Commentary

Innovation, nanotechnology and industrial sustainability by the use of natural underutilized byproducts

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Abstract

Nanotechnology can have a positive impact on environmental problems and aid in the development of new green technologies. In this direction, two EU projects have been set up, called BioMimetic and n-Chitopack as well as an Italian one, named Chitofarma. Chitin nanofibrils (CN), coming from fishery waste, and biopolymers, extracted from vegetable biomass, are among the basic polymers used. These raw materials of natural origin are skin and environmentally-friendly. They can be conjugated or cross-linked by bio-mimetic processes to create innovative products, such as specialized cosmetics, food packaging and non-woven antiaging tissues. A description of these research projects together with their expected results will be briefly reported.

Innovation entails the modernization of regulatory science and policy by adapting new approaches and advanced technologies, capable to safeguard humans and the environment. According to Roco *et al.* (1999) of the Interagency Working Group on Nanoscience, Engineering and Technology (IWGN), "*Nanotechnologies have the potential to significantly impact the generation and remediation of environmental problems through understanding and control of emissions..., development of new green technologies..., and remediation of existing waste sites and polluted water sources*". In this regard, the most important advances in the life sciences come from "transitioning" our thinking of materials and their properties to the nanoscale rather than the macro or even microscale. Towards this direction, two EU research projects, BioMimetic (www.biomimetic-eu-project.eu), coordinated by Procter & Gamble-Italy, and n-CHITOPACK (www.n-chitopack.eu) coordinated by MAVI sud Italy, have been setup.

The objective of the Bio-Mimetic project is to develop an effective bio-mimetic glue by the use of biomass and similar enzymatic processes utilized by marine organisms. Mussels, for example, transform proteins into strongly cross-linked ones, with the unique feature of strong surface adhesion in aqueous environments. Thus, biomass-based precursors can be transformed into new bio-based polymers. These will be conjugated with peptides or cross-linked with chitin nanofibrils (CN) to create biocompatible detergents or innovative cosmetic products and non-woven tissues, respectively. Thus, the biomimetic processes of conjugation, inspired from and mimicking the natural biopolymerization of mussel adhesion and insect cuticle hardening, known as *bleu biotechnology,* are natural productive processes concerned with the application of molecular biology methods to marine and freshwater organisms. The electropositive polymer CN comes from the same natural origins (Morganti & Li 2011, Morganti *et al.* 2011a, 2011b, 2012a). In addition, chitin is the second most abundant skin-friendly polymer present as bio-waste, after cellulose (Faruk 2012, Joan 2008, Kurita 2006).

The n-Chitopack project, by the casting technology, has the objective to produce functional bacteriostatic films and rigid packaging for use in the food industry, utilizing as its main components the same natural chitin nanocrystals (CN), together with other natural polymers. Of note, about 50% of Europe' s food is packed in plastic packaging (British Plastic Federation, 2013). Film-packs, currently used in the food industry, are made, for example, of polyethylene, a thermoplastic polymer that is non-biodegradable, having generated an impressive waste of 14 millions tons in the long term (Eurostat, statistical data, 2009).

At this point, it is important to underline that approximately 18,000 pieces of various plastics are present on each square kilometer of the world's ocean surface. In certain regions, the amount of this *confetti* is six times higher than that of sea plankton!

Thus, the use of chitin and the other natural polymers used in both the Bio-Mimetic and n-Chitopack projects would have many benefits, as they are biocompatible, naturally biodegradable, safe, and non-toxic. Moreover the use of chitin from waste materials, will reduce the need for primary raw materials, maximizing resource productivity, and minimizing waste from processing along the value chain. In other words, both EU projects are based on the use of environmentally friendly processes, involving the use of natural compounds to produce bio-based products.

It is interesting to underline that CN may also be used to produce non-woven tissues by electrospinning technology. This method is the basis of another project, named Chitofarma**,** coordinated by MAVI sud, Italy. The objective is to generate innovative, advanced medications, through the use of natural skin-friendly biomaterials and eco-compatible processes, useful for treating skin burns and other serious diseases (Vauthier & Couvreur 2007). In this regard, nanomaterials and biotechnology have recently drawn a lot of attention from the industry; not only because of their potential market, but also because of their technological maturity (Woodrow Wilson Center 2013). Thus, Chitofarma encompasses a disciplinary field, from regenerative medicine, based on the non-woven tissues' capacity to restore the structure and function of damaged skin (Mezzana 2008, Muzzarelli *et al.* 2007) to health maintenance through the use of cosmetic products (Morganti 2011, Morganti *et al.* 2012b). Therefore, a deeper understanding of the above fields is necessary for the development of more effective nanoscale systems for treatment, therapy and diagnosis. It should be noted that the physicochemical properties of the tissue' nano-fibers, made by CN and other natural polymers, may be engineered at molecular level, and their shape, size, and electrical charges can be controlled. Similarly, the surface density of the designed targeting ligand can be functionalized and optimized for specific applications (Euliss *et al.* 2007, Jana 2004, Morganti *et al.* 2013). In addition these nanostructured fibers may be designed to have dimensions smaller than the human cell. Any effective/therapeutic nanocarrier requires, in fact, high-throughput optimization of many physicochemical parameters, including surface hydrophilicity, surface charge, surface functional groups, particles size, core materials, linker composition and nano-fiber shape, in order to optimize its therapeutic or cosmetic efficacy and pharmacokinetic parameters, as well as reduce its toxicity. This is the reason why nanotechnology could be defined as a group enabling technologies capable to develop structures, systems, and devices in a scale ranging from 1 to 100 nanometers (nm). To give an idea of this scale, the diameter of a hair is about 50.000/100.000 nm, while the size of a red cell is in the order of 7.000 nm, and a bacterium is about 1.000 nm long.

Certainly non-degradable nano-fibers and/or nanoparticles that accumulate intracellularly, are likely to have a number of toxic effects and, therefore, need to be designed and targeted for rapid excretion. In this regard, tissue engineering approaches need to be versa-

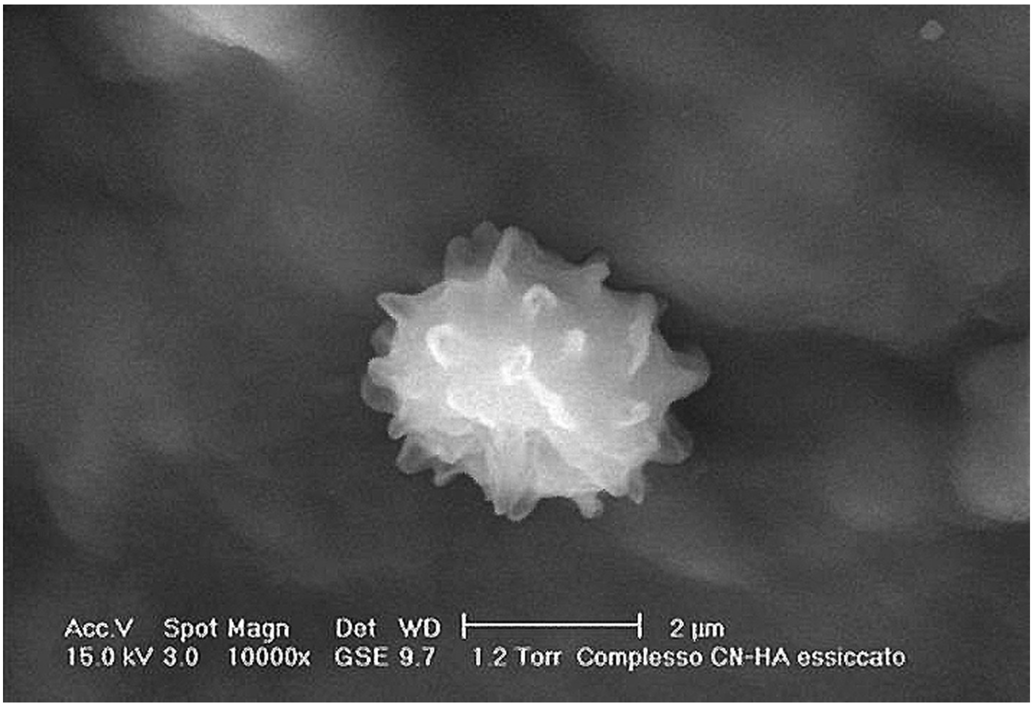

Figure 1. Block-co-polymer chitin nanofibrils-hyaluronic acid at scanning electron microscopy.

tile; restoring the lost or aged skin tissue structure and function requires the right cues to guide tissue regeneration and rejuvenation.

The interactions between cells, the extra cellular matrix (ECM) and biological signals are crucial for normal tissue structure and function. Disruptions in these processes often lead to skin diseases and/or degeneration and premature aging. In a similar way, the surface charge and functional groups of nanoparticles or nanofibers depend on the electronegative polymer used by the gelation process and can affect their interactions with the skin microenvironment (Lundqvist *et al.* 2008). Thus, in the Chitofarma, Biomimetic and n-Chitopack projects, collaborations between clinicians, biologists, chemists, plastic surgeons and engineers are essential for obtaining the desired results. Numerous fields, in fact, have to be involved in assisting in the R&D of biomaterials, including, but not limited to, material, mechanical, and medical engineering; clinical medicine, molecular cell biology, bioethics, regulatory affairs, business administration, and commercialization transition (Roco *et al.* 2011).

Towards this direction, most tissue engineering strategies, composed of single or three key components (scaffolds, cells, and instructive signals) are designed and optimized for specific needs of certain tissues. The scaffold (crystal chitin in our project) that serves as temporary matrix to support the skin regeneration, may also be considered as a reservoir system capable to release biological signals. These signals, coordinating many physiological necessities, play an important role during the normal tissue development process and mediate the tissue remodeling during injury (Bu & Callaway 2011). Nano-fibers and the non-woven tissues, made by the Chitofarma project, will be designed and developed to obtain a scaffold architecture capable to take important roles in sustaining cell proliferation and facilitating the diffusion of the nutrients, the active ingredients entrapped into CN, as well as wastes and signaling molecules at different levels of the skin layers. A better understanding of the cell-niche interactions, as well as appropriate CN engineered fiber models will be crucial for developing functional non-woven tissues capable to repair a diseased or aged skin.

In any way, scaffolding materials, such as CN, play a critical role in tissue engineering by acting as substitutes of cellular ECM, providing temporary mechanical support for the cells, mimicking their native microenvironment. The normal ECM network, comprising of fibers, such as collagen, hyaluronan, and soluble molecules provides the biophysical and biochemical cues to guide cell behavior within tissues, similarly to CN-non-woven multilayered tissue. The latter has its own cicatrizing activity, that is increased by the presence of Hyaluronan, peptides and other natural compounds that are electrospun.

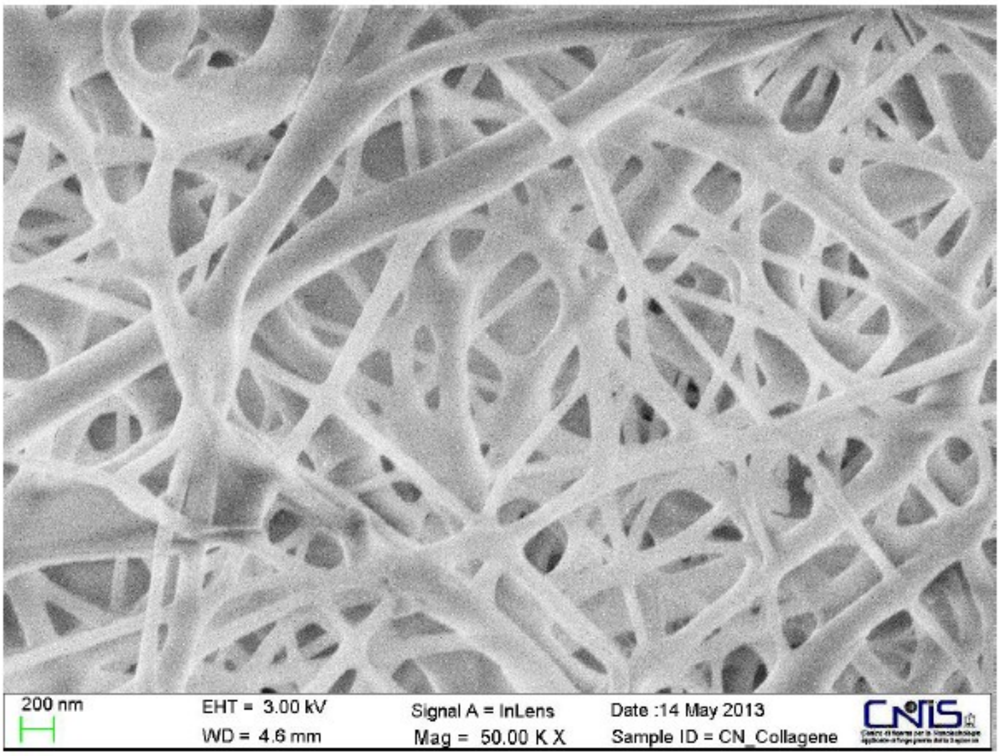

Figure 2: Block-co-polymer chitin nanofibrils-Collagen at scanning electron microscopy, on kind permission of CNIS.

Figure 3. Chitin nanofibrils advanced medication obtained by electrospinning technology.

From an economical point of view, nanotechnology is a growing market, representing almost 1,300 products that are being commercialized (Roco *et al.* 2011). The market of nanotechnology-based products reached $254 billion in 2009 and is expected to rise to $1 trillion worldwide by 2015. The market of natural products in Europe is projected to grow towards €250 billion by 2020, while the regenerative medicine field that is based on nanotechnological ingredients is estimated to have a worldwide market of $500 billion, according to the US Department of Health and Health Services (Bu & Callaway 2011, Mantovani *et al.* 2010). On the other hand the actual world demand for food containers is higher than $15 billion.

In conclusion, product multifunctionality is the key advantage of these chitin nanofibrils over other polymers. By this new technology it is possible to produce innovative block copolymeric nanoparticles and cross linked polymers for cosmetic emulsions by the gelation method (Figure 1), advanced medications by electrospinning technology (Figure 2), and transparent films (Figure 3) to be used as food packaging by the casting process. All these products can have a profound impact in the market of innovative goods and also change consumer management in the near future. Industrial sustainability is another advantage of these specialized products. The consumption of raw materials coming from waste resources and the use of methodologies that consume low amounts of water and energy are necessary to protect human health and the environment.

Finally, it should be noted that processing the wastes of crab, shrimp and fisheries has become a serious issue in coastal areas (FAOSTAT 2011, Islam *et al.* 2004, Kim & Venkatesan 2013). Selective isolation of bioactive material, such as CN, is the simplest way to decrease not only the environmental pollution due to the disposal of these underutilized byproducts, but also to increase the production of these innovative biomaterials. The generous support of the EU funds is pivotal towards this end.

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