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Use of CHITIN Nanofibrils from Biomass for an Innovative Bioeconomy

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Outline:

Introduction

Managing natural resources in the right way is a vital start to reduce environmental footprints and promote a healthy bioeconomy. Turning raw materials into consumer products, in fact, generates waste both from agricultural and manufacturing [1] (Fig. 1.1). But the waste depends on the technology used, the nature of raw material processed and how much of it is discarded at the end of the chain. However, it is necessary a global new vision of our living, by producing and consuming goods and services in more efficient and less pollution ways [1].

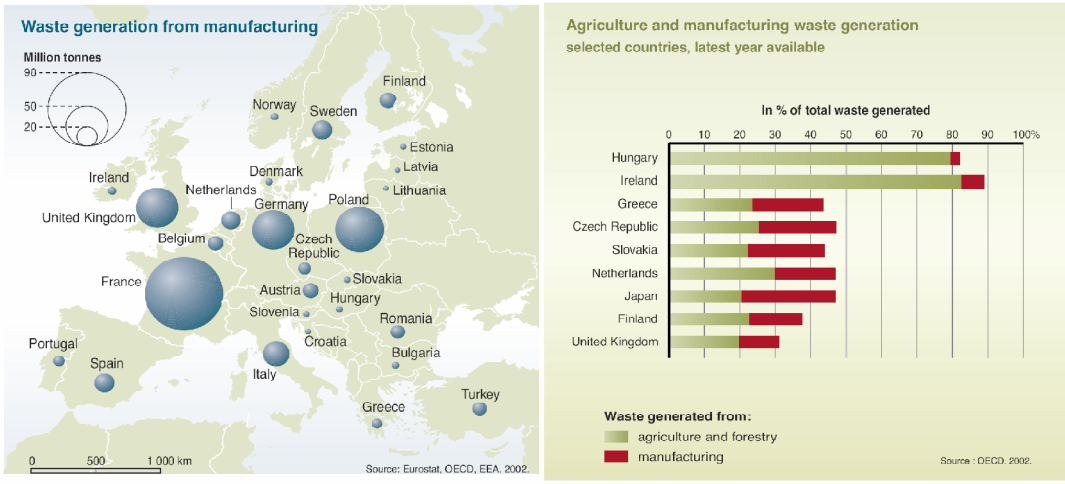

FIGURE 1.1
Left: waste generation from manufacturing. Right: agriculture and manufacturing waste generation

First of all, it is important to consider the full life cycle of products, to get a comprehensive overview of the amount of waste generated together with its financial and environmental cost (Fig. 1.2) [2].

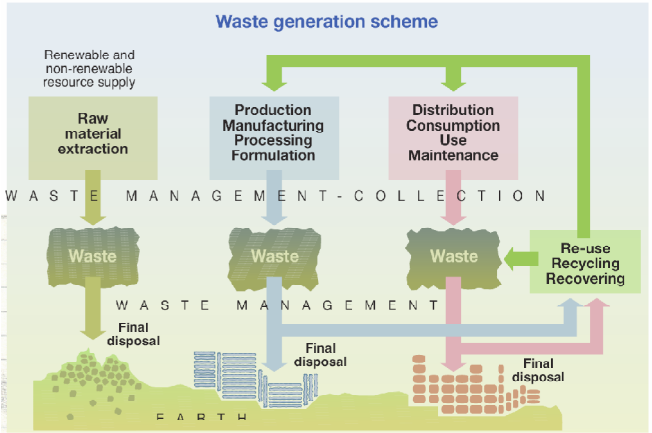

FIGURE 1.2
Waste generation scheme. Source: CECO 2002

Secondarily, it is important to underline that while waste is generated in all sorts of ways, its composition and volume largely depends on both consumption patterns and the industrial and economic structures in place [3]. Moreover, it has not to be forgotten that waste-contaminants in the soil and groundwater can harm plants when they are taken up through their roots, as well as can impact human health, and eating plants or animal that have accumulated soil contaminants. In addition, air and water pollution can cause respiratory and other adverse health effects, when absorbed from the respiratory system or the skin. Last but not least, it is to underline how the global fast consumption of key raw materials is quickly impoverishing our planet of its natural resources. At this purpose, over the 20-year period ending in 1994, the world population increased by 40%, while the world consumption of cement increased by 77% and plastics by about 200% [2, 3].

Thus today, the ecological footprint, measuring the amount of the global productivity necessary to support the relative consumption of goods and production of waste, is exceeding the amount of the available raw materials. It is, therefore necessary to use by-products coming from both industry and agriculture, reduce consume of water and energy, contemporary decreasing the amount of waste generated. That means changing our consumption patterns, for example, by choosing products that use recyclable material, marketing fresh produce instead of canned food, using less packaging and easily recyclable containers [4]. Recycling, collecting, processing, and reusing waste materials become, therefore, a must of our society.

According to UNEP [2], it has to underline that between 1993 and 2001 the amount of waste crisscrossing the globe increased from 2 million tons to more than 8.5 million tons, e-waste representing the biggest and fastest growing manufacturing by-product on the move (Fig. 1.3).

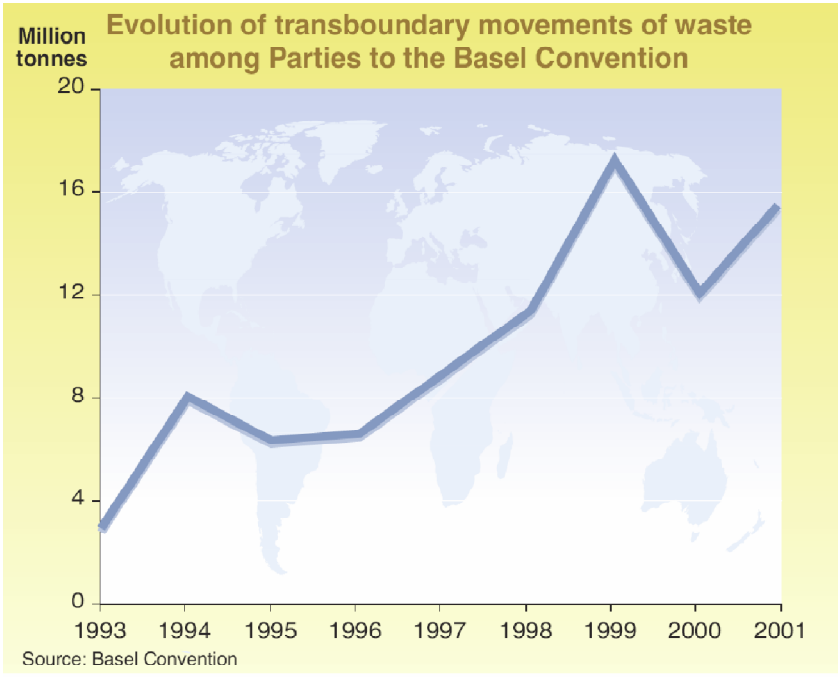

FIGURE 1.3
Evolution of transboundary movements of waste among Parties to the Basel Convention

According to US Environmental Protection Agency [5], it is estimated, for example, that there are over a billion personal computers in the world with an average life span of only 2 years, while in the USA alone there are over 300 million obsolete computers. In addition, disposal and treatment of waste can produce emissions of several greenhouse gases (GHGs), such as methane and carbon dioxide. Thus, waste prevention and recycling help address global climate change by also decreasing the amount of GHGs and saving energy [5, 6].
In conclusion, addressing all these challenges properly requires understanding of a major use of the biomass by modern nanobiotechnologies for preserving the natural habitat and biodiversity of our planet (Fig. 1.4).

FIGURE 1.4
The planet biodiversity

The forestry sector as well as the fishery's biomass can provide, in fact, great potential for the cascading use of renewable raw materials to produce a wide range of innovative value-added products. This is the reason why, an increased focus on entrepreneurship transnational sciences and regulations, accompanied with technology transfer, can help move beyond this goal.
According to the EU programs "the transition from a dependence on fossil fuels, to a situation where agriculture not only will continue to provide food security but also biomass as a renewable raw material for industry, has to be the basis of the coming integrated bio-economy" [7].

Chitin from biomass

Chitin, as principal structural polysaccharide of crustaceans (lobsters, shrimps and crabs) and cell wall of fungi, is a natural occurring fibre-forming polymer that plays a protective role in many lower eukaryotes similar to that of cellulose in plant. The molecular chains of chitin are associated

together in a highly ordered manner to form a crystallite of a mean diameter of 2.8nm. In the alpha-chitin the molecular chains of these crystallites, involving ~20 chains with the dimensions of 2.8 x 2.8 mm^2, are arranged in an anti parallel form and packed in a hexagonal or pseudo hexagonal form [8].

As second most abundant organic compound after cellulose, it has been estimated that 10^{10} 10^{12} tons of chitin are biosynthesized each year [9]. Because of ~ 40-50% of crustaceans total weight goes as waste, these by-products result in collection, disposal and pollution problems [10, 11].

Thus the necessity of a proper use of this waste material that may allow recovery of value added goods in expanding area of biomedicine, pharmaceutical, food technology, agro-bioscience and cosmetic dermatology [12-14].

Chemically chitin is made of N-acetyl glucosamine residue linked through Beta-1,4 covalent bonds, while its deacetylated form is known as chitosan, and its purest crystalline and patented form is named Chitin Nanofibril (CN) [15].

Due to their biocompatible, anti microbial and nontoxic properties, both chitin and chitosan have been widely studied for applications as biomedical and cosmetic/drug delivery materials [16-20]. Taking into account the role played by chitin in different biological structures, its metabolic process of biosynthesis and degradation results essential for different morphogenic events. On one hand, it may act as substrate for the production of proteoglycans which, for example, gives hydrophilicity to cartilage and skin, as well as it seems to be a promising biomaterial for tissue engineering and stem cell technologies [21]. On the other hand, looking to the molecular structure of this natural polymer, it possesses the same backbone of hyaluronic acid (HA) (Fig. 1.5), which as important component of the skin Extra Cellular Matrix (ECM), helps to provide mechanical support and regulation to cell activities.

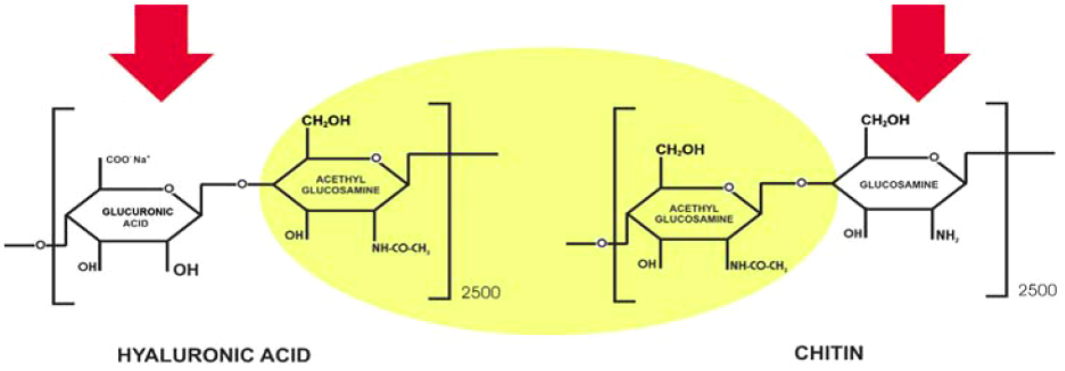

FIGURE 1.5
Chitin and Hyaluronic Acid have the same backbone

These are the reasons why CN, produced as the needle-like polymer purest crystallite (Fig. 1.6), promises to change the use of chitin for biological, biotechnological or biomedical applications, such as repairing wound healing and burns or restoring healthy tissues.

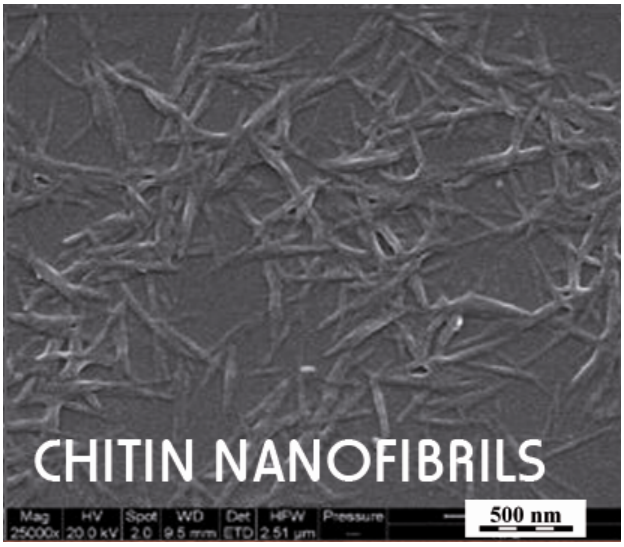

FIGURE 1.6
Chitin Nanofibrils at TEM

Chitin Nanoparticles

Chitin Nanofibril appears as a single crystal with the medium dimension of 240x7x5 nanometers (nm) and a medium weight evaluated to be equal to 0.074x 106 ng. At pH between 2 and 4 one milliliter of the aqueous colloidal suspension, obtained by the productive process, contains about 300 trillions of nanocrystals enveloped with water molecules, which prevent their flocculation. The protonation of free amino groups present on the CN surface provides the positive charges of this crystalline polymer [22].
This is the reason why CN, bonded to a negatively charged polymer obtained from the plant biomass, has the capacity to form nanolamellae or nanoparticles (Fig. 1.7) which, embedded into nanoemulsions produce innovative cosmetics.

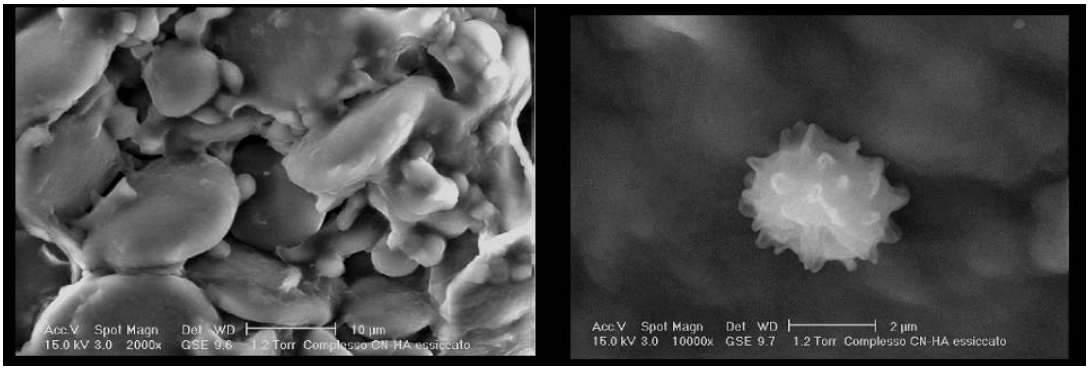

FIGURE 1.7
Nanolamellae and Nanoparticles of CN-HA at SEM

When electrospun together with other polymers, this natural crystal can produce nanofibrous matrices (non-woven tissues) capable to mimic the structure and biological function of ECM (Fig. 1.8) [23].

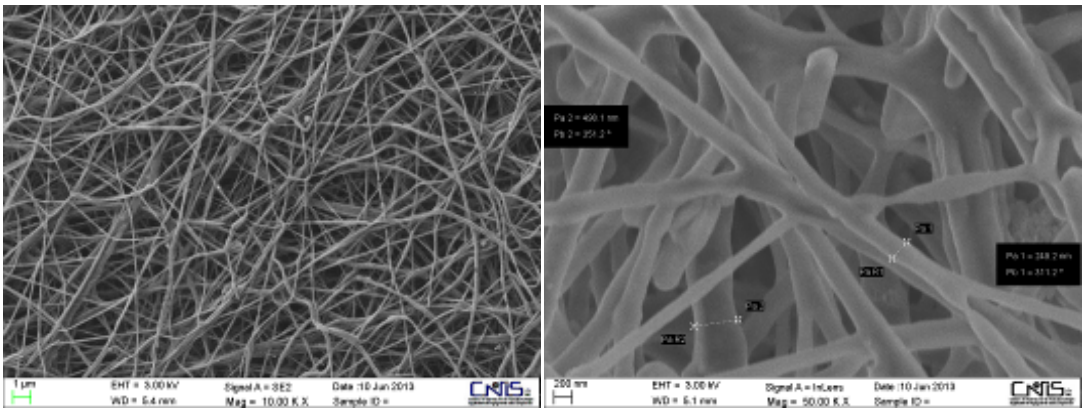

FIGURE 1.8
The electrospun Chitin Nanofibril shows spaces mimicking the ECM organization

The ~15,000 amino groups positively charged, covering the surface of CN crystallites, give the possibility to produce block co-polymeric nanoparticles by a self-assembling with electronegative polymers, as hyaluronic acid or lignocellulosic macromolecules. The self-assembled nanoparticles, obtained by the gelation method (fig 1.9), are molecular assemblies that are formed spontaneously by mixing water suspensions of electropositive macromolecules/polymers with electronegative ones.

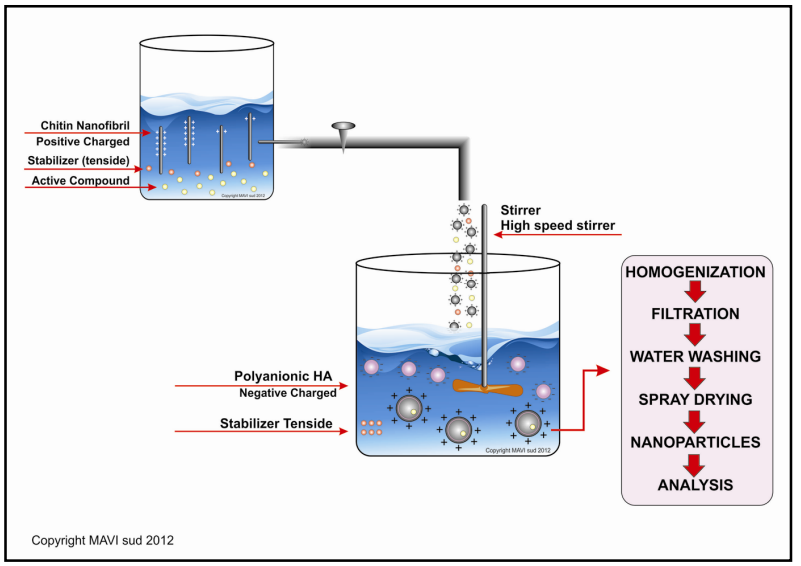

FIGURE 1.9
The gelation method to make the block-co-polymeric nanoparticles

The key idea of a self-assembly process is that the final structure is close to a thermodynamic equilibrium, which has to be obtained by the global methodology adopted. Moreover, during the preparation of particles one or more active ingredients may be embedded or adsorbed onto their surface, according to the adopted process parameters. It is interesting to underline that the nanoparticles made by our method, assembling CN with HA, have shown the capability to slowly release the entrapped lutein during 45 days (fig 1.10) [24].

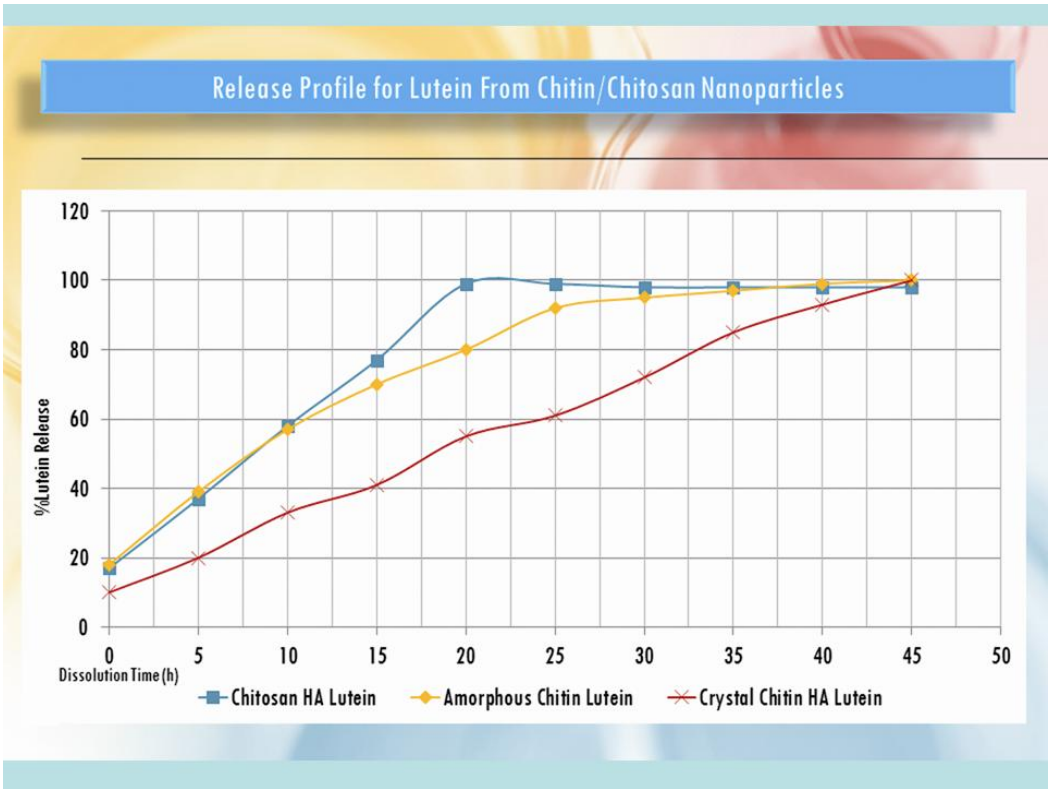

FIGURE 1.10
Release of Lutein entrapped by CN-HA

It has been also demonstrated that the rate of release could depend upon the nanoparticles size and the charges covering their surface (Unpublished data). On one hand, the release, in vitro, from smaller size was faster than those from the large size nanoparticles due to the larger surface area of contact with the dissolution medium.

On the other hand in vivo, it has been shown that CN-HA nanoparticles, whose periphery was covered by positive surface charges, had probably the ability to disturb the tight lamellar layer of the stratum corneum, enabling a better diffusion through the skin of the ingredient entrapped (Fig.1.11) [25].

The CN-HA mean size ,width distribution and zeta potential of nanoparticles were determined by a Zetasizer (Nano ZS model Zen 3600,Malvern Instruments, Worchester, UK) on samples dried by Buchi Mini B-190 spray drier (Flawil, Switzerland) and re-suspended in distiller water. The Scanning Electron Microscope (SEM/EDY, Philips XL30) was used to physically control their relative size [26].

It is interesting to remember that, as Nanoparticles move through the skin or the body they can be exposed to different biological micro environments, including the blood, the extra cellular matrix (ECM), the cytoplasm, and cellular organelles. Consequently, the interactions that occur at the nanobio interface may impact the function of bio molecules, cellular components and tissue structures, eliciting toxic responses [27]. This is not the case of CN-HA which are completely safe compounds metabolized to physiological compounds, normally present in our organism.

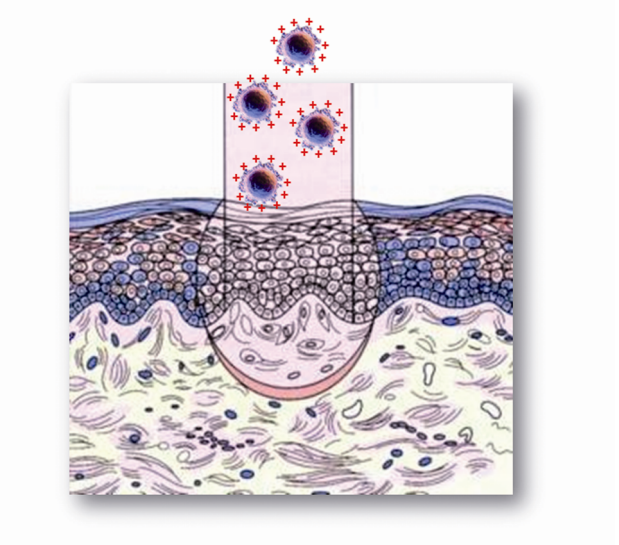

FIGURE 1.11
Space of penetration created by CN-HA nanoparticles positively charged on their surface

Electrospinning and Chitin Nanofibrils

Electrospinning is an electrostatic fiber processing developed for the generation of ultra thin polymer fibers with nanometer-scale diameters [28]. The fiber is electrospun when the electrical forces at the surface of a polymer solution or suspension overcome the surface tension and cause an electrically charged jet to be ejected. The union of the ejected fibers forms geometrical sheets with a morphology depending on the process parameters, solution concentration, applied field strength, and the feeding rate of the precursor solution.
Alternatively, nanoparticles can be entrapped not only into emulsion but also into fibers (a non-woven tissue) produced by the electrospinning technology.
By this technique it is possible to combine a different variety of polymers in an interesting, ease, and versatile way, useful to produce nanofibers, at low cost and high speed, by the use of a vast selection of materials.
Additionally the electrospinning allows control over fiber diameter and porosity to obtain a nanofibrous structure, characterized by high and regular porosity microstructure and arrangement [29]. The possibility to combine different polymers, particulate nanofillers, and biological active ingredients has leaded our group to develop new nanocomposites mimicking the skin ECM. These new matrices have been used to make innovative advanced medications by the use of CN, bonded with Ag+ ions by an electrospinning anti-bacterial pre-processing (Fig.1.12).

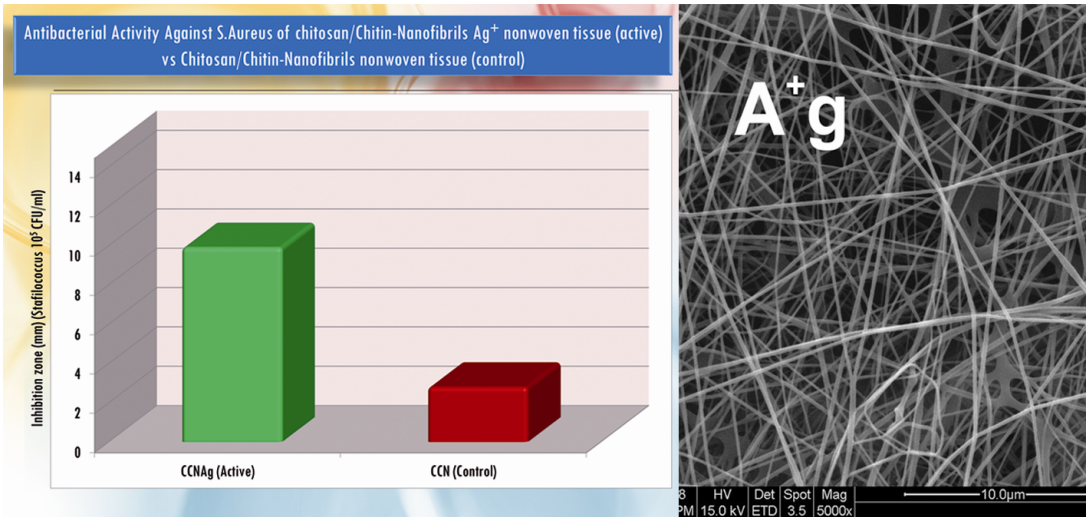

FIGURE 1.12
Antimicrobial activity of CN-Ag

By this functionalization with the elemental silver, it has been possible to obtain good anti microbial properties, as reported by an in vitro study showing the reduction of the skin burden bacteria (Fig. 1.13) [30].

Assessment of the Antibacterial Activity of the Nanocomposite CN-CS and CN-CS-Ag Films after 18 h Incubation at 36°C on Agar Containing the Culture of Bacteria Taken from Bioburden Skin Tissue

Sample	Bacterial Growth (CFU/g)
Agar + culture of bacteria from bioburden skin tissue (CB)	10^7
Agar + CB + CS-CN nanocomposite film	10^5
Agar + CB + CS-CN-Ag nanocomposite film	10^3

FIGURE 1.13
Antibacterial activity of CN-Ag on skin bioburden bacteria

On the other hand, a recent in vivo study has underlined that the combined activity of silver (linked to CN chain in ppm concentration) and chitin nanofibrils (bonded to lignocellulosic polymers) result in a faster reduction of the bacteria accompanied by the quick regeneration of skin affected by burn (Fig. 1.14) [31]. Thus, by virtue of the available high surface/volume ratio supported by micro/nano fibers used to produce the non-woven tissue and the silver incorporated in low quantity into CN, the final product seems to offer a very promising efficiency in removal skin microorganisms, minimizing the formation of biofilm on the surface of the burden wounded skin and contemporary presenting a very low toxicity.
These and other studies have been developed by our group to control the capacity of electrospun CN to make advanced non-woven tissue capable to repair the wounded or burned skin. Other parallel studies have gone in the direction of making stable CN nanoparticles to be embedded both

into normal cosmetic emulsions and/or natural fibers [unpublished data]. As previously reported, these nanoparticles were obtained simply mixing the electro positive CN with other electronegative polymers or other large molecules of natural origin by the use of the gelation method [32].

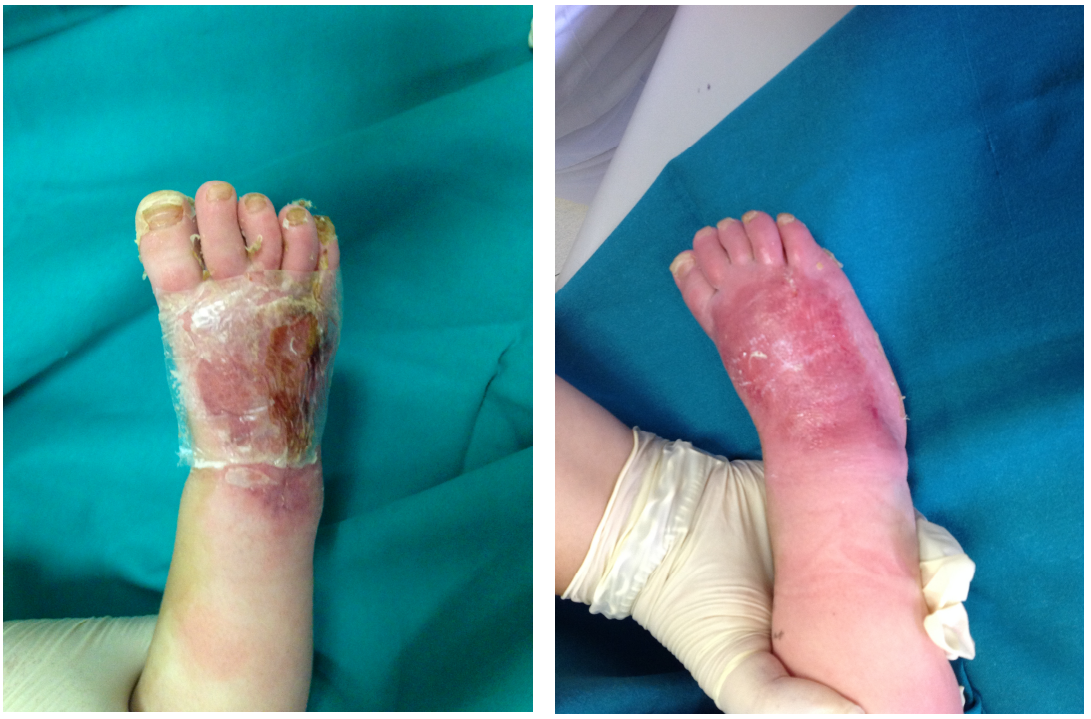

FIGURE 1.14
Regenerative activity of the advanced medication made by Chitin Nanofibrils on baby's foot affected by a II grade burn. Left: day 0; Right day 7

During each single preparation the nanoparticles, personalized by the entrapment of different active ingredients, were selected according to the de-signed and expected activity. After a further process of refinering, the different obtained nanoparticles have been embedded into different kind of water in oil (w/o) or oil in water (o/a) emulsions. Finally safeness and effectiveness of both the nanoparticles and the different final products were verified by in vitro and in vivo studies. The different obtained results are shown regarding, for example, their activity as anti acne ingredients (Fig.1.15) [33], as anti-inflammatory compounds capable to repair the skin barrier (Fig.1.16) [34], as carrier to deliver anti-aging ingredients through the skin (Fig.1.17) [35] for slowdown the wrinkling appearance, or as specific complexes to whitening the hyper pigmented skin (Fig.1.18) [36], or to reduce the microorganisms density on people affected by Seborrheic dermatitis (Fig.1.19 and 1.20) (37).
The increased use of cosmetic product, ranging worldwide the turnover of about 200 billion € [38] is principally due to the actual mentality of considering and giving importance to our wellness and exterior aspect. We are living longer and, understandably, we wish to be healthier as we age. In reality we do not wish to age more, dreaming to appear day by day younger! It is estimate that by 2050 the number of people aged 65 and over, will reach 16% of the global population (Fig.1.21) [39]. Thus the necessity to make an ever-growing arsenal of new biological ingredients that,

recognized from the cells, may be used as material of support for producing, for example, new collagen, the synthesis of which is reduced during the aging process [40].
Researchers, in fact, have harnessed the cell's ability to interact with other cells to develop new material with any kind of biological/living component useful to make new and innovative, effective and healthier pharmaceutical and cosmetic products.

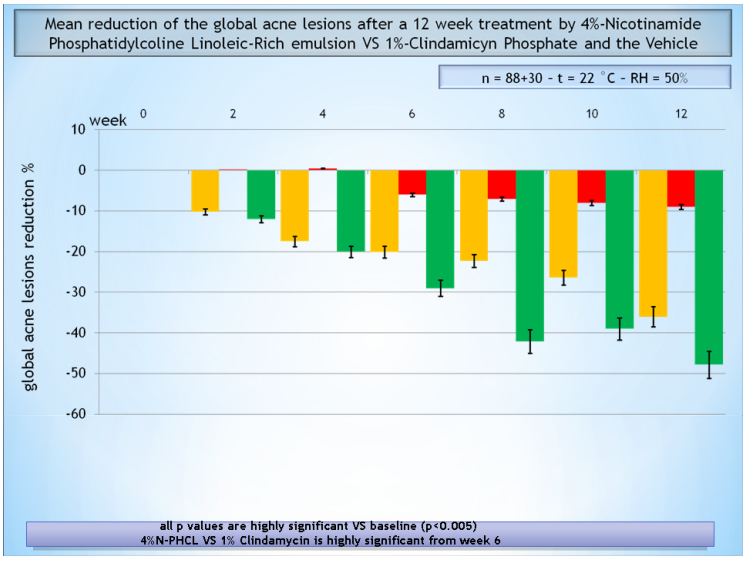

FIGURE 1.15
Anti-acne activity of CN emulsion entrapping nicotinamide

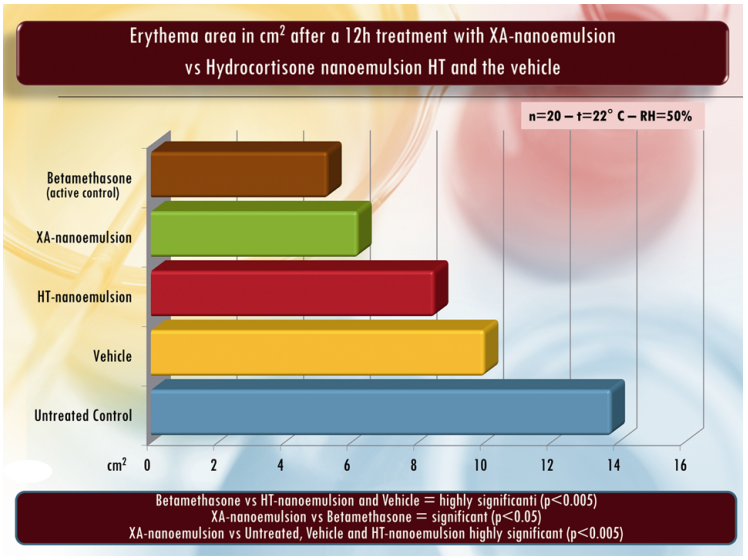

FIGURE 1.16
Anti-inflammatory activity of CN-HA emulsion (XA –nanoemulsion) in comparison with the vehicle and a corticosteroid cream

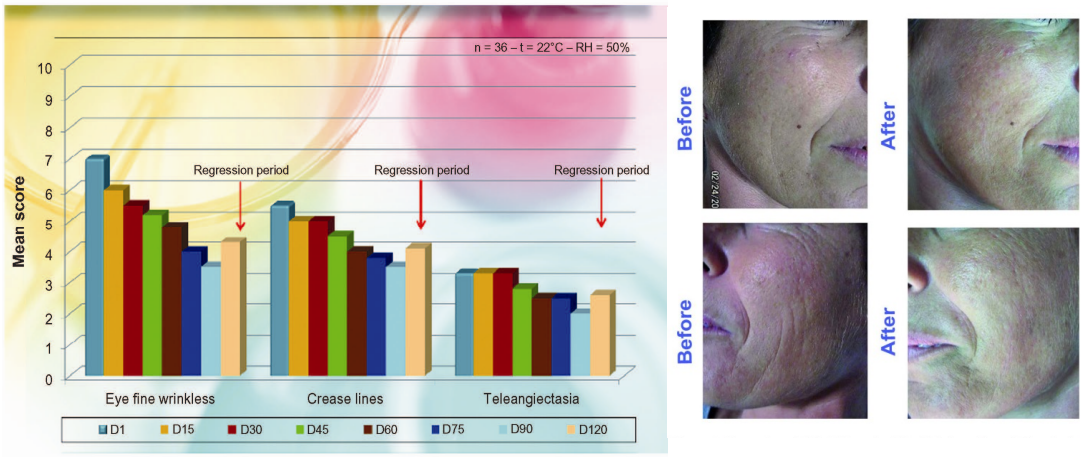

FIGURE 1.17
Anti-aging activity of a CN-HA emulsion embedding different active ingredients

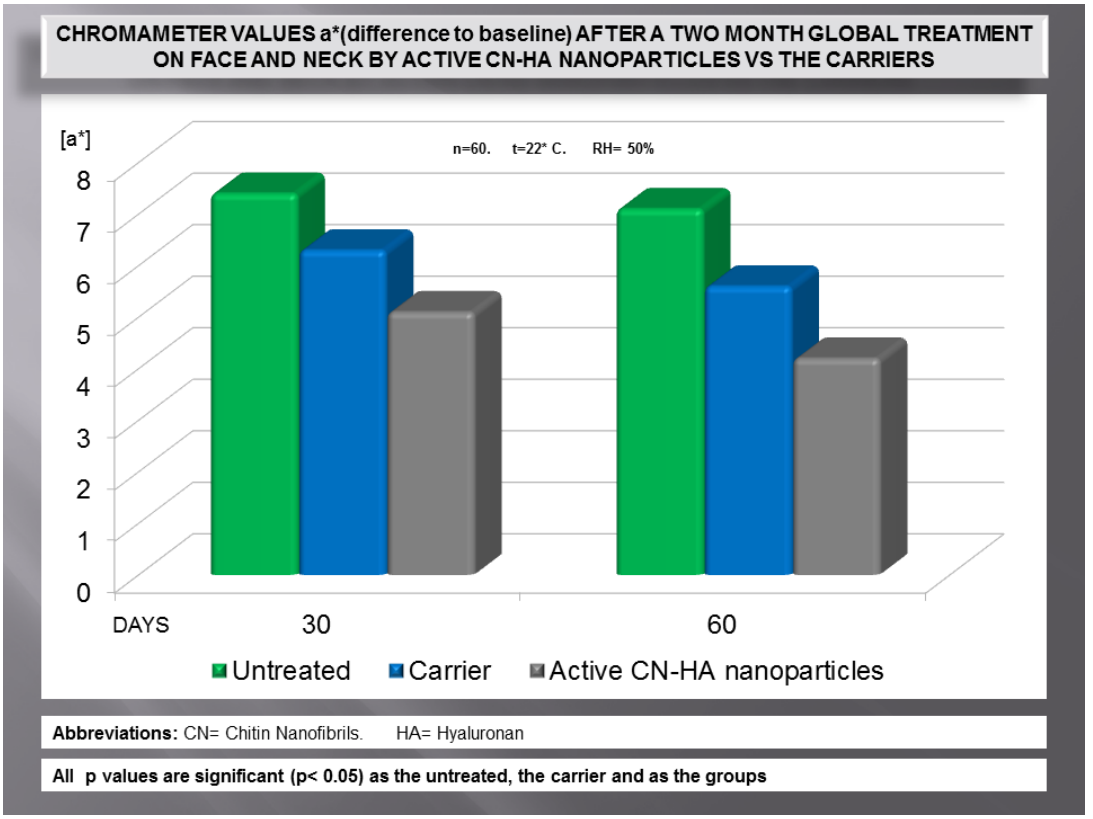

FIGURE 1.18
Whitening activity of a CN-HA emulsion embedding different active ingredients

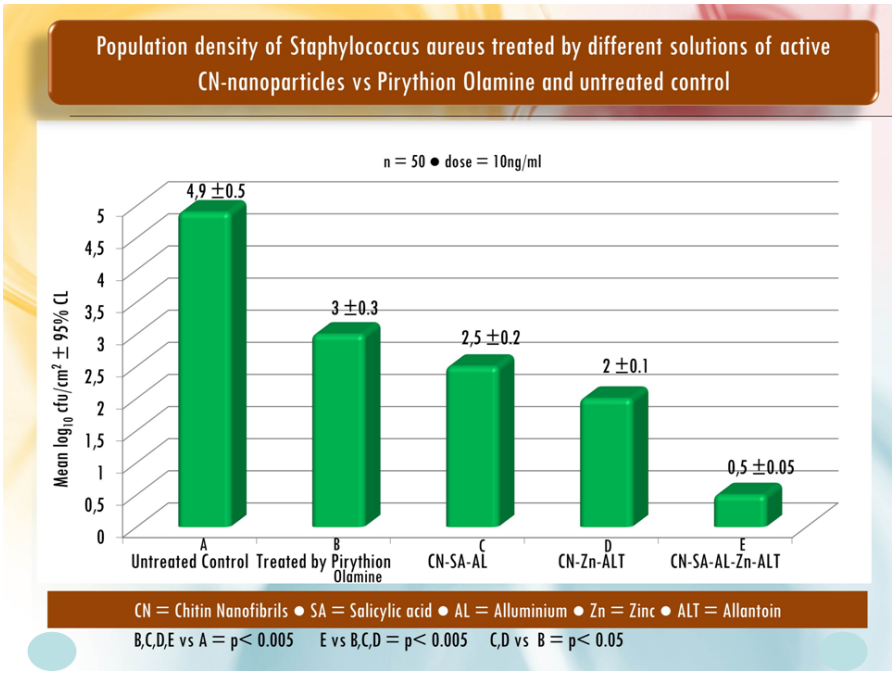

FIGURE 1.19
Antibacterial activity of CN nanoparticles

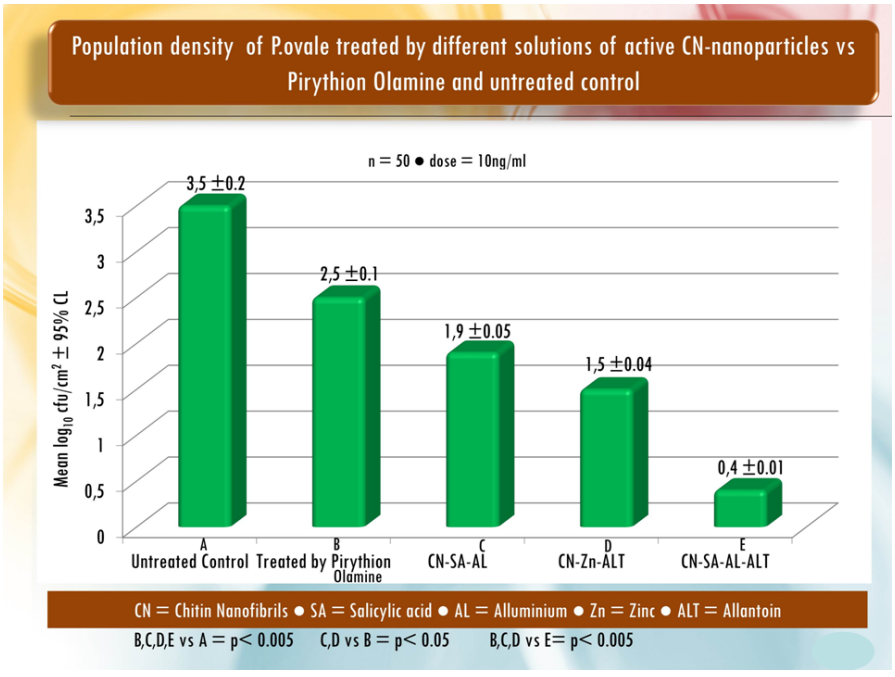

FIGURE 1.20
Antimicotic activity of CN nanoparticles

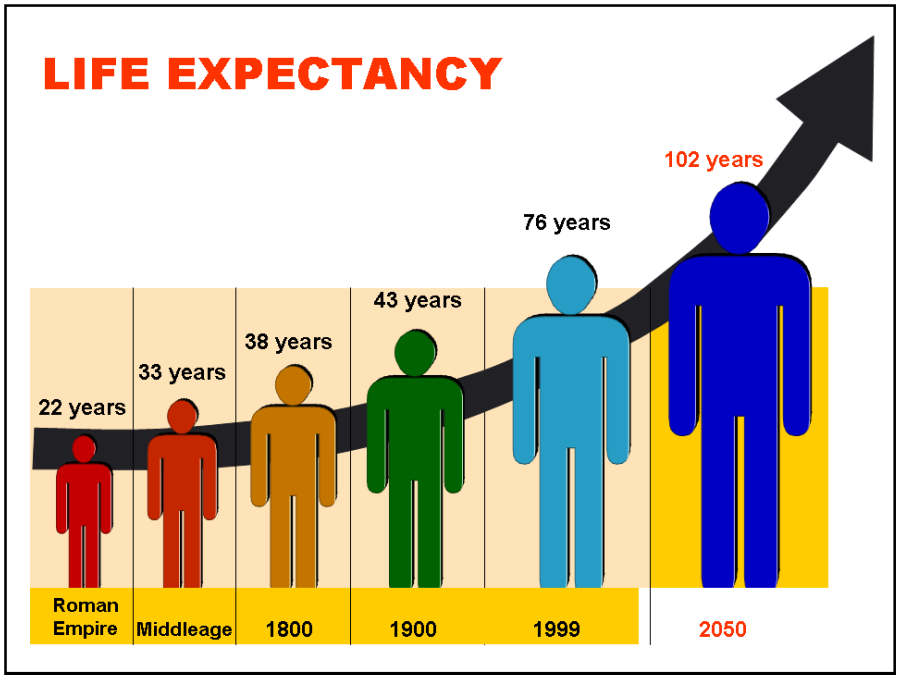

FIGURE 1.21
Life expectancy

European Bioeconomy Strategy for a sustainable development and a cleaner environment

According to the EU Knowledge Based Bioeconomy (KBBE) [41] the term bioeconomy means an economy that utilizes biological resources from the land and the sea as well as waste, including food wastes, as inputs to industrial and energy production by the use of bio-based processes for arriving to a green industry. However, the proposed action plan towards a sustainable and inclusive growth economy by 2020 has to substitute the actual use of biological raw material with biomass and biotechnology, as much as possible [42-44].
Biomass, including organic fishery's waste and plant-based resource, is sought as a substitute for fossil fuels whose economic value must be extract and transformed. Thus, the EU plan has been focused to obtain three bio-economical objectives, (a) developing new nanobiotechnologies and proc-esses, by investments in research and innovation; (b) developing markets and competitiveness in different industrial sectors, by the use of biomass and waste streams, as well a improving the resources efficiency; and (c) pushing policymakers and stakeholders to work more closely together, enhancing synergies and coherence throughout the whole value chain. [42-45].
These objectives have the scope to:

- reinforce European leadership and creativity in the bio sciences;
- optimize Innovation and transfer of knowledge;
- improve the efficacy of agricultural, food, and industrial production and distribution;

- make rural and costal economies more sustainable;
- maintain the competitiveness of EU industry and agriculture;
- increase research for obtaining more safe nutritional and affordable food;
- building low-carbon Industries;
- reduce emission of GHGs and waste.

Therefore, the bio-based economy has to encompass agriculture, forestry, fisheries, food together with nanobiotechnology and industrial sectors, ranging from the production of energy carriers and chemicals to buildings and transport. Thus, this new economical branch has to replace fossil-based re-sources making more widespread use of biomass and biotechnology in the production of fine chemicals and pharmaceuticals. In addition a bio based economy applies feed stocks in the industrial production of synthetic materials, such as bio-plastics.
For all these reasons OECD [46] defines sustainable development as: "the design, manufacture and use of efficient effective, safe and more environ-mentally benign products and enzymatic processes, obtained by the use of waste materials for developing durable goods that can be re-used and recycled". The sustainable development has to be based, however, on three fundamental pillars (Fig. 1.22):

- social equity
- environmental preservation and
- economical viability

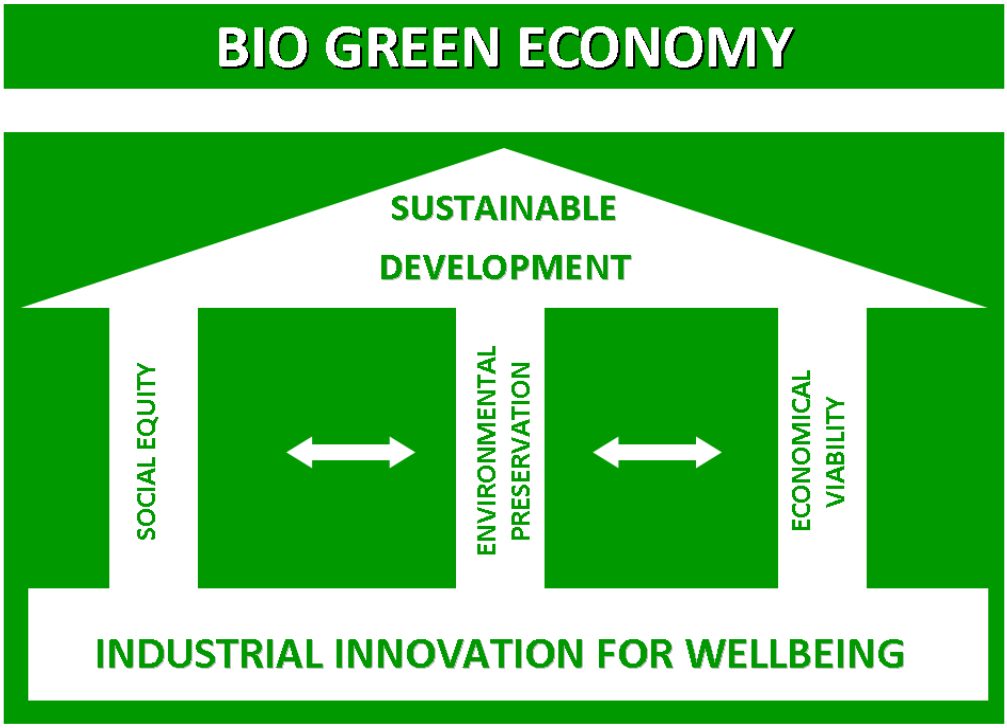

FIGURE 1.22
Bio-Green Economy

In conclusion, a responsible bio-economy needs multi-stakeholder partner-ships involving a broad range of civil groups, such as scientists, opinion leaders, farmers, SMEs and consumers in addition to the representatives of the different bio-based industries. According to Clark and Dickson [47] "sustainability and economy, in fact, are focused, on the dynamic interactions between nature and society". The economy is dependent upon society as well as society is dependent upon the environment [48]. Economy could not survive without its context within society, while society (i.e. humans) requires resources from the environment and relies on the services of its functioning.

Conclusive remarks

The study of engineered biomaterials and nanoparticle's delivery systems necessary to technological applications in nanomedicine and in nano enabled consumer products, is an ever-expanding discipline for the unusual and particular properties these compounds possess. Biomaterials, in fact, are defined as material or combination of materials man made or natural in origin, which can be used to repair, replace or model tissues or organs in vitro and in vivo [49]. Nanoparticle delivery systems offer the ability to design a delivery vehicle that maximizes the effectiveness of an active ingredient entrapped into nanoparticles [50]. In particular CN is an engineered nanopolymer obtained by an industrial patented green process [15].

The free amino groups, present on the surface of this natural polymer and providing its positive charges, give it the possibility to make block copolymeric nanoparticles with many electronegative polymers or macromolecules, as previously shown.

It is interesting to underline that this phenomenon of self-assembly requires low quantity of energy and water. Moreover these particular nanoparticles, made by the use of CN (obtained from the fishery's waste) and successively bonded with other lignocellulosic polymers (extracted from the plant-biomass), are considered skin friendly and environmentally friendly com-pounds [51-53]. Interestingly these nanoparticulate systems can be used not only as vehicles for the liberation of a wide variety of active ingredients, but as active ingredients also. As an example, the block copolymeric nanoparticle made by the complex CN-HA has shown to possess different activities.

Acting as vehicle it (a) facilitates the ingredients transport, increasing their efficacy and protection from oxidation; (b) modulates the time of permanence into the skin of all the entrapped ingredients, minimizing their transdermal absorption; (c) releases the different ingredients in the designed specific areas; (d) minimizes their eventual, toxicological side effects.

Thus as vehicle CN-HA can protect the payload from degradation and enable sustained and controlled active ingredient release. Furthermore, these natural nanoparticles have the potential to decrease clearance and improve accumulation of the "actives" in the designed skin layers, thereby increasing their effectiveness and reducing side effects. Moreover, these block copolymeric nanoparticles are composed of natural polymers known to be non-toxic and totally biodegradable.

In addition both CN and HA are effective as active ingredients. CN can be metabolised by the endogenous body enzymes Chitotriosidases [54], producing glucosamine and acetyl glucosamine, which, as active molecules, may be used for cartilage effectiveness and probably to modulate the glycation process [55] (Fig.1.23).

Moreover, it may produce glucose, indispensable for the cellular energy. On the other hand, HA can be utilized as support for the ECM composition and the glucosaminoglycans' production.

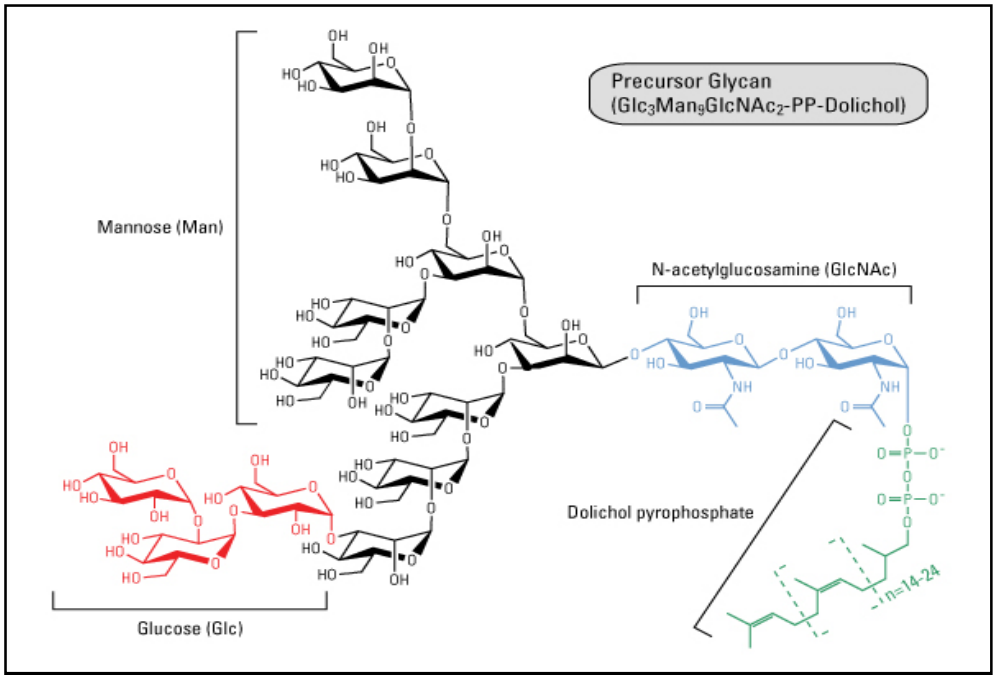

FIGURE 1.23
Physiological process of glycosilation involving glucose and acetyl glucosamine

For all these reasons CN, as pure nanocrystal, is particularly studied as carrier or drug/cosmetic delivery system for innovative cosmetic and pharmaceutical micro/nanoemulsions , as well as for the production of nanocomposites made by the electrospinning to make advanced medications and innovative beauty masks (by the use of biomimetic materials) or to make soft and hard films for food packaging (Fig.1.24) [56,57], according to the results obtained by the EU research projects n-Chitopack (www.n-chitopack.eu) and Bio-Mimetic (http://www.biomimetic-eu-project.eu/).

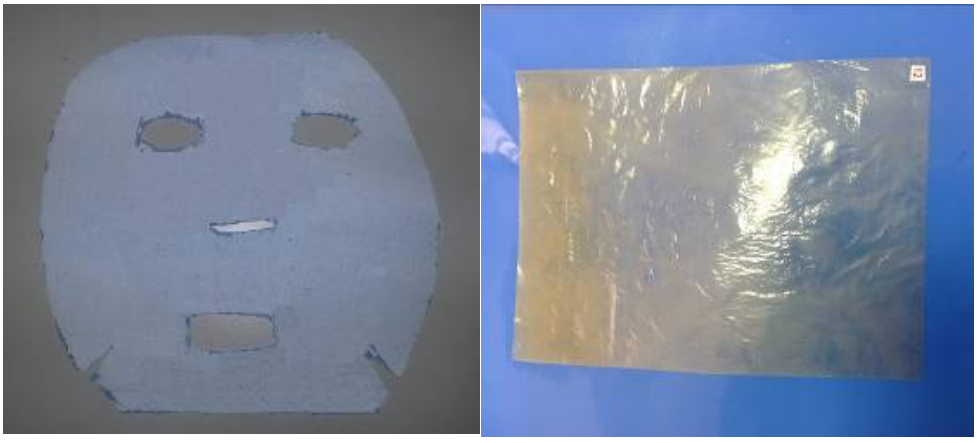

FIGURE 1.24
Beauty Mask and Food Packaging films

Last but not least, for its multi-functional activity CN and other natural polymers, obtained from fishery's and plant biomass, could have a fundamental role as innovative and economic biomaterials useful to produce different kind of eco-compatible goods, necessary to link the innovation with a sustainable economical growth [58]. It is, therefore, important to create a green low-waste production chain able to secure public goods and food supply in the actual contest of climate change and growing population.
This new bio-green-economy, based on knowledge and innovation, has to increase both industrial and agricultural productivity, whilst maximizing the efficiency and resource used, contemporary minimizing the environmental impact. Thus, the necessity to involve scientists from different disciplines together with all the industries of the supply chain, as well as farmers, consumers and society at large. This is the challenge to realize a real sustainable development for ameliorating the quality of life, maintaining the earth' biodiversity.

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