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Chitin Nanofibrils, a Natural Polymer from Fishery Waste: Nanoparticle and Nanocomposite Characteristics

Pierfrancesco Morganti, Gianluca Morganti and Maria Luisa Nunziata

Abstract: Chitin nanofibrils (CNs), obtained by a patented industrial process, is a pure linear alpha-crystal polysaccharide of acetyl-D-glucosamine and D-glucosamine with a mean dimension of 5 × 7 × 240 nm. By the process a colloidal aqueous suspension, containing ~300 billion of positively charged pure nanofibrils, is obtained. For their physicochemical character CNs form easily block copolymeric nanoparticles (NPs) with macromolecules or natural polymers, negatively charged. These NPs, capable to entrap active ingredients, can be embedded into micro/nano cosmetic pharmaceutical emulsions or into nanocomposite fibers to make non-woven tissues. NPs not only have the capacity to increase the effectiveness of ingredients protect them from environmental aggressions, but also to release them in different skin/mucous layers at different times, depending on the formulation methodology used. Effectiveness and safeness of chitin nanoparticles are reported and discussed in this chapter.

1. Introduction

Chitin nanofibrils (CNs) [1,2], are pure crystalline structures obtained by an industrial patented process free of any waste material [3]. They are made of linear alpha polysaccharides of *N*-acetyl-D-glucosamine and D-Glucosamine with a mean dimension of 5 × 7 × 240 nanometers (nm) and the same backbone of hyaluronic acid (Figure 1) [4,5].

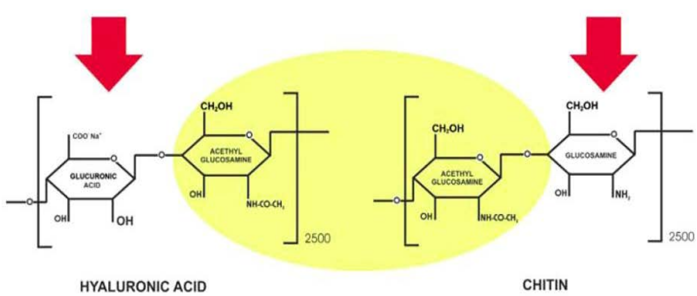


Figure 1. Chitin and hyaluronic acid have the same backbone (courtesy of MAVI SUD, Italy).

By this patented process a colloidal aqueous suspension of CNs are obtained, containing about 300 billion pure nanofibrils per milliliter, as shown elsewhere (Figure 2) [4,5]. A nanometer, with a range equivalent to the billionth of a meter (80,000 times thinner than a human hair), covers sizes smaller than the wavelength range of visible light but bigger than several atoms (Figure 3) [6,7].

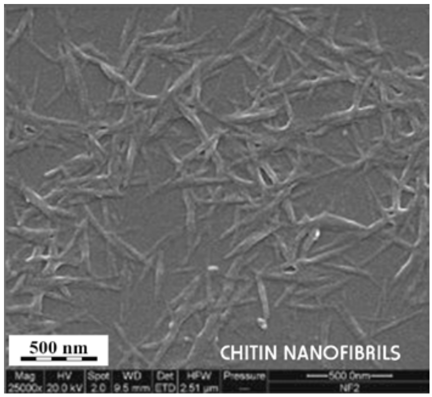


Figure 2. Chitin nanofibrils at SEM.

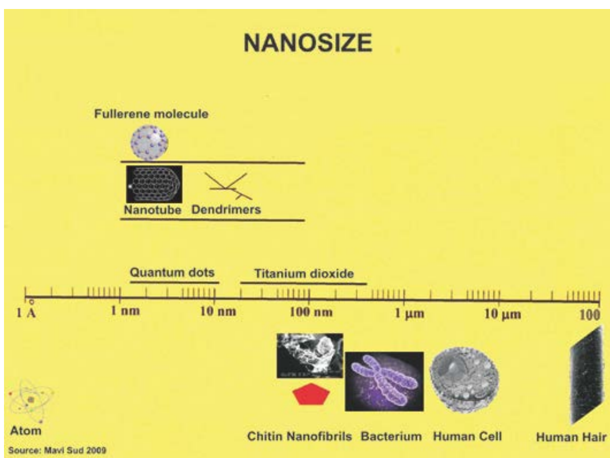


Figure 3. The nanometer dimension [7].

These electropositive nanocrystals with interesting physicochemical characteristics and properties (Figure 4) easily form block copolymeric micro/nanoparticles with electronegative compounds, and give more mechanical strenght to natural or man-made polymers, rendering their activity more effective [8–13].

The higher acetylation degree of chitin can, in fact, contribute to the formation of hydrogen bonds, stabilizing the crystalline structure [8], giving not only a greater resistance to the composite fiber made, for example, with PLA or chitosan [9], but also showing antibacterial activity and lower toxicity [10]. On the one hand, nanocrystals could institute a bridge between single molecules and bulk systems, modifying and changing the polymer characteristics [11]. On the other hand, the nanometer range and high-surface-area-to volume ratio of CNs allow them to interact closely with microbial membranes; they display most significant antibacterial and antifungal effects different from those of the bulk counterparts [11,12]. Moreover, these nanocrystals, covered by positive charges on their surface and capable to entrap active ingredients, have the ability to disturb the tight lamellar layers of the Stratum Corneum (SC), enabling better diffusion of the ingredients through the skin layers [13].

On the contrary, when the nanoparticles are negatively charged, the active ingredients remain at the level of the outermost skin. So, it is possible to modify the activity and effectiveness of the CN block-copolymeric nanoparticles not only by selecting the active ingredients, but also by modulating the electrical charges covering their surface. However, these fibrillar bio-nanoparticles are characterized by remarkable properties such as outstanding stiffness and strength, thermostability, barrier properties, degradability, and sustainability, with a global availability from renewable resources and food waste [5,12,13].

Thus, CNs find many applications in foods, advanced medications, cosmetics, smart textiles, waste water treatments, and other biotechnological products [14–16] (Figure 5).

For this purpose it is interesting to underline that the significant amount of underutilized waste resulting from the industrial processing of seafood and plant biomass became a problem both for the environment and human health.

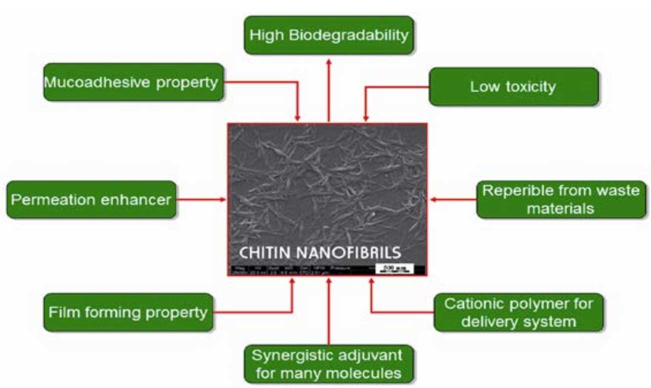


Figure 4. Chitin Nanofibril characteristics. Source: MAVI SUD 2010.

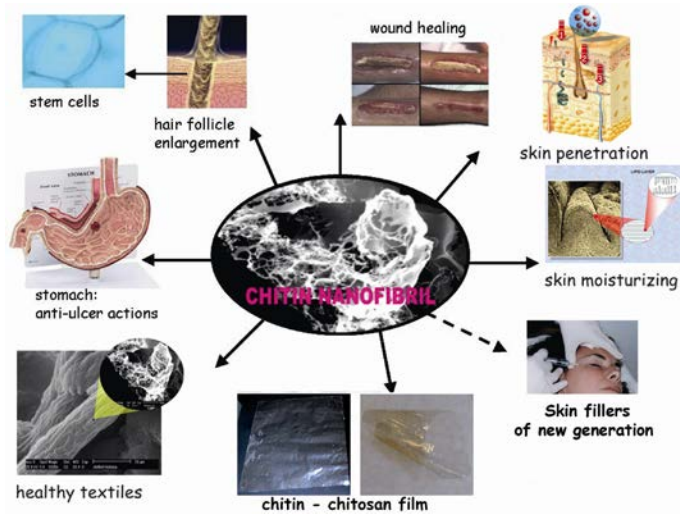


Figure 5. Different uses of Chitin nanofibrils. Source: MAVI SUD 2010.

According to the Food Agricultural Organization (FAO) Yearbook, in fact, the annual total production of crustacean and fishery's, has reached 148.5 million tons in 2010, 45%, producing ~50–70% waste [17]. On the other hand, 140 billion tons of plant biomass are generated every year from agriculture according to the United Nations Environment Program (UNEP) [18]. Therefore fisheries and plant biomass, widely available and renewable materials still largely underutilized byproducts represent an important source of raw material at a low cost (virtually free).

Aside from being carbon-neutral biomass used for energy and innovative goods it could reduce greenhouse gas (GHG) emissions and dependency on fossil fuels, closing the carbon cycle loop and contributing to climate change mitigation. Thus, the main industrial objectives are to select raw materials (possibly obtained from wastes and byproducts), identifying and assessing environmentally sound technologies to convert chitinous and lignocellulosic biomass into energy and innovative goods.

The use of chitin nanofibrils to produce nanoparticles and nanocomposites is the object of the following section.

2. Chitin, Chitosan and Chitoolisaccharides

While chitosan is the low acetyl substituted form of chitin, composed mainly of Beta (1–4)-2-deoxy-2-amino-D-glucopyranose residues [19], chitoolisaccharides are the smallest chitosan oligomers, characterized by different molecular weights with unusual biological activities [20] (Figure 6).

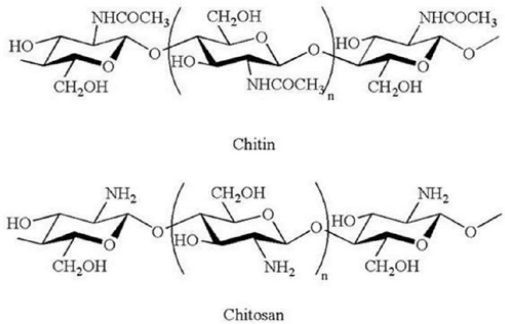


Figure 6. Chemical structures of chitin and chitosan. When the degree of *N*-acetylation (DA) is greater than 50%, the polysaccharide is considered to be chitin. When the DA is less than 50%, the polysaccharide is considered to be chitosan.

These natural polymers, which elicitate defence responses in mammals and plant tissues, because of their mucoadhesive property, low toxicity and antifungal/antibacterial activity, have found a variety of applications in different fields such as the biomedical, pharmaceutical, food and environmental industrial [21], as previously reported. Moreover, the presence of amino groups makes chitin and its derivatives easier to modify by chemical reactions than cellulose [22]. In addition, CN, for its crystalline structure, nanosize dimension and natural origin, has been shown to be not only an interesting active carrier for innovative pharmaceutical and cosmetic products, but also a good candidate for reinforcing polymer nanocomposite fibers to be used for advanced medications and food packaging films [23,24].

Specifically in the case of composites and films, the use of biopolymers has emerged as an interesting alternative to fossil fuel-based products. With the impending fossil fuel crisis, the search for and development of alternative chemical/material substitutes is pivotal to reduce human dependence on fossil resources. The various advantages of natural fibers over man-made glass and caron fibers include their low cost, low density, comparable specific tensile properties, reduced energy consumption, lower health risk, renewability, recyclability, and biodegradability, all necessary to safeguard both the environment and human health [25]. Moreover, owing to the increase in the concept of ecological safety and utilization of renewable materials towards a greener society, the application of natural fibers in industry as bio-filler/reinforcement materials in composite has considerably increased in recent years [26]. These composites are, in fact, eco-friendly to a greater degree and offer a lower density, better matrix–fiber compatibility, and recyclability compared to conventional ones [27,28].

For all these reasons, CN has shown interesting properties for both its crystallinity and nanodimension. In any case, chitin nanofibrils and chitosan possess interesting characteristics qualifying their use in wound healing for their capacity to (a) attract and activate macrophages and neutrophils initiating the healing process; (b) promote granulation and re-epithelialization of the tissue; (c) limit scar formation and retraction; (d) show analgesic and haemostatic activity; (e) activate the immunocompetent cells function; and (f) stimulate the cellular activities by the release of monomers and oligomers of glucosamine and *N*-acetyl glucosamine, used as building blocks in the synthesis of the natural Extra Cellular Matrix (ECM) [29–34]. Moreover, they show interesting skin protective activity and antimicrobial/antifungal effectiveness [10,15].

In addition, CN and chitosan, as polymers characterized by their good adsorption and attraction ability towards transition metal ions and electronegative polymers, easily form stable chelate compounds and block co-polymeric nanoparticles, respectively (Figure 7). This complex-forming ability, useful to clean air and water or produce specialized pharmaceutical and cosmetic carriers, mostly depends on polymer parameters such as de-acetylation degree, polymer chain length and crystallinity [35,36], as well as on its own absorptive properties and physical form of the adsorbent selected, connected also with its composition, pH, and ionic strength.

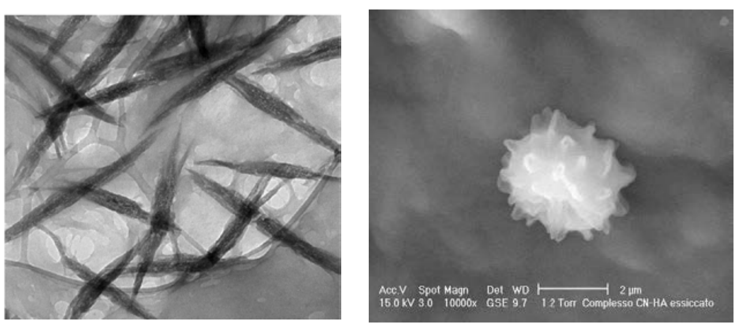


Figure 7. Left: Chitin nanofibrils bonded to metal ions (courtesy of G. Tischenko); Right: single CN–Hyaluronan nanoparticle (courtesy of Morganti et al. [36]).

3. CN Nanoparticles and Nanocomposites

On the one hand nanoparticles, obtained combining the electropositive CN with the electronegative hyaluronic acid [36], have been used recently to design cosmetic products characterized, for example, by their antiaging effectiveness on skin folds has been shown (Figure 8) [37], anti-acne activity treatment with an evident decrease of lesion counts (Figure 9) [38] and melanin synthesis inhibition verified on melanocytes cultures (Figure 10) [39], or for their elastic activity on damaged hair exposed to UV (Figure 11) [40] and wound healing activity (Figure 12) [32]. On the other hand, they are also considered as high-potential filler material for the improvement of the mechanical and physical properties of the nanocomposite polymer matrix (Figure 13) [41,42].

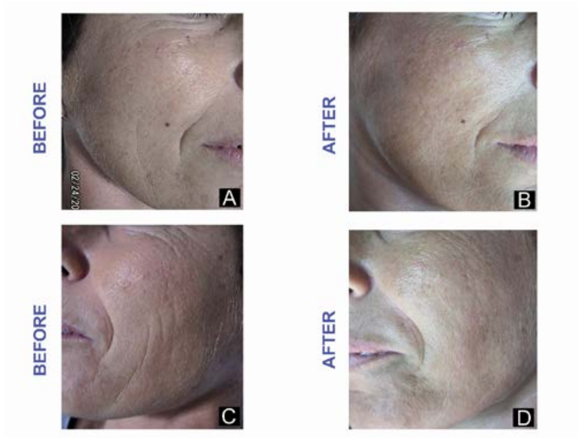


Figure 8. Antiaging effectiveness on nasolabial folds and mid-cheek before (**A**-**C**) and after (**B**-**D**) treatment by the active block-polymer-nanoparticles (BPN) at 30 days (courtesy of Morganti et al. [37]).

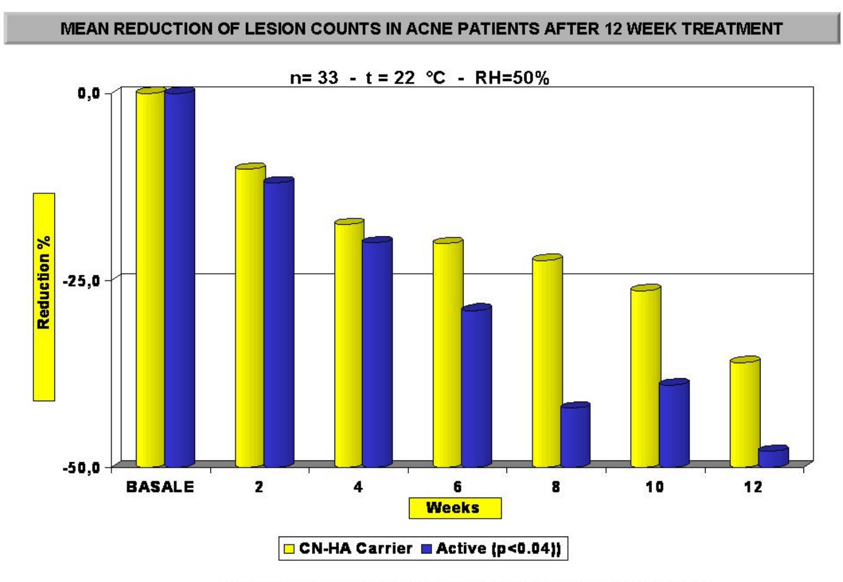


Figure 9. Anti-acne treatment effectiveness by active block-polymer-nanoparticles (courtesy of Morganti et al.).

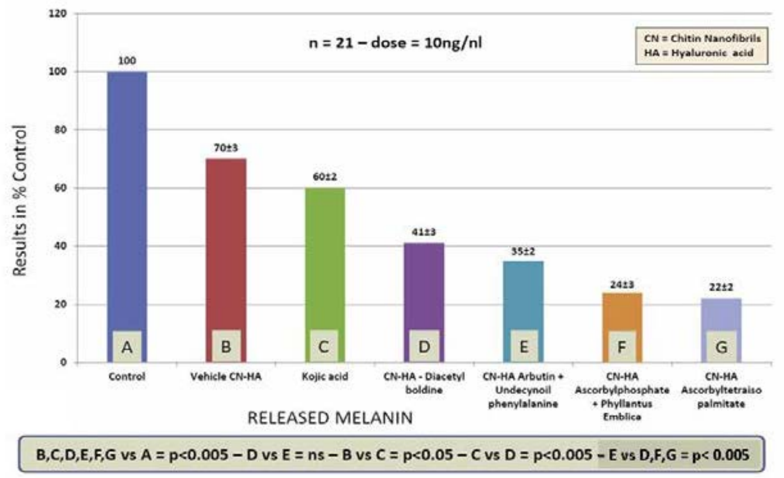


Figure 10. % Melanin synthesis inhibition on melanocyte cultures treated by CN–HA entrapping active ingredients vs. control and vehicle [39] (courtesy of Morganti et al.).

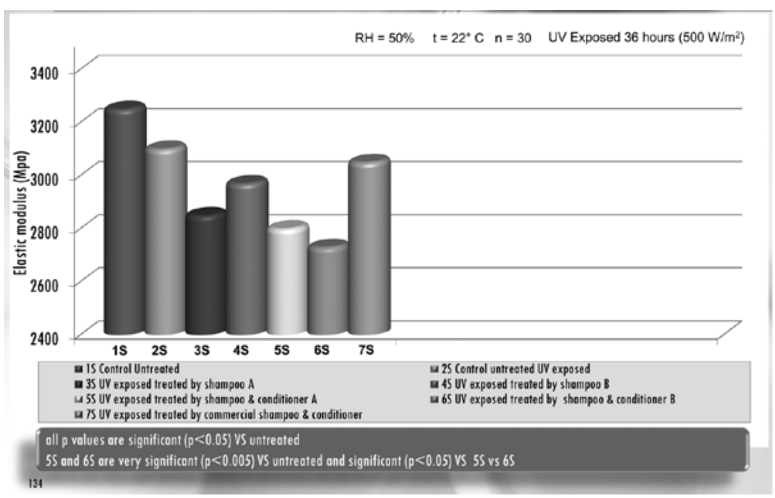


Figure 11. Decrease in elastic modulus of hair exposed to UV and treated with a Zn–CN shampoo and conditioner [40] (courtesy of Morganti et al.).

Figure 12. Wound healing activity of CN–HA nanoparticles (courtesy of Dr. P. Mezzana).

Composite Fibers	Tensile Strength MPa	Tensile Modulus MPa	Elongation at break, %
Chitosan 100%	199	7950	7.2
+0.5% Chrysotile	292	13740	7.6
+1.0% Chrysotile	220	8510	8.5
+1.5% Chrysotile	241	11370	8.5
+2.0% Chrysotile	187	7310	4.8
+3.0% Chrysotile	214	9200	4.7
+ 5% CN	**391**	**18240**	**6.2**
+ 20% CN	**411**	**20700**	**3.9**

Figure 13. Mechanical properties of chitosan/CN on composite fibers [40] (courtesy of V.E. Yudin).

4. Nanoparticles and Regenerative Medicine

4.1. Nanoparticles

Nanoparticles are used in nanomedicine as diagnostic imaging agents and therapeutic delivery vehicles to treat different disorders such as cancer, infection diseases, neurological modifications, etc. [42–49].

The primary amine groups of Chitin Nanofibril (CN) [50], assessing the special properties to this crystalline compound as material of choice for developing micro/nanoparticles, make it very useful, especially in biomedical applications [51]. The CN nanoparticles, in fact, have the ability to control the release of active ingredients, avoiding the use of hazardous organic solvents, since they are produced by the gelation method in aqueous solution by the use of electronegative, natural polymers (Figure 14) [36].

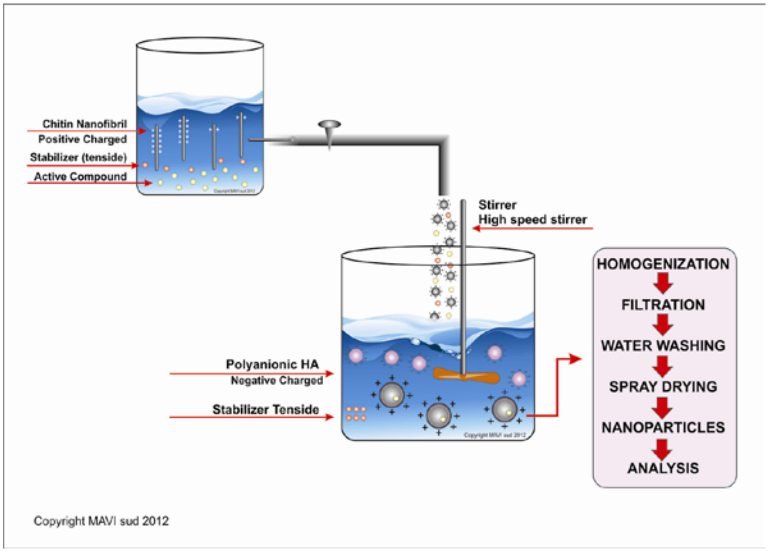


Figure 14. The gelation method. Hyaluronic Acid = HA. Source: MAVI SUD, Italy.

As an electropositive polymer, CN, when in contact with electronegative compounds, easily forms block copolymeric nanoparticles, also having the ability to entrap different active ingredients during the gelation process (Figure 15).

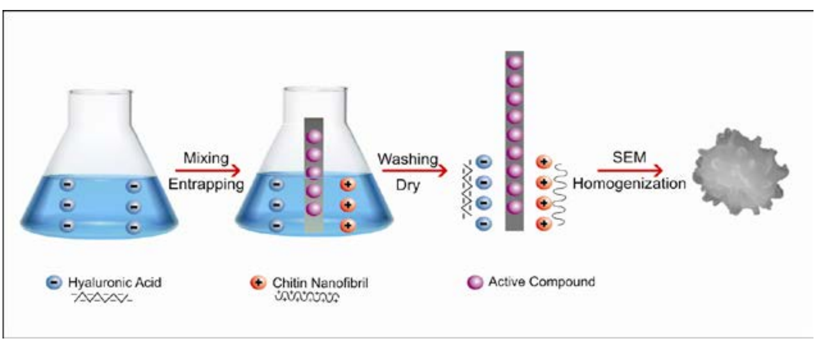


Figure 15. Entrapping active ingredients by CN–HA during the gelation method. Source: MAVI SUD, 2013.

Both CN and CN-derived nanoparticles are biocompatible with living tissues, breaking down to harmless amino sugars by the activity of the chitotriosidase (families of chitinases), secreted by humans [52]. This specific enzyme degrades chitin and chitosan primarily by the endo-processive mechanism, showing an absolute preference for acetylated sites compared with deacetylated ones. Thus CN is more easily degraded than chitosan because of its higher content of acetylated glucosamine, probably acting as a template for both the regular synthesis of hyaluronan and glucosaminoglicans, inducing the normal and regular dispositions of the fibers into the ECM (Figure 16). The facility to modulate the collagen synthesis could explain why its use may reduce the risk of hypertrophic formation of scars and keloids, also slowing down the adhesion of intra-peritoneal and intestinal structures [29,30,53,54].

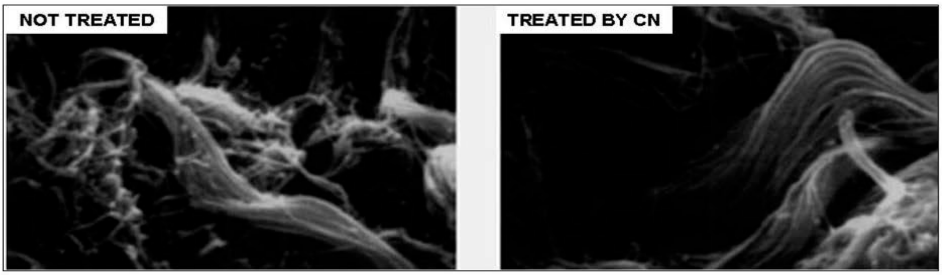


Figure 16. Disposition of collagen fibers on wounded tissue treated (**right**) by a CN-enriched gel emulsion compared to the control (**left**). Courtesy of M. Tucci et al. [29].

Thus, when used as carrier, this natural polymer could modulate the penetration through the skin layers of the entrapped/encapsulated active ingredients and the healing process by its own metabolized components (e.g. glucosamine and acetyl glucosamine) [29,30].

During the wound healing process, in fact, glucosamine and *N*-acetyl glucosamine groups should serve as a reinforcement substratum of the epidermis for keratinocyte activity at level of the wounded tissue. At dermis level, fibroblasts can be activated to produce the right quality and quantity of fine collagen fibers, necessary in the early period of the tissue rebuilding. Thus, CN could constitute a micro-environmental stimulus for the cell that, by influencing its correct trophism, could ameliorate and modulate the skin granulation process, enhancing the activity of defensines. Moreover, they modulate the activity of both metalloproteinases and angiogenesis favouring the regular deposition of the collagen fibers necessary to repair the dermo–epidermal lesions [55,56].

4.2. Regenerative Medicine

The aim of regenerative medicine is to repair and replace damaged tissues or organs by mean of natural regeneration processes. In fact, million people worldwide had an increase in life expectancy, while millions of patients are suffering from the skin and cartilage defects caused by trauma, injury and age-related degeneration. For example, the main cause of hospital admission and death in Brazil is injuries caused by accidents. In 2004 alone, the National Health Care System has spent US$585 million on orthotics and prosthetics [57,58].

According to The WHO Report on Disability [47], there are more than 1 billion people with disability worldwide (i.e., about 15% of the global population) who would benefit from prosthetics and orthotics services. The presence of disability is rising because of the aging population and the global increase in chronic diseases. Thus, 30 million people in Africa, Asia and South America require 180,000 rehabilitation professionals and devices whose cost is unsustainable for poor people. However, the mass production of these devices can lower their cost, using universal and innovative ingredients that are administered widely. Therefore, it becomes imperative to develop biomaterials, such as CN, with the main purpose of regenerating tissues and organs, possibly at low cost and without side effects.

In a regeneration strategy, biomaterials have to promote new tissue formation by providing adequate porosity and an appropriate surface to foster and direct cellular attachment, migration, proliferation, favouring the desired differentiation of specific phenotypes throughout scaffolds where new tissue formation is needed [59]. Thus films, fibers and bulk materials, based on the natural polysaccharide CN, could represent an elective biomaterial combining bioresorption properties, absence of cytotoxicity and low environmental impact during processing and use [60,61].

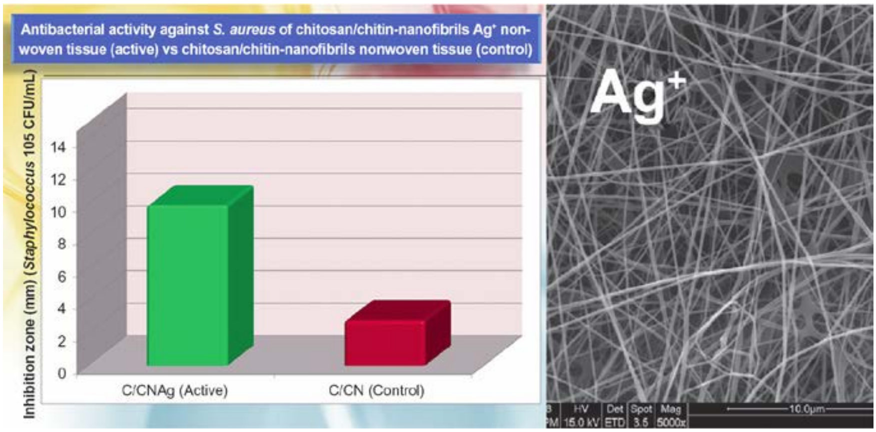
5. Nanocomposites

Nanocomposites, as the most advanced and adaptable engineering material, are considered to belong to the group called nanomaterials, where a nanoparticle (nanofiller) is distributed into a matrix [62].

Generally, a nanocomposite is a multiphase dense material in which at least one of its phases has either one, two or three measurements lower than 100 nm [63].

The perfect combination of the right polymeric matrix and reinforcing natural fibers produces composites possessing the finest properties of each component. However, while the term natural fiber-reinforced composite usually refers to natural fibers in any sort of polymeric matrix (natural or man-made), the nanofillers (nanoparticles) in a nanocomposite material are the component constituted of inorganic/inorganic, inorganic/organic or organic/organic sources.

Polymer/inorganic nanoparticles find applications in diverse areas, including biomedical applications. While on the one hand the polymer component has structural functions, also tuning the mechanical features and processability of the final material, on the other hand inorganic components such as TiO_2, ZnO, or the metals Ag, Cu and Bi, can not only reinforce the mechanical and thermal properties, but can characterize the final product by their anti-inflammatory, antibacterial and anti-fungal activities (Figure 17), necessary, for example, to accelerate skin regeneration by the use of advanced medications, appositely designed (Figure 18).



Abbreviations: S. aureus; Staphylococcus aureus; C: chitosan; CN: chitin-nanofibrils; Ag+: silver ions; CFU: colony forming unit.

Figure 17. Antibacterial activity of Ag+ treated chitosan/chitin fibers. Courtesy of Morganti et al. [55].

Thus, before starting the electrospinning and/or casting process to make non-woven tissues, Ag nanoparticles have been bound to CN fiber by our group [16]. This methodology allows the inorganic particle to be either physically trapped within the matrix or ionically bound to the polymer [64], depending on the productive process selected. However, both electrospinning and casting are technologies for fabricating fibers at nanometer dimension, which for their specific high surface areas and their ability to mimic the native ECM are very useful for developing nanofibrous cellular scaffolds for human tissue engineering.

All the tissues of human organs, such as bone, cartilage, tendon, ligaments, skin, nerve, and blood vessels, in fact, are hierarchically organized into fibrous structures with fiber dimensions down to the nanometer scale [65].

Advanced medications made by the use of electrospinning or casting technology can provide an environmental or physical cell scaffold, promoting cell growth and function towards the synthesis of ECM over time. This is the reason why natural, biodegradable, nanofibrous materials that mimic the ECM nanostructure have been investigated as ideal components for many human tissues.

Therefore, nanostructured biomaterials such as nanoparticles, nanofibers and nanocomposites made by the use of CN have gained increasing interest in regenerative medicine, so that recently they have been investigated for the capacity to emulate the nanofibrous features of ECM components and modulate the regeneration of burned skin in a faster way (Figure 18) [53,66].

Figure 18. Scar-forming and antibacterial activity of chitosan/chitin fibers treated with Ag+ on burned baby skin treated for six days. Courtesy of M. Palombo et al. [53].

The general idea of nanocomposites is based on the concept of creating a very large interface between nanosized building blocks and the natural/manmade polymer matrix [67]. In any case, the performance of natural composites is influenced by several factors, such as the fiber's microfibrillar angle and its architectural structure, the physicochemical properties and composition, as well as the cell dimensions, and the mechanical properties connected with the interaction between the fiber and the polymer matrix. For these reasons, in recent years reinforced composites containing natural fibers have received considerable attention. Thus, their use increased rapidly because of their high performance in mechanical properties, significant processing advantages, biodegradability, low cost and low density [68].

Natural fibers are, in fact, renewable and cheaper, and pose no health hazards, providing a solution to environmental pollution by finding new uses for waste materials. At this purpose CN from crustaceans' waste, and lignin from plant biomass, seem to have good potential as byproduct resources for industrial uses, probably for their capacity to form non-woven tissues or films with an extremely high surface-to-volume ratio, and tunable porosity underlined for their non-toxic and skin-friendly character, as reported in other chapters of this book.

As natural compounds, diffuse in nature in great quantity, lignin represents a structural material for plant cells, and chitin (CN) is a defense and protective material for crustaceans. However, to understand the properties of naturally reinforced composite materials, it is essential to recognize and control in advance the mechanical, physical and chemical composition/properties of the fibers selected, together with their naturalness, safeness and effectiveness [69]. Natural polymers such as oligosaccharides, in fact, are hydrophilic, enzymatically degradable compounds capable of retaining the stability of incorporated drugs, thereby increasing their therapeutic effects.

This is why the term bio-nanocomposite has been coined, as well as naturapolyceutics, born from the union of polymer and pharmaceutics [70].

In any case, bio-nanocomposites are regarded as an emerging group of nanostructured materials classified as (a) nanocomposite materials developed from renewable and sustainable nanoparticles like cellulose, chitin and lignin, (b) petroleum-derived polymers like polypropylene (PP), polyethylene (PE) and polyethylene oxide (PEO), and nanocomposites derived from bio polymers like polylactic acid (PLA) and polyhidroxyacids (PHA) or inorganic nanofillers like carbon nanotubes and nanoclay.

In conclusion, nanoparticles, nanofibers and nanocomposites, made by the use of CN and other natural polymers or macromolecules, represent new families of polymeric carriers and matrices able to enhance the mechanical and barrier properties of emulsions, films, and non-woven tissues, used to produce innovative cosmetics, food packaging and advanced medications together with many other composite-based industrial applications (Figure 19).

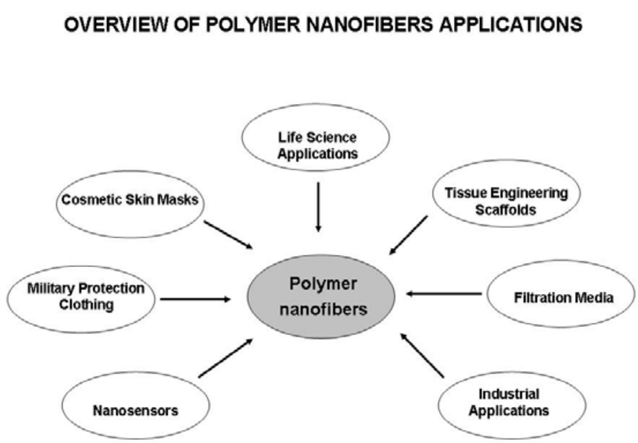


Figure 19. Nanofibers' applications.

Specifically, CN nanoparticles enhance the performance and properties of emulsions and composites, showing great value for both innovative pharmaceutical and cosmetic formulations, and fiber-reinforced composite-based products. This is the reason why bionanotechnology is estimated to contribute at least US$3 trillion to the worldwide economy by 2020 [71].

Furthermore, it has been expected that industries based on nanotechnology might require at least six million workers to sustain them by the end of the decade, hence contributing to a solution to the international economic crisis. Apart from the benefits and safety aspects of bionanotechnology-based products such as nanoparticles and nanocomposites, public opinion and attitudes (Figure 20) towards this new sector are extremely important for the development of this emerging area and business extimated to reach US$172 billion by 2025 [72], according to the research study of Nanotechnology Industries Association (NIA) [73].

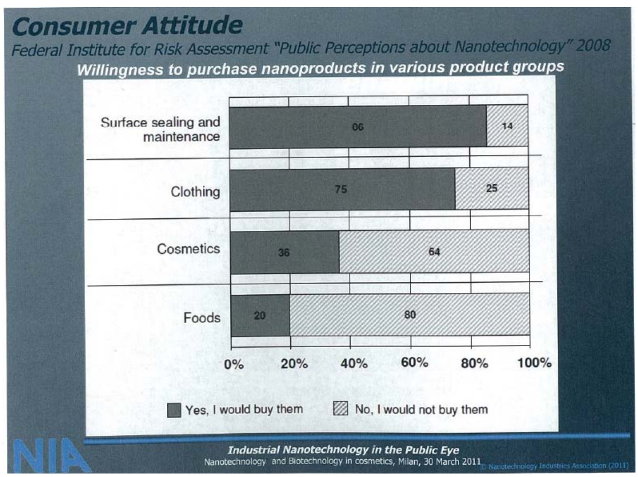


Figure 20. Consumer attitude to purchasing nanoproducts in different industrial areas (courtesy of D. Kolsov) [72].

6. Concluding Remarks

The extraordinary mechanical and biological properties of Chitin nanofibrils seem to be related to their highly layered hierarchical structure, when produced as pure crystals by the right treatment and purification methods [74]. They are natural polymers possessing unique properties like biodegradability and chelating activities, and have been shown to have antibacterial, antifungal, and anti-inflammatory effectiveness also [75]. However, the relationship between its hierarchical structure and the biological properties has to be further explored.

In anyway CN is a biomaterial that seems capable of stimulating the growth of cells in contact with it, interacting with the biological systems.

Finally, its extraction from waste materials of natural origin, the low cost and its wide applicability make it suitable to be used in many industries involved in the production of pharmaceuticals, food, cosmetic products, and packaging materials.

However, more studies must be undertaken in order to recognize in a deeper way all the possibilities these new technologies and chitin nanofibrils have for contributing to effective industrial innovations. It is, therefore, fundamental to underline the necessity of using more waste materials and industrial byproducts to produce goods that will not impoverish our planet and will help maintain its biodiversity [76].

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Conflicts of Interest: The authors work at the R&D Centre of Nanoscience, Mavi Sud, s.r.l, Italy.

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