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4

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International Society of Cosmetic Dermatology



ISCD
International Congress
Wellness and Beauty outside in:
East & West working together

Rome - October 21-23, 2009

PROGRAMME and ABSTRACTS

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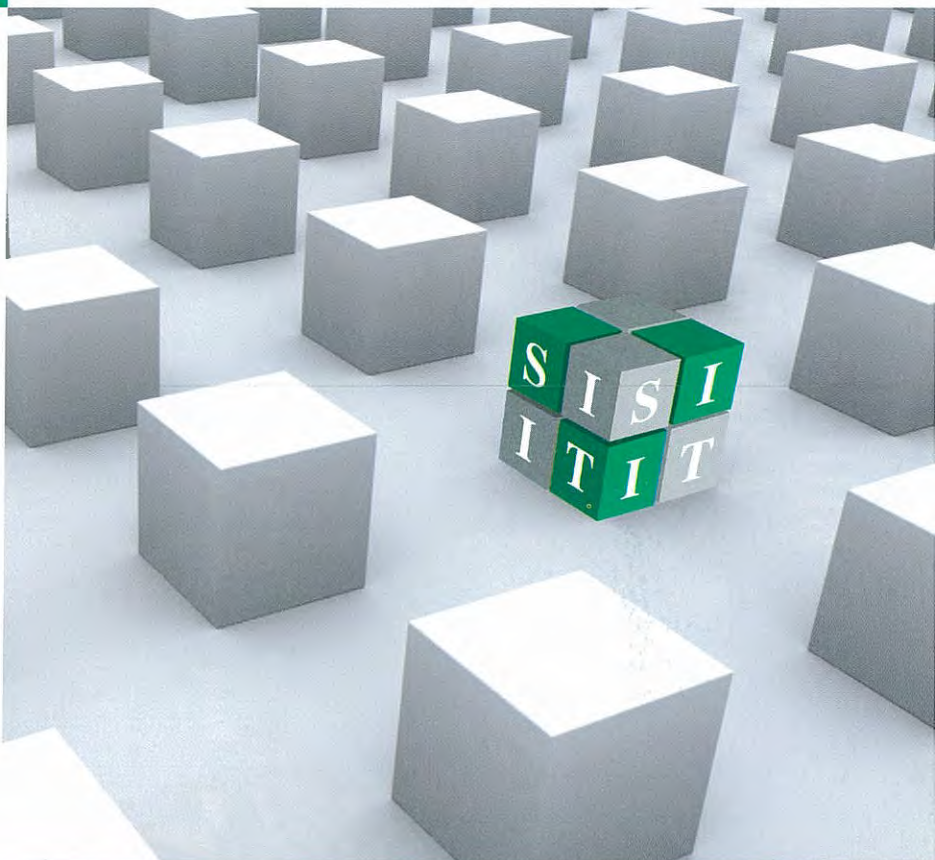
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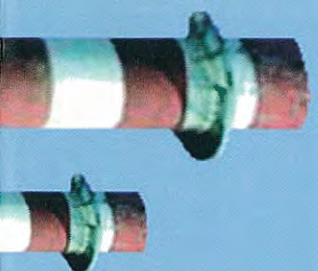
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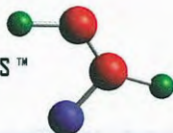


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**IX ISCD INTERNATIONAL MULTIDISCIPLINARY
CONGRESS**

**Wellness and Beauty Outside In:
East & West working together**

Rome, 21-23 October 2009

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Welcome from the Congress Presidents

Today, formulating cosmetic products and diet supplements performing more than one function are more likely to succeed in the marketplace. In fact, multifunctional products are becoming increasingly popular for three key reasons: increasing consumer expectations, maturing technology and expanding marketing demand. This is the reason of increasing demand for *cosmeceuticals*, combining the aesthetic appeal and benefits of traditional cosmetic products with therapeutic components. All *cosmeceuticals* are multifunctional because they try to have both cosmetic and therapeutic properties, without being classified as drugs or medical devices.

This new approach to formulate innovative products, helps the development efforts focused and leads to more efficient cosmetic and diet supplements. At this purpose, many industry professionals together with dermatologists, biologists and pharmacologists agree that there is a need for a better understanding and definition of the cosmetic products's mechanism of activity. And this important topic will be discussed in a special round table of the Congress.

The challenge of cosmeceutical formulation is, in fact, to evaluate the feasibility of combining active compounds and vehicles to create products that yield the therapeutic benefits.

For these reasons new biological and clinical techniques are available that have demonstrated how substances such as water and petrolatum once though to be inactive may alter the structure and function of skin. Thus, the necessity of multidisciplinary studies where cosmetic chemists work together with dermatologists, biologists, pharmacologists and other scientists involved in Cosmetic Dermatology, to demonstrate the efficacy and safeness of cosmetics products.

However, knowing deeply the cosmetic mechanism of action and how the consumer will use the product and how the product will be dispensed from the package, can aid in creating formulations that maximize the therapeutic benefits of actives.

Thus, the efficacy of cosmetic products represents the key lecture of the Congress.

Therefore, a big space has been reserved to speakers from Academia and Industry introducing the NICE concept-in which the Nervous, Immune, Cutaneous, and Endocrine system, i.d. NICE, all work together to activate our *mind-body* connection. This *mind-body* skin care represents a bridge between the ancient Chinese culture based on *yin* and *yang* holistic activity and the West more pragmatic activity.

Combining East and West way of thinking and living will surely ameliorate the quality of our Future life.

Hong Duo Chen M.D.
President of the Congress

Rodolfo Paoletti M.D.
President of the Congress

Welcome from the ISCD

Cosmetics and Functional Foods are, today, effective, safe and meet consumer's demand for high efficacy.

They fulfil these requirements for both the raw materials and the active ingredients used, and have a low rate of side-effects because of the numerous tests manufacturers carry out with great care.

At this purpose, the innovation has continuously given strong support to clarify the physiological relationship and mechanism of action of the ingredients used in order to increase the efficacy and safety measures of both Cosmetics and Functional Foods.

Thus, with claims that can mirror the effect of injectable products, like botulin toxin, hyaluronic acid and collagen, the so-called cosmeceuticals, attract consumers seeking for high-level performance, and hoping to save on a trip to the dermatologist or the plastic surgeon.

Unfortunately the actual EU regulatory status do not classify the cosmetics' mechanism of action; so that many products available on the market are borderline between drugs and medical devices.

However, in terms of products, the latest innovation in the cosmetic field is the development of active cosmetics based on the NICE concept, in which the Nervous, Immune, Cutaneous and Endocrine systems work together to activate the body skin physiology. An entire session will be dedicated to this interesting topic.

For these reasons, special round tables have been organized with expert scientists to talk about the mechanism of activity the cosmetic products have and to verify the means necessary to control their efficacy and safeness. Finally special room will be dedicated to highlight the problem of the nano-structures used in Cosmetic Dermatology.

With the functional approach, entering today also in the contest of nutraceuticals, products became diversified and started to claim a multitude of new biologic activities.

The modern concept of Quality of Life (QoL) and the competitive environment pushed manufacturers to promise more and more to consumers, and to develop Cosmetics and Functional Foods of ongoing better quality and higher efficacy.

This 9th World Congress of the International Society of Cosmetic Dermatology (ISCD) has been carefully thought to give the opportunity to scientists coming from Industries and Academia to report and discuss the obtained results of the latest studies proving and sustaining the efficacy of the new mind-body skin care activity... from outside in.

Being sure you will find this Congress a source of an innovative biologic and holistic experience, I welcome you to Roma.

*Pierfrancesco Morganti Ph.D.
ISCD President and Secretary General*

Congress Opening Remarks

Today, we regard dermatology as one of the most inspiring arena of clinical medicine. Some of the sub-specialities in dermatology are booming, among which cosmetic dermatology being one of the most prominent. The flourishing of cosmetic dermatology comes not as unexpected. It is human nature to seek nice and healthy skin, for self-content and appraisal. The economical development has enabled more and more people affordable for their care of the skin. Most importantly, with the advent and help of molecular medicine and other basic sciences, cosmetic dermatology has been pushed far beyond the era when it was regarded merely as a luxurious makeup. Lasers, new formulations, and various well characterized functional ingredients have revolutionized the treatment options for many cosmetically related skin problems, such as pigmentary disorders, vascular disorders and skin aging. In addition, some traditional methodology and therapies are still playing important role in cosmetic dermatology, while in up-to-date approaches. For example, licorice has long been used in traditional Chinese medicine to treat some pigmentary disorders, sandalwood has been used as an anti-aging agent, to name a few. Now we know through modern technology, that some of the characterized ingredients in herbs play main roles in their clinical efficacy. There is a huge reservoir of Chinese medical herbs that are worthy of exploring. Skin is the biggest, while not an isolated, organ of human body. Dysfunction of some internal organs may have manifestations on skin, and vice versa. Different studies have demonstrated that stress delayed the rate of recovery of skin barrier function to certain extent. Melasma is an acquired circumscribed facial hyperpigmentation commonly seen in Asian women. Dysregulated hormones play very important roles in the pathogenesis of the disease. In addition, a number of clinical observations have shown that when the melasma patients are physically exhausted or emotionally distressed, the facial skin hyperpigmentation becomes more obvious. We recently found an intimate contact between the intraepidermal nerve fibers and melanocytes in human skin, a substantial proof that nervous system links to skin pigmentary constituents. Coincidence or not, the psycho-neural impact on melasma was described as early in 1742 in an ancient textbook of traditional Chinese medicine entitled "The Golden Mirror of Medicine". It says that "Dark dyschromia comes to face due to the blood deficiency and malnutrition resulting from anxiety and depression". In another of our study on lichen simplex chronicus, a psychodermatological condition exacerbated by stress or anxiety, we found close contact of nerve fibers with Langerhans cells in the epidermis. One of the most prominent features of traditional Chinese medicine is the emphasis on holism. In the view of traditional Chinese medicine, skin is a mirror that reflects the state of health. Oriental philosophical thinking and modern studies allude that the nervous, immune, cutaneous, and endocrine systems (N.I.C.E) - all work together to internally influence physiology of the skin. The N.I.C.E concept is emerging. Thanks to the thoughtful planning and organization by Prof. Morganti and other friends, the present congress covers a wide variety of interesting topics concerning multi-facets of cosmetic dermatology. Environmental influence on wellness and skin health is an eternal subject that can never be overlooked; evaluation of efficacy and safety of both natural and synthetic cosmetic products is a constant task for dermatologists, pharmacologists, other scientists and relevant regulatory bodies; novel technology such as nano-materials and lasers is pushing the development of cosmetic dermatology at an unprecedented speed; harmonious interchange of skin care culture between the East and the

West is expected to go much farther beyond the skin, but to the integration of the different views on wellbeing.

The last episode of the congress will be a relaxing and exciting event-tasting of wine, coffee and tea. Whatever in your cup, dear friends, let's make a big toast and a good wish for the success of the 9th ISCD International Congress in Rome.

*Hong-Duo Chen, M.D.
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A special thanks goes to the Agriculture Council of Lazio Region and to ARSIAL for the special contribution given in sponsoring this Congress.

SCIENTIFIC PROGRAMME

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SESSION	I
	<p>ENVIRONMENTAL INFLUENCES ON WELLBEING</p> <p>CHAIRMEN: <i>Hong Duo Chen (PRC) - F. Franchina (I) - P. Morganti (I)</i></p>
8.30	<p>Introductory remarks <i>P. Morganti (I), Hong Duo Chen (PRC)</i></p>
9.00	<p>Public - private connections in support of innovation <i>R. Menia (I)</i></p> <p style="text-align: right;"><i>pag. 139</i></p>
9.15	<p>Sustainable products: the innovation strategy for the European chemical industry <i>A. Collina (I)</i></p> <p style="text-align: right;"><i>pag. 140</i></p>
9.30	<p>Toxicity indexes in the food production chains: an innovative approach <i>C. Frazzoli, R. Dragone, L. Campanella and A. Mantovani (I)</i></p> <p style="text-align: right;"><i>pag. 141</i></p>
9.45-10.00	<p>DISCUSSION</p> <p>CHAIRMEN: <i>L. Campanella (I) - S. Ma (PRC)</i></p>
10.00	<p>Whitening agent from natural plant <i>S. Ma (PRC)</i></p> <p style="text-align: right;"><i>pag. 142</i></p>
10.15	<p>Photosensor of ecopermanence and its application to cosmetic Pao determination <i>L. Campanella (I)</i></p> <p style="text-align: right;"><i>pag. 143</i></p>
10.30	<p>New environmentally friendly products for a better way of living <i>G. Zappelli (I)</i></p> <p style="text-align: right;"><i>pag. 144</i></p>
10.45	<p>Chemoprevention of photoaging and photocarcinogenesis by soybean isoflavone genistein <i>H. Wei (USA), Xing-Hua Gao (PRC)</i></p> <p style="text-align: right;"><i>pag. 145</i></p>
11.00-11.15	<p>DISCUSSION</p>
11.15-11.30	<p>COFFEE BREAK</p>

SESSION

II

**COSMECEUTICALS & NATURAL COSMETICS
Part I**

Natural cosmetic: a technical reality or an oxymoron?

CHAIRMEN: *L. Andreassi (I) - M.C. Rabagliati (I)*

11.30	New bio-chemicals from sea to save the skin <i>M.L. Ciavatta (I)</i>	<i>pag. 146</i>
11.45	Natural and/or chemical compounds? First of all skin friendly <i>L. Andreassi (I)</i>	<i>pag. 148</i>
12.00	Food to bettering the way of living: the involvement of Lazio Region <i>M.C. Rabagliati, G. Somma (I)</i>	<i>pag. 149</i>
12.15	Protective effects of green tea extracts on photoaging and photoimmunosuppression <i>Hong Duo Chen, Yuanhong Li, Yan Wu (PRC)</i>	<i>pag. 150</i>
12.30	Effective Cosmetic Treatments: the importance of Spa environment <i>B. Scorza (I)</i>	<i>pag. 151</i>
12.45	Molecular Design and sustainable development <i>S. Viticoli (I)</i>	<i>pag. 152</i>
13.00-14.00	BRUNCH CHAIRMEN: <i>J. Arct (P) - A. Chianese (I)</i>	
14.00	Physiological modulators <i>U. Cornelli (USA)</i>	<i>pag. 153</i>
14.15	Polyphenols recovery from olive vegetation wastewater <i>M. Parisi, A. Chianese (I)</i>	<i>pag. 154</i>
14.30	Lipoic acid: a natural antioxidant compound <i>G. Orlandi (I)</i>	<i>pag. 155</i>
14.45	Natural compounds for effective cosmetics <i>J. Arct, K. Pytkowska (P)</i>	<i>pag. 156</i>
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CHAIRMEN: *C. Gelmetti (I), S. Viticoli (I)*

15.15	Safe and skin friendly cosmetics for sensitive skin: is lanolin included? The dermatologist opinion <i>C. Gelmetti (I)</i>	<i>pag. 158</i>
15.30	Lanolin - Dispelling the myth of lanolin allergies <i>W. Cannon (UK)</i>	<i>pag. 160</i>
15.45	Bio-functional textiles facing the future by the NICE concept <i>P. Morganti (I)</i>	<i>pag. 161</i>
16.00	Unique and unexpected cosmetic applications of an innovative Chinese spice extract <i>C. Artaria, G. Appendino (I)</i>	<i>pag. 162</i>
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16.30-17.00	SESSION CLOSURE	
17.00-20.00	WELCOME CEREMONY (Protomoteca del Campidoglio)	

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Part II	
<i>Cosmeceuticals: are they a scientific approach? Scientific or marketing necessity?</i>	
CHAIRMEN: <i>B. Berra (I) - Y. Li (PRC)</i>	
8.30	Cosmetic itinerary: an innovative educational program for future cosmetologists <i>E. Mignini (I)</i>
	<i>pag. 165</i>
8.45	Cosmeceuticals for Asians who are living in the tropics <i>R.I.S. Tranggono (Indonesia)</i>
	<i>pag. 167</i>
9.00	A comprehensive approach to the treatment of acneic skin: formulation aspects and clinical results <i>F. Cuppo, M. Terno, D. Ganassini (I)</i>
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9.15	New strategies for skin barrier and microcirculation recovery <i>G. Guglielmini, E. Berardesca (I)</i>
	<i>pag. 169</i>
9.30	Science based cosmetics: the way into the future <i>K. Lintner (F)</i>
	<i>pag. 171</i>
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CHAIRMEN: <i>G.P. Littarru (I) - P. Perego (I)</i>	
10.00	Antioxidant add protection to a broad-spectrum sunscreen <i>Yuanhong Li, M. Matsui, Y. Wu, Xing-Hua Gao, Hong Duo Chen (PRC)</i>
	<i>pag. 172</i>
10.15	Microalgae to save health, beauty and environment <i>P. Perego (I)</i>
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10.30	Stem cells from plants for cosmetic and oral applications <i>I. Montañó, D. Schmid, C. Schürch, P. Blum, F. Zilli (CH)</i>
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10.45	Coenzyme Q₁₀ and skin protection <i>G.P. Littarru (I)</i>
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11.15-11.30	COFFEE BREAK

10.30-11.30	PRESS CONFERENCE The NICE concept: a bridge between West (biological based) and East (mind-body based) skin care culture.
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SESSION	III	
		CHAIRMEN: <i>C. Anselmi (I) - X.H. Gao (PRC)</i>
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	<i>A. Braca, B. Perfetto, A. Melito, M. Carteni, M.A. Tufano (I)</i>	<i>pag. 177</i>
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CHAIRMEN: <i>S.Ma (PRC) - R.A.A. Muzzarelli (I)</i>		
14.00	Chitin Nanofibrils and microparticles: no connection with allergy and asthma <i>R.A.A. Muzzarelli (I)</i>	<i>pag. 185</i>
14.15	Clinical efficacy of innovative cosmeceuticals based on Chitin Nanofibrils <i>P. Morganti, G. Fabrizi, P. Palombo G. Morganti (I)</i>	<i>pag. 187</i>
14.30	Chemico-physical & toxicological properties of a natural raw material: the Chitin Nanofibrils <i>F. Carezzi (I)</i>	<i>pag. 188</i>
14.45	Challenges on safety assessment of cosmetic products containing nano-material <i>L. Manzo, E. Roda, R. Butera, T. Coccini (I)</i>	<i>pag. 189</i>
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15.30	A new, biologically compatible physical sunscreen, with skin firming properties <i>L. Brucato (I)</i>	<i>pag. 191</i>
15.45	Nanotechnology in cosmetics and sunscreens: is there a health risk? <i>G.J. Nohynek (F)</i>	<i>pag. 192</i>
16.00	Greening with Silicones <i>T. O'Lenick, K. O'Lenick (USA)</i>	<i>pag. 193</i>
16.15	Responsible development to ensure health and environmental safety of manufactured nanomaterials <i>A. Marconi (I)</i>	<i>pag. 194</i>
POSTER	Chitin Nanofibrils: in vitro effects on wound repair <i>B. Perfetto, A. Melito, E. Albano, A. Baroni, P. Morganti & MA. Tufano (I)</i>	<i>pag. 196</i>
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CHAIRMEN: <i>G. Bertoja (I) - P. Morganti (I)</i>		
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8.45	Establishment and change of NICE approach <i>J. Hosoi (F)</i>	<i>pag. 200</i>
9.00	A new approach to antiaging technologies - biology, technology and psychology <i>P. Matts (USA)</i>	<i>pag. 201</i>
9.15	Cosmetic science in skin ageing: achieving the efficacy <i>P. Morganti (I)</i>	<i>pag. 202</i>
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10.30	Anti-inflammatory and retinol-like activities coming from nature <i>F. Pflücker, C. Carola, R. Graf, H. Epstei², C. Wirth (D)</i>	<i>pag. 205</i>
10.45	Soft vesicular systems for efficacy and safeness in cosmetic products <i>E. Touitou (Israel)</i>	<i>pag. 206</i>
11.00	Skin bleaching agents in legal and illegal market. The use of some depigmenting cosmetics out of the rule, illegally imported and consumed in Italy from foreign people <i>A. Morrone (I)</i>	<i>pag. 207</i>
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THE PROTECTION OF INTELLECTUAL PROPERTY

*To expand, strengthen and protect your presence
on the global market*

CHAIRMEN: *L. Andreassi (I) - A. Chianese (I)*

11.30	TRADEMARK: for promoting your image: First Part <i>A. Morganti (I)</i>	<i>pag. 209</i>
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12.00	PATENT: for protecting your innovation <i>S. Borrini (I)</i>	<i>pag. 210</i>
12.15	TRADEMARK LICENSE: for enhancing your position on the international market <i>G. Rubino (I)</i>	<i>pag. 211</i>
12.30	INFRINGEMENT: are you sure you know what counterfeiting is? <i>P.L. Roncaglia (I)</i>	<i>pag. 212</i>
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	CHAIRMEN: <i>P. Morganti (I) - R. Paoletti (I) - L. Wei (PRC)</i>	
	<p align="center">The overlapping regulatory definitions of drugs, topical medical devices and cosmetics</p>	
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10 min	<i>L. Gramiccioni, R. Marcoaldi (I)</i>	pag. 216
10 min	<i>S. Selletti (I)</i>	pag. 217
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	<p align="center">The necessity to define the mechanism of action of cosmetic products The efficacy of cosmetics on normal skin and minor skin disorders</p>	
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CHAIRMEN: *B. Berra (I) - B. Scarpa (I)*

8.30	Organic lycopene from tomatoes: the way to obtain a unique product <i>M. Bleve, L. Rescio, M.S. Lenucci, G. Dalessandro, F. Boari, S. Vanadia (I)</i>	pag. 229
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9.00	Melatonin as an antioxidant, radical scavenger and anti-aging molecule: role in the skin physiopatology <i>B. Berra (I)</i>	pag. 232
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10.45	The effect of an oral intake of hydrolyzed collagen on skin properties. Results of clinical studies <i>V. Fabien-Soulè (F)</i>	pag. 240
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12.00	Non-ablative laser for skin rejuvenation <i>M. Palombo (I)</i> <i>pag. 244</i>
12.15	Skin Rejuvenation: non surgical strategies, from Lasers to Cosmeceuticals <i>P. Mezzana (I)</i> <i>pag. 245</i>
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13.15	Treatment of facial port-wine stains with intense pulsed light <i>L. Zhang (PRC)</i> <i>pag. 249</i>
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Public-Private Connections in Support of Innovation

R. Menia

Deputing Ministry of Environment and Sea Protection - Italy

NOT RECEIVED

Sustainable Products: the Innovation Strategy for the European Chemical Industry

Amilcare Collina

Responsible Relationship with Scientific Community - Sustainable Chemistry Mapei S.p.A., Milano - Italy

The Chemical Industry claims to be science and technology enabling a number of innovations, to provide solutions for the overall objective of conserving natural resources and the environment and protecting people's health: to sum up, it claims to be aimed at improving the quality of life. In other words, Chemical Industry claims to be part of the solution, which is true, and does not recognize to be part of the problem, which is true also.

Sustainability must be the key factor which will dictate the progress of the European Chemical Industry in the next decade.

Europe can get a leadership position because of the following reasons:

- The market is ready to accept new sustainable products; moreover it is asking for such a products. A huge market is there.
- The European Parliament voted in favour of the REACH Regulations thus interpreting the requirements of the general public.

Europe has a lead time over the other Countries.

- Without a doubt, the new Regulations will force the chemical industry to carry out a severe, costly assessment on how to implement them. It is an opportunity to take advantage of, not a threat.

The Chemical Industry is at a crossroads. It may choose the road which leads to resisting the changes, by trying to postpone the obligations required by the new standards and to ignore the demand from the market for as long as possible, but this is only a short-sighted, losing approach.

The alternative is to bravely choose the road which leads to product innovation, considering sustainability as the guiding star for this path. Sustainability may represent a factor for competitiveness, as long as the characteristics of sustainability are explicitly illustrated in the performances of the products, and are acknowledged by the market as a value, which means information and education strategies aimed at consumers and industrial users, the definition of a coherent standards programme and a legislative programme which provides incentives for sustainable solutions.

In so doing, the European chemical industry may construct legitimate barriers against the entry of products from other markets with sustainability characteristics which do not meet the European standards. European Chemical Industry has the challenge to become the most sustainable Industry over the world.

Europe has a solid base of tradition, culture, knowledge, business capacity and resources to take up this road successfully.

Toxicity indexes in the Food Production Chains: an Innovative Approach

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Food security and nutrition security have to integrate with food safety, in a framework of health-promoting choices, prevention-based strategies and early management of risks.

Innovation is pivotal to develop an efficient and up-to-date risk assessment, especially in more vulnerable food supply systems, as well as to provide markers and cost-effective tools for toxicological HACCP; screening toxicity indexes may allow to detect early warnings of hazards as well as to target timely risk management.

Herewith we describe a new device, developed and patented by ISS in collaboration with CNR and the Sapienza University of Rome, the (Bio)Sensors' system in Food Safety [BEST].

BEST is based on a flexible combinations of probes working in parallel (battery).

The aim is to provide farms and facilities with an efficient and effective device for in continuum monitoring of the compliance with quality and wholesomeness indexes of their routine productive life.

The system can be used to monitor the relevant Critical Control Points (CCPs) along specific food production chains, providing early warnings as well checking the effectiveness of corrective actions foreseen by the HACCP plan.

The output is an integrated dataset obtained with proper grid of a-specific and specific biological and chemical-physical parameters. BEST is at laboratory prototype stage, awaiting optimization; market targets are enterprises involved in food production and control.

BEST-driven early warning and risk management along the food chain would minimize economic losses due to contamination, alarms, as well as costly instrumental analyses at chain's end.

BEST's cost-effectiveness and user-friendliness will eases its practicality.

Wireless connection allows the centralized management of a system of BESTs even working in remote CCPs.

Acknowledgements

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Whitening Agent From Natural Plant

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The development of effective skin-lightening agents from natural plants is an increasingly interesting area of research in the field of cosmetic dermatology.

The knowledge of melanocyte biology and melanogenesis process have made remarkable progress over recent years. Tyrosinase is the key enzyme for the melanin synthesis. Many natural plants of skin lightening agents exert inhibit effect on this enzyme, such as Arbutin, extracts from Licorice, Grape seeds, Aloe extract(Aloesin),

The peel of citrus, Promegranate extract and Mulberry etc. Screening from traditional Chinese herbs also provided many promising agents with whitening effects.

Scutellaria, Ramulus cinnamomi, Galla chinensis and Fls carthami were proved to inhibit melanogenesis *in vitro*.

Chamomilla recutita was found to have the effect of reducing the melanin synthesis as an Endothelin(ET) antagonist.

Since the melanogenesis pathway and regulation of tyrosine function are complicated, The mechanism of skin whitening needs further investigation.

Photosensor of Ecopermanence and its application to cosmetic PAO determination

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Ecopermanence is a very significant property as related to thermodynamic stability and so to the time of the possible interaction of a tested compound with human organism and ecosystem.

The photosensor here described measures the value of ecopermanence basing on the combined action of uv light, TiO_2 as semiconductor photocatalyst, microwaves, on the time needed by the oxidative degradation to start (activation) and on the rate of the oxidation expressed as amount of carbon dioxide produced in the time unit.

An easy algorithm allows to calculate the value of the ecopermanence index.

This photosensor was applied to toxicity evaluation and to the determination of the "period after opening" (PAO) of cosmetics.

This determination was possible as artificially aged known cosmetics show a behaviour characterised by a sharp decrease of ecopermanence at an ageing time corresponding or very near to PAO value.

According to the conditions of the artificial ageing the correlation coefficient of this correspondance assumes different values and can be optimized.

New Environmentally Friendly Products for a Better way of living

Giordano Zappelli

Solvay Chemicals - Senior Vice President - SODA ASH Solvay - Italy

The NEUTREC® process - an integrated solution for flue gas cleaning and the recovery of residues. Air quality preservation and environmental protection are a priority for both peoples health and primarily for the safeguard of our societies.

Air quality control and emission monitoring of gases that are released into the atmosphere are among today's major issues and challenges for the public, for local authorities and for industrial companies. In this context, industrial flue gases must meet the requirements of an increasingly binding legislation.

NEUTREC® is a simple and efficient process based on the injection of dry, finely ground sodium bicarbonate into the flue gases that need to be cleaned.

Sodium bicarbonate, thanks to its physico-chemical grain structure, neutralises the acids (hydrochloric acid, sulphur dioxide, hydrofluoric acid, and its etc....) with a very high degree of efficiency. When active carbon or lignite coke are injected as well, the gases are also cleaned of heavy metals and dioxins/furans down to within the most stringent legal limits.

As the process is totally dry, neither water is consumed, nor any aqueous effluent is created which otherwise would have to be treated as well, and thanks to the operating conditions the plume of water vapor at the stack is significantly reduced.

The NEUTREC® process offers an alternative to tipping the gas cleaning residues: their sodium content and the available technology allow them, in most cases, to be purified and recycled.

In the case of municipal and hospital waste incineration, and where double filtration is used for flue gas cleaning, the Residual Sodium Chemicals collected at the second filter, consist mainly of sodium chloride, sodium sulphate and sodium carbonate. They also contain impurities such as part of fly ash, activated carbon and heavy metals.

As part of the NEUTREC® process, SOLVAY has developed, patented and industrialized an original technology which makes it possible to produce a brine with a level of purity that allows it to be recycled as a raw material.

It is thanks to the fact that Sodium Bicarbonate is a neutral, non corrosive, non irritant and non toxic product, and also easy to handle, transport and store, that this process is very simple.

Sodium Bicarbonate is a simple molecule and has, dependently on its granulometry and purity, an incredible number of other applications: from blasting to detergents, from feed and food to pharmacy; in cosmetics (alone or associated to other simple minerals) it is used in toothpastes, deodorants and in the treatment against head lice, nymphs and nits on the hair and scalp.

Sodium Bicarbonate: a simple solution for clean air and people wellness.

Chemoprevention of photoaging and photocarcinogenesis by soybean isoflavone genistein

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There has been accumulating evidence that ultraviolet (UV) radiation plays a key role in premature skin aging and the increasing incidence of skin cancer in humans.

Genistein is an isoflavone richly present in soybean and exhibits a variety of anticancer activities. We have investigated the anti-cancer and anti-aging effect of genistein in hairless mice and human subjects.

We demonstrated that topical application of genistein significantly inhibited UVB-induced skin carcinogenesis at both initiation and promotion stages in a chemo-photo animal models. Furthermore, chronic application of low dose of genistein substantially prevents the skin carcinogenesis and skin wrinkling by low level of UVB exposure.

In human clinical trials, genistein significantly prevented the cutaneous erythema and discomfort index by UVB irradiation in human dorsal skin.

Further studies showed that genistein inhibited UVB-induced oxidative photodynamic DNA damage, suppressed phosphorylation of EGF receptor in human keratinocytes, down regulation of c-fos and c-jun expressions, and reverse the expression of proliferating cellular nuclear antigen (PCNA) by UVB irradiations in both mouse and human skin.

In conclusion, genistein exhibits promising anti-photoaging and anti-photocarcinogenesis activity with well-defined mechanisms of action.

New biochemicals from the sea to save the skin

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Natural products (NPs), especially those from plants and microbes, have been for long time a traditional source of drug molecules. But the role of NPs in drug discovery has undergone many changes in the past 30 years. In particular since 2000, after a few years of partial abandon of the field as a result of the large investments of pharmaceutical industries in drug development processes based on home-made synthetic libraries, there has been a rediscovering of NPs as the most convenient sources of drugs leads. Among NPs, those derived from the sea represent a very promising and relatively unexplored family. The interest in marine natural products (MNPs) has risen in the late 1950s when the technologies (mainly scuba diving) to collect the source organisms were widely used.

Nowadays, the first drug from the sea, ziconotide, a peptide isolated from a tropical cone snail, was approved in 2004 under the trade name of Prialt for the treatment of chronic pain, whereas a second drug, trabectedin (Yondelis) from a tropical sea-squirt, has been on the market since 2007 for the treatment of soft-tissue sarcoma. Several other MNPs are currently being evaluated in Phase I-III clinical trials for the treatment of various cancers (1).

But how to select a new drug? Two different approaches are generally utilized to select bioactive compounds from natural sources: a) bioassay-guided fractionation of extract; b) bioactivity screening on purified molecules. Due to the difficulties that the marine supply present compared to the terrestrial counterpart, a third strategy, the "ecological filter", could be the selection of molecules that play a biological role in the organisms (chemical defense, trophic relationships, etc) (2). From this point of view, marine opisthobranchs seem to be an excellent source of bioactive molecules. Indeed, these naked animals have lost the physical barrier of the shell but have elaborated a series of chemicals as defensive strategies.

The observation and the understanding of the "*in vivo* function" of these compounds are important tools for driving these molecules to potential application in different fields such as pharmaceuticals, nutritional supplements, cosmetics, etc (3).

To this regard, sacoglossans are opisthobranch molluscs that live in superficial waters closely associated with green algae, and are able to sequester chloroplasts that remain active for many days. These molluscs, even though they have lost the external barrier of the shell, are rarely predated. In addition, living closely associated with algae, they have elaborated strategies to reduce the damage of a too prolonged solar exposition. In fact, they biosynthesise some metabolites, the polypropionates, that are implicated as mediators in chemical defence and tissue regeneration (3).

But additional intriguing properties of these molecules have been demonstrated because of their transformation when exposed to sunlight.

In this communication the photochemistry of the sacoglossan molluscs will be presented and the natural function of these molecules against solar radiation might suggest the use and the development of these molecules for skin UV protection and anticancer treatments (4).

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Natural and/or Chemical Compounds? First of all Friendly

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The chemistry and technology of cosmetic products have accomplished enormous progress both in the preparation of vehicles and in the synthesis of new substances to be used as ingredients. This has led to the development of products able to interact with the structures and functions of the skin.

The new sector has currently known as "cosmeceuticals", with a name that may seem ambiguous, but it is really appropriate for defining products that can evoke effects similar to those of drugs without therapeutic activities.

One of the most ambitious aims of cosmeceuticals is to counteract the damages induced by skin aging, particularly those caused by external factors, as solar radiation. In this context an important role is played by antioxidants and above all those of natural origin.

Carotenoids, polyphenols and vitamins are some of the antioxidants used by the cosmetic industry in the preparation of anti-aging products.

These substances have shown to be mostly active when obtained by extraction processes, probably because they consist of mixtures, which represent the combinations developed by nature to counteract electromagnetic radiation without suffering their damage.

The wide use of antioxidants in the anti-aging products has led to a reevaluation of natural ingredients in the preparation of cosmetics and cosmeceuticals, and such occurrence was warmly welcomed by consumers. The use of extractive ingredients may offer some drawbacks, such as the possible variability in the composition of products and also the possibility of using substances that are not tolerated by the skin. For these reasons it is important that the extraction procedures are carefully standardized and it is also imperative that the products are clinically tested before being placed on the market.

Food to Bettering the Way of Living: the Involvement of Lazio Region

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The modern image both for females and males is that of an attractive individual who posses the skills to improve not only the beauty but also the health of the skin and body. Thus we are entering in the era of Beauty outside in so that the term wellness become synonymous with beauty, health and longevity. Moreover, in the new millennium especially large cities as Rome have become multicultural embracing all cultures and different food, fashion and way of living.

Thus, Lazio Region has been working from many years to promote and highlight the quality of its own food and wines. To achieve the deserved national and international acclaim for the quality of its regional food and wines, known from the ancient period of antique Rome, the Lazio Region organizes numerous promotional and sales initiatives to present its famous specialties in a cultural and social context for diffusing and enhancing the excellent qualities of these products.

The varied types of terrain and tradition present in the Lazio Region guarantee a very broad range of different food and wines of different tastes but all of high quality standards.

The concept of wellbeing and need for care were well known in ancient Rome, which may claim to be the crib of famous food, wine and Thermalism becoming a fashion in the whole Roman world and, of course, throughout the Lazio Region.

Therefore I hope you all should have the possibility to visit and stay happy in Rome, tasting the typical regional food, wine and coffee offered from the Lazio Region by the Congress' s Organization.

Protective Effects of Green Tea Extracts on Photoaging and Photoimmunosuppression

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Green tea has been consumed as a popular beverage throughout the world, especially in Asian countries. It has recently gained greater popularity because of its purported antioxidant and anticarcinogenic effects.

We have investigated whether green tea extracts in sunscreens protect ultraviolet irradiation (UVR)-induced photoaging and photoimmunosuppression.

Our results showed that UVR substantially induced cutaneous erythema, thickening of epidermis, over-expression of cytokeratin 5/6, cytokeratin 16, matrix metalloproteinase-2, matrix metalloproteinase-9, and depletion of Langerhans cells.

The sunscreens containing different concentrations of green tea extracts offered a significant protection against the above events of photoaging and photoimmunosuppression. Interestingly, the protective effects were not parallel to the concentrations of green tea extracts, with 2% and 3% green tea extracts showing most efficacious photoprotection.

In conclusion, the green tea extracts-containing sunscreens have the potential photoprotective effects on the UVR-induced photoaging and photoimmunosuppression.

Effective Cosmetic Treatments: the Importance of Spa Environment

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It is well known that Spas, nowadays, offer individuals the most coveted of escapes: soothing music, pampering and a brief respite from daily stresses and responsibilities. However, spa treatments also offer a wealth of benefits to people seeking longevity, a youthful appearance and a wellness care that incorporates aspects of mind, body and soul to achieve enhanced pleasure and sense of wellbeing with life in general.

As the connection between Mind and Body is considered to be one of the most important factors for the effectiveness of cosmetics products and integrators, a supporting care environment is necessary in order to reach that state of mind that allows individuals to take full advantage of their treatment program.

Spas meet most needs of clients in a single location whose ambience provides quiet, relaxing and soothing surroundings complete with aromatherapy and take-me-away-from-it-all music. Furthermore, a spa always provides traditional spa therapies such as massage, reflexology and more, which are well-known to help our body to recover from stress and fatigue, as well as prepare it to receive further treatment and enhance the effectiveness of Cosmetics and Dietary Supplements.

Medical spas are distinctive from other spas due to the fact that they have medical doctors on staff, as well as licensed, well-trained and experienced staff to meet individual needs and offer quality medical care in fields such as cosmetic surgery, dermatology and wellness care techniques and programs.

In its constant commitment to Guest's satisfaction and well-being, Atahotels has successfully created a Resort Spa at Tanka Village in Sardinia, and has recently inaugurated a fully equipped Medical Spa at Petriolo Spa & Resort, in Tuscany near Siena. The next step, and future flagship of the company, is the opening of a very elegant, brand new City Spa at Villa Pamphili, in Rome.

Molecular Design and sustainable development

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NOT RECEIVED

Physiological Modulators

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The Physiological Modulators (PM) are natural products present in food, or used as food supplements, characterized by the activity on the human metabolic system. This concept represents the evolution of the "essential nutrients" such as some vitamins, minerals and fatty acids.

For example, Vitamin C, Omega 3, Phytosterols are typical PM and follow the classical paradigm of nutrition that indicates that both lack or excess of the intake of a given nutrient may modify a metabolic pathway and can initiate a disease.

It is common knowledge that lack of Vitamin C intake causes scurvy and bleeding, whereas it is not known that excess of Vitamin C generates carbonilation of proteins and a consequent metabolic disease.

Beta-carotene at low dosages reduces the severity of hearth ischemic disease and also protects skin from sun exposure, whereas high dosages can reduce the activation of Vitamin D.

PM undergo a massive media advertising and people is stimulated to use them without criticism in the believe that "what is good for somebody is good for everybody". Testimonials are taken to push up the intake without considering that the dosage of PM should be controlled with care.

Appropriate clinical demonstration of the activity declared for any PM is necessary.

The old statement "an apple a day takes the doctor away" has to be reviewed with the indication that maybe 10 apples are to much and that ...an apple creates already plenty of problems to Humanity (genesis).

A new way of considering the entire matter starting from the biochemistry and clinics represents the essential step to give doctors the tools to control therapies and to set up the prevention of chronic diseases.

Polyphenols recovery from olive vegetation wastewater

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Polyphenols may have antioxidants characteristics with potential health benefits. They may reduce the risk of cardiovascular disease and cancer. Since synthetic antioxidant compounds may be dangerous for human health, there has been a growing interest in the use of alternative natural antioxidants: polyphenols are the major plant compounds with antioxidant activity /1/.

In this context, the interest of the scientific community has been focussed on the extraction of antioxidant compounds from inexpensive or residual sources from agricultural industries, such as tomato wastes and olive vegetation wastewaters /2/.

In this work, the removal of polyphenols from olive vegetation wastewater ("OVWW") by adsorption on polymeric resins were experimentally investigated. In particular Amberlite XAD16 resin, a polystyrene-based material with a high surface area, was used to remove mixture of polyphenols from OVWW. The desorption was accomplished by hydro-alcoholic solutions.

First of all, the adsorption kinetics and equilibrium were investigated at isothermal conditions by using a mixed suspension of Amberlite particles in OVWW. The concentration of polyphenols was measured by means of the Folin-Ciocalteu method. The obtained experimental data were handled to determine the parameters of both the isothermal equilibrium and the adsorption kinetic equations. Adsorption experiments were, then, performed by using a cylindrical column, 4 cm in diameter and 19 cm in height, in order to evaluate in first approximation the breakthrough curve.

Finally, the specific polyphenols in the feed stream and in the hydro alcoholic stream from the desorption operation were identified by a Spectra-Physics liquid chromatography (Model Agilent 1200). The main compounds present in the feed stream, i.e. Tyrosol and Hydroxytyrosol, were recovered to great extent by the adopted technique.

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Lipoic Acid: a Natural Antioxidant Compound

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Alpha Lipoic Acid (ALA) was first identified as a nutrient in the 1950s.

The body needs ALA to produce energy in the cells. It was initially believed to be a vitamin but in 1988 it was identified as a powerful antioxidant. The extent of its power is still being explored but already researchers have declared it a stronger antioxidant than Vitamin C or E.

Alpha lipoic acid is made by the body and can be found in very small amounts in foods such as spinach, broccoli, peas, brewer's yeast, brussel sprouts, rice bran, and organ meats.

Alpha lipoic acid supplements are available in capsule.

ALA is capable of neutralizing free radicals in both the fatty and watery regions of a cell, it is a sulfur-containing fatty acid found inside every cell of the human body.

Lipoic acid plays a key role in a variety vital energy-producing reactions in the body that turn glucose (blood sugar) into energy.

It is a potent biological antioxidant that has been shown to slow the oxidative damage in cells, and in many cases stabilize or even reverse cell damage, it is so effective as an anti-oxidant because it works on both water and fat-soluble free radicals that cause oxidation and cell damage in the body.

Experimental studies show that alpha-lipoic acid may exhibit a renal protective effect in individuals with diabetes.

ALA increases glucose uptake in the cells and appears to reduce symptoms of diabetic complications including cataract formation, vascular damage, and polyneuropathy (nerve damage).

Natural compounds for effective cosmetics

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Wide application of natural actives in cosmetology observed nowadays, has two fundamental causes. The first is cosmetic-drug borderline legislated by Cosmetic Directive limiting to a considerable degree possibility of applying xenobiotics in cosmetics. The second, one should find in the huge wealth of topically active substances present amongst botanicals.

The term „topically active” in this case should be understood as biological activity manifesting itself on the molecular level. It is possible to explain the mechanism of this kind of activity on the classic biochemical receptor theories basis. Biological activity can be resulted from evolutionary processes, which linked products of the secondary metabolism of plants with specific reception networks of the Mammals. The activity can be also a coincidence of physicochemical resemblance and the low selectivity of receptors.

We know thousands of natural substances having an influence to selected physiological pathways of the skin, however only few from them show the real efficacy in cosmetology. The way from the activity determined *in vitro* on keratinocyte or fibroblast cellular cultures for cosmetic activity *in vivo* is very long. A bioavailability of compound becomes the basic condition. An excellent example of it are polysaccharides from the group of mannans, belonging to unusually strong immunostimulants - they have no chance of permeating through lipid barriers of stratum corneum. As a result their activity after topical application on the undamaged skin is scarce.

The second group of factors influencing activity are metabolic processes during the penetration. In the result penetrating compound can be activated – on the way of conversion into the biologically active form. In the case of many natural glycosides, inability of enzymatic systems of the skin for aglycon release is a cause of the lack of activity *in vivo*.

As a result, as mentioned above, a number of natural cosmetic actives is limited. Natural actives are usually able to effectively scavenge free radicals, it means the constant of the reaction rate with primary or secondary radicals is appropriately high – tocopherols, tocotrienols, ascorbic acid, flavonoids etc. are good examples. Substances inhibiting or regulating inflammatory processes form the second group – some triterpenes, bisabolol, azulenes, glycyrrhetic acid and its derivatives, asiaticoside etc. Compounds of similar activity (as eicosanoid precursors) are EFA. To extremely interesting substances showing the ability to activate hormone receptors belong isoflavones (from soybean, clover etc.) and sterols and other compounds from Cucurbitaceae seeds. Finally, flavonoids form undervalued and not entirely well known class of natural compounds, they are a huge group of substances of strongly diversified, multidirectional activity, which we still cannot fully exploit.

Recently one can observe the astonishing career of the substances of natural origin coming straight from our organism - LMW peptides. They are toxoforic fragments of HMW transmitters from our tissues, synthetically modified in general to improve activity, bioavailability and stability and decrease the price. Undoubtedly the introduction of LMW peptides into cosmetic raw materials market opened the new chapter in natural actives applications.

Ingredients of the natural origin were ones of the first cosmetic raw materials. They survived throughout the period of the invasion of synthetic products, their significance then grows again. The cause is the safety, of course, as well as the high efficacy in certain applications.

At the same time we can observe the newest trend, applying products modeled on natural, based on structural alterations guaranteeing increasing effectiveness and unchanged mechanisms of the natural activity of the prototype.

Safe and skin friendly cosmetics for sensitive skin: is lanolin included?

The Dermatologist opinion

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Sensitive skin is an elusive term that could include many individuals, but it is sure that atopic dermatitis is a good example of sensitive skin. In considering that one of main characteristics of atopic dermatitis is a dry and more permeable skin, emollients are perhaps the most important part of the therapy for mild/moderate cases.

Different classes of moisturisers are based on their mechanism of action. Patients may be prescribed different moisturizers depending on their particular preference, their age and type of AD but also on environment conditions. Practically speaking, only ointments such as petrolatum and pure tocopherol acetate do not contain preservatives, while other topicals must include them.

Recent findings indicate that some cosmetics may have more pronounced effects in the skin than previously considered.

The increase of emollients can decrease the use of topical steroids and a combined treatment (topical steroids+emollients) is more effective when compared with the monotherapy (topical steroids). Emollients play an important role in rehydrating dry atopic skin so that the International Consensus Conference on AD II has stated that: "Emollients keep the skin hydrated and can reduce itching. They should be applied regularly at least twice during the day, even when there are no symptoms of disease". Many new molecules are coming into the field of AD: among them sunflower oil distillate that should stimulate the endogenous synthesis of lipids; hydroxydecine influencing the filaggrin production; ALIAmides able to counteract the mastocytes-induced reactivity. In addition, extracts coming from grapevine (*vitis vinifera*), green tea (epigallocatechin-3-gallate; an antiprotease) and *Vitreoscilla filiformis* (a non photosynthetic bacterium) could be favourably added to skin care emollients formulated for AD.

Among the old substances, lanolin has an ambiguous fame. Lanolin had the reputation of being an important contact sensitizer so that the market place abounds with products that are labeled "lanolin free". Using the word of Kligman [1] "...lanolin is at most a weak contact allergen.

The supposed hazards of sensitization to lanolin products are a resultant of faulty science and failure to appreciate the limitations of patch testing". It can be observed that lanolin in topical therapeutic agents can sensitize a high proportion of patients, whereas the same lanolin is 'safe' in cosmetics so widely used by millions of individuals. This is demonstrated by the fact that patients with an allergic contact dermatitis to lanolin in a medication applied to a stasis ulcer can nevertheless use lanolin-containing cosmetics without experience a negative reaction.

According to some authors there are too many false-positive and false-negative results using the

standard patch test tray and patch testing with 30% wool wax alcohols used in the standard patch test tray cannot be considered a reliable method for detecting and confirming lanolin allergies.

Coming back again to Kligman: "Lanolin allergy is a myth created mainly by overzealous professional patch testers. No one has succeeded in sensitizing animals or humans to lanolin or wool wax alcohols. Most of the case reports are false positives, in association with the angry back syndrome" Besides that it must be noted that the prevalence of allergic patch-test reactions to lanolin in North America patch-test populations is decreasing (2).

Current relevance of reactions was high, but occupational relevance was low. Moreover a recent study showed that neonates treated with olive oil/lanolin cream showed statistically less dermatitis than did neonates treated with emollient/bepanthenol cream (3).

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Lanolin - Dispelling the myth of lanolin allergies

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A walk through lanolins history of use in the field of dermatology covering its highs, lows and current positioning as a product of choice.

How such a beneficial product for the promotion of skin health can be tarnished by the misrepresentation of excellent clinical reports and how 50 years on as an industry we are still dispelling the myth.

Bio-functional textiles facing the future by the NICE concept

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The today interest in bio-functional textiles is mainly focussed on the use of such textiles supporting therapy and prevention dermatology. Moreover, many published studies on the activity of cosmetic products led to the NICE concept in which, Nervous, Immune, Cutaneous and Endocrine systems all work together to internally activate wellbeing. Thus, *mind-body* skin care become to appear on the market. In the same way textiles, interacting with the skin surface may have not only a general protective biological activity but a more specific function against ultraviolet irradiation and thus an anti-ageing activity.

At this purpose we tried to incorporate into fibres of cellulose acetate chitin nanofibrils pre-linked with lutein, a well known antioxidant and anti UVA and bleu light filter.

Due to the demonstrated UV-screening and anti-ageing activity of chitin nanofibrils pre-linked with lutein, melatonin and other well known antioxidant compounds, we try to control the efficacy of new fibres by *in vitro* and *in vivo* studies.

The obtained results will be reported and discussed.

Unique and Unexpected Cosmetic Applications of an Innovative Chinese Spice Extract

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The Sichuan pepper is a commonly employed spice used in the Chinese and Japanese gastronomy. It is the archetype for the “tingling” sensation, a kind of electrical sensation induced by the alkylamides contained in the spice: it in fact creates a tingly numbness mainly due to alpha-hydroxy-sanshool.

In vitro investigations on a nerve-muscle preparation have shown that the product has a transitory action on the neuromuscular synaptic transmission. This activation quickly leads to the depletion of the neurotransmitter.

The action is mediated by the voltage-dependent Na⁺ channels, by closing them at the suggested dosages and in this way, by blocking the electric signal.

Hydroxy- α -sanshool has demonstrated *in vivo* to show an interesting activity on thermal and tactile sensitivity, making the extract containing it a suitable ingredient to remove skin discomfort and itching.

ABSTRACTS

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Cosmetic Itinerary: an innovative educational program for future cosmetologists

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Background

Cosmetic graduates are looking for educational experiences aiming to improve their capability in cosmetic product and process development to assist them to be introduced into the working chain.

Most of the options now offered by the educational market usually require time and budgets far from the availability of the youngsters. The lack of specific post-graduate courses conjugating scientific, managerial and practical skills obliges cosmetic companies to invest resources in "on-the-job" training, often without the appropriate competence to make profitable the investment.

The SICC/IFSCC offer to provide the qualified skill in both technological and managerial fields; in addition, cosmetic knowledge improvement is one of the most important objective of both Societies. Qualified Suppliers and Cosmetic Companies are keen to provide support to the students to show their capability in innovation; therefore, they are ideal partners to maintain reasonable the cost of the course.

In addition, the involvement of qualified Universities can guarantee the learning efficacy and validate the certificate, which can be used by the students as a tool for their job improvement.

Objective

To train future cosmetologists in project management, team work and virtual working groups

To optimise the student's capability to apply the appropriate formulation and "marketing mix" strategies

To "vest" products with packaging, image and communication

To train young cosmetologists in products/ranges prototyping

To increase the student's potential on the working market

Courses Structure

The following monographic Courses are part of the educational project; the complete cycle of 4 courses covers all the learning needs of a well-trained cosmetologist:

Emulsion technology: Skin treatment & Body Care; Detergent technology: Body, Hair and Oral Hygiene; Colour Cosmetics: Make-up, Camouflage and Hair Colorants; Fragrance Technology: Perfumes, Deodorants & Antitranspirants. The following scheme, lasting six months, is applied to each course:

1st Module: The basic and complementary cosmetic disciplines are delivered to the students; the first module can be attended also as a stand-alone course. All the most innovative ingredients, formulations, evaluation methodologies and delivery systems are introduced as creative inputs to be followed during the virtual and practical development work; in this

contest, concept like NICE as starting point for a new way to evaluate the activity of cosmetic products and nanotechnologies as new threat/opportunity for the cosmetic business are at the moment amongst the teaching disciplines.

- 2st Module:** Elements of project management and virtual working groups procedure are delivered to the students; at the end, a Marketing Brief for the development of specific products/ranges are assigned by a Mentor to each group of min. 5/max 9 students. The groups organise themselves assigning the technical (Formulation,, Packaging, Evaluation and Quality, Marketing and Communication) and Managerial (Coordinator, Time Keeper, Innovator, Facilitator, Communicator) responsibilities.
- 3st Module:** Virtual groups work at home and produce “virtual prototypes”; a specific Forum is supplied to the group to exchange their opinions and findings.
- 4st Module:** Physical prototypes are produced taking advantage of laboratories supplied by suitable Companies, Organisations and Institutes that have agreed to collaborate; the prototypes are complete of packaging, brand name and image, communication and Marketing plan for launch.
- 5st Module:** Prototypes and group experience are presented to the Steering Committee and at the first available National/International Cosmetic Conferences, where the best projects are prized and celebrated.

The output of a few groups will be presented at this Conference

Cosmeceuticals for Asians who are Living in the Tropics

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There are many differences in environment between tropical and subtropical country. So are between skin color and aesthetic behavior of Asians and Caucasians. Not all cosmetics which are suitable for Caucasians in subtropical countries are also suitable and safe for Asians, especially who are living in tropical countries.

Some oily cosmetics which are good for dry Caucasian skins might be acnegenic for the oily Asian skins in the tropics. Sun protection product for Asians in the tropics should not contain photosensitizers agent that cause the skin tanned quickly, contrary to the Asian's tendency of opinion that fair or white skin is a beautiful one. That was different with Caucasians in the sub tropics, which have aesthetic opinion that tan skins are healthy and beautiful. Besides, Asian skins contain more melanin pigment as compared to Caucasian skins.

The melanin of Asian skins, mostly are eumelanin, have black brown color, larger, more solid and difficult to degrade.

Tropical climate, with high temperature and humidity, make Asian skins become more oily and humid. Asian skins in the tropics were exposed by UV radiation from the sun more intensely because of the geographical location of their countries. So Asian skins in the tropics need a total UV protection (include UV A and UV B protection) because UV radiation has been implicated in the formation of sunburn, free radicals, skin cancers, suppression of the immune system and aging skin. Following UV-exposure, free radicals and reactive oxygen species (ROS) play a major role in producing lipid radicals that seem to be responsible for the destruction of the cell membrane and ultimately the cell.

Regarding the influence of cosmetics products for Asian skins in the tropics, factors to be considered are environment factor, human factor, cosmetic factor, and interaction of these three factors (The Science of Beauty, Tronggono, 1983).

Cosmeceuticals contain active ingredients such as sunscreens, vitamins, antioxidants, and skin lightening can help maintaining skin and protect skin from various insults. Some cosmeceuticals need a proper delivery system, and then it could enhance the skin quality.

A comprehensive approach to the treatment of acneic skin: formulation aspects and clinical results

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Acne vulgaris (commonly referred to as acne) is a frequent skin condition, most usually encountered during adolescence; in fact, it affects more than 85% of teenagers, and frequently continues into adulthood. When the onset of acne occurs during adolescence, it generally stems from an increase in male sex hormones, which people of both genders accrue during puberty. Beside the dermatological and cosmetic aspects, in such cases the acneic condition certainly involves most important psychological and social aspects.

An appropriate treatment of acne depends, firstly, on the degree and overall gravity of the condition. While medical treatment is certainly required in severe cases, an integrated cosmetic treatment may prove very effective in the presence of milder forms.

We recently developed a new anti-acne cosmetic line, composed of i) a mild detergent for daily use, ii) a topical treatment in the form of an emulsion, with skin-smoothing, sebonormalizing and anti-bacterial properties, mainly directed to an effective short- and mid-term approach to the acneic condition and iii) a moisturizing, soothing, sebonormalizing emulsion, this latter especially designed for a longer-term maintaining treatment.

This newly developed cosmetic treatment has been clinically tested on 40 volunteers of both genders, between 15 and 35 years of age, in order to assess the skin tolerability and the cosmetic efficacy. The encouraging results that were obtained are presented.

New strategies for skin barrier and microcirculation recovery

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Objects

A new technique for solubilising lipids on a natural basis, able to incorporate over 30% of lipids, has been used as vehicle in order to obtain innovative cosmetic ingredients, ideal for delivering a reduced amount of actives by keeping a high level of efficacy, in form of clear and jellying emulsion. Technique of micro-encapsulation by homogenization into lipophilic vehicle constituted by lecithin has been recently used, in Sinerga Research Centre, to obtain a matrix of Phospholipids / Water / Carbohydrates in which particular and high effective lipids are incorporated, able to form spontaneously nanoparticles too, when dispersed in water.

Materials

Innovative combinations of effective ingredients have been obtained and presented as useful for the relevant activities:

- A.** High performance microcirculation modulator with an improvement of superficial blood vessels flow with increased blood perfusion, ideal for treatments where modification of microcirculation is present (cellulitis, heavy legs,).

From *Olax dissitiflora*, a pure product has been purified (Ximeninic acid) a long chain fatty acid, with a double and triple bond (11-octadecen-9-ioic acid). By further esterification, a semisintethic fluid oil has been obtained, that is Ethyl Ximenynate. As demonstrated by the advanced capillaroscopic technique (Laser Doppler Flussimetry), in a study on volunteers, ximeninic acid ethyl ester resulted endowed with a vasokinetic activity, due to its affinity to PUFA structure.

Its usage in cosmetics is suggested for products for ameliorate circulatory disease of legs, particularly when an alteration of capillary permeability is present, such as heavy legs, body firming-up and cellulite.

- B.** High performance skin barrier recovery with better control of moisturization and protection of epidermal barrier, restoring a deranged barrier, by restructuring the intercellular lipid network and providing immediate moisturizing effect on superficial stratum corneum, ideal for any treatment where a recovery of skin barrier is necessary (atopic dermatitis, psoriasis, dry skin...)

The possibility to have in the same cosmetic ingredient a combination between members of all key lipid classes (i.e., cholesterol, ceramide, and free fatty acid or their precursors) can provide a useful support in managing skin barrier disorders. In particular, since barrier alterations are usually related to dry skin conditions, the association in the same compound with a humectant sugar such as trehalose can improve dramatically stratum corneum hydration.

Antioxidants Add Protection to a Broad-spectrum Sunscreen

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Exposure of human skin to ultraviolet radiation (UVR) results in short term damage such as erythema and pigment darkening as well as long term effects such as skin cancer and photoaging. In addition to conventional organic-chemical and the physical-mineral type sunscreens, other non-sunscreen protective strategies have been investigated, including anti-oxidants and topical DNA repair enzymes. Sun protection factor (SPF) and persistent pigment darkening (PPD) do not accurately reflect the photoprotective benefits of these latter materials, in part, because many have multiple mechanisms of action and protect against "unseen" damage such as immune suppression and induction of matrix metalloproteinases (MMPs).

In this study, the anti-oxidants ascorbyl phosphate (0.1%) and tocopherol acetate (0.5%) plus botanical extracts with anti-oxidant properties (caffeine, Echinacea and Chamomile) were added to a broad spectrum sunscreen (SPF 25 containing benzophenone, parsol 1789, avobenzone and methoxycinnamate) and efficacy of the supplemented sunscreen against several endpoints of solar simulated ultraviolet radiation (ssUVR) was compared with both vehicle and unsupplemented sunscreen.

Human subjects were irradiated or sham irradiated on multiple sites once a day for four consecutive days, visual evaluations performed and biopsies taken for analysis. Although anti-oxidants alone protected against Langerhans cell depletion, anti-oxidants alone were no different than vehicle for protection against erythema or pigmentation.

In contrast, addition of anti-oxidants to sunscreen enhanced protection against UV-induced epidermal thickening, over-expression of MMP-2, MMP-9 and depletion of CD1a+ Langerhans cells.

This study demonstrates that non-sunscreen materials such as anti-oxidants can contribute value when added to an SPF 25 sunscreen and applied topically to human skin *in vivo*.

Microalgae to save health, beauty and environment

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Microalgae are able to enhance the nutritional content of conventional food preparations and hence, to positively affect the health. In the early 1950's, the increase in the world's population and predictions of an insufficient protein supply led to a search for new alternative and unconventional protein sources and microalgal biomass appeared at that time as a good candidate for this purpose.

The interest in the commercial production of microalgae is due to some nutritional properties such as high digestibility, lower concentration of nucleic acids, high content of protein, and quantitative importance of essential amino acids. In their biomass, there are also pigments such as phycocyanin and β -carotene, essential fatty acids as α -linolenic, which has therapeutic effect in humans, vitamins and antioxidants. These properties are important to evaluate the algal biomass quality. Recently, the importance of studying these organisms is due to its therapeutic properties and presence of antioxidant compounds. It has been demonstrated experimentally, *in vivo* and *in vitro*, that these properties are effective for the treatment of certain allergies, anemia, cardiovascular and viral diseases, hyperglycemia, hyperlipidemia and other inflammatory processes.

Currently, most products launched to serve the health food market are supplied as tablet and powder, for example: Chlorella health drinks (Chlorella growth factor), Arthrospira liquid CO₂ extracts (antioxidant capsules) and Dunaliella carotenoid-enriched oily extracts (capsules).

Photosynthetic pigments including chlorophyll a (Chl a), lutein, β -carotene, phycocyanin (PC) and allophycocyanin (APC) are the major bioactive compounds in Arthrospira sp. These compounds have been used as nutrients for human consumption, as natural dyes for food and cosmetics and as pharmaceuticals. The harmful effect of synthetic dyes and the tendency of society to use natural products in food and cosmetics has led to exploitation of microalgae as a natural dye.

Microalgae can also be used in cosmetic products; their extracts can be mainly found in face and skin care products; as well as represented in sun protection and hair care cosmetics.

In environmental field microalgae could be used as a possible source of biological material for the production of biodiesel, in particular because of their lipid content; in fact microalgae have higher photosynthetic efficiency, higher biomass production and faster growth compared to other energy crops. Moreover, they are able to use refuse products like carbon dioxide, coming from various industrial processes. From this point of view the microalgae can also be seen as simple CO₂ sequestrants to use in plants for greenhouse gas emissions control (ET—Kyoto Protocol).

Nowadays, the microalgal biomass market produces about 5000 t of dry matter/year and generates a turnover of approximately US\$ 1.25x10⁹/year. The commercial applications are dominated by four strains: Arthrospira, Chlorella, D. salina and Aphanizomenon flos-aquae.

Stem Cells from Plants for Cosmetic Application

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Only stem cells retain the capacity to divide and thus to provide new tissue cells. Fast regenerating tissues such as the epidermis in the skin, are particularly dependent on their stem cells. Skin stem cells have a limited life expectancy and are at risk of premature death due to intrinsic or extrinsic stress factors. Their depletion is regarded as the primary cause of skin ageing.

Stem cells of an old apple cultivar with very good storage properties were produced by applying plant cell culture technique. The extract of the cultured apple stem cells was shown to enhance the viability of umbilical cord blood stem cells, to reverse senescence signs in human fibroblast cells and to increase lifespan of isolated human hair follicles.

A novel Progenitor Cell Targeting technology was used to isolate human epidermal stem cells. This special, fully defined cell culture medium leads to an enrichment of so called keratinocyte progenitor cells (stem cells). These keratinocyte progenitor cells were incubated with the apple stem cell product.

Compared to a control culture, the CFE was stimulated by up to 100 per cent in the presence of the plant stem cell ingredient. This clearly shows that the apple stem cell product improves the maintenance of the stem cell characteristics of epidermal stem cells. Cell proliferation was reduced in the presence of the apple stem cell product, indicating again the higher percentage of slowly dividing epidermal stem cells. PhytoCellTec™ Malus Domestica, a cosmetic ingredient based on encapsulated extract of cultured apple stem cells, was tested in a clinical trial over 4 weeks with 20 subjects. This new ingredient was found to significantly reduce wrinkles in the crow's feet area.

Coenzyme Q₁₀ and skin protection

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The first observation on the involvement of CoQ₁₀ in skin metabolism goes back to the early 90s, when we found that levels of CoQ₁₀ are higher in light-exposed compared to unexposed skin (1). Later on a physiological decline of CoQ₁₀ with age was described, as for other organs (3). CoQ₁₀ plays a key role in the energy transduction mechanisms of the inner membrane of mitochondria and, at the same time, in its reduced form (CoQ₁₀H₂ ubiquinol) is a potent antioxidant, active in the lipophilic environment.

The bioenergetic and the antioxidant roles of CoQ₁₀ are the prominent ones also at skin level. CoQ₁₀ and vitamin E are present in sebum and they exert their antioxidant function against UV induced free radicals, protecting squalene depletion. In fact the same UV dose, when applied in the absence of vitamin E and CoQ₁₀ produced a 90% decrease of squalene (2). Pretreatment of H₂O₂ exposed keratinocytes with CoQ₁₀ was able to maintain glutathione levels at about those found in unstressed cells. Also DNA damage produced by UVA irradiation in keratinocytes was minimized by CoQ₁₀ treatment of the cells (3).

Aging skin becomes functionally more anaerobic, showing an increase in glucose uptake; this additional glucose uptake in keratinocytes of old donors goes almost entirely towards lactate production (4). The loss of mitochondrial membrane potential by UV irradiated keratinocytes was very efficiently prevented by topical application of CoQ₁₀ (4). The antiwrinkle effect of CoQ₁₀, originally described by Hoppe et al. (3), was based on its function of cutaneous energizer and antioxidant.

Recent data point out that some CoQ₁₀ effects might be due to a gene induction mechanism (5). UVA induced upregulation of collagenase is inhibited by CoQ₁₀ *in vitro* (3).

UVA and UVB stimulate fibroblasts to produce matrix metalloproteinases (MMPs) which cleave collagen and elastic fibres and basement membrane leading to wrinkle formation by reduced normal collagen fibres and degradation of elastic fibers. Normal human keratinocytes exposed to UVB greatly increased their production of cytokines (IL-1 α and IL-6). The content of IL-6 in the cells treated with 20 μ M CoQ₁₀ was significantly reduced compared to controls. The production of matrix metalloproteinase (MMP-1) in cultured fibroblasts was greatly suppressed if these cells were incubated with a CoQ₁₀ enriched medium (6).

Therefore, besides its antioxidant and energizing effect, recent studies indicate that CoQ₁₀ inhibits the production of cytokines in keratinocytes exposed to UVB irradiation, leading to decreased collagenase production by fibroblasts and therefore to wrinkle reduction.

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Bombesin: a possible role in wound repair

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During tissue regeneration and wound healing of the skin, migration, proliferation and differentiation of keratinocytes are important processes.

We assessed the effect of a neuropeptide, bombesin, on keratinocytes during regeneration from scratch wounding. Bombesin is one of the active neuropeptide purified from amphibian skin, and is homologue of mammalian gastrin releasing peptide (GRP) and neuromedin B(NMB). This peptide is also active in mammals and its pharmacological effect extends into various physiological aspect: hypertensive action, contractive effect on uterus and colon, stimulating action on gastric secretion, hyperglycemic effect or increasing insulin secretion. Bombesin exerts its effect by binding to two cell surface receptors: gastrin releasing receptor (GRP-R) and neuromedin B receptor (NMB-R).

In vitro it shows a hyperproliferative effect and an increase of motility on different experimental models.

The aim of our study was to elucidate the effect of bombesin in an *in vitro* experimental model on a monolayer of human keratinocyte (HaCat) mechanically injured.

We evaluated different mediators involved in wound repair such as Il-8, TGF β , Il-1 β , COX-2, VEGF and Toll-like receptors 2 and 4. We also studied the effects of bombesin on cell proliferation and migration and its direct effect on wound repair by observing the wound closure of mechanical injury. We also evaluated the involvement of bombesin receptors GRP-R and NMB-R. Our results show that bombesin, at a concentration of 10^{-8} M, increased: the growth and migration of cells, the expression of Il-8, TGF β , COX-2, VEGF and Toll-like receptors 2, while decrease the expression of Il-1 β .

In addition we show that NMB-R was more involved in our experimental model compared to GRP-R. All this data show that in an experimental model in which human keratinocytes were mechanically injured, treatment with bombesin modulated the expression of several important biological parameters in skin repair and favored migration, proliferation and neoangiogenesis in the damaged tissue. The identification of the pathway involved in wound healing is a matter of great interest both for the characterization of the physiological abnormalities leading to an aberrant skin repair in acquired or inherited wound healing disorders and for improvement of current pharmacological treatments. Bombesin could be used in combination with conventional therapy in the resolution of skin damage.

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Multifunctional Natural Active Compounds to Rejuvenate the Skin

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Aging skin, especially photoaging skin, is a distressful condition for the elderly (sometimes even in relatively young people with premature aging). The desire to rejuvenate the skin is boundless. Natural compounds have been widely used in rejuvenating the skin, either orally or topically. Seeking natural compounds for the purpose seems more vehement in China, due to the long traditional use of natural compounds in Traditional Chinese Medicine.

The natural compounds could be derived from plants, animals, fossils, etc. Different compounds serve different purposes in rejuvenating the skin, such as antiwrinkling, whitening, etc.

Here we present some the compounds that are available or under development, their uses and safety issues.

Perfluoropolyethers in skin care: a study on the protective activity of new innovative formulations based on linear Fomblin® HC/V

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Perfluoropolyethers (PFPEs), trade name FOMBLIN® HC, are a well-known family of cosmetic ingredients having a unique combination of properties (hydro/lipophobicity, vapor and oxygen permeability, ability to form a protective film, without clogging the skin's pores allowing the skin to breath). They are odorless, colorless, non greasy, transparent, liquid polymers having an excellent chemical and thermal stability and solvent resistance. Besides a safe toxicological profile, Fomblin HC perfluoropolyethers show remarkable cosmetics characteristics: like the absence of comedogenic activity, the aesthetics, and the capability to impart a "velvet effect" on the skin.

The results of the first clinical investigations on creams containing Fomblin HC Classic perfluoropolyethers highlighted the high potential of these polymers in the protection of the skin and paved the way for further developments (including chemically modified perfluoropolyethers, Fomblin HC Functional family).

The availability of a new type of "neutral" perfluoropolyethers having a linear chain structure and an higher average molecular weight in comparison with Fomblin HC Classic range at the same viscosity values, suggested us to investigate their efficacy in skin protection, also in combination with Fomblin HC Functional products and other new co-polymers.

A double blind, controlled study was conducted on 10 healthy volunteers of both sexes, aged between 18 and 50 years, in order to evaluate the protective activity of 5 topical products (single application, before chemical/mechanical skin insult) on experimentally induced erythema by repeated skin stripping and by sodium lauryl sulphate (SLS) 5%, applied in occlusive conditions (patch test). Moreover, the re-epithelizing activity, "repairing activity", of the 5 products (among which, one was the placebo, not containing any Fomblin HC perfluoropolyether) was investigated.

Skin analyses were conducted through different techniques: clinical evaluation (visual assessment), optical densitometry, electrical capacity of skin (hydration) and epicutaneous pH.

The results of the study showed that optical densitometry is the most efficient instrumental technique to score the erythema index. Erythema index is considered to be the most important parameter in the evaluation of protecting and repairing activity.

Product 2, containing the new Fomblin neutral perfluoropolyether combined with a Fomblin HC Functional (perfluoropolyether phosphate) showed a significant and clinically important protective and repairing activity both after stripping and SLS patch.

A protective lutein for innovative cosmetics

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Lutein is one of over 600 known naturally occurring carotenoids.

From the chemical point of view lutein belongs to the xanthophylls, natural liposoluble pigments contained in many food stuff of animal (i.e. eggs) and of vegetable origin (spinaches, kales, corn). Numerous studies have shown that lutein may protect against photodamage of the retina by filtering out blue light, which is not stopped by the cornea and lens, and which can damage the retina over time. It also acts as antioxidants against the formation of reactive oxygen species and subsequent free radicals, with consequent benefits to the eyes and to the human skin.

Unfortunately, as many other antioxidants, this carotenoid is a very unstable molecule. Therefore, to be able to improve its physical and chemical stability and the possibility to introduce it inside a cosmetic formulation, its incorporation in micro- or nano- carriers is necessary.

In order to have a large spectrum of use, we have studied both lipophilic and hydrophilic nano and microsystems.

To check if it could be better to use nano or microencapsulations, we have realized liposomes and lipospheres, as to lipophilic delivery systems.

In parallel, we have used cyclodextrin and developed a new polymeric matrix to deliver lutein in hydrophilic carrier.

From these experiments we have been able to demonstrate that these carrier systems allow a better formulation of lutein, improving its stability and its availability.

Food supplement: beauty and wellness from inside

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Wellness and functional food's market in 2009 has prove to be an anticrisis sector.

Food supplement market in pharmacy and mass market has developed a turnover 1,3 bilion euros with a 7% increase.

From several years a lot of cosmetic company support their traditional product with food supplements for beauty treatment "from inside".

We analyze the Italian food supplement market, in particular for:

- Tan food supplement

- Anticellulite food supplement

- Hair food supplement

ABSTRACTS

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Chitin Nanofibrils and microparticles: no connection with allergy and asthma

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Chitin has been erroneously associated to allergy or asthma in some articles. Certain authors equivocated about the chemical form of chitins occurring *in vivo*: they arbitrarily assumed that chitin in mites, helminths, worms, fungi and bacteria is similar to the packaged industrial chitin.

Certain published rudimentary illustrations are misleading because they translate the images of living organisms into the chitin chemical formula.

The notion that chitin *in vivo* is orderly combined with other macromolecules is amply accepted: in fungi, chitin is covalently linked to glucans, while in arthropods it is covalently linked to proteins and tanned by quinones, while in bacteria chitin is diversely combined according to the Gram(+/-) classification. Therefore, at the nano level, chitin is a highly associated structure that has been recently refined in terms of regularity, nature of bonds, crystallinity degree, etc.

The purpose of this communication is therefore to re-assess the beneficial role of exogenous chitin in the human organism.

The effects of *Streptomyces griseus* chitinase on Ca²⁺ signaling in human airway epithelial cells has been investigated: the exogenous chitinase was found to cleave a peptide representing the cleavage site of protease-activated receptor-2 (PAR-2) and enhanced IL-8 production.

Therefore, the exogenous chitinase is a potent proteolytic activator of PAR-2 that can directly induce Ca²⁺ signaling in human airway epithelial cells. The meaning of this is that the mammalian organism recognizes the secreted water soluble chitinase produced by a pathogen, rather than the insoluble and well protected chitin.

This is followed by the secretion of the acidic mammalian chitinase (AMCase) and/or chitotriosidase, as an ancestral and universal defensive means against invasion. Direct inhibition of hyphal growth could be achieved with the use of AMCase; in fact, the *in vitro* antifungal activity of AMCase was studied against *Candida albicans*, *Aspergillus fumigatus* and *Trichophyton rubrum* strains. The growth of all three dermato-pathogenic fungi was clearly inhibited by recombinant and natural AMCase, especially the natural one.

Those authors who claimed the involvement of chitin in asthma insurgence in workers exposed to crustaceans, did not pay attention to the possible presence of N-acetyl-β-D-glucosaminidase (NAGase) in those hypothetically inhaled aerosols where they pretended that insoluble chitin particles are present (not demonstrated), nor, even worse, they paid attention to the real allergens, tropomyosin in primis, a soluble compound coming from crustacean flesh. More specifically, NAGase is present in the epidermis of crustaceans (under hormonal control) where it is responsible for the resorption of chitin in the early stage of the molt.

This methodological error remained undetected for several years, and the arbitrary equivalence chitin = allergen was taken for granted by journalists and other persons not particularly skilled in this matter.

Nearly 3 decades ago, Japanese authors demonstrated that chitin and chitin derivatives stimulate macrophages to produce cytokines that confer anti-tumor activity and non-specific host resistance against bacterial and viral infections. Since then, more immunologic activities of chitin have been reported: the immunological effects of chitin *in vivo* and *in vitro* using phagocytosable small-sized chitin particles included significant priming effects of chitin particles in alveolar macrophages and NK cells.

Intravenous administration of chitin microparticles (1-10 μm) into the lung activates alveolar macrophages to express cytokines such as tumor necrosis factor- α (TNF α), IL-12 and IL-18, leading to INF- γ production mainly by NK cells. A mannose receptor mediates the internalization of the chitin particles that then are degraded by lysozyme and NAGase in human and animal macrophages.

These studies indicated that chitin uses specific signaling pathways in immune regulation.

Intranasal application of chitin microparticles into the lung also significantly down-regulated allergic response to Dermatophagoids pteronyssinus and Aspergillus fumigatus in a murine model of allergy. The chitin treatment substantially reduced the allergen-induced serum IgE levels, peripheral eosinophilia, airway hyper-responsiveness, and lung inflammation. Similarly, intranasal application of water soluble chitosan attenuated mucus production and lung inflammation induced by Dermatophagoids farinae.

The ample evidence that chitin is a potent innate immune stimulator of macrophages and other innate immune cells raises the possibility that chitin could affect allergen-induced adaptive type 2 responses as well, but, generally, type I cytokines are produced by innate immune cells and it has been shown that type I cytokines down-regulate type 2 allergic immune responses.

Thus, it is reasonable that chitin negatively modulates allergen-induced type 2 inflammatory responses.

It was further demonstrated that application of microgram quantities of chitin microparticles had a beneficial effect in preventing and treating histopathologic changes in the airways of asthmatic mice. All these studies strongly support the fact that chitin depresses the development of adaptive type 2 allergic responses. From the clinical point of view, the regulatory function of chitin on Th2 adaptive immune response is therapeutically important because it can be applied to control a variety of type 2 allergic diseases.

In conclusion, the administration of chitin is beneficial because it acts as an immunoadjuvant, and depresses the insurgence of Th2 inflammation and allergy, besides a multiplicity of favorable actions. As a matter of fact, the use of nanocrystalline chitin in hemostasis and in wound healing did not produce any detrimental effect. Chitosan, on the other hand, is being used as a vehicle for drugs to be administered by the nasal and the pulmonary route.

Clinical efficacy of innovative cosmeceuticals based on Chitin Nanofibrils

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Biocompatibility and capacity to promote the synthesis of hyaluronan are, among others, the main characteristics of chitin-derived compounds, whose biological significance depends largely on the activities some enzymes exert on human skin.

The resulting penetration of chitooligomers stimulate various cells, while the released monomers, glucosamine and N-acetyl-glucosamine, are phosphorylated and incorporated into hyaluronan, keratin sulphate and chondroitin sulphate at level of intracellular matrix and connective tissue.

The industrial production and reperibility of chitin' pure nanocrystallites (Chitin Nanofibrils, -CN) gave us, the possibility to investigate in a better way its activity both on healthy and diseased skin.

The objective of the study was to control the anti-aging activity of a cosmetic emulsion based on the use of CN enriched with lutein, melatonin and alfa-lipoic acid as antioxidant compound and ectoin as immunomodulant agent.

Methods

A double blind study vs vehicle on 42 photoaged women medium age 37 years for a period of 60days by a twice daily topical application of the emulsion, verifying superficial skin lipids, hydration, TEWL by 3C System /Dermotech-Rome); lipid peroxides by MDA method and skin colour by Chromameter 300.

Results

It was obtained an increase of skin lipids (42%) and skin hydration (71%) with a decrease of TEWL (47%), lipid peroxides (68%) MDA (38%) and age spots (43%).

Conclusion

The use of CN-emulsion enriched with the antioxidant and immunostimulant compounds used may be considered a good mean to fight skin aging ameliorating the quality of our life.

Chemico-Physical & Toxicological Properties of a Natural Raw Material : the Chitin Nanofibrils

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Chitin Nanofibrils (CN) as nano-crystals, represent the pure sugary molecular portion of alpha-chitin obtained after the elimination of the protein portion. The production process brings the formation of a stable water suspension of nanofibrils containing 300 billion nano-crystals per milliliter. The extremely small size (240 nm about) of these nano-crystals, separated from each other and bound with water, and their mostly electropositive electric charges arranged along the axis of molecule, allow this polyglucoside to remain stably suspended in water solution, ready to bind with other molecules via ionic bonding. Chemically CN is a natural polysaccharide made up of glucosamine and acetyl-glucosamine bound together by a typical beta-1-4 bond.

Being a pure polyglucoside it doesn't cause allergic reactions, which on the contrary can be caused by the protein portion of the fish shells which is totally eliminated during the production process. Moreover, in contact with the skin, this sugary polymer is transformed by cutaneous enzymes into disaccharides and/or tetra-saccharides in depending of the time of contact with the horny layer and the emulsion entrapping it.

In conclusion CN is *natural* because present in nature, and *safe* to use because, being recognizes by human enzymes, it is *bio* and *eco*-compatible.

Challenges on Safety Assessment of Cosmetic Products Containing Nanomaterials

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Several studies indicate that nanomaterials (NMs) may have different proprieties from their macro-scale counterparts. The combination of small particle size, large surface area, and ability to generate reactive oxygen species has been demonstrated to be a key factor in induction of cell injury following exposure to certain engineered NMs. Nanostructure can be associated with modification of biological properties and toxicological effects of ingredients used in cosmetics. However, the issue is controversial. Contrasting results have been obtained with TiO₂ and ZnO.

Preliminary evidence of nanoscale-dependent toxicity exists for certain ingredients of hair dyes.

From a toxicological perspective, there are two controversial issues that significantly impact on regulatory aspects and safety assessment strategies for nanotechnology-derived products. The first is as to whether nano-sized particles have to be considered new chemicals, or whether the use of existing materials at the nano-level should be considered a "new use" of an existing chemical. Addressing this question is of crucial importance to define adequate strategies and establish whether NM-tailored testing methods should be added to the conventional toxicity testing battery in safety assessment of NMs to comply with regulatory demand. A second issue is whether the classical toxicity testing methods and strategies that are currently used in the hazard evaluation of macroscale chemicals are adequate when applied to NMs.

NMs used in cosmetics can be divided into two groups: labile nanoparticles which disintegrate upon application to skin into their molecular components (e.g. liposomes microemulsions, nanoemulsions) and insoluble nanoparticles such as TiO₂, fullerenes and quantum dots. It is currently believed that for labile nanoparticles, conventional risk assessment methodologies may be adequate whereas for the insoluble particles specific toxicological and physicochemical parameters and modifications in current risk assessment procedures must be considered. At the present time the production and commercialisation of manufactured NMs do not trigger additional safety testing. However, the European regulation of chemical substances (REACH), which effectively shifts responsibility from authorities to industry to assess safety of chemical substances, is likely to represent a significant challenge in resolving the conflict between progress and protection of cosmetics containing NMs.

Acknowledgements

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Nanotechnology/Nanobiotechnology in Cosmetic Dermatology: Status and Perspectives in China

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Many skin conditions, such as dry skin, oily skin, hyper-, hypo- pigmentation, vascular deformities or neoplasias, photoaging, benign or malignant skin tumors, are major concerns in cosmetic dermatology.

Nanoparticles were defined as particles with a diameter range of smaller than 100nm. Nanoparticles have diversified properties, often distinct from their counterpart macroparticles, due to their surface physical-chemical activities.

The use of nanomaterials or development of nanotechnology is only at the starting point in the field of cosmetic dermatology in China. China has a unique medical system, in that it has hundreds of schools for Traditional Chinese Medicine (TCM), of course, hundreds of Western style school of medicine as well. There are potentially boundless supplies of single or combine materials used in TCM, some of them has been used in cosmetic dermatology. Some researchers are developing nano-based TCM in cosmetic product for better efficacy. In addition, some Chinese researchers are developing new drug delivery systems(DDSs) including the Sustained and Controlled DDS, the Targeted DDS, the Transdermal DDS, the Bioadhesive DDS, and the Self-Emulsifying DDS and their applications.

In the future, problem oriented products will be fully considered and developed, due to the unlimited need in the innovative cosmetic products in China.

A new, biologically compatible physical sunscreen, with skin firming properties

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A new skin-friendly, micro-dispersed mineral active has been discovered, which provides significant UV-B rays protection enhancement. Its performances are comparable or even superior to those of Titanium dioxide, without any blue-white appearance and at lower costs in formula. Indeed, it does not react with dibenzoylmethane UVA sunscreens. It enhances by 10% the COLIPA standard P3 UV absorption and replaces perfectly Titanium dioxide in W/O emulsions set at SPF 30 and 50+.

Due to its physiological components, it has also been tested in a series of evaluations related to anti-age efficacy on a panel of women (40-70 y old).

Significant improvements have been obtained, in comparison to placebo, in terms of biologic elasticity and maximum rugosity parameters. Moreover, the raw material provides significant soft focus effect on the skin.

Nanotechnology in Cosmetics and Sunscreens: is there a Health Risk?

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Modern cosmetic formulations contain nano-sized components including nanoemulsions and microscopic vesicles (nanocapsules, nanosomes, niosomes or liposomes), which consist of traditional cosmetic materials. Numerous studies suggest that vesicle materials do not penetrate human skin beyond the superficial layers of the *stratum corneum*.

When compared with the skin absorption / penetration of ingredients in traditional formulations (solution, gels or creams), nano-sized formulations may somewhat enhance or reduce skin absorption of ingredients, albeit at a limited scale. Modern sunscreens contain insoluble titanium dioxide (TiO₂) or zinc oxide (ZnO) nanoparticles (NP), which filter UV more efficiently than larger particles. The results of a large number of safety studies suggest that insoluble NP do not penetrate into or through human skin. Recent intravenous toxicity studies of TiO₂ or ZnO nanoparticles in rats suggested that these particles are non-toxic. A number of *in vivo* toxicity tests revealed that TiO₂ and ZnO NP have low toxicity and a good skin tolerance.

A series of *in vitro* cytotoxicity, genotoxicity and photo-genotoxicity studies on TiO₂ and ZnO NP found no difference in the safety profile of micro- or nano-sized materials, all of which were non-toxic.

A recent comparative study between TiO₂ micro- and nanoparticles suggested similar acute toxicity, genotoxicity and ecotoxicological properties. Although some *in vitro* investigations on TiO₂ or other insoluble particles reported uptake by cells, oxidative cell damage or genotoxicity, these data should be interpreted with caution since they may be secondary to phagocytosis and overload of cells exposed to excessive concentrations of insoluble particles.

Data from studies on surgical implant-derived wear debris nano- and micro-particles or magnetic resonance contrast agents (iron oxide nanoparticles) and other insoluble particles support the traditional view of toxicology that toxicity of small particles is generally related to their chemistry, rather than their particle size.

There is little evidence supporting a general rule that adverse effects of particles to the skin or other tissues increase with smaller particle size, or produce novel toxicities when compared with those of larger particles.

Overall, the weight of current scientific evidence suggests that nano-sized cosmetic or sunscreen ingredients pose no or negligible potential risk to human health, whereas their use in sunscreens has large benefits, such as the protection of human skin against skin damage, including skin cancer.

Greening with Silicones

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Today's consumer has very sophisticated if not contradictory attitudes when it comes to the selection of cosmetic products.

On one hand, the consumer will neither accept products that are not formulated to minimize the impact on the environment. On the other hand, the consumer will not accept products that fail to meet the performance expectations.

This results in a basic contradiction; how does one get the performance that one has come to expect, while having concern for the environment. This has been a problem for marketing over the last decade and will become a defining problem for our industry.

The use of the properly chosen silicone in both water based, oil based and emulsion technology, results in products with a high level of green attributes and the required consumer benefits.

Talk will concentrate on oil based products.

Responsible Development to Ensure the Health and Environmental Safety of Manufactured Nanomaterials

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Engineered nanoparticles and nanomaterials offer many potential socio – economic, health, and environmental benefits as a result of novel properties and behaviour that materials can exhibit when manufactured at the nanoscale. While the production of nanomaterials is undergoing exponential growth, their biological effects and environmental fate and behaviour are relatively unknown.

There is a lack of scientific knowledge on the effects of nanomaterials, particularly nanoparticles, on human health and the environment. Governments around the world are keen to understand, reduce and manage any risks associated with these new materials through a responsible and co-coordinated approach to ensure that potential safety issues are being addressed at the same time as the technology is developing.

The behaviour of nanoparticles is critically dependent on several characteristics, including size, surface area and surface reactivity, and the risk assessments related to both human health and the environment have to be based on these characteristics. It is important to know if the existing guidelines are suitable for nanomaterials and which need to be adjusted to take the properties of nanomaterials into account. It is even possible that new test guidelines will be needed. It might also be necessary to draft guidance to describe how existing test guidelines can be applied to nanomaterials, in the light of their special properties.

The European Commission Strategy and Action Plan on Nanotechnologies emphasises the importance of a safe and responsible approach to risk assessment with every step of the life cycle of nanotechnology-based products. There is now a need to assess the suitability of current risk assessment methods in more detail in order to guide how to deal in practice with nanomaterials in an appropriate manner. The practical implementation of different areas of Community legislation dealing with chemical substances, including the legislation on new and existing substances (REACH), may be eventually affected by nanotechnologies. It is possible that nanomaterials may require a different classification and labelling compared to the bulk material.

For the determination of dose – response relationships, special attention should be given to the expression of the metrics of the nanoparticle dose since mass concentration is not necessarily the best description of dose for these materials and number concentration and surface area are likely to be more appropriate.

Not all nanoparticle formulations have been found to induce a more pronounced toxicity than the bulk formulations of the same substance. This suggests that the evaluation of nanoparticle formulations should be carried out on a case by case basis and it is important that it is determined whether test procedures will be predictive for human health hazards for all types of nanoparticles. With respect to environmental exposure, the validity and appropriateness of existing technologies are not

clear. In the absence of sufficient data on the fate and effect of nanoparticles on the environment, it is neither feasible nor appropriate to propose firm rules on how substances in nanoparticle form should be evaluated. Instead the applicability of existing methods for risk assessment of nanoparticles should be evaluated. There is therefore a need for new standardized ecotoxicity tests for nanoparticles.

In this context OECD is playing a major part and a large body of work is being developed. Under its Chemicals Committee a Working Party on Manufactured Nanomaterials (WPMN) has been established.

The objective of this Working Party is to promote international co-operation in health and environmental safety related aspects of manufactured nanomaterials, in order to assist in their responsible development.

The activities of the Working Party will ensure that the approach to hazard, exposure and risk assessment is of a high, science-based, and internationally harmonised standard.

Chitin Nanofibrils: *in vitro* effects on wound repair

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Over the course of a lifetime the skin undergoes numerous modifications as a result of aging and photoaging as well as infectious diseases, neoplasia, allergies and trauma. In all these cases, characteristic modifications to the resident cell lines and matrix occur. These modifications involve collagen and elastic fibres, which are primarily responsible for cutaneous elasticity. Fibroblasts and keratinocytes play a key role in regenerating wound tissue and restoring the normal cutaneous architecture by producing chemical mediators and interacting with immunocompetent cells.

Cosmetology and aesthetic medicine are studying new strategies to fight cutaneous damage, such as autologous cellular regeneration, the use of lutein as a cutaneous antioxidant, and the production of chitin nanofibrils.

Chitin nanofibril is a natural raw material obtained from crab and shrimp shells. It is a crystalline polysaccharide capable of interacting with enzymes, platelets, and other cell compounds present in living human tissue. In addition, it can be recognized and broken down by endogenous enzymes. The aim of this study is: 1) to evaluate the effects of different concentrations of chitin nanofibrils alone or in association with lutein, ectoine, melatonin, and collagen polypeptides (kindly provided by MAVI Sud srl) on wound repair; 2) to analyze the effect of chitin nanofibril solutions on the production of proinflammatory cytokines (IL-8, TNF- α ;) immunomodulatory cytokine (TGF- β), integrins, growth factors, metalloproteinases and natural peptides such as beta-defensin from resting and stressed human keratinocyte monolayers; 3) to study the effects of chitin nanofibril solutions on cell migration and proliferation.

For the wound repair experiment, a keratinocyte monolayer grown on collagen cut with a yellow tip was used, and the cells were observed during the following 48-72h.

The preliminary results obtained show that the solutions used at all concentrations and in all associations are not toxic in our experimental mode

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Amarone: the history of a great, old and NICE wine

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Italy is distinguished throughout the world for its typical, historical and high-quality production of great wines. One of the multitude of types produced is called *Amarone*, originating from the province of Verona and, geographically, produced in nearby Valpolicella. *Amarone* evokes far-off times: indeed, the occurrence of vines in the Veronese area goes back to the Middle Eocene (about 40 million years ago), as revealed by fossil findings of Ampelideae, *Ampelophyllum* spp., discovered in the 19th century at Bolca, in the neighbouring province of Vicenza.

It has also been hypothesised that this botanical species may have been the originator of *Vitis vinifera*. Pips of *Vitis silvestris* going back to the Bronze Age have been found in the lake-side settlements of Lazise, Pacengo and Peschiera del Garda, all on Lake Garda.

Vitis vinifera sativa also appears in the Iron Age, probably from the Etruscans, in the VII-V centuries BC.

In Roman times, vine cultivation expanded considerably, as shown by widespread examples, e.g., letters carved on stone tablets by a person of Tenazio's family, by Theodoricus and Suetonius, who stated that the Emperor Augustus was accustomed to serving at his table a "*Vinum Rhaeticum*" (aged in amphorae), noted by Pliny the Elder and Martial as a typical Veronese wine. Lastly, some finds in the rustic Roman villa (III-II centuries BC) between San Pietro in Cariano and Fumane and the famous description of the "Acinatico" of Cassiodorus (cultivated a few centuries later) attest to the practice of withering.

The *Amarone* of Valpolicella is famous worldwide for its many excellent properties: the peculiar way in which it is worked (thanks to the singular technique of withering and fermentation), it seems for good protection (when consumed in moderate quantities) against cardiovascular diseases (thanks to its contents of polyphenols), high anti-oxidising properties, and the contemporary presence of procyanidines, which protect against radiation treatment, excessive smoking, breast cancer and fatty liver disease. It is also interesting to note how the recently introduced, beneficial *wine therapy* has highlighted the explicit capacity of wine to act at the level of the Nervous, Immune, Cutaneous and Endocrine systems, as the felicitous acronym *N.I.C.E.* indicates.

This will be an interesting and indeed enthralling journey, which will show you how, starting from the historical and cultural traditions of a certain territory, this great wine can be served both at table during mealtimes and also outside them, at moment of relaxation and leisure.

This "nice" wine, pleasant to the palate, exalts our wellbeing, improves the quality and style of our lives, and enables us to achieve what we Italians call "Beauty and Serenity": "*Bellezza e Serenità*".

Establishment and Change of NICE Approach

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We have discovered the anatomical association of skin immune cells with nerve fibers (1). Functional analyses revealed the bidirectional interaction between nerve factors and immune cells in the skin (2). Endocrinological factors also regulate skin functions. Harvard group reacted these findings and named the system NICE (3).

Last year German group proved that mental stress decreased Langerhans cells (4). Certain odorants stimulate and others suppress skin immune functions (5, 6).

Cosmetics to meet the NICE system were developed from some companies. Recently, we paid attention to the homeostasis of the body, self healing function in other words. DHEA is considered as an anti-stress hormone.

The combination of the odorants which increase DHEA level and agents which stimulate the effects of DHEA was found to be effective to improve the skin condition by single treatment with acute stress and also by daily use of the novel skin care. Fusion of local and total treatment and the idea to take advantage of the homeostasis can provide tender and effective skin care.

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A New Approach to Anti-Ageing Technologies, Biology, Technology and Psychology

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Today's anti-ageing skin care formulations are more sophisticated than ever.

It is now possible to deliver meaningful, consumer-noticeable "anti-ageing" benefits beyond those traditionally associated with "moisturisers", out of a chassis with outstanding skin compatibility and exceptional aesthetic / multi-sensorial acceptability.

One could be forgiven for thinking however that, based on the technologies and marketing campaigns of the last 20 years, "anti-ageing" equals "anti-wrinkle", when this patently not the case.

As the title suggests, this presentation will discuss another approach by considering the biological structures that drive the optics responsible for human skin appearance, paying particular attention to internal light transport and the role of chromophore concentration and distribution in young and aged facial skin.

We will also consider new research where we have collaborated with Evolutionary Psychologists to demonstrate, for the first time, the link between these skin structures and the perception of age, health and attractiveness.

Finally, we will consider the importance of using both an understanding of skin optics and the psychology of perception to deliver a new generation of anti-ageing technologies to the consumer.

Cosmetic Science In Skin Ageing: Achieving the Efficacy

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Besides the anatomical links between brain and skin, keratinocytes in the epidermis and fibroblasts in the dermis, actively take part in the control of the epithelial homeostasis interfering with immunological, endocrine and nervous processes.

The skin, in fact, control all the environmental changes, generating stimuli transmitted to the nervous system via different mediators, such as cytokines and catecholamins. These mediators contribute to the interconnection of the three systems controlling homeostasis: the nervous, immune and endocrine systems. Both keratinocytes and fibroblasts are buried in a complex mesh of extracellular matrix, the ECM, which works not only as a physical support, but also as an exchange and communication area. Collagen, elastin, proteoglycans, fibronectins and other glycosilated proteins are the main molecules forming the ECM.

The long term detrimental effects on these cells and macromolecules is characterized by wrinkles loss of skin tone and resilience, evidenced as ageing. Thus skin ageing appears as a consequence of chronological aging effects, in a manner similar to other organs, and UV-generated reactive oxygen species (ROS) which deplete its non-enzymatic and enzymatic antioxidant defence systems, overwhelmingly contributing to a premature aging. Therefore, UV-rays activity, largely contributing to these detrimental effects on the skin, is the main cause of premature ageing of the skin.

However, it has been also demonstrated as the prolonged anxiety and tension promote the secretion of adrenocorticotrophic hormone (ACTH) from the anterior pituitary gland, which promotes the secretion of cortisol, leading to a reduction of immunological Langerhans cells and rough skin.

Moreover, as known from aromatherapy, fragrance may have favourable effects on the mind stimulating the mind-body connection.

In conclusion, skin protection and activity seems to be a result of an improvement of the balance of whole body rather than only a local improvement of skin condition. Therefore to achieve an higher efficacy of cosmetic products it should be necessary not only to use ingredients with a demonstrated biological activity at level of keratinocytes, fibroblasts and ECM, but also capable to activate and modulate the secretion of all the mediators produced from the nervous, immune, cutaneous and endocrine system for balancing and stimulating the *mind-body* connection.

As the immune molecules can trigger feelings of sluggishness, sleepiness and loss of appetite, they may also activate the defence cascade of cytokines and hormones. Thus, they may contribute to ameliorate the skin homeostasis and reduce the skin alterations associated with aging, by a better interconnection with the nervous and endocrine systems.

This the new way for obtaining innovative anti-ageing cosmetics.

Neuroscience is the future of innovative Cosmetic and Functional Food, innovation is the lifeblood of progress.

A Good, Naturally Balanced Diet: Healthy, Beautiful Skin

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Beauty is certainly a sign of good health: we cannot be fine outside and therefore be beautiful if we are not fine inside. Our 'inside', our organs and systems, which are all, none excepted, interconnected, as highlighted by the acronym N.I.C.E. (which shows how closely related they are to a nice look as well), feed on stimuli, on relations but above all on food. We are, and we look, what we eat. Because what we eat, and how we eat, if we do eat well, enables the nervous system (N), the immune system (I) and the endocrine system (E) to work efficiently, thus making our skin healthy and young-looking (C). Actually skin blemishes are basically the end result of alterations of the functional balance of such systems, which is disrupted, much more often than we think, by simple, ordinary as well as gross dietary mistakes.

Despite his appearance and the common opinion, man is still a real animal, moulded over hundreds of years in the savannah, and, as such, he must completely rethink his own diet, both qualitatively and quantitatively. The quantity and quality of what modern man eats nowadays is actually too different from what our body can still recognise and asks us as the optimum diet to maintain our health and live as best as we can.

The key components of a complete, healthy diet, such as proteins, carbohydrates, vitamins, fibre, minerals, must certainly be of excellent quality (for instance "good" fats), but basically they must be taken at different times from what we usually do. More often than not, we just count the total calories of our meals, thinking this is enough to eat well. Instead, all such components must be well balanced over the day, starting with breakfast, but above all they must be well balanced in every single meal. Few high-calories and/or imbalanced meals lead therefore to a state of overloading or deficiency, which our organism cannot appropriately respond to, and pave the way to different stages of metabolic disorders, from liver to pancreas disorders, from skin to general disorders.

Of course any functional alteration, even minimal ones that are well below the threshold of a full-blown pathology, of a major organ or system will have repercussions on our general wellbeing, first and foremost on our mental and therefore our psychological wellbeing.

Nowadays, technology and research provide us with certainties about the quality, source and purity of such components, on the lack of pollutants. Likewise, over the last few years, research has led us to understand the importance for our health, wellbeing and therefore for our outward appearance, of some essential components, such as antioxidants and microcirculation regulators (nitric oxide), which the diet of people who take care of the quality of their skin cannot be lacking in.

New topical agents for the ageing face

A. Puri Ph.D.

President, Cosmeceutical Solutions - UK

There is a famous saying nothing succeeds like success !! that is absolutely true in case of new topical agents for the face. Success of Cosmeceuticals which are now tipped to be the fastest growing sector of the cosmetic business over the next few years particularly in the face & under eye area has resulted in discovery and introduction of a very impressive number of very efficacious new 'Actives' to the market.

Their activity can be broadly divided into the following categories:

1. Retinol and derivatives
2. Vitamin and vitamin derivatives
3. Peptides
4. Antioxidants
5. Hydroxy Acids
6. Depigmenting agents
7. DNA & Cell Protection and stimulation
8. Growth factors
9. Others

The presentation will highlight the latest and the most effective topical agents ie. 'Actives' recently introduced for the ageing face.

Anti-inflammatory and Retinol-like activities coming from nature

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Ethnobotany is a discipline that studies valuable traditional knowledge regarding the use of medicinal plants and the relationship between people and plants. Two different active ingredients are discovered from nature out of a variety of plants used in traditional Chinese and Japanese medicine against diverse skin ailments. The aim of the present study is to demonstrate that those benefits from plants can also be utilized for cosmetics as shown for both (1) tiliroside, and (2) di-hydroxymethylchromone (DHMC).

(1) To investigate anti-inflammatory effects of tiliroside an inflammation is provoked by UV-radiation using a solar simulator in a placebo-controlled *in vivo* study on 20 human volunteers with dry skin. The development of erythema is examined after application of emulsions containing tiliroside prior to and after treatment. (2) DHMC has been investigated by an *in vivo* anti-wrinkle study on 40 human volunteers over 28 days with twice-daily application.

The cutaneous relief has been assessed before and after application with a PRIMOS 3-D device. Furthermore the gene activation pattern of DHMC has been compared to Retinol by means of cDNA analysis of human keratinocytes *in vitro*.

(1) Anti-inflammatory studies with tiliroside formulations (use level 0.1%) show a statistically significant decrease of skin reddening (Chromameter) after 6 and 48 h versus the placebo. In parallel the tiliroside containing verum suppresses the capillary flow after 6, 24 h as well as 48 h after UV-irradiation with statistical p-value of about 0,002. (2) A similar gene activation pattern as described for Retinol is achieved when DHMC is used. DHMC stimulates the synthesis of collagen while reducing the activity of collagenase and elastase *in vitro*. Finally *in vivo* studies with DHMC confirm a statistically significant decrease of 12% in average roughness in 80% of the volunteers.

In conclusion tiliroside and dihydroxymethylchromone are very effective ingredients coming from nature for normal and sensitive skin. They offer a multitude of cosmetic claim opportunities such as calming/soothing skin, anti-inflammatory, and anti-ageing/anti-wrinkle. DHMC could be identified as efficient alternative for Retinol especially due to its superior skin tolerance and stability.

Soft Vesicular Systems for efficacy and safeness in cosmetic products

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Nanotechnology is surging ahead in the cosmetic industry. It is mainly used in personal care and sun-screen products. Soft nanovesicles are an important addition to technologies that will generate sophisticated formulations and could have a major impact on the future of nanocosmetics.

Phospholipid soft vesicles can efficiently target both hydrophilic and lipophilic actives to the various layers of the skin and improve their skin penetration.

One major characteristic of these vesicles is their fluid bilayers. It is noteworthy that these nanostructures, while delivering the agent to the deep layers of the skin, are not absorbed intact through the skin. This important feature together with the lack of skin irritation and any side effects contributes to their safety as carriers for cosmetic use.

The ability of soft vesicles to enhance delivery of active agents to the deep skin strata and pilosebaceous units could lead to the development of safe and efficient new cosmetic products for a wide range of active agents for skin barrier repair, whitening, anti-aging, moisturizing, skin nutrition, anti-cellulite and hair-growth.

These nanovesicular carriers are made of safe and approved ingredients, generate compositions with esthetic appeal and are easy to manufacture.

Skin bleaching agents in legal and illegal market. The use of some depigmenting cosmetics out of the rule, illegally imported and consumed in Italy from foreign people

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The bleaching products usually contain drugs and substances able to inhibit or prevent the synthesis of melanin.

According to the mechanism of action, they are divided in:

- inhibitors of the synthesis of tyrosinase (such as the heavy metals),
- inhibitors of the activity of tyrosinase (such as the anti-oxidants, that bind to the O i.e: idroquinone, arbutin and glycolic acid) – the most popular
- agents with selective cytotoxicity towards the melanocytes
- inhibitors of the transfer of melanosomes to keratinocytes (cytochines)
- agents able to keep the melanin in the reduced form, making it clearer (peroxides)

The bleaching agents include hydroquinone, hydroquinone derivatives (hydroquinone monobenzylether and monomethylether), strong steroids, mercurials (mercuric oxide 1–3% or mercuric chloride 6–8%), kojic acid, alpha hydroxyl acids, plant-derived products (that may contain active agents such as arbutin) and even hydrogen peroxide.

Skin bleaching agents are marketed as cream, lotion, oil, gel, soap or pomade formulations and are typically obtained from non-medical sources, including open markets and beauty stores. Sometimes, various ingredients from the domestic environment (toothpaste, washing liquid, washing soda, hair straighteners, sand, cement and even battery fluid) may be mixed in homemade concoctions that are used for their caustic effect.

The unregulated trade in cutaneous depigmenting agents involving non-medical individuals has fuelled an international trafficking business, which needs to be curtailed. Moreover, the risk of side-effects occurring with skin bleaching depends on the nature and concentration of products used. This is complicated by the fact that these products may contain a higher concentration of active agents than stated on their packages. Additional contributory factors for the development of side-effects with skin bleaching include the concurrent use of several active principles, application of products over widespread areas of the body and for prolonged periods (months to years) and lack of sunscreen application.

The current focus within the dermatological community on the safety and regulation of hydroquinone presents a unique opportunity to raise awareness on the occurrence and dangers of skin bleaching. Aesthetic and systemic side-effects of skin bleaching not only remain a public health problem in most parts of sub-Saharan Africa (but not only), but also may increasingly impact many other com-

munities around the world. It is also important that we educate individuals that use the legal formulation of these drugs for the treatment of pigmentary problems to seek dermatological care for their dermatoses, in order to avoid the self-medication or use illegally obtained cutaneous depigmenting agents.

However, this would not be enough to reduce the global burden of skin bleaching. Instead, a multifaceted approach is required.

Some studies in the field of human sciences, to consider the sociological and psychological factors that are responsible for the search of a lighter complexion (which may vary among different communities) are required to guide the development and implementation of appropriate public health prevention campaigns. In addition, international cooperation between governmental, nongovernmental and medical agencies is required to decrease the international trafficking of illegal depigmenting agents.

Continued rigorous scientific studies, especially in Western, Arab and Asian countries where such studies remain scarce, are required to critically evaluate the global burden and adverse health effects associated with skin bleaching.

Finally, more research directed towards the development of alternative safer agents for the inhibition of skin pigmentation is required.

TRADEMARK: for promoting your image: First & Second Part

A. Morganti, A. Klein

FIRST PART

Know what qualifies as a trademark or service mark: A trademark is any name, symbol or slogan that is used to distinguish a particular product or service from others in the marketplace and/or identify the source of a particular product or service (the company that makes or provides it). Business names, logos, packages, domain names and distinctive product designs can all qualify as trademarks. Know what types of trademarks qualify for maximum legal protection (called 'distinctive' or 'strong' trademarks): Unique logos or symbols such as the Nike Swoosh design; made-up words such as SHISEIDO or LANCOME; fanciful marks or words that evoke imaginative images such as CLINIQUE or BIODERMA; arbitrary marks that are surprising in the context in which they're used, such as APPLE and marks that suggest but don't outright describe a product's qualities, such as Netscape Navigator (web browser). How an arbitrary and fanciful mark may become generic or descriptive like RIMMEL.

SECOND PART

No one doubts that the term SEPHORA for instance, a logo, or their combination are trademarks. However, the shape of a packaging, a piece of music, a colour, a smell, that are not traditional trademarks are not always identified as trademarks. However unusual, it is true that people rely on the presentation of a colour, a packaging to locate a product on the shelves of large supermarkets. Similarly, taste, touch and sound may also help in identifying a product. Since according to national laws registration of colours, sound, smells are not always possible, a short list of do's and don't's will be presented.

INFRINGEMENT: are you sure you know what counterfeiting is?

Pier Luigi Roncaglia

Studio Legale SIB, Firenze - Italy

The main menace to businesses' IP assets is no doubt the evergrowing phenomenon of counterfeiting and piracy. Notwithstanding international recognition of the gravity of the problem and the successful efforts achieved with legal tools to strengthen national enforcement and anti-counterfeiting laws all over the world, counterfeiting remains a booming business everywhere.

While, the soft spot of counterfeit consumers is traditionally fake luxury goods bearing status symbol trademarks, counterfeiters have expanded to new fields such as children's toys, pharmaceuticals, foods, auto parts and airplane components, where health and safety issues heavily come into play.

To combat the counterfeiting phenomenon we need to tackle it on all possible fronts, from the political and legislative side to the enforcement and social awareness perspective. This last aspect is particularly important. In fact, it is crucial to make people aware of the extent of this problem as well as of its gravity, because counterfeiting is not just about the small time street vendor trying to make a living – he is only the weakest link in the entire chain –, but is really about a huge underground market that can cause serious damage to important and delicate social interests.

While it is impossible to successfully prevent or exterminate counterfeiting, completely and permanently there are legal strategies that permit to control this problem, reducing both the risks that it arises and its entity.

ROUND TABLE

THE COSMETIC EFFICACY MYTH OR REALITY?

The Opinion of ...

Introductory Remarks

Pierfrancesco Morganti

President & Secretary General ISCD- Roma -Italy

Professor of Applied Cosmetic Dermatology, II University of Naples, Pavia - Italy

Visiting Professor of China Medical University, Shenyang - China

According to the well-known dermatologist AM Kligman “petrolatum penetrates into the lipid-rich intercellular space of Stratum Corneum (SC), enhancing its barrier properties and making the horny layer pliable so that it does not crack when deformed”.

Moreover, M Mao-Qiang and PM Elias have demonstrated by interesting studies as this hydrocarbons compound promotes wound healing and prevents ultraviolet-induced tumors also. Thus, it should be underlined as this old oil compound used to produce cosmetics and the simplest cosmetic emulsions penetrate through the SC and induce modifications on the skin physiology.

These are the conclusions of all the studies reported in the scientific papers of the last 30 years. Therefore, Cosmetic Products when well formulated and controlled by *in vitro* and *in vivo* studies support and restore the biological functions by their activities. But, how define their function and which is their mechanism of action?

Without a shadow of doubt cosmetics interact with the physiological mechanisms of the skin without having a therapeutic function but *protecting or keeping in good condition any suffered cell* by simple biological mechanisms.

This round table has been organized to give the opportunity to all the participants to give your opinion to this fascinating theme. Therefore, the function of cosmetic products and their mechanism of action will be considered and discussed to clarify and define their overlapping with drugs and medical devices of topical activity.

Moreover, it is intention of the Congress' Organizers to report the final conclusions of this multidisciplinary panel of expert at EU level for trying to review the actual regulatory state of cosmetics, medical devices and drugs.

The Opinion of

L. Gagliardi

Director Dept. Complementary Natural & Complementary Drugs Safety Cosmetic Products, Italian Institute of Health - Italy

The scientific developments derived from biological researches applied to dermatology have deeply changed numerous concepts in skin physiology and physiopathology. According to current EU legislation a cosmetic product is so defined:

A 'cosmetic product' shall mean any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition.

According to current EU and Italian legislation on medicinal products the distinction between drugs and cosmetics, biocides and medical devices seems clear and unequivocal as reported at art. 2 of the Directive 2001/83/CE:

Article 2

- 1) This Directive shall apply to medicinal products for human use intended to be placed on the market in Member States and either prepared industrially or manufactured by a method involving an industrial process.
- 2) In cases of doubt, where, taking into account all its characteristics, a product may fall within the definition of a 'medicinal product' and within the definition of a product covered by other Community legislation the provisions of this Directive shall apply.

Taking into account the advancement of science of cosmetology it is necessary a deep revision of European rules in order to better classify such categories.

The Opinion of

Luciana Gramicciani, Roberta Marcoaldi

Director Dept. Environment and Medical Devices Natural, Italian Institute of Health - Italy

In the last years, since the Council Directive concerning medical devices has been adopted, we assisted to a large improvement in the sector of topic products.

These products, which do not achieve their principal intended action in or on the human body by pharmacological, immunological or metabolic means, can be considered like medical devices also because they be used for human beings for the purpose of diagnosis, prevention, monitoring, treatment or alleviation of disease.

The comparison between the definitions of medical devices, cosmetics, medicinal products and biocides underlines the possibility to find a borderline product.

A misclassification can be due to the presence of ancillary effects. These ancillary effects are permitted if however it is possible to show that their function is only a function of assistance to the principal effect.

For this reason it is more and more important conduct reliable studies about the principal intended action of the various component substances, about their ability to penetrate the skin and the mucous membranes, and about their "therapeutic" function.

In every case it is important to remember that the principal intended action of medical device always must be carry out by a mechanical and a physical effect.

The Opinion of

S. Selletti

Astolfi Associated Law Office, Milano - Italy

The rules governing the marketing of health and wellbeing products contain precise definitions meant by the Legislator to mark the identification of the various classes of products and correctly determine their implementation field.

It has in any case been proved that scientific and technical progress often confers the health products such original and innovative features as to make it more difficult their classing as to legal definition due to the overlapping that can occur among the different areas.

The cosmetic sector is an emblematic example of such a situation.

Research and progress have favored the notion of functional cosmetics which can interact with physiological functions, without interfering, on the action level, with mechanisms typical of other classes of products (for instance, medications).

The basic issue is therefore identifying which is actually the frame for functional cosmetics within our current legal classification. In order to do so, we must first say that the definition of cosmetic comprises functional profiles that when effectively interpreting the development and the progress in the cosmetic field, broadens the interpretation limits until it becomes necessary to proceed on a "case by case" basis as indicated also the Judges of the European Court of Justice, when asked to decide upon the interpretation of rules in borderline situations, in such a case, supported by the "Handbooks" drawn by the Work Groups and by the Guidelines on Borderline products issued by the Union, that, although not binding at a legal level, are certainly effective interpretation tools to correctly orient the enterprise and interpreters' performance.

Without claiming to give an exhaustive view on this issue, may we give some hints about the assessment frame. Therefore, taking into account typical cosmetic functions, if no interpretation issue can be raised about the commonest functions such, for instance "perfuming", on the contrary, reference to "protection" and "keeping in good condition" the parts of the body which the cosmetic can be applied on, reminds of activities which, with much greater difficulty, can be classified and determined a priori to establish abstract classification schemes.

A cosmetic protective function can in fact occur in various areas, so as the keeping in good state, and the space for the correct classification of the products is precisely close to these limits. It is apparent that the protective function and the keeping in good state can not imply therapeutic functions, but this does not prevent the cosmetic from having protective adjuvant function together with the use of medication for skin care and such property from having action mechanisms not interfering with other product classes.

Still, the cosmetic definition, with regard to the product aim, involves the issue of the "exclusive or prevailing" use, thus granting access to the representation of primary and ancillary functions. In such cases the legal limit is of course the former prevailing on the latter, in order to respect the cosmetic functionality domination with regard to secondary areas.

As you can see the frame for the assessment of cosmetic effectiveness "between myth and reality" is still wide, but also thanks to this fact, there remains a wide margin for progress, science and the interpreters' work.

The Opinion of

Stefano Dorato

Director Regulatory and Scientific Affairs, UNIPRO, Milan - Italy

Looking and feeling good brings confidence and success in of our lives. Cosmetics help people taking care of themselves and play a role for a better quality of life by providing feelings of well-being (by using a shampoo, a makeup or a fragrance), protecting from climate impacts and consequent skin/hair damage (by applying sunscreens or skin moisturizers or hair conditioners) and ensuring good hygiene practices (by means of soaps and oral care products).

Colipa (*The European Cosmetics Industry Association*) guidelines and recommendations (e.g. on safety assessment, product information file, undesirable effects, cosmetic efficacy) represent an important tool for the industry, providing useful information on the practical interpretation and application of legal requirements.

Recently Colipa has published revised guidelines for the efficacy evaluation of cosmetic products. Methodologically sound research is essential for the efficacy evaluation and the guidelines offer an overview of the established different testing methodologies, providing data on the performance of cosmetics products.

Cosmetic claim substantiation is an integral part of product development and design and validated evaluation methodologies grant an appropriate and effective tool to assess the validity of product efficacy.

Moreover efficacy claims and the methods substantiating them need to be included in the product information file, by the person placing the product on the market, according to the current Cosmetics Directive and the future Cosmetics Regulation.

However some product efficacy claims, even when scientifically substantiated, might fall outside the scope of the Cosmetics Directive. Concerning the delicate question of borderline products among the scope of the Cosmetics Directive and other pieces of EU Regulation, like the Medicinal Product, the Medical Devices, the Biocides, the Food and the General Product Safety Directives there are several guidelines produced by the EU Commission to help both the national Competent Authorities and the industry.

The Manual on the scope of the application of the cosmetics Directive is the latest guideline and it is the result of the effort of a working group chaired by the Commission (DG Enterprise) and composed of representatives of all Member States of EU and EFTA, the European Organisation of Consumers (BEUC), the European Federation of Cosmetic Products (COLIPA) and other industry associations.

In the EU a product can have only one regulatory status at a time, as reiterated also in the Recital no. 5 of the Cosmetic Directive 76/768/EEC “[the Cosmetic Directive] is not applicable to the products that fall under the definition of cosmetic products but are exclusively intended to protect from disease”. Recognizing the existence of a borderline area with definitions overlapping to some extent did not, in any case, induced the regulators to introduce mid way categories (e.g. cosmetic/drugs) even in the recent recast of the Cosmetics Directive which ended with the approval of the new Cosmetics Regulation.

The EU Court of Justice in various judgements indicated that, in case of definitions overlapping, should be applied the most rigorous legal regimen.

Nevertheless the different Commission guidelines, published on its Internet site, contain principles laid down by case law:

- global assessment of the characteristics of the product (e.g. function, composition, method of use, frequency of application, application site, distribution, familiarity of the consumer with the product, potential risks, labelling, packaging, claims, target population etc.) must be taken into account in order to avoid that a single characteristic is enough to arrive at a definite judgement;
- the intended main function of the product (i.e. cleaning, perfuming, changing appearance, correcting body odours, protecting, keeping in good condition) takes precedence when making a decision and a secondary, ancillary function for 'preventive' purposes does not necessarily classify a product as a drug or a biocide;
- the question whether a product or its substance(s) restores, corrects or modifies physiological functions by exerting a pharmacological, immunological or metabolic action has to be taken on a case-by-case basis. Cosmetics may modify physiological functions without affecting the metabolism in a significant way, i.e. not any minor modification of physiological function suffices to render a product a medicinal product by virtue of function;
- if a substance is also contained in a drug as active ingredient, it is not decisive for the classification of a product but this may be an indicator for a pharmacological, immunological or metabolic action of the substance independently of the question whether the product is ingested or used topically;

The EU Court of Justice is of the opinion that: *"As regards the meaning of 'restoring, correcting or modifying physiological functions', it is clear from the aim of health protection pursued by the Community legislature that the phrase must be given a sufficiently broad interpretation to cover all substances capable of having an effect on the actual functioning of the body. However, this criterion does not serve to include substances such as certain cosmetics which, while having an effect on the human body, do not significantly affect the metabolism and thus do not strictly modify the way in which it functions."*

The conclusion of this short summary is that the answer is in the hand of the Company producers which must use brain, money and time not far away from what is made when something, that interact with health, is produced.

The Opinion of

Bruno Berra

Physiology and Biological Chemistry Institute Milano - Italy

A cosmetic product is the result of a simple or complex chemical procedure.

In this view, it must be seen as a scientific creation based on very well-known ingredients and following a rational pathway. For this reason, the answer is that cosmetic efficacy is a reality!

However, science and marketing are very often in contrast: the low of marketing is so that the mechanism of action of a cosmetic product is not well-recognized and defined and it is not taking care of the real efficacy of the ingredients. For this reason, the answer is that the cosmetic efficacy is seldom a myth!

One must become aware of this situation by three means:

- Considering how many of the cosmetic products are made; in many cases I personally informally observed that the invention of a new product is only the result of the average composition of goods already present in the market.
- Looking at the sentences issued in Italy by the "Istituto di Autodisciplina pubblicitaria" which are published in the website of IAP (www.iap.it).
- Evaluating the actual national and international regulations which are to be followed in order to put on the market a new product.

The Opinion of

Fabrizio Guarneri, Biagio Guarneri

Institute of Dermatology – University of Messina - Italy

Cutaneous absorption can occur through an intercellular path, an intracellular path, or through hair follicles. Although active captation is possible, the transport of substances happens mainly by passive diffusion: in this model, absorption depends on the gradient of concentration of a substance between the outer and the inner layers of the skin. However, for the aforementioned reasons, the cutaneous barrier does not act as a simple membrane, and absorption is also significantly influenced by several factors, such as the physical and chemical features of the molecule(s) applied on the skin, the structure and condition of the skin itself, and environmental variables.

For which concerns penetration in the skin, one of the most important characteristics of a molecule is its partition coefficient (also known as distribution coefficient), not only between a hydrophilic and a hydrophobic phase, but also between the stratum corneum and the vehicle used in the compound applied on the skin. The size of the molecule is similarly important: smaller molecules can penetrate more easily than bigger ones. Less important features are the presence of polar chemical groups on the surface of the molecule, electric charge, hydration, and volatility. Of course, for all the above parameters, modifications possibly occurring on the cutaneous surface must be kept into proper consideration.

Percutaneous absorption also depends on several subjective parameters, some with interindividual variability, such as age, sex, ethnicity and hereditary features, others with both interindividual and intraindividual variability (significant differences among various body areas), such as skin thickness, skin aging, cutaneous hydration and pH, number of hair follicles, cutaneous blood flow.

Finally, microenvironmental conditions at the site of application, such as temperature, humidity and occlusion, can influence the interaction between a compound and the skin barrier, and consequently the local permeability of the barrier itself. However, Major alterations of the barrier can occur during cutaneous diseases and also in some cases of systemic diseases, and play often a significant role in maintaining or aggravating the disease itself.

In our opinion, the lack of reference to the effects of topical products on the functions of the components of the skin barrier is a major problem of the laws, and no real progress can be made in the regulatory field without solving this problem.

Moreover, in the last decades, the continue evolution of cosmetic research progressively introduced an increasing number of components with pharmacological or “nearly-pharmacological” activity, as well as highly technological delivery systems (not different from those used for medicinal products), into cosmetic products. This makes the boundaries between the current legally recognized categories even more blurry, and further underlines the distance between laws and scientific reality.

The Opinion of

Aran Puri Ph.D.

President, Cosmeceutical Solutions - UK

EC Cosmetics Directive 1973 7th amendment states cosmetics A “cosmetic product” shall mean any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition

Regulations when they are drafted are based on available science at that time. Technology and science has made an exponential leap since the EC Cosmetics Directive 7th amendment was first enacted and numerous amendments which update have been added along the years. Many of these are focused to various aspects of safety.

However the regulatory authorities have not felt the need to redefine or extend the meaning of cosmetics.

In the early 1980's Prof Albert M Kligmann, MD Ph.D. Professor Emeritus of Dermatology University of Pennsylvania coined the word 'Cosmeceuticals' of products in the category intermediate between cosmetics and pharmaceuticals..

Since that time the word Cosmeceuticals has been increasingly chosen and used by many cosmetic scientists and segments of the cosmetic industry to describe cosmetics which contain 'Actives' with specific efficacy.

I would define Cosmeceuticals as high performance cosmetics with a specific 'Activity' and demonstrable efficacy to improve and enhance the appearance.

Regulatory constraints on efficacy claims can in principle restrict cosmeceutical development because products claims can be made in terms of their ability to improve skin appearance but not function. Evidence of improved function would remove cosmetics from the cosmetic category and place it in the drug category and that is a dilemma facing the industry.

The Opinion of

Luigi Manzo

University of Pavia Department of Internal Medicine, Maugeri Foundation Medical Center, Pavia - Italy

That a cosmetic must be inactive with no biological or physiological interactions with cells and tissues is an ambiguous concept often contrasting with scientific evidence.

The simplest cosmetic emulsion composed of oils and water is known to induce physiological modifications on skin and is effective in increasing biological activity or promoting absorption of other active ingredients. Experimental and clinical studies of cosmetic products have indicated a range of biological activities that are compatible with their observed (desired or adverse) effects.

In principle, the ability to modify a biological function may be interpreted as an indicator of possible pharmacological activity. However, knowledge of the mode of action and accurate scientific evaluation of effects observed at various levels of biological complexity are fundamental approaches to distinguish a cosmetic from a pharmaceutical product. In this respect, the advancement in biomedical research and application of new molecular methods such as omics techniques offer new opportunities to characterise biological effects of cosmetics and determine whether these biological activities do not reflect unacceptable toxicity and are compatible with the intended cosmetological applications.

Advanced molecular techniques are increasingly used to assess the mode of action of cosmetics and the ingredients that are currently found in the cosmeceutical marketplace such as retinoids, B vitamins, peptides, antioxidants, and polyhydroxy acids.

These methods also be valuable to determine the biological effect profile of other emerging topical agents such as peptides, growth factors, nanotechnology-derived products, and a range of products proposed for natural skin defence, lightening and depigmentation.

Recent findings obtained by these new techniques indicate that the boundaries between cosmetics and dermatological products are fading away rapidly.

Accordingly, certain cosmetics have been proposed in the treatment of minor skin disorders and mild skin abnormalities based on the hypothesis that they may be effective as adjuvant of physiological processes by mechanisms not implying direct pharmacological action. These dermatological applications should be decided case by case based on prudent evaluation of safety and risk-benefit issues. Cosmetic treatment of minor skin disorders may indeed represent a valuable alternative to therapy with potentially dangerous drugs such as antiinflammatory agents and antibiotics. However, in the absence of expert medical advice, cosmetics may have unfavourable effects such as, for example, modification of the wound healing process or masking early manifestations of serious skin disorders. In such instances, treatment with pharmaceuticals, cosmetics or both should be decided after accurate medical evaluation.

The Opinion of

P. Minghetti

Institute of Pharmaceutical Chemistry, University of Milano - Italy

According to the current EU legislation a cosmetic product is intended as any substance or preparation used exclusively or mainly, to cleaning, perfuming, changing appearance, and/or protecting or keeping in good condition epidermis, hair system, nails, lips, external genital organs, teeth and or mucous membranes of the oral cavity.

This definition states also the difference with medicinal products, which must have a therapeutic effect, and with medical device, which must have the purpose of diagnosis, prevention, monitoring, treatment or alleviation of disease or a physiological process.

All these products have to be safe and efficacy.

Therefore, main issue, for cosmetics, is not only if the efficacy is a "myth or reality", but which kind of efficacy we have to speak about.

The latter question results particularly critical since a secondary prevention purpose is admitted and a definition of "disease" does not exist.

As a consequence, statements or claims reported in the label cannot be always clearly referred to a determinate type of product.

As far as cosmetic products are concerned, the legislation provides that they must not cause damage to human health. Following this provision methods of safety assessment have been developed ,and nowadays, many of them are validated.

As concern the efficacy, EU legislation sets that the proof of the effect claimed for the cosmetic product should be given, where justified.

So, while, there are no problems regarding safety, the demonstration of the efficacy is still lacking.

The Opinion of

Rocolfo Paoletti

Professor of Pharmacology, University of Milano - Italy

NOT RECEIVED

The Opinion of

Flavio Papadia

Trust-Buster Authority of Market & Competition

Tales about marvellous mysterious countries, that sometimes are only the result of imagination while sometimes do refer to existing places, all share the characteristic of being full of emphasized descriptions and extraordinary details. You can have a feeling similar to the one raised by such tales when exposed to advertising, whose task itself is to depict a given product or service in such a way as to lure consumers into buying it.

For cosmetics in particular this situation is magnified by the nature of the products, whose nature is closely related to the improvement of the appearance of a person, both in the eyes of others and in the eyes of that very person.

The distinction between myth and reality is the main subject matter of the repression of misleading advertising.

The relevant regulation in Europe has changed recently following the adoption of the Directive 2005/29/EC on Unfair Commercial Practices, which set new rules enhancing consumer rights. Among other things, the new legislation outlines "sharp practices" which are prohibited throughout the EU, such as misleading and aggressive marketing. Enforcement of the rules is the task of national consumer protection authorities and courts.

It is worthwhile considering how this change in consumer protection legislation determinates an evolution in the assessment of marketing practices in general and in the cosmetics sector in particular. A few cases have already been decided by the Autorità Garante della Concorrenza that supervises misleading and aggressive marketing In Italy, with rulings in which it is possible to see the continuity that exists with the consolidated jurisprudence in the field and elements introduced by the new regulation.

The Opinion of

Liu Wei, M.D., Ph.D.

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Vice-Chairman, National Standard Committee of Cosmetics - China

Efficacy is a fundamental character of cosmetics. In broad sense every cosmetic product has an efficacy, for example, cleaning, moisturizing, nutrition, skin and hair care, beautifying and so on. With the progress of science and technology especially in the field cosmetic industry and skin physiology, many new types of cosmetic products have been developed and in consequence more and more functional usages have been claimed by cosmetic products such as whitening, anti-aging, sunburn protection, anti-acne, etc. In China there is a special category of cosmetics, namely special using cosmetics including nine kinds of products claiming hair-growing, whitening, sunscreens, bust-beautifying, body-slimming, depilatory, deodorant, hair-dye and perming, which were based on a series of corresponding active ingredients added in their formulas. Such products, so called cosmeceuticals, represent a boundary products between cosmetics and drug., and put on a pressing challenge to the basic concept of cosmetics and the cosmetic regulations worldwide.

Many methods, both *in vitro* and *in vivo*, have been established in recent years to evaluate the efficacy of cosmetics. Animal test is banned now in Europe and human become the victim. Fortunately non-invasive techniques are developing rapidly and human subjects may survive from such tests. The real problem of the matter is that we have no international standard method in evaluating the efficacy of cosmetics with the exception of SPF test of sunscreen. Acceptable criteria and standard operation procedures (SOP) are necessary in evaluating the efficacy of cosmetic products especially in clinical trials. Such standards are deadily needed by cosmetic industry in developing new products, by consumers in selecting suitable goods according to the claims of cosmetics, and by governments worldwide in monitoring and regulating the market.

We have done a lot of works in this field and a book has been published in recent year titled with 'SKIN BASIC SCIENCE AND FUNCTIONAL EVALUATION OF COSMETICS' (editors: Liu Wei and Zhang Huailiang, Chemical Industry publisher, Beijing, 2005).

The Opinion of

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Infiltrating knowledge from biological sciences has fundamentally changed our view on dermatology. Yes, histologically, human skin is always the same as what we used to look at it to be. The skin is composed of epidermis, dermis, subcutaneous tissue and several adnexal units. The epidermis is mostly composed of stratum corneum, granular cell layer, prickle cell layer and basal cell layer. The intricate biological reactions and interactions among viable constituents of the skin are hard for our visual observation to understand. Rather, we have to rely on modern biological principles and techniques to tackle the complicated machineries of the skin. Understanding of the skin is far more complicated in diseased skin conditions, in regard to the fact that there are thousands of categorized skin diseases.

Here we take the outmost layer of skin—stratum corneum (SC), as an example. Until several decades ago, many people thought SC was a layer of nonviable terminal junk of the epidermis that would eventually slough off. Now we see SC, albeit nonviable in the sense of living cells, contains many molecules that are indispensable for the homeostasis of the human skin. SC plays an important role in the so-called skin barrier function, which is measurable in terms of transepidermal water loss, water content, lipid content, to name a few. Genetic or environmental factors might disturb the skin barrier function. For example, functional mutated filaggrin gene causes ichthyosis, a heritable skin condition manifesting as dry and scaly skin; over-exposure to detergents that wash off or disturb the sebum component in the SC causes xerosis or even xerotic eczema; extreme weather conditions such as dry and windy season would exacerbate the symptoms of dry skin. Molecular studies showed that decreased amount of natural moisturizing factors, low level of ceramide, and decreased activity of certain proteases, contributed to skin barrier function of SC, among an array of other factors.

Moisturizing cream is a prototype of cosmetic products. Topical application of moisturizing creams has long been used to alleviate the dry skin condition. Nowadays, moisturizing creams with functional ingredients such as ceramide, urea or some small molecule proteins can do much better than the traditional “pure” moisturizing creams, in improving the dry skin condition.

Myth or reality? As long as a cosmetic product is designed, developed and tested in a scientific fashion, has a measurable efficacy and manageable safety profile, a cosmetic product will have a solid ground in aiding the skin care.

Organic Lycopene from Tomatoes: the way to obtain a unique product

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Lycopene is a carotenoid found in a wide variety of vegetables and fruits. There are more than six hundred natural carotenoids, but only twenty of those have been found in human blood and tissues. Lycopene is the most abundant carotenoid in human blood, followed by β -carotene, lutein and zeaxanthin (1).

The purpose of this work was to obtain a natural, solvent-free lycopene extract from red-ripe tomato fruits. This project was developed in three different steps finalised to control and optimise the entire productive cycle starting from fresh tomatoes and finishing with the production of organic lycopene. The first step of this work was the accurate selection, experimentation and production of organic grade certified tomato varieties characterised by high-lycopene content (2), followed by the biochemical analyses of their antioxidant characteristics (3).

The second step was the setup of a process to obtain a freeze-dried tomato matrix suitable for the extraction by supercritical carbon dioxide (SC-CO₂) from the new selected high-lycopene varieties (4). The last step was the optimization of SC-CO₂ lycopene extraction from a defined blend of the tomato matrix with a co-matrix composed of roughly crushed hazelnut seeds.

This procedure allowed the simultaneous extraction of lycopene from the tomato matrix and oil from hazelnut co-matrix which improves the solubility of the pigment and increase the yield of recovered end-product, according to the Pierre S.r.l. Galatina patented co-extraction technology (5,6).

The extract is an over-saturated solution of lycopene in hazelnut oil (oleoresin).

This innovative procedure has high lycopene extraction yields. The oleoresin represents a healthy and high added-value source of lycopene, suitable for nutraceutical, cosmetic and pharmaceutical purposes. It was registered as the first organic grade lycopene. This innovative product is characterized by: 1) the absence of toxic impurities such as solvents, pesticides, heavy metals and dioxins; 2) high natural bioavailability, increased by the presence of the co-extracted natural components from hazelnuts and tomatoes; 3) high antioxidant activity, due to the presence of other carotenoids from tomato and of tocopherols and phytosterols from the hazelnut oil.

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The Global Activity of Lutein in Human Health

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Lutein and its isomer zeaxanthin are oxycarotenoid naturally present in the typical human diet through sources such as green leafy vegetables. Lutein is one of the few carotenoids absorbed by the body and detectable in appreciable concentration in the serum (1).

Lutein is concentrated in the eye and the skin and deposits in fatty tissues. The rationale for the protective role of lutein in the human body, stems from the ability of this carotenoid 1) to filter short-wavelengths of visible blue light, 2) to function as an antioxidant and 3) to stabilize membrane integrity (2).

These biological functions are believed to play an important role in helping in reducing light-induced oxidative damage caused by reactive oxygen intermediates. Lutein is well known for its role in eye health: research indicates that it plays a protective role in the macula and the lens of the eye and that is associated with improvement in visual performance (3-5). The role of lutein in skin health is an emerging area of research. Like the eyes, the skin is constantly exposed to potential damage from light and the environment.

Therefore, the skin may also benefit from lutein's biological functionalities.

Several human intervention studies using lutein in combination with other carotenoids and/or other antioxidants indicated a promising role of lutein in helping protect human skin (6, 7).

A double-blind, multi-center, clinical study offers considerable evidence that lutein (FloraGLO™ Lutein) administered orally, topically or as a combined oral and topical treatment may provide specific skin health benefits. In fact, the results show that lutein may positively modulate skin hydration and elasticity, skin lipid peroxidation and in particular provide skin photoprotective activity and increase superficial skin lipids (8).

Future studies may provide additional support for the beneficial role of lutein in skin health and may help elucidate the mechanism of action supporting the efficacy of lutein in specific skin health conditions.

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Melatonin as an Antioxidant, Radical Scavenger and Antiaging Molecules: Role in the Skin Physiopathology

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Melatonin, which interact with the neuroendocrine axis and with circadian rhythms, was recently recognized as a free radical scavenger, antioxidant and antiapoptotic agent. The protective effect of melatonin may be associated with the increases levels of several antioxidative enzymes such as Mn SOD dismutase and Cu-Zn SOD dismutase.

The wide range of antioxidant enzymes induced by melatonin includes GPRX, catalase and SOD dismutases. In addition, levels of some prooxidant enzymes such as lipoxygenase and NOS are depressed after melatonin treatment.

It is well known that tissue aging is characterized by a progressive deterioration of circadian time keeping and that melatonin is reduced during aging.

Melatonin exerts many of its physiological actions by interacting with membrane MT1 and MT2 receptors and intracellular proteins such as quinone reductase 2, calmodulin, calreticulin and tubulin. MT1 and MT2 receptors are G protein coupled receptors expressed in various parts of the CNS and in peripheral organs (including skin).

The effects of melatonin comprise changes in intracellular cyclic nucleotides (cAMP, cGMP) and calcium levels, activation of certain protein kinase C subtypes, intracellular localization of steroid hormone receptors and regulation of G protein signaling proteins.

One main role of melatonin is to control mitochondria homeostasis improving the bioenergetics of the cell.

Melatonin, is produced by and metabolized in the skin where its functions are mediated by cell-surface and putative-nuclear receptors expressed in skin cells. The function is protect against oxidative stress and ultraviolet radiation-induced damage.

The properties of endogenous melatonin suggest that this molecule is an important effector of stress responses in the skin as reported by Slomisky A. (2007).

The predominant receptors is MT1, one found in both whole skin and cultured cells.

PPARs which are members of the nuclear receptor super family that regulate lipid, glucose, and aminoacid metabolism were recently in skin where regulate important cellular functions including cell proliferation, differentiation and inflammatory responses together with DAF, a transmembrane protein which contain a glycosily phosphatidyl inositol (GPI) anchor.

The links between PPARs, DAF and Delta-6 and Delta-5 desaturases involved in long chain polyunsaturated fatty acid synthesis are the following:

LC PUFAs increase cell membrane fluidity and enhance a number of receptors, serve as endogenous ligands of PPARs and regulate the balance between pro and anti-oxidant; daf-7 codes a transforming growth factor beta (TGF-beta) type signal while daf -16 enhances superoxide dismutase (SOD)

expression. On the other hand, melatonin has an antioxidant actions similar to daf-16, TGF-beta and SOD. These interconnected effects suggest that the activities of Delta-6 and Delta-5 enzymes play a critical role in the expression and regulation, besides other molecules, of daf genes and melatonin. These new evidences seem to create a link between long chain PUFA, melatonin and skin abnormalities.

Beyond Caffeine. Unexplored Potentiality of other Coffee Compounds

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Many studies have shown positive effects of moderate regular coffee-drinking on various aspects of health, ranging from psychoactive responses to neurological and metabolic disorders. Among approximately 850 volatile and 700 non-volatile substances, caffeine is the coffee compound which plays the most relevant role in the health impact of coffee consumption, and up to few years ago, it has been considered the only one biologically active coffee compound. However, coffee brews are characterized by properties, such as antioxidant and antibacterial activities, which cannot be exclusively related to the presence of caffeine. Moreover, several recent studies put in evidence that coffee beverage is rich in many other biologically active substances, some of them naturally occurring (polysaccharides, polyphenolics, sterols, tocopherols, etc.), some others generated by roasting (quinides, melanoidins, nicotinic acid, nicotinamide, etc.).

The scope of the present work is to provide an overview of several coffee non-volatile compounds, other than caffeine, with potential benefits or adverse aspects on human health.

Coffee compounds presence and concentration in the beverage is determined by many factors such as coffee botanical species and varieties, raw material processing, blending, roasting process and brewing method. Up to now, these factors have been exploited to offer coffee products able to satisfy consumer taste, flavour and mouthfeel needs, in the future, however, they could be used to modulate physiological effects and then to personalize the coffee health impact.

The Dietary and Antioxidant Properties of Virgin Olive Oil

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For a long time olive oil's health benefiting action was attributed to its acidic composition; high in monounsaturates, low in polyunsaturates and an optimum μ -6 to μ -3 ratio. Current scientific studies, while not excluding the importance of its balanced acidic composition, have shown that olive oil's health value is mostly due to some minor components with antioxidant activity, such as α -tocopherol, some carotinoids (β -carotene and lutein), the phytosterols, the feofitins, the triterpenic hydrocarbons (squalene) and particularly the phenolic compounds.

Presently more and more studies have verified the strict relationship between peroxidation by free radical oxygen (ROS) and the aging process as well as the pathogenesis of many diseases. Apart from many external and internal factors, an increase in peroxidation can be due to an insufficient introduction of antioxidant agents or to an excessive introduction of polyunsaturated fatty acids.

Notable attention has recently been focused on μ -6 polyunsaturated fatty acids that possess a particular tendency to give up a hydrogen atom placed between the two double bounds. Once formed, polyunsaturated free radicals can consequently react with oxygen to form other peroxidized free radicals, that, following a chain reaction, form hydroperoxides and products of degradation with inevitable damage, even serious, to the organism's wellbeing.

Extravirgine olive oil, besides containing mostly monounsaturates (resistant to peroxidative risk), possess a low amount of μ -6 polyunsaturates as well as an adequate quantity of μ -3 and an optimum ratio between the two series. Interest in its protective antioxidant action is however due to its wealth of phenol compounds or simply polyphenols, that have been shown to intervene in many aspects of the disease forming process. Of particular note are hydroxytyrosol that inhibits cyclooxygenase activity reducing thromboxane formation as well as inhibiting phospholipase A2 and consequently the release of arachidonic acid (pro-inflammatory), oleouropein, with anti-inflammatory and endothelial protective action, and the lignans with anti cancer activity.

Other important antioxidant agents like tocopherols (present in its active form, which is to say the alpha form), β -carotene with antiateroscleoritic and skin protecting properties, lutein which prevents cataracts and senile retinal degeneration, and squalene that besides being an antitumor agent has an evident skin protective property by acting as a scavenger to an oxygen singlet inhibiting the peroxidation caused by UVA.

It must also be remembered that Olive oil is easily digestible activating at the duodenal level the secretion of cholecystokinin-pancreozymin thereby stimulating the emptying of the gallbladder and pancreatic lipolysis activity.

Phytochemicals and antioxidant activity: hype and facts

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In the past decade, research on phytochemicals has been very active and prolific, with hundreds of studies published all over the world.

The importance of phytochemicals grew over time, as researchers explored their protective and antioxidant properties that neutralize free radicals in our body, thus protecting our cells and DNA from oxidative damage. These compounds appear to have also different mechanisms of protection: stimulation of the immune system, regulation of gene expression in cell proliferation and apoptosis, hormone metabolism, antibacterial and antiviral effects.

Epidemiological studies have consistently shown that regular consumption of plant food is strongly associated with reduced risk of developing chronic diseases, such as cancer and cardiovascular disease. Based on the results of these studies, many food products, beverages and even cosmetics have been developed claiming antioxidant properties and antiaging action. However, the real benefits of all these products are far from being demonstrated.

In fact, the antioxidant activity of a food or of a single component measured *in vitro* is not enough to claim the observed health benefits of diets rich in fruits and vegetables.

Beside, the antioxidant activity of a food may not be directly related to the health benefits in the organism. There are in fact other factors to be considered.

First of all it is necessary to determine if the bioactive molecules are absorbed through the intestine, then if they can act as supposed, i.e. neutralization of free radicals *in vivo*. Most importantly, it is crucial to investigate if there are interactions among phytochemicals and other components of the diet that may lead to the inactivation of the healthy compounds.

Recently several research groups have proposed a new approach showing that the antioxidant and antiproliferative activities of plant food reside in the combination of phytochemicals. This means there is an additive and synergistic effects of phytochemicals ingested, so the health benefits of a diet rich in fruits and vegetables are due to the complex mixture of phytochemicals present in whole foods. This explains why no single antioxidant can replace the combination of natural phytochemicals in plant food to achieve the health benefits, as shown in several clinical studies.

The evidence suggests that antioxidants and bioactive compounds are best acquired through whole-food consumption.

The international recommendation to eat 5 to 10 servings of a wide variety of plant food daily is the best strategy to significantly reduce the risk of chronic diseases and to slow down cellular aging.

Assessment of Novel Probiotic Lactobacillus Strains Isolated from Elderly Persons for the Production of Functional Foods

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Probiotics are defined as live microorganisms which when administered in adequate amounts confer a health benefit on the host. The probiotic potential of Lactobacillus strains isolated from human faeces (1,2) was investigated.

The strains were identified and examined for resistance to gastric acidity and bile toxicity, adhesion to HT-29 cells, antimicrobial activities, antibiotic susceptibility and plasmid profile (3).

From the results obtained, two strains, *L. rhamnosus* IMC 501 and *L. paracasei* IMC 502, tolerated well low pH and bile acids. In antimicrobial activity assays, both strains showed inhibitory properties towards selected potential harmful microorganisms, particularly against *Candida albicans*. The two selected strains expressed good *in vitro* adherence to HT-29 cells increasing this characteristic when they are used in combination and they were resistant to vancomycin, colistin sulphate, gentamicin, oxolinic acid and kanamycin. The suitability of a combination of the two probiotic strains (1:1) (Synbio composition, Synbiotec S.r.l., Camerino, Italy) as food additive was tested and its ability to retain viability in the food environment was evaluated.

The two probiotic strains were found to withstand the tested foods manufacturing process and to survive during storage without negative effects on the quality of the products.

The Synbio composition was used in a 3-months human feeding trial during which the survival of the probiotic strains through human intestine was examined. Also the improvement of the intestinal functionality during the probiotic consumption was evaluated.

The two strains were recovered from stools of volunteers after the feeding trial and a better intestinal regularity, an adequate faecal volume, a reduction of constipation and flatulence was detected during the probiotic consumption. *L. rhamnosus* IMC 501 and *L. paracasei* IMC 502 present favourable strain-specific properties and their higher adhesion ability when used in c.

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Italian Wine to Increase the Healthy Activities of Chinese Food: Role of Resveratrol and Wogonin

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Chinese food are known to produce health effects through its functional components; on the other hand the Italian cuisine is also highly appreciated for its important role in prevention of many diseases. The properties of Chinese food are recognized mainly by the use of traditional herbs. On the other hand the main Italian functional foods known are olive oil and wine. In my presentation I will particularly focus on two molecules, resveratrol and wogonin probably not so acknowledged by the general population.

Resveratrol is a diphenol synthesized by some species of spermatophytes; it is also found in peanuts, groundnuts and *Vitis vinifera*. Epidemiological studies reveal that the low mortality of CHD was correlated with red wine consumption. This effect was evoked by resveratrol by different mechanism (regulation of NOS activity, relaxation of isolated aortic rings and prevention peroxidative degradation of LDL).

Resveratrol was found to improve other metabolic disturbances due to inappropriate dietary habits. In animals fed a high-calorie diet, orally administered resveratrol decreased mortality and improved motor functions. It was suggested the resveratrol can also modulate the secretion of leptin, and important adipokine performing a significant role in regulation food intake and energy expenditure. The important activity of resveratrol, concerning regulation of metabolism, is due to its binding and enhancing the activity of Sirt1 (seen below), a NAD⁺-dependent histone deacetylase.

Wogonin, isolated from herbal plants *Scutellaria baicalensis* exhibits antioxidant and anti-inflammatory properties. Wogonin inhibits PMA-induced COX-2 protein and its mRNA levels. Wogonin also inhibited PMA-induced AP-1 activation and the expression of c-Jun, a key component of AP-1. Down-regulation of NF- κ B appears associated with anti-inflammatory Sirtuins are a conserved family of proteins. The first known sirtuin, SIRT2 was isolated by *Saccharomyces cerevisiae*. The mammalian sirtuin family consists of seven members SIRT1―7.

SIRT1 is the human ortholog of the yeast SIRT2 protein. It is an NAD⁺-dependent protein histone deacetylase with many known substrates that affect a wide variety of cellular processes.

In particular it is a regulator of mitochondrial biogenesis, as done by the putative SIRT1 activator, resveratrol. Moreover SIRT1 as been linking to caloric restriction mediated longevity even if the mechanism by which it extends live span in mammals in know fully understood.

Altogether these date indicate a real synergistic results when traditional food of Chinese and Italian cuisine are used together.

The effect of an oral intake of hydrolyzed collagen on skin properties. Results of clinical studies

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Rousselot® has carried out two clinical studies to evaluate the effect of an oral intake of 10g per day of Peptan Hydrolyzed Collagen on skin properties and tolerance.

The two studies were double-blind placebo-controlled trials of oral supplementation of Peptan Hydrolyzed Collagen conducted by two global independent skin health research organizations based in Japan and in France.

The Japanese study was conducted in Tokyo by SOUKEN on 33 women from 40 to 59 years old for 8 weeks during winter. 10 grams of Peptan were ingested once a day in liquid form.

The French study was conducted in Lyon by DERMSCAN on 47 women from 35 to 55 years old. 10 grams of Peptan were ingested, 5 grams in the morning and 5 grams at night, as a powder to be dissolved in a drink.

The first assessment of Peptan was its moisturizing effect. Measurements with a Corneometer® CM825 showed a significant improvement for the Peptan test group of skin hydration by 28% compared to placebo after 8 weeks. 91 % of Peptan volunteers saw their skin hydration increased after 8 weeks. This result was particularly visible in Japan.

The second assessment of Peptan was its anti-aging effect. The number of micro-relief furrows decreased by 26 %. The number of deep wrinkles increased by 30 % with the placebo group while remaining stable within the Peptan Group after 12 weeks in the French study.

Peptan Hydrolyzed Collagen when taken daily up to 12 weeks improves the basic skin condition and structure: it improves skin moisture level, skin suppleness and skin smoothness by reducing the number of micro-relief furrows and prevents the formation of deep-wrinkles.

A self assessment by the volunteers confirmed the impression of improvement of skin hydration and skin suppleness in both studies. Other Rousselot experiments on cell cultures have given some clues on the mechanism of actions of hydrolyzed collagen confirming data provided by the literature. Peptan hydrolyzed collagens added to a culture of fibroblasts do not increase the number of fibroblasts in the cell culture but enhance the production of Type 1 collagen by fibroblasts themselves. This may explain the decrease of wrinkles shown by the clinical studies and the increase of skin hydration.

The results of the Rousselot clinical studies supported by *in vitro* data demonstrate that Peptan hydrolyzed collagen is one of the new potent ingredients for the nutricosmetic market.

Topical and systemic use of isoflavones and phytoestrogens as skin rejuvenating agent

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The skin is one of the largest organs of the body significantly affected by the aging process and menopause. Both estrogen receptor isoforms (ERalpha and ERbeta) have been detected on the cellular components of the skin, and estrogens have been shown to exert a profound influence on this tissue.

Accordingly, dermal cell metabolism is affected by the hypoestrogenic state of menopause, leading to changes in the collagen content, in the concentration of glycoaminoglycans, and, most importantly, in water content. Thus, by altering the basic components of the skin, menopause actually exacerbates the deleterious effects of age on this tissue.

Obviously, Hormone Replacement Therapy (HRT) cannot be recommended solely to treat skin aging, and topical estrogen application is usually administered in this clinical setting, although the highest effective concentrations of estrogens that can be used without the risk of possible systemic side-effects, need to be further investigated. Notably, while great strides have been made in developing effective therapy for other menopausal symptoms, the challenge of developing an effective estrogen alternative for skin aging treatment still remains.

Phytoestrogens are a broad group of non-steroidal compounds of different structure that bind to ERs. There are three main classes of phytoestrogens: isoflavones, coumestans and lignans. Among the isoflavones, genistein and daidzein are the most investigated.

Phytoestrogen isoflavones are increasingly being considered ideal candidates as skin rejuvenating agents, with the potential ability to retard skin aging processes linked to intrinsic (estrogen-dependent) or extrinsic (environmental-dependent) causes. Indeed, isoflavones can both act as steroidal mimics, by filling the stereochemical space of the ER ligand-binding pocket, and via other mechanisms such as prevention of lipid peroxidation, reduction of collagen degradation, increased collagen deposition, and increased production of hyaluronic acid. It is this special chemistry that supports the claimed effects of many phytoestrogen-based herbal supplements or topical preparations as anti-aging skin therapy.

Overall, however, available data are quite limited, and their possible side-effects need to be investigated in more detail and this area remains a very new, interesting and promising field of study and researches.

Domestic animals as irreplaceable and therapeutic friends for our wellbeing

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During the evolutionary history of the human race, we have passed through and are still completing a different approach, at least in the most highly developed countries, towards pets and other domestic animals.

Dogs and cats in particular, but also rodents, some species of birds, aquarium fish, iguanas, snakes and, last but not least, some felines and other exotic animals, are increasingly coming closer to human beings - no longer as an end-product in the form of food, but as cherished friends and also, in many cases, irreplaceable adjuncts to doctors and therapists.

There are many cases and reports, especially from young people and children, who have gained psychophysical benefit, a significant and highly appreciated sense of relaxation, and greater possibilities of socialisation and dialogue in the presence of domestic animals and pets.

I would merely make the observation that our love of animals, domestic or otherwise, must always be interpreted and experienced with respect for those animals which are close to us. And, for our part, we should understand that, as well as their adapting themselves to our daily lives, we should also try to adapt ourselves to theirs.

I think we are morally obliged to insist upon a relationship of mutual respect: animals are indeed irreplaceable friends and much more, but we cannot always insist that they sit down when we want them to, get up when we want them to, look at us affectionately when they eat, and so on.

In 1972 in England, the Doctor William Tuke began to treat patients with mental disorders in the presence of domestic animals, finding clinically positive benefits: this was the beginning of *Pet Therapy*. Since then, beneficial therapy granted to humans and obtained by working with animals has developed throughout the world.

Pet Therapy is evolving not only thanks to the direct actions of animals as true and unique friends of mankind, but also in the form of *Animal Assisted Activities and Therapy (AAA/T)*, distinguishing between the role of *Activities* (e.g., occasional and/or periodic visits with animals to hospitals, in order to create a moment of relief and happiness to its patients), and that of *Animal Assisted Therapy* (in which several people are involved, collaborating in detailed research on specific psychophysical, social or healthcare rehabilitation aims).

In the latter case, I would like to present in detail my personal experience of "*Pet Therapy in Water*", still a unique scientific study in this field in Italy. It was carried out on children with language problems (dyslexia), autistic and genetic syndromes, together with their parents a veterinary surgeon, a psychologist, a pediatrician and a neuropsychological speech therapist.

This example may and must be a scientific and social stimulus, for continued and further improvements in the study of the various types of treatment which can involve Pet Therapy.

Global skin treatments for the best results

Paolo Palombo

Director Dept. Plastic Surgery Burn Center, S. Eugenio Hospital, Roma - Italy

As the population has become increasingly older, it falls to the plastic surgeon to treat the most common of all skin diseases, aging. And the goal in treating the dynamic picture of the face is to reestablish its youthful appearance, in which the restoration procedure produces the illusion that only the eyes and lips are visible. In fact, the way that we look not only influences how others treat us, but also affects our own attitudes, behaviours, and accomplishments

It must be remembered that patients frequently seek surgery because they have experienced or they anticipate some negative changes in their lives, ranging from divorce to loss the job.

They perceive these losses, real or imagined, to be related to how they look and say that a youthful appearance made them forget about their true chronological ages also.

Thus, the successful interaction between the available procedures and the topical treatments used is crucially important in treating the aging face.

The primary goal of plastic surgery is to reduce abnormalities to a reasonable minimum given the circumstances, not to create a perfect face or to match a specific look that the patient may wish to imitate. Therefore, surgeon has not to achieve the maximum results, but the best for the patient. However, patient-surgeon psychological rapport is essential to satisfaction with the surgery. It is the task of the surgeon to help patient to develop realistic expectations.

The best procedures and cosmetic treatments used will be reported and discussed.

Non-ablative laser for skin rejuvenation

Marco Palombo

Head Plastic Surgery Center, CTO Hospital, Roma - Italy

The face is of profound importance in the psychological and social world, thus creating a more youthful appearance has become today a must of our Society.

Attractiveness is often the first reason that people put forward to explain their desire to look younger. Those who have built their careers in the media and elsewhere on the basis of physical attractiveness may find that their careers falter as they get older.

In this new century ,public-sector work and traditional manufacturing is given way to an economy dominated by the media, service industries and the world of internet; all are types of work associated with the young. About all ,youth represents life and future.

Thus, growing older is lived as a serious threat to the social and economic status.

Economical development has ,in fact , disrupted traditional social patterns. It may be that older men find younger women socially desirable and they may look to their younger partner as a reflection of their own sense of youthfulness. On the other hand many younger women have more economic power and do not necessarily seek an older man for financial security. The older man cannot, therefore, necessarily attract the younger women on the basis of age and financial status alone. He then begin to invest in facial treatments to seek facial rejuvenation surgery to look younger, healthier and more tempting to the younger and more assertive female .

However, people seek facial rejuvenation treatment to improve their psychological and social well-being and not only for technical reasons. At this purpose, different techniques are used for the improvement of cutaneous changes seen with aging and photoaging .

Non-ablative laser and light sources have been recently introduced as an alternative modality for skin rejuvenation. It has been suggested that tissue ablation, leading to collagen shrinkage and new collagen deposition contributes to the clinical results after traditional laser resurfacing. Moreover, this system offer minimal adverse sequelae and no recovery time is necessary.

Finally by the combined use of other available rejuvenation procedures and long-term treatments by selective cosmetic products involved in the NICE concept, it is possible to obtain the best results to ameliorate the ageing appearance. Just to remember, in the NICE concept: the Nervous, Immune, Cutaneous and Endocrine system all work together to internally activate the skin activity balancing and stimulating the mind-body connection.

In summary, non-ablative laser resurfacing has been shown to be more or less effective in skin rejuvenation in depending of the technique and first of all the selective pre and post-operative treatments used also.

Different non-ablative laser techniques and selective cosmetic treatments linked with the innovative NICE concept will be reported and discussed.

Skin Rejuvenation: non surgical strategies, from Lasers to Cosmeceuticals

Paolo Mezzana

Plastic, Reconstructive & Aesthetic Surgery Specialist G.B. Bietti Eye Foundation-IRCCS Roma - Italy

Skin changes in the elderly have been considered an inevitable and irreversible part of the aging process, with the undesirable texture and appearance masked with the use of cosmetics.

Recently, however, there has emerged a clearer understanding that aging of the skin is the total of two processes: intrinsic changes associated with aging and extrinsic damage, particularly the accumulative effects of repeated exposure to actinic radiation, referred to as photoaging.

Non surgical skin rejuvenation using laser, intense pulsed lights (IPLs) or radiofrequency techniques are becoming increasingly popular because of the aging population's desire for fresher, younger looking skin. More and more patients are seeking noninvasive, no-downtime techniques to obtain smoother skin, diminish age spots and discoloration, and eliminate visible blood vessels.

At the moment there is a clear understood that photoaging is a complex process, so the treatments involved in its correction have to be done at different levels. Not only a machine or a cosmeceutical but the deep intergration of different strategies.

The integration of different procedures to correct photoaging signs is a new concept in aesthetic medicine.

This is a method of global skin care, and this let us obtain better results with less morbidity in skin texture and firmness changes compared with the use of a single procedure alone.

Treating acquired telangiectasia

A. Rusciani Scorza

Dermatologist, Roma - Italy

NOT RECEIVED

Treatments of Ageing Hands

Leonardo Marini, Aleksandar Kronic

SDC The Skin Doctors' Center, Trieste - Italy

Chrono and photo-ageing are powerful allies working synergistically together to progressively modify function and beauty of UV-exposed skin.

Permanently uncovered body areas like face, neck, and hands are more affected. Irregular blotchy pigmentation, epidermal dryness, dermal thinning, sagging and wrinkling are most prominent signs. Modern Dermatologic Surgery can offer many different treatment options to slow down and improve clinical aspects of chrono- and photoageing. Superficial and medium chemical peels, high intensity pulsed polychromatic light sources, 532nm Q-S lasers, Er:YAG and CO₂ ablating fractional dermo-epidermal remodelling, 5-ALA photodynamic rejuvenation, LED photo-biomodulation are presently used either alone or in combination.

Clinical results obtained with this treatments are quite impressive, particularly when started at a relatively younger age.

Tissue and body metabolism need to be sufficiently active to effectively conclude all sequential steps involved in healing processes.

Anti-oxidant and UV-photo-ageing preventive measures are extremely important in prolonging beneficial effects of dermatologic surgery procedures.

Skin care cosmeceuticals should be also carefully selected to maintain epidermal function within acceptable normal limits.

Dermatologists and Dermatologic Surgeons play a key role in selecting patients for specific treatment strategies to improve chrono- and photo-ageing related skin alterations.

Combination Treatments for the Ageing Face

Luigi Rusciani Scorza, M.D.¹, Antonio Rusciani Scorza, M.D.²

¹ Head Dept. and Professor of Dermatology University of Sacro Cuore, Roma -Italy

² Dermatologist, Roma - Italy

In the last years the treatment of the aging of the face has suffered drastic in partnership modifications to the necessity to make such procedures less possible invasive.

The lasers not invaded you, the radiofrequency and the pulsated light have supplanted the ablative lasers and the surgery.

The combination of such procedures, in relationship to the type of damage that the patients introduce, it guarantees a good aesthetical result not submitting the patient to annoying times of recovery.

We bring our experience.

Treatment of facial port-wine stains with intense pulsed light

Li Zhang

The First Hospital of China Medical University, Shenyang - China

Background

Intense pulsed light (IPL) have been reported in the treatment of fresh or laser-resistant port-wine stains localized in different body regions.

Objective

Our aim was to assess the effectiveness of the IPL in the treatment of fresh facial port-wine stains.

Material and Methods

32 patients with facial port-wine stains without previous treatment were enrolled in the trial. Patient demographics, treatment setting, outcome of clearing, and treatment complications were noted.

Results

The treatment intervals were 3 to 4 weeks for three to four treatment. Mild improvement (30%-50%) was achieved in 62.5% of the patients. Moderate improvement (50%-75%) was achieved in 37.5% of the patients. Complete clearing was not seen in 32 patient after four treatment sessions. Pigmentation formation in 5 patients occurred after healing blister. They fade away 3 to 6 months later. Except for the side effects, long-term complications were not seen.

Conclusion

Effectiveness was achieved with IPL treatment in the facial port-wine stains.

CHITIN

Chemically, chitin is a natural polysaccharide made up of glucosamine and acetyl glucosamine bound together by a typical Beta-1-4 bond (1).

Extracted from by products in the shell fish industry, in variable amounts from 10^{10} to 10^{12} tons per year, this natural bio-polymer has a similar structure as hyaluronic acid having in common with it the presence of acetyl glucosamine (2). (Fig.1)

Being a pure polyglucoside it doesn't cause allergic reactions, which on the contrary can be caused by the protein part of the fish shells which however is totally eliminated during the production process.

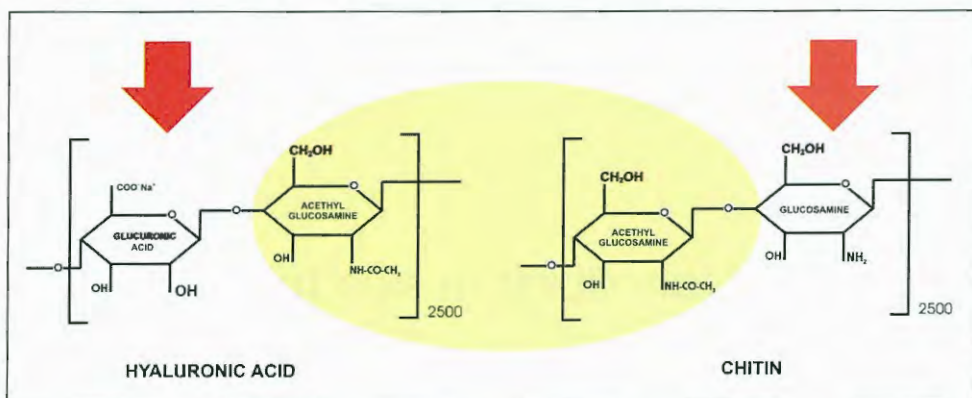


Fig. 1 Hyaluronic acid and Chitin have the same basic makeup.

Made up of polysaccharide chains bound together as a zipper, this biomaterial has a reparative/equilibrating (3)(Fig.2) role in nature, due to its ability to entrap growth factors, active endogenous and exogenous substances and water molecules (3,4).

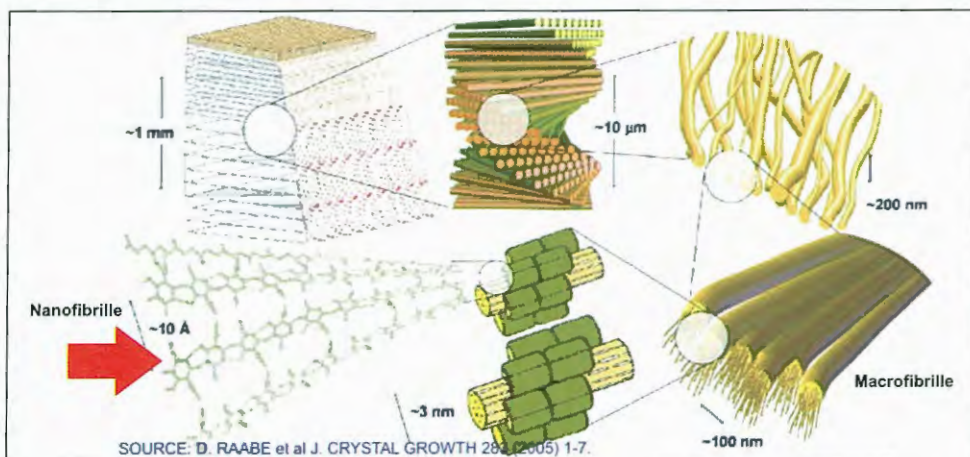


Fig. 2 Chitin containing crystalline fibers and nanofibrils, is organized as in the shape of a zipper.

CHITIN-NANOFIBRILS

Dimensions and characteristics

Chitin-nanofibrils (CN), as nano-crystals, represent the pure and sugary molecular portion of alpha-chitin obtained after the elimination of the protein portion. Since they are easily metabolized by our body using endogenous enzymes, they are used in the cosmetic as well as in biomedical sectors (5).

These crystals are called *nano* due to their average size of 240x7x5 nanometers (nm), and *fibrils* because of their shape as thin needles. Moreover they are *natural* because present in

nature and *safe* to use because, being recognized by enzymes, they are *bio* and *eco*-compatible.

These nanofibrils' average size (6,7) being one-fourth of a bacterium, 1 gram of product develops a surface of 400mt (Fig.3)

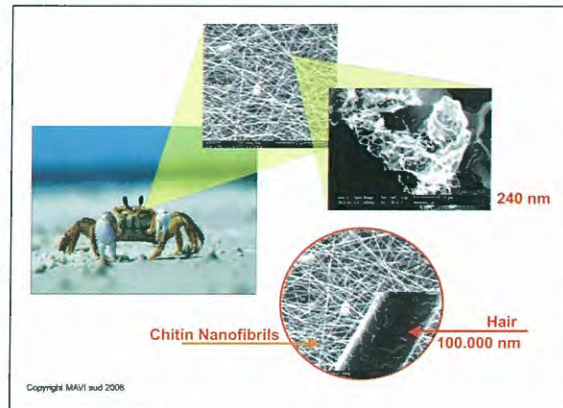


Fig. 3 Size of chitin-nanofibrils compared to the thickness of hair.

Physio-chemical behavior

The extremely small size of these nano-crystals, separated from each other and bound with water, and their mostly electropositive relative electric charges arranged along the axis of the molecule, allows this polyglucoside to remain stably suspended in water solutions, ready to bind with other molecules via ionic bonding (8). (Fig.4)

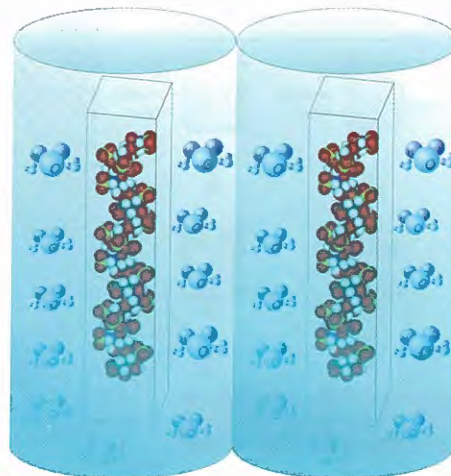


Fig. 4 The presence of innumerable moles of water separates the nanofibrils and keeps them stably in suspension in polarized liquids.

Therefore, given the particular chemical structure similar to hyaluronic acid, CN tends to combine with many active components normally used in cosmetics, both hydro or liposoluble. Naturally, the type of compounds CN forms with antioxidants such as *lutein*, *melatonin*, *lipoic acid*, or with immune modulators as *ectoin* or *beta-glucan*, depends on the environment in which it reacts and consequently on the intermolecular bonds it establishes with the various molecules. (Fig.5)

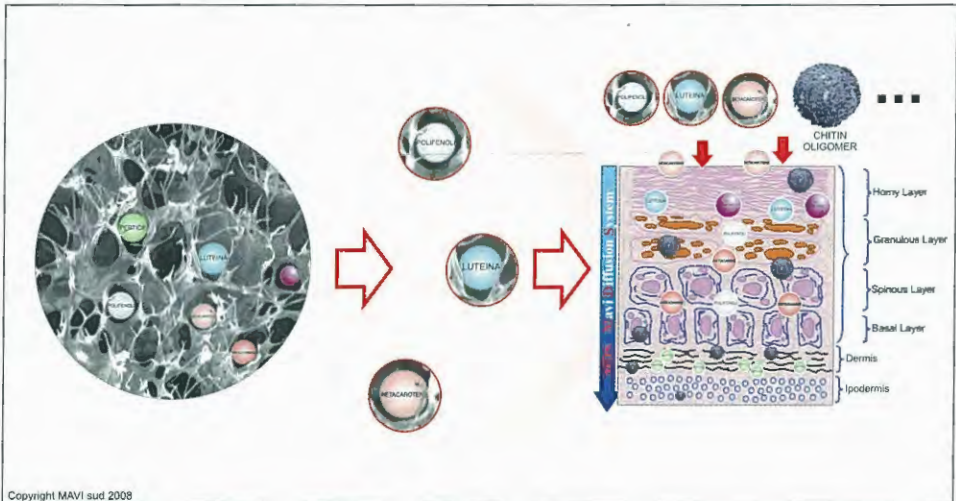


Fig. 5 The different oligomers arising from the enzymatic hydrolysis of nanofibrils are able to penetrate into the stratum corneum releasing the relative active substances to the various layers and even at different time intervals .

However, of fundamental importance is the carrier (micellary o lamellary) in which these compounds are inserted (9) (Fig.6) and which influences their thermodynamic activity and the consequent interaction with skin.

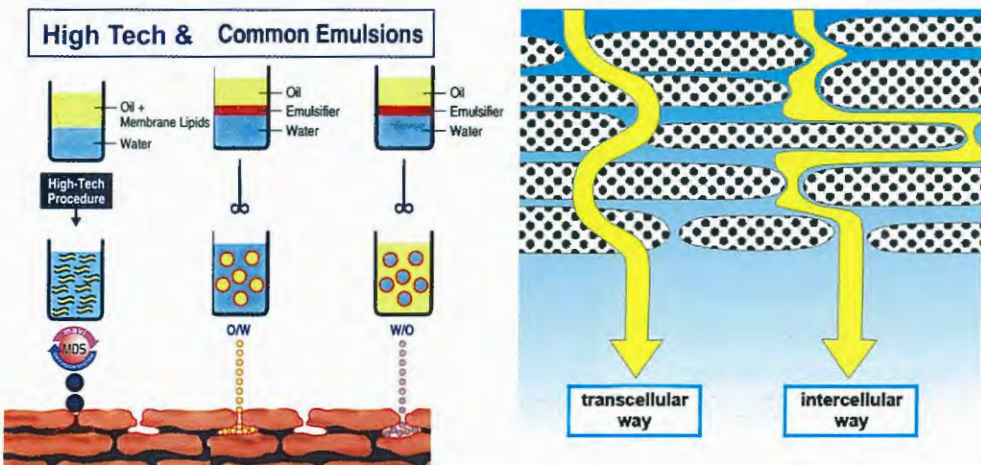


Fig. 6 The various types of emulsions, whether micellary or lamellary, heavily influences an inter- or transcellular penetration.

BIODEGRADABILITY

Chitin-nanofibrils, as with all its derivatives even if transformed into material, are hydrolyzed to oligomers by hydrolytic enzymes as lysozyme, N-acetyl-D-glucosaminidase and the lipases. In this reductive process even nitric oxide (NO) can play a role. Also, these oligomers further reduced to N-glucosamine and to glucose can be incorporated into glycoproteins or eliminated as CO₂. It's interesting, however, to point out how all the chitin-oligomers can act as founding for the synthesis of hyaluronic acid.(10-14)

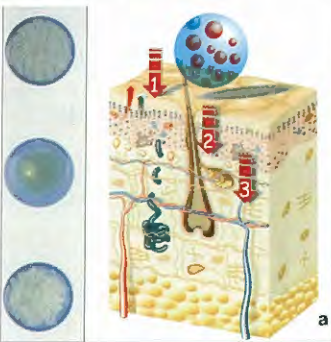
PRODUCTION METHODOLOGY AND FIELDS OF APPLICATION

Chitin-nanofibrils represent a techno-scientific innovation internationally patented by MAVI both as regards the production process (Fig.7) as well as for its use in the **cosmetic**, **biomedical** and **bio-active material** sectors (15). (Fig.8)

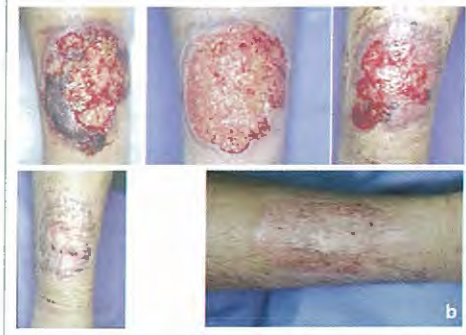


Fig. 7 The industrial process necessary to produce nanofibrils

Cosmetical sector



Biomedical sector



Biofunctional textiles



Fig. 8 CN are active as ingredients in cosmetics (a), as active components to accelerate and optimize skin healing (b), and to make textiles bio-active (c).

The production process of chitin-nanofibrils is characterized by a safe and non polluting ecological methodology that brings about the formation of a stabile aqueous suspension of nanofibrils containing 300 billion nanocrystals per milliliter. Also produced is a secondary solution rich in glucosamine, acetylglucosamine and oligomers; molecules useful in the treatment both of skin and hair, giving a particular shine and manageability to the latter (16).

MECHANISM OF ACTION IN THE COSMETIC AND BIOMEDIC SECTORS

When linked with CN the active principles show a more intense and effective biologic activity resulting in an increase in their bioavailability.

In this way, depending on the type of complex and the emulsions obtained, it's possible to produce innovative cosmetics able to achieve their specific activity at the level: (16-22)

-of the stratum corneum (sun screens) (Fig. 9)



Fig. 9 CN is a potent booster, that reinforces sun screen protection both with UVB and UVA.

-of the epidermis and the dermis (antioxidant and anti-aging cosmetics) (Fig. 10)

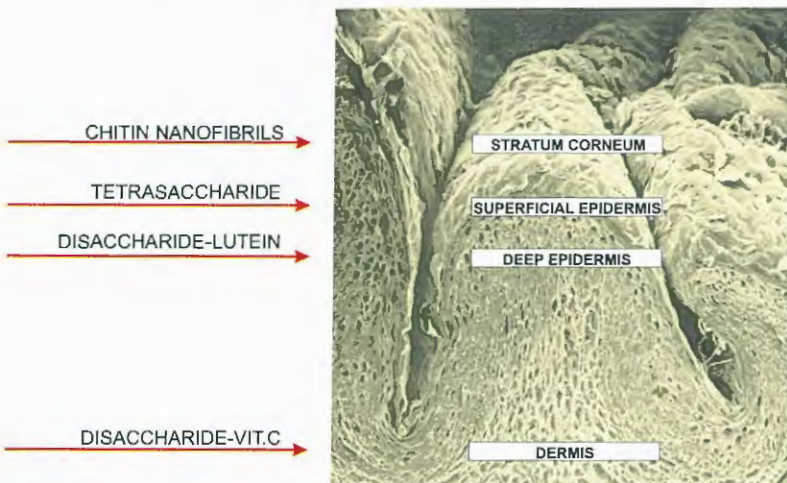


Fig 10 The different transepidermal or transdermal skin penetration and relative products effectiveness will be directly tied to the used emulsion, to the size of the chitin oligomer, and to the bonds established between the oligomer and the different active compounds.

- of **specific cellular components** like melanocytes (depigmenting agents) (Fig.11)

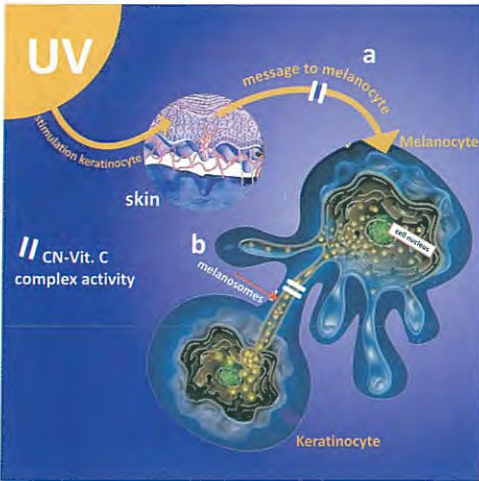


Fig. 11 Depigmenting activity takes place on two levels: a) interruption of the message from keratinocyte to melanocyte; b) impeding the transfer of melanosomes to the keratinocyte

- of **sweat glands** (deodorants and antiperspirants) (Fig. 12)



Fig. 12 The complex CN-Aluminum salts reduces the lumen of sweat duct and the relative sweat flow, neutralizing all's irritating action.

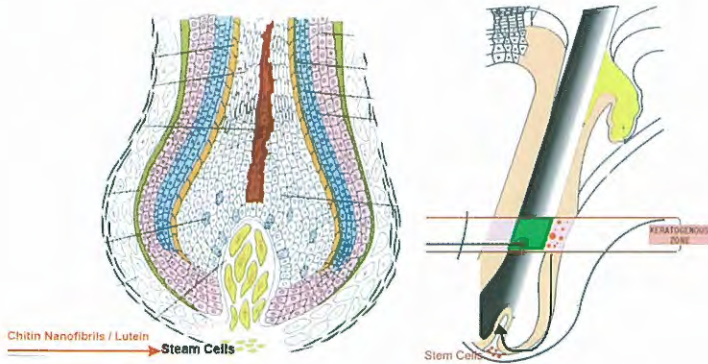


Fig. 13 CN complexes with various active substances has a double optimizing action: a) the production of stem cells at the hair bulb level; b) increments the production of high-sulphur keratin compounds at the site where synthesis takes place.

- of **hair follicles** (anti- hair loss) (Fig. 13)

In conclusion all these new compounds are able to function in a very specific way and with totally original mechanisms making them more effective and without side effects. Thus, due to their high molecular weight nanofibrils are unable to penetrate the inner cell, nor to enter the circulatory system, but they can be metabolized by skin enzymes and transformed into dimers or tetramers, with the subsequent formation of glucosamine and methyl glucosamine. These molecules can in turn be used exactly as they are or further catabolized to glucose and glutamic acid; the former takes part in cell energy production while the latter is a part of essential protein molecules.

BIOAVAILABILITY

The *bioavailability* of the different compounds of CN-active substance, fundamental for their effectiveness and safe usage, begins at the stratum corneum level, and goes to the cellular sites in response to the type of emulsions used (micellary or lamellary) (23,24). (Fig.14)

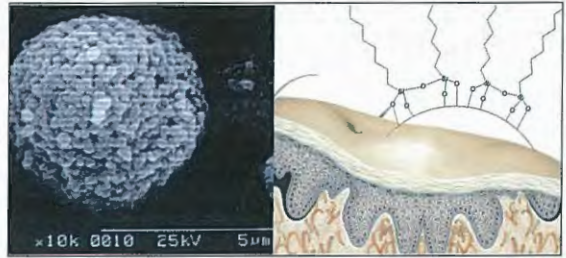


Fig. 14 The transepidermal or transdermal penetration and the bio-availability of the active substances depends on the type of carrier used; whether micro, nano or lamellary, as well as on the various compounds formed.

I stage - On contact with the skin the polymer CN pre-bonded with the active substance is transformed into *disaccharides* and/or *tetrasaccharides*. (Fig. 15)

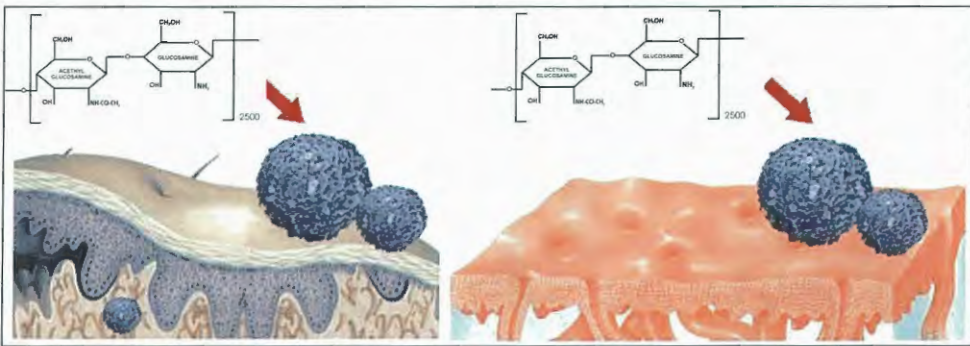


Fig. 15 The emulsion on skin contact causes the nanofibrils to adhere to the stratum corneum or to the mucous membranes and once hydrolyzed penetrates into the different skin layers releasing the various bonded substances

II stage - *Disaccharides* and *tetrasaccharides*, able to cross the stratum corneum will be localized in the various regions of the epidermis and/or of the dermis ready to release the *active* substance combined with it and thereby perform its designated function (Fig.16).

The greater or lesser transcutaneous penetration will be directly tied to the size of the oligomer (whether dimer or tetramer) and the relative compound formed with the active substances and, naturally, to the thermodynamic activity of the carrier.

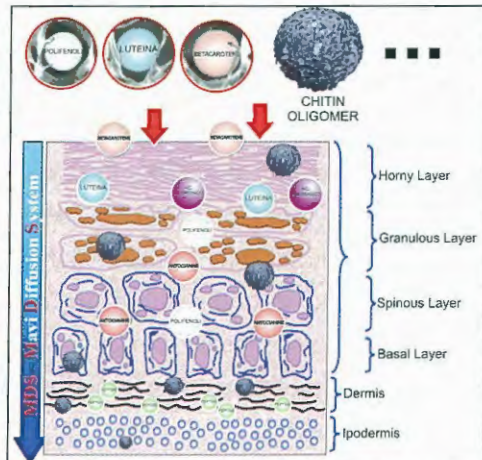


Fig. 16 Transcutaneous penetration of chitin-oligomers.

It's interesting to point out how, similar to what happens with hyaluronic acid, these dimers /tetramers seem able to enzymatically repolymerize themselves at the level of both the lipidic lamellae and the extra cellular substance of the dermis. Later on, attracting and binding many water molecules, they act precisely like real natural sponges. (Fig.17)

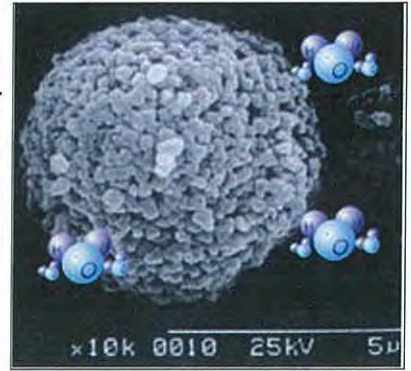


Fig. 17 The chitin-nanofibrils hydrolyzed to dimers or to tetramers and binding water increase the hydrating ability of the lipidic lamellae improving the skin barrier functions.

Thus, thanks to its prevalence of electropositive charges, CN is able to easily form ionic bonds with the sulfurated part of the glycosaminoglycans or with certain areas of hyaluronic acid where there is a prevalence of electronegative charges. (Fig.18)

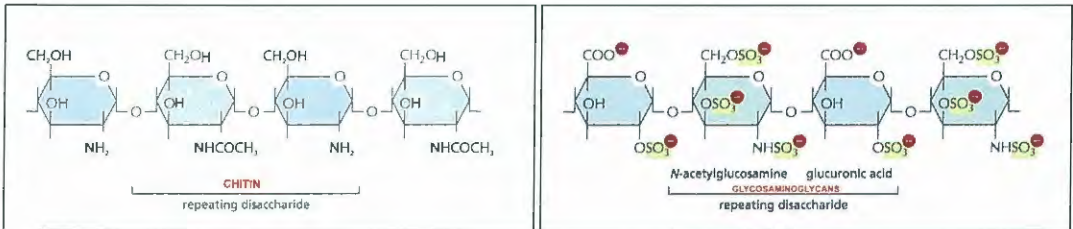


Fig. 18

Besides disaccharide/tetrasaccharide repolymerization, a more complete CN hydrolysis can occur giving way to the formation of *glucosamine* and *acetyl glucosamine* that, as their precursors, can be used also for the synthesis of glycosaminoglycans, fundamental components of extra cellular liquid. (25). On the other hand, as described above, the glucosamine, synthesized by the body through the reaction between *glucose* and *glutamic acid*, can once more generates these two important molecules, glucose for energy and glutamic acid for protein building.

An interesting data seen in the degeneration of the cartilage of ligaments, tendons, and bone structures, besides that of elastic fibers, is that the enzyme elastase activity, playing a role in these pathologies, increases its efficacy with aging.

N-acetylglucosamine (a component of chitin) inhibits elastase in a dose dependent relationship, playing an important role for the maintenance of elastic fiber functionality.

RESEARCH STUDIES CONDUCTED BY MAVI

In the last few years MAVI has done various studies centered not only on the methodology necessary to produce these chitin nanocrystals (CN) industrially, but also aimed at highlighting their specific biologic activity, that takes place mainly at the human skin level and in adjacent tissues (26-29). (Fig.19)

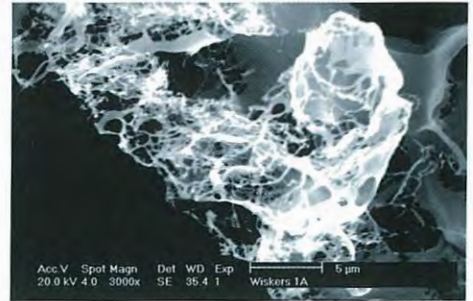


Fig. 19 Detail of CN with scan electronic microscope.(SEM).

It was thus possible to show their ability to complex other molecules, strengthening their specific activity, such as at the cell stem level. (26).

Furthermore, it was possible to show how this polyglucoside can facilitate penetration into the epidermis, the follicle and dermis levels of various molecules compounded to it. These can then perform specific activity within various cells of the different skin layers (27). (Fig.20)



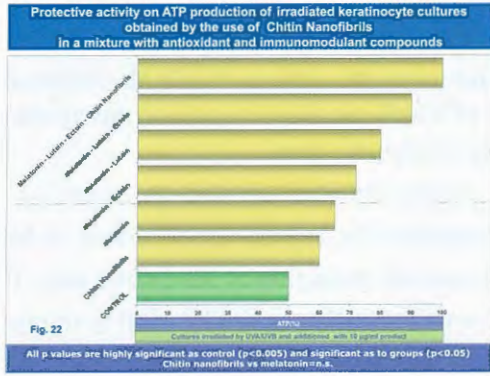
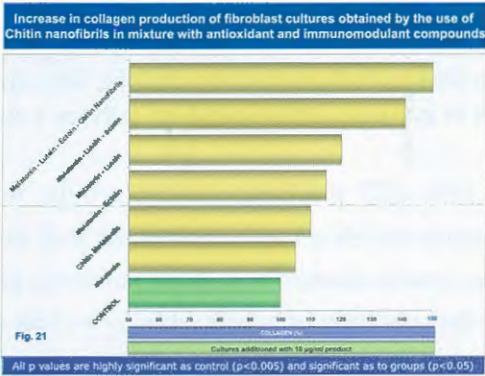
Fig. 20 The CN-active substance compounds are able to penetrate the skin more or less deeply according to their physio-chemical characteristics.

With these studies carried out *in vitro* and *in vivo*, it was possible to show that CN is capable of *synergizing* both the activity of certain antioxidants, as melatonin, lutein, and lipoic acid, as well as the immune-stimulating activity of ectoin or betaglucan (28,29).

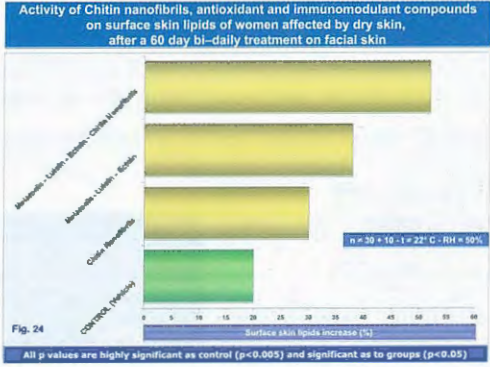
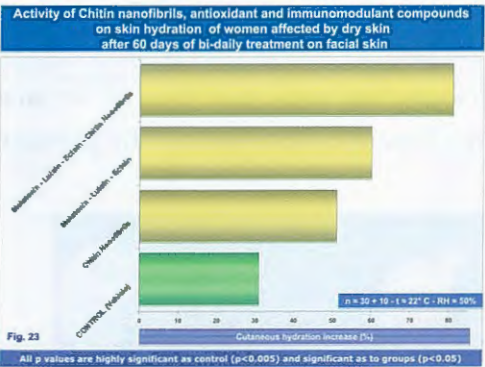
COSMETIC EFFECTIVENESS

In an *in vitro* study achieved by a lamellary cosmetic emulsion, it was possible to show the ability of CN to increase the reproduction of fibroblasts with a subsequent increase in collagen synthesis. (Fig.21)

In vitro - This increase gave rise to an even greater production of ATP, necessary as the cell's energy source. (Fig. 22)

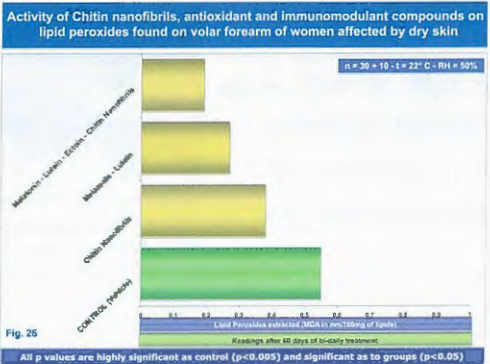
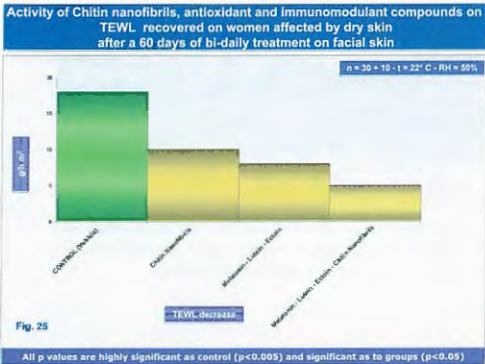


in vivo - As a consequence of the *in vitro* activity on photo aged subjects it was possible to obtain *in vivo*:



* the subsequent reduction of TEWL (Fig. 25)

* a reduction of lipid peroxides.(Fig.26)



These studies once more demonstrate the strict relationship between the activity carried out by the antioxidants, like melatonin and lutein especially if combined with CN, and the life of skin cells. (30-36). These molecules regulate, in fact, the rhythm of cellular growth or death, neutralizing free radicals and maintaining an efficient barrier. Thus, with the passing of time the mitochondria, the main electron transporters and enactors of the oxy/redox system, lose their efficiency in ATP synthesis bringing about an abnormal production of ROS (Radical Oxygen Species) and of RNS (Radical Nitrogen Species). For this reason the cell, no longer able to provide for its own vital necessities, dies sooner (apoptosis). Furthermore, the deficit of ATP, the increase in free radical production and the subsequent lack of water can induce a precocious apoptosis in mitochondria dependent cells, as a result of the oxidative stress.

The results obtained showed an increased in vitro ATP production at the cellular level, accompanied by in vivo improvement in hydration and skin barrier action, as well as the simultaneous reduction of lipid peroxides. These results showed how these particular types of cosmetic emulsions can be used to improve the condition of xerotic skin as well as skin damaged by photo aging (28,29).

NANOFIBRILS AND PHOTOPROTECTION

Chitin-nanofibrils don't act naturally as sun screens, but, when they bind to the stratum corneum they enact an interesting booster function, increasing the protective factors of sun screens UVB (SPF) o UVA (PA++). (Fig.27)

On the other hand, if bonded to lutein, to melatonin or ectoin, they reinforce the photo protective effects against UVR and blue light, as well as the antioxidant, hydration and immune-protective efficacy of these molecules (37).

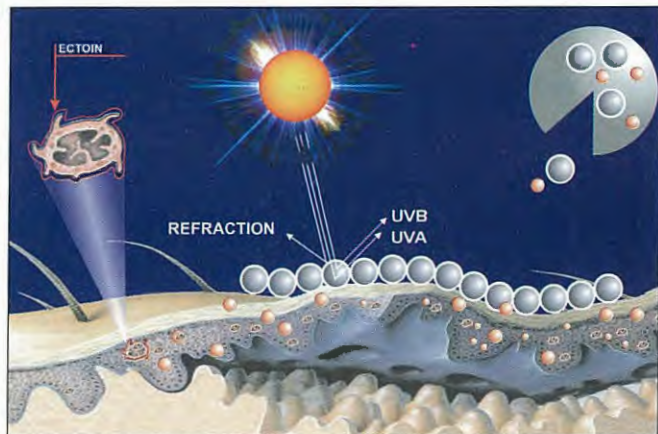


Fig. 27 The transepidermal or transdermal penetration and the bio-availability of the active substances depends on the type of carrier used; whether micro, nano or lamellary, as well as on the various compounds formed.

NANOFIBRILS AND HAIR

Chitin-nanofibrils and relative oligomers, due to their electropositive characteristic, are able to make strong bonds with Keratin scales as well as with hair cortical cells. This not only makes hair more manageable but also repairs damages incurred by excessive use of dryers, brushes, combs and color stripping agents. (38) (Fig. 28).



Fig. 28 Reparation enacted on hair through the use of special CN-oligomer compounds.

The early experimental data at our disposal has further shown that this polyglucoside may be able to promote hair follicle activity increasing the presence and maturing of keratin stem cells. CN seem to bind, in fact, to CD44 (26) cell receptors. (Fig. 29)

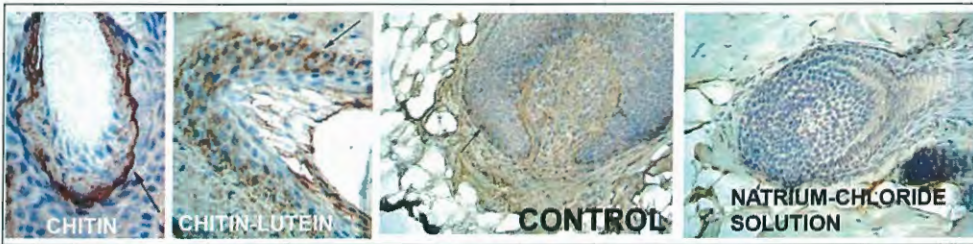


Fig. 29 Nanofibril dimers are able to stimulate cell stem reproduction at the hair bulb level.

NANOFIBRILS AS SKIN MOISTURIZERS

Due to its physical and chemical conformation very similar to that of hyaluronic acid (many OH groups present in the molecule) CN manages to bind a great quantity of water to skin tissue. Nanofibrils' particular hydro affinity allows their usage as is or in association with other well known moisturizers, as PCA and hyaluronic acid, for the sole purpose of keeping the skin tissue moist for long periods, or to repair damaged skin barrier and/or to neutralize free radicals. The prevalently cationic character of CN and its complexes allows a tight adherence and high affinity both with skin and hair keratin as well as with the protective gel that lines the body mucosa. In this way it can increase the elasticity of these tissues helping cells to optimize their ability to uptake and fix water. Consequently there's an increased resistance towards external aggressions. The particular affinity with water molecules make CN particularly useful even with dry wounds that, in the presence of certain aqueous carriers, can thus be kept moist, to facilitate tissue granulation (39,40).

EFFECTIVENESS IN BIOMEDICINE

The first results obtained on subjects affected with *photo-aging*, using cosmetic formulas were followed by other studies aimed at wound healing. With these studies it was possible to demonstrate how CN, inserted in suitable medical devices is capable of playing a fundamental role in the process of tissue granulation. In fact it promotes and modulates collagen production, avoiding its excessive and irregular synthesis, as is often seen during wound healing. (27,39-41) (Fig.30)

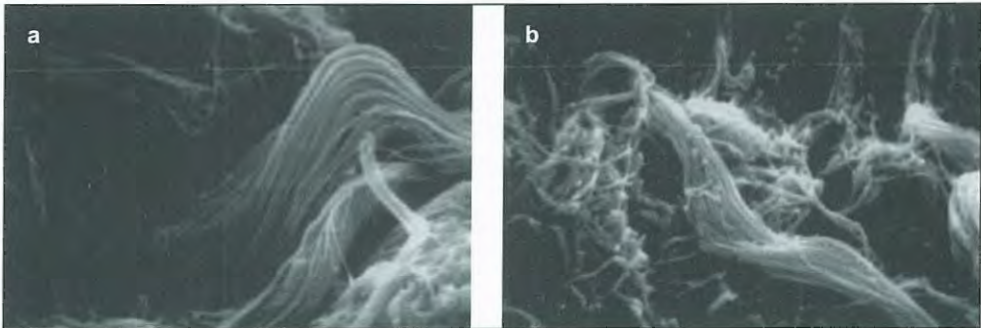


Fig. 30 CN dimers are able to stimulate fibroblasts making them produce the correct quantity of collagen structured in a regular formation (a) contrary to what happens in the non treated wounds in which a chaotic structuring of collagen fibers is seen(b).

In fact, as many studies have shown, these particular polyglucosides are capable of activating the proliferation of *keratinocytes* as well as of *fibroblasts*, regulating not only collagen synthesis but also that of cytokines and macrophages.

In this way the immune-protective and healing properties of skin tissue is increased, thus encouraging a physiologic healing with a drastic reduction of altered scar phenomena as hypertrophism or hypotrophism (keloids, hyper or hypotrophic scars). (Fig.31,32)

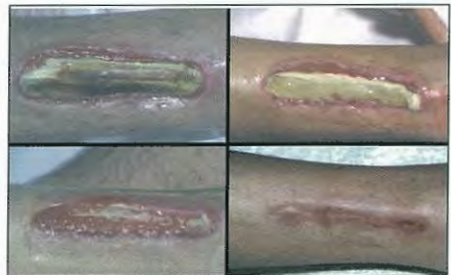


Fig. 31 Healthy scar activity enacted by CN.

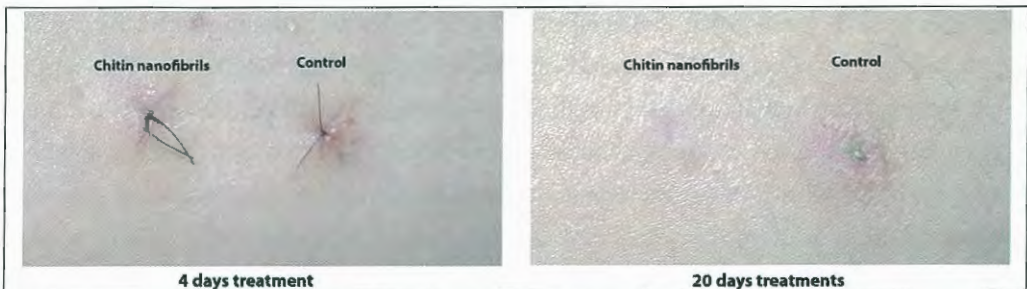


Fig. 32 Healthy scar activity enacted by CN.

CONCLUSIONS

The results coordinated in MAVI's R&D department enabled the Company to introduce new active principles in their formulas or to use already know ones, made innovative and more effective due to their complexing with *chitin nanofibrils* using innovative pharmaceutical and technical methods of advanced bio-engineering.

Chitin-nanofibrils as sugary polimers have multiple biological functions. These functions are strictly connected not only with the nature of the carrier but also with the sophisticated physical & chemical technologies used, which give these interesting molecules the ability to bond with other hydro or liposoluble molecules, including of course omnipresent water. In this way the different bonds formed with other active molecules allows CN a wide range of functions both in the strictly medical sector, as well as in the cosmetology and/or biomedical material sectors as reported schematically below (Fig. 33): (42,43)



Fig. 33 The multiple functions performed by CN and its compounds.

As a consequence of the use of CN and the relative applied technology, MAVI products are particularly active, also because their efficacy and the absence of negative side effects are continually and attentively evaluated *in vivo* and *in vitro* (Fig. 34).

The effectiveness depends not only on a scrupulous selection of active principles, but also on the type of emulsion, the emollient activity, the specific emulsifier and methodology used in making the emulsion,

as well as the organization and relative size of the micelles and lamellae obtained which strongly influence the transcutaneous or transdermal penetration of cosmetic products.

All these studies, conducted in collaboration with many Italian, European and Extra-European Universities and Research Centres, and presented in many national and international Meetings, have showed MAVI with varied acknowledgements ^{Meet. 1-21}.

Thus the prestigious Best Innovator award received in 2006 and the Confindustria's Certificate of Excellency awarded in 2007 allowed the Company to be considered one of the most innovative European businesses, with its inclusion into the exclusive European Best Innovator Club.



Fig. 34

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In copertina / Front cover

Tessuto biofunzionale di acetato di cellulosa con nanofibrille di chitina e luteina.

Foto al microscopio elettronico a scansione (SEM). Su gentile concessione dell'Istituto di Morfologia Umana Normale, Università Politecnica delle Marche, Ancona, Italia.

Biofunctional tissue of cellulose acetate with chitin nanofibrils and lutein.

Scanning Electron Microscopy (SEM). On kind permission of the Institute of Human Normal Morphology, Università Politecnica delle Marche, Ancona - Italy.

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