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Smart Tissue Carriers for Innovative Cosmeceuticals and Nutraceuticals

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Abstract: The present review was conducted to investigate the possibilities in realizing novel nanostructured tissues containing functional molecules that can be commercialized as solid products (without using emulsifiers and preservatives) for cosmeceutical and nutraceutical applications. After considering the principal concepts regarding skin and mucous features and physiologies, the possibilities in using bio-based, biodegradable and biocompatible materials was explored by investigating the correlations between their structures and morphologies with respect to the characteristics of the skin extracellular matrix (ECM). Regarding the new smart type of biodegradable tissues, their possible composition was reviewed in relation to the skin aging process and to the current contest for novel, innovative cosmeceuticals and nutraceuticals that consider the "beauty from within" concept. The barriers to the development of these new tissues were mainly identified due the necessity in defining the claim regarding green products. Moreover, the market growth data regarding these novel products were highlighted to support the idea that the diffusion of smart tissue-based cosmeceuticals and nutraceuticals is an opportunity for new sustainable industrial chains in the development of bioeconomies.

Keywords: chitin nanofibrils; nanolignin; carrier; microplastics; cosmeceuticals; nutraceuticals; nutricosmetics

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1. Introduction

The vehicles/carriers used to make cosmetics (cosmeceuticals) and diet supplement (nutraceuticals) in the so-called "Beauty from Within" context (i.e., the contemporary use of the same ingredients by cosmetics and diet supplements, i.e., cosmeceuticals and nutraceuticals) are currently based on emulsions and solutions [1]. These carriers, which are rich in water, also include the use of emulsifiers, preservatives, fragrances, colors and other chemicals, and they often cause allergic and/or sensitizing reactions [2]. Moreover, many of the used active ingredients are made with petrol-derived compounds, as well as with fossil plastic-derived polymers, and these are utilized to package the final product. The extensive use of plastic polymers as packaging material or as skin peeling particles is provoking an unsustainable invasion of waste and pollution in land and in the oceans, and it is also becoming dangerous for the state of human food worldwide. In fact, after being transformed into microplastics by environmental activity, these micro/nano particles entire the normal food of fish, birds and sea mammals. Therefore, it seems necessary to use renewable and degradable polymers, including polysaccharides and active

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ingredients that, as they are obtained from food and agriculture waste, seem useful for producing innovative and biodegradable tissue carriers. These unusual and novel vehicles have been shown to be useful for realizing innovative skin and environmentally friendly cosmeceuticals and nutraceuticals [3,4]. These tissue carriers should be smart and efficient; thus, they are made of specific materials that give them the ability to facilitate the penetration of the active ingredients through the skin and mucous membranes' barriers. These active ingredients are easily released at the level of skin layers at the designated dose and time, as reported by some of the studies of our research group. Our proposal is to realize these novel vehicles with the use of polysaccharides and natural polymers, such as chitin and lignin, as alternative carriers for *nutricosmetics* (cosmeceuticals and nutraceuticals). Therefore, it seems possible to obtain the so-called *green/organic* cosmetics and diet supplements requested by consumers today. These innovative tissues, which are free of water, emulsifiers, preservatives, fragrances, colors and other chemicals, might represent a new alternative to the currently widely diffused emulsions and solutions. This is the aim of our research investigation.

2. Skin and Mucous Barriers

Cosmetic products show their effectiveness when applied to a skin surface, where they deliver active ingredients—which are embedded in their emulsified carriers across the Stratum Corneum (SC) and into the deeper skin layers, including the epidermis and dermis—when topically applied to the skin [5]. Among others, the most common carriers (vehicles) include ointments, emulsions, gels and lotions (selected and used), and these are administered according to the features and conditions of the skin areas to be treated, as well as with respect to the activity of the selected products, such as whether they are drugs, medical devices, cosmetics or diet supplements.

The carriers, in fact, have to optimize the contact with the skin or mucous membranes surface as this is necessary to help the penetration and effectiveness of the selected active ingredients, as well as to successfully release them at the level of the different layers of these different structures [5]. Moreover, both ingredients and carriers should be characterized for their effectiveness and safeness, and they should possibly be made with natural ingredients and sustainable technologies that respect the environment. Lastly, the final products should be packed without the use of fossil fuels and non-recyclable plastic polymers but they should still be sold at a low cost, as requested from the majority of consumers [6,7].

Just to understand the importance of the ingredients and carriers used, it was considered necessary to investigate the skin structure.

The skin, as the largest, as well as multifunctional, organ of the human body with a surface area of 1.5–2 m², is composed of several layers and structures, including the epidermis, dermis, subcutaneous fat, hair follicles and sebaceous glands [2]. As the principal barrier between the environment and interior organs, this structure, in balancing both body temperature and skin water content, is able to avoid infections, the physical damage of ultraviolet radiation (UVR), and it also protects and maintains the entire organism' homeostasis [8,9].

However, the real skin barrier is represented by the outermost stratum corneum (SC) layers, which—through being organized by dead differentiated keratinocytes (i.e., the corneocytes *brick*)—are embedded in a continuous intercellular lipid matrix that is organized and packed by lamellae (*mortar*). Therefore, this particular network creates a two compartment model of *bricks* and *mortar*, which are made of the polymeric lamellar sheets of corneocytes [9,10]. Perpendicular to this lamellar structure, the lipids are organized in either orthorhombic, hexagonal or liquid crystallin form, and they are necessary to modulate the skin penetration of any kind of compounds applied to its surface (Figure 1) [11].

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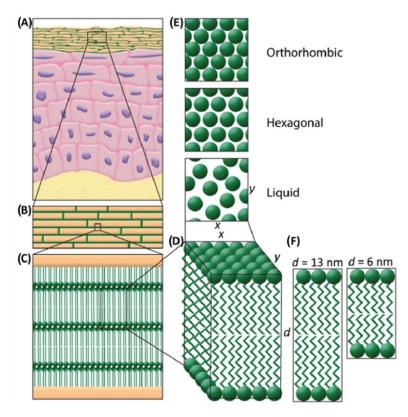


Figure 1. Lipid organization in the stratum corneum. The brick and mortar structure of the lipid matrix at the level of corneocytes (A–C) with a lipid lamellae organized structure (D–F) (diagram courtesy of Berkers et al. [11]).

However, it seems important to underline that skin penetration—which is achieved through two principal ways (i.e., intercellular and trans-cellular (Figure 2))—is affected and depends on the integrity of SC, as well as on the particle size, the lipophilic–hydrophilic gradients, the pH and the isoelectric point of the products applied to its surface [11,12].

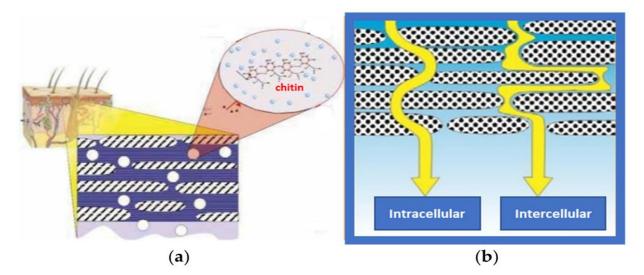


Figure 2. The main penetration pathways of active ingredients through the skin layers, including chitin nanofibrils (**a**) supposed penetration of chitin nanofibrils; (**b**) intercellular and intracellular penetration (diagrams courtesy of Morganti et al. [12] and 2023 copyright of the authors).

It is also important to remember that one of the fundamental cosmetic functions for both skin and mucous membranes is to maintain their flexibility and hydration state with Cosmetics 2024, 11, 20 4 of 19

the presence of the right content of bound water, which has to be greater than 10%. In healthy skin, in fact, as well as via the process of maturation and differentiation, the cornecoytes connected by corneodesmosomes and aggregated by intercellular lipids release filaggrin to maintain the SC barrier function, thereby contributing to skin flexibility and hydration via the activity of the so-called natural moisturizing factors (NMF) [13,14].

Therefore, these specialized cells, which are constantly removed and renewed by the continuous skin turnover, are the main cause of the filaggrin fragmentation at the level of mRNA lipid lamellae and keratins, and this is achieved via the release of the amino acids and NMF that are obtained by the activity of different enzymes, such as bleomycin hydrolase, calpain-1, caspase-14 and Kallikrein 5 and 7 [13–16] (Figure 3).

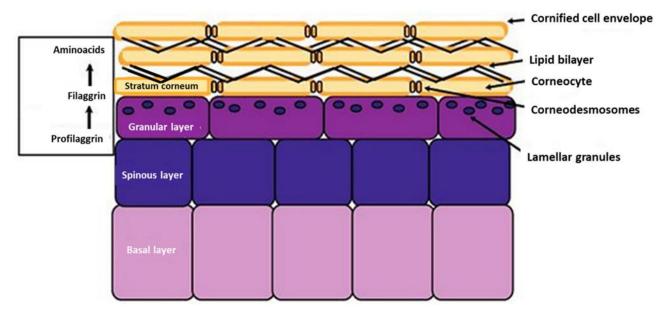


Figure 3. Via the skin turnover involvement and the filaggrin's function in the amino acids and normal moisturizing factors (NMF), the stratum corneum is able to retain water (diagram courtesy of Morganti et al. [12] and 2023 copyright of the authors).

Thus, the cosmetic active ingredients that are embedded in the right carriers have not only the capability of penetrating skin and mucous membranes for the purpose of maintaining the flexibility and hydration of their structures, but they are also effective and safe, thus resulting in skin and environmentally friendly properties. This is why younger generations are requiring cosmetics characterized by environmental sustainability, effectiveness and safeness [17]. Thus, according to Millennials (26–44 years old) and Generation Z (16–26 years old), skincare products should be fundamentally based on natural and safe ingredients that are extracted from the agro-food sector and plant products (including their by-products). They should also be manufactured without the use of fossil fuels or non-recyclable plastic packaging [17]. Due to this, consumers—as they are interested in using specialized products for their skin, body and haircare treatments, including fragrance and beauty masks—are shifting from the beauty of "objectives from aesthetic perfection to holistic wellbeing" (mental, emotional, psychological and physical) [15]. Therefore, and first of all, young people are looking for natural and technologically oriented skincare cosmetics (the so-called cosmeceuticals) to be used by the contemporary oral intake of immune-boosting diet supplements (the so-called nutraceuticals). These products, formulated by the same active ingredients and are obtained from the agro-food sector and plants, should have the aim of obtaining the so-called Beauty from Within (Beauty from the Inside and Outside) context [18–30].

For all these reasons, McKinsey estimated that the global beauty industry will record over USD 580 billion of retail sales, growing at 6% per year by 2027, which is in addition to the current day USD 1.5 trillion global wellness market [19]. Meanwhile, the global

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nutraceutical market has been valued, by the time of 2022–2027, at USD 650 billion, growing at a CAGR of 8.13% [31].

On the other hand, the oral and gastrointestinal mucous membranes could represent barriers for the penetration and release of the active ingredients selected for diet supplements [32-34]. Similar to skin structure, the oral mucous membranes consist of epithelial cells, which—through their physical and microbiological immune and saliva barrier functions—form a continuous layer that is able to protect the body from all environmental exposures, including physical, chemical and microbial [34]. Different from skin, this particular network protects the deeper gastrointestinal tract tissue from mechanical insults, and it also functions as a portal for food, selected microbiota and airborne particles entering into the body while preventing the entry of pathogenic bacteria and toxic substances [25]. Additionally, mucous, which is produced by numerous salivary glands, is maintained constantly in a moisturized condition in the epithelial oral mucosa. Due to this and simply to understand the existing difference levels of the absorption that characterize the oral tissues, it is necessary to distinguish the hard palate and gingiva mucosa from buccal and sublingual mucosa. The first consists of a keratinized epithelium that is attached to the underlying tissues via a collagenous connective tissue, while the buccal and sublingual mucosa comprise a nonkeratinized epithelium that is supported by a more elastic and flexible connective tissue, as reported in Figure 4 [35].

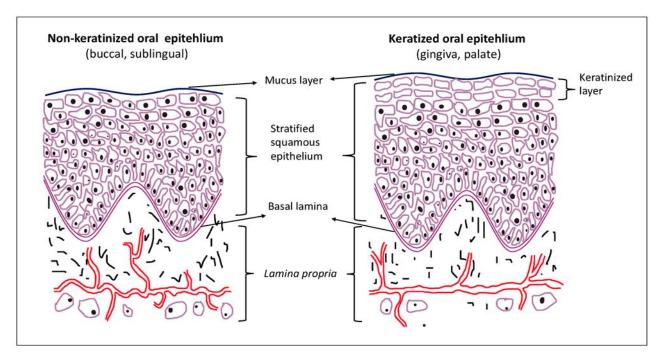


Figure 4. The non-keratinized and keratinized structures present in different areas of oral epithelium (courtesy of Senel [35]).

To satisfy the actual requests of consumers, different skincare products should be skin and environmentally friendly, and they should be made with natural-derived ingredients at low consumptions of water and possibly packed in biodegradable containers [35,36]. Unfortunately, both cosmeceuticals and nutraceuticals are made with emulsions, ointments and solutions, which—through containing preservatives, emulsifiers, fragrances, colors and other chemicals with consumptions of water between 60 and 90%—may often be the cause of allergic and/or sensitizing phenomena. In addition, they can also be non-sustainable for the environment because of the non-biodegradable and non-recyclable plastic materials that they are packaged in [37,38]. It is thus necessary to find new active ingredients with innovative carriers and packaging, which—due to being skin/mucous and ecofriendly—should be made by natural, effective and safe raw materials.

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With respect to this purpose, our research group proposed the use of natural polymers to make biodegradable packaging [6], as well as tissues to be used as new smart containers and carriers for producing innovative cosmeceuticals and nutraceuticals that are human body and environmentally friendly [12].

3. Biopolymers, Skin Function and Consumer Opinion

Due to the consumer request of innovative skin and environmentally friendly products, it has become urgent to use natural biopolymers, such as polysaccharides, for replacing the majority of the polymers derived from petrochemicals [38,39]. These biodegradable polymers, in fact—because of their high bio- and eco-compatibility and non-toxicity—might be used in different fields, including textiles, agriculture, electronic, as well as food, cosmetic and pharmaceutical products [39,40]. Moreover, these products, as represented due to a great variety of compounds that naturally occur in living organisms such as plants, animals, microbes and other natural sources, may be obtained by different methods, which are synthesized from bio-derived monomers that are directly extracted from food waste and agro-forestry biomasses, or are alternatively produced by microorganisms, as reported in Figure 5 [40]. Monomers, in fact, are represented by small organic molecules, and they can be polymerized to produce linear, branched or crosslinked macromolecular structures.

Among the many available bio-based polymers (Figure 5), polysaccharides are the most used in making cosmeceuticals and nutraceuticals because they are considered more effective and safer. These polymers, which are made by lengthy chains of monosaccharides connected by glycosidic linkages, are easily modifiable as they act on the distinct functional groups present in their monomeric units. With respect to their natural bio-characteristics, polysaccharides may have a wide range of applicability in cosmetic and biomedical areas, where they act, for example, as ingredient delivery carriers, tissue scaffolds, wound dressing materials and/or edible films, among others [40,41]. Just as an example, biopolymers from starch, cellulose, chitin, chitosan and lactic acid may be obtained at a low cost, while the presence of —-OH groups and/or the protonated amino groups in their structures may determine different properties like solubility, reactivity, adsorption and biodegradability. Moreover, due to actual technical advancements, obtained composites have been brought into the market owing to their similar performance with synthetic polymers in terms of configuration, resistance and applications [42]. With respect to their specific bio- and eco-compatibility, consumers think that these sugar-like ingredients, which are present in natural sources such as monomeric units, are capable of enhancing not only the skin appearance, but also global body well-being and immunity. In addition, they also work to probably modify the microbiome dynamics [43-45]. Consequently, consumers are still willing to pay a premium for natural products, which, as they are believed to deliver genuine value, could support skin beauty with overall health. Therefore, 60% of people worldwide and 42% of Europeans wish to maintain health and beauty for the long term as they recognize the importance of emotional wellbeing, immune health and happiness, as well as due to thinking that "healthy skin facilitates healthy ageing" [46,47]. However, consumers, due to wishing to know the global composition of their purchased nutricosmetics (cosmeceuticals and nutraceuticals), are looking for innovative products made with biodegradable ingredients and which are packaged with bio-based and compostable materials. They, in fact, think that the use of regenerative and biodegradable materials could have the capability of contemporarily increasing body health and beauty, thus maintaining effectiveness and safeness along all of the supply chain of products [46–48].

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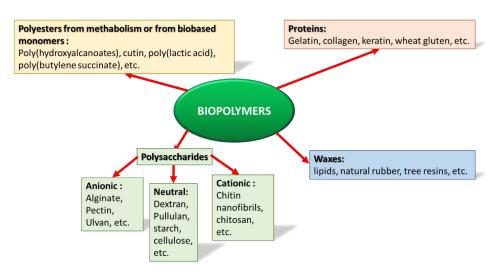


Figure 5. Bio-based and biodegradable polymers.

3.1. Characteristics of Bio-Based Polymers

As previously reported, biopolymers consist of repeated units of monomers, which are attached together by covalent bonds and, via the basis of their sources, are divided into natural polymers (i.e., starch, alginic acid, cellulose, gums, chitin, etc.), semisynthetic polymers (silicones and celluloses derivatives) and synthetic polymers (nylon, polyethylene, etc.). On the basis of the structure that they may be divided in, we have the following categories: (a) linear polymers, in which monomers are arranged in a straight-line chain; (b) branched polymers, which possess small monomer chains attached to other straight chains; and (c) crosslinked polymeric chains, which are attached by cross bonds. Among polymers, polysaccharides are the most used in human healthcare because they are made with glucose units and are found in nature at a low cost as biocompatible compounds. Moreover, they are non-toxic, easily biodegradable and therefore recognized by scientists as the most robust material that mimics nature [39-42]. These biopolymers, made via a synthetic or natural origin, are preferably fabricated through the electrospinning technique that affords nanomaterials [43] in the form of micro and nano fibers [44,45] (Figure 6). The electrospinning machines that can produce tissues from polymer solutions are the most widely diffused. Polysaccharides, due to the dependence of their molecular weight, can be suspended in water and easily electrospun. The polysaccharides that are anionic or cationic (Figure 5) in slightly acidic or basic solutions can benefit from an improved processability because of their increased solubility and increased solution homogeneity.

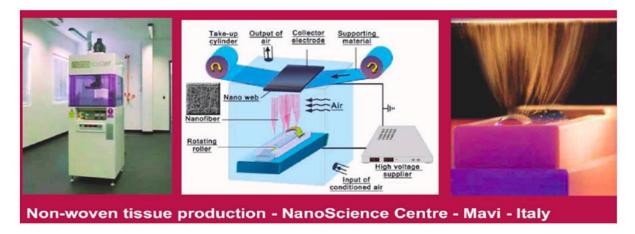


Figure 6. Electrospinning technology transforms a nanocomposite gel in micro/nanofibers via a high voltage supply (copyright of the authors).

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This technology, based on a high voltage supply (power supply), a collector (electrode) and a syringe (spinneret), are organized with a rotating roller and supporting selected materials, thus offering simplicity of use and versatility [43,44]. Moreover, the obtainable uniformity of nanofibers' mat organization—which is produced via small diameters that are associated with a large surface area-to-volume ratio and natural electrospun materials such as, for example, collagen and hyaluronic acids—results in fibers and tissues that possess a high porosity [47–50]. This is why it is possible to make and obtain scaffolds that, having the same structure of the natural skin extra cellular matrix (ECM), possess enhanced cellular adhesion, proliferation and differentiation' properties, thus providing a physiological relevant platform (Figure 7) [45–53].

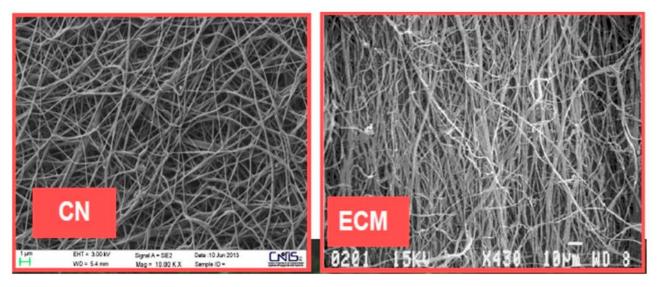


Figure 7. The realized electrospun insoluble chitin tissue (CN) on the left has the same morphology of the natural ECM (copyright of the authors).

3.2. The Nature and Function of the Skins' Natural ECM

The skin is a self-organized organ that, where the ECM comprises the fibrillar collagen and associated proteins recovered in the basement membrane, influences its normal homeostasis, as well as the modified structure and content recovered in aging phenomena, wound healing and diseases [51]. Therefore, by playing a pivotal role in the skin structure, this natural network is able to establish and maintain tissue/cell organization and functions. Therefore, its activity is important in providing an anchorage stage to cells, thereby maintaining their division, migration and polarity [48]. Thus, every strategy and/or scaffold that are able to manipulate the cell-ECM interactions, including the following proposed tissue carriers, may be useful for easily repairing diseases, wounds and burn' alterations, as well as for modifying and slowing down the superficial fine lines and wrinkles that appear on prematurely aged skin. Due to this purpose, the following proposal of using tissue carriers as scaffolding/vehicles for innovative cosmeceuticals and nutraceuticals seems to be a useful strategy for repairing wound and burn alterations, as well as for slowing down superficial fine lines and wrinkles by regenerating and rejuvenating their altered structures [3,50,54–58]. As a consequence, the necessity of using innovative biopolymers, carriers and tissues, via mimicking the ECM network, may be useful for producing smart cosmeceuticals and nutraceuticals that are characterized by their effectiveness and safeness [3,51,54–58].

According to our experience, these new cosmetic nutraceuticals have shown the ability to load and carry natural ingredients, and they can release them at the designated skin layers, dose and time because they realized by the production of innovative tissues, thereby functioning as smart carriers for the cosmetic and diet supplements of a new generation [3,54–

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58]. These tissue carriers are considered *smart* due to having the ability to modify their penetration activity in relation to the polymers and active ingredients used [3,54–58].

4. Smart Biodegradable Tissues

The strategy explained in the present review consists in producing nanostructured tissues loaded with functional biomolecules that can be applied on wet surfaces (skin, mucosa, etc.) so as to release the beneficial substances onto them. According to our research studies [53-58], the composite materials used to realize these biodegradable tissues have been shown to possess an interesting hierarchical structure, which, based fundamentally on the use of chitin nanofibrils and nanolignin complexes, resulted in effective and safe use, most likely due to their particular ECM-like morphology structure (Figure 7) [53,54]. In fact, as shown by some of our studies, electrospun tissues can be prepared from chitin nanofibrils and these complexes (Figure 7). The use of different chitin nanofibrilnanolignin (CN-LG) complexes consisting of nanostructured micro-particles are differentiated by the encapsulation of various active ingredients, which are bound to the tissue fibers, and this results in the effective amelioration and repair of the skin affected by wounds and burns or those who have precociously aged [55,56,59]. These tissues seem able to transmit the biochemical signals that are useful for sequestering, preventing and orienting the many morpho regulatory molecules necessary for skin cells, which are differentiated by attachment and growth [3,53–56].

4.1. Composition of the Proposed New Tissues

These smart tissue carriers have been realized by the use of different natural polysaccharides. They are characterized by different structures and functions, and they are obtained from waste organic materials at low consumptions of water and energy, which makes them useful for reducing the global consumption and use of water and natural ingredients.

The polymers used to make these innovative carriers are, in fact, water insoluble or water soluble according to the kind of compound considered useful for obtaining the different products and functional effectiveness of the designed and realized cosmetic nutraceuticals. Just as an example, an interesting water-soluble tissue [57] was obtained through the use of pullulan, which was embedded via different active ingredients. A tissue was obtained by inserting CN-LG powder via dry powder impregnation into a nanostructured pullulan tissue that was produced by electrospinning. The obtained tissue was used to prepare beauty mask prototypes [58]. These masks produced effective results in the skin: in vivo studies indicated that the beauty mask significantly decreased the area, length and depth of forehead and crow's feet wrinkles, and they also significantly increased moisturizing levels in the skin. The developed beauty mask was also seen to increase skin firmness, and it did not show skin irritation after the test.

More recently [3], CN-LG complexes were incorporated into pullulan tissue that was deposited via electrospinning as a nanostructured tissue on a non-woven bamboo. This bilayer system was characterized before and after the rapid washing of the sample with distilled water and liquids mimicking physiological fluids. The viability of keratinocytes and antioxidant activity, which are protective activity toward UV light, the metalloproteinase release of aged fibroblasts and the inhibitor activity against collagen degradation, were studied. Immunomodulatory tests were also performed to investigate the anti-inflammatory activity of the bilayer system and its indirect antimicrobial activity. The results indicated that the bilayer system can be used in the production of innovative, sustainable cosmeceuticals. These versatile functional pullulan-based tissues, which are embedded in chitin nanofibrils, nanolignin and specifically selected biomolecules, could be used to make-for example-specific nutraceutical or medical device products that are able to respectively modulate the oro-pharyngeal or genital commensal microbiota and the immune system when applied on the oral or feminine mucous membranes for alleviating local irritative phenomena [3,60,61]. Due to this, our research group designed and prepared various cosmeceuticals, nutraceuticals and medical devices in a laboratory Cosmetics 2024, 11, 20 10 of 19

environment, whereby the tissue carrier activity were characterized by embedding their fibers into the different active ingredients selected. These were then encapsulated in the CN-LG complexes during the electrospinning process [60], as evidenced in several studies [61–68]. Chitin nanofibril, being, in fact, positively charged, may be complexed via the gelation method with negative-charged polymers [69,70], including lignin and hyaluronic acid, which may also encapsulate the selected active ingredients (Figure 8).

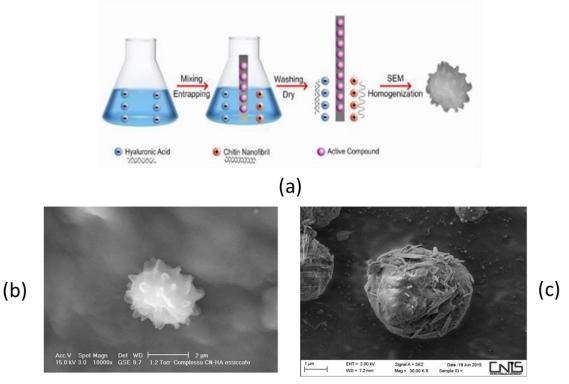


Figure 8. The gelation method (a) adopted to produce micro-nanoparticles between chitin nanofibrils and hyaluronic acid (b) or nanolignin (c). (Copyright of the authors).

Regarding the activity of these tissues, it is interesting to underline that, many years ago, it was shown that polysaccharides could have an interesting effectiveness in modulating the disposition of collagen fibrils when applied topically on a wound skin in comparison with an untreated control (Figure 9) [65]. This is probably one of the reasons for the effectiveness and hemo-compatibility shown by the obtained tissues in treating wound healing, as well as in ameliorating premature aged skin [71,72]. Due to this, both chitin and lignin—when selected at a nanosize—have shown antioxidant, immunomodulant and skin repairing activities as they are able to neutralize the excess of the radical oxygen and nitrogen species (ROS and RNS) recovered in, for example, aged and photoaged skin. Both these biopolymers, in fact, contain active molecules that include glucosamine and polyphenols, which are effective as repair and anti-aging agents [73–78]. ROS and RNS, in fact, are some of the key components that accelerate, for example, the skin aging processes [78].

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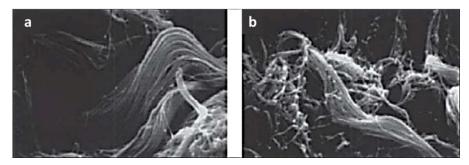


Figure 9. The effectiveness of polysaccharides in modulating the regular disposition of collagen fibrils (a), as well as those that favor the wound healing of skin treated in comparison to non-treated ones (b). (Courtesy of Tucci et al. [64].)

4.2. The Activity of ROS and RNS on the Aging Process

The effectiveness of the nanostructured tissues is explained with the knowledge of the aging process. In fact, oxygen, which is necessary for all living aerobic organisms, may be the reason for toxicity and skin aging when it is present in excess or is inappropriately metabolized at the tissue level. Accordingly, the excessive production of ROS and RNS is provoked by xenobiotics, which occurs in certain diseases as result of toxic insults and may be the cause of the so-called oxidative stress and/or unusual melanogenetic processes [73,74]. These particular conditions, due to an imbalance in the prooxidant/antioxidant equilibrium, result in the critical maintenance of tissue homeostasis and are therefore determinants in skin ageing [73–79]. As a consequence, the antioxidant and aged protective activity in skin cell membranes—which are recovered by topical treatments with polyphenols, as well as the vitamin C and E encapsulated in the chitin/lignin complexes bound to the tissue carriers—has shown to be able to neutralize and inhibit the formation of the free radicals triggered by the ROS and RNS recovered in age-related diseases and aged skin (Figure 10) [72–78].

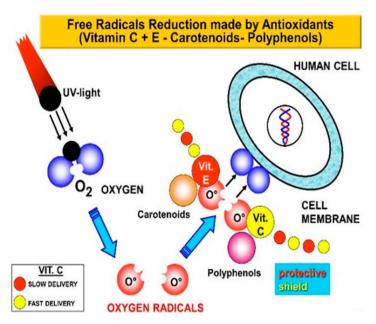


Figure 10. The protective antioxidant activity of some natural antioxidant ingredients in human cell membranes. (Copyright of the authors).

Consequently, the activity of the proposed innovative cosmetic nutraceuticals seem to go in the direction required from consumers who are looking to change their lifestyle by firstly using so-called "green cosmetics" that are considered useful in reducing skin fine line and wrinkle formation [20,32,78].

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4.3. The Contest for Novel Tissues: The Meaning of the Expression "Beauty from Within"

Consumers, because of the excessive consumption of petrol-derived polymers in cosmetic and food plastic packaging, are looking for so-called green cosmetics as they are worried about steadily growing environmental damage (Figure 11) [33,79–81]. Moreover, because of the continuous and contemporary growth of pollution and climate change, it is time to transfer the actual linear resource flow into circular ones, which can be achieved by implementing a nature-based solution [32–34]. The waste that is present in land and the oceans represents the source of climate change, which is producing continuous worldwide disasters such as extreme weather conditions, deforestation and water scarcity [32– 34,78,79,81]. Therefore, the well-being and wealth of future generation will depend on our ability to change the current linear economy, which is based on redesign-reduce-reuse and take-make-use-dispose waste, to a circular economy, which is based on redesignreduce-reuse-recovery and could possibly produce zero waste [30-32]. Consequently, contemporary consumers are oriented to so-called "green cosmetics", and they wish to know not only the composition and sustainability aspects of purchased products, but also the packaging material used to make their containers [75,76]. It is thus necessary to adopt a climate-friendly lifestyle that is focused on reducing production and the use of the nonbiodegradable materials, which will be achieved through modifying the current way of living by reducing food loss and cosmetic waste along all supply chains [76,78-80]. It is necessary to produce and use more products and carriers that are based on plant-based ingredients. Therefore, it is useful to make natural-oriented cosmetics and diet supplements (i.e., cosmeceuticals and nutraceuticals) via a reduced production of waste and consumption of energy and water [76,78–80].

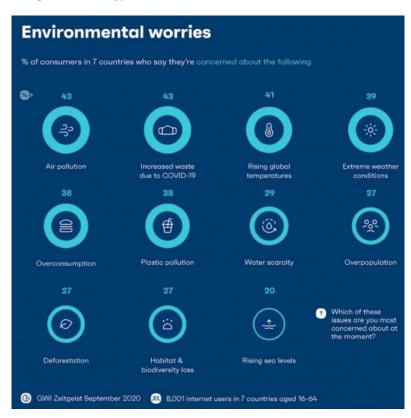


Figure 11. Environmental consumer worries (courtesy of Giles. GWI [34]).

4.4. Barriers to New Tissues: The Necessity in Defining the Claim Regarding Green Cosmetics

Although green cosmetics might eliminate the use of hazardous ingredients when developed in accordance with the principle of Green Chemistry, until today, there has been no exact definition on their significance by the cosmetic directives of the USA, the

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EU and Brazil [79-82]. Consequently, in order to address the gap regarding the lack of worldwide government definitions on green cosmetics, voluntary certification systems have been developed in different countries, including BDIH (Germany), Evicert (France), ICEA (Italy), Natrue (Belgium) and IBD (Brazil) [80-82]. These systems, which are characterized differently from country to country, have been used for verifying not only green organic ingredient sources and the raw material storage methods, but also the productive processes and labeling used with the energy consumed and the waste released and managed. All these considerations are necessary for assessing the effectiveness and safeness of both ingredients and raw materials in terms of obtaining skin and eco-sustainable products [81]. However, in our opinion, it is necessary to establish specific and standardized regulations, which can be achieved by uniformly certifying all the green cosmetics distributed worldwide in order to eliminate the confusion regarding their definition and thus determining the extent of their real impact on human health and the environment. Due to this, there has new progress in a 2023 EU directive, which is named the "Proposal for a Directive on Green Claims" [82]. This directive aims to eliminate the misleading environmental messaging across EU markets by setting out the EU's first detailed company market rules regarding environmental impacts and performances. Last but not least, and in accordance with consumer requests, more time and studies have to be dedicated to recover and change the materials used to pack food and cosmetic products, whereby petrolbased ingredients should be substituted with biodegradable and natural-derived ones [83]. Packaging, in fact, has become another "critical enabler for everyday lives of most consumers" due to their awareness of sustainability, as well as due to the increasing positive attitude toward recycled materials and the new-born movement against plastic straws (which has recently increased due to certain striking images of packaging leakage into oceans [82,83]).

Our proposed use of polysaccharides for making innovative carriers and biodegradable green cosmeceuticals and nutraceuticals seems to go in the direction of a realistic sustainability [84–93]. The reported smart tissue carriers, in fact, result in a low consumption of water and are free of preservatives, emulsifiers, colors, fragrances and other chemicals, and they might be considered of interest as new skin and environmentally friendly vehicles.

5. Market Growth as an Opportunity for Novel Tissues

As previously discussed, consumers have a holistic approach to beauty and wellness, which are considered so closely connected each other that healthy and hydrated skin are nearly always associated with vibrant energy and overall happiness [80,81]. Thus, 55% of people worldwide are looking to improve both their physical and mental well-being, and they are seeking cosmeceuticals and nutraceuticals that are made by natural-derived ingredients and sustainable technologies [82–84]. Therefore, beauty and wellness is particularly important to Baby Boomers (57-75 years old), Generation X (41-56 years old) and Millennials (26-44 years old), who are all looking for green ingredients that are environmentally sustainable and are packaged with upcycled waste materials (i.e., the transformation of a by-product or waste stream to usable ingredients) [83,84]. On the other hand, Generation Z (16–20 years old), who represent 25% of the global population, are focusing on the prevention of environmental and mental health problems by considering the role of social media and technology as the main influencers of their purchasing decisions [80– 83]. The preservation and protection of the environment and oceans, in fact, have become a "collective anxiety of the actual consumers" [82,83,94,95]. Moreover, they are also searching for personalized services and wish to be informed by advertising and messages on all of the offers and prices that meet their specific needs [36,96–100].

As a consequence, the green/organic segment of the beauty and personal care market, which was estimated at 19.3 billion in 2021, is expected to increase by a Compound Annual Growth Rate (CAGR) of 19.3% from 2022 to 2030 thus representing 3.3% of the global cosmetic market [94,95]. On the one hand, the smart and US Healthcare Market size was estimated at about 50 USD billion in 2022, and it is expected to witness a CAGR of 11.3%

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from 2023 to 2030 [98,99]. On the other hand, the consequential global digital health market size, which was valued at USD one billion in 2022, is projected to grow at a CAGR of 18.6% from 2023 to 2030 [101–103], thus further influencing the global beauty and healthcare market [103,104].

Therefore, as previously reported, the adoption of a sustainable nanotechnology that is able to make specific carriers and innovative cosmeceuticals and nutraceuticals has to be taken into greater consideration [104–107].

Due to this, the use of nanomaterials could exhibit different physicochemical and biological properties because of their tiny size and large surface-area-to-volume ratio when compared to their bulk dimension. However, it is necessary to better understand the nanomaterial-to-cell interactions at level of both skin and mucous membrane layers to avoid the possible adverse effects of nanoparticles in healthcare applications [54]. Consequently, and according to consumer requests, the discussed proposal of using novel tissue-based carriers to realize innovative, effective and safe cosmeceuticals and nutraceuticals seems to be moving in the right direction [104–107]. The proposed nanostructured tissue, in fact, is able to ameliorate the active ingredients' penetration by overcoming the skin and mucous membrane barriers, and it has been shown to be human health and environmentally friendly since it is also packaged in biodegradable containers [106–110]. In addition, these innovative structures, which are free of water, preservatives, emulsifiers, fragrances, colors and other chemicals, might reduce the consumption of water and could therefore avoid certain allergic and sensitization skin phenomena when used as a substitution of current cosmetic emulsions.

6. Conclusions

The present review considered the correlation between the structure of skin, mucosa, the extracellular matrix and novel nutraceutical and cosmeceutical tissues by considering both their morphologies and compositions. The biopolymers most suitable for these tissues are polysaccharides, which are mostly used in human healthcare because they are made with glucose units and are found in nature at a low cost as biocompatible compounds. Furthermore, they are non-toxic, easily biodegradable and therefore are recognized by scientists as the most robust material that also mimic nature. From these biopolymers, nanostructured tissues can be fabricated through the electrospinning technique. For instance, pullulan can be successfully used for this purpose.

The proposed biopolymeric tissues, which are embedded in the chitin–lignin complexes that encapsulate the selected natural active ingredients, could be useful for making specific, biodegradable and innovative tissue carriers as a novel and original solution for making novel bio- and eco-cosmetic nutraceuticals. With these smart tissues, in fact, it will be possible to realize skin and environmentally friendly *nutricosmetics* that are characterized by effectiveness and safeness. These products will contribute to reduce pollution, as well as aid in reducing allergies that occur due to toxic additives and non-degradable fossil plastics invading our lands and oceans in an extensive and non-sustainable way.

These products have a good compatibility with consumers who are looking for a healthier life; in addition, the market growth of the cosmeceutical and nutraceutical sectors was also evidenced. Therefore, these novel products seem ready to activate new businesses and sustainable industrial chains in the development of bioeconomies.

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