

Review

# From Cosmetics to Innovative Cosmeceuticals—Non-Woven Tissues as New Biodegradable Carriers

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**Abstract:** Due to pollution and climate-change fear, further increased by the COVID19 pandemic, consumers are looking for body and mind health by the request of more effective and safe products, including the anti-aging skincare cosmeceuticals. The term “cosmeceuticals” was coined in 1962 as a fusion of cosmetic and pharmaceutical to cover a new class of products able to achieve aesthetic and drug-like benefits. They not only improve the skin’s appearance, but also treat different dermatological conditions, through a physiological activity, shown by in vitro and in vivo studies. This new category of cosmetics should contain no recognized drugs, but nonetheless have medicinal value. Consumers, in fact, are looking for products able to regenerate the skin and maintain not only a youthful appearance together with well-ness and well-being, but preserving the environment also. Consequently, they are searching for cosmetics and food made with high-quality natural ingredients, packaged with biodegradable materials and realized by sustainable technologies, possibly at zero waste. Consumers, in fact, are afraid of the pollution and plastics invading lands and oceans, causing many frequent disasters on our planet. New and smart tissues and films, made by polysaccharides and natural active ingredients, are proposed as innovative cosmeceuticals. These non-woven tissues, embedded by micro/nano complexes of chitin and lignin encapsulating different active ingredients, could represent a new category of vehicles that are characterized for their high effectiveness and safeness. Moreover, they do not induce allergic nor sensitizing phenomena, being biodegradable; skin- and environmentally friendly; and free of preservatives, emulsifiers, colors, fragrances and any kind of chemicals. Last but not least, polysaccharides, chitin and lignin may be obtained from industrial and agro-forestry waste, safeguarding the natural raw materials for the future generations.

**Keywords:** cosmetics; cosmeceuticals; health; well-being; wealth; polysaccharides; chitin nanofibrils; lignin COVID-19



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## 1. Introduction

The lockdown period and ongoing distancing measures have seen a decline of some cosmetics categories, such as color cosmetics, fragrances and hair removal, with a growth in skincare promoting well-being and self-care able to slow down the skin-aging phenomenon.

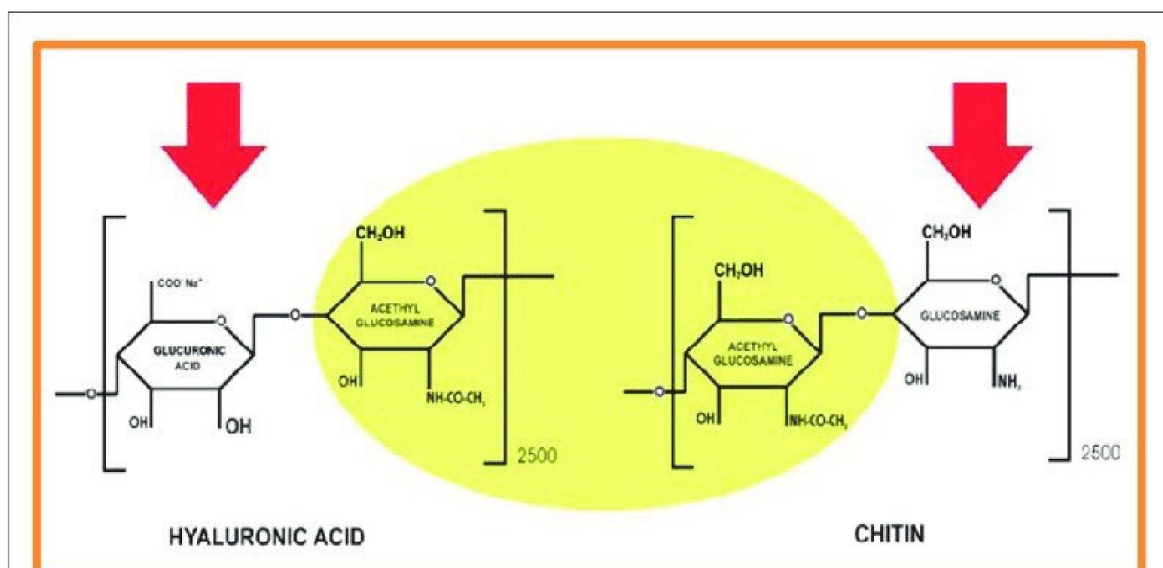
People, in fact, do not want to get old and unhealthy, also because the unattractive elderly individuals are perceived as being significantly less favorable, according to the actual stereotype [1]. “Older person who have aged well”, preserving their appearance, in fact, “are associated with the personable quality of being young healthy”. Attractiveness in the elderly is really equated with youthfulness, and “What is beautiful is good” [1,2]. Consequently, individuals who take advantage of cosmetic products with a real effectiveness have a better chance to enter into a more positive cycle [1]. Thus, “cosmetics can be viewed as therapeutic interventions to help a person feel” and look better, being used “as

a vehicle to promote health care and general psychological and social, wellbeing" [1,3]. Therefore, in this specific field, due to the lack of the actual international rules, the so-called "cosmeceuticals" might represent a new category of topical products placed between cosmetics and pharmaceuticals. The term "cosmeceuticals" was coined by Raymond Reed in 1962 who, receiving a medal award for his studies in the cosmetic field, defined them as "products closely related scientifically to many topical pharmaceuticals" [4]. Thus, they were characterized as products with "desirable aesthetic properties capable not only to enhance the appeal attractiveness, beauty and health of human being", but also "to meet rigid physicochemical and medical standards, delivering all their benefits without endangering the health of user" [4]. However, the term "cosmeceutical" became well-known in 1984, thanks to the study on retinoic acid as anti-aging agent, reported from the famous dermatologist professor Albert Kligman [5]. He successively wrote that "whether one approves or disapproves the use of term cosmeceutical, it has permanently entered the vocabulary of skin-care science" [6]. In any way, cosmeceuticals represent a new category of products which, placed between cosmetics and pharmaceuticals, are intended for the enhancement of both health and beauty system. Unfortunately it is to underline that, 30 years after the term was coined, is not yet officially recognized from the international cosmetic rules, also if the need of new regulations is claimed from many scientists, and the term "cosmeceuticals" dominates in dermatology literature, academic books, discussions, symposia and lectures all around the world [7–12]. Moreover, some actual ambiguities regarding the actual definition of cosmetics, drugs and medical devices [13], as well as the classification of some category of cosmetics, have to be reported. For example, antiperspirant products, anti-dandruff shampoos and sun preparation are regulated as drugs in the USA and as cosmetics in the EU [14,15]; in Japan, those cosmetics termed "quasi-drugs" may contain pharmacologically active ingredients, providing that the medicinal effects are only mild and the products' safety has been demonstrated [16].

Therefore, the challenge of innovative cosmeceuticals is to evaluate the feasibility of combining many active ingredients to create products that yield the expected "therapeutic" benefits, as previously reported many years ago [17]. The efficacy of a cosmetic product, in fact, depends not only on the active ingredients, but also on the delivery system selected [18]. Thus, the carrier able to load the ingredients and releasing them at the right skin layer, in the right dose and at the right time results in being fundamental to reach the effectiveness and safeness desired for the cosmetic formulation selected [19–23]. Moreover, consumers are not just looking for cosmetics characterized for their effectiveness and safeness, but also for their naturally derived ingredients and production through sustainable technologies [20–23]. Sustainability, in fact, has become a priority especially after the COVID-19 pandemic that, pushing for the necessity to increase health, well-being and wealth, has "further pushed the notion that natural is not always better when it comes to ingredients safety and shelf life" and to biodegradable packaging saving the environment [22,23]. In conclusion, in our opinion, cosmeceuticals based on tissue-carriers can be considered today as innovative personal-care formulations. These cosmeceutical-tissues, made by natural ingredients obtained from renewable sources and sustainable technologies and packed by biodegradable containers, have been supported by *in vitro* and *in vivo* studies which have shown their effectiveness and safeness as skin- and environmentally friendly products. Thus, we have the proposed use of polysaccharides as natural polymers to make innovative and biodegradable tissues. At this purpose, chitin and lignin have shown to be particularly useful to make micro-nano capsules, which, loaded with specific active ingredients, may be bound to the fibers of these natural tissues, characterizing their effectiveness and safeness. It is also interesting to underline that polymers and ingredients used may be easily obtainable from agro-forestry and industrial waste at a low cost, thus preserving the environmental raw materials for the future generations.

## 2. Why the Use of Polysaccharides

The growing search of greener products made by natural resources free of chemicals and the increasing concern with healthcare and lifestyle has notably changed the consumer trends driving demand for natural, bio-based cosmetics [21–25]. Consumers, in fact, are increasingly aware of the depletion of natural resources, and the increase of air and water pollution, which, with the extensive use of non-renewable and non-biodegradable raw materials, are causing climate changes with the consequential worldwide disasters [26]. Thus, there is an increased request for polysaccharides which, arranged from linear to highly branched chains, are polymers comprising 10 to up a thousand monosaccharides. Chemically and practically, they take on a variety of forms and functions, depending on which monosaccharides and carbons are connected. Therefore, because of their structure, some of these polymers are used for storing energy, while others result useful to send messages or provide support to cells and tissues. However, polysaccharides have gained high popularity due to their biodegradable and skin-friendly and environmentally friendly nature [27–30]. They are biological macromolecules which, together with proteins and polynucleotides, play important roles in the growth and development of living organisms as important component of higher plants, and membrane of cell wall of animals and microbes [28,29]. Polysaccharides act also as basic compounds for the realization of immune and antimicrobial systems of plant and animal tissues, including human breast milk. This is the reason why natural and some synthetic polymers, being also biodegradable and biocompatible ingredients with interesting mechanical properties and low toxicity, have been shown to be useful for specialized biological functions [27–30]. Therefore, they result in being appropriate materials for making natural-like scaffolds for the development of novel controlled skin delivery systems, as well as for innovative tissue-engineering (TE) and immunomodulating scaffolds for regenerative medicine and innovative cosmeceuticals [30–32]. TE, in fact, is a multi-stage process that requires the development of different components to design and make new-tissues by new biomaterials able to meet local environments, such as burns, wounds and aged skin [33,34]. Naturally, the right biomaterials have to satisfy appropriate characteristics necessary to stimulate the biological crosstalk between scaffold and tissue, for inducing the cells proliferation, adhesion and activation [35]. By these polymers, therefore, it is possible to make natural composite cell-supporting systems that are capable of setting up the matrix for building and regenerating the skin tissues or being used as active delivery devices [33,34]. Polysaccharides, in fact, are considered interesting carriers for drug and greener cosmetic ingredients, due to their easy delivery process, programmable target, cellular uptake, low toxicity, known metabolism and pharmacokinetic, and greater half-life in term of repeated topical administration of the loaded active ingredients effective and safe for the consumer's health [27–31]. However, by an advanced understanding of the signals by which the cells communicate with each other, it will be possible their up- or downregulation to influence the host responses by the interaction with the immune system [36]. At this purpose, the modulation of the immune system is believed to occur by binding hyaluronic acid (HA) to the CD44 receptor of eukaryotic cells for regulating cell–cell communication [36]. Remember, in fact, that HA is an anionic hydrophilic linear glycosaminoglycan composed of repeating units of N-acetyl-D-glucosamine and D-glucuronic acid, linked via Beta-1, 4 glycosidic bonds. Thus, as possible major component of the extracellular matrix (ECM) of mammalian tissues, the polymer could act as an adhesion for attachment to CD44 helper cells on human keratinocytes, thanks to the disaccharide units and its backbone containing -OH and -COOH groups [36]. In conclusion, HA has the role to promote cellular, survival, adhesion, migration, differentiation and proliferation in tissue, by transduction of specific signals and promotion of angiogenesis and wound healing. It is interesting to underline that chitin, having a backbone similar to HA (Figure 1) could have the capability to “trap” growth factors, stimulating the cell proliferation [37].



**Figure 1.** Backbone of hyaluronic in comparison with chitin.

Thus, by a morphological and immunohistochemical study, it was shown that “CD34positive radicular-follicular (i.d. stem) cells of Winstar rats appeared to be more expressed in skin treated with chitin nanofibrils (CN) and CN-Lutein than with untreated cutis (control) or with saline-treated” (Figure 2) [38].



**Figure 2.** The CD34 radicular–follicular cells of rat-skin treated topically by CN and CN–lutein (by the courtesy of Biagini et al. [38]).

Moreover, it was evidenced that CN may be considered “an important vehicle for the diffusion of derma-cosmetological molecules biologically active” [37]. Therefore, polysaccharides and chitin nanofibrils could be used as carriers for cosmeceuticals, emulsions and tissues. We should consider them as a new category of products which, placed between cosmetics and pharmaceuticals, have the function to enhance both skin health and beauty [4–11,39].

### 3. Chitin and Its Complexes

Chitin with cellulose is one of the major structural polymer occurring in nature, found in fungi, algae and the exoskeleton of arthropods, including insects, plankton and krill. It is a highly crystalline, cationic, and hydrophobic linear polysaccharide structure with strong hydrogen bonding, consisting of (1-4)- $\beta$ -N-acetyl-D-glucosamine units, while its deacetylated form, chitosan, is a mixture of N-acetyl-D-glucosamine and D-glucosamine [40]. Industrially produced, chitin may contain around 50% and more of glucosamine, while in chitosan it ranges a concentration from 70% to 98%. The polymer, such as cellulose and keratin, is arranged by nanosized and strong nanofibers in an antiparallel fashion made by fibril units bound each other to forms a hierarchical organization. These nanofibers provide a three-dimensional structure that mimic the native Extracellular matrix (ECM) useful, for the tissue regeneration, as happens in arthropods, plant and animals. Differently to cellulose rich of -OH groups, chitin/chitosan contain many -NH<sub>2</sub> group attached to the side-chains of the monosaccharide (Figure 3). Moreover, it is important to underline the



proposed role of chitin size as immune regulator molecule in response to the pathogens' aggression. [41]. This large polymer, in fact, released from pathogenic organisms and activated by the macrophages and cytokines' production, is degraded to intermediates pro-inflammatory chitin (40–70 millimicron) that in turn is further degraded in small anti-inflammatory chitin (<40 millimicron) (Figure 4) [41,42]. Therefore, the micro-size dimension of the polymer results a fundamental option to obtain the anti-inflammatory effectiveness. Thus CN as well as HA could induce cytokine production, leukocyte recruitment and alternatively macrophage activation. Due to these reported characteristics and activities, our group produced microspheres prepared by complexation between the cationic electropositive chitin nanofibrils and the poly-anionic hyaluronan (HA) and lignin (LG), respectively. The gelation method and water as solvent were used (Figure 5).

However, before complexing CN with LG, it was possible to solubilize different active ingredients, including vitamin C and E, niacinamide, glycyrrhetic acid, etc., which were successively and separately encapsulated into the two polymers. Soon after, the suspension was spray-dried to obtain micro-nanoparticles (NPs) (Figure 6) which were then successively coating, grafting on, or bound to the fibers of natural and natural-made polysaccharide nanocomposites for making innovative non-woven tissue and films by the electrospinning, casting or extrusion technologies, respectively. The obtained tissues/films have been shown to possess specific and interesting antioxidant, immunomodulatory and skin-repairing properties, being effective in regenerating, wounded, burned and aged skin [44,45]. Naturally, NPs were analyzed by Scanning Electronic Microscopy (SEM), Dynamic Light Scattering (DLS), Transform Infrared Spectroscopy (ATR-FTIR) and other techniques to verify their superficial charges, dimension and distribution on the tissue fibers, as well as the concentration of the active ingredients encapsulated into the CN-LG polymers, and the porosity and mechanical strength of the tissues/films (Figures 7 and 8). We must also underline that the encapsulation of biological material into the reported bio-polymeric microparticles not only ensures the protection and target delivery of the selected active agents, but also offers a controlled release with higher effectiveness and environmental safety for the consumer.

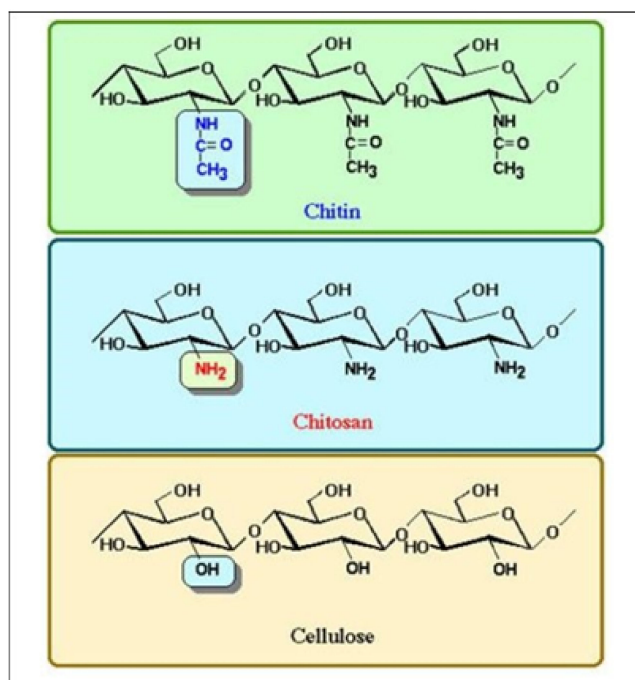
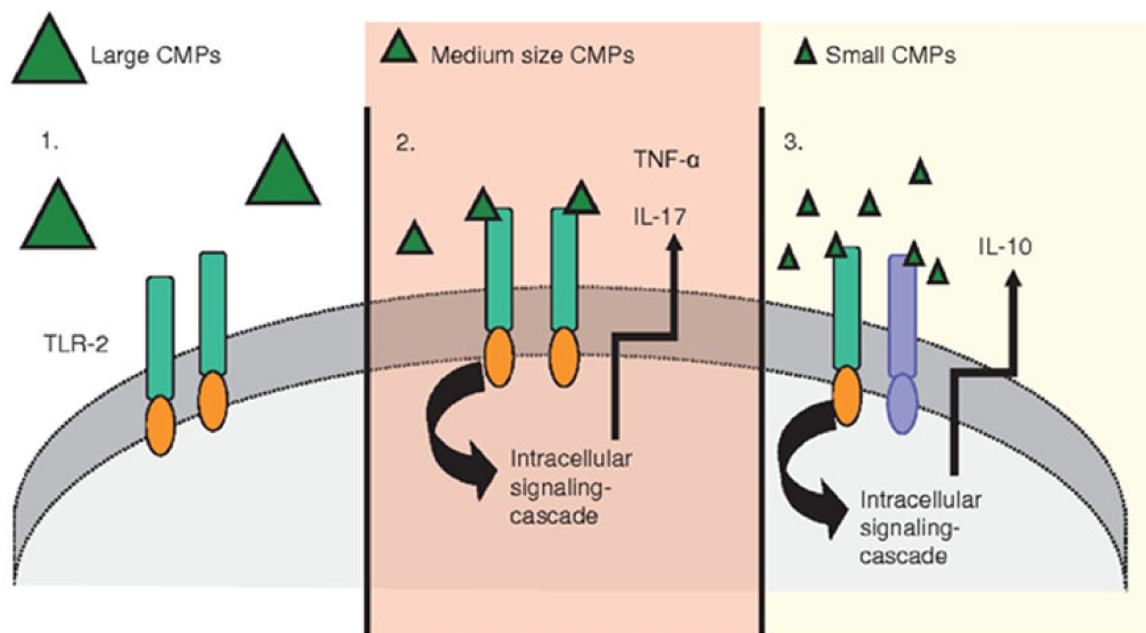
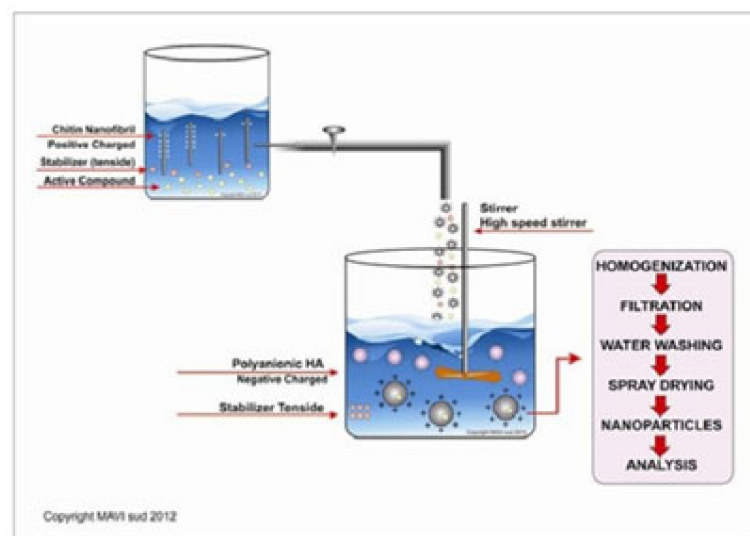


Figure 3. The different chemical groups characterizing cellulose from chitin and chitosan.



**Figure 4.** The pro-inflammatory or anti-inflammatory activity of chitin depends on its size (by the courtesy of Reference [43]).



**Figure 5.** The complex chitin–lignin obtained by the gelation technology.

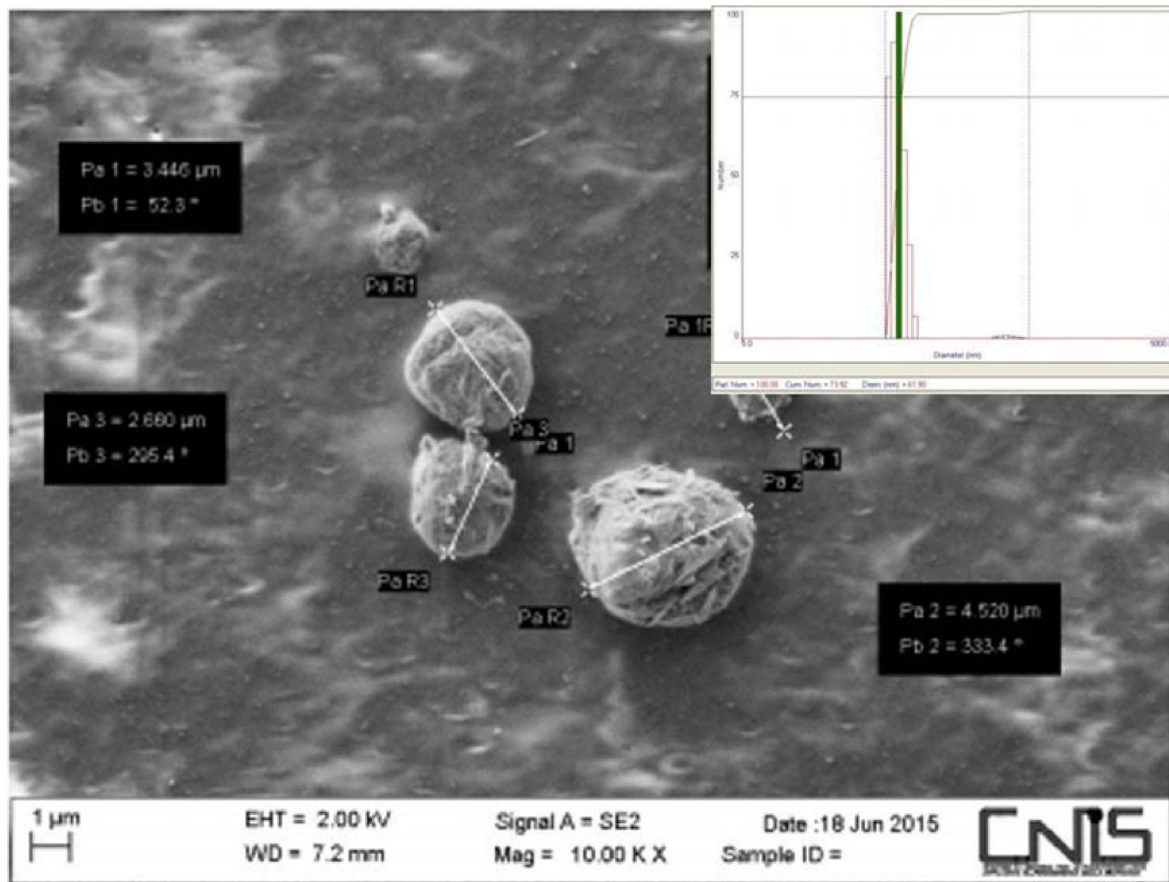
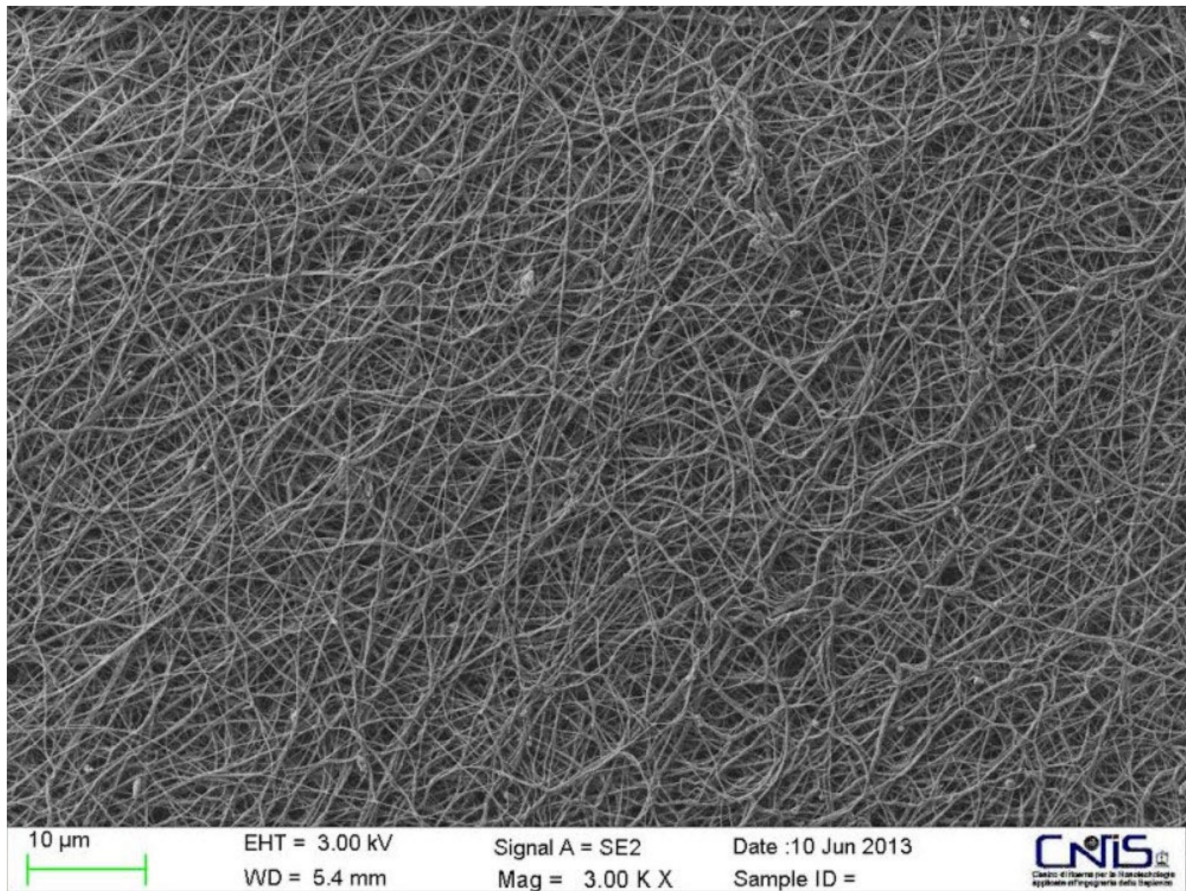


Figure 6. Micro capsules of chitin-lignin and their size at SEM.

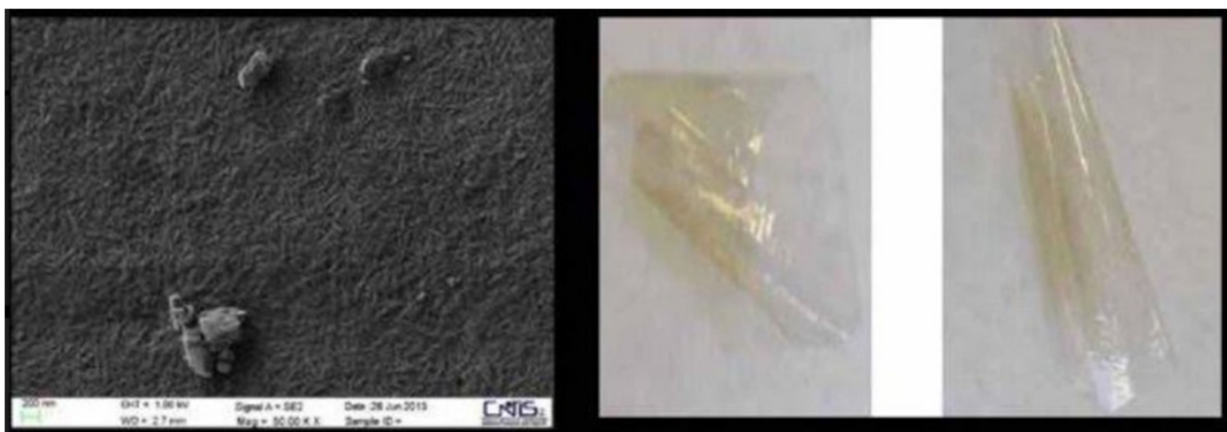


Figure 7. Cont.





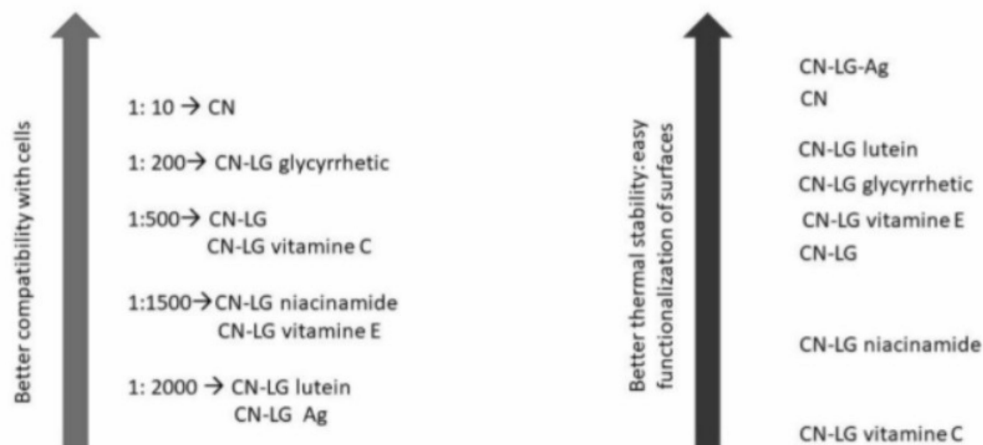
**Figure 7.** Chitin non-woven tissue (up) and its photo at SEM (down) where longer microfibers appear with the right interfibrillar porosity.



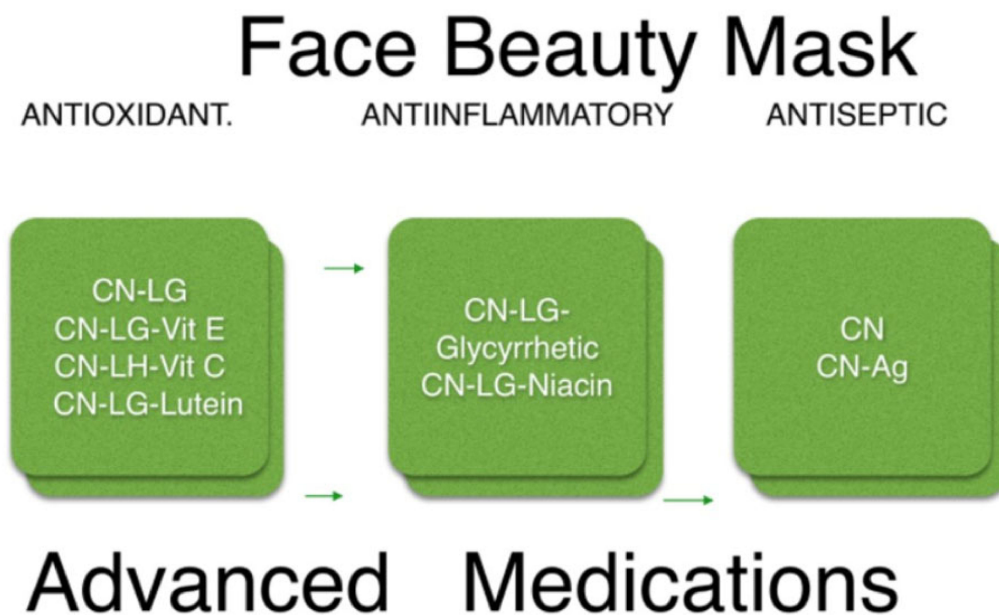
**Figure 8.** Chitin films (on the right) with its photo at SEM (left) where shorter fibers with no porosity appearing.

Moreover, by *in vitro* [46–48] and *in vivo* [49–51] studies, the effectiveness and safety of the final product were verified. Thus, by the first obtained results, it was possible to establish the better biocompatibility and thermal stability (Figure 9) of the various active ingredients encapsulated into CN-LG, as well as their effectiveness as antioxidant, anti-inflammatory or antibacterial agents when used to make surgical or beauty masks (Figure 10) [45–48,51–58].





**Figure 9.** Increased compatibility and thermostability of CN-LG microparticles encapsulating different active ingredients.



**Figure 10.** Effectiveness of various active ingredients encapsulated into CN-LG micro capsules bound to the fibers of beauty masks and surgical tissue-masks.

However, these smart tissues have been realized with the aim to make cosmeceutical tissues to be used as an alternative to the normal cosmetic emulsions because of their effectiveness to repair burned, wounded and aged skin [44–48,52,53,59], as well as to realize biodegradable surgical masks and one-day doctor’s dressings [55–57], because of their skin-repairing activity [51,54–58].

The natural polymeric nanostructured biocomposites used to make films and tissues, in fact, need their stability, size, shape, surface charge and chemistry, mechanical strength and porosity to be verified. Therefore, these properties have to be tailored towards the specific functionalities designed to meet the needs of the biomedical or cosmeceutical target required from the consumers. The efficacy of the realized tissues, in fact, depends upon the properties of the polymer(s) used, and the active ingredients coated on their surface or embedded into or bound to the fibers, the solvent used, and all the other methods adopted to reduce consume of water and energy, eliminating also any kind of waste. The reasons for proposing these biodegradable tissues as carriers for future innovative and smart cosmeceuticals are as follows: being reproducible; stable after application on the skin; easy to use with significant absorption properties; and non-immunogenic or sensitizing

activity the tissues in fact are free of emulsifiers, preservatives, colors, fragrances and chemicals (44–46). Moreover, the CN–LG nanoparticles used to encapsulate the active ingredients successively embedded into the tissues show other advantages, including a greater surface to weight ratio, facility to be produced and used, and characterized for their relatively low cost, being skin-friendly and environmentally friendly also [58]. Finally, they may be packed by biodegradable materials, such as paper and aluminum foils.

In conclusion, a greater cosmetic use of polysaccharides has to be considered important not only for their safeness and effectiveness as carriers and active agents, but also for being sustainable polymers obtainable from the food and industrial waste. It is important to reduce the increasing and unsustainable pollution invading our planet, saving the natural raw materials for the future generations.

#### 4. Cosmetics, Beauty/Health and Plastic Pollution

COVID-19 pandemic has affected people in the sense that they are looking to change their current consumption for making life more convenient and safer [51,54–58]. Thus, consumers are searching “for holistic, resilient and more thoughtful consumption” for dressings, food and cosmetics also. Regarding the sustainability sentiment before the pandemic, 64.3% of consumers desired to reduce plastic use, 59.7% food waste, 47.2% energy and 36.4% carbon emissions respectively, while 61% worried about climate change, 58.8% were oriented to recycle products and 30.6% to eat less meat [60]. After the COVID-19 pandemic, therefore, people have been taking social and environmental issues more seriously, believing sustainability initiatives critical for their lifestyle. Moreover, this pandemic disease “is causing a devastating wave of mental health issues, so that the number of people seeking help for depression and panic attack has increased dramatically” [61], it is also to underline that 88% of deaths in the first year of COVID-19 disease were in countries, including USA, UK, Germany and France (Figure 11), where more than half of the population was overweight [62].

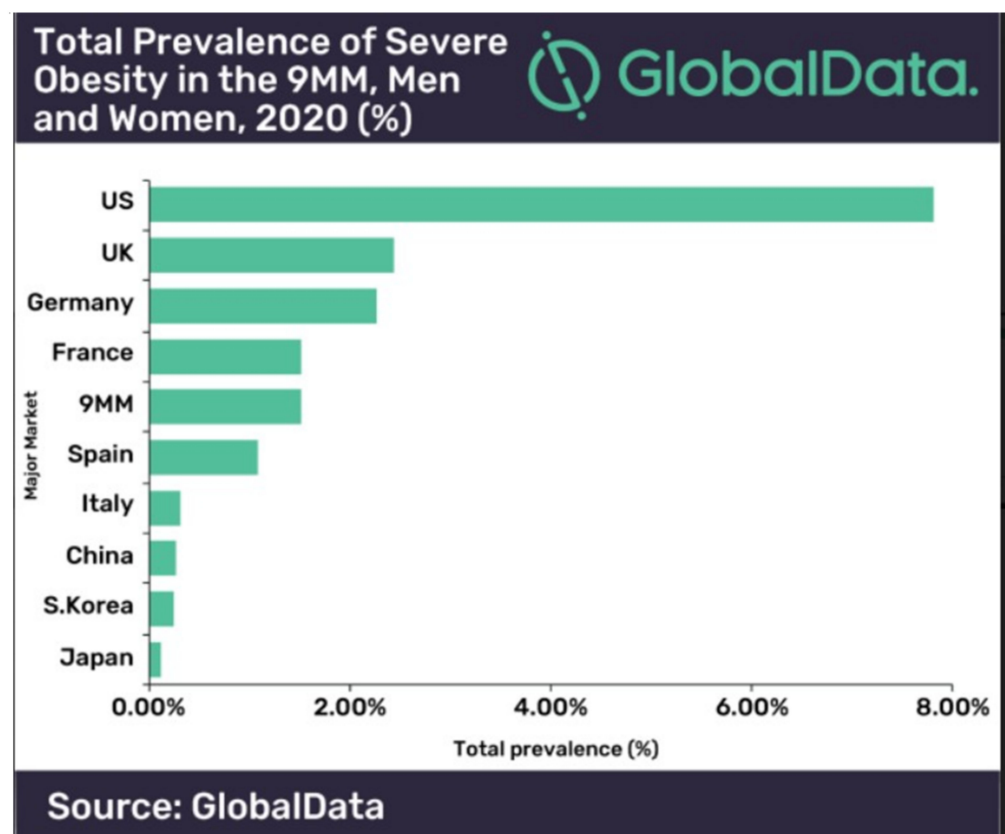


Figure 11. People overweight in USA and Europe (by the courtesy of GlobalData).

For these and other reasons, 43% of people worry about the increasing pollution and waste, while 41% for global rising of temperature, and 38% for plastic pollution [63] (Figure 12), thus the majority of people is looking to change their lifestyle.



Figure 12. Consumer environmental worries (by courtesy of GWI [61]).

Consequently, this pandemic crisis has accelerated the focus on sustainability and planetary changing, increasing the people's concern for their own and planet health. Thus, consumers have a major interest in cosmetic ingredients' quality and provenience, the content of the final product and its overall environmental impact from the production to its consumption [64]. Consequently, the demand for products made from natural ingredients and attractive for their biodegradable packaging boost the global cosmetic market, generating an estimated USD 380.2 billion in 2019 and projected to reach USD 463.5 billion by 2027 with an estimated Compound Annual Growth Rate (CAGR) from 5.3% to 7% from 2021 to 2027, with a high increase of natural products (Figure 13) [64].

Regarding the regions, Asia-Pacific accounted for the highest share, contributing in 2019 more than one-third of the market. Moreover, according to the Cosmetic Europe data [65] in the global market with a value of USD 286.7 billion. Europe remains the largest market in the world with a value at retail price of USD 79.8 billion and in 2019 with over 2 million jobs (Figure 14), in comparison with USD 73.7 billion in USA, 54.9 in China, 32.6 in Japan, 23.4 in Brazil, 12.0 in India and 10.3 in South Korea, respectively (Figure 15) [65].



Figure 13. Global Cosmetic Ingredients market, driven by natural-oriented compounds (by the courtesy of Technavio).

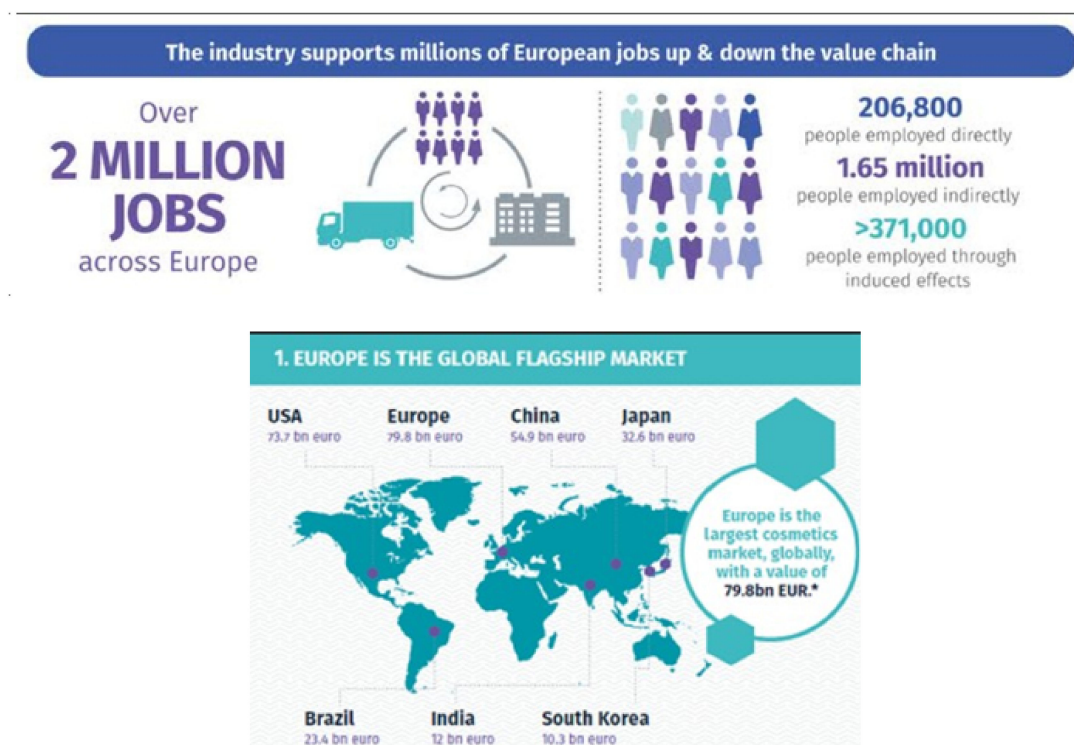


Figure 14. The EU jobs in 2019 involving cosmetics production and market (by the courtesy of Cosmetic Europe 64).





**Figure 15.** The worldwide provisional Beauty and personal care cosmetic markets 2019–2025 (by the courtesy of Common Thread Collective).

However, as previously reported, the COVID lockdown has led to a decline in consume and demand of  $-8\%$  for certain categories of products, also because self-isolation and limited social interactions have altered consumers' ordinary habits. Regarding the global economy, it has been estimated that the ongoing COVID-19 crisis will cause a total loss in global output of at least of USD 10 trillion losses in global output over the period 2020/2021, accumulating to USD 22 trillion over the period 2020/2021 [61].

For all these reasons it is time to change the way of producing, consuming and living. Thus, there is a necessity to stop the natural world's destruction through the continuous deforestation, modifying not only the actual intensive farming and eating, but also eliminating plastic waste and air and water pollution. Doing so will make it possible to slow down the increasing global warming, ameliorating both human and environment health together with the economic crisis.

Just to remember, around 11 million metric tons of plastic is added each year to the actual 150 million pervading the oceans as tiny particles (i.e., micro-nanoparticles) [66], further increased from the last medical waste due to surgical masks, personal protective

equipment, disposal syringes, catheters, and other tools, used daily for the COVID-19 pandemic [54–57,66–69]. Thus, the global cumulative amount of plastic waste generated from 1959 to 2015 was ~6.3 billion tons, 9% of which was recycled, 12% incinerated and 79% accumulated in landfills or the natural environment, releasing dangerous ingredients. Consequently, and unfortunately, it is estimated that the 5.25 trillion macro and micro pieces floating on the ocean today kill 1 million seabirds and 100,000 marine mammals every year [66,70]. This plastic waste, in fact, releases toxic chemicals which, eaten by plankton, krill, fishes and sea mammals, are entering into human food, recovered in tea [71] and human placenta also [72]. Among the toxic ingredients, there are phthalates acting negatively on our health, cause hormone disruption, infertility and breast cancer [73,74], as well as the heavy metals and bis-phenols have shown with potential effects on the placenta–brain axis (Figure 16) [74,75].



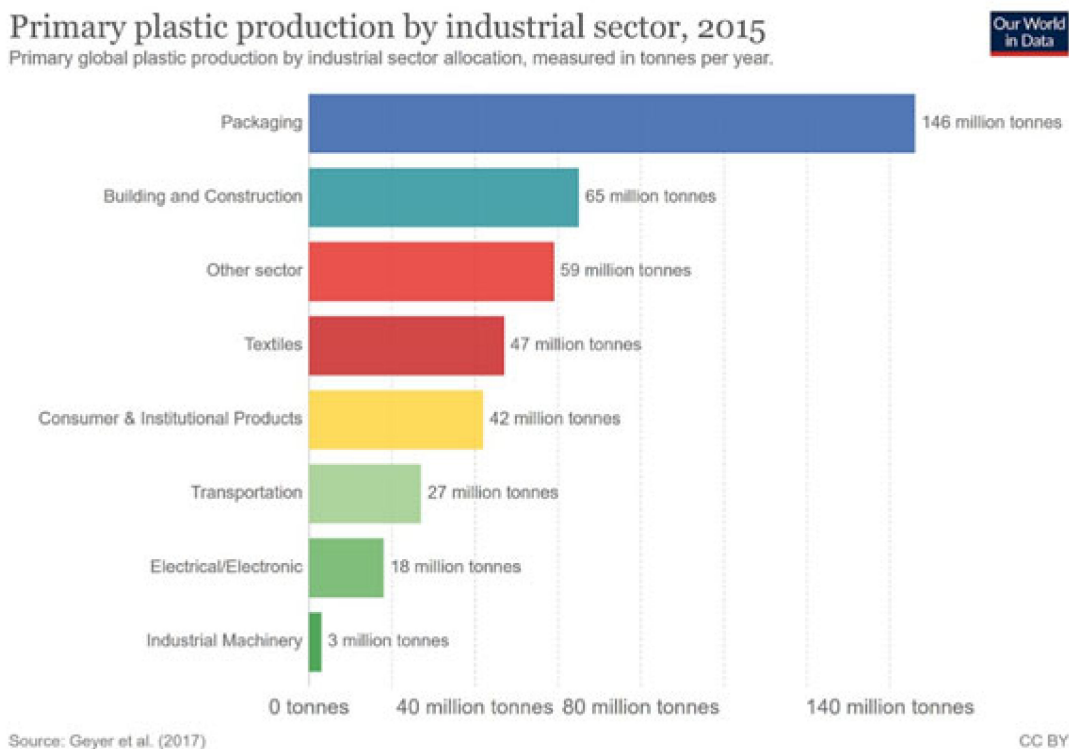
**Figure 16.** Some of the chemical toxic contaminants from plastics involving the animal and human health (by the courtesy of MADESAFE).

However, which of the industry's sectors are consuming the highest quantity of plastic polymers?

The principal end-use sectors using plastics are packaging, construction and textiles (Figure 17).

For the reported reasons, it is considered an exigent problem to first adopt the circular economy first of all in these three industrial sectors by the use of sustainable technologies and natural biodegradable raw materials, possibly obtained from waste and recycled materials. By doing so, it will be possible to eliminate waste and pollution, which is necessary to ameliorate the human and planet health. Just to remember, 80 billion pieces of new clothing are purchased each year, which, translating to USD 1.2 trillion annually, has created millions of tons of textile plastic waste in landfills by unregulated settings and injustices in low- and middle-income countries [76]. A majority of these fast-fashion clothes, in fact, are assembled in China and Bangladesh, while USA consumes more clothing and textiles than any other nation in the world! On the other hand, the cosmetics industry has

produced 142 billion packaging units in 2020, and 95% of which have been thrown out after just one use, with 79% ending up in landfills [76]; meanwhile the sector of construction has produced 65 million tons of plastic waste!



**Figure 17.** The major industrial sectors using non-biodegradable plastic fibers (by the courtesy of Our World in Data).

## 5. Conclusions

As amply focused on by recent papers also [77–79], cosmeceuticals already exist as scientifically designed products with biologically active ingredients that supposedly have medical or drug-like benefits. [1,4–8,13]. However, also if not recognized from the actual international rules, it has been supposed that these specialized cosmetics will reach USD 72.2 billion by 2022, with a CAGR of 7.4% and 400 suppliers and manufacturers [80].

Therefore, in our opinion, it is time to recognize the biological activity of cosmeceuticals!

Many research papers, in fact, have shown that some components of cosmetic emulsions and part of the active ingredients used today penetrate the skin layers, inducing, for example, modifications of the trans epidermal water loss, as well as the keratinocytes cohesion of the skin's horny layer [51,53,54,81–83]. Therefore cosmeceuticals may have the possibility to reduce some of the skin environmental damages acting by these mechanisms of action. Thus giving healthy benefits [43,84]. Thus by a controlled trans-epidermal penetration it will be possible to increase both cosmetic effectiveness and safeness which naturally depend on the physicochemical properties of the active ingredients selected, the nature of the vehicle and the skin conditions. Consequently, there is the necessity to select ingredients and carriers for formulating cosmeceuticals with highly effective and safe, as the proposed natural-made cosmeceutical-tissues [44,45,52,59]. As previously reported, in fact, consumers are searching out products which might be not only natural-based and respective of the environment, but also capable of giving them a more youthful appearance and improving their health. They, in fact, are looking for wellness, well-being, wealth and longevity. Therefore, the proposed innovative cosmeceutical-tissues, made by biodegradable polysaccharides [85,86] and sustainable packaging realized by a nanotechnological

approach [86–88], could represent a new way to treat both the human face and body, with the goal of ameliorating the quality of life and reducing the use of non-biodegradable chemicals and plastics. Thus, it is considered a future priority for the production of goods and cosmeceuticals to have better management of natural resources with the use and realization of innovative bio-machines. In conclusion, by an increased ability to understand and engineer biology, introducing innovation in biomolecules, bio-carriers, bio-systems, bio-machines and bio-computing, it will be possible to understand how nature works, thus realizing the dream of the so-called bio-revolution [89–91].

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