suffer throughout their lifetime.

What is beautiful is good; unattractiveness is perceived significantly less favourably.

Thus benefits that can accrue from cosmetic enhancement, exercising, right eating and a good lifestyle need to be emphasized!!

Therefore aesthetic medicine, Beauty and Fitness Centers and SPA (salus per aquam) contributing to ameliorate general appearance and global health are at the base of well being.

Skin care versus skin therapeutic: who animates the user?

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Vienna - Austria

At first sight, the answer to this crucial question seems to be simple: doctors prescribe and control skin therapy, cosmeticians and pharmacists are responsible for skin care. But over the last decades, the frontiers between dermatological therapy and skin care became less and less distinct. Worldwide, most dermatologists do not only treat diseased skin but they offer skin care and more invasive methods of skin (and beauty) restitution, including peelings, fillings of folds, botox injections, Laser treatment, liposuction and face lifting. This development endangers the medical reputation of the dermatologists, as their main task, the diagnosis and treatment of dermatoses is often underestimated by the public.

The motivation of a patient to see a dermatologist is clear: medical concern, unpleasant sensations like itching and burning, and awkward changes of her or his appearance. However, minor lesions of the skin often are considered to be a cosmetic problem, not worth to be shown to a dermatologist. Dry scales, pigmented spots, pimples, comedones, wrinkles and folds, are primarily shown to non-medical personal. Instead of skin therapy, the patient receives skin care products and advices for gentle skin cleansing. Thus, symptoms of underlying diseases may be overlooked. This statement does not only apply for changes of the skin itself but for the skin appendages as well. In beauty saloons, infected nails are covered with artificial nail plates to hide the disturbing symptoms, and hair loss is discussed with hair dressers or employees of hair institutes. As a result, oral vitamins and ions are recommended together with special shampoos and hair-lotions but no medical diagnosis is searched for.

The typical borderline cases between dermatology and cosmetology are pre-acne, couperose, prematurely aged skin (chronic ultraviolet damage), and itching skin. A good cosmetician will be of great help but only if he is responsible enough to admit the necessity of a medical consultation when appropriate.

The numerous reports on restitution of beauty and youth in the media as well as the personal, occupational, and social environment force most people to obtain and to retain an optimal appearance. Reading the pertinent articles in the yellow press and listening to the recommendations of colleagues, friends (and enemies), an amelioration of the personal outlook is sought. However, in many instances, there is absolutely no reason to start rigorous actions. The abundant application of cosmetic devices does not always produce the desired effects, and therefore more and more products and corrective measures are used the results of which are uncritically reported in the yellow press

The animation of the consumer stems from his personal motivation, regardless whether therapeutic measures or skin care products are used. The most important point is the medical concern which induces the patient to see a dermatologist. But for many people, an unpleasant appearance, true or imaginary, is almost as important. To whom should the public rely when medical or cosmetic skin-problems arise? The competent person to consult about skin therapy and skin care products should

be the dermatologist who knows the advantages and disadvantages of all the medical, surgical, and cosmetic measures developed to restore and to retain healthy and youthful looking skin. By his knowledge, his skills, and his aesthetic judgement, the dermatologist is in the position to diagnose and treat patients with skin diseases and to advise persons unhappy with their outlook on appropriate skin care.

Skin Care: Intelligent Partnership between Medical and Beautician Communities

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The clientel visiting a SPA come to aquire health, beauty and wellness. A dermatologist at a SPA should be a specialist for all kinds of non-invasive rejuvenation technics and in anti-aging politics. A sortiment of topical anti-aging and hormonal treatments as well as substitutional therapies in the battle against signs of aging and reduced skin health. Beauticians work in the dermatological team as competence center for the local therapy treatment, as advisor in all decorative cosmetics and for camouflage and as an important feedback between patients and doctors. Maximized teamwork only make it possible to reach the main goal of a SPA cure: health, beautiness and wellness.

The Use of Bergamot Oil in Aromatherapy and Aromachology for Wellbeing

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First of all, it is necessary to understand the significance of aromachology, a science dedicated to the study of the relationship between psychology and technology of the fragrances that provoke a variety of emotions. On the contrary aromatherapy is a scientific methodology by which essences of botanical origin are used as therapeutic means to alleviate or eliminate symptoms of many diseases.

How a fragrance may act at the emotional level?

The odours to be perceived have to arrive to the higher area of the nasal cavities where the nervous cells, excited by the odours molecules, transform chemical energy in electric pulses stimulating the olfactive centres of the anterior cerebral cortex. From here the olfactive message goes in other brain's areas, the limbic system where the emotional area is located.

Differently from the other senses, the olfactive stimulations go directly to the cortical brain area without being filtered from thalamus.

Therefore memory and sensation provoked from an odour or a fragrance may immediately evoke certain long-lasting events accompanied by very pleasant or fearful emotions apparently forgotten. These sensations are always more intensive than other evoked by a sound or an image.

In conclusion aromachology is a new and important branch of general culture to better understand the activity of fragrances at level of our emotional phenomena. In this frame the use of Bergamot oil both in the cosmetic and functional food fields will be presented and discussed.

Role of Extra-virgin Olive Oil to preserve the consumer's health

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The current momentum toward the Mediterranean Diet based on extravirgin olive oil has solid biological foundation and does not represent a transient fashion or simply a business.

Successful research has proved that animal fats has to be used with caution because of the presence of saturated fatty acids which favour the plasmatic cholesterol and act as starters for some kinds of cancer.

Many vegetable oils must be used with caution because the polyunsaturated fatty acids of which they are mainly composed are a target of ROS (Reactive Oxygen Species) and consequently of peroxidated lipids, main cause of skin ageing.

On the contrary the extra-virgin olive oil, rich of anti-oxidant agents such as tocopherol, phenolic compounds, and squalene, being self protecting does not undergo the peroxidative process.

Moreover some recent studies have highlighted also its specific protective property versus the P-54 gene.

The antioxidant capacity of extravirgin olive oil and its main use in functional food will be evaluated and discussed.

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The role of peptides of the extra cellular matrix in modern cosmetics

Claude Dal Farra, Eric Bauza, Nouha Domloge
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The extra cellular matrix (ECM) represents a diversity of critical multifunctional molecules that are very important for skin integrity, appearance, regeneration, wound healing, and the fight against aging. The interest of developing ECM-like peptides is based upon the crucial role that each of these ECM constituents plays in the skin.

Fibronectin is an important skin matrix glycoprotein that is involved in cell adhesion, differentiation, and migration. Fibronectin contains different domains that have binding sites to important macromolecules and other molecules on the cell surface which induce cell adhesion. Moreover, fibronectin also plays an important role in wound healing. These functions are necessary for skin regeneration and the fight against aging. Laminin, another very interesting ECM molecule, is made of multidomain glycoproteins and is thus directly involved in many biological functions. To date, many laminin isoforms have been identified. They are large disulfide-bonded heterodimers composed of three genetically distinct polypeptide chains: alpha, beta, and gamma. Laminin plays a critical role in cell behavior, is a potent cell adhesion molecule, and is involved in some skin pathologies. Moreover, its role as an important key in basement membrane care and skin aging has been evoked recently.

In addition to the two molecules mentioned above, another essential ECM molecule is collagen. Collagen plays a crucial role in maintaining skin structural integrity, tissue remodeling, and wound healing, and is also very important for cell adhesion and migration.

The objective of these studies is to demonstrate that the ECM-like molecules of synthetic peptides (such as fibronectin, laminin and collagen peptides) exhibit very interesting effects on the skin and are of great interest in modern cosmetics. Analytical reverse-phase HPLC studies confirmed both the great stability of these synthetic peptides in water and their exceptionally low surface adsorption when stored in plasticware. Furthermore, incubation of these synthetic ECM-peptides with culture media taken from human cultured cells exhibited only a low degradation.

These peptides enhance both cell adhesion and uniform spreading on the matrix, followed by greater differentiation. Their presence stimulates cell synthesis of ECM molecules and their ligands, which reinforce epidermal cell cohesion and the expression of adhesion integrins, as well as better stratum corneum formation.

The effect of some of these peptides (such as fibronectin-like and laminin-like peptides) on laminin-5 synthesis, an essential component of the basement membrane, lead to very interesting results including regenerative and functional improvement, as well as enhancement of the basement membrane structure. Interestingly, studies on dermal repair showed that ECM-like peptides (such as fibronectin and collagen peptides) significantly help dermal repair, regeneration and wound healing.

In conclusion, ECM-like peptides, with their remarkable biological effects on the multiple layers of the human skin, are crucial to the development of modern anti-aging cosmetics and skin care products.

Cell-energizing active ingredients in modern cosmetics

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In the process of developing effective modern active ingredients for skin care and the fight against aging, cell production and energy-use have become crucial considerations and are increasingly at the heart of cell biology investigations.

It is now well-established that cell energy metabolite decrease can be caused by different factors including aging and stress, especially UV stress.

Studies have shown that, although aging does not seem to cause any alteration in baseline levels of energy metabolites, energy rebound in response to stress significantly decreases in the skin.

Moreover, among UV damage mechanisms, UV-induced oxidative stress and accumulated UV-induced mt DNA mutations disrupt cellular energy metabolism, and cause ATP depletion as well as cell death. Furthermore, other data has shown that both cell death and accelerated cell aging under stress are modulated by the level of energy metabolism.

Therefore, cell energizers and metabolism activators are of central importance to modern cosmetics and skin care products.

Energizers and activators function on one of the essential mechanisms of cell activation and signal transduction pathways. Specifically, the activation of cell membrane-related receptors (such as G-protein-coupled receptors) which trigger a second messenger responsible for a cascade of cellular responses.

The use of active ingredients (such as APnA peptides) that activate this G-protein-receptors path revealed an interesting effect: a rapid increase in cellular energy metabolites and ATP level. Another important cellular signaling path is tyrosine kinase receptor activation, which results in PKC phosphorylation and activation by diacylglycerol (DAG), which, in turn, induces different important cellular responses such as cell differentiation and rapid cell activation.

Furthermore, studies revealed a calcique response after the administration of such energizers, which suggested the activation of different cell signaling pathways.

In conclusion, these studies demonstrate that APnA peptides and other energizing active ingredients trigger combined mechanisms that lead to cell activation (such as G-protein-coupled receptors, tyrosine kinase receptor activation, and Ca^{2+} signalling).

Energizing active ingredients are then of great interest in the field of skin care products and offer much promise in future anti-aging products.

Sodium L-ascorbyl-2-phosphate shows *in vivo* and *in vitro* efficacy in the treatment of acne vulgaris

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Acne vulgaris is the most common inflammatory skin disorder which involves a complex relation among several causes. It affects about 80% of adolescents and young adults. Two main causes in the typical acne cycle may be on the one hand colonisation of microorganisms like *P. acnes* to produce antigens and inflammatory. On the other hand lipid oxidation produces free radicals and may result in further inflammation. Sodium L-ascorbyl-2-phosphate (INCI: Sodium Ascorbyl Phosphate) is a stable derivative of vitamin C which ensures the beneficial use of vitamin C in cosmetics by delivering the active molecule in a stabilized form. We were able to show a strong anti-microbial efficacy of Sodium L-ascorbyl-2-phosphate in a dose-dependent manner. We tested *P. acnes* in anaerobic devices, which are the physiologically relevant conditions. A standardized time kill study was running over 48h. After 4h we calculated already a 100fold reduction and after 8h all bacteria were killed. On the back of 20 subjects Sodium L-ascorbyl-2-phosphate significantly prevents the UVA-induced sebum peroxidation. 20 subjects were pretreated with each 5% Sodium L-ascorbyl-2-phosphate, 1% vitamin C or vehicle in O/W formulations twice daily for 7 days. After UV-A irradiation induced stress squalen and squalenehydroperoxide were then analysed by HPLC. 5% Sodium L-ascorbyl-2-phosphate was as effective than 1% vitamin C. In conclusion these data shows that Sodium L-ascorbyl-2-phosphate is efficient in the treatment or prevention of acne, which is supported by two different modes of actions shown here as anti-microbial and anti-oxidant agent. Sodium L-ascorbyl-2-phosphate can be used as a non-antibiotic and effective treatment or co-treatment of acne with nearly no side effects, which makes it additionally accessible for cosmetic purposes.

Potassium undecylenoyl hydrolyzed wheat protein: a new surfactant with dandruff control properties

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Undecylenic derivatives are well known in cosmetics and widely used; undecylenic soaps, amides and betaines have been already on the market for many years in antidandruff and mycotic growth control field. In order to obtain a new mild surfactant with multifunctional properties undecylenic acid was grafted to hydrolyzed wheat protein residue obtaining so Potassium Undecylenoyl Hydrolyzed Wheat Protein.

The work will show the properties of this molecule in the dandruff control field.

The results of an *in vivo* test made using Piroctone olamine as control will be shown. Potassium undecylenoyl hydrolyzed wheat protein used at 4% (as it is) was shown to be as effective as 0.75% Piroctone Olamine in dandruff control.

Furthermore the sensitization power of this molecule compared with classical antidandruff agents will be described using Interleukine-1 α secretion as parameter to be evaluated.

At 18 hours the Interleukine 1- α secretion on a 3D epidermidis caused by the product (4% as it is) was much more lower than the values obtained with 0.75% Piroctone Olamine and 1% Zinc Pyrithione.

Potassium undecylenoyl hydrolyzed wheat protein is also effective against Epidermophyton and Tricophyton Mentagrophyte (responsible for different types of tinea).

Mildness to skin and hair has been also evaluated with *in vivo* and *in vitro* test.

Permeation and distribution of sunscreens in the reconstituted skin

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Introduction: The continuous sun exposition can cause serious problems in the skin like photoaging or skin cancer. Then, it is essential to protect the skin from sun radiation with photoprotectors as sunscreens.

The most important peculiarities of sunscreens are water resistance, photochemical stability, good compatibility with eccipients and no toxicity associated to a good affinity for the skin. All these characteristics are joined in a single word: substantivity of a sunscreen.

The efficacy of a topically applied sunscreen, without showing toxic effects, depends on its good capacity of distribution in the skin layers without reaching the systemic circulation.

This study had the purpose to evaluate the permeation and the distribution of two different sunscreens, octyl-metoxycinnamate (Uvinul® MC80, BASF) and octyl-triazone (Uvinul® T150, BASF), through reconstituted skin, EpiDerm™ 606 (MatTek).

Experimental methods: In vitro release tests and skin distribution studies of Uvinul® MC80 and Uvinul® T150 were performed using different formulations (alkyl-citrate solution and O/W and W/O emulsions) containing 6% sunscreen. Permeation tests through reconstituted skin, were carried out using Corning Costar diffusion cells in which the donor phase consisted of the tested formulation and the receiving phase of pH=7.4 phosphate buffer solution (PBS) for Uvinul® MC80 and pH= 7.4 PBS added with 0.01% Brij® 98 for Uvinul® T150. In all cases 1 ml of each formulation was applied. Each perfusion experiment continued for 5 hours; then the skin was removed, sectioned by cryomicrotome in 20 mm slices and the amount of sunscreen in each section was determined by HPLC.

Result and discussion: The results of permeation tests through reconstituted skin EpiDerm™ 606 showed formulations (alkyl-citrate solution and O/W and W/O emulsions) did not allow the permeation of sunscreen in the receiving phase.

The results of distribution tests highlighted that Uvinul® MC80 showed the same trend for all formulations: the skin recovery of Uvinul® MC80 did not depend on the kind of vehicle. Uvinul® T150 accumulated in the upper skin layers. In the deeper layers the concentration decreased in a gradual way for both emulsions (W/O and O/W), whereas the solution showed another concentration peak at 60 mm. Moreover, Uvinul® T150 concentration in the upper skin layer after application of W/O emulsion was 70-fold higher than the values obtained from other two formulations. It was evident that the oil vehicle enhanced the penetration of sunscreen through the double lipidic layer of the skin. The results highlighted that reconstituted skin appears a good substrate for topic formulation screening avoiding the animal use.

Ethosomal suspension for topical administration of a natural antiinflammatory agent: *in vitro* and *in vivo* evaluation

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Ethosomes are a vesicular carrier that present several advantages for the dermal administration of active compounds [1].

In particular we evaluated the potentialities as carrier for ammonium glycyrrizinate (AG), a natural antiinflammatory agent, for the treatment of sun-erythema.

In this work we investigated the ethosomes' ability to enhance the permeation of AG with a non invasive technique as reflectance spectrophotometry.

MATERIALS AND METHOD

Ethosomes were made up of Phospholipon 90 (2 % w/v), ethanol (45 % w/v) and 2% of AG. *In vitro* skin permeation experiments were carried out using adult human skin samples (mean age 32±6 years) obtained from abdominal reductive surgery. Subcutaneous fat was trimmed and the skin samples were immersed in distilled water at 60±1°C for 1 min; then stratum corneum and epidermis (SCE) were peeled off. The experiments were carried out with Franz diffusion cells. AG permeated was analyzed by HPLC.

Skin erythema was induced by UVB irradiation using an ultraviolet lamp which emitted in the range 290–320 nm with an output peak at 302 nm. The flux rate measured at the skin surface was 0.80 mW cm⁻². For each subject, the minimal erythema dose (MED) was determined preliminarily and an irradiation dose corresponding to the double of the MED was used throughout the study. Skin sites were exposed to UV-B irradiation and then 200 µl of ethosomal suspension were immediately applied to irradiated sites for three hours using a Hill Top chamber (Hill Top Research Inc., Cincinnati, OH). For each subject two skin sites were left untreated but exposed to UVB radiation (control), and two sites were treated with an aqueous solution of AG. At the end of the pretreatment the chambers were removed, the skin surfaces were gently washed with water to remove the formulations; the induced erythema was monitored using the reflectance spectrophotometer.

RESULTS

In vitro experiments showed that ethosomes are able to increase significantly the AG permeated through the human skin at the end of the experiment. To verify the AG-loaded ethosomes ability to reduce a UVB-induced erythema, we carried an *in vivo* experiment on human healthy volunteers. The results show that ethosomes were able to reduce the UVB induced erythema in a time 2-fold lower respect to the AG aqueous solutions. In particular 24 h after the UV-irradiation, skin sites treated with AG-loaded ethosomes showed no erythema, whereas in the sites treated with the free drug an erythema is still present. These findings showed that AG-loaded ethosomes may be employed as

topical protective treatment against UV radiation-induced skin damage.

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Microemulsions-loaded: evaluation of in vitro percutaneous permeation and anti-inflammatory activity

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INTRODUCTION

Ketoprofen is used both systemically and topically for the treatment of several diseases. The systemic administration of this drug, similar to other NSAIDs, presents gastrointestinal side effects, while the topical treatment is often limited by the poor percutaneous permeation through human skin. For this reason, the realisation of topical formulations, which are able to improve the percutaneous permeation of anti-inflammatory drugs, can be of particular importance for the success of topical therapeutic approaches.

The aim of this work was to investigate the potential application of highly biocompatible o/w microemulsions as topical drug carrier systems for the percutaneous delivery of anti-inflammatory drugs, i.e. ketoprofen. In particular, lecithin microemulsions were compared with various conventional topical formulations: w/o and o/w emulsions, and a hydrophilic gel.

EXPERIMENTAL SECTION

SL microemulsion was prepared by dispersing the lecithin (Epikuron 200) at 40 °C in the aqueous solution of ketoprofen (1 % w/v). The lipophilic phase made up of Myglitol 812 N was added under continuous stirring at room temperature. Then, n-butanol was added. The microemulsions were kept for 24 h at room temperature to allow the stabilisation of the colloidal phase. OA-SL microemulsion was prepared by adding OA in the hydrophobic phase. Various ketoprofen-loaded topical formulations were prepared to be compared with microemulsions, that is w/o and o/w emulsions, and a hydroalcoholic gel. Samples of healthy adult human skin (mean age 35±8 years) were obtained from abdominal reduction surgery. Stratum corneum and epidermis were isolated as elsewhere reported [1]. Skin permeation studies were carried out by using Franz-type diffusion cells. The receptor was filled with a 33 mM phosphate buffer (pH 7.4). The acceptor phase (100 ml) was withdrawn and analysed by HPLC. Skin acceptability was tested in human volunteers. A 48 h test for primary irritation was performed [2]. An occlusive patch bearing the formulation was applied to the outer part of the upper arm for 23 h. One hour after removal, skin sites were assessed and scored for signs of skin irritation [2]. Wistar rats were intradermally injected with a single dose of a suspension of *Mycobacterium butyricum* at the level of subplantar area of the right hind paw [3]. Various formulations were topically applied twice a day for five days, starting from the 7th day after inflammation induction. Anti-inflammatory activity was expressed as percentage of oedema regression.

RESULTS AND DISCUSSION

The ability of various topical formulations to delivery ketoprofen through the human skin stratum

corneum was reported in Figure 1. OA-SL microemulsion is characterized by the highest ketoprofen permeation, while the hydrophobic w/o cream showed the lowest permeation profile. The gel presents an intermediate permeation profile, probably due to the penetration enhancing effect triggered by the presence of ethanol as a component of the topical formulation. The presence of OA in the microemulsion formulation seems to poorly influence the permeation of ketoprofen through human skin.

The significant difference in ketoprofen percutaneous permeation between conventional formulations and the two microemulsions was probably due to various factors: i) size of oil droplets (smaller in the case of microemulsions); ii) a solubilizing effect of the drug elicited by the microemulsion lecithin matrix; iii) a penetration enhancer effect mediated by the lecithin component.

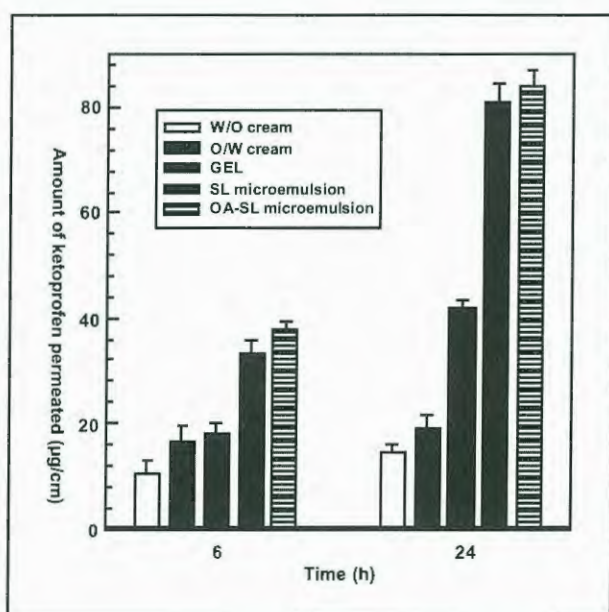


Figure 1 Permeated ketoprofen through the human skin from various topical formulations. Each value is the mean value of three different experiments $\pm$ SD.

The potentiality of a topical formulation to be used as a transdermal drug delivery device should be evaluated also in terms of tolerability. Microemulsion formulations showed the highest skin tolerability. It is interesting to note the higher tolerability of OA-SL microemulsion with respect to OA aqueous dispersions containing the same amount of OA (data not reported). The incorporation of OA in the microemulsion structure and the impossibility to strongly perturb the stratum corneum skin lipids could be the reason for the reduced skin irritation.

The increased percutaneous permeation of ketoprofen when delivered by microemulsion corresponds to an improvement of the anti-inflammatory activity of this drug. In fact, in vivo experiments on rats showed that a ketoprofen-loaded SL microemulsion was much more effective in reducing the

induced oedema than ketoprofen vehicled in other topical formulations (Table 1).

Table 1 <i>Anti-inflammatory activity of various topical formulations containing ketoprofen as percentage of the oedema regression</i>	
Sample	Oedema Regression (%)
O/W cream	3.9 ± 2.7
W/O cream	-15.4 ± 3.1
Gel	8.5 ± 2.7
SL microemulsion	25.3 ± 3.6
OA-SL microemulsion	33.7 ± 5.1

In conclusion, the percutaneous absorption of ketoprofen from topical formulations depends both on the mean size of the oil droplets and on the vehicle constituents. In fact, a suitable choice of the components is essential to minimise the irritancy effect and to determine an improvement of both the percutaneous permeation and the anti-inflammatory efficacy of the drug.

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Niosomes for topical application. *In vitro* percutaneous permeation and bilayer-inducing perturbation properties

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The basic constituents of niosomes are surfactants that undergo self-aggregation into bilayer structures when dispersed in water. Niosomes can entrap various kinds of active ingredients. Niosome constituents can be integrated into the skin, thus altering the intercellular lipid material of the horny layer [1]. The aim of this work was the evaluation of the possible correlation between the capability of niosomes to mix with bilayer structures and the percutaneous permeation of a fluorescent marker through the human stratum corneum from various niosome formulations.

MATERIALS AND METHOD

Niosomes were prepared by the thin layer evaporation method. Various Span and Brij were used to prepare different niosome formulations. Cholesterol was added (20 % mol) to obtain the niosomes. Samples of healthy adult human skin (mean age 35±8 years) were obtained from abdominal reduction surgery. Skin permeation studies were carried out by using Franz-type diffusion cells. Human skin was mounted with the stratum corneum side up. Occlusive conditions were used. The receptor was filled with 33 mM phosphate buffer (pH 7.4). The acceptor phase (100 µl) was withdrawn and spectrofluorimetric analysis was carried out. The various samples (40 µl containing ~2 mg of lipid material) were sealed in an aluminium pan and submitted to DSC analysis. The calorimetric experiments were performed on a Mettler DSC12E equipped with a Haake D8-G. The detection system was a Mettler Pt100 sensor. The reference was an aluminium pan containing 40 µl isotonic phosphate buffer. Various samples were submitted to heating and cooling cycles in the temperature interval 20-60 °C at a scanning rate of 1°C/min.

RESULTS

Brij 92 and 96 determined a fluidification and a depression of the main transition peak of DPPC biomembranes. These two non-ionic surfactants determined thermotropic changes similar to those caused by oleic acid. This evidence suggested that niosomes, made up of either Brij 92 or Brij 96, may behave, similarly to oleic acid, as colloidal penetration enhancers by favouring the transdermal adsorption of topically applied substances. The limiting factor in the transdermal enhancing properties of niosomes may be represented by the mixing rate of non-ionic surfactants with skin lipid components. Brij 30 determined a phase segregation of the DPPC bilayer, rather than a fluidification effect. These findings show that the thermotropic effect is modulated by two factors in the case of Brij: i) the type and length of the alkyl chain, ii) the length of the polyoxyethylene chain. In the case of niosomes made up of Span, the effect on DPPC vesicles is modulated by the alkyl chain. In fact, Span 40 and 60 elicit a phase segregation but do not fluidize the DPPC bilayers. While Span 20 signi-

ificantly lowers the transition temperature of DPPC bilayers (fluidising effect) and also elicits a loss of co-operativity due to a phase segregation.

The percutaneous permeation of calcein from various noisome colloidal suspensions through human skin stratum corneum was carried out to evaluate a possible correlation with the thermotropic effect on bilayers. Brij 96 niosomes ensured the highest The percutaneous permeation of a hydrophilic molecule, i.e. calcein, from niosomes seems to be correlated to the fluidization effect on the bilayer structure rather than to the segregation of ordered lipid phases.

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Evaluation of cosmetic efficacy of oleuropein

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Oleuropein, phenolic compound derived from olive leaves and oil, is known to possess several biological properties, many of which may be attributed to its antioxidant and free radical-scavenger activity. Nevertheless, up to now, cosmetic activity of this molecule has not been extensively investigated. The aim of this work was to evaluate the cosmetic properties of oleuropein against induced UVB erythema. To this aim, emulsion, gel and lotion containing oleuropein were prepared, applied and evaluated on healthy volunteers undergone to UVB irradiation to investigate its protective and/or lenitive activity. Protective effect was assayed by application of topical preparations before irradiation instead of the lenitive effect was evaluated after erythema induction. Vitamin E is used as reference compound. Our study was carried out by using non invasive techniques to assess specific skin parameters: barrier function (Tewameter, Courage & Kazaka), color (Chromameter Minolta 200), and microcirculation (Periflux, Perimed). The study allowed us to point out the lenitive property of oleuropein, opening the way to further trials to deepen our specific knowledge about this natural molecule, which could be used in association with other active ingredients in cosmetics to repair UV damages.

Tewameter TM300 vs tewameter TM210 - is there really an evolution?

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Trans-Epidermal Water Loss (TEWL) is a major representative of the barrier function, in normal or pathological conditions. Systems generally known by "evaporimeters" are frequently used to quantify this variable. But limitation related to the instruments reproducibility still constrains its use. Innovation in TEWL measurement is permanent and recently, the new Tewameter TM300 was proposed as a clear progress in the field. In this study the authors compare the TEWL results obtained with the new TM300 and the old TM210 in order to confirm the accuracy and reproducibility conditions of these two devices.

TEWL from healthy volunteers (n=15, both gender, 21-45 y.o.) was obtained by Tewameters TM300 and TM210 (CK Electronics, Germany). The time to stabilization, the reproducibility and the repeatability was measured in order to compare the instant measures behaviour. POST experiments were also performed with a 24h of occlusion period. Continuous data from POST experiments was analysed by a compartmental model and $t_{1/2\text{evap}}$ was evaluated. Non parametric statistics included the Wilcoxon sign rank test, and a significance level of 0,05 was adopted.

Results show that the time to stabilization significantly decreases with TM300. The reproducibility of the TM300 is slightly higher than TM210 mainly because it's a more sensitive device. However these differences are not statistically significant and, under these conditions, do not represent a worst result for the TM210 unit. The $t_{1/2\text{evap}}$ dynamical measurements show significant differences. TM300 shows faster decay rates than TM210, probably due to a faster time of response to water changes. Finally, these results suggest that the new TM300 is a clear evolution of its predecessor for the introduction of the automated calibration routine, ease of operability, and stabilisation time, reinforcing its precision and reproducibility.

Modelling TEWL desorption curves: a new practical approach for the quantitative *in vivo* assessment of skin barrier

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The cutaneous *in vivo* water content is a well known conditionant of the skin physiology and pathophysiology, and it is the result of the dynamic water balance established between the deep and the superficial skin structures. The mathematical modelling of the transepidermal water loss (TEWL) curves that result from a plastic occlusion stress test (POST) is a useful tool in the study of this delicate equilibrium. The objective of the present work is to test the discriminative capacity of this model by studying variations in the cutaneous barrier that are the result of insults inflicted to the skin or of differences in three distinct anatomical regions.

Nine volunteers participated in this study after informed consent. In all subjects one site was marked in each volar forearm: site A was the untreated control and B the treated site. On the treated site one of three different insults to the skin barrier were performed: tape stripping, lipid extraction with ether: acetone or skin surface biopsy. Both sites were then submitted to a POST, involving the application of an occlusive patch for 24 hours, after which the desorption curves were recorded. Data points were continuously registered for 30 minutes. The same procedure was applied to the study of anatomical differences. The occlusion and measurements were performed in the volar forearm, in the leg and in the wrist. The mathematical model was adjusted to the data points using a specially modified simplex routine and the ADAPT software written in Fortran. Calculated parameters considered relevant to the study were $t_{1/2\text{evap}}$ (evaporation half-life) and DWM (dynamic water mass).

Results indicate differences in the parameters obtained in the control and treated sites, which suggests differences in the water dynamics after the damage was inflicted and shows that the method is valid for the objectives proposed. There were also significant differences in the parameters obtained in the wrist, volar forearm and leg, which indicates that the method is also sensitive to variations in skin thickness and anatomy.

Studying the burn injury healing process by transcutaneous indicators

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Burn wound healing assessment by transcutaneous techniques has grown motivated by the ease of use and capacity to provide fast, quantitative non-invasive readings. In the present study the authors characterise the evolution of thermal burn lesions, after auto-grafting, in order to identify the most useful indicators in the wound lesion process.

Ten human volunteers (both gender, 25-62 years old) selected from the hospital burn unit were included after informed written consent. All patients suffered autologous split-thickness skin grafting. Biometrical follow-up included TEWL (Tewameter TM210, CK), microcirculation (LDF) and transcutaneous (tc) pO₂ measurements from week (W)8 post-surgery until W52. Both grafted (GL) and donor (DL) areas were assessed and the respective contra lateral (normal) areas used as control. A POST methodology was also applied with a 24H skin occlusion in order to test the epidermal water dynamics with a mathematical bi-compartmental model previously developed. Non parametric comparisons were performed using Mann-Whitney and Wilcoxon statistical tests. The significance level was 0,05.

Results show that local blood flow normalizes earlier GL (W6) than in DL areas (W8). No differences between GL and DL were found for tcPO₂ measurements. However, full functional recovery occurs earlier in DL, while for GL, statistically significant differences ($p < 0.05$) between the lesion and the control area are still present in W26. Barrier function evolution also reflects different evolutions in the healing process. In GL the barrier is re-established after W 8 while in DL, full re-establishment is achieved 1 year after grafting. These results help to characterize different evolutions for different trauma origins, and demonstrates the usefulness of these indicators to follow-up the cutaneous wound healing process.

Development of quali-quantitative methodologies for the assessment of the cutaneous wound pathophysiology

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Transcutaneous indicators such as transepidermal water loss (TEWL) laser-doppler flowmetry (LDF) and transcutaneous gases (tcpO₂ in particular) have been shown to be extremely useful to assist clinical evaluation, allowing new insights into the mechanisms involved in vascular pathology. A close relationship between transcutaneous flow variables and other skin functional parameters is often suggested but poorly explored, and these may be important to better understand the complex wound healing pathophysiology. Recent studies suggesting that TEWL may also be influenced by the local flow conditions, centres again the interest into these variables, helping to search for better and more precise ways to quantify the mechanisms involved. The present study investigates the relative influence of the local flow conditions on multiple aspects of the wound healing process.

Data was collected from several patients (n=11), selected from the burn unit and vascular medicine services. after informed written consent (18 to 54 y.o.). Cutaneous microcirculation (Laser Doppler Flowmetry, Oxford Optronix, UK), partial tensions of O₂ and CO₂ (TINA, TCM3, Denmark), TEWL and skin biomechanical behaviour (Tewameter TM300 and Cutometer SEM575 respectively, from CK electronics, Germany) were registered in basal conditions and during the healing process of different cutaneous wound conditions. Descriptive statistics and non-parametric tests were executed and the significance level of $p < 0.05$ adopted.

Results clearly confirms that (laser Doppler) flow, tcPO₂ and TEWL are true indicators of the healing process in its different phases. tcPO₂ correlates well with the flow profile evolution, but no statistical correlation with flow is found for the other skin variables. In any case, many of these can be used as objective methods to follow-up the process and the authors propose a systematic qual-quantitative scale that may help to compare results.

Non-invasive methods for tests on the scalp

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NOT RECEIVED

On the influence of the applied amount of sun protection products on their efficacy and photostability

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NOT RECEIVED

THE EUROPEAN CHEMICAL INDUSTRY CONFRONTING IN BRUXELLES

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Recent studies of the European Commission highlighted the constant loss of industrial competitiveness Europe is going through because of its poor innovation: the EU research is fragmented, the intraEU projects are still insufficient and few are the institutions producing "knowledge". Hence it is necessary a huge investment in the R&D activities which implicates:

- a better R&D integration with project, design, production, marketing and customer support.

As recently declared by Ezio Andreta, Director of the DG Industrial Technologies Research of the European Commission: "a better integration of human resources and technology will lead to the creation of a new living frame able to connect directly the consumers to the innovation". Therefore it is necessary that the industries rethink their own value in terms of knowledge and not in terms of mere material property.

So investments aimed at creating a synergic relation on formation of the employees at various levels, will be necessary in such a way that human resources get the proper multidisciplinary skills apt to support the innovation in the whole working process.

In this way only the European industries could be able to compete with the emerging Asiatic industrial world.

Does the new European regulation's proposal for the chemical industry called R.E.A.C.H. (Registration, Evaluation, and Authorisation of Chemicals") move in this direction?

The answer will be negative unless its last draft, approved by the European Parliament on October 29, 2003, is modified (Fig.1).



Fig. 1 A view of Bruxelles Parliament

In fact the present equilibrium between rules and bureaucracy is still strongly precarious and onerous especially for the small-medium enterprises (SMEs) destined to loose those resources necessary to make them knowledge based enterprises. For knowing the critical opinion of the European chemical industries involved in the R.E.A.C.H., on March 4 at the Bruxelles European Parliament, it has been held a public forum promoted by the European Popular Party, represented by honourable members: Werner Langen (Germany), Francesco Fiori (Italy) Ria Oomen-Ruijten (Holland), Alejo Vidal-Quadras Roca (Spain) (Fig. 2).

The aim of this forum was to better evaluate the impact that this regulation could have on all the operators involved: industries, researchers and institutions.



Fig. 2 From the left: Alejo Vidal-Quadras Roca MEP (EPP-ED, Spain), Vice-President of the European Parliament, Ria Oomen-Ruijten MEP (EPP-ED, Netherlands), Werner Langen MEP (EPP-ED, Germany) and Mario Schwetz, Representative of the EPP-ED Group in the European Parliament.

This new regulation's proposal that will replace more than 40 directives and rules, at present in force at community level, is of great importance since it states rules about the whole living cycle of chemical substances, dangerous and non dangerous.

The R.E.A.C.H. requires to both manufacturers and importers the registration and the evaluation of about 30.000 chemicals in the next 10-15 years.

Hence, the key element of this evaluation would be represented by the priorities that will be assigned from a scientific and practical point of view. First of all, it will be necessary to identify such priorities carefully evaluating the quantity of chemicals/products imported and the risk/benefit of each chemical product on human health and on environment.

In order to find a solution, 16 industrial experts have been invited in Bruxelles to represent the needs of both SMEs and big companies, producers and importers of chemical products (Fig. 3). All the speakers asserted the necessity of this regulation to uniform the European productions to a unique standard, able to reduce the environmental impact and to protect human health.

But it is necessary that the present regulation's

draft is changed in such a way that the rules contained are made easier and less expensive to apply.

Since the first draft of the R.E.A.C.H. results still too onerous for the SMEs and for the industries operating in fine chemicals and specialties, it is indispensable to pursue the sustainable development, paying attention to the competitiveness of the European industries in a more and more globalized world. Hence the necessity to apply the better regulation's principle, encouraging and sustaining the scientific research.

These results will be possible only if the R.E.A.C.H. would make the chemical substances' selection and evaluation on the base of the risk/benefit principle of the actives and not on the mere quantity produced.

To achieve these goals, it is required the establishment of an European Agency as the sole responsible of the chemical products assessment.

This Agency, in which experts from the Member States should operate, will express the European professional super partes judgement.



Fig. 3 Some of the experts invited Form the right: Werner Langen MEP EPP-ED, Willem van Loo, CEMBUREAU Dr. Cristianus de Rooij, Solvay, Pierfrancesco Morganti, MAVI SUD S.r.l., Dr. Bruno Stephan, FECC, and Mario Schwetz, EPP-ED.

These are the conclusions of the experts invited. The Agency, totally independent, should be responsible for the coordination of the technical and scientific resources that Member States will

place at its disposal and supported by :

- 1 committee for the Risk Assessment;
- 1 committee for the Socio-economical Analysis;
- 1 committee for the Member States Representatives;
- 1 forum for the Exchange of Information or Enforcement;
- 1 Secretariat

The experts urged this Agency not to be only a mere secretariat collecting data as foreseen by the first draft of the R.E.A.C.H., but a real institution with decisional power.

The regulation's first draft states also that producers and importers of chemical substances and down stream users should provide for their own chemical safety assessment.

For the first time the assessment's responsibility, consisting on using and manipulating chemical substances in such a way that human health and environment are safe, is passed directly to the categories above mentioned. The duty to reduce the risk is therefore identified in the safety assessment.

Hence the duty to give to the EC Member States all the information about the chain production or at least the following documents: a Safety Data Sheet in conformity with the directive 91/155/CEE; a Chemical Safety Report; the number of registration and authorization and all other information useful to define a correct risk management.

In this information system manufacturers and distributors are involved also.

The most revolutionary aspect of the R.E.A.C.H. is the change of the responsibility passing from public authorities to producers, importers and users of chemical substances. Of course this change requires a careful attention based on the proportionality's principle.

In fact the proportionality's principle is undoubtedly the pillar of the European Legislation and consists on 3 fundamental elements:

1. the measures must be suitable and effective

for the achievement of a legitimate objective;

2. the measures must be necessary to achieve the objective and must represent the least restrictive alternatives available;
3. the measures must be reasonable and not disproportionate for the achievement of the final objective. This third element is generally renowned as basilar for the "proportionality" *stricto sensu*.

The European Community Jurist (ECJ) is generally strict in applying the proportionality's principle and very careful about the fundamental principle of free circulation of goods, services, capitals and people.

The norms adopted must be less restrictive about these principles considered basilar.

In conclusion, with the R.E.A.C.H. proposal the fundamental rights of property will be at risk, as, for example, when limitations on chemical substances production and trade are applied.

These limitations deeply interfere with complexity of activities that constitute the work core of producers, importers and final users. Moreover, they interfere also with the profession rights protected by art. 5 of the European Charter of Human Rights.

These are some of the final considerations reported by the 16 experts invited in Bruxelles, resulting from a careful examination of the problems the R.E.A.C.H. could create especially for the European SMEs that at present are suffering from the commercial incoming of the Asiatic companies, such as the Chinese ones.

They urged to consider chemical industries no more as a cause of the environmental pollution but as a primary resource for progress and well-being.

In fact the industrial segment represents only 1% of the human activities producing soil degradation (Fig.4) while the progress had in pharmaceutical chemistry, with the production of even more effective drugs, reduced drastically man mortality.

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