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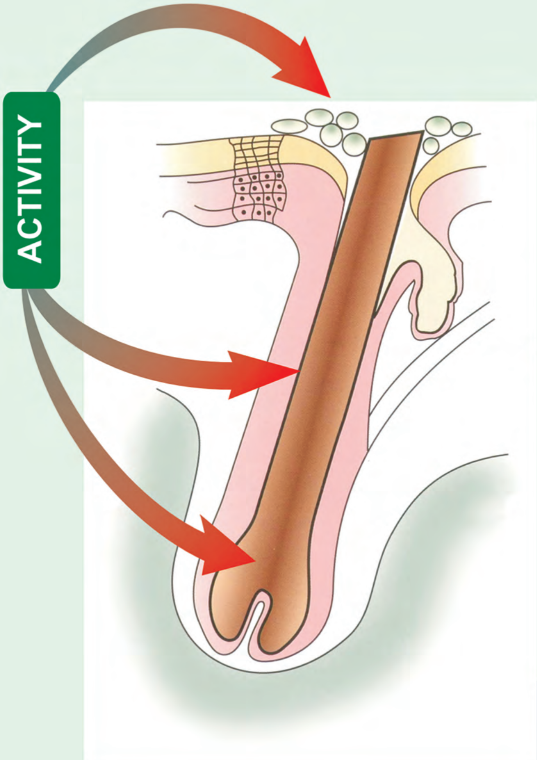

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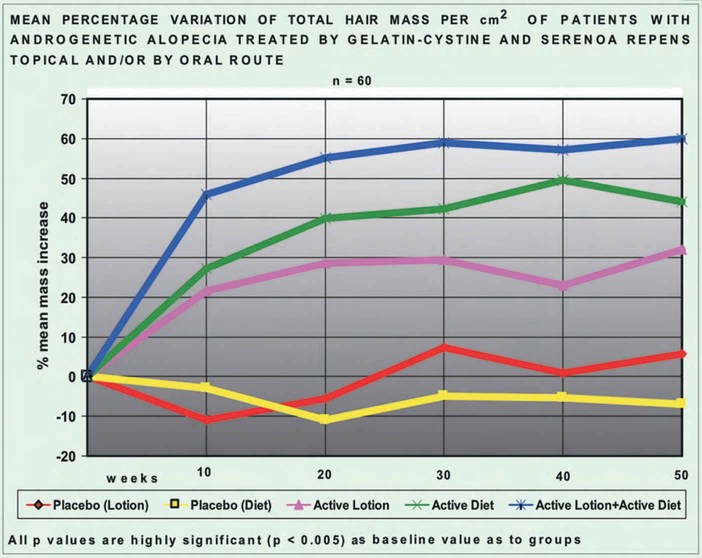

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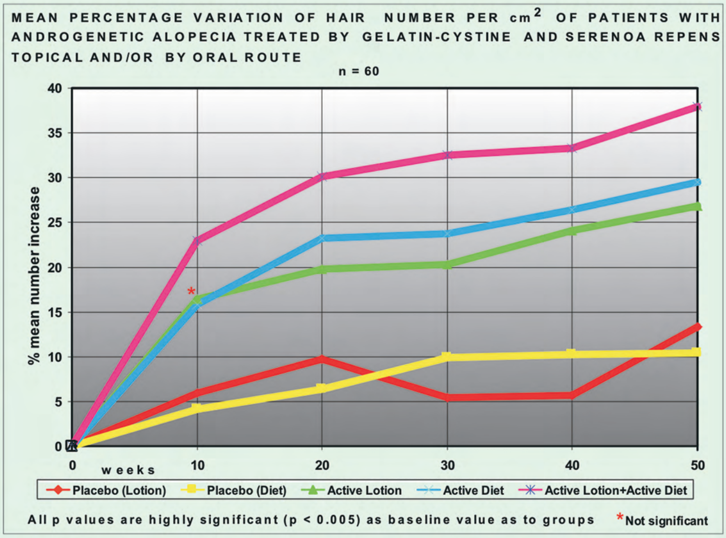

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1

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Contents

J. Appl. Cosmetol. **33,** 1-7 (January/June 2015)

'Quick Kill Effect' of a Herbal Shampoo versus Contact Time

Janani S, Gayathri Rajagopal
Dr. JRK's Siddha Research and Pharmaceuticals Pvt., Ltd., Kundrathur, Chennai - India

Received: *March, 2015*

Key words: *Anti-dandruff; Herbal extracts; Quick kill effect;*

Summary

The quick kill effect (QKE) of the ingredients of a herbal shampoo* formulated with *Acacia sinuata, Aloe vera, Trigonella foenum graecum, Hibiscus rosa sinensis, Indigofera tinctoria, Psoralea corylifolia* were tested individually against *Candida albicans* cells. The cells treated with varying concentrations of the extracts and incubated at different time points were stained with methylene blue.
The number of live versus dead cells was ascertained against the concentration and treatment time of the respective extracts.
The findings of the study show that 2mg/ml concentration of *Acacia sinuata, Trigonella foenum greacum and Psoralea corylifolia* in two minutes exposure has caused death of yeast cells with percentage of 26 to 31.
The quick kill effect of these herbal extracts suggests their outstanding value in wash-off products like shampoo as anti-fungal agents.
Most of the anti-dandruff shampoo preparations despite having effective anti-fungal agent show poor efficacy mainly due to short contact time. The present study clearly state that when a shampoo is formulated with these herbal extracts with their quick kill effect seem make such formulations superior.

Riassunto

In questo studio è stata controllato l'effetto antimicrobico degli ingredienti di uno shampoo formulato con *Acacia sinuata, Aloe vera, Trigonella foenum graecum, Hibiscus rosa sinensis, Indigofera tinctoria, Psoralea corylifolia* e testato nei confronti della *Candida albicans*.
Le cellule trattate con differenti concentrazioni degli estratti ed incubate in tempi diversi, sono state colorate con blu di metilene. Il numero di cellule vive verso le stesse morte è stato verificato con tempi e concentrazioni variabili dei diversi estratti.
I risultati dello studio, dimostrano come con concentrazioni di 2mg/ml di *Acacia sinuata, Trigonella foenum greacum and Psoralea corylifolia* causa la morte delle cellule del lievito con percentuali che vanno dal 26 al 31%.

** Trade name: Lumina herbal shampoo by Dr. JRK's Siddha Research and Pharmaceuticals Pvt., Ltd., Chennai.*

Pertanto, il rapido effetto "killing" di questi estratti vegetali ne suggerisce l'uso nei prodotti a risciacquo quali gli shampoo antiforfora, considerando anche che la maggior parte degli shampoo antiforfora mostra di possedere una bassa efficacia antifungina a causa del loro scarso tempo di contatto con il cuoio capelluto.
I risultati di questo studio evidenziano come gli estratti vegetali utilizzati sembrino risultare più efficaci.

INTRODUCTION

The demand for anti-fungal agents from herbal sources for the treatment of dandruff is increasing globally due to the increased incidence of dandruff (1). Although, the ingredients like Climbazole, Zinc pyrithione, Octopirox, etc. have proven anti-dandruff effect, due to their chemical nature their global acceptance is diminishing (2). Several herbs are known to possess strong anti-dandruff activity and one such proven ingredient is Tea tree oil (3).

Siddha system of medicine is one of the ancient health practices followed in Southern part of India. Siddha system has rich mention of several herbs having curative value against dandruff and other scalp disorders (4).

The tested herbal shampoo is a proprietary siddha medicine (shampoo) of Dr. JRK's Siddha Research and Pharmaceuticals Pvt Ltd, Chennai. The shampoo is formulated with select herbs such as *Acacia sinuata, Aloe vera, Trigonella foenum graecum, Hibiscus rosa sinensis, Indigofera tinctoria, Psoralea corylifolia*.

Traditionally, *Acacia sinuata and Hibiscus rosa sinensis* were widely used in hair care/hair wash preparations (5). Similarly, *Trigonella foenum graecum* is used in the treatment of dandruff (6). Although most of the anti-fungal ingredients do exhibit anti-fungal activity *in vitro* against various fungi such as *Candida albicans, Pityrosporum* ovale, but their efficacy in shampoo system is highly limited. One of the reasons for the above is the short contact time of shampoos and wash-off products in the scalp. Therefore, the evaluation of anti-fungal shampoos and wash-off products must be done with reference to their contact time than their real time activity.

The present paper reports the anti-fungal efficacy of the ingredients in the herbal shampoo with reference to their contact time. Methylene blue and Trypan blue staining techniques were employed for the above.

MATERIALS AND METHODS

Composition of the herbal shampoo

Acacia sinuata	: 10mg
Aloe vera	: 2mg
Trigonella foenum graecum	: 2mg
Hibiscus rosa sinensis	: 5mg
Indigofera tinctoria	: 5mg
Psoralea corylifolia	: 2mg

Preparation of extracts
Acacia sinuata

The quality checked *Acacia sinuata* pods were powdered and treated with liquid nitrogen for 30 minutes with continuous mixing. After treatment, the extract paste was presented in aqua base, filtered and then the filtrate was used. The concentration of the extract was adjusted to 2mg/ml.

Aloe vera

The quality checked *Aloe vera* pulp was treated with liquid nitrogen for 30 minutes with continuous mixing. After treatment, the pulp paste was presented in aqua base, filtered and then the filtrate was used. The concentration of the extract was adjusted to 2mg/ml.

Trigonella foenum graecum

The quality checked *Trigonella foenum graecum* seeds were powdered and treated with liquid nitrogen for 30 minutes with continuous mixing. After treatment, the extract paste was presented in aqua base, filtered and then the filtrate was used. The concentration of the extract was adjusted to 2mg/ml.

Hibiscus rosa sinensis

The quality checked flower of *Hibiscus rosa sinensis* was treated with liquid nitrogen for 30 minutes with continuous mixing. After treatment, the extract paste was presented in aqua base, filtered and then the filtrate was used. The concentration of the extract was adjusted to 2mg/ml.

Indigofera tinctoria

The quality checked *Indigofera tinctoria* leaves were powdered and treated with liquid nitrogen for 30 minutes with continuous mixing. After treatment, the extract paste was presented in aqua base, filtered and then the filtrate was used. The concentration of the extract was adjusted to 2mg/ml.

Psoralea corylifolia

The quality checked *Psoralea corylifolia* seeds were powdered and treated with liquid nitrogen for 30 minutes with continuous mixing. After treatment, the extract paste was presented in aqua base, filtered and then the filtrate was used. The concentration of the extract was adjusted to 2mg/ml.

Determination of contact time versus killing rate

To evaluate the killing effect of different herbal extracts on *Candida albicans* cells with reference to contact time methylene blue staining was performed.

Preparation of inoculum

The 24 hour culture of *Candida albicans* was prepared in normal saline and the size of the inoculum was adjusted to an absorbance of 0.7 at 450nm. The 20 microliter of the adjusted inoculum was taken in a clean glass slide and was treated with varying concentrations of different herbal extracts separately.

In the extract suspension 0.5% of glycerin was incorporated in order to prevent the drying of *Candida albicans* cells. The extract treated yeast cells were incubated at RT for 2, 4, 6, 8 and 10 minutes. After incubation for the specified time, the methylene blue dye was added & mixed gently and then the slide was examined microscopically (7).

Ten fields at random were chosen and the number of dead (blue colored) cells versus unstained live cells was recorded. The percentage of dead cells was calculated by averaging their number from all the ten fields.

Similarly, the untreated cells were incubated for the above period of time in order to understand the percentage of death of *Candida albicans* in untreated condition.

Climbazole at a concentration of 0.1% was used as positive control for the above experiment.

Evaluation of possible mechanism of action of different herbal extracts

To understand the role of different herbs in either damaging the cell wall, the treated cells were stained with Trypan blue dye. The cells were examined microscopically to differentiate the stained versus unstained cells. The Trypan blue dye would permeate into the cell only when there is a definite damage to the cell wall. Otherwise, the cells would appear colorless.

RESULTS

The two minutes of exposure of yeast cells to varying concentrations of the extracts of Acacia sinuata, Aloe vera, Trigonella foenum graecum, Hibiscus rosa sinensis, Indigofera tinctoria, Psoralea corylifolia showed that the killing effect of these plants depends on two factors viz concentration and contact time.

The Psoralea corylifolia, Trigonella foenum graecum and Acacia sinuata were more effective in causing death of the cells in two minutes of contact time than other herbs (Table I).

When yeast cells were exposed to 2mg/ml concentration of different extracts at different time intervals viz. 2,4,6,8 and 10 minutes revealed that longer the contact time, the percentage of death increased marginally. The marginal increase in the death of yeast cells from the treatment period of 2 minutes to 10 minutes, suggests that although the anti-fungal activity of these extracts are quick in action however are definitely concentration dependent. May be at higher concentration these extracts are likely to exhibit greater killing effect on yeast cells at short contact time. Climbazole at 0.1% has caused 90% cell death even at two minutes contact time (Table II). The survival of yeast cells in untreated group was unaffected for 20 minutes.

TABLE I

Concentration versus killing effect.

Name of the Herbs	Concentration and Percentage of death			
	2 mg	1 mg	0.5 mg	0.25 mg
Acacia sinuata	26	14	0	0
Aloe vera	8	0	0	0
Trigonella foenum graecum	29	16	0	0
Hibiscus rosa sinensis	18	9	0	0
Indigofera tinctoria	15	8	0	0
Psoralea corylifolia	31	18	0	0

TABLE II

Contact time versus dead cells.

Name of the Herbs	Contact time versus % dead cells				
	2 mins	4 mins	6 mins	8 mins	10 mins
Acacia sinuata	26	30	34	37	40
Aloe vera	8	10	13	16	19
Trigonella foenum graecum	29	33	35	39	44
Hibiscus rosa sinensis	18	15	18	22	24
Indigofera tinctoria	15	21	25	27	32
Psoralea corylifolia	31	40	42	49	56
Combination of extracts (equal proportion)	60	63	65	66	69
Climbazole (0.1%)	90	90	95	95	98
Untreated cells	0	0	0	0	1

DISCUSSION

The present study clearly reveals that the herbs used in the shampoo have definite anti-fungal activity. The short contact period of these extracts was sufficient to cause death of the yeast cells. When these extracts individually exhibit such quick effect, the synergistic effect of the combination of the above extracts is naturally expected to be superior. In our study, the combination of the above herbs exhibited high killing rate of yeast cells accounting to 60% in two minutes contact time.

The quick kill effect (QKE) of these extracts in short time ideally qualifies these extracts to be the best anti-dandruff candidate in wash-off products such as shampoo, cleansers, etc. These wash-off products must deliver the anti-fungal effect in short time as they are used and are immediately washed off. Therefore, any effective wash-off formulations and anti-dandruff preparations must have ingredients that are quick in action (7).

The Herbal shampoo is formulated with herbs such as Acacia sinuata a natural cleanser (8), the hair conditioning herb Hibiscus rosa sinensis (9) and Indigofera tinctoria, the scalp calming agent Aloe vera, and the anti-fungal active herbs such as Trigonella foenum graecum (10) and Psoralea corylifolia.

The Acacia sinuata, Trigonella foenum graecum and Psoralea corylifolia all of them have exhibited QKE against yeast cells in two minutes exposure.

To understand the possible mechanism of action, the extract treated yeast cells were stained with Trypan blue dye.

However, none of the cells treated by any of the extracts or their combination, had taken up the Trypan blue dye suggesting the effect of these extracts in causing death of the yeast cells may not be due to cell wall damage.

The release of these extracts from the shampoo base was difficult to ascertain. However, we have studied the effect of these individual extracts along with the surfactants like SLES (data communicated elsewhere). The findings of the above study showed that the SLES or other surfactants in the herbal shampoo neither complemented nor acted against the efficacy of these extracts. The above finding suggests that the activity of these extract are quite stable and non-pH and surfactant dependent.

The quick kill effect of the herbal ingredients which are unaffected by either the pH or the ingredients of the shampoo base against yeast cells strongly support their interesting anti-dandruff efficacy. Further, their quick effect also favours their use in wash-off products like shampoo. The anti-fungal efficacy of the well-known ingredient like Climbazole is affected by various conditions of the shampoo system (2). Not considering these conditions when using Climbazole as the principle anti-dandruff agent in shampoo system might cause such products to be less effective. In our present study, none of the herbs used in the herbal shampoo showed any such sensitivity like Climbazole.

The 2mg of combination of the extracts at equal ratio exhibited synergistic effect in killing about 60% of yeast cells in two minutes of exposure. This finding suggests the likely strong anti-dandruff activity of the herbal shampoo.

The herbal shampoo is well received by the dandruff sufferers in India. In the light of the above findings, we presume that the global acceptance of the herbal shampoo tested by us (marketed under the trade name Lumina herbal shampoo) may be due to its superior effect.

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Innovation in Cosmetic and Medical Science. The role of Chitin Nanofibrils Composites

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Summary

The main substrate of interest in cosmetic dermatology are hair, covered with hard keratin-scales, and skin Stratum Corneum (SC), being with corneocytes the outermost cell layer of the skin. Both, directly exposed to onslaught of pro-oxidative stressors and composed of dead cells filled with specific type of lipids and cross-linked proteins in the form of alpha-helix structure, represent the barrier of our body to the environment. The barrier function of both skin and hair depends, therefore, on the physicochemical properties of corneocytes and scales, which by their lipid-keratin structures, regulate and interchange water loss, oxygen and carbon dioxide, modulating the penetration of active ingredients and preventing the entrance of pathogenic microorganisms. While the skin lipid structure consists predominantly of ceramides (~50%) connected with fatty acids and cholesterol, the hair epicuticle membrane (scale) contains highly cross linked proteins (~75%) and adsorbed fatty acids (~25%), 18-methyleicosanoic acid (18-MEA) being the most abundant. In addition, skin and hair are equipped with a network of enzymatic and non-enzymatic antioxidant system, that counteract the oxidative injury. An imbalance of this complex structure leads to modifications of DNA, lipids, and proteins, resulting in loss of functionality of the barrier key components of both hair and skin. As a consequence, skin wrinkling appears and hair lose luster and alignment, decreasing its thickness and combability .

The challenge of cosmetic dermatology is to produce effective and safeness cosmetic products capable to modulate both the keratin-lipid production and the antioxidant synthesis at level of skin and hair. These innovative products should slowdown skin wrinkling formation and ameliorate structure and function of the hair, giving the body a more younger appearance.

For obtaining these results it is necessary to develop topical systems capable to deliver the *right* concentration of the *right* active ingredient to the *right* site in the body in the *right* period of time (4 R's),

without disrupting the respective protective structures, but having the capability to stimulate the synthesis of both skin extra cellular matrix (ECM) and hair cortex components. These results have to be produced by a low consume of water and energy and by the use of *green* raw materials extract, for example, from fishery's waste, as Chitin Nanofibrils, and plant biomass, as lignocellulosic compounds. Thus, natural material, and biodiversity of our planet will be preserved.
In this paper innovative products realized by two EU research projects Biomimetic (www.biomimetic-EU-project.eu) and n-Chitopack (www.n-Chitopack.eu) will be presented and discussed. These products, made by the use of biopolymers such as Chitin Nanofibrils (CN), Lignin (LN) and Polylactic acid (PLA), are in accordance with the incoming *Bio-green economy* supported by EU and UNEP. The use of these biopolymers, is, in fact, necessary to reduce the production of the actual petrol-derived polymers and stop the plastic waste in the land and in the oceans where 5 trillion pieces afloating, have been recovered, ranging a weight of over 250,000 tons.
Finally it is to underline that this plastic waste causes the death of ~1 million bird and ~100,000 sea-mammals every year, so that scientists, opinion leaders and politic people worldwide have to work all together to solve this important problem!

Riassunto

I principali *attori* della dermatologia cosmetologica sono i capelli costituiti da una struttura proteica ricoperta da tegole di cheratina, e la cute, il cui strato esterno è formato da corneociti, anch'essi ricchi di cheratina. Entrambe queste strutture, direttamente esposte agli attacchi ossidativi ambientali e composte da cellule cheratinizzate legate tra di loro da lipidi, rappresentano la barriera difensiva del nostro organismo che si oppone alle molteplici aggressioni esterne.
La funzione barriera sia della pelle che dei capelli dipende dalle proprietà fisico-chimiche dei corneociti e delle tegole cheratiniche che regolano l'interscambio di acqua, ossigeno e anidride carbonica, modulando la penetrazione delle sostanze nutritive e prevenendo l'ingresso dei microorganismi patogeni.
Se da una parte i lipidi cutanei sono rappresentati da cerammidi, che rapprensetanto il "collante" delle cellule (50%), acidi grassi e colesterolo, dall'altra parte le tegole cheratiniche dei capelli sono formate da proteine (~75%) legate tra loro da acidi grassi (~25%) con preponderanza dell'acido 18-metileicosanoico (18-MEA). Inoltre, sia la cute che i capelli sono equipaggiati con un sistema antiossidante composto da enzimi e molecole specializzate in grado di controbattere gli attacchi ossidativi dell'ambiente. Qualsiasi sbilanciamento di questa complessa struttura provoca modifiche a livello del DNA, dei lipidi e delle proteine, causando perdita di funzionalità della barriera cutanea e dei capelli. Come conseguenza sulla pelle appaiono le rughe del volto, mentre i capelli perdono lucentezza e spessore con conseguente riduzione della pettinabilità.
La sfida della dermatologia cosmetologica è di produrre cosmetici sicuri ed efficaci in grado di regolare sia la produzione delle cheratine e dei lipidi, che la sintesi degli antiossidanti a livello di cute e capelli.
I cosmetici innovativi dovranno essere in grado di rallentare la formazione delle rughe, migliorando contemporaneamente la struttura e le funzioni dei capelli per donare a tutto il corpo una più giovanile apparenza.
Per ottenere questi risultati è necessario sviluppare sistemi topici capaci di liberare la *giusta* concentrazione del *giusto* ingrediente attivo, nella *giusta* area del corpo e nel *giusto* periodo di tempo (4 G).

Naturalmente questa attività dovrà essere svolta non soltanto senza alterare le rispettive strutture difensive, ma anche con la capacità di stimolare la sintesi dei componenti la struttura extracellulare cutanea (ECM) e della corteccia dei capelli. Inoltre, gli ingredienti attivi utilizzati dovranno essere prodotti con basso consumo di energia ed acqua e attraverso l'uso di materie prime *verdi*, ricavate per esempio dagli scarti della lavorazione dei crostacei, come le nanofibrille di chitina, e/o dalla biomassa vegetale, come i derivati ligno-cellulosici. In questo modo si potranno preservare le materie prime naturali salvaguardando anche la biodiversità del nostro pianeta.

In questo lavoro verranno presentati i risultati di due progetti di ricerca finanziati dall'Europa: Biomimetic (www.biomimetic-EU-project.eu) e n-Chitopack (www.n-Chitopack.eu).

I prodotti realizzati mediante l'uso di polimeri naturali quali le nanofibrille di chitina, la lignina e l'acido polilattico sono stati realizzati mediante le tecnologie *verdi* volute e sostenute sia dalla EU che dall'UNEP. Infatti, l'uso di questi polimeri naturali biodegradabili e compostabili è necessario per ridurre la produzione dei derivati del petrolio con il conseguente inquinamento da plastica non biodegradabile che ha raggiunto la ragguardevole cifra di 250.000 tonnellate, pari a 5 milioni di pezzi che galleggiano sugli oceani.

È infine utile ricordare come l'eccessivo uso di plastica da petrolio causi ogni anno la morte di 1 milione di uccelli e di circa 100.000 mammiferi che rimangono impigliati o mangiano direttamente questo materiale tossico e indistruttibile. Pertanto, è tempo che tutti gli studiosi, i politici e gli uomini di buona volontà cerchino di occuparsi e risolvere questo problema non più rimandabile.

INTRODUCTION

The main substrate of interest in cosmetic science are hair and skin stratum corneum (SC), representing the outmost 10-20μm cell layers of the skin made by corneocytes (Fig.1) (1, 2).

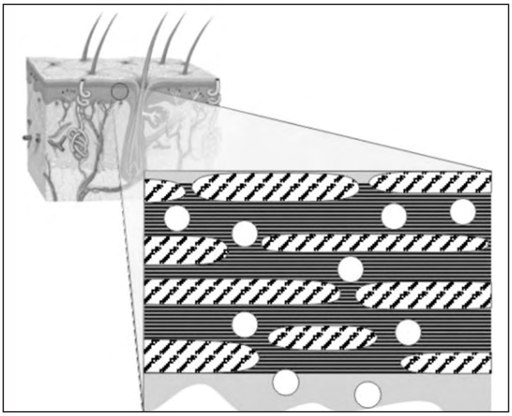

Fig. 1 *The Stratum Corneum made of corneocytes embedded into lipidic layers.*

Both are composed of dead cells filled with specific type of cross-linked proteins, represented by crystalline keratins in the form of alpha-helix structure (Fig.2). Thus, on the one hand the skin Stratum Corneum (SC) is composed of keratinized corneocytes enclosed by a keratinic envelop, surrounded by a semi-continuous matrix of lipids - the so-called *lamellae* - characterized by a repeating structure with alternating *hydrophilic* and *hydrophobic* domains oriented parallel to the corneocytes. In this complex structure, the keratins provide a superbly adapted covering for the underlying tissues, being chemically nonreactive, hard, waterproof, elastic and resistant to abrasion and physical insult. However, the composite architecture of SC is essential for the skin physiological functions and it is continuously renewed via the epidermis' turnover (Fig.3).
On the other hand hair (3-5) can be considered a bio-composite material made by structural components named *cortex*, covered by protective layers of overlapping cuticular scales (Fig.4).

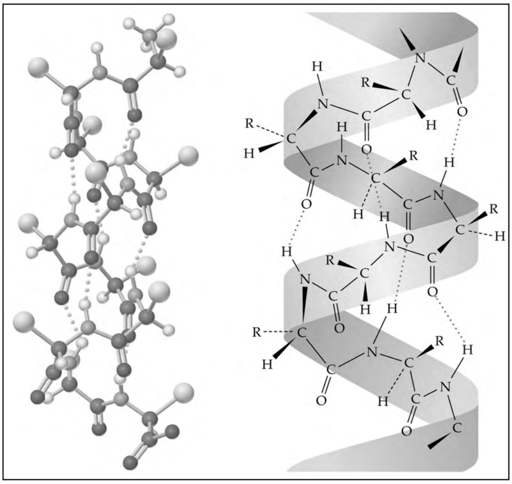

Fig. 2 *The alpha-helix structure of keratins.*

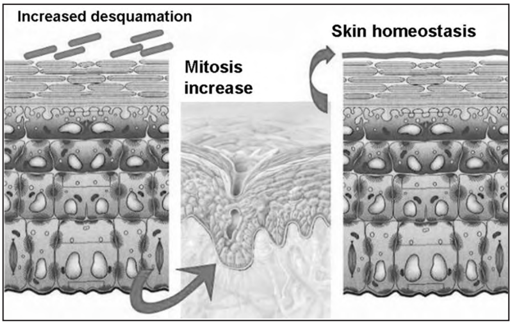

Fig. 3 *The skin turnover.*

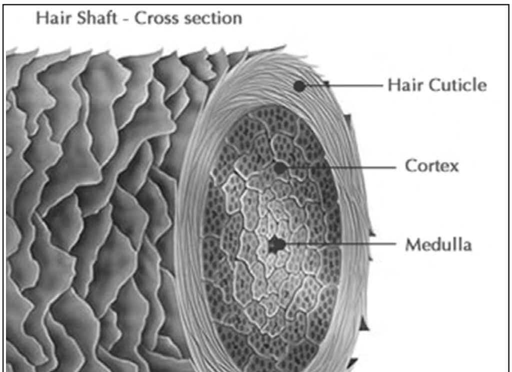

Fig. 4 *The hair made by cuticle scales protecting cortex and medulla.*

The cortex, formed of elongated cells aligned along the axis of the fiber is filled with keratins, arranged in a coiled-coil configuration (Fig.5).

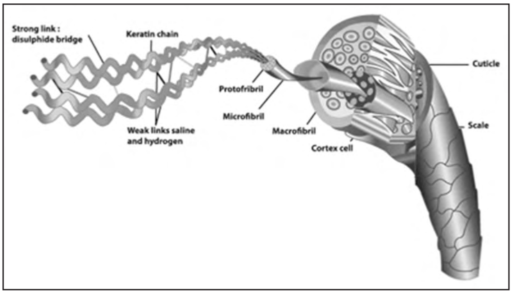

Fig. 5 *The hair coiled configuration.*

The cuticle is a thin laminar-like structure comprised of layers of overlapping, flat, scale-like cells acting as a protective hair sheath, as well as the cornified envelope of corneocytes acts as a reinforcing material of the skin barrier. Structure, assembly, and cohesion in the cells of both keratins and lipidic lamellae, give the hair and stratum corneum their specific mechano-elastic properties (5). Because they are located at the interface with the environment, SC and hair are directly exposed to an onslaught of pro-oxidative stressors, including air pollutants, ultraviolet rays (UVR) chemical oxidants, and microorganisms. Thus, the integrity of keratins and surface lipids of both hair and skin may be affected by protein alteration and uncontrolled loss of water and ions. The barrier function of skin and hair depends, therefore, on the physicochemical properties of keratinized corneocytes and lipid lamellae for the skin, and keratinic scales covered by lipids, for the hair (6).

The skin lamellar fashion, consisting predominantly of ceramides (CER) (about 50% by weight), fatty acids (FFA) and cholesterol (CHOL) in the molar ratio 1:1:1, comprises about 10% of the dry weight of *young* SC. (7). The hair epicuticle membrane contains highly cross linked proteins (~75%) and adsorbed fatty acids (~25%), the 8-methyleicosanoic acid (18-MEA) being the most abundant (50% w/w). The outermost surface of the hair' cuticle cells, in fact, seems to be covered by a layer of covalently bound fatty acids (8). The absence of this fatty acid is considered one of the reasons for the increased interfiber friction that influences the sensory perception of hair, such as feel and difficult combing (9).

The cuticle surface, in fact, affects the hydrophobic-hydrophilic properties of hair, modifying its luster and alignment in the wet environment, particularly in the case of damaged hair (8, 9). An important cosmetic role of 18-MEA, therefore, could be to allow hair fibers to lie flat and parallel with respect to each other in wet environments by providing low surface friction (Fig.6). By these protective structures, both skin and hair regulate and interchange water loss, oxygen and carbon dioxide, modulating the penetration of active ingredients and preventing the entry of pathogenic microorganisms.

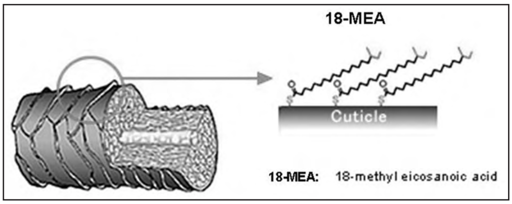

Fig. 6 *MEA positioning on hair surface.*

SKIN AGING

As exterior barrier and dynamic cover of our body in direct contact with the environment, the skin is the guardian of the body and the *defence* mean of our health.

During the years, as a result of the multiple daily stresses, a slow but cumulative destruction of the macromolecules of both dermis and the dermal-epidermal junction appears, underlined by the formation of wrinkles as evident sign of aging (10). Moreover, an increased average lifespan, bringing the global life expectancy to future 102 years (Fig.7), has increased the number of people looking for a more youth appearance. Thus, prevention of premature skin aging is constantly increasing of importance to the general population, and, as a consequence, the mainstay of skin protective strategies is increasing day by day.

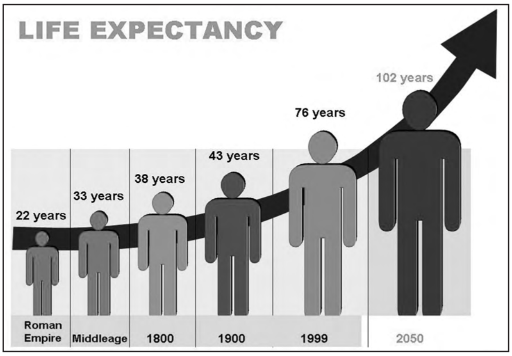

Fig. 7 *The life expectancy.*

But which the main causes of skin aging? On the one hand it is to be considered the more frequent appearing of the oxidative stress, due to an unbalanced activity among antioxidant compounds, such as vitamin A, E, and C. On the other hand a minor functionality of the skin turnover for a loosed synchronization between cell differentiation and proliferation, has to be underlined (10). Both these phenomena may cause an impaired barrier function, resulting in the appearance of inflammatory reactions by an increased expression of several cytokines (11). The cells tend to hyper proliferate in different skin areas, moving toward the surface very fast, as in the case of psoriasis and atopic dermatitis (12). In addition, the inflammation may create phenomena of hyper-pigmentation and the skin appears dry, less flexible and rich of black spots. When skin cells move up faster, in fact, there is less time for cell differentiation, keratinization, and lipid secretion so that the skin barrier is affected. In conclusion, a reduced presence of antioxidant compounds (13, 14), a loss of synchronization between the cells, and a slow down of their regular turnover cause loss of homogeneity and a premature skin aging.

Moreover, the increased inflammation phenomena activate immune cells and metalloproteinase enzymes that destroy specific components of the extra cellular matrix (ECM) in the dermis together with key elements of the basal membrane (BS). Thus, the synthesis of collagen I, III and IV (15) appear reduced and the increased melanocytes production provokes formation of the so-called aged spots.

It is also to remember that human skin, equipped with a network of enzymatic and non-enzymatic antioxidant systems, counteracts the oxidative injury (14). An imbalance between reactive oxygen species (ROS) and these antioxidant protection mechanisms leads to oxidative modifications of macromolecules such as DNA, lipids, and proteins, resulting in loss of structural and functional integrity of key components of both skin and hair barrier (16).

In conclusion, skin moisturizing and flexibility, hairstyle and manageability, depend to great extent on surface properties of these complex bio-structures. To maintain their homeostasis, it seems possible to modify the keratin-lipids interaction at level of skin and hair by the right selection of carriers and active ingredients.

So doing it will be possible to make cosmetic products useful to slow down the appearing of skin wrinkling, contemporary improving and ameliorating structure and surface properties of the hair. These results could be obtained developing topical systems that, capable to deliver specific active ingredients to the viable epidermis and/or the hair complex organisation, can penetrate through both horny layer and hair barrier, without disrupting the respective protective structures. Thus the basic idea, elaborated and designed into the Nanoscience Centre MAVI, has been to formulate innovative cosmetic gels and beauty masks capable to reduce the wrinkling appearance and the skin irritative processes respectively, stimulating and balancing the synthesis of both lipids and keratins, involving enzymes, oxidatively inactivated during the aging and photo aging process (17). These cosmetics could be used to modulate and/or restructure skin and hair by the use of different bio-carriers and right active ingredients. At this purpose and to prevent damages to lipids and proteins, an antioxidant strategy has been established, based on the use of vitamins A, E and C and anti inflammatory/immunomodulant compounds, such as allantoin and ectoin entrapped into patented innovative carries.

NANOCOMPOSITES MADE BY THE USE OF CHITIN NANOFIBRILS

According to the EU Bio-mimetic project (www.biomimetic-eu-project.eu), block copolymer micro-nano/lamellae or nanoparticles (Fig.8) made by the use of Chitin Nanofibrils (CN), hyaluronic acid, and different kind of refined lignin compounds were realized.

These innovative nanoparticles, controlled for their diameter, distribution, and physicochemical characteristics at the Department of Chemical Engineering Materials, and Environment, University La Sapienza, Rome, Italy (Fig.9) (18) and for their safety and efficacy at the Department of Experimental Medicine, 2nd University of Naples (Fig.10), were embedded into gels and non-woven tissues made in the Nanoscience Centre MAVI, Aprilia (Lt), Italy.

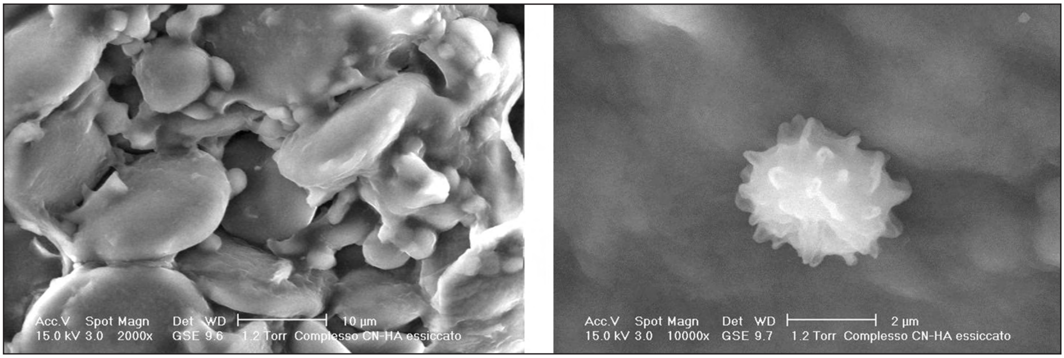

Fig. 8 *Nanolamellae and Nanoparticles made by the chitin-nanofibrils-hyaluronan acid block copolymer, at SEM.*

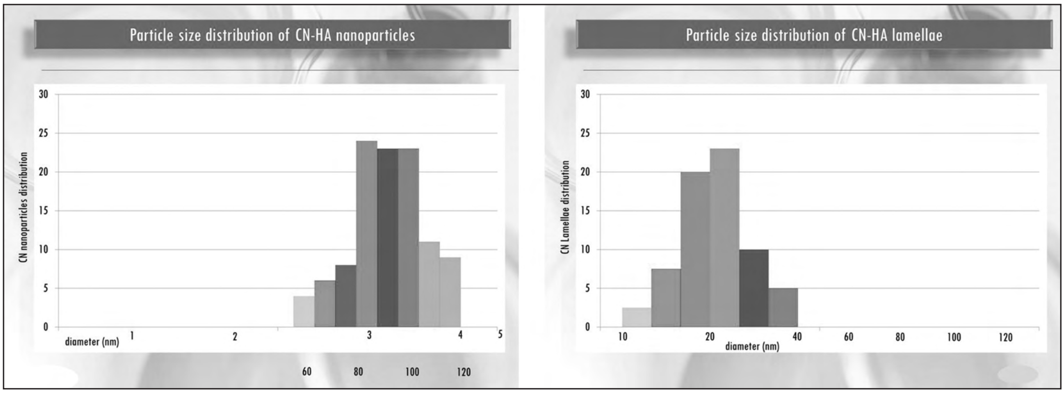

Fig. 9 *Distribution and size of nanoparticles (right) and nanolamellae (left).*

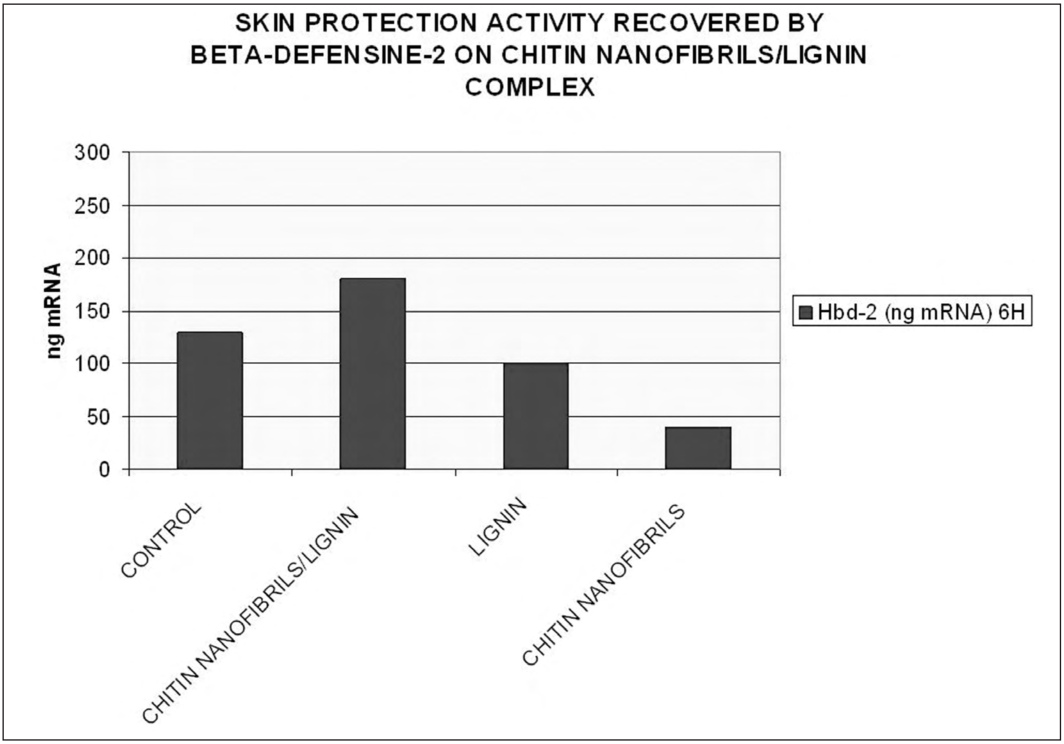

Fig. 10 *Protective activity of chitin-lignin nanoparticles by release of human defensines.*

According to the patented methodologies of the Company (19), the obtained nanoparticles have been entrapped with different active ingredients before their inclusion into gels and fibers, used to make innovative cosmetics and non-woven tissues Beauty Masks (Fig. 11 and 12).

The studies *in vitro*, made by cultures of keratinocytes and fibroblasts have shown interesting protective properties of both gels and beauty masks, showing their interesting anti inflammatory (Fig.13), and antibacterial activities (Fig.14) together with an increase of collagen synthesis (Fig.15), confirmed by the *in vivo* antiageing effectiveness (Fig.16).

Fig. 11 *Innovative cosmetics made by Chitin Nanofibrils (CN) - Hyaluronic Acid (HA).*

Fig. 12 *Innovative non woven masks made by non-woven tissue.*

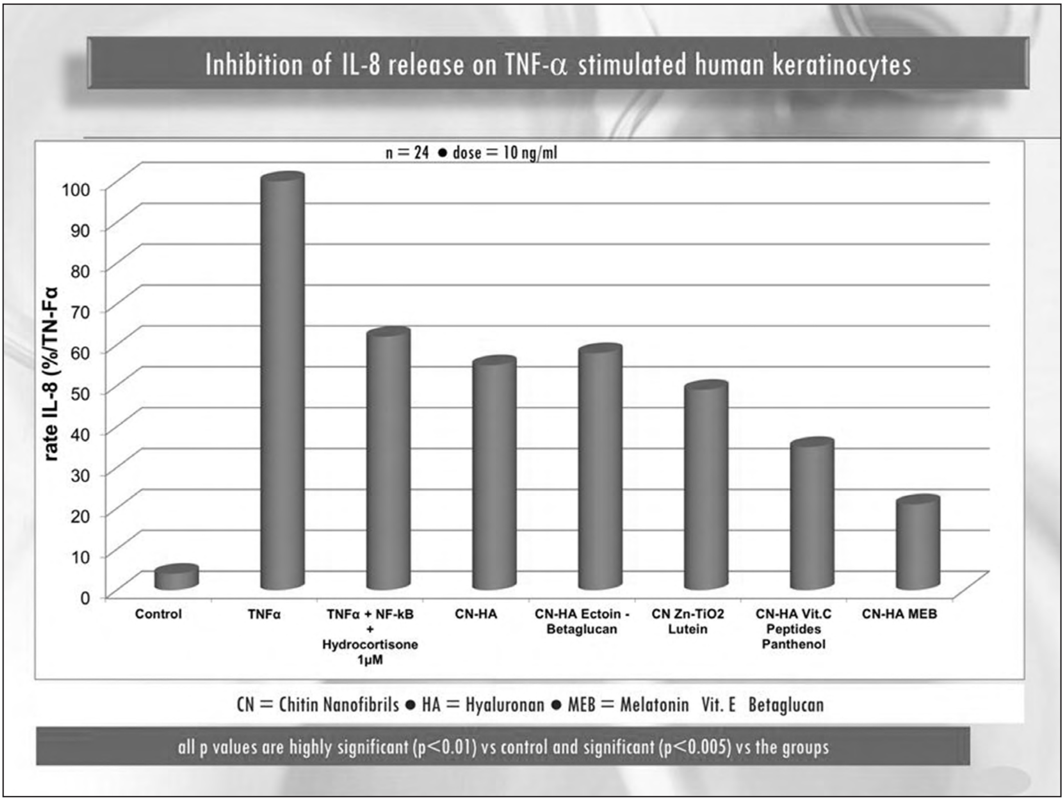

Fig. 13 *Antinflammatory activity of CN-HA shown in vitro on human fibroblast cultures by the release of IL-8.*

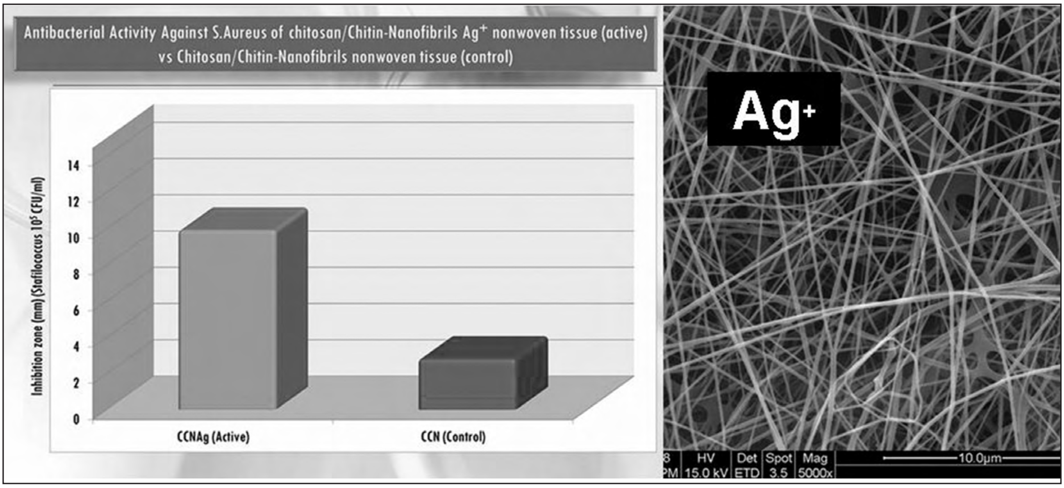

Fig. 14 *Antibacterial activity of CN non woven tissue bonded with* Ag^{+} *iones.*

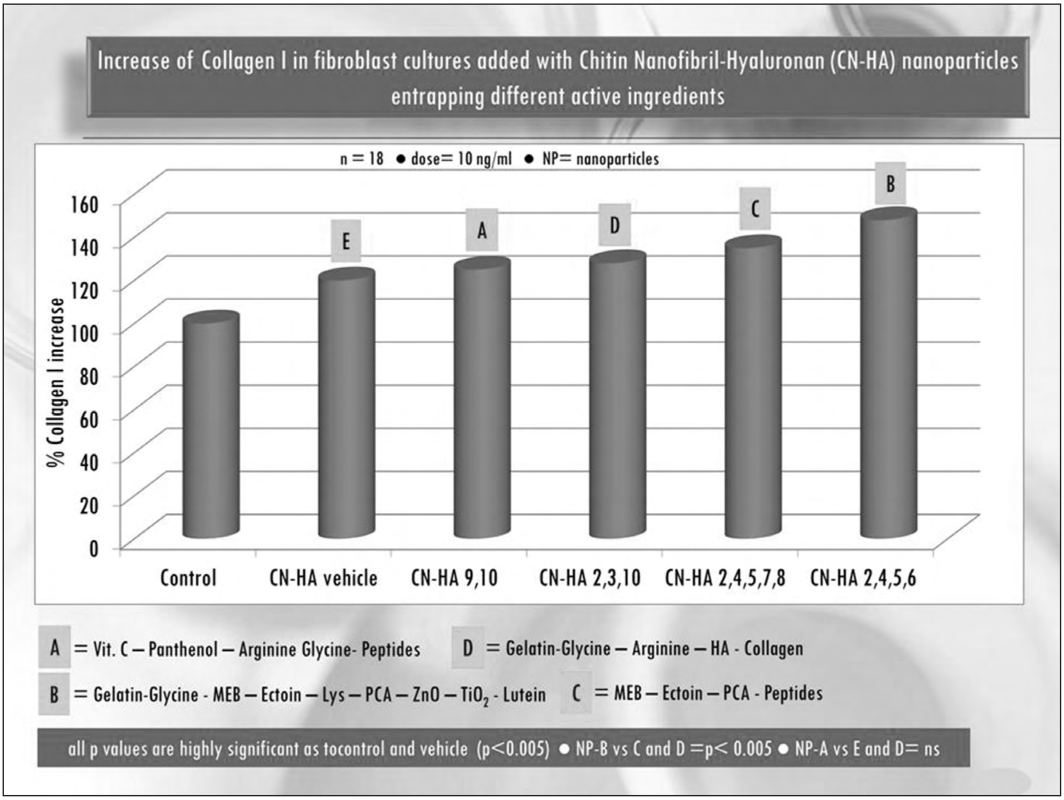

Fig. 15 *In vitro activity of CN-HA on the synthesis of collagen type I.*

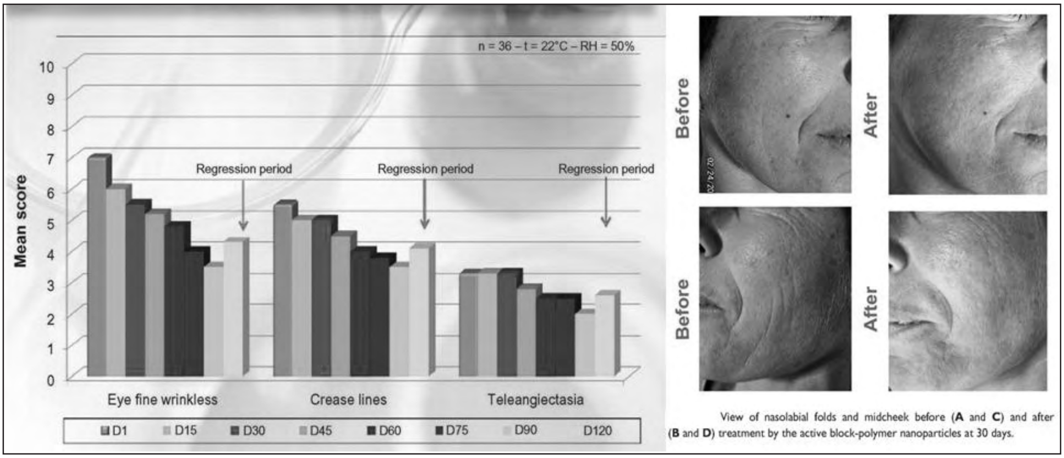

Fig. 16 *In vivo anti-wrinkling activity of CN-HA emulsion.*

It is interesting to underline how the bonds established between CN and lignin seems to be represented not only by ionic and Van der Waals forces but also by more stable bonds, according to the study realized in the Department of Chemical Science & Technology of Torvergata University, Rome (20).
In any way the interesting activity shown from these innovative masks, CN-HA and CN-lignin, seems due to the specific antioxidant and cicatrizing activity of both the block polymer complexes capable to enhance the particular anti wrinkling, moisturizing, immuno-modulating, and anti-inflammatory activities of the selected active ingredients used. CN-lignin, for example, has a double activity: as carrier it can transport the active ingredients at the right sites of skin and hair, and as active agent it is capable to show an interesting antioxidant, anti-inflammatory and restructuring activity due to the polyphenolic structure of lignin (Fig.17) and the hyaluronan-like backbone of chitin (Fig.18) (21).
Moreover, the nanoparticles of CN-Hyaluronan, entrapping different active agents and embedded into a cosmetic gel, has shown to regenerate the wounded skin in a short time without formation of hypertrophic skin or keloid, as shown in figure 19 (22).
In addition, CN has shown to be effective in extreme wounded condition also, without the use of topical, or systemic antibiotic therapy (Fig. 20 and 21).

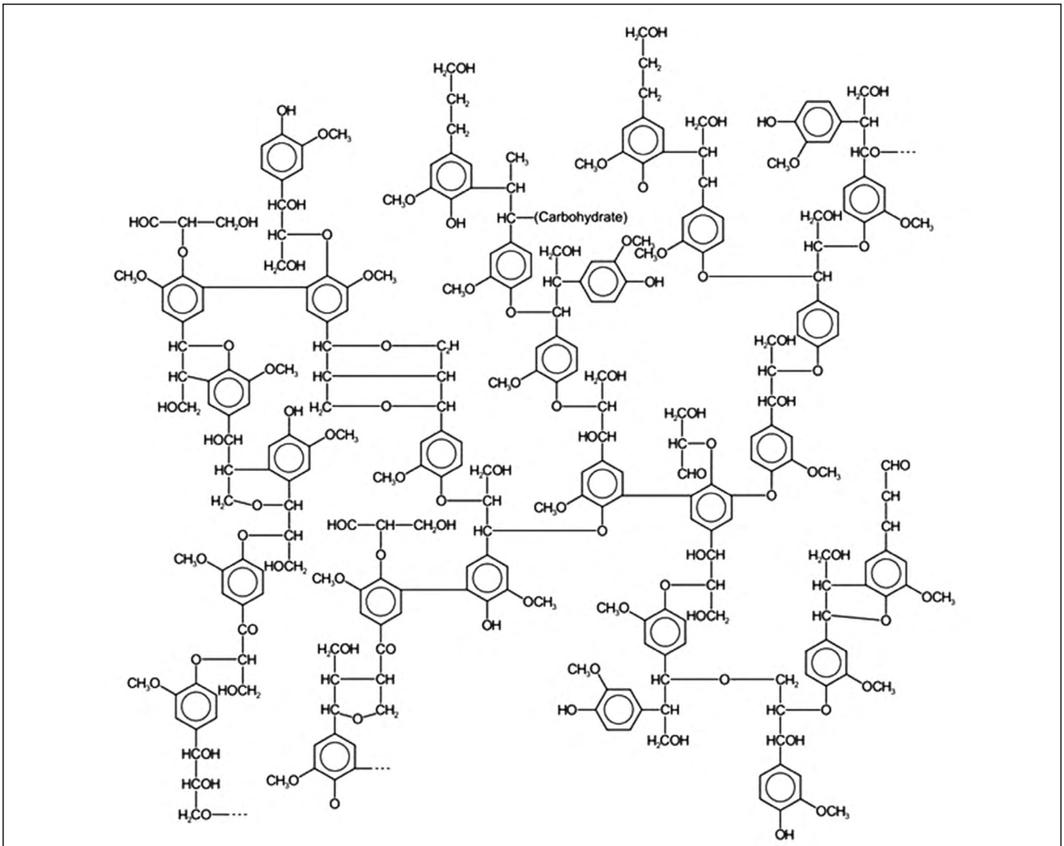

Fig. 17 *Polyphenolic structure of lignin.*

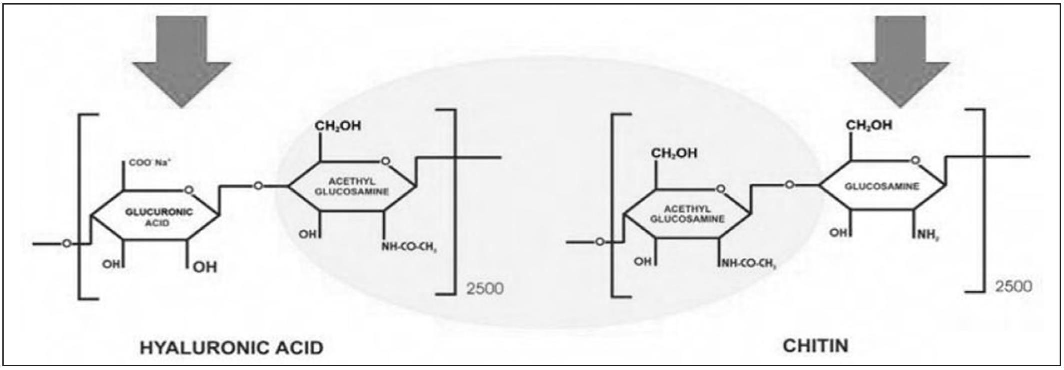

Fig. 18 *Chitin backbone structure compared to Hyaluronic Acid.*

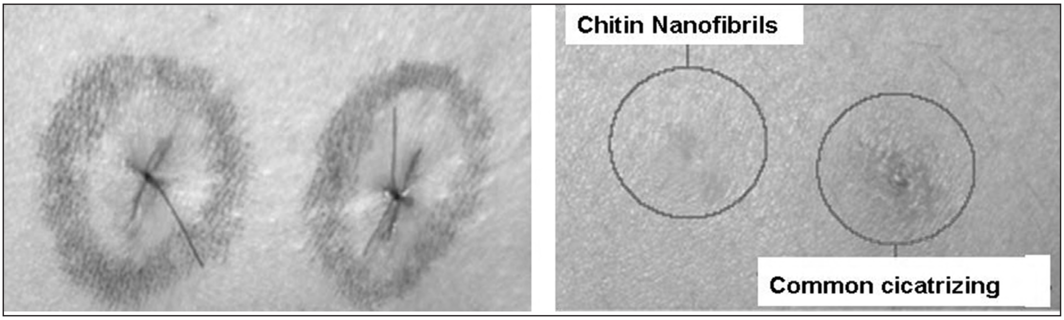

Fig. 19 *Cicatrizing activity of CN in comparison with a standard medication (before on the left, and after on the right, 15 days-treatment).*

Fig. 20 *Activity of CN on wounded skin.*

Fig. 21 *Activity of CN on wounded skin.*

Finally CN-fibers pre-bonded with Ag+ ions and electrospun with PEOX and PVA have shown to be effective in regenerate the skin affected by a 2nd-grade burn (Fig. 22 and 23) (23).
It is interesting to underline that these results have been obtained by one medication only, maintained on the skin for 6 days without the appearance of bacteria infection.
This new advanced medication seems to be useful for regenerating the burned skin in a shorter time, notably reducing the hospitalization cost also. Same effectiveness has been obtained by the use of CN-Hyaluronan (CN-HA) which, entrapping antioxidant and immuno-modulanting ingredients, has shown an interesting anti-aging activity on both skin and hair (15, 24). By these *in vitro* and *in vivo* studies it has been underlined that CN has not only the capacity to increase the production of new collagen reducing the wrinkling formation, but has also an interesting reparative activity on damage hair that appear more shining (Fig.24).
From new in progress studies (unpublished data) it seems that CN-HA and other block polymeric nanoparticles could result effective as: (a) glue at level of the hair superficial scales, acting as reparative agent to ameliorate its tensile and brightness properties, repairing the split ends also; (b) absorptive compound of environmental toxic agents with a protective activity, against any kind of heavy metals and colouring and de-colouring agents used in permanent waves; (c) reparative compound capable to improve the ability to align the hair fibers in a more parallel configuration, for obtaining an increased flexibility and combability; (d) colour-retention agent capable to maintain a longer benefit for the colour-treated hair, giving them a more shining aspect.

Fig. 22 *Activity of CN-Ag+ non woven tissue on baby burned skin (6 days-treatment).*

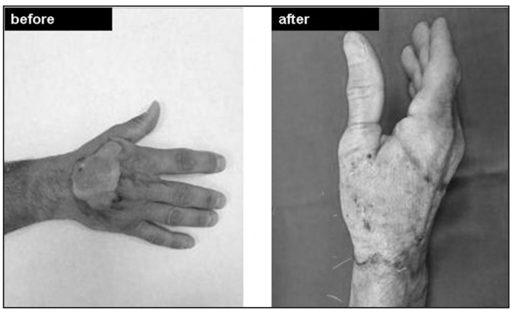

Fig. 23 *Activity of CN-Ag+ non woven tissue on old man burned skin (6 days-treatment).*

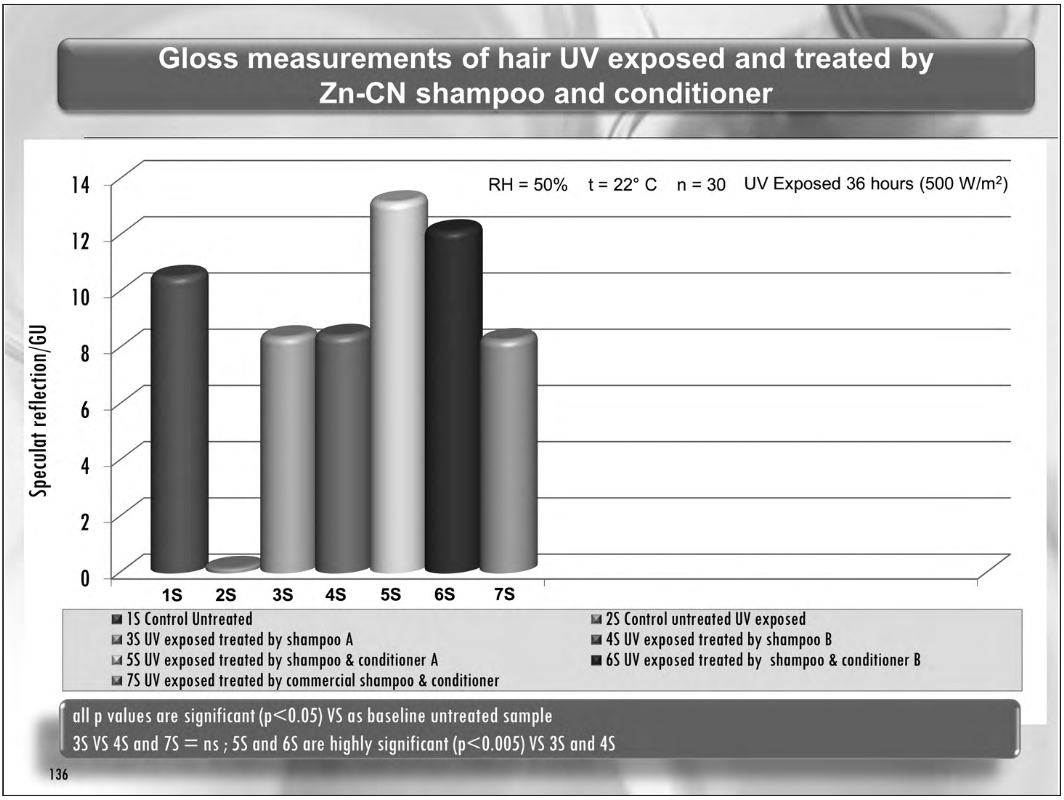

Fig. 24 *Repairing and shining activity of CN on damaged hair.*

In conclusion, by the use of different CN block copolymeric nanoparticles it seems possible to formulate innovative cosmetic products and advanced medications useful to ameliorate our well being maintaining the earth' equilibrium. CN and the other polymers used to formulate these new products are, in fact, ingredients obtained from Fishery's waste and plant biomass with a low consume of water and energy, according to the incoming bio-green economy (25).

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Aquous Lubrication. Natural and Biomimetic Approaches

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This book about water lubrication in nature, covers the current state of our understanding of the principles of aqueous lubrication with gels and materials. Organized in 8 chapters it covers the lubrication phenomena of natural articular joints as well as of Food and Cosmetic emulsions, Ceramics and Polymer Brushes, reported and discussed underlining their tribological and nano tribological effectiveness.

Tribology deals with friction, wear and lubrication, representing one of the least developed classical science to date. Nanotribology is a branch of tribology which studies friction phenomenon at the nanometer scale. Thus, it is concerned with experimental and theoretical investigation of processes ranging from atomic and molecular scales to the microscale, occurring during adhesion, function, wear, and thin-film lubrication at sliding surfaces.

The reason is that like nanoscience is neither truly to a single discipline nor well represented by steady state processes. However, the viscosity of the lubricating film is recognized as one of the most influential parameters for the film thickness and lubrication regime, so that it is reasonable to expect a beneficial effect on its tribological performance. Another important consequence of surface charge due to the repulsion and/or attraction between the surfaces and debris is the effect on the mechanical properties of the newly formed electro-tribochemical layers. In conclusion tribology like nanoscience involves all the complexities of nano-constrained materials that are experienced over a wide range of scales during a shear occurrence.

Tribology plays therefore a very important role in improving the design and making successful biomaterials for cosmetic and medical use. At this purpose, biomaterials used to date are metal ceramics with polymers, biopolymers and related composites.

Hyaline cartilage is a smooth, white tissue that covers the surface of all moving joints in the human body, playing an important role in determining the friction coefficient in different situations. The most abundant substance in cartilage is water, which makes up 70 to 80% of the weight. The remained material includes type II collagen, which forms the fibrous network, and the proteoglycans aggregate, a large complex comprising hyaluronan. The mechanical properties of cartilage are attributed to the highly hydrated aggregate trapped in a matrix of collagen, makes up approximately 50-75% of the dry weight of articular cartilage. Thus, articular cartilage coefficient plays a role in determining the friction coefficient. Therefore, in order to compare the friction coefficient in different experiments, it must be considered not only the changes in the lubricant but also changes in the bulk cartilage or articular surface. Additionally, a change in the friction coefficient of this tissue indicates some changes in the tribological system, which may be the lubricant, substrate, environment and/or the tribological conditions.

On one hand, the articular surface seems to have special properties that, enhancing the cartilage lubrication, protects itself against wear; on the other hand, a number of other requirements may be part of the articular surface in order to fit its functions, such as the ability to allow nutrients to permeate, to show resistance to non-specific protein adsorption, and integration with the opposing cartilage surface.

The structure, surface, friction and wear of articular cartilage, together with lubricant studies and theories on the activities of the fluid films during the swing phase of walking, are all reported and discussed on the **Chapter 1:** *Tribology of Natural Articular Joints*.

Chapter 2, *Sticky and Slippery: Interfacial Forces of Mucin and Mucus Gels*, deals with natural lubricating mechanisms as found in mucous membranes. Mucosa plays a protective role by secreting slimy and adherent mucus layers, represented by hydrogel networks formed from macromolecules called *mucin*. Mucin, known as lubricant for biological systems, is a glycoprotein, which, accounting for 70-80% of carbohydrate chains, is responsible of the mucus-gel's hygroscopic nature.

In addition, mucin/mucus possess other biological functions, such as bioadhesion, cell signal transduction, diagnostic marker in cancer, bacterial inoculation, immune response, inflammation, and tumour genesis.

The chapter reports and discusses the recent studies on the characterization and understanding of interfacial forces arising and involving mucins/mucus gels. These studies, in fact, have been performed in the contest of researches that include mucoadhesion for drug delivery, understanding the lubricating properties of saliva in food science and ontology, masticatory food consumption in food science; smooth gliding of endoscopy in biomedical science, and fundamental understanding of mucin lubricating behaviour in biotribology.

At this purpose, the chapter is composed of two main parts, covering molecular mucins and mucus gels/mucosa. The molecular mucins offer an opportunity to understand the fundamental force-interaction mechanisms at interfaces, while mucus gels offer an opportunity to understand in systems the interacting forces of physiological relevance. However, unlike other biomolecules that are known to be responsible for the lubrication of biological systems, mucin/mucus gels have both adhesive and slippery characteristics.

Lubrication is also an important factor in the oral processing of food. However, it is difficult to interpret the tribological response of food products due to their innate complexity in terms of rheology and microstructure, also because they contain multiple phases and components of emulsions that are interfacially active.

Aqueous Lubrication and Food Emulsions are the topics focused on **Chapter 3**. Emulsions are an important class of aqueous-based lubricants as they can be designed to deliver essentially the same lubricating properties as oils do, under low-temperature situations. However, although there is some general understanding and know how on food-emulsion lubrication, their predictive properties and surface characteristics are still in development.

Foods are also highly complex in terms of microstructure, rheology and composition so that more research is still needed to both characterize and understand the lubricative properties of complex food systems under well-defined conditions and biosubstrates. Moreover, the influence of saliva on food-emulsion lubrication has to be better understood. In any way, the utilization of modern tribometers could provide fundamental insights into the mechanisms by which the friction coefficient is defined in a soft-tribological contact for a complex food or emulsion system, particularly when the system is well defined in terms of surface toughness and surface chemistry.

Lubrication and tribological issues are also involved in many cosmetic products, in which water plays not only an important role to deliver a particular activity or properties, but has to be considered also an active ingredient, improving, for example, skin hydration or hair feel. Thus, while creams are expected to improve texture and feel of skin, hair-styling lacquers improve adhesion between hair fibers to set a specific shape while nail varnishes decrease wear in nails. This is why lubrication and in general tribological issues are involved in many cosmetic applications. Therefore when dealing with biological surfaces, such as skin and hair, it is important to understand the importance of the substrate that cannot be underestimated.

Water, in fact, acts like a plasticizer on both skin and hair. Human hair is a nano composite biological fiber which, by the fiber-to-fiber interactions of its cuticle, plays an important role in fiber-assembly behaviour. The inter fiber forces play a significant role in hair combing and manageability, and therefore in the overall appearance of the whole head. Thus, friction coefficient tends to rise when hair is wetted or ambient humidity is high, as well as excess sebum can stick together several hairs to form little swatches, which characterize greasy hair.

Under wet conditions, the value of friction coefficient is nearly multiplied by 3, while with the addition of a *cationic surfactant* the coefficient drops drastically to the level of dry hair. This is why cationic surfactants and cationic polyelectrolytes are widely used in cosmetic treatments, to affect the maintenance and grooming processes. For these reasons, the nanoscale characterization of the cellular structure, and the tribological properties of hair are essential to evaluate and develop more effective cosmetic products and to advance the understanding of biological and cosmetic science. Hairstyle and manageability depend, in fact, on numerous parameters such as the geometry of the fibers, the topography of the hair coverage, the fiber-to-fiber interactions and, in other words, to a great extent on the surface properties.

In any way, many people who use hair/skin care products regularly might think that the tribology of hair and skin/mucous surface is more important than the lubrication of moving metal surfaces! These the topics focused on **Chapter 4**, *Aqueous Lubrication in Cosmetics*, which reports a general view of the hair surface properties, describing the current understanding of the lubrication mechanisms of the common ingredients used, evaluating also the effects on friction properties of specific conditioning ingredients.

Chapter 5, *Hydrogel a Friction and Lubrication*, covers the current status and principles governing the gels' aqueous lubrication. Sliding friction and frictional behaviour of polymer gels is one of the most important practical subjects in physics. It depends on the chemical structure, property and geometry of the gels, the surface properties of sliding counter surfaces with their measurement conditions.

A gel has many features in common with other soft cross-linked polymers in terms of its cross-linked polymer structure and viscoelastic properties. In contrast to a rubber, a gel contains a large amount of low molecular weight component and water. The water content in biological gels such as cartilage is, in fact, ~70-80wt% while, in synthetic gels, the water content can be as high as 99.9%.

Due to the large presence of water, strongly solvated to the polymer network, the internal friction of a gel is much less than that of a cross-linked polymer melt or rubbed. Moreover, the surface structure and, therefore, friction of a gel strongly depends on the substrate on which the gel is synthesized. Thus, when gels are synthesized between a pair of glass substrates they have a mirror-like smooth surface.

On the contrary, when synthesized between two different plates, one hydrophobic and the other hydrophilic, heterogeneous gelation occurs. In any way, the friction events in biological systems mostly occur between soft and wet tissues, mediated by viscoelastic polymeric gel fluids such as synovial fluid or mucus. Mucus, for example, adheres to many epithelial surfaces, where it serves as a diffusion barrier against contact with noxious substances and as lubricant to minimize shear stresses. Mucus is, therefore, an important component of lubricating saliva, as well as articular cartilage is a natural fiber-reinforced hydrogel that, contributing to the joint functions of the tissue, involves ultra-low friction, distribution of loads, and adsorption of impact energy.

For these reasons, it is important develop specific gels as therapeutic agents and substitutes of synovial fluid for the damaged cartilage, a tissue extremely difficult to regenerate. Thus, design and production of hydrogels with a low surface friction and high mechanical strength are crucially important in the biomedical applications such as contact lens, catheter, artificial articular cartilage, and artificial oesophagus.

Nature's effective lubrication mechanisms are mostly based on sugar-decorated polymers-glycoproteins- that utilize the facility with which they can be hydrated in order to hold a significant amount of water at the surface to be lubricated.

Charge, hydrophobicity, and hydrogen bonding all play significant roles in the behaviour of natural lubricant molecules. Brush coating, for example, is a way to control the friction in skin and teeth product interactions thus, in attempting to mimic the lubricating function of the natural molecules, a class of polymer brushes has been produced. They appear to function by means of their ability to separate hard, sliding counter surfaces while presenting a solvent-rich, low-shear-strength interbrush layer, providing fluid-film lubrication without the need for hydrodynamic forces.

Brush coating represent, in fact, polymer layers developed on a supporting surface by tethering long polymer chains with a sufficiently high grafting density. Because of the main challenge, facing polymer brushes, appear to be resistance to wear, inter penetration of polymer brushes, response to applied load, effect of pressure on the lubricity of surface-grafted polymers, and macro-micro-nano-tribological measurements on different charged systems, all phenomena reported and discussed on **Chapter 6**, *Aqueous Lubrication with Polymer Brushes*.

Moreover, the efforts to apply aqueous lubrication are focused on **Chapter 7**, *Water-like Lubrication of Hard Contacts by Polyhydric Alcohols*.

Water has a low viscosity so that it isn't a good lubricant for hard steel contact. However, liquid and vapour water is known to have some ability to lubricate diamond and amorphous carbon materials in the boundary regime at high contact pressure and slow speeds. It is also interesting to notice that ceramic materials are easily lubricated by water and that tribochemical reactions lead to smooth surfaces and subsequent water hydrodynamic lubrication.

This chapter reports the tribological results obtained with glycerol and other polyol molecules on steel and diamond-like coatings. All these molecules, small and with different shapes such as spherical, crab shape or spider shape, seem to be progressively dissociated under the effect of pressure shearing and liberating water. Thus, the formation of water molecules may be an important mechanism for friction reduction by polyhydric alcohols and glycerol. They, however, do not contain aliphatic chains, distinguishing them from most of the amphiphilic molecules used as traditional lubricant additives.

Chapter 8 reports how the electrochemical parameters ,such as surface charges and the associated pH, zeta-potential or solubility, affect the properties of the surface layer, the physicochemical and load-carrying properties of the lubricating film, together with the tribochemical reactions and the tribolayer failure modes of water-lubricating contacts. It is, however, suggested that a more complete set of tribo-electro-chemical effects should be considered and controlled in the aqueous lubricating film of ceramic systems, and that more refined models should be developed to enable a more accurate prediction of the contact conditions in future aqueous, boundary-lubricated-ceramic tribosystems.

At this purpose several groups of parameters that directly influence the properties of the lubricating film and the severity of the contact conditions have been suggested.

In this interesting book, where the mechanisms of aqueous lubrication in nature are reported and discussed for trying to understand and imitate them for practical purposes, various cellular structures of human hair and body have been described. Friction and lubrication of skin, for example, play a major role in product development for cosmetics, textiles, artificial turf, medical devices, floor cleaning, etc. Characterizing the friction and wear properties of hair and skin is, in fact, essential to develop more effective shampoos and conditioners that leave hair untangled and skin hydrated looking natural while feeling smooth.

Thus, nanomechanical properties such as hardness, elastic modulus, tensile deformation, fatigue, and scratch resistance have been discussed, as well as nanotribological properties such as roughness, friction, adhesion and wear have been presented. All these tribological properties are essential to evaluate and develop cosmetic and biological products, and to advance the understanding of cosmetic and biological science. During all the pages of the book the remarkable properties of water as the main and important lubricant in nature is continually discussed and explained in simply way so that its lecture is to be considered useful for all the scientists, such as dermatologists, biologists, gynaecologists, paediatricians, marketing managers, and also students of both the chemical and medical community who wish to better understand the biological and biomimetic role the water has for the human body and for many human activities involved in producing smart textiles, innovative cosmetics, medical devices and other innovative products where skin represents one of the interacting surfaces in relative motion.

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Bio-Inspired Nanomaterials and Applications

by Donglu Shi

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Proliferation and release into the environment of nanomaterials arise important ecological and human health concerns, because of nanosurface properties affecting the biological systems by the use of the so called *green* chemistry. Its main feature is the *atom* economy capable to take full advantage of each raw material in the molecular process of acquiring and transforming new material at *zero emissions, without* producing pollution.
Nanoparticles are a part of Nanomaterials where at least one characteristic dimension is less than 100 nanometers (nm). It is to remember that 1nm is a billionth of meter and at this scale, the nanomaterials show new and interesting properties not seen in their conventional bulk counterparts. For these reasons, the increased necessities for a better knowledge of materials science and engineering as a field concerning with the studies of the structure, properties and processing of all bulk solids.
Nanomaterials, in fact, arise concerning the interfaces between nanoparticles and cells, where nano surface properties affect the biological behaviours such as endocytosis and toxicity, and nano size effect on transport kinetics in a biological system. Thus the necessity of new research studies involving chemists, biologists, medical doctors and material scientists in conventional and nanosized materials to develop new nano carrier systems of high versatility with multiple functionalities of cell targeting, drug storage, optical imaging, and effective means of treatment such as magnetic and photo thermal hyperthermia, photodynamic therapy, and drug release via innovative smart mechanisms. At this purpose, a new medical terminology *theranosics* has been used. It implies simultaneous therapy and diagnosis. This book, organized with 10 chapters, not only describes the most fundamental topics of Nanoscience but also deals with critical clinical issues of translational medicine.
Up-Conversion Nanoparticles (UCNPs) for *Early Cancer a Diagnosis* is the topic reported and discussed on **Chapter 1**. Compared with traditional down-conversion fluorescence imaging, the NIR light excited up-conversion luminescence (UCL) imaging, relying on UCNPs, exhibits, in fact, improved tissue penetration depth, higher photochemical stability and is free of auto-fluorescence background. Thus, the up-conversion process of UCNPs may be utilized to photosensitive therapeutic agents for applications in cancer treatment, as well as UCL shows promise in biomedical imaging with high sensitivities. For this reasons much attention has been paid to the development of UCNPs-based composite nanostructures with multiple functions by coating or integrating them with other inorganic nanoscale components. However, UCNLs may be coupled with many functional nanomaterials, also if silica coating is one of the most popular techniques for the fabrication of nanocompo-

sites, not only to facilitate surface coating with biocompatible polymers and bio conjugation, but also to render the obtained nanocomposites more functional. In any way better design of novel multifunctional agents, based on UCNPs for simultaneous medical diagnosis and combined cancer therapies, are still needed in the future to realize real-time monitoring of treatment progress as well as to achieve synergistic therapeutic effects.

An ideal drug delivery system fulfils the objective of maximizing the therapeutic effect while minimizing toxicity. With the progress in time and advances in science and technology dosage forms have evolved from simple mixtures to sophisticated systems known as innovative drug deliver systems.

Polymeric nanoparticles (NPs) have recently emerged as novel candidates for targeted and controlled drug delivery. Ideal NPs, possessing high drug loading levels, are able to deliver drugs to specific pathological sites within the body, and the capacity to rapidly release their drug load at the site of action. Since the high redox potential of the intra cellular compartments limits the efficient therapy, it is possible to incorporate redox-responsive signals into the polymer architecture of NPs to overcome this extracellular barrier.

This modification can lead to a more controlled and/or triggered intra cellular release of therapeutic agents. Thus stimuli responsive polymeric NPs, releasing drugs in response to intra cellular tumour signals, have been recently used as a promising platform to overcome the aforementioned barriers.

Recent advances in polymer chemistry have facilitated, in fact, the precise control of polymer architecture and composition in the synthesis of polymeric NPs. It has been evidenced that the core material, the surface polymers, and the encapsulated payload agents are the three main design components necessary for these polymeric nanoparticles. Moreover, NPs can also be conjugated or grafted with affinity ligands to increase the selectivity for diagnosis and treatment of tumour cells. However, while a vast variety of redox-sensitive polymeric NPs have been reported, only a small number of systems have been tested in preclinical, *in vivo* models.

Redox-Sensitive Polymeric Nanoparticles for Intracellular Drug Delivery has been focused on **Chapter 2** where the advances in the world of these particular nanoparticles have been highlighted.

Transfer of genetic material in nanocarriers may be an approach for the treatment of genetic disorders, caused by lack of enzymatic factors for missing of defective genes. Thus gene therapy has emerged as a novel method to treat a broad spectrum of human diseases caused by gene defects. At this purpose, gene delivery vectors play an important role in escorting exogenous genes into targeted somatic cells. Polyethylenimine (PEI) is one of the most efficient polymeric gene delivery vector due to its strong gene binding ability and unique buffering capacity for endosomal escape. For this reason much effort has been made in the development of biocompatible PEIs and derivatives as safe and potent gene delivery vectors. This topic has been widely discussed on **Chapter 3**: *Design of Biocompatible PEIs as Artificial Gene Delivery Vectors*.

Human body temperature is normally maintained at 37°C so that, when gets ill, it defends itself by increasing the temperature to fight disease-causing agents such as bacteria and viruses. Based on the phenomenon of natural fever, thermal therapy, i.e. hyperthermia, has been developed and applied in clinical practice, so that the use of laser with infrared or near-infrared (NIR) for the treatment of cancer is termed Photothermal Therapy (PTT).

Cancer cells, in fact, can be destroyed at 42.5° C, whereas normal cells can survive at 44°C. A possible mechanism for photo thermal conversion is associated with the localized surface plasmon resonance (LSPR) response of the metal containing nanoparticles to NIR laser resonance. The use of

magnetic iron oxide nanoparticles as heating mediators for cancer therapy is therefore attractive for clinical applications for both doctors and patients.
The principle of magnetic hyperthermia, induced by an alternating magnetic field(AMF) of nanoparticles, can generate in fact, heat by loss of hysteresis, easily controlled by changing the AMF parameters or the amount of nanoparticles in the tumours.
On **Chapter 4**, *Magnetic Fe3O4 Nanoparticles fir Cancer Photothermal Therapy*, the current knowledge on PTT of the Fe3O4 nanoparticles *in vitro* and *in vivo* induced by NIR laser irradiation has been discussed, as well as the magnetic resonance imaging guiding cancer PTT has been reported with its limitations.
Environmental pollution has become a global issue so that novel sensors for environmental safety received special attention worldwide. Heavy metals, toxic gases, organophosphorous compounds and wastewater are, in fact, the major environment pollutants produced from industrial and people activity that damages our ecosystem. Thus, the necessity to develop and produce advanced selective sensors with high sensitivity, as well as simple low-cost detective methods to monitor these toxic substances for protecting our health. At this purpose, sensors are comprised of two functional components: the receptor and the transducer.
The first is designed to identify the toxic ingredient, while the second has to give the response signals in chemical or physical ways, such as electrochemical, optical, thermal or piezoelectric, depending on the sensor devices used. Because of the unique properties of nanostructured materials, it is possible to develop an innovative sensing and monitoring technology. Therefore, the design and fabrication of nanomaterial-based chemosensors has generated great interest into the scientific communities from biological and environmental sciences to engineering.
Chapter 5, *Nanomaterial-Based Sensors for Environmental Monitoring*, is focused on the recent progress in nanomaterial-based sensors for environmental pollution monitoring, where the use of Au and Ag functionalized nanoparticles became the dominant candidates for metal-based sensors.
Functional group containing S, O and N elements, in fact, play important roles in ligands, such as thiols, carboxyls, aminos, and hydroxyls. Among these, thiol is one of the main functional group for Au nanoparticle decoration, due to the strong Au-S bond. However, colorimetric sensors based on Ag nanoparticles have also been well developed. On the other hand, graphene-based gas sensors have been constructed for the detention of a range of gases including H_2O, NH_3, CO, NO_2, and NO, as well as metal oxide and hollow oxide structures have also been the main focus enhancing the gas sensing performance.
The ability of block copolymers to form nanoparticles and nanostructures in aqueous solutions makes them particularly useful for biomedical applications, such as therapeutics delivery, tissue engineering and medical imaging. Therefore, the critical question appears to develop multi-surface nanostructures capable to utilize in the best way, the intrinsic properties of nanomaterials. Thus nanocarriers, for example, must have different functionalities, such as the capability to conjugate biological moieties, to possess an imaging capability and, naturally, to be nontoxic for clinical applications.
At this purpose, cell studies have proven that the Janus nanocomposites successfully combine targeting and controlled drug release. This structure, in fact, offers more possibilities for assembling multifunctional carriers involving the change in affinity between monomers and polymers, among polymers or between the generated nanoparticles and the aqueous phase.

One common approach is growing polymers through emulsion polymerization on the presynthesized polymer seeds of another kind. On the other hand, regarding the copolymer blocks ABC, the middle block B can connect with the two ends A and C to form a two-module Janus nanocomposite. However, methods employed include chemical functionalization, electrostatic attraction and metal evaporation.

Ligands are also used to bridge two distinct parts to form a Janus nanostructure that has shown to be a versatile platform for biomedical applications. This the topic reported on **chapter 6**, *Janus Nanostructures and Their Bio-Medical Applications*.

Being the analysis a mean to uncover the ultimate secrets of life in details, Single Molecule Detection (SMD) method has aroused significant interests of many disciplines. The combination of nanomaterials which possess remarkable optical, electrical and mechanical properties with single molecule techniques generated a new branch of biomedical detections. This innovative technique, in fact, can provide information on structures, functions, interactions of various molecules at single-molecule level, which can be difficult or impossible to obtain using conventional ensemble averaging techniques.

Differently from conventional techniques, SMD may provide information such as conformational states and dynamics, and the relationship between the conformational states and functions of a single molecule. Moreover, it can be used to track the distributions and time trajectories of the objective molecules which would be suited to study the intermediates and follow time-dependent pathways of biochemical reactions, generally difficult or impossible to synchronize at the ensemble level.

Chapter 7, *Nanomaterial-Involved Optical Imaging/Spectroscopy Methods for Single-Molecule Detentions in Biomedicine*, reports the recent progress of nanomaterials involving optical imaging/spectroscopy techniques for SMD, including the related preparing methods of nanomaterial probes, the instruments and analysis methods for SMD detections, and the current application assays of nanomaterial-inspired SMD.

Owing to the advanced microscope apparatus which has broken the light diffraction limit, quantum dots (QDs) have found their stride in single molecule tracking, also if new nanoparticles with improved fluorescence properties and lower bio toxicity are required. The brilliant spectral properties and photo stability of semiconductor nanocrystals, known as QDs, in fact, enlighten scientists to replace traditional organic dye molecules with these inorganic nanomaterials, introducing also various functional nanomaterials to other SMD methods.

Chapter 8, *Surface Functionalized Carbon Nanotubes for Biomedical Applications*, reports an update on carbon nanotubes (CNTs) technology, representing today one of the most widely used class of nanomaterials. They, in fact, have many advantages including unique intrinsic physical and chemical properties together with the ability to be decorated with various functional materials and biological species. Moreover, CNTs possess the ability to penetrate into the cells, which justifies their worth in being intensively exploited for potential nanobiomedical applications. Thus, for example, the design and fabrication of specific multifunctional nanohybrids can improve the early detection and diagnosis of some diseases, having the possibility to be used as the matrix of the nanohybrid synthesized.

These special compounds on one hand have a large surface area to load nanoparticles in one-dimensional direction, preventing the aggregation of nanoparticles in solution. On the other hand they can readily penetrate into cells either by endocytosis or non-endocytosis mechanism, increasing their

sensitivity and efficiency for detection as diagnostic agents.
In any way, an ideal nanotube can be considered as a hexagonal network of carbon atoms that has been rolled up to make a seamless hollow cylinder. These hollow cylinders can be tens of micrometers long, but with diameters as small as 0.7 nm, and with each end of the long cylinder "capped with 6 pentagons". Single-walled nanotubes, having a cylindrical shell with only one atom in thickness, can be considered as fundamental structural units which form the building blocks of the molecule.
Despite safety concerns over CNTs, which have shown to induce oxidative stress and pulmonary inflammation, many studies have reported their successful use in many biological applications. At this purpose, future interdisciplinary research needs to be devoted to the development of intelligent and integrated multifunctional CNTs based nanosystems, capable to perform controlled actions such as switching on/off the drug release, signalling to the sensing device, recognizing a specific cell, and monitoring the concentration level in a biological and living system.
Novel tools for evaluating gene function *in vivo* such as ribozymes and RNA interference (RNAi) are emerging as the most highly effective strategies.
Intracellular siRNA Delivery by Multifunctional Nanoparticles is the topic focused and discussed on **Chapter 9**.
Numerous studies indicate, in fact, that RNAi could be efficient ways to investigate the gene work mechanisms and screen novel drug targets for therapeutics. At this purpose, nanoparticles exhibite much promise due to their multifunctional properties and easily targeted modifications for Intracellular siRNA delivery both *in vitro* and *in vivo*. Moreover, chemical modification in addition to conjugation strategies with biodegradable nanosystems will play a pivotal role in the transition of siRNA from a laboratory knock-down tool into a valuable platform for the development of therapeutics towards clinical applications. However, RNAi efficiency is largely dependent on the development of many delivery vehicles that can deliver the siRNAs to target cells.
Cationic liposomes and polymers, for example, represent one of the few multifunctional nanoparticles that can meet these requirements of intracellular nucleic acid delivery. These agents, in fact, are composed of positively charged lipid bilayers that can be complexed to negatively charged siRNA duplexes. However, still lipid-based systems have important drawbacks, including the lack of specific targeting and variation arising during fabrication. Cationic polymers siRNA delivery vectors can be divided into synthetic and natural vectors. The former include Polyethyleneimine (PEI), poly (lactic-co-Glycolic) acid (PLGA), poly (amido amine) dendrimers (PAMAM), etc. The latter include chitosan and its derivatives, cyclodextrin inclusion compounds, etc. In any way, cationic polymers are more stable, easier to change molecular weight and shape and have the possibility to be modified for optimizing the systems and their sensitive detection by the use, for example, of quantum dots, gold or magnetic nanoparticles.
Nanostructural semiconductors exhibit properties that make them superior to their bulky counterparts, including electrical, magnetic, optical, thermoelectric and chemical traits. These properties can be attributed to the quantum effects of electronic conduction, high density of electronic states, diameter-dependent band gap, enhanced surface scattering of electrons and photons, increased excitation binding energy, high surface to volume ratio, and large aspect ratio. Therefore, nanostructural semiconductors have potential applications in electronic, photonic, biological, energy, and magnetic devices, possessing many advantages over conventional materials because of their excellent sensitivity.

The application of semiconducting nanowire transistors in chemical and biological sensors, as well as their synthesis and surface functionalization are review on **Chapter 10**, which represents the end of the book.

The innovative properties of nanomaterials have open new possibilities of collaboration between the biomedical and physical science to obtain more functional information on the activity of human organs, tissues and cells as well as to discover new drugs and therapies. The effectiveness of a drug depends, in fact, to the capacity of delivering it at the right concentration, reaching the right site in the body for a sufficient and correct period of time. Therefore, the active compound should reach its site of action intact to exert its biological activity during its transport also and has not to be inactivated by metabolism nor becoming toxic. The effect of a drug increases, in fact, with increasing of its concentration at the site of action, until a concentration is reached where the effect starts to become toxic.

Thus, for example, a great challenge in cancer diagnosis is to locally biomark cancer cells for maximum therapeutic benefit. And tumour cell targeting is until now a complex issue in medical diagnosis and therapy by the use of nanotechnology, also if new delivery mechanisms have to be identified from the perspectives of materials science and biomedicine.

This book, written in a very clear language, may be of interest of both the physicochemical and medical community as well as may be of great help for students in chemistry and medicine who like to have an update on the more modern medical nanodevices used for diagnosis and therapy.

P. Morganti
Editor-in-Chief

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Contents

In vivo Studies of Chitosan Fiber Resorption

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Key words: *Chitosan fibers; Resorption; Endomysium; Perimysium;*

Summary

Scanning electron microscopy and histologic analysis were used in the comparative *in vivo* study of resorption of chitosan fibers implanted into endomysium and perimysium of a rat *latissimus dorsi* muscle. It was demonstrated that the mechanism and rate of chitosan fiber resorption depend on the position of fibers in muscular tissue. After implantation of chitosan fibers into endomysium (when chitosan was in direct contact with muscle fibers), the formation of cross-sectional cracks, fragmentation of implanted fibers and its partial resorption were observed in 14 days. Complete chitosan resorption in endomysium occurred after 30 days only. Chitosan fibers implanted into perimysium preserved integrity for 7 days, and fibrous tissue was formed around implants. After 45 days of exposure, no signs of chitosan fiber destruction were registered in this case.

Riassunto

Le analisi con il microscopio a scansione sono state utilizzate assieme ad indagini istologiche per verificare il riassorbimento *in vivo* di fibre di chitosano a livello di endomisio e perimisio del muscolo del dorso del ratto. È stato dimostrato che il grado di assorbimento ed il relativo meccanismo d'azione delle fibre di chitosano dipendono dalla posizione specifica delle fibre nel tessuto muscolare.

Dopo 4 giorni dall'applicazione del chitosano nell'endomisio (quando cioè il chitosano era in diretto contatto con le fibre muscolari), sono state osservate fessurazioni e frammentazioni a livello delle fibre impiantate a cui ha fatto seguito un loro parziale assorbimento.

Le fibre di chitosano impiantate nel perimisio hanno conservato una loro integrità per 7 giorni con formazione di tessuto fibroso che le ricopriva.

Dopo 45 giorni il chitosano veniva completamente riassorbito.

INTRODUCTION

The development of materials capable of substituting for lost organ or its parts is the main goal of tissue engineering and transplantology (1-3). The chitosan (polysaccharide obtained from natural polymer chitin) is of great interest for development of scaffold materials. It is known that chitosan is biocompatible and decomposes in biologically active media (4,5).

A literature analysis demonstrates that the resorption rate of chitosan materials depends on its deacetylation degree (6,7), molecular mass (8), porosity (9), the presence of nanoparticles or other polymers in film and bulk samples (10). The majority of data on chitosan resorption were obtained during *in vitro* experiments, in lysozyme-containing media or *in vivo* after subcutaneous implantation of the studied chitosan material.

As a rule, the used objects were small films or plates. There are virtually no publications concerning *in vivo* studies of the mechanism of chitosan fiber resorption, although these fibers may be used as one-dimensional matrices in tissue engineering (e.g., prototypes for nervous tissue, muscles and ligaments). Therefore, information about kinetics of *in vivo* resorption of chitosan fibers is of special interest.

The aim of the present work is comparison between the mechanism of resorption of chitosan fibers implanted into endomysium (when maximum contact between chitosan and muscular tissue is observed) and into perimysium (in close proximity to muscular tissue, but without direct contact to a muscle).

MATERIALS AND METHODS

Chitosan (Fluka Chemie, BioChemika line) with a molecular mass of 225 kDa, deacetylation degree of 80% and ash content of 0.5% was used.

The fibers prepared from this chitosan by the method described elsewhere (11) were used in the work too. Their tensile strength, tensile modulus, deformation at break of the chitosan fibers were 220 ± 10 MPa, 900 ± 100 MPa and 8 ± 1 % correspondingly.

The experiments were performed using 20 female white Wistar rats in accordance with good laboratory practice, the principles of the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (Strasbourg, 1986) and the World Medical Association's Declaration of Helsinki (1996) concerning humane treatment of laboratory animals.

The weight of test animals was 180-200 g, the age was 6 months.

In the studies of the *in vivo* resorption, a bundle of chitosan fibers 20 mm in length containing 10 monofilaments with a diameter of 80 μm was sterilized in 70 wt.% ethanol for 1 h.

The operated animals received inhalational anesthesia (3% isoflurane). The fibers were placed into a *latissimus dorsi* muscle, and then the wound was stitched up layer wise with atraumatic suture needles using a Prolen 4-0 thread.

Chitosan fibers were implanted into the latissimus dorsi muscle in the endomysium between individual muscle fibers and perimysium between bundles of muscle fibers.

The position of the fibers during implantation is shown in Figures 1 a, b. Implantation of chitosan fibers into endomysium was performed using 10 animals. Muscle fibers were spaced about 2 mm apart with tweezers, and no more than two chitosan fibers were introduced into the resulting cavity (20-25 mm in length), see Figure 1 a.

In the experiments with other group of animals (10 individuals), a bundle of chitosan fibers was applied over a bundle of rat *latissimus dorsi* muscle, i.e., into perimysium (Fig. 1b).

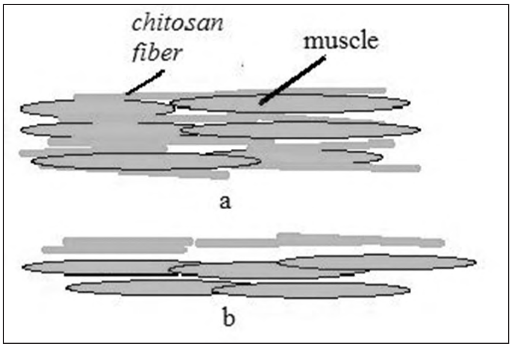

Fig. 1 *Implantation of chitosan fibers into endomysium (a) and perimysium (b).*

After suturing, animals were kept in individual cages and had free access to water and the standard fodder. All animals were active after surgery; no negative influence of implantation was revealed. The implanted fibers were extracted from animals at 7 days intervals.

Histologic analysis

Morphological studies were performed in 1 and 6 weeks after the surgery using muscle tissue with chitosan fibers and adjacent connective tissue. The samples were fixed in 10% neutral phosphate-buffered formalin (pH=7.4) for 24 hrs, dehydrated in a series of ethanol solutions of increasing concentrations and embedded into paraffin blocks according to the standard histological technique. Transverse sections of muscle and chitosan fibers 5 μm thick were prepared. The sections were colored with hematoxylin and eosin (Bio-Optica, Italy) and according to the Mallory method (Bio-Optica, Italy).

Microscopy analysis was performed with the use of a Leica DM750 light microscope (Germany) at x100 and x400 magnifications. Photographic survey was performed with a Leica DM750 microscope and an ICC50 camera (Leica, Germany).

Fiber samples before and after implantations were fixed on object tables and spattered by gold. The samples were studied using a Supra 55VP scanning electron microscope (Carl Zeiss, Germany) in the secondary electron mode.

RESULT

Resorption of chitosan fibers in endomysium

Figure 2 presents a micrograph of chitosan fiber surface (Fig. 2 a) and its cross-section made in liquid nitrogen (Fig. 2 b). It can be seen that the surface of the fiber is smooth and contains no defects. The cross-section of a fiber is also dense; no large pores or cracks were detected. After implantation of these fibers in a rat muscle (endomysium), in 7-14 days cross-sectional cracks are formed on the surface. The width of these cracks increases with exposure time. Figures 2 c, d gives micrographs of fibers exposed in endomysium for 14 days. It may be presumed that these cross-sectional cracks result from mechanical dynamic load which affected chitosan fibers placed in direct contact with muscles. Throughout the experiment, all animals were active; their muscles were repeatedly stretched and constricted in different directions, thus leading to destruction of chitosan fibers contacting with muscle tissue.

The studies of implantation area have demonstrated that after 14 days the fragments of fibers 3-5 mm long are formed, and these fragments are partially resorbed. It should be noted that resorption process virtually does not change fiber diameter and their biodegradation starts from the ends.

This fact is evidenced by the results of the studies of fiber cross-section after exposure in animal organism (endomysium). Figures 2 e and 2 f demonstrate the presence of a large amount of pores in the interfibrillar space (which were not observed in the initial fibers). It can be assumed that the active biological medium containing enzymes and macrophages penetrates into interfibrillar spaces of fragmentary fibers at the expense of capillary forces and leads to intensive chitosan degradation.

Observations of the implantation zone demonstrated that after 21 days only low amount of fiber fragments is present.

The main portion of chitosan fiber degrades, and degradation products are removed from the implantation zone during metabolic processes. In 30 days, neither fibers nor their fragments were observed in the implantation zone; all chitosan fibers were completely resorbed.

The resorption process is shown in Figure 3.

The important thing to note is that throughout the experiment (30 days) no connective tissue was formed around chitosan fibers or their fragments, and thus, encapsulation did not occur.

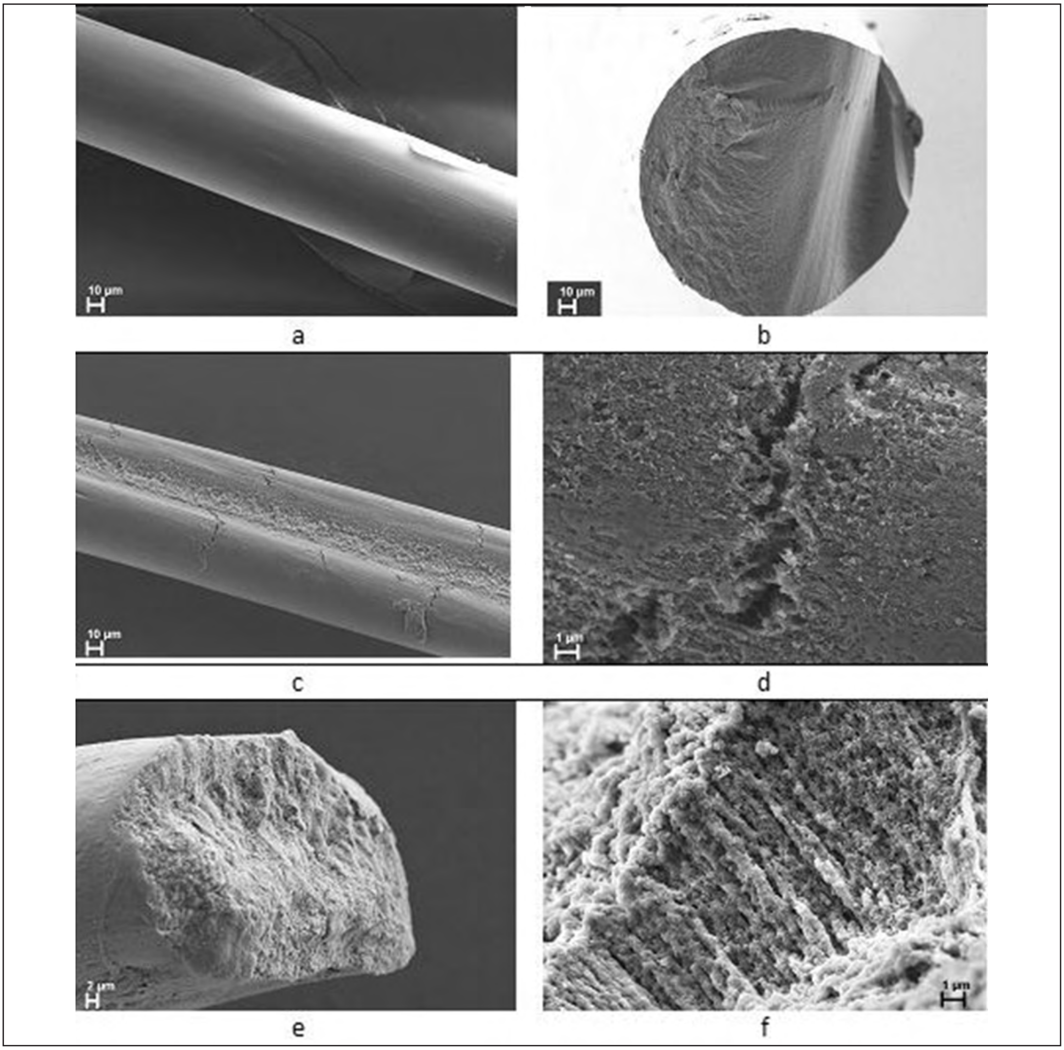

Fig. 2 *Micrographs of lateral surface (a) and cross-section (b) of the initial chitosan fibers and the fibers removed after exposure to rat endomysium for 14 (c, d) and 21 (e, f) days.*

Resorption of chitosan fibers in perimysium

Another picture was observed after implantation of the fibers into perimysium. The studies of the implantation zone showed that after 7 days the fibers remained intact. After prolonged exposure (6 weeks) no qualitative changes in the implanted fibers were observed, but fibrous tissue was formed around them, as evidenced by histological analysis of the chitosan fibers exposed to rat organism (Fig. 4).

It is clearly seen that fibrous capsules were formed around every chitosan fiber. Cell infiltrate of fibrous tissue includes individual multinucleated cells of foreign bodies and insignificant amount of macrophages, monocytes and lymphocytes, this indicating aseptic chronic inflammation.

Considerable differences in behavior of chitosan fibers implanted into muscle endomysium and perimysium may be explained by mechanical stresses appearing in rat latissimus dorsi muscles due to animal activity and affecting the fibers implanted into endomysium.

These multidirectional dynamic loads have an impact on the implanted chitosan fibers and facilitate their degradation.

The important factor influencing accelerated fiber resorption is an intensive metabolism in muscle tissue. Besides, it is expected that continuous shear stresses affecting the implanted fibers, their mutual friction and friction between chitosan and muscle bundles (due to muscle stretching and contracting) prevent the formation of connective tissue around chitosan fibers.

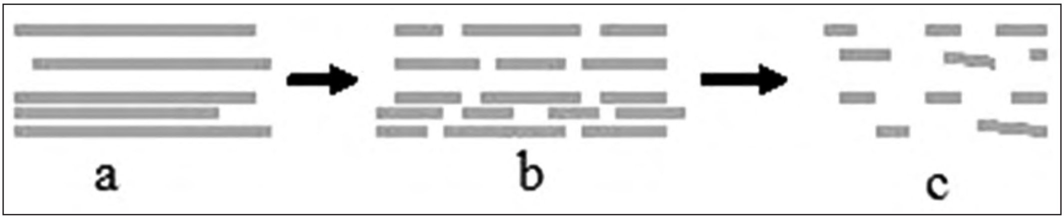

Fig. 3 *Resorption of chitosan fibers in rat latissimus dorsi muscle endomysium: a — the initial fibers; b, c — the fibers exposed to endomysium for 14 (b) and 21 (c) days.*

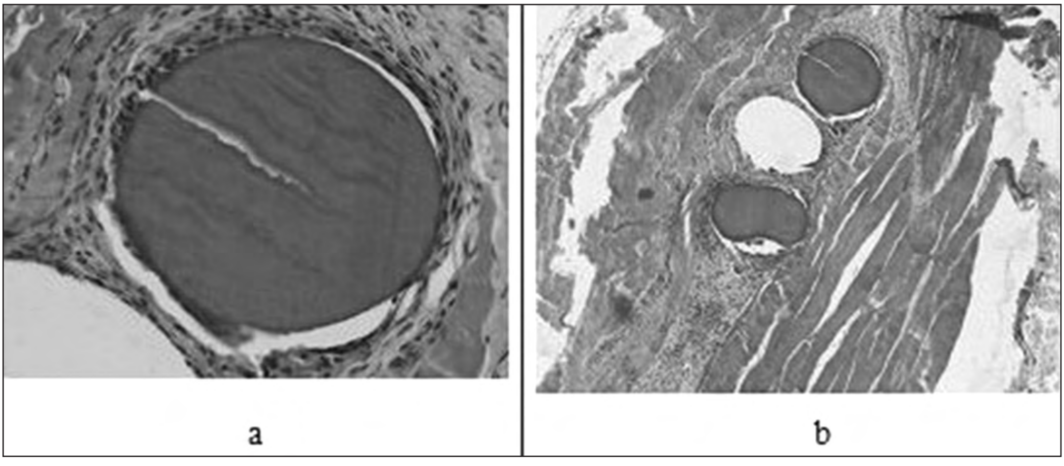

Fig. 4 *Cross-section of the chitosan fibers after 6 months implantation in perimysium; colored with hematoxylin and eosin; magnification a - x400 and b - x100. Around fibers revealed fibrous capsule.*

Considerable differences in behavior of chitosan fibers implanted into muscle endomysium and perimysium may be explained by mechanical stresses appearing in rat *latissimus dorsi* muscles due to animal activity and affecting the fibers implanted into endomysium.
These multidirectional dynamic loads have an impact on the implanted chitosan fibers and facilitate their degradation.
The important factor influencing accelerated fiber resorption is an intensive metabolism in muscle tissue. Besides, it is expected that continuous shear stresses affecting the implanted fibers, their mutual friction and friction between chitosan and muscle bundles (due to muscle stretching and contracting) prevent the formation of connective tissue around chitosan fibers.
Chitosan fibers implanted into perimysium were subjected to smaller mechanical loading, and metabolism in these areas is rather slow. Therefore, the implanted fibers were encapsulated in a fibrous capsule.
The resorption rate in this case is significantly lower.

CONCLUSION

The studies of resorption of chitosan fibers implanted into rat *latissimus dorsi* muscle demonstrated that the position of these fibers in muscle tissue has a strong influence on the resorption mechanism.
The fibers located in endomysium (in direct contact with muscle tissue) were subjected to multidirectional loading. This loading led to the formation of cross-sectional cracks and fragmentation which took place 14 days after the surgery.
Diffusion of active biological medium (containing enzymes and macrophages) into interfibrillar spaces of fiber fragments facilitated their complete resorption in 30 days.
Chitosan fibers implanted into perimysium (where mechanical stresses and metabolism rate are lower than those in muscle interfibrillar space) were encapsulated in 7 days after the implantation.
The resorption process was significantly slower as compared to the previous case.

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How to get what you ought to~ A New Insight on Anti-dandruff Evaluation

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Received: *April, 2015*

Key words: *Anti-dandruff; Anti-scaling scalp shampoo; Herbal actives;*

Summary

The anti-dandruff efficacy of the anti-scaling scalp shampoo* was evaluated in liaison with the way such products are used by the AD sufferers.
The findings of the study proves that the above shampoo was active even at higher dilution (1:500), which resisted different qualities of water and exerted quick killing effect on the target microbe.
Further, the level of activity of key AD agents in the shampoo such as Climbazole and ZPTO was well preserved in the shampoo formulation suggesting the non-interference of shampoo base in the AD activity.
This is the first study to the best of our knowledge to establish the AD activity of a shampoo in liaison with its usage at *in vitro* level with the scope of its likely real activity *in vivo*.

Riassunto

In questo studio è stata valutata l'attività antiforfora dello shampoo specifico secondo le modalità d'uso dei consumatori. I risultati dello studio evidenziano come tale shampoo rimanga sempre attivo anche ad alte diluizioni (1:500) non essendo influenzato dalla qualità dell'acqua.
Il livello dell'attività antiforfora di agenti quali il climbazolo e lo zinco piritione inseriti nella formulazione rimane invariato suggerendo che la base formulativa non influenza la loro efficacia. Questo è il primo studio di nostra conoscenza, che stabilisce *in vitro* l'attività antiforfora di uno shampoo nelle normali condizioni d'uso.

* *Trade name: Verdura anti-scaling scalp shampoo by Dr. JRK's Siddha Research and Pharmaceuticals Pvt., Ltd., Chennai.*

INTRODUCTION

The anti-dandruff (AD) efficacy of most of the wash off anti-dandruff preparations like shampoos is greatly influenced by the method of use and the quality of water (1). Hence, the usage instruction must be arrived carefully in order to preserve and achieve maximum effect from anti-dandruff shampoos.

The anti-dandruff shampoos are the most preferred agents for the treatment of dandruff (2). Considering the growing consumer need and the opportunity, many anti-dandruff products have come to market (3).

However, still an appreciable relief after use of such products is elusive (4). In general, the dandruff sufferers use 3-5 ml of the AD shampoo per wash. 3-5 ml of shampoo is directly placed in the vertex region of the scalp. Then, the shampoo is diluted directly in the scalp with approximately 500ml of water. Then, the hair is washed and rinsed (5).

The likely contact time of shampoo in the scalp and reaching every part of the scalp are quite poor because it is washed off immediately. This is considered to be one of the reasons why the desired benefit the dandruff sufferers are not achieving even after using many effective AD shampoos (6).

Evaluation of the anti-dandruff effect *in vitro* by determining minimum inhibitory concentration (MIC) is widely followed (7). Irrespective of the level of effectiveness of such shampoo preparations at *in vitro* level, still can fail to control dandruff due to the likely short contact period during usage. Therefore, the evaluation of the anti-dandruff effect of shampoos must be done keeping in view of the above limitation in order to achieve the logical extrapolation of the likely AD activity.

The present study report the anti-dandruff efficacy of the anti-scaling scalp shampoo established exactly in liaison with the way the shampoo is used by the end user.

Further, we also present a clear usage instruction to achieve maximum AD effect from the above product through our intense study. The findings of the study are discussed.

MATERIALS AND METHODS

Details of the shampoo

The anti-scaling scalp shampoo tested for the study is a licensed cosmetic preparation of Dr. JRK's Siddha Research and Pharmaceuticals, Chennai. The shampoo contains 1% each of Climbazole and Zinc pyrithione as AD agents.

Efficacy evaluation of Anti scaling scalp shampoo in liaison with its usage.
Preparation of shampoo dilution

One and four milliliter of the shampoo was taken separately. The shampoo was then diluted in 500ml of water.

Testing of anti-fungal effect by measuring zone of inhibition

Agar well diffusion method was used (8) for testing the anti-fungal activity. Sabouraud's dextrose agar was used for the above purpose. 20 ml of molten media was poured into petri dish and allowed to solidify and then 0.5 ml of the culture suspension of *Candida albicans* adjusted to 0.4 at 450 nm was spread evenly on the plate. After 10 minutes of incubation, 2 mm well was made in the center of the media. 20 microliter of the diluted shampoo viz 1:500 and 4:500 were placed in the well and incubated at 26°c for 24 hours. Similarly, 20 microliter of undiluted shampoo was used as positive control.

The Zone of inhibition around the well was measured and the efficacy of the shampoo vis-à-vis

their respective dilutions was ascertained.
Similarly, water with different qualities such as:
1. Water with high Total Dissolved Solids
2. Brackish water
3. Distilled water
4. Chlorinated water

were also used to prepare the shampoo dilutions. Influence of the quality of water in the AD effect of shampoo was evaluated by using the above method.

Influence of shampoo base in the activity of Climbazole and Zinc pyrithione[9]

In order to understand the activity of Climbazole and Zinc pyrithione individually (without shampoo base) and in combination, zone of inhibition assay was done using the procedure describes earlier. Similarly, the shampoo base without Climbazole and ZPTO was also tested.

Preparation of the dilution of Climbazole and Zinc pyrithione

1% solution of Climbazole and Zinc pyrithione was prepared in distilled water in lieu of shampoo base. From the above, 1 and 4 ml of the solutions were re-diluted separately in 500 ml distilled water. This was done in lieu of 1 and or 4 ml shampoo being diluted with 500 ml water during usage described earlier. 20 microliter of the re-diluted Climbazole and ZPTO were separately subjected to zone of inhibition assay.

Killing effect vs contact time[10]

In order to understand and extrapolate the zone of inhibition of shampoo with reference to the percentage of death of the organism, methylene blue staining procedure was employed by treating the yeast cells with the respective shampoo dilutions.

Results

Except chlorinated water, the quality of water such as distilled water, water with high TDS and brackish water did not influence the effect of the shampoo. Further, the extent of dilution i.e., 1:500 or 4:500 also has not significantly influenced the anti-fungal activity as the zone of inhibition for the above was more or less similar (Table I).

TABLE I

Efficacy evaluation of Anti scaling scalp shampoo in liaison with its usage.

S.No.	Quality of water	Method of dilution of shampoo (sample)	Zone of inhibition for 20 μl sample
1	Distilled water	1:500	14 mm
		4:500	14 mm
2	Water with high TDS	1:500	14 mm
		4:500	15 mm
3	Brackish water	1:500	15 mm
		4:500	16 mm
4	Chlorinated water	1:500	No inhibition
		4:500	No inhibition
5	Shampoo as is	Undiluted	26 mm
		Undiluted	28 mm

Compared to Climbazole, ZPTO exhibited greater activity. The combination of both ZPTO and Climbazole showed only marginal increase in the zone of inhibition and that may be due to issues relating to their diffusability. The shampoo base devoid of the above ingredients didn't show any activity (Table II).

Irrespective of the quality of water used for dilution of shampoo, the killing effect of shampoo remains unaffected. However, lower the dilution greater was the killing effect. The killing effect of shampoo was perfectly in line with the killing effect of either the respective agents individually or their combination (Table III).

TABLE II

Influence of shampoo base in the activity of Climbazole and Zinc pyrithione.

S.No.	Tests	Method of dilution of Sample	Zone of inhibition for 20 μl sample
1	1% Climbazole	1 ml in 500 ml water	3 mm
		4 ml in 500 ml water	4 mm
2	1% Zinc pyrithione	1 ml in 500 ml water	8 mm
		4 ml in 500 ml water	11 mm
3	Combination of Climbazole & Zinc pyrithione (1% each in water)	1 ml in 500 ml water	12 mm
		4 ml in 500 ml water	14 mm
4	Shampoo base as is	Undiluted	No inhibition

TABLE III

Killing effect versus contact time.

Water used for dilution		Percentage of dead cells versus dilution of shampoo – 2 minutes contact time	
		1:500	4:500
Shampoo	Distilled water	27	48
	Water with high TDS	37	56
	Brackish water	23	34
Distilled water used for dilution	Climbazole	24	29
	Zinc pyrithione	28	31
	Combination of Climbazole & Zinc pyrithione	33	38

DISCUSSION

The present study undoubtedly proves that the anti-scaling scalp shampoo tested by us is quite effective in limiting dandruff. The evaluation of the activity in liaison with the usage pattern of anti-dandruff shampoos by the end users re-iterates the superior efficacy of the anti-scaling scalp shampoo. This may be due to the complementing effect of the shampoo base, herbal actives such as *Cassia alata, Aloe vera & Wrightia tinctoria* and the actives (Climbazole or ZPTO). Further, the shampoo base was found to have no negative effect in limiting the activity of either Climbazole or ZPTO.

Although, both the above ingredients are known to have superior AD effect (11), the influence of the shampoo base both in their release and their efficacy are not well known. Similarly, the effect of the three herbal actives present in the anti-scaling scalp shampoo in the efficacy of Climbazole or ZPTO is also not understood.

Further, the likely short contact period of AD shampoos is going to be yet another limiting factor on their performance (6).

Therefore, the AD shampoo must preserve its activity even at greater dilution, must able to spread and reach the entire scalp surface and must quickly exert the killing effect on the organism. The anti-scaling scalp shampoo is formulated by keeping all the above considerations as reflected by our test findings.

The quality of water used by the dandruff sufferers do differ greatly from region to region. Hence, the consideration of the likely influence of the quality of water in the activity of AD shampoo is essential while formulating the same. In our present study, we found that except chlorinated water, the water with high TDS and brackish water didn't influence the activity (1).

The relatively comparable activity of both the ingredients and for the shampoo suggests that the activities of the ingredients are well preserved in the shampoo system. Further, the three herbal ingredients also didn't influence the above.

This is the first study to the best of our knowledge proving the anti-dandruff efficacy of shampoo exactly in liaison with the way such products are used by the dandruff sufferers. Therefore, we believe that besides testing MIC, the study methodology should mimic the actual usage pattern of such products in order to capture the real activity.

The above findings strongly suggest that the anti-scaling scalp shampoo (marketed under the trade name Verdura anti-scaling scalp shampoo) is very effective, quick in its action, withstand higher dilution and exhibit instant killing effect.

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Bionanotechnology & Bioeconomy for a Greener Development

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Summary

According to Europe 2020 strategy, a sustainable, more competitive, and greener economy is regarded as development that meets the today needs without compromising the needs of the future generations. The new green growth is to be based on a low carbon, climate resilient, and resource-efficient economy, minimizing waste and pollution and protecting-restoring the earth ecosystem. In addition a *green economy* can create new jobs trying to solve both the EU problem of youth unemployment and the preservation of natural resources by the use of waste material from animal and plant biomass. Young people, in fact, are the group most adaptable to the changes, easily accepting jobs in the new and unexplored areas of bionanotechnologies, by the use of industrial by-products representing ~300 billion/year of unused available and precious raw materials. Thus, the green economy has been recognized as a potential source of employment and a contributor to economic recovery, representing both a challenge and an opportunity for the labour market and the environment preservation.
MAVI as producer of Chitin Nanofibrils (CN), obtained from the crustacean waste by a green technology, has been involved in different EU research projects to produce innovative biocomposites for pharmaceutical and cosmetic use and/or food packaging. By the Biomimetic project (www.biomimetic-eu-project.eu/) innovative emulsions and non-woven beauty masks have been realized; by Chitofarma (www.mavicosmetics.it) advanced medications have been made by biodegradable non-woven tissues; by n-Chitopack (www.n-Chitopack.eu) different food packaging have been made completely biodegradable and compostable. It is to underline that all the projects, based on the production of *green* biocomposites, have been based on the use of crystal-CN and other natural polymers, all obtained from waste material by a low consume of energy and water, according to the EU, OECD, and UNEP guidelines. The origin of chitin and its crystallinity has determined, in fact, the structure, morphology and the particular properties of CN used as filler, as well as the other bio-based polymers have represented the matrix of the composites obtained into the university of Pisa.
In conclusion the different green products resulting from the projects will be shown by this paper, focusing the discussion on the present necessity for a sustainable development. A green economy in fact, implies not only a right economic, social and environmental development but also a bettering of the quality of life, through education and training in line with labour market demands, and human

knowledge. At this purpose it is to remember that a young-looking is psychologically connected with the necessity to show a healthy appearance also. Thus, a healthy and beauty body, as well as an increased and ameliorated education is one of the priorities of the EU 2020 strategy, along with labour productivity growth, lower unemployment, better insertion of young people in the labour market, increasing public participation in education, and lifelong learning. Recent EU studies reported, in fact, that by 2020 2.8 million jobs are expected to be created by the *green economy*.

Riassunto

Lo sviluppo di un'economia più ecocompatibile in grado di salvaguardare le future generazioni dovrà essere alla base di un'industria più competitiva e sostenibile, secondo le linee strategiche dettate dall'Europa da qui al 2020. La nuova crescita *verde* dovrà risolvere le attuali necessità senza compromettere le necessità future, pur basandosi su una bassa emissione di gas serra che salvaguardi e protegga gli ecosistemi del nostro pianeta. Questa bioeconomia innovativa sarà sicuramente in grado di creare nuovi posti di lavoro per risolvere l'attuale tasso di disoccupazione, soprattutto giovanile, preservando le sorgenti naturali di materie prime e utilizzando gli ingenti scarti di lavorazione delle biomasse. Infatti, il mondo giovanile è più propenso alle innovazioni, si adatta facilmente ai cambiamenti, accettando con entusiasmo di eseguire lavori in aree ancora inesplorate basate sull'uso delle nuove bionanotecnologie e di materie prime industriali inutilizzate, preziose e di recupero che hanno raggiunto un volume pari a circa 300 miliardi di tonnellate l'anno.

Così la cosiddetta *economia verde*, che rappresenta attualmente una sfida ed un'opportunità per il mercato del lavoro ed è riconosciuta come potenziale sorgente di nuovi impieghi, sembrerebbe in grado di rafforzare l'economia globale, preservando anche l'ambiente.

MAVI, come produttrice di nanofibrille di chitina (CN) ottenute dagli scarti di lavorazione dei crostacei attraverso una tecnologia verde, è stata coinvolta in diversi progetti di ricerca europei per produrre bio compositi adatti all'uso farmaceutico, cosmetico ed alimentare. Attraverso il progetto Biomimetic (www.biomimetic-eu-project.eu/) sono state realizzate emulsioni cosmetiche e maschere di bellezza a base di tessuti senza trama completamente biodegradabili contenenti ingredienti ad attività anti-aging; attraverso il progetto Chitofarma (www.mavicosmetics.it) sono state prodotte medicazioni avanzate, sempre a base degli stessi tessuti senza trama contenenti ingredienti attivi adatti a facilitare la cicatrizzazione di cute alterata; attraverso il progetto n-Chitopack (www.n-Chitopack.eu) sono stati realizzati imballi per alimenti completamente biodegradabili e compostabili.

Da sottolineare come tutti i progetti, basati sull'uso di biocomposti *verdi*, siano stati realizzati con l'uso di polimeri naturali, quali CN ottenuti da materiali di scarto e con basso uso di energia ed acqua, in accordo con quanto voluto dalle linee guida dell'EU, OECD e UNEP.

L'origine della chitina e della sua cristallinità ha determinato la struttura, la morfologia e le particolari proprietà di CN utilizzato cone filler, cosi come gli altri bio polimeri realizzati presso l'università di Pisa hanno costituito la matrice dei compositi.

In conclusione, i diversi prodotti realizzati con i progetti verranno descritti in questo lavoro che mette in evidenza come l'attuale economia necessiti di uno sviluppo sostenibile. L'*economia verde*, infatti, implica non soltanto uno sviluppo economico sociale ed ambientale corretto, ma anche la necessità di migliorare la qualità della nostra vita attraverso una corretta educazione ed un vigoroso sostegno al mercato del lavoro. Attraverso studi recenti è stato messo in evidenza come entro il 2020 l'Europa si aspetta che l'economia *verde* sia in grado di creare 2,8 milioni di nuovi posti di lavoro.

Gli studi riportati in questo lavoro vanno in questa direzione.

INTRODUCTION

Bioeconomy, that encompass all industries and sectors, is based on the values of biological materials (including organic waste), such as agriculture, forestry, and fisheries. For these reasons, EU supports research and innovation under an investment of about €80 billion by the Horizon 2020 program by which over €4 billion will be invested on bioeconomy-related research in the period 2014-2020 (1).

This new bioscience is based on the knowledge and innovation, involving many technologies such as engineering, chemistry, biology, computer science and nanotechnology. So far, it refers to the sustainable production and conversion of biomass for a range of food, advanced medications, cosmetics and other industrial products as well as energy, translated into new sources of goods, environmentally-friendly and human-friendly, necessary to ameliorate the social wellbeing. For all these reasons it has been estimated that bioeconomy will contribute a global average of 2.7 percent to GDP by 2030, according to the a Organization for Economic Cooperation and Development (OECD) (2). On the other hand, the market incorporating bionanotechnology is a growing and attracting interdisciplinary technology seen as the industrial revolution of the new millennium, estimated to reach US$ 3 trillion by 2020 (Fig.1) (3, 4).

In terms of component the bionanotechnology market can be segregated into nanomaterials, nanostructures, and nanotechnologies (Fig.2), comprising the sectors of electronics, energy, defense, cosmetics, medical, food and agriculture. In any way, bionanotechnology encompasses the production and application of physical, chemical, and biological systems at scales ranging from individual atoms or molecules to around 100 nanometers (nm) (1 nm representing a billionth of a meter), as well as the integration of the resulting nanostructures into larger systems. This specific technology makes use of phenomena and fine-tuning of materials at atomic, molecular and macromolecular scales where properties differ from those at larger scale. Just to understand this dimension, a single human hair is about 80,000 nm wide, a red blood cell is ~ 7,000 nm wide, a DNA molecule 2 nm and a water molecule almost 0.3 nm.

Thus, the innovation in the sector of bionanotechnology is pulled by manufacturers and producers because of the beneficial new properties of nanomaterials, attracting large-scale research investments.

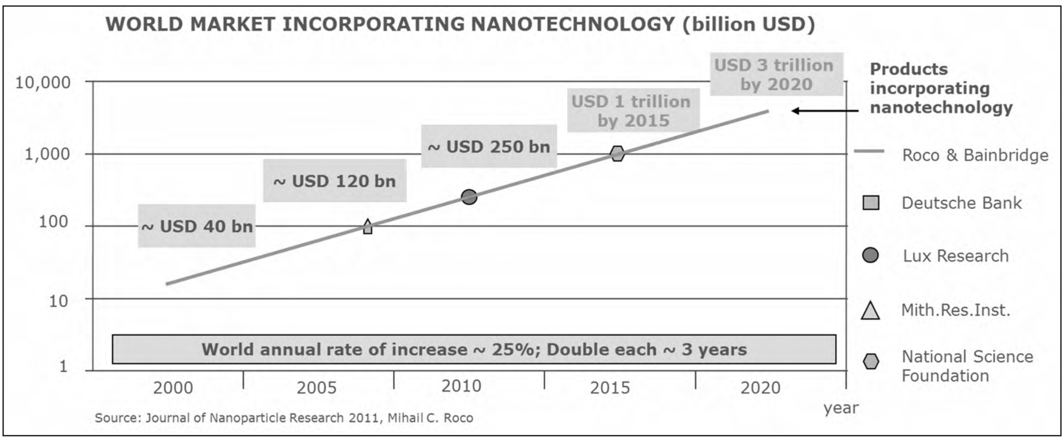

Fig. 1 *Previsional market of nanotechnology.*

New devices and tools like nanocapsules, nanoparticles and nanofibers are examples for the detection and treatment of diseases, the delivery of active ingredients to specific sites, and water treatment processes (Fig.3).

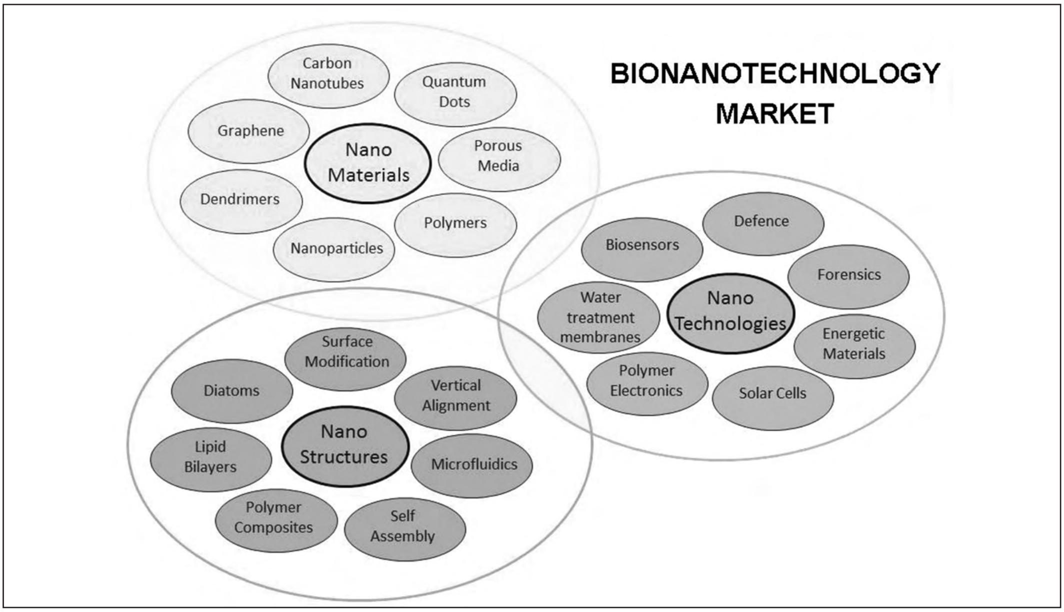

Fig. 2 *The Pillars of nanotechnology.*

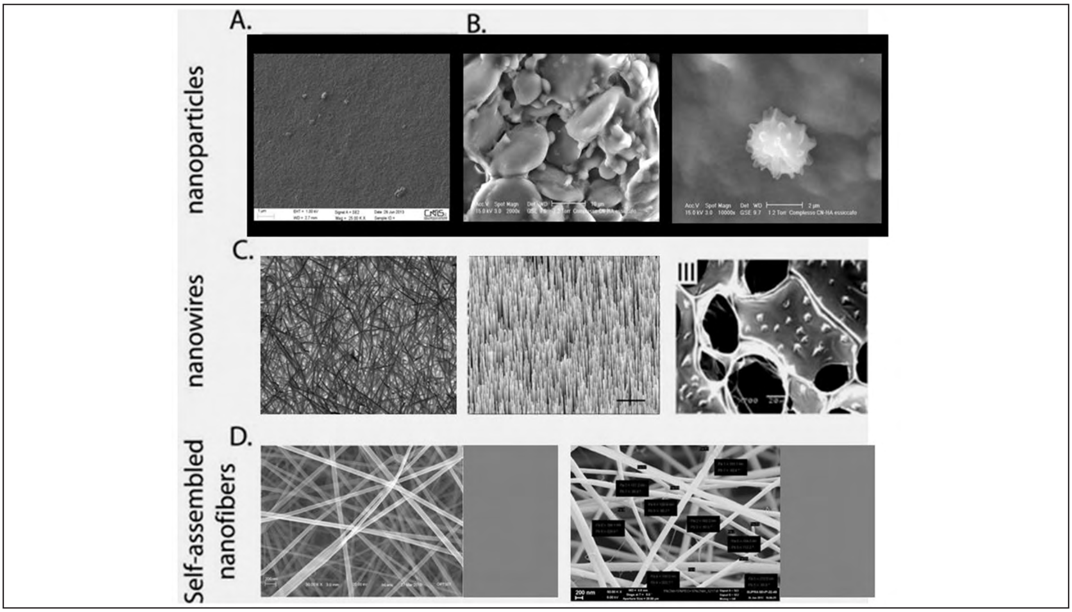

Fig. 3 *Nanoparticles, nanowires and nanofibers used for many purposes.*

At present bioeconomy, towards a circular economy based on a zero-waste program (Fig.4) and the use of bionanotechnology, is regarded as the solution for climate change, resource scarcity, conservation of biological diversity, safeguarding nutrition, energy transitions, post-fossil chemistry, while safeguarding a sustainable growth and competition.

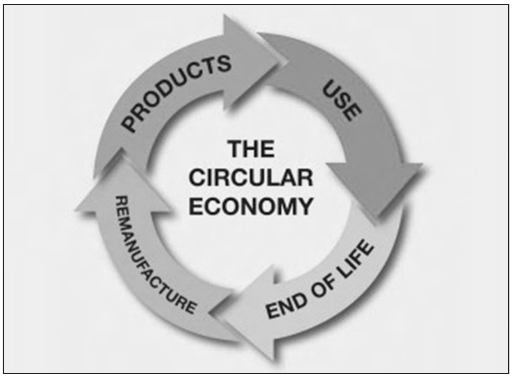

Fig. 4 *The circular economy system for a zero waste program.*

Thus, bionanotechnology, often referred as an *enabling technology*, is having a major impact in development of many sectors. By 2020 it will be a broad-based technology, seamlessly integrated with the most novel technologies and potential applications from electronics, optical communications, and biological systems, to new materials (5).

However it has been predicted that bioeconomy, as new scientific discipline, will achieve previously unavailable solutions in productivity, sustainable development, medicine and health to obtain a better quality of human life. It has to be considered a framework for policies that, harnessing the innovation growth, can face and solve the social grand challenges of food security, climate change, healthy living, and energy efficiency (Fig.5).

EU strategy

Innovation will be at the centre of the EU's growth strategies for the coming decade. The EU 2020 strategy (6), announced since 2010, includes the bioeconomy as an important component, according to 3 main priorities: (a) *smart growth*, obtained by the development of knowledge and innovation-based economy; (b) *sustainable growth*, obtained by a more resource efficiency, and a more greener and competitive way to use the available raw materials; (c) *inclusive growth*, fostering a higher employed economy and delivering a better social and territorial cohesion. Thus, according to OECD and EU (7, 8), bioeconomy has to be considered not a simply science, but an integration of science with business and society (9). The financial sector, in fact, will have a key role in transferring technology knowledge from the research centres to the industry and the market, safeguarding the poverty.

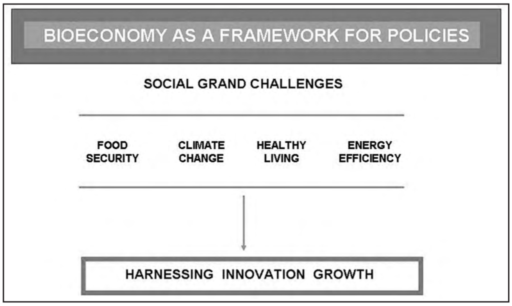

Fig. 5 *The four pillars of Bioeconomy.*

On the other hand, bionanotechnology is recognized by The European commission (EC) as one of the six key enabling technologies (KETs) that shows applicability in several different sectors such as medicine, biotechnology, electronics, material, science and energy technology (Fig.6) (8, 10).

By these supports, the bioeconomy is expected to increase security, producing healthier food, and reducing the environmental impact of agriculture, fisheries, and manufacturing industries. In this way, the climate change will be stopped, the greenhouse gas emission reduceds, and food and water preserved for the future generations.

These the reasons why the EU bioeconomy has a turnover of nearly € 2 trillion, employing more than 22 million people, and a program by 2025 to trigger 10€ for each euro invested in research and innovation (8-10).

At this purposes and by the program *Horizon 2020*, (Fig.7) the European Community will invest ~€3.7 billion in bio-based innovations over 2014-2020. The *Horizon* contribution will be €975 million, while the biobased Industries Consortium will contribute €2730 million (11, 12). By these investments it will be possible to obtain a greener market and more environmentally sustainable growth together with a significant reduction of its dependency on fossil-based products (Fig.8).

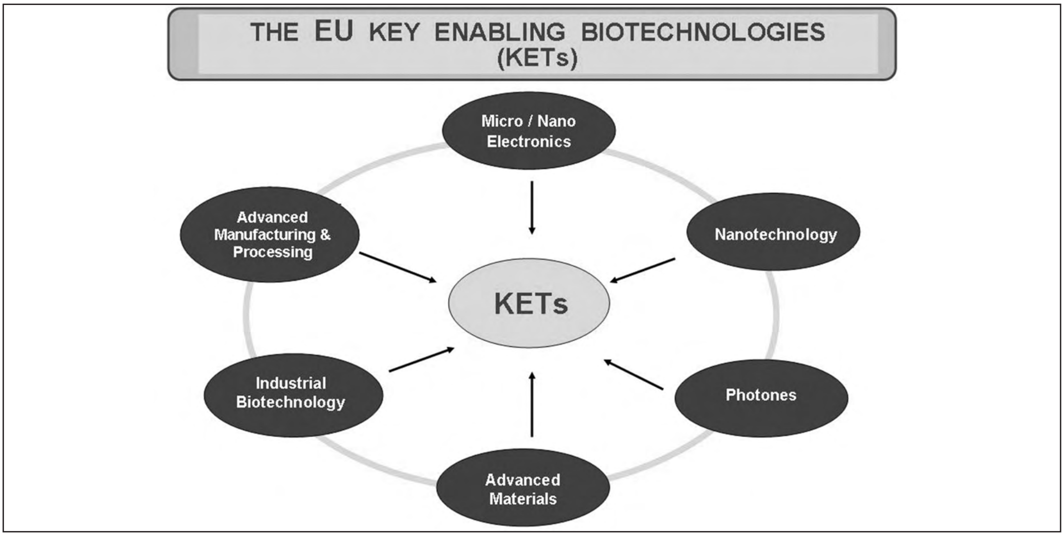

Fig. 6 *The EU emerging technologies.*

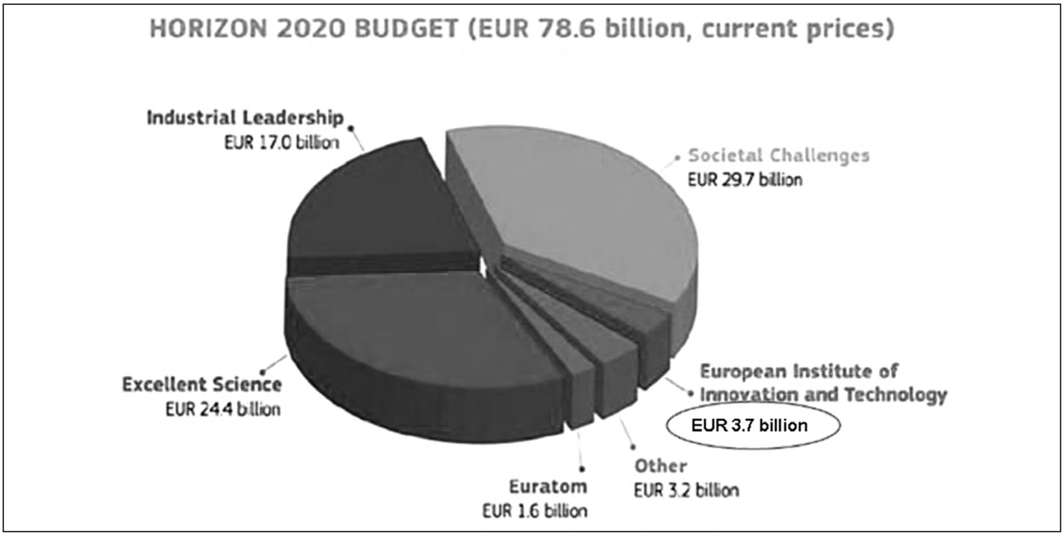

Fig. 7 *Budget Horizon 2020*

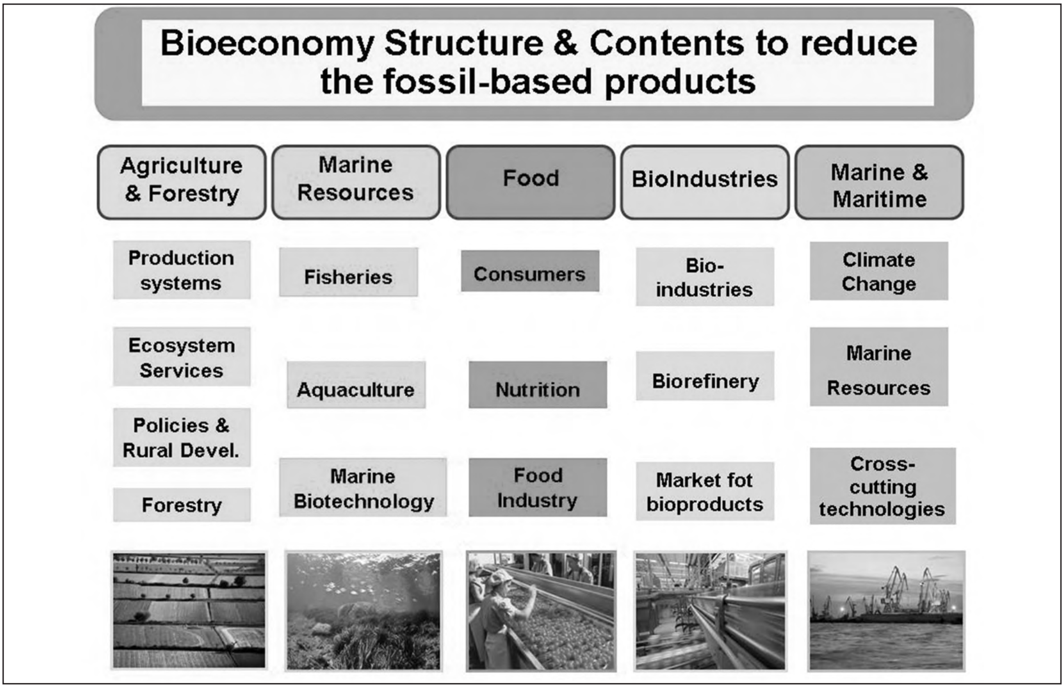

Fig. 8 *Mainstrays of Bioeconomy.*

Bionanomaterials

Bionanomaterials (BNMs), defined as any matter, surface or construct that interacts with biological systems, has to have at least one dimension between 1 and 100 nm in size. According to their size, surface area, and charge, BNMs have different mechanical, chemical, electrical, and optical properties that make them suitable for technological and biomedical applications. Among them, the one-dimensional (1-D) nanostructures have found broad applications especially to make biomedical reinforcement biocomposites used as nanofibers in tissue engineering, drug delivery and wound dressing.

Biocomposite materials, in fact, have several advantages being made from renewable and not from petroleum-derived products, having a cost that can be reduced with large-scale use. Moreover, their biodegradability could eliminate potentially harmful effects related to materials processing and disposal.

The foremost requirements for nanofibers to serve as biomaterials are, in fact, (a) biocompatibility for not causing any toxicity or inflammation to the tissue/organ, (b) biodegradability to avoid the post-removal process after their application into the biological systems, (c) biological inertia for not causing any immune response/biological reaction to the host organism, and (d) to have a good tunable rigidity for facilitating the process diffusion of the active ingredients loaded into the tissues/organs (13).

It is to remember that nanocomposites are made by dispersing a filler material into nanoparticles that form flat platelets distributed into a polymer matrix. This structure, creating a complex barrier of multiple parallel layers, forces gases and water vapour to flow through the polymer in a *tortuous* path. As more tortuosity is present in a polymer structure, higher barrier properties will result.

Naturally, the extent of the nanocomposite properties will dependent on the type of polymer selected and filler used, as well as the extent of dispersion of the nanoparticles in the polymer matrix (14).

For all these reasons our group designed to use chitin nanofibrils (CN) and lignin, both obtained from biomasses, for producing not only advanced cosmetic emulsions, but also innovative beauty masks (Fig.9) and topical medications (Fig.10) made by natural nanocomposites of non-woven tissues or transparent films (flexible packaging), 100% biodegradable and produced by green processes of electrospinning and casting technology (15-17). Both these technologies give rice to nanofiber meshes exhibiting unique properties such as high specific surface area, flexibility in surface functionalities, and excellent mechanical properties. Moreover the electrospinning, allowing the control over fiber morphology, is capable of being scaled-up for mass production (18). On one hand it is interesting to underline that these nanocomposites (the non-woven tissues and films) were made by the use of waste materials such as CN and ligno-cellulosic polymers obtained from fishery's and plant biomass respectively (19-21). The realized nanocomposites represent an innovative technology that recently gained momentum in mainstream commercial packaging (22).

Fig. 9 *Innovative beauty masks made by the casting technology.*

On the other hand, it is important to remember that, for example, the flexible packaging consumption's represent today a rapid growth market of US$:8 billion (23). Therefore, these the reasons why our group, by the EU Research projects n-chitopack. (www.n-chitopack.eu) and Bio-Mimetic (http://www.biomimetic-eu-project.eu/), investigated the environmental impact of processing and manufacturing green composites from engineering natural fibers obtained from the biomass,such as chitin nanofibrils, lignin, polylactic acid (PLA) etc to produce non-woven tissues (24, 25).

Fig. 10 *Advanced medications made by Electrospinning.*

So far it has been shown that a small amount of CN or lignin added to the bioplastic PLA or to the electrospinning/casting mixture made the resulting composites stiffer, stronger, tougher and more scratch-resistent, improving their electrical or thermal conductivity, and ameliorating their compostability also (26) (Fig.11).

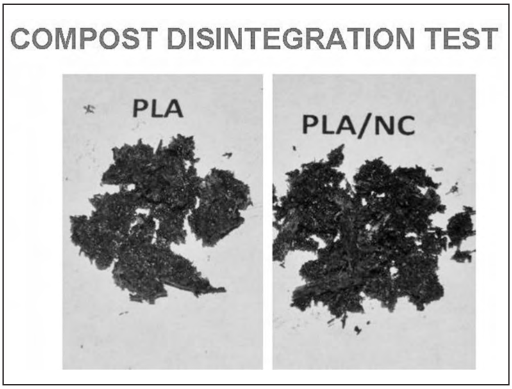

Fig. 11 *The better compost disintegration test of a biocomposite made by polylactic acid (PLA) and chitin nanofibrils (CN).*

Thus, these new nanocomposite films, utilizing CN nanoparticles as filler, may have numerous applications also, for their properties such as: gas/oxygen, water vapour barrier function, high mechanical strength, thermal and chemical stability, recyclability, dimensional stability, heat resistance and good optical clarity (27-30). Moreover, while the electrospun non-woven tissue made by the use of chitin nanofibrils have comparable structure to the extra cellular matrix (ECM), the carrier film matrix has shown to possess (a) compatibility with both the skin and the mucous membranes, (b) stability during the time of drug delivery (c) adequate mechanical properties, (d) facility in fabrication cost, (e) appreciable swelling in water and softening point above 37°C (Fig.12).

Finally, unlike their physical properties, *in vitro* and *in vivo* degradation of these films occur less rapidly as their degree of deacylation become higher. At this purpose, it has been shown that the enzymes chitotriosidases, belonging to 18 families of chitinases secreted by humans, show preference to degrade the acetylated units, so that chitin is degraded more quickly than chitosan (31).

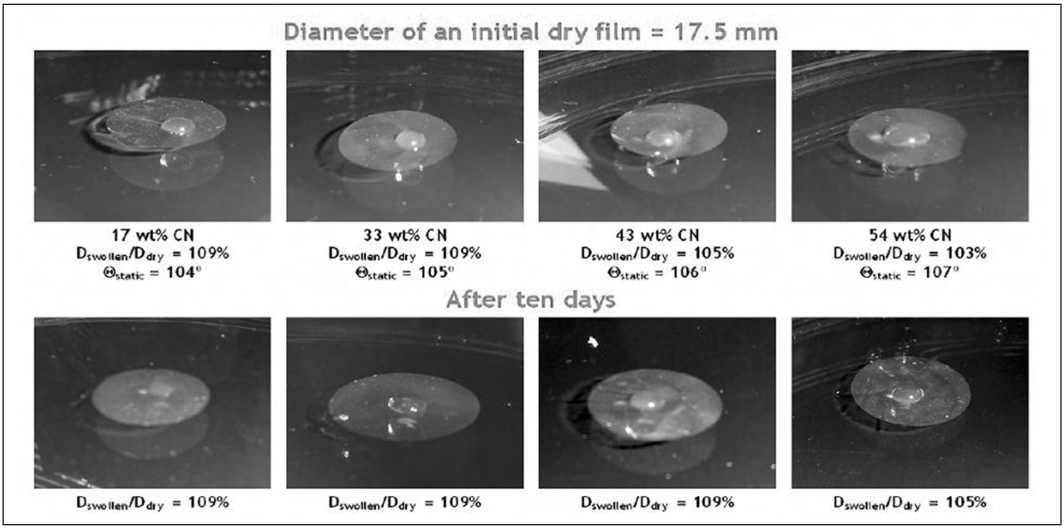

Fig. 12 *Swelling capacity of the CN-Chitosan film made by the n-Chitopack EU research project.*

This is the reason why films and non-woven tissues made by the prevalent use of CN, have found applications for cosmetic and pharmaceutical use to produce beauty masks and wound dressings (32-35). They have, in fact, the possibility to carry cargos, such as cells for tissue repair, and active ingredients for tissue regeneration, because of the activity of the natural nanofibers used for making the non-woven tissues. Moreover, nanofibers have a close connection with our body where every type of tissue are made by fibers from micro- to nanoscale, generally in the form of bundle structures, which function to provide strength enforcement and elasticity, conduct nervous impulses and movement of the whole body or within organ (36, 37). At this purpose non-woven tissues produced by the use of CN have shown to possess a repair and regenerative capacity on skin tissue because of their large-surface-area-to-volume ratio, as large as ~1000 times that of a microfiber, and their capacity to accelerate the skin granulation processes, because of their same hierarchical organization of ECM (38). Moreover these innovative non-woven tissues, made by biomaterial of natural origin, have evidenced to be bioresorbable and non toxic and, therefore, applied and used as wound dressings.

As previously reported, they can be broken down from the skin enzymes, avoiding the need of the removal process with the associated surgical functional problems to the patients and plastic surgeons. In conclusion the non-woven tissues, based on the use of CN properly treated, have shown to be active not only for their capacity to accelerate the skin regeneration processes, but also for their effectiveness against the bacteria bio-burden formation (15, 38). These advanced medications, in fact, possess special properties, being free of binder and chemicals, having an high economical efficiency of production and at the same time, offering lower weight and 100% biodegradability. For all these reasons, they have many possibilities to compete in the international market, also for their capacity to impart the desired properties and stand out for many advantages, compared with other commercializes medical non-woven tissues.

The market of medical devices

The global nanotechnology-based market of medical devices is expected to grow at a significant increase of 11-12% during the forecast period 2014-2019 (39), mainly driven by the growth in aging population, increased use, and rising R&D expenditure in this new technology. In addition, the governments of several countries are investing heavily in developing and commercializing new nanotechnological products, so that in 2013 North America accounted for the largest share to the global nanotechnology-based medical devices market, followed by EU and Asia Pacific. However, Asia Pacific is expected to be the fastest-growing region during the forecast period owing to the rapidity aging-populations, rising adoption of advanced nanotechnology-based medical devices, increased accessibility to health care facilities and rising R&D and health care expenditure (10, 39).

Sustainable development

In the Report of the World Commission on Environment and Development: Sustainability has been defined as «development that needs the needs of the present without compromising the abilities of future generation to meet their own needs» (40). Thus, bioeconomy has to encourage the sustainable use of the so-called *green* goods, while affecting an alternative to the regulated market economy (41). At this purpose, with an increased green market (Fig.13) there is a great need not only for innovative products made by the use of renewable raw materials, but also for sufficient renewable energy which not cause environmental harm, being produced by industrial *green* processes. Sustainable development relies, in fact, not only on the development of novel processes but also on the use of raw materials derived from fishery's and plant biomass, for decreasing dependence from fossil fuel resources.

Fig. 13 *The expected world green market in the 2011-2020 period.*

For these reasons, on one hand chemical industries have been moving toward the development of innovative processes as the awareness that a sustainable and *green* development is becoming essential for their competitiveness and for saving human wellbeing and the environment (42) (Fig.14). Nanotechnology leads, in fact, social and economic innovations useful in day to day life (Fig.15).

On the other hand, according to UNEP, a *green* economical policy may deliver social and economic benefits by improving resource efficiency and inducing domestic companies to innovate for obtaining a competitive edge (43). Moreover, this kind of policy seeks to drive growth, jobs, environmental improvement, poverty eradication and social equity by shifting investments towards clean and efficient technologies, natural capital and social infrastructure.

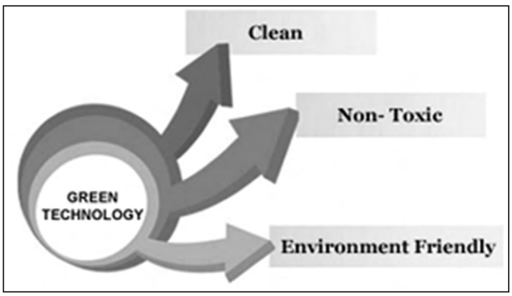

Fig. 14 *Main reasons for a green technology.*

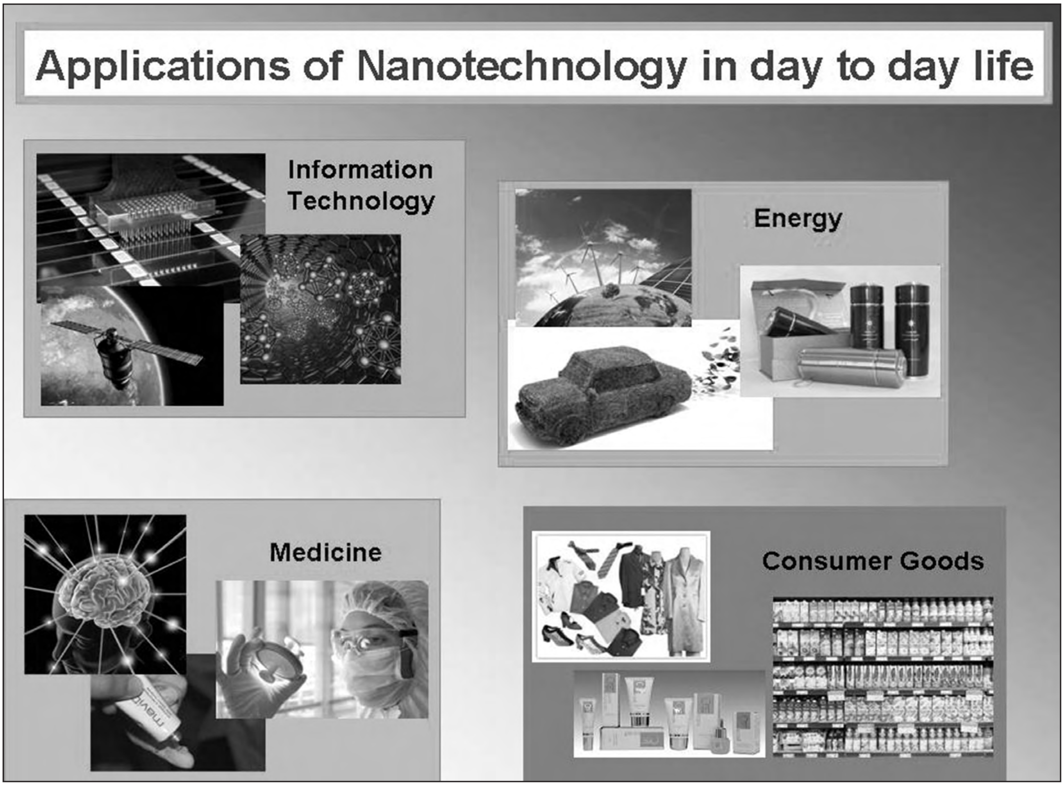

Fig. 15 *Nanotechnology in day-to-day life.*

However, greening the economy will involve large scale investment in new technologies, equipment, buildings, and infrastructures.

Thus composite and innovative policies, under the form of direct investments by the government will result necessary to create knowledge and technology to generate new forms of capital, pushing the industry to advance in a particular direction and helping a country to attain technological leadership.

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Innovative and Sustainable Bio-Polymers for Household and Beauty Care Products. Final results of the EU BIO-MIMETIC Project.

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Summary

Into the charming and historical location of Villa Mondragone with the final report in Unindustria Latina, the EU Research Project BIO-MIMETIC, coordinated by Anju Brooker from P&G, has been closed during a three days meeting from June 23 to 25c.a. The project has received funding from the European Union's Seventh Framework Program (agreement nr 282945) for developing *New bio-inspired processes and products from renewable feedstocks*, as strategic alternative to fossil fuels.
As first result and starting from different biomass sources, the BIO-MIMETIC consortium has been able to obtain homogeneous constant and purified batches of lignin and lignin oligomers. Successively, lignin, as interesting, abundant and renewable source of aromatic groups has been transformed in new bio-polymers and bio-based products by environmentally-friendly enzymatic processes developed within the project, involving the enzymes laccases, oxidases and lipoxygenases. Moreover, it was possible to bind the by-product lignin, obtained from plant biomass, with chitin Nanofibrils, as natural polymer obtained from crustacean waste by a simple and *green* process. Finally, by the use of these new bio-polymers, household and beauty care consumer bio-products have been realized: an Automatic Dishwashing, a Compact Hard Surface Cleaner, and Anti-aging/Anti-inflammatory Skin Creams and Beauty Masks. In addition a stakeholder's analysis has been performed while a life cycle assessment has explored the environmental sustainability of both the new bio-polymers and the consumer products realized.

Riassunto

Nella storica e bellissima Villa di Mondragone e presso le sedi UNINDUSTRIA Latina, dal 23 al 25 giugno, è stata organizzata la chiusura del progetto di ricerca BIO-MIMETIC terminato dopo 3 anni di intenso lavoro.
Il progetto è stato parzialmente finanziato dal settimo programma quadro dell'Unione Europea (n. 282945) con lo scopo di mettere a punto nuovi processi e prodotti biologici con l'utilizzazione di materiali di recupero, in alternativa all'uso del petrolio.

Come primo risultato, il consorzio BIO-MIMETIC è stato in grado di ottenere diverse tipologie di lignine purificate e loro oligomeri. Successivamente la lignina, abbondante fonte rinnovabile di polifenoli, è stata trasformata in oligomeri e prodotti biologici innovativi, attraverso l'uso di processi enzimatici bio ed eco compatibili. Inoltre, è stato possibile complessare la lignina ottenuta dalla biomassa vegetale con le nanofibrille di chitina ricavate dagli scarti di lavorazione dei crostacei.
Infine, attraverso l'uso di questi biopolimeri, sono stati realizzati prodotti di largo consumo per la casa quali un prodotto per lavastoviglie, un detergente per superfici solide, e cosmetici innovativi quali maschere di bellezza e gel di nuova concezione. Ovviamente sui prodotti realizzai sono state eseguite tutte le analisi necessarie alla loro commercializzazione e ne è stata valutata la compatibilità ambientale del loro ciclo di vita.

INTRODUCTION

Transition to an integrated Bioeconomy is the way to secure a sustainable future for the succeeding generations. If higher quality, renewable raw materials will be produced sustainably, food security, biodegradable and/or compostable goods, and a healthy environment will continue to be assured, according also to the theme of EXPO 2015, Milan, Italy (Fig. 1).

***Fig. 1** The tree of life in EXPO 2015.*

The development of innovative production systems and an optimized use of agricultural and industrial by-products will be necessary to address this challenge, because of the increasing demands of natural resources from a growing population at global level.

New products can be created from biomass to replace those based on fossil fuels, for obtaining a reduced emission of greenhouse gases (GHGs). In addition, the use of bio-based products, obtained by enzymatic reactions as alternative to currently-used toxic organic solvents, may help to increase the resilience of the industrial production in the face of climate changes. Downstream processing, which uses bio-catalysis to replace chemical processing, can save, in fact, billion tons of CO_2 emissions across a range of industrial sectors. This is the meaning of the *synthetic biology* that will enable scientists to discover, design, and construct artificial micro-organisms, new biomaterials and green industrial processes to be used in the production of renewable chemicals, bio fuels, renewable specialty and fine chemicals, food ingredients and health-care products.

In the Bio-mimetic project for example, scientists from Dyadic Netherlands (www.dyadic.nl) discovered and developed single target laccase enzymes (Fig. 2) useful to catalyze the oxidation of the lignin' phenols, successively used by Claudia Crestini and her group from Torvergata University in Rome, Italy (www.uniroma2.it) to fractionalize and functionalize the lignin oligomers (Fig. 3).

Bio-mimetic project (www.biomimetic-eu-project.eu) has been based on the production of household and beauty care consumer products obtained by the use of renewable raw materials, such as lignin from plant biomass, produced by CIMV (www.cimv.fr) and Chitin nanofibrils (CN) from crustaceans waste, produced by MAVI (www.mavicosmetics.it). In any way, basic and applied biological research has the potential to produce a whole generation of new knowledge and technologies necessary to mitigate human impact, restore the environment ecosystems for ameliorating and enriching our quality of life.

In addition, industries making products such as households, cosmetics, and textiles have to move toward bio based goods and away from use of petrochemical products for manufacturing in a *green* way and cleaning-up the environment, by the alternative use of biologically derived enzymes more human-friendly, environmentally-friendly, and cost effective.

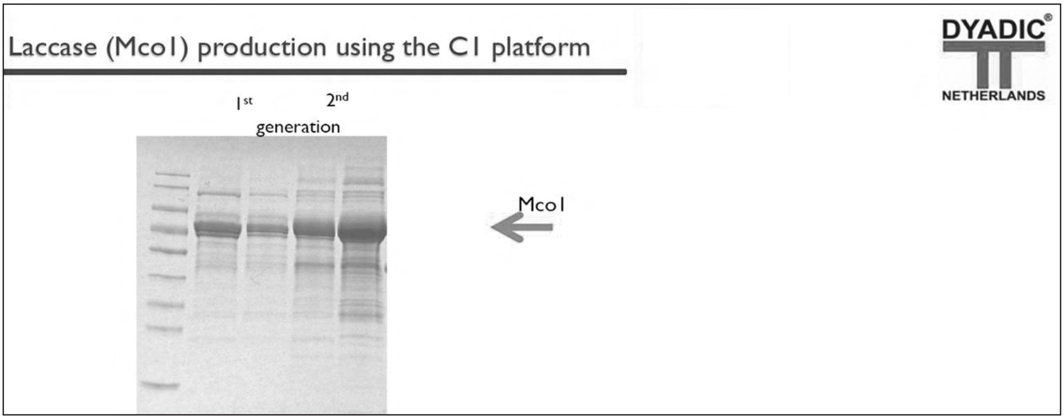

Fig. 2 *Generation of Laccase production by the C1 platform.*

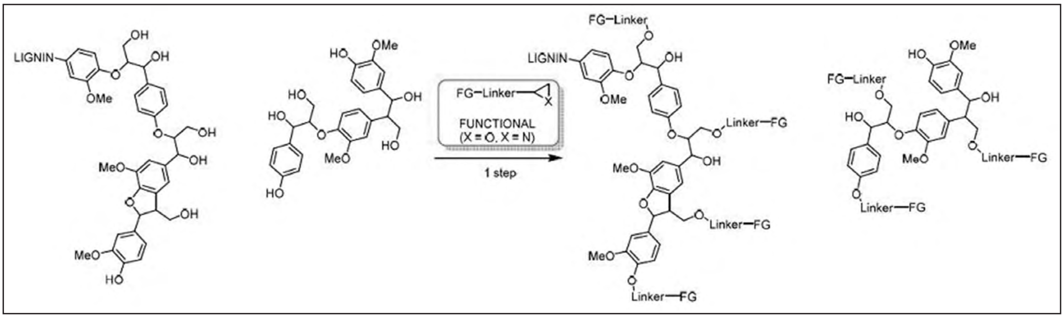

Fig. 3 *Functionalization of lignin.*

THE MEETING

On June 23-24, into the charming historical location of Villa Mondragone (Fig. 4-6), last scientific data on Bio-mimetic project were discussed; on day 25, into the location of Unindustria Latina, final scientific presentations have been held by all the scientists, participating into the research project. After welcome addressing, the meeting was opened from the guest of the day, Vladimir E. Yudin, head Institute of Macromolecular Compounds RAS, Saint-Petersburg, Russia, by the lecture: *Polymer Nanocomposites for tissue Engineering and Transplantation*.

The interesting lecture of Prof. Yudin has shown the possibility to develop biodegradable matrices made by biocompatible and biodegradable polymers used in medicine for tissue engineering under the form of fibers, films, or sponges (Fig. 7).

These matrices, produced by different processes in his laboratory (Fig. 8), can be made by natural material, such as montmorillonite, hydroxyapatite, chitosan, chitin nanofibrils etc.

Chitin nanofibrils (CN) may reinforce the strength of other natural fibers as chitosan, being useful for different medical applications, such as wound coating, fibroblast cells cultivation etc, and used under the form of films (Fig. 9) or sponges (Fig. 10).

Thus it has been shown that films, made by chitosan/chitin fibers increase the intensive reproductions of the fibroblasts and stem cells at wound level (Fig. 11 and 12), without any toxic effect.

Fig. 5 *Views of Villa Mondragone.*

Fig. 4 *Front side of Villa Mondragone.*

Fig. 6 *A particular of Villa Mondragone garden.*

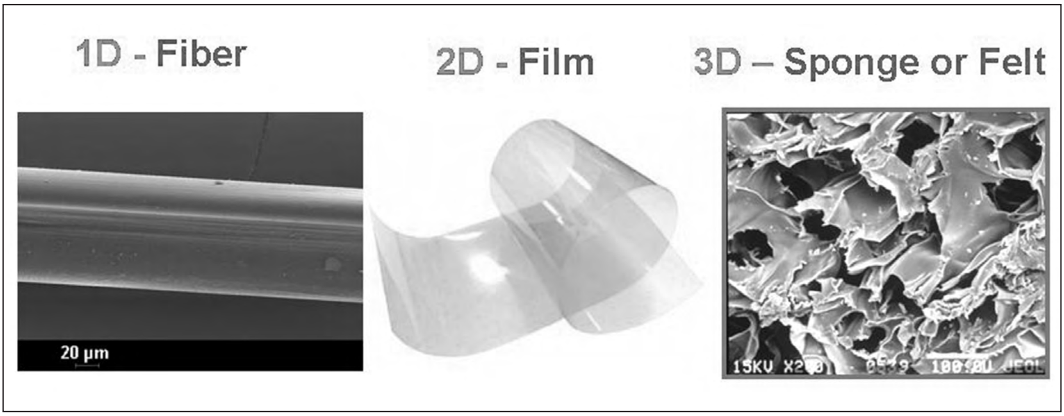

Fig. 7 *Different biodegradable matrices used for tissue engineering.*

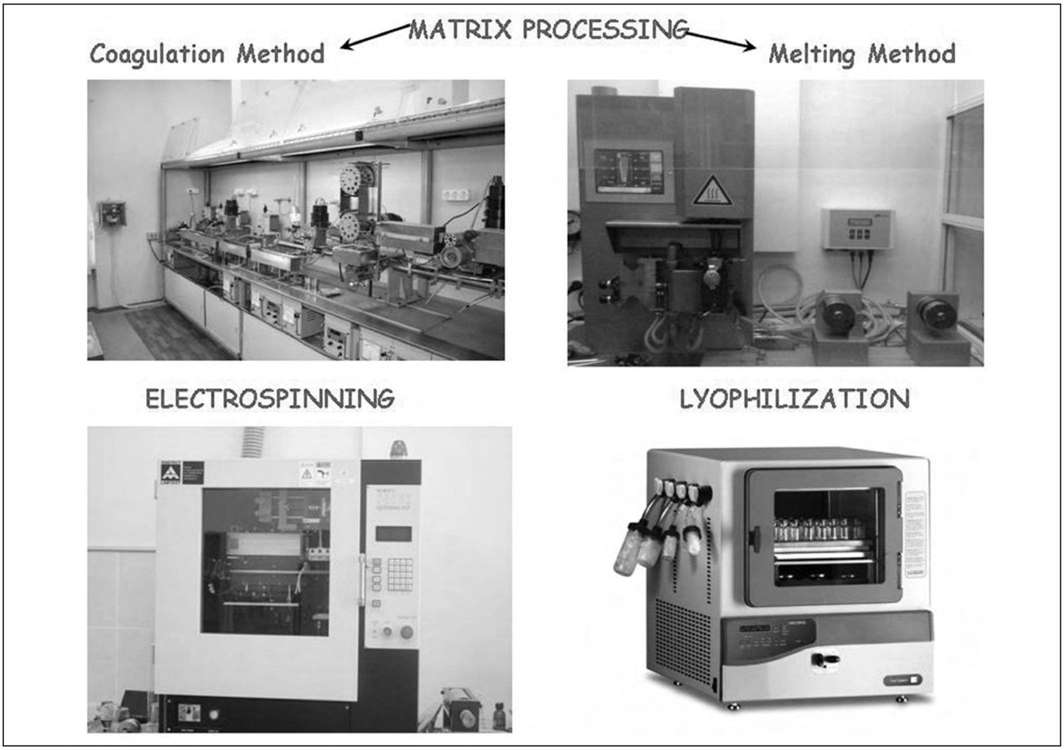

Fig. 8 The different methods adopted in IMC for matrix processing

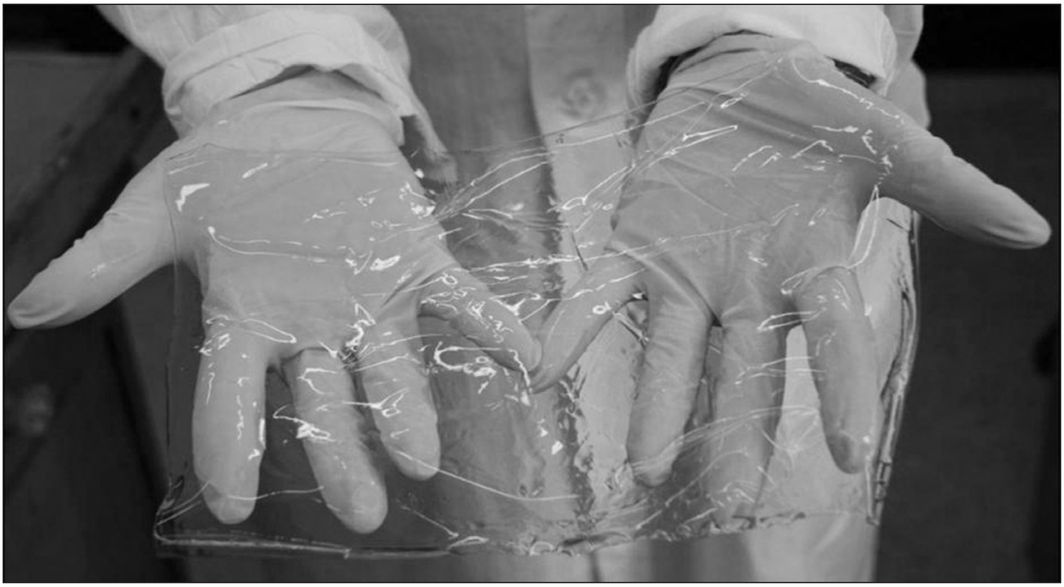

Fig. 9 The obtained Chitin Nanofibrils films.

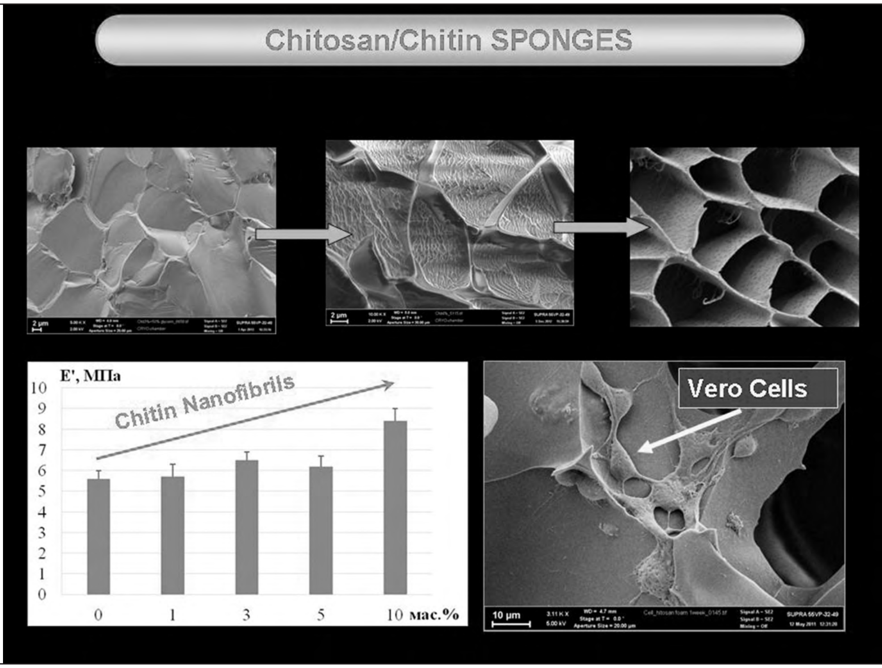

Fig. 10 Chitosan- Chitin sponges.

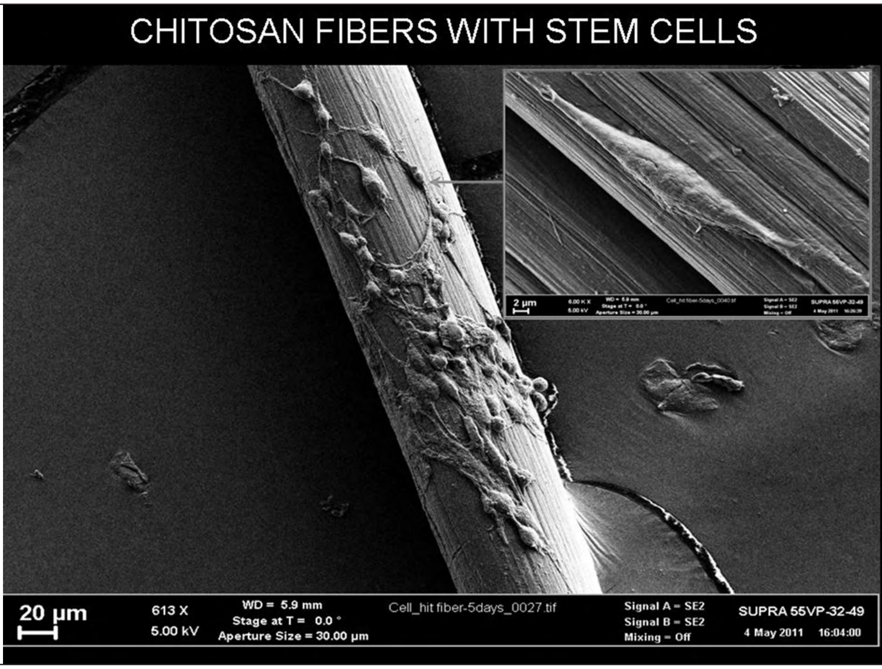

Fig. 11 The survival of stem cells on chitosan fibers.

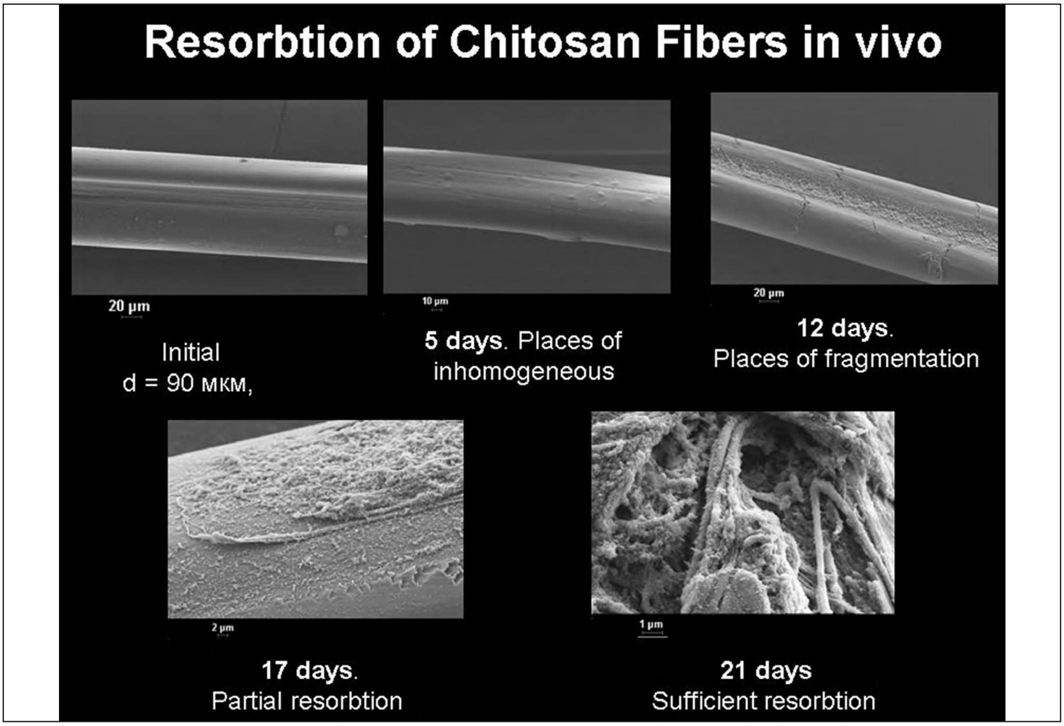

Fig. 12 *Resorption of chitosan fibers in vivo.*

As previously reported, it is important to use resources efficiently reducing waste and minimizing the negative impact on the environment, ameliorating also our wellbeing, and preserving the natural ecosystem for the future generations. Thus, the stewardship of the environment refers to protect its integrity through recycling by conservation, regeneration, and restoration of any produced good (Fig. 13).

For all these reasons, any industrial organization has to maintain an environmental stewardship by organizing *green* buildings, *green* offices, *green* procurement and *green* purchasing to maintain a life cycle, making the most efficient use of resources, such as materials, energy, and water. This was the topic of Diederik Schowanek from P&G BIC: The *use of renewable feedstocks to produce industrial chemicals as part of the corporate sustainability strategy of consumer goods company*.

Fig. 13 *The pillars of sustainability: reduce, reuse, recycle.*

The Company P&G from many years established a systemic set of procedures for compiling and examining the inputs and outputs of material and energy together with the associated environmental impacts, directly attributable to the functioning of every product or service system throu-

ghout its life cycle (Fig. 14).
Thus, by an organized Life Cycle Analysis (LCA), P&G compiles an inventory of all the relevant inputs and outputs of the products and evaluates the potential environment impact, interpreting the results and the phases in relation to the shelf-life of each product. The LCA work in the Biomimetic project was conducted in collaboration with The University of Manchester and integrated into their CCaLC tool, which is discussed below.
However, LCA involves cradle-to-grave analysis of every production system and provides comprehensive evaluation of all upstream and downstream energy inputs and multimedia environmental emissions, also if it is costly and time-consuming.

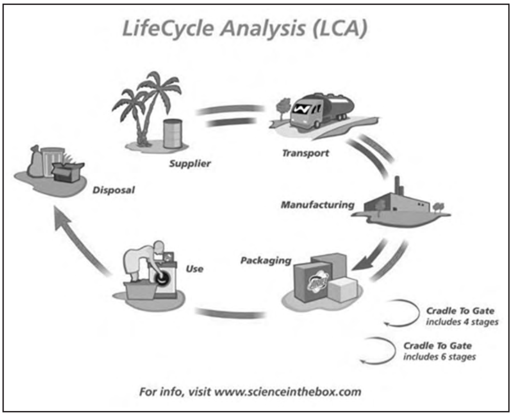

Fig. 14 *Life cycle Analysis.*

Lignin and its oligomers represent the main components used to make the household and beauty care products realized from the Research project by the support of CIMV (www.cimv.fr) and Tor Vergata University. Thus Bouchard Benjelloun, director R&D of CIMV, France, through the description of -*Biorefinery process: an advanced technology to produce a high quality lignin*, has presented advanced methodologies, covered by 9 patents, to obtain *bio-lignin* from different renewable resources, such as forest residual, wheat straw, sugar cane, corn straw and rice straw (Fig. 15).
According to the resources and methods used, it is possible to produce bio-lignin, xylose, glucose, cellulose pulp and bio-ethanol (Fig. 16).
The biolignin produced by CIMV has been successively refined by Claudia Crestini from UNITOV, Rome, Italy (www.uniroma2.it) to produce different functionalized oligomers, obtained by chemical and enzymatic application approaches.
By the different strategies reported by the topic Lignin *Biorefinery: Advanced and Challenges chemoenzymatic Functionalized Lignin-based Oligomers*, it has been possible to obtain different fractions of lignin-oligomers, selected by different weights. (Fig. 17 and 18).
The basis of innovation are the adopted strategies, such as the direct use of lignin functionalities, and the convenient short and scalable synthesis of functionals. Such tailored lignins may be of potential use in detergents for hard surfaces and laundry, and in cosmetic applications.
Alternative synthetic approaches based on the use of enzymes have been developed. More specifically polyphenol, oxidases, laccases and lipoxygenases have been used on graft lignins with suitable functional groups.

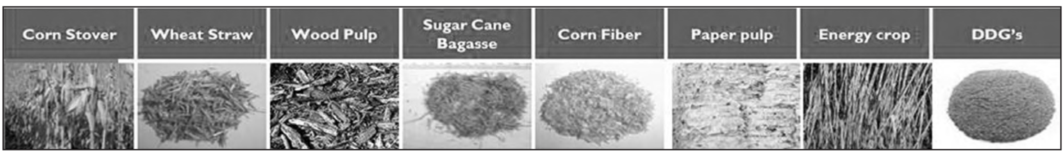

Fig. 15 *The raw materials used from CIMV process.*

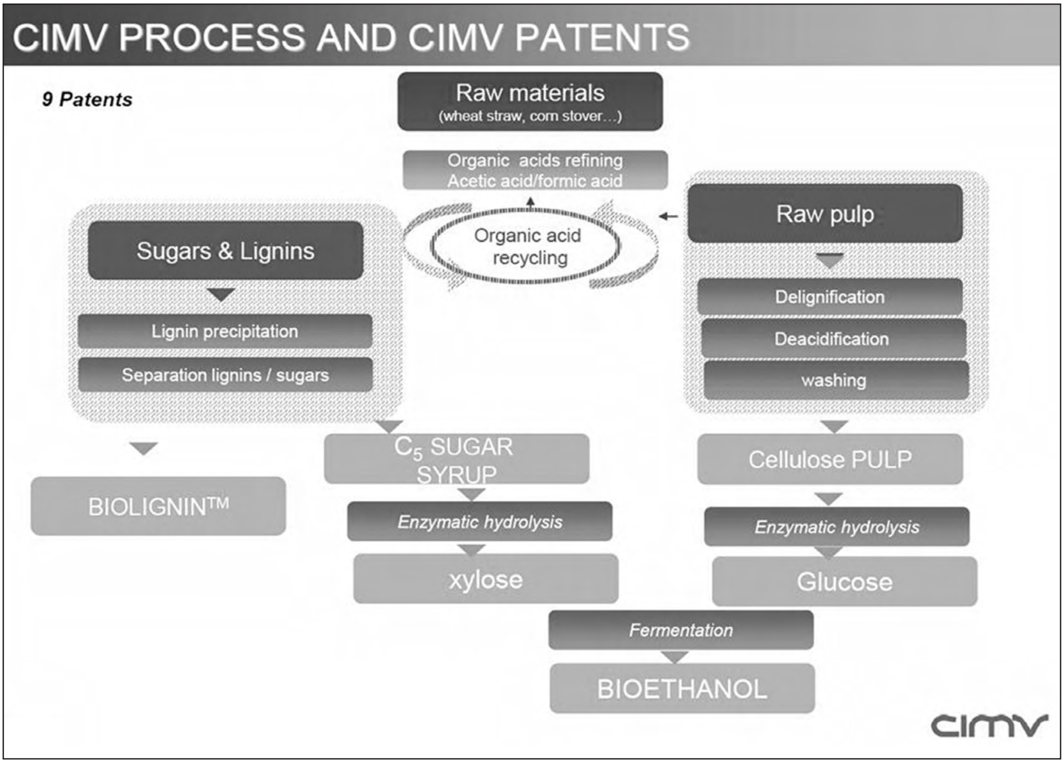

Fig. 16 CIMV process.

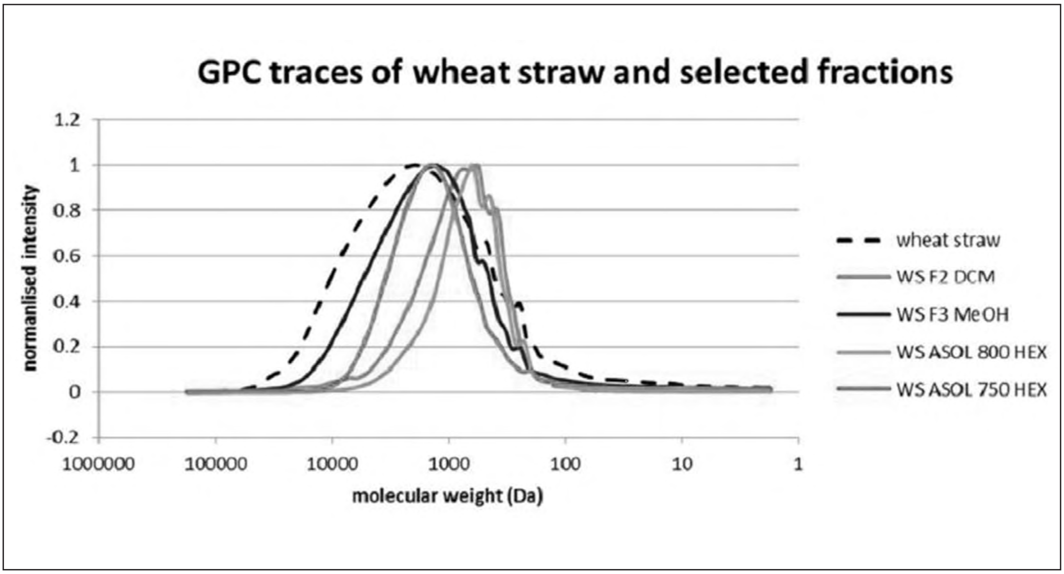

Fig. 17 Functionalization of lignin.

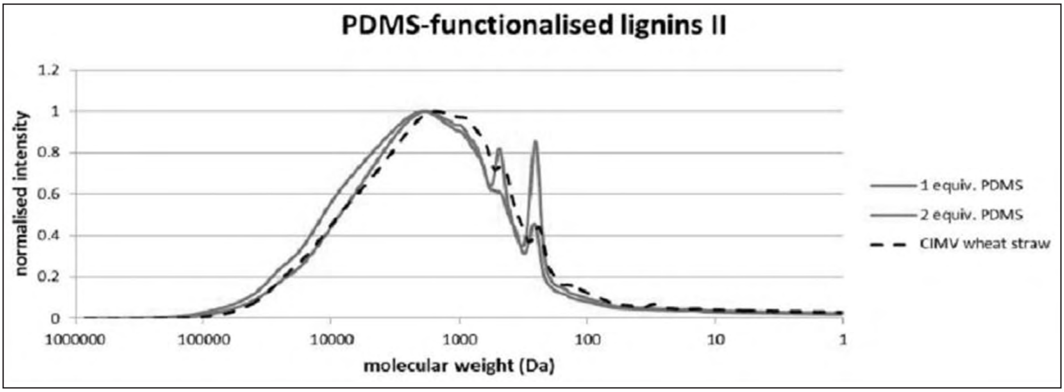

Fig. 18 *PDMS functionalized lignins.*

The use of lipoxygenases allowed an enzymatic functionalization with a regiochemistry that was not achieved through the chemical functionalization.

The different enzymes used to produce and functionalize the biolignin oligomers, realized and produced by the Dyadic Netherlands BV team (Fig. 19) (www.dyadic.nl), have been presented from Martijn Koetsjer by the topic: *The Cl-Enzyme Platform for the Production of Industrial Enzymes*.

Fig. 19 *DYADIC Team.*

The Dyadic library has composed by more than 100 functional single homologous enzymes, among which a special laccase has been developed in the Bio-Mimetic project. Laccases, in fact, are able to catalyze the oxidation of lignin phenols. However, by the Dyadic Cl methodology it is possible to screen single target enzymes (Cl-library) from a defined enzyme mixture, producing relatively *pure single* enzyme or dedicated enzyme combinations (Fig. 20).

It is however to underline that the enzymes developed in the project, could be valuable tools in the valorization of lignin biomass, also outside the scope of the Bio-Mimetic project, such as the production of paper pulp, textile, food or bio energy.

The topic presented by MAVI: *Innovation in Cosmetic Dermatology and Medical Science for a Greener Planet* has gone into the hearth of the project to produce *green* cosmetics and non-woven beauty masks. Thus, block co polymeric micro/nanoparticles of CN-lignin and CN-Hyaluronan were produced and embedded into cosmetic gels and tissues.

The final products were verified for their safeness and effectiveness in the department of experimental dermatology 2nd University of Naples, Italy, while size and stability of the micro/nano particles and the elasticity and strength of non-woven tissues were controlled at the Engineering department of La Sapienza University, Rome, Italy.

The obtained block polymeric CN-HA nanoparticles, entrapping different active ingredients, have shown the interesting property of increasing *in vitro* the collagen synthesis in culture of fibroblasts (Fig. 21), having also an anti-aging activity *in vivo* (Fig. 22).
On the other side the block co-polymeric nanoparticles CN-lignin, embedded into cosmetic gels or entrapped into CN fibers of non-woven tissues, have shown to increase the skin synthesis of defensines (Fig. 23) reducing the release of metalloproteinases (Fig. 24).
Finally, the *in vivo* activity of the beauty masks seems capable to reduce the skin face wrinkling, slowing down the black spots formation.
As it has been supposed in fact, the chemical and porous structure of the non-woven tissue seem to promote the adhesion of stem or somatic cells, ensuring all the metabolic processes necessary for the effective proliferation and differentiation of the cells. Thus, the anti aging and anti-inflammatory activities verified both *in vitro* and *in vivo*, have shown a high effectiveness without providing any toxic effects.
The innovation achieved by MAVI is related to the possibility of using CN-Lignin or CN-HA as both active ingredients and carriers to be embedded into micro/nano emulsions and entrapped into natural fibers to produce innovative cosmetic emulsions and non-woven tissues characterized by high effectiveness and safeness.

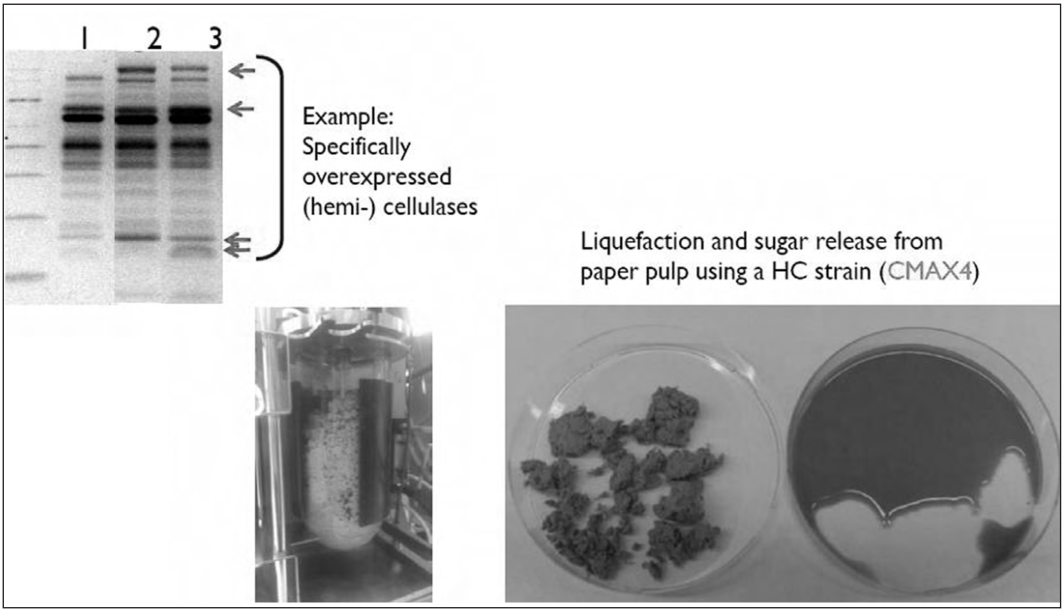

***Fig. 20** HC strains used to produce tailor-made enzyme mixtures.*

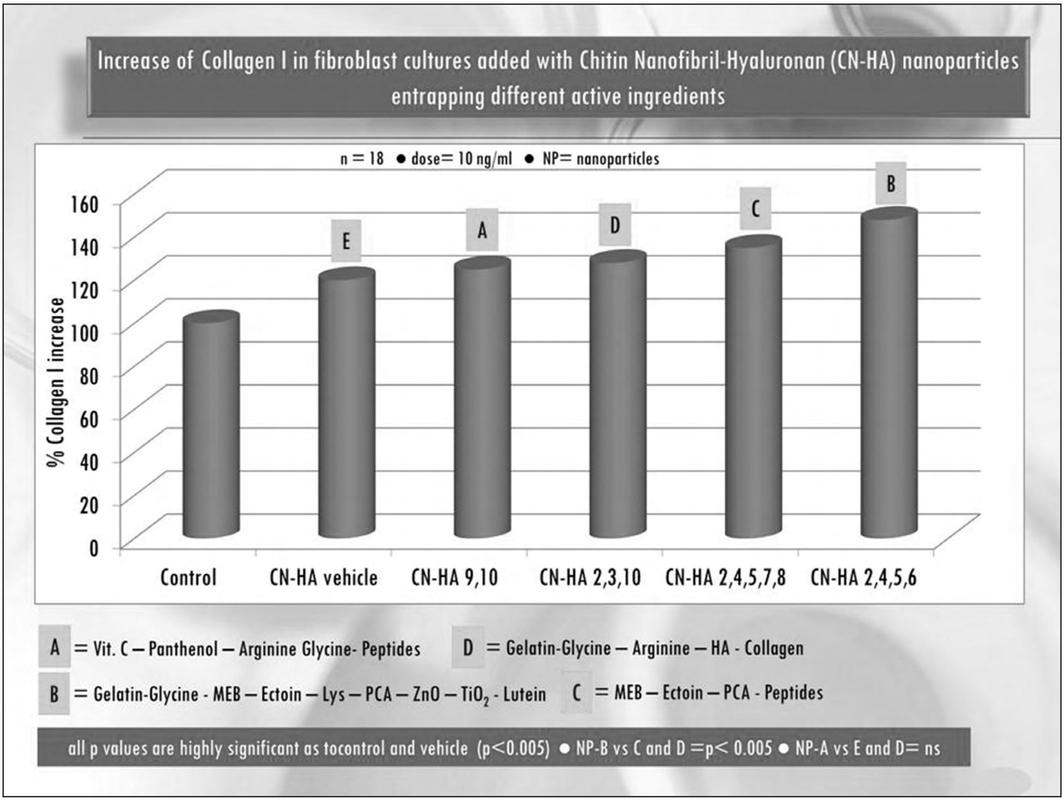

***Fig. 21** Increase of collagen synthesis in a fibroblasts culture.*

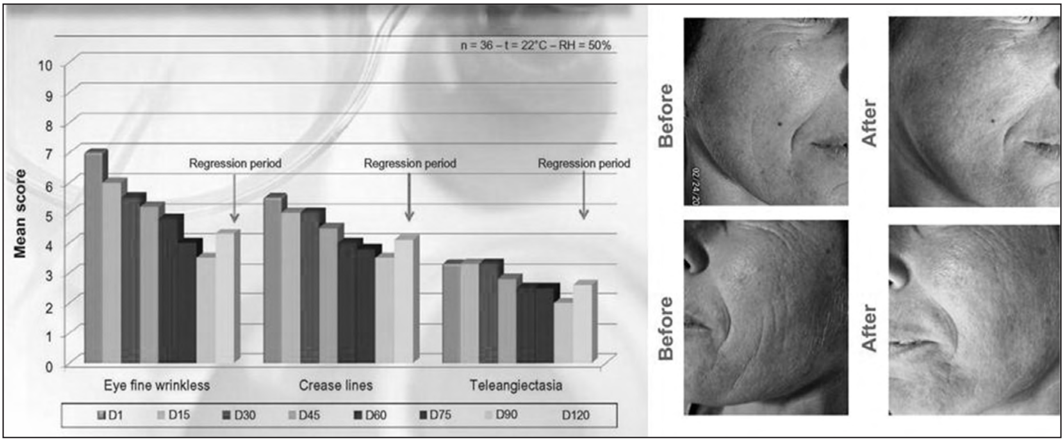

***Fig. 22** Antiaging activity of CN-HA nanoparticles.*

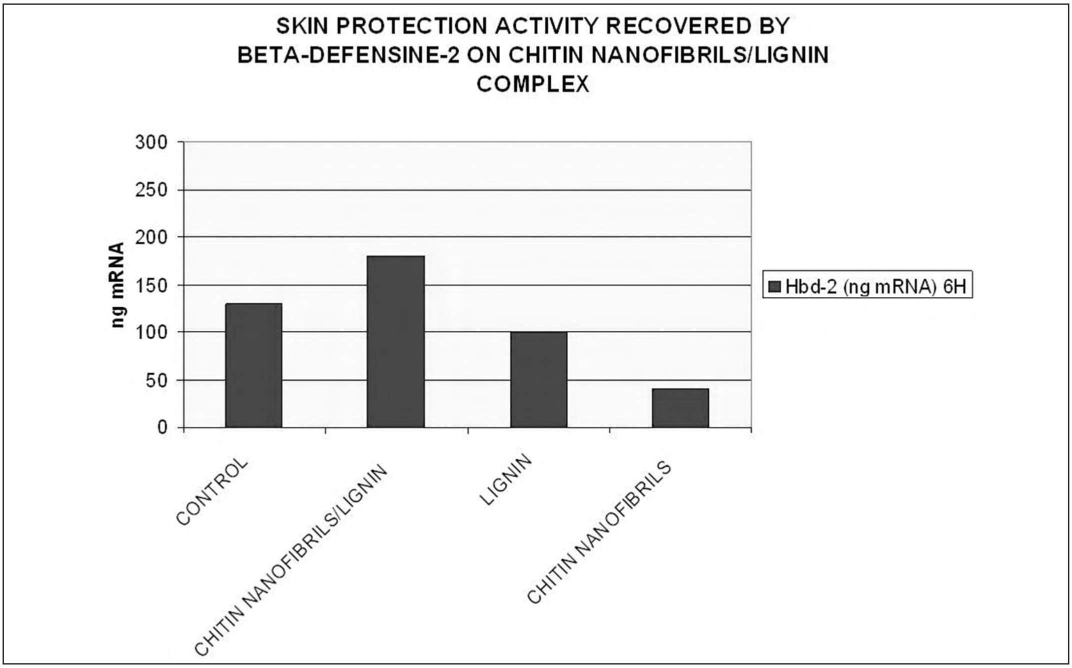

Fig. 23 *Defensine increase in a keratinocytes culture.*

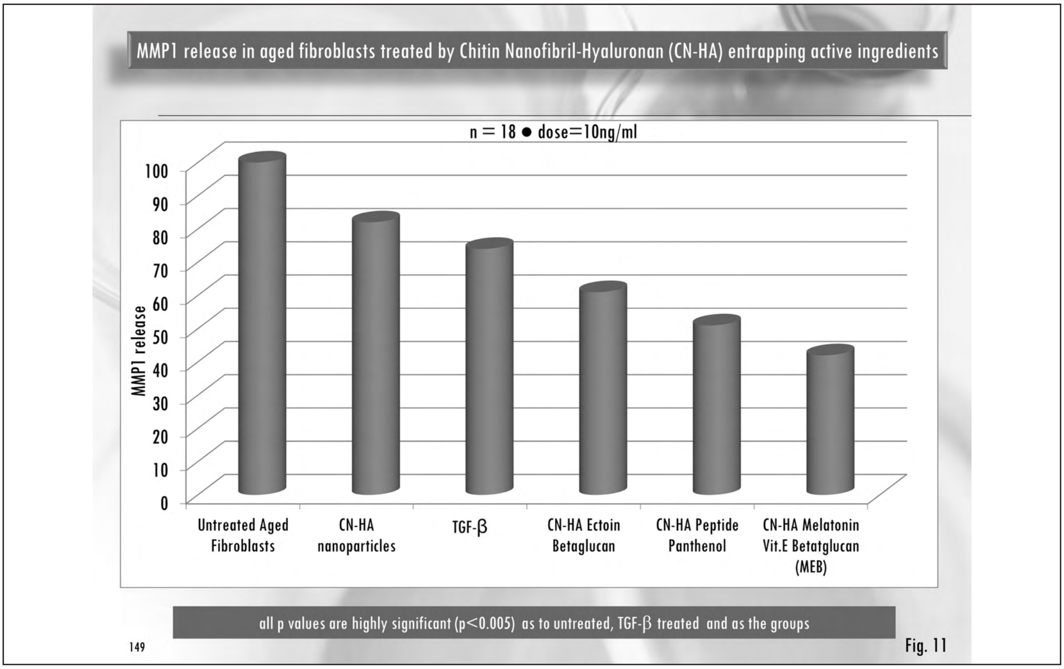

Fig. 24 *Release of metalloproteinase in a fibroblasts culture.*

Using the COSMO engineering approach coarse-grained, Culgi developed molecular models (Fig. 25) to be able to perform dissipative particle dynamics (DPD) simulations that were in turn verified by all-atom molecular dynamics simulations (Fig. 26). Once the coarse-grained parameterization and verification were performed actual DPD simulations of the interaction with surfaces and interaction between oligomers were performed (Fig. 27).

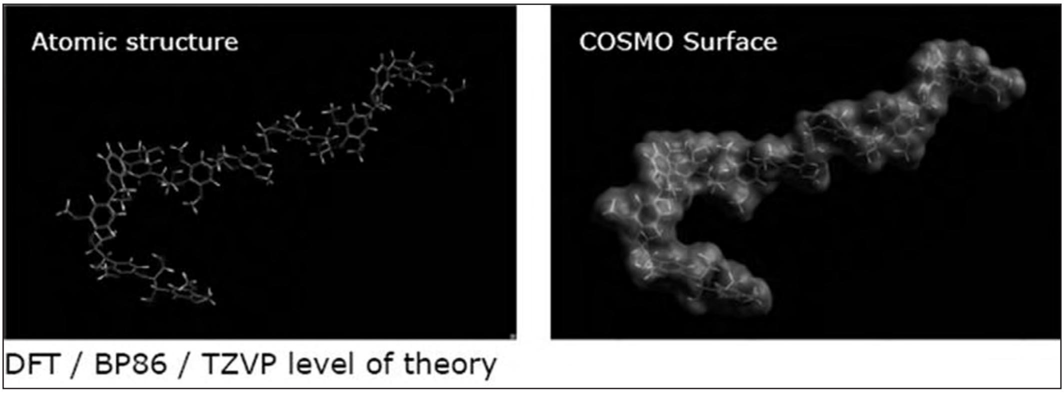

Fig. 25 *Computation of the coarse-grained interaction parameters was performed with COSMO engineering approach.*

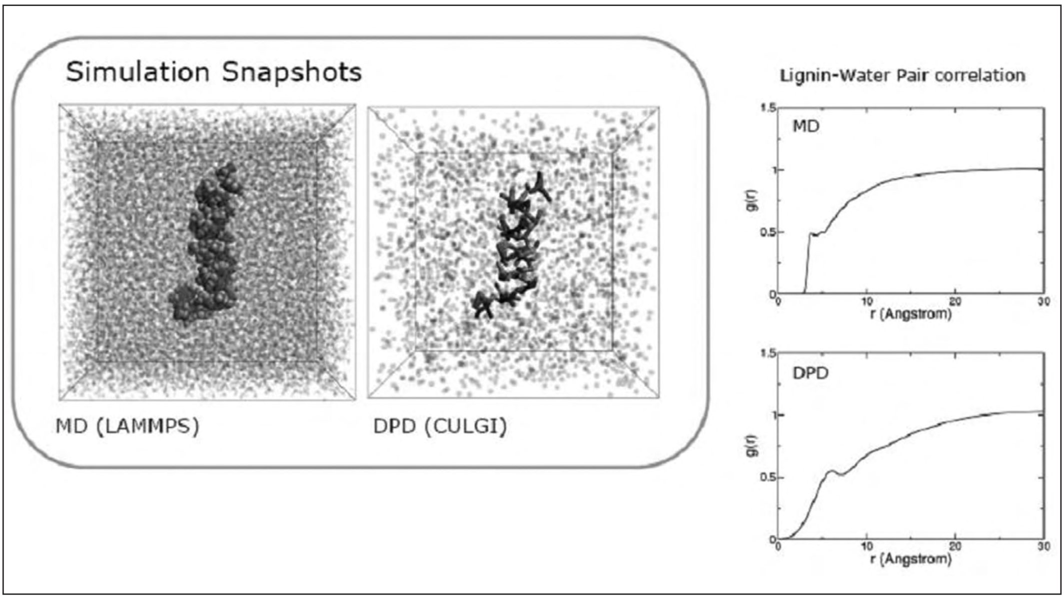

Fig. 26 *Simulation of lignin-water oligomer in an aqueous solution.*

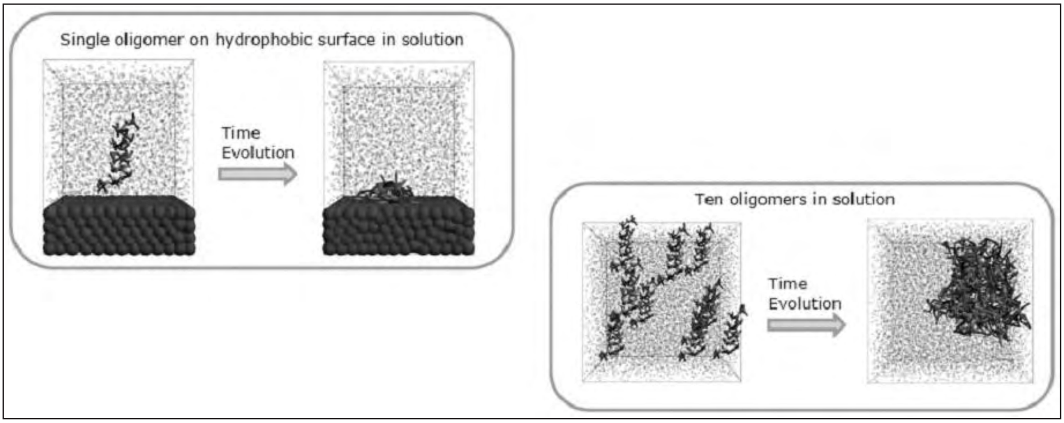

Fig. 27 *Simulation of interaction with surfaces and interaction between oligomers.*

In conclusion, based on 2D-NMR data, the Culgi team in collaboration with Fraunhofer IFAM have realized a new simulation model to be used in an R&D environment, capable to specially address the interaction of active agents derived from bio-based feed stocks, as lignin, with surfaces such as cotton, glass and plastic. Thus, the fragmentation algorithm and the parameterization scheme used could handle the complex chemical diversity of lignin, while the logP and coarse-grained simulation results indicate that unfunctionalized lignin is not water soluble. IFAM's goal has been to identify the detailed molecular mechanisms of lignin-based compounds, predicting their interaction with polymers and different surfaces in the field of detergents and gels for home care and cosmetics. As final part of the morning meeting, Patrizia Circelli from Ciaotech/PNO (www.ciaotech.com) gave a clear picture on the Horizon 2020 (Fig. 28), underlining the 3 Pillar structure on which the EU Research project is based (Fig. 29). Soon after Anju Brooker, coordinator of the Biomimetic 3-year project, thanked all the participants involved in these interesting studies and all the attendants at the meeting. During the afternoon Laurence Stamford of the University of Manchester (www.manchester.ac.uk) has shown how to use the CCaLC, software (freely available from www.ccalc.org.uk) that provides a simple user interface and access to a large amount of data licensed from commercial databases. CCaLC allows user to map the entire life cycle of their products, including raw material acquisition, processing steps, waste management, storage use and transport giving the possibility to SMEs also to conduct their own LCA without need to outsource.

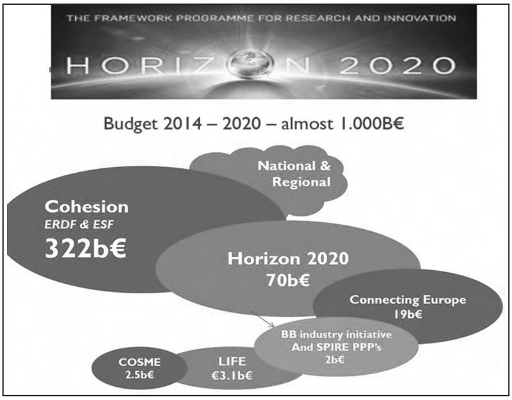

Fig. 28 *Horizon 2020 budget.*

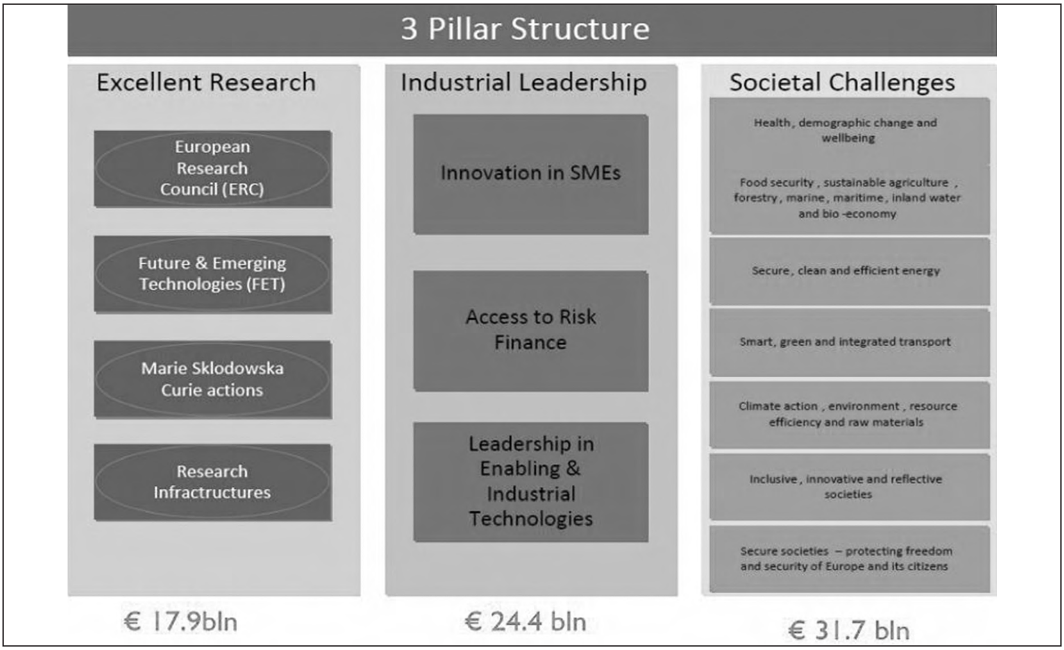

Fig. 29 *The 3 pillars structure of EU investments.*

CONCLUSION

Bioeconomy and sustainable industry are based on the use of innovation in biological science and nanotechnologies to create economical activity and public benefit. However, a growing of world population requires increased health services and more resources such as food, animal feed, fibers for clothing and housing, and sources of a *green* energy and bio-chemicals for manufacturing.

By 2050, in fact, the world population is estimated to reach about 9 billion, compounding the need for food and goods! Thus, the industrial and environmental nanobiotechnology can contribute to make production processes more resource efficient and environmental friendly, developing more sustainable bio-based products as for the Bio-Mimetic project, by which different and innovative household products and skin care cosmetics have been realized by biological technologies, without the use of petrol-derived chemicals.

This is also the reason why the final meeting has been held into an historical location to underline that the progress has to be increased on the base of technological innovations without forget but using the experience of historical heritages, as reported in the final photo of the scientists involved in the Bio-Mimetic project (Fig. 30).

Fig. 30 *The Bio-mimetic Team at Villa Mondragone.*

References

1) **IFAM (2014)** Chemistry of Natural Resources. Presented at 249th Meeting, 22-26 March, Denver, Colorado, USA.
2) **UNITO (2013)** Biorefinery analytics. Presented at COST FP Meeting, Finland and Turku.
3) **MAVI (2015)** A Green Bieconomy for a Sustainable Cosmetic Dermatology. Presented at the 11th International Congress of Cosmetic Dermatology, 26-28 November, Beijing, China.
4) **CULGI (2014)** A fragment-based Computational Approach to Study the Phase Behavior of Biopolymers. Presented at 248th ACS National Meeting, 10-14 August, San Francisco, California, USA. All simulations presented in this paper were performed wih Culgi 8.0 and 9.0 (Culgi B.V., Leiden, The Netherlands).
5) **CTETCH (2014)** Nanotechnology. Presented at NANOTECH Italy, 26-28november, Venice, Italy.
6) **CIMV (2015)** Influence of organosol process parameters on lignin structure. Industrial Crops and Products.
7) **P&G (2015)** Internal section and management review Meetings, Brussels,10 February.

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SYMPOSIUM
PROGRAM PLAN
12TH INTERNATIONAL CONGRESS OF COSMETIC DERMATOLOGY

	Saturday 2 April 2015		
07.00 – 08.00	Registration		
08.00 – 08.30	Opening Ceremony		
PLENARY SESSION	**What's New in Cosmetic Dermatology**		
08.30 – 09.00	New Horizon in Cosmetic Dermatology : Prof. Pierfrancesco Morganti		
09.00 – 09.30	Trends and Future in Skin Aging Treatment :		
09.30 – 10.00	Acne : Prof. Giuseppe Micali		
10.00 – 10.30	Coffee Break		
SYMPOSIA 10.30 – 12.00	**I. Acne**	**II. Recent Advances in Botox and Filler**	**III. Aging Skin Update**
	Update on Pathogenesis - Prof. Dae Hun Suh	Recent advances in Botox	Stem Cell for Aging Skin – Dr. Yohanes Widodo
	Dermocosmetics in Acne – Prof. Giuseppe Micali	Recent advances in Filler	Hormones for Aging – dr. Edwin Djuanda
	International Consensus in Acne Management – Dr. Cheong Wai Kwong	Filler Application	Aging and Grey Hair: News from Melanocyte Biology and Clinical Practice – Prof. Torello Lotti
	Keefektifan Krim Nicotinamide Plus (ABA+ZINK) Sebagai Terapi Adjuvan Krim Adapalen Pada Pasien-pasien Acne Vulgaris Moderat di Indonesia (Uji Klinis Acak, Tersamar Ganda, Multisenter) – dr. Yulia Farida Yahya	How to Treat Lines and Folds – dr. Lis Surachmiati	PRP + Fat Grafting – Dr. Alfredo Callanta (tentative)
12.00 – 13.00	Lunch		
SYMPOSIA 13.00 – 14.30	**IV. What's New in Cosmetics**	**V. New Update on Light Sources in Dermatology**	**VI.Antioxidant Update**
	Emerging Cosmetics and Cosmeceuticals – dr. Sjarif M.W.	Phototherapy for Rejuvenation – Dr. Henry W. Lim	Controversies in Antioxidant Pros and Cons – Megalife
	Enhancement of Topical Delivery of Drugs – HIKI	Phototherapy for Acne Vulgaris – Dr. Keyvan Nouri	The Role of Antioxidant in Acne Management – Dr. Sewon Kang
	Herbal Cosmetics – Dr. rer.nat. Anna Setiadi Ranti, Apt.	PDT for Aesthetic Indication – Dr. Henry Lim	Antioxidant in Aging Skin – Prof. Theresia
	The Side Effect of Cosmetics – Prof. Dr. Retno Widowati	Indication – IPL for Aesthetic – TBA	Antioxidants and Low Dose Oral Cytokines and Growth Factors - The Novel Paradigm in Photoprotection and in Photoaging. - Prof. Torello Lotti
14.30 – 16.00	**VII. What's New in Laser & Light**	**VIII. Nanotechnology in Cosmetics**	**IX. Free Paper Communication**
	Laser for Tattoo Removal – dr. M. Yulianti Listiawan	Technological Aspects of Nanocosmetics – Ketua HIKI Batam (Djayadiningrat)	

	MERZ - Ulthera	Plus and Minus in Nanocosmetics – dr. Sjarif MW	
	Laser for Hyperpigmentation Disorder – Prof. Goh Chee Leok	Nanotechnology in Cosmetic Dermatology – Dr. Vladimir Yudin	
	Laser for Hypertropic Scar and Keloid - TBA	Indonesian Regulation on Nanocosmetics - BPOM	
16.00 – 16.30	Coffee Break		
16.30 – 18.00	**Ballroom 1**	**X. Hair Disorders**	**XI. Free Paper Communication**
		Evaluation and Diagnosis of Patient with Hair Loss – Dr. Rataporn Ungpakorn	
		Update on Dandruff Management – Dr. Dae Hun Suh	
		Hair Transplant – Dr. Gunawan Budisantoso	
		The Latest Treatment of Alopecia – dr. Iwan Trihapsoro	

	Sunday 3 April 2015		
PLENARY SESSION			
08.30 – 09.00	Challenges for Dermatologist in Cosmetic Dermatology : Prof. Xing Hua Gao		
09.00 – 09.30	Melanocyte Biology: Prof. Amit G. Pandya		
09.30 – 10.00	Regulation and Ethical Aspects of Cosmetic Dermatology : Dr. Nasser		
09.30 – 10.00	Coffee break		
SYMPOSIA	**XII. Acne Scar Management Update**	**XIII. Hyperpigmentation Update**	**XIV. Free Paper Communication**
10.00 – 11.30	Pathogenesis of Acne Scars – Dr. Sewon Kang	Update on Management of Hyperpigmentation Disorder - Prof. Amit G. Pandya	
	Treatment of Acne Scar – Prof. Goh Chee Leok	Combination Peel for Hyperpigmentation – dr. FX. Hanny Suwandhani	
	Sunscreen and Acne – dr. Irma Bernadette, SpKK(K)	Management of Erythema and Hyperpigmentation Post Acne – dr. Lili Legiawati	
	Pros and Cons Moisturizer for Acne Prone Skin – dr. Rataporn Ungpakorn	Pro and Cons in Hyperpigmentation Management – dr. Rointan Simanungkalit	
11.30 – 12.30	Lunch		
SYMPOSIA 12.30 – 14.00	**XV. Pharmacology of Cosmetic Agent**	**XVI. Hypopigmentation Update**	**XVII. Free Paper Communication**
	Pharmacology of Cosmetic Ingredients - Prof. Widji	Vitiligo Update – Prof. Xing-Hua Gao	
	Green Ingredients in Cosmetic Dermatology – Prof. Morganti	Other Hypopigmentation Than Vitiligo – Dr. Tjut Nurul Alam	

	How to Set Up and Successfully Run An Industrial Cosmetics - dr. Retno I. Tranggono	Punch, Blister and Cellular Grafting for Vitiligo – Prof. Amit G. Pandya	
	Men's Cosmetic Update- dr. Reti Hindritiani	Melanocyte Response to Therapeutic Interventions – Prof. Amit G. Pandya	
14.00 – 15.30	**XVIII. Skin Tightening**	**XIX. Aging Skin Update**	**XX. Miscellaneous**
	Threadlift: Does It Really Work? – dr. Abraham Arimuko	Current Practice in Management of Aging Skin – dr. Sri Aryani Sudharmono, SpKK(K)	Laser for Nail Disorders – Dr. Keyvan Nouri
	Mini Facelift – dr. Syarief Hidayat	Other Skin Problem Possibilities in Aging Skin – dr. Susanti B	Picosecond Modalities for Pigmentation - Neoasia
	Laser Skin Tightening – dr. Soedarto Oeria	Kudzu Acetic Acid: A New Natural Peel for Facial Rejuvenation – Dr. Kim Won-Serk	Management of Acne Scar with Fractional Devices - Neoasia
	Neoasia	Growth Factor – Dr. Ahmed Al Qahtani	Metals in Cosmetic Ingredients – dr. Sondang P. Sirait
15.30 – 17.00	**XXI. Moisturizer**	**XXII. Cosmetic Dermatology for Skin Color**	**XXIII. Invasive Procedures in Cosmetic Dermatology**
	Molecular Aspect of Skin Hydration - TBA	Traditional Eastern Cosmetic – dr. Anis Irawan	Face Anatomy Unit for Flaps and Grafts - dr. Sri Lestari
	How to Choose Moisturizer - TBA	Cosmetic for Aging Skin - TBA	- dr. Susanti Budiamal
		Cosmetic for Baby and Children - Unilever	Bromhidrosis - dr. Indah Julianto
		Farmasi - TBA	
17.00 – 17.30	Door Prize and Closing Ceremony		

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Chiuso in tipografia: Giugno 2015
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