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Biomimetic Materials Mimicking Nature at the Base of EU Projects

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Author's contribution

The whole work was carried out by the author PM.

Original Research Article

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ABSTRACT

Many marine organisms, such as mussels, are able to produce viscoelastic adhesive materials made of polymeric protein-polysaccharides, active in aqueous environment also. Some EU research groups are working to identify the same materials and processes for producing ecologically -friendly glues, at industrial scale. To obtain this and other goals, innovative bio-polymers will be produced by the use of plant biomass and by-products from fishery waste. These biopolymers will be used for making eco-friendly non-woven tissues by the electrospinning technology to obtain advanced medications, and producing food-packaging films by the casting technology. The multi-functionality of the bio-polymers obtained, useful to produce innovative goods, will be of great importance to reduce pollution and save the environment, also because they have to substitute the use of petrol-based compounds.

Keywords: Biomass; fishery waste; biopolymers; bionanotechnology; chitin nanofibrils.

1. INTRODUCTION

Many specialized biological systems are able to make firm attachments to various substrata, in aqueous environment also, by the production of viscoelastic adhesive materials made of polymeric protein-polysaccharide complexes (Fig. 1) [1,2].

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Fig. 1. Attachment of mussels on surface under the sea. (image taken from http://en.academic.ru/dic.nsf/enwiki/353104)

These naturally produced adhesives are known for their superior strength and durability compared with man-made materials. Examples of biological systems that generate adhesives include bacteria, spider, sea cucumbers, barnacles, and mussels. developed adhesive strategies to deal with the dynamic ocean environment, so that many sea invertebrates attach permanently or temporarily to inanimate and sometimes living surfaces [3]. In particular marine mussels, such as *M. Edulis,* attach to a variety of surfaces in an aqueous *Mitylus edulis* environment by using a natural adhesive, incredibly strong,durable,and impervious to water and turbulent sea forces. For all these reasons, research efforts have focused on identifying the same environmental strategies and protein synthesis adopted by mussels for producing these adhesive compounds. The production-scale availability of these processes will enable bind materials ranging from glass, plastics, metals, and organs such as bone, teeth, skin, and other biological organs.

Many of the mussel adhesive proteins identified to date are polyphenolic 38 polymers, known for their non-toxicity, low immunogenic qualities, anti-inflammatory and antioxidant properties. According to many authors, these natural bioadhesives may consist mostly as a combination of proteins, polysaccharides and lipids, the most common constituent being the amino acid DOPA(3,4-dihydroxyphenylalanine), mediates adhesion to substratum [4-7]. It has been shown, in fact, that DOPA not only mediate adhesion to the surface, but is also a cross-linking agent contributing both to the competition with water and cohesive strength of the mussel adhesive plaque. In any way, the cohesive and adhesive proteins produced by mussels contain, 4-dihydroxyproline, 4-dihydroxyarginine, and o-phosphoserine [8-11], while the concentration of non-oxidized DOPA (> 20%) seems to be critical for the quality of adhesion [12].

Thus being highly hydroxylated and positively charged, these molecules have the possibility to form numerous and strong hydrogen bonds with negatively charged hydrophilic polymers [11] and marine mineral surfaces [13]. However, it is interesting to underline how the production of these marine adhesives is similar to that involved on the majority of commercial synthetic adhesives: small monomers are first cross-linked to form larger chains that further interact during the curing of the adhesive: the 3kD protein is thought to be the smallest subunit polymerizing to complex molecules in biological adhesives

2. USE OF NANOTECHNOLOGY AND BIOTECHNOLOGY

According and inspired to these premises, the EU research project Bio-Mimetic www.biomimetic-eu-project.eu) has been designed to develop effective biomimetic glues by the use of biopeptide-based materials (pseudo-peptides precursors) obtainable by enzymatic processes that converts these precursors into more reactive compounds. Subsequent non enzymatic reactions will lead to further linking processes such as the polymerization of monomers, the conjugation of polymers and the formation of cross- linked structures. The main *industrial* objective of Bio-Mimetic is, therefore, to set the base for full scale exploitation of new bio-processes and bio-polymers as eco-innovative solutions for a wide range of goods, such as household products, cosmetics and bio- non-woven tissues. The obtained bio-based polymers, resembling natural peptides, will be conjugated or cross-linked to create respectively: [1] *bio-conjugated copolymers* useful for producing skin-friendly glues and household products, replacing the petrol-based copolymers with environmentally friendly alternatives; [2] *bio cross linked block copolymeric nanoparticles* for making innovative cosmetics and non-woven tissues. What is interesting to underline in this project is not only the adopted *blue biotecnology processes,* but also the use of raw materials extracted by the plant-biomass [14,15] and *chitin nanofibrils* (CN) obtained from the fishery and crustacean waste, both necessary to reduce the environmental pollution [16-18]. By the use of CN and the fabrication of nanoparticles and non-woven tissues made by the electrospinning process, the project' participants will also enter into the fascinating new field of *nanotechnology* and specifically of *nanobiotechnology. Nanotechnology* mainly consists of the processing and utilization of materials, devices, and systems through the control of matter on the nanometer-length cale, in the range between 1 and 100nm (i.e.at level of atoms, molecules and upramolecular structures) (Fig. 2) [19]. Naturally, these nanostructures, exhibiting novel physical, chemical, and biological properties and phenomena, play important roles in many diverse 91 isciplines, such as physics chemistry, engineering, computer simulation, biology, medicine, and material science. Just to have an idea of the nanoscale, 1 nanometer (nm) is a billionth of a meter, so that the hair diameter is between 50,000 and100,000 nm, the size of a red blood cell is in the order of 7000 nm, while a bacterium is about 1000 nm long (Fig. 3). On the other hand, *Nanobiotechnology* is the branch of nanotechnology that deal with the study of iological and biochemical activities used for medical application, such as therapy and diagnosis, to make innovative drug delivery systems, biomaterial, innovative non woven tissues, nanoparticles and cosmetics, nanoelectronic biosensors for imaging and nanorobots [20- 25].This is the reason why many efforts in nanomedicine are focused on understanding and engineering the properties of already available therapeutic and diagnostic modalities, rather then development of novel therapies. The physicochemical properties of *rather than* nanoparticles can be engineered, in fact, at the molecular level, so that their shape, size and charge can be controlled and optimized for specific applications [26-28]. By this new technology it is possible to develop a nanocarrier that will accumulate in certain issues, owing to its physicochemical properties, as well as will select a therapeutic load, based on the distribution properties of the nanocarriers. Lipid nanoparticles, for example, have shown to be able to form monolayer on the skin surface retaining the skin's moisture, while some polymeric natural nanoparticles may improve the carrier penetration through the skin layers, when covered by positive charges on

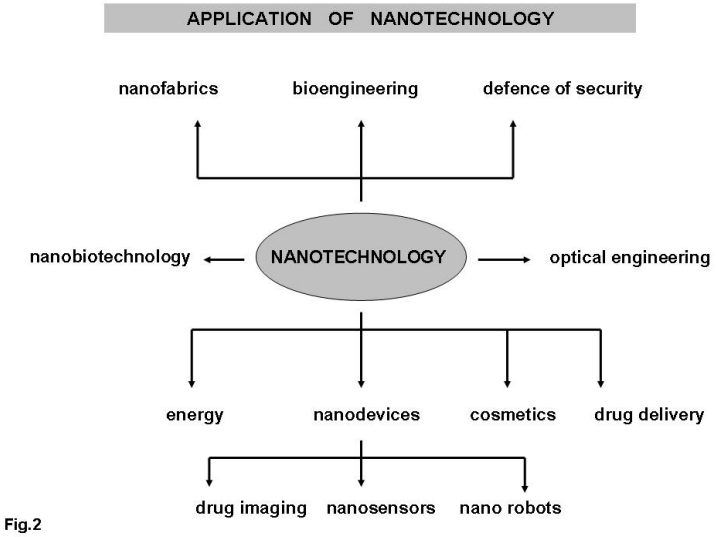

Fig. 2. Application of nanotechnology.

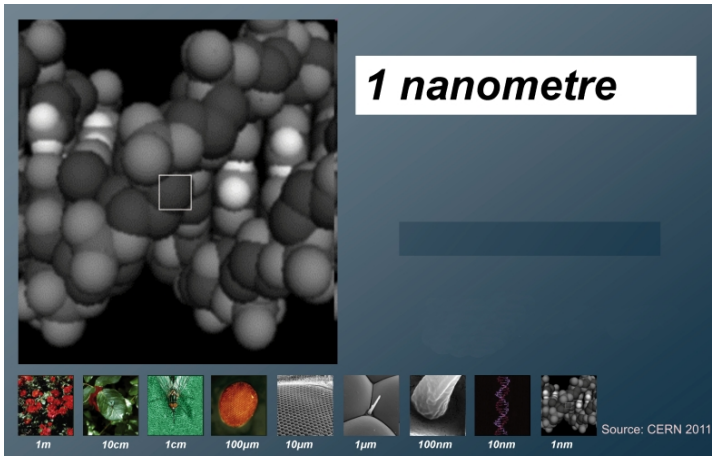

Fig. 3. Nanoscale.

their surface [29,30]. Size, surface charge and lipophilicity seem, in fact, controlling factors in transcutaneous transport of nanoparticles. In any way, nanoparticles used in nanomedicine could be made of a wide variety of biomaterials, including polymer matrixes (nanospheres), block copolymers (nano/micro lamellae or nanospheres) (Figs. 4,5),polymer shells (nanocapsules),lipid particles such as liposomes,dendrimer-like structures,carbon-based structures such as adamantine, fullerenes, ultra-nanocrystalline diamond, etc. [25,29,30]. Together with the design of nanocarriers, a major consideration in tissue engineering is also the pursuit of scaffolds, providing an architecture on which seeded cells may proliferate and differentiate to form new tissues and organs [31]. These structure, based on the use of natural polymers such as collagen, hyaluronate, alginate, gelatin and manmade polymers as polyethylene, polyvinyl alcohol,play a critical role in tissue regeneration because surface and structural properties of the obtainable biomimetic scaffolds directly influence the cell viability,

migration, proliferation, and differentiation. The synthesis of biomimetic nanomatrices can be obtained, in fact, by the electrospinning technology by which can be fabricated caffolds with nanoscale fibers that mimic the size and arrangement of native collagen fibers (50-500 nm), also because electrospun scaffolds possess a high surface to volume ratio and interconnecting pores (Fig. 6). In this way, cell adhesion and formation of cell-cell junctions is facilitated [32,33]. Additionally sequential multilayering spinning of different polymers, synthetic polymers alone and in combination with natural proteins, enhances the mechanical integrity and dimensional stability of electro spun meshes [33-35].In any way, nanofibrous scaffolds induce favorable cell-ECM (Extra Cellular Matrix) interactions, increase cell proliferation rate, maintain cell phenotype, support differentiation of stem cells and activate cell-signaling pathways [36,37].Naturally, scaffolds must be designed and based upon the tissue with which they would interface and must be biocompatible and biodegradable, as well as flexible and clinically manageable. Moreover, compared to other scaffolding materials, electrospun nanofibers have the advantage of higher mechanical strength and may be created from organic and inorganic materials of high Young's modulus [38,39].

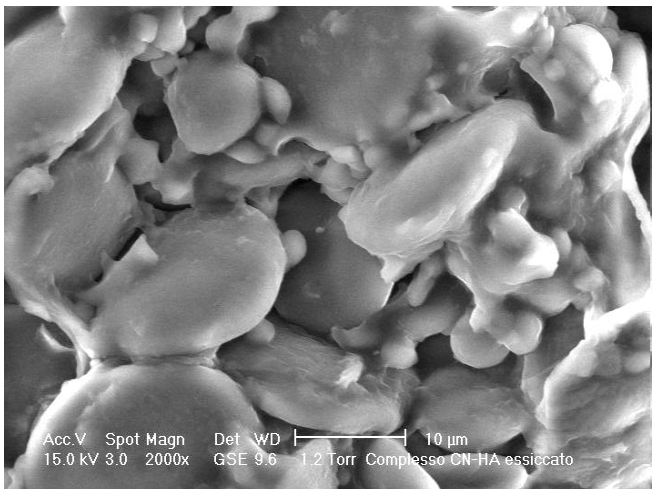

Fig. 4. Nanolamellae of chitin nanofibrils block polymers at SEM.

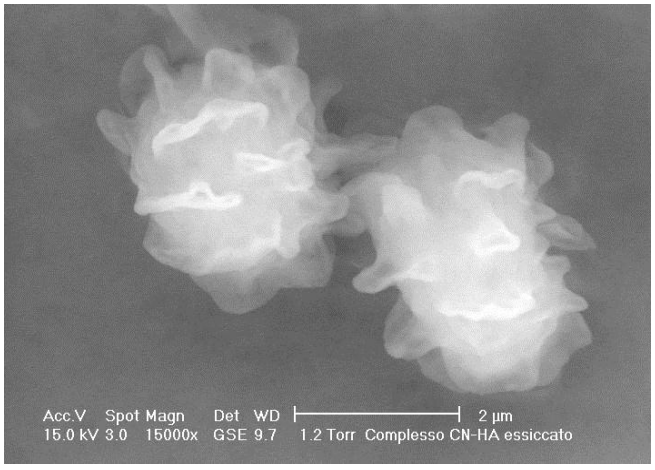

Fig. 5. Nanoparticles of chitin nanofibils block copolymer at SEM.

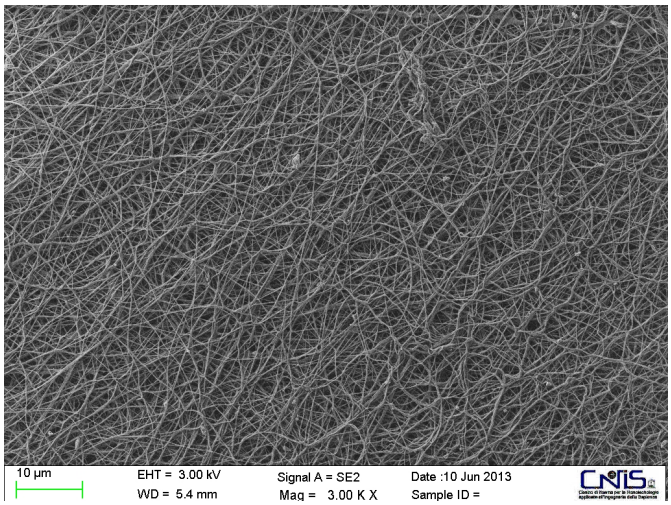

Fig. 6. Electrospunscaffold made by chitin nanofibils.

3. BIO-POLYMERS BASED ON THE USE OF CHITIN NANOFIBRILS

It is to remember that electrospinning is a method of fabricating unlimitedly long nanofibers. (100-200 nm in diameter) from viscous polymers extruded from syringe needles by a direct current (DC) power source. During fabrication, the polymer is highly charged (10-100kV) by the DC power and is stretched by electrostatic repulsion toward the polymer molecules. For all these reasons the nanotechnology and nanobiotechnology are two very important sectors that gave rice to the large market of nanomaterials and nanoparticle technology. Moreover the necessity to utilize natural ingredients, contemporary reducing the environmental pollution, has revealed the huge potential that offers the selective isolation of bioactive aterial from industrial underutilized by-products, such as *biopolymers* from plant biomass and *Chitin Nanofibrils* from the fishery and crustacean waste. Processing the wastes of crab, shrimp, and fishes has recently become a serious issue in coastal areas of the Pacific, Atlantic, and Indian oceans, as well as in the worldwide land by the great quantity of underutilized plant biomass [40-42].

Thus, while about 70% of marine capture fisheries are utilized for processing, its discards exceed 20 million tons/year, so that the consequent chitinous shellfish waste is considered hazardous for their high perishability and high polluting effect, if disposed off-shore [40-42]. In the sea it rapidly leads to eutrophication with an high oxygen demand, while on land it quickly becomes colonized by pathogens and spoilage organisms, causing environmental and public health concerns [43,44]. On the other hand, world production of biomass is estimated at 146 billion metric tons/year, mostly represented by 182 plant growth [45]. At this purpose it is interesting to underline the generation of organic plant residues and substrate waste, coming from the forced systems in horticulture. Thus, a surface area of greenhouse cultivated crops of 30,000 ha, generates, in fact, approximately 1,000,000 tons of solid waste per year [46]. The Greenhouse industry residues cause serious environmental and visual pollution, making it necessary to look for new ways of their elimination. According to Callejon et al. [47], the biomass not only acts as a host for pests, microorganisms, rats and insects, but has other harmful environmental effects, such as pollution of the soil and rivers, emitting also bad smells. In any way the assessment of the environmental impact of this potential waste-plant treatment has shown that it would be better its recycle, than to try to obtain

energy through combustion. However, since the realization of global sustainability depends on renewable sources of materials and energy, there is an ever-increasing need to develop, for example, environmentally-friendly bio-based polymers able to replace petroleum-based ones.

Research in this field has shown strong potential in generating high-performance unctionalized polymers from plant, grass biomass and fishery by-products. With the potential large-scale production of lignocellulosic biomass and fishery discards, cellulose and hemicellulosic polysaccharides as well as, chitin, chitosan, and oligopolysaccharides will be abundantly available representing renewable feedstocks for biopolymers and biocomposites with physicochemical properties that match or exceed those of petroleum-based compounds [48-50]. It is,therefore,clear that these innovative biopolymers can provide an alternative to a number of petroleum-derived polymers and enable the development of bio-compatible compounds, some times with properties that exceed those of synthetic polymers made from petroleum.Thus new scientific and technical basis for a new era of sustainable chemical production will be created, becoming an indispensable consumers' behavior beyond the *oil age* from fossil resources (Biomimetic: www.biomimetic-eu-project.eu). Based on these considerations other two research projects become a reality: n-Chitopack (www.n-Chitopack.eu) that has the goal to produce transparent films and soft/rigid food-containers, and Chitofarma that has to make advanced medications. Both the projects, in progress from about one year are coordinated by the Italian PMI MAVI, patent holder of Chitin Nanofibrils (CN) [WPO/PTC (26/10/2012) WO/2012/14875]

About the waste materials to take in consideration, it is to underline that the world demand for food containers is estimated to increase nearly 3.8% per year, ranging over US$ 115 billion in this year, due to an increase in the global output of food and an influence towards fast foods to meet fast-paced lifestyle. The petrol-based polymers are today widely used for packaging materials because of its cost effective and barrier properties in meeting the arket needs, but they are generally not bio-degradable in the long run, generating in Europe an impressive 14 millions tons/year of waste [51].Thus the necessity to find significant alternative source of potential renewable feedstock for polymers to be used as food packaging. At this purpose and by the n-Chitopack project, the EU group involved is developing different technologies based on the use of Chitin and other natural polymers to obtain nanocomposite films and rigid containers with bacteriostatic and UV resistant properties for producing innovative food packaging of high performance and environmental compatibility. But which characteristics and dimension CN has? It is a natural sugar-like polymer of 240x7x5 nm in dimension, that made of 18-25 molecules of glucosamine and acetylglucosamine, appears at SEM as a needle (Fig. 7).

In a water colloidal dilute dispersion, its crystalline structure is prevalently covered by positive charges and enveloped by water ions which prevent its flocculation [52,53]. The ncorporation of CN and other nano-sized reinforcement ingredients to produce biopolymers opens new possibilities for improving not only their properties, but also their cost-price-efficiency [54,55],also because of its ability to form film, complexing active ingredients, chelate metal ions, and retain water. In addition CN, because of its geometrical and opological architecture which mimic the native state of ECM in living tissue, may be utilized to make non-woven tissues for advanced medications. This is the goal of **Chitofarma** project based on the use of CN and other natural polymers transformed in technology, previously reported. At this purpose, it is to remember that the in study advanced medications are designed to solve the problem of burned skin and wound healing. Tissue healing, in fact, is a complex process which involves an orchestrated interaction between many different types of

cells including immune, vascular and stromal cells in addition to the tissue-specific cell [56]. In the later stages of this process fibroblasts are recruited to the wound, depositing ECM proteins such as collagen, fibronectin and hyaluronic acid, leading to new tissue regeneration [57].Therefore, the activity of the CN252 scaffold and the active ingredients embedded into the designed elextrospun fibers used for the no-woven construct, has to profoundly affect and accelerate the skin healing process. In any way, being the normal skin' healing process characterized by a complex sequence of events, the design of the solution to be used by the electrospinning technology has been developed with the strategy in mind to not only replace wounded tissues but also to regenerate the native tissue lost. At this purpose the antiinflammatory/reparative activity CN has shown to possess, seems to be of great help for obtaining efficacious advanced medications [58]. In conclusion, the use of biomimetic and multifunctional material of natural origin as CN and plant biopolymers may be useful to solve different problems, ameliorating our way of living. The integration of new nanobiotechnologies, such as electrospinning to made nanofibers for medical application, and casting to make thin and transparent films for food packaging, or the adoption of new enzymatic methods to produce specific biopolymers necessary to produce innovative and safe household and cosmetic products, will give many benefits to Humans and the environment, first of all when underutilized by-products as plant biopolymers and chitin will be used. necessary, in fact, to below costs, reducing also pollution and saving the environment [59]. However, according with the EU research programs, the biotechnological ingredients have to be designed and made by the same material- structure of the life, learning from nature to produce goods by the same enzymatic processes used from living organisms.

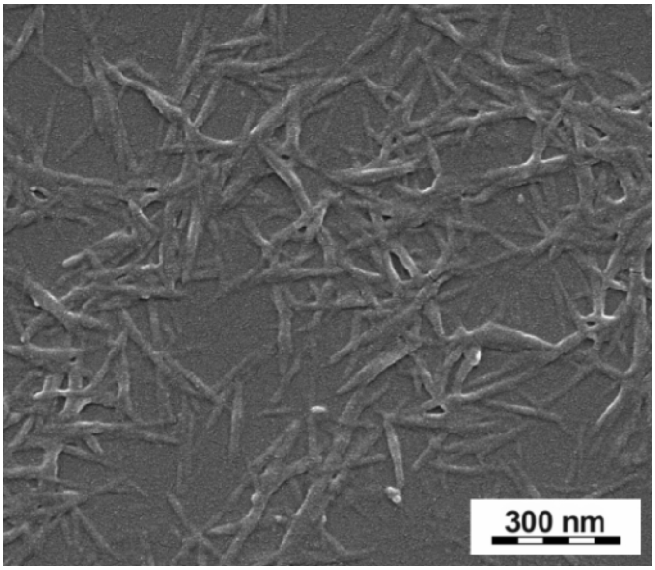

Fig. 7. Chtin Nanofibrils' needles at TEM.

4. CONCLUSION

According to the scientist Fritjof Capra [60,61] "development of these new technologies will represent a great intellectual challenge because until now we have not been capable to understand processes developed from nature during the billion years of evolution". Spider,

for example, is capable to rapidly produce fibers for its spiderweb that, according to their thickness are more resistant than steel. Abalone makes a shell two times more resistant than our ceramics produced by the more modern technological processes, while some butterflies mimic different colors by the use of specialized chitin' nano crystallin constructions reflecting sunlight (Fig. 8) [62]. By what kind of technology and means are these animals producing their biomaterials, by a low consume of energy, at ambient temperature, and without producing any toxic waste? The solution to these problems is at the base of the biomimetic projects, organized by the use of innovative anobiotechnologies, just to mimic the molecular structures and processes adopted in nature [63]. This is the challenge of the EU projects, Bio-mimetic, n-Chitopack, and Chitofarma reported and focused by this paper.

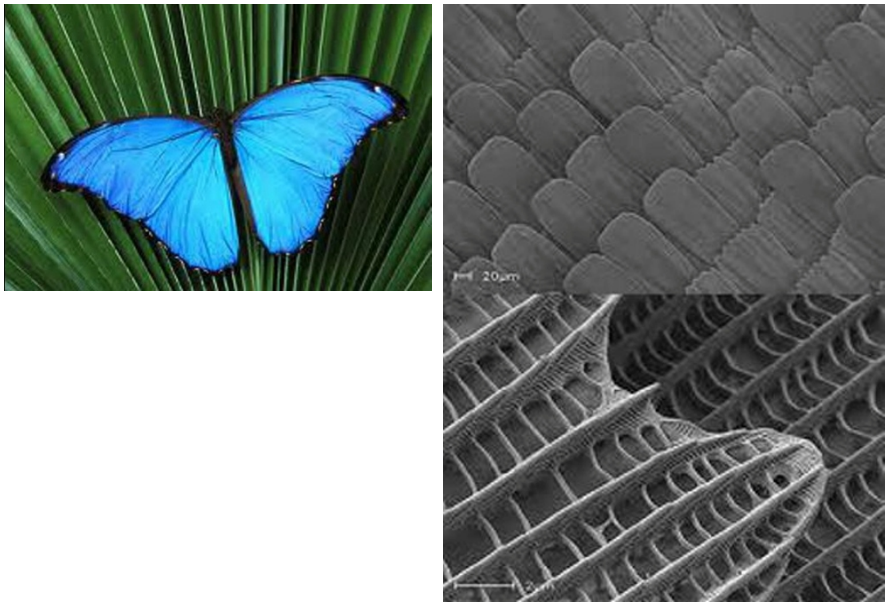

Fig. 8. Chitin nanostructured crystals of butterfly wings (*Morpho didius*).

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COMPETING INTERESTS

Author has declared that no competing interests exist. The opinion expressed in this article represent those of the authors only and not of the European Community.

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