

Review

# Active Ingredients and Carriers in Nutritional Eco-Cosmetics

Pierfrancesco Morganti <sup>1,2</sup>, Alka Lohani <sup>3</sup> , Alessandro Gagliardini <sup>4</sup>, Gianluca Morganti <sup>5</sup>  
and Maria-Beatrice Coltelli <sup>1,6,\*</sup> 

<sup>1</sup> R&D Unit, Academy of History of Healthcare Art, Lungotevere in Sassia, 3, 00193 Rome, Italy

<sup>2</sup> Dermatology Department, China Medical University, Shenyang 110122, China

<sup>3</sup> School of Pharmaceutical Sciences, IFTM University, Moradabad 244001, India

<sup>4</sup> R&D Unit, Texol Srl, Via C.D'Ascanio, 3 Zona Industriale, 65020 Alanno, Italy

<sup>5</sup> ISCD Nanoscience Center, 00165 Rome, Italy

<sup>6</sup> Department of Civil and Industrial Engineering, University of Pisa, Via Diotisalvi 2, 56122 Pisa, Italy

\* Correspondence: maria.beatrice.coltelli@unipi.it

**Abstract:** Beauty and personal care became a significant part of the global economy for two reasons: (1) The elderly growing in the global population and (2) the desire of women and men to appear younger and more attractive. Thus, both young and old people are looking for revolutionary nutritional eco-cosmetics (combined use of cosmeceuticals and nutraceuticals) manufactured by natural active ingredients, using biopolymers as substrates, and made by innovative and sustainable technologies. Consequently, the market of both cosmetics and diet supplements is continually growing together with the request of natural active ingredients, including bio-peptides and biological macromolecules such as chitin and lignin. Therefore, both consumers and industry need to recover innovative active ingredients and carriers (vehicles), naturally derived and supported by advanced methods for controlling their effectiveness and safeness on skin and mucous membrane layers. The use of selected bio-ingredients, such as hyaluronic acid and bio-mimetic peptides, obtained by advanced, innovative and sustainable bio nanotechnologies, will be of interest to develop smart cosmeceutical and nutraceutical formulations. Innovation is considered the key business strategy to drive sustainable economic growth. For trying to reduce waste and produce sustainable, biodegradable and innovative products, the realization of new non-woven tissues, used as carriers for making innovative cosmeceuticals and nutraceuticals was considered. Both carriers and active ingredients have been obtained from food waste to reduce loss and pollution. This review will report a brief description of the skin functions, trying also to focus and discuss some of the active ingredients and carriers used in nutritional eco-cosmetics to clarify the supposed mechanism of action, effectiveness and safeness of both active ingredients and carriers, as well as the supposed activity of beauty and personal care products.

**Keywords:** cosmetics; biopeptides; biomimetic peptides; cosmeceuticals; nutraceuticals; diet supplements; skin; active ingredients; natural ingredients; carriers; beauty market



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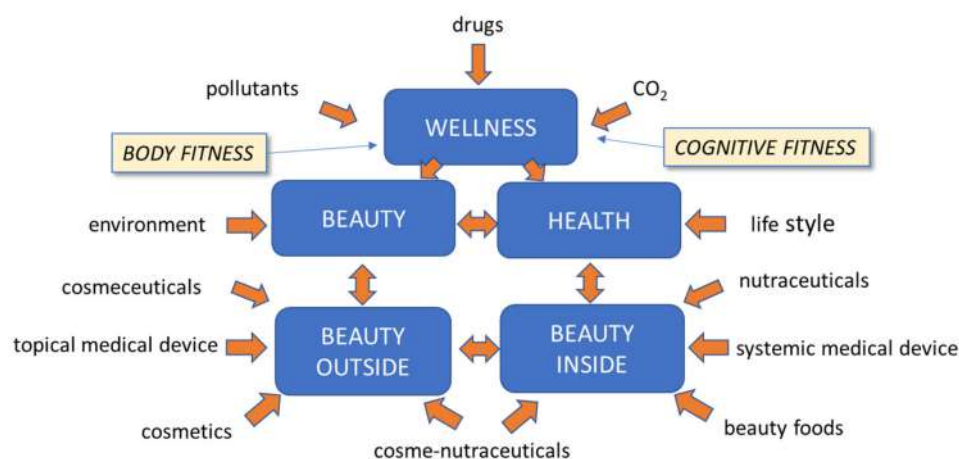
## 1. Introduction

Beauty/personal care is an important economic sector of the worldwide economy with a global market revenue of around USD 565 billion in 2022, projected to be worth USD 758 billion by 2025 and expected to grow annually by a compound average growth rate (CAGR) of 4.76% in the forecast period 2022–2026 [1].

It represents one of the fastest growing consumer markets, driven by the entering of young consumers, women and men, and reinforced by social media and the increasing of e-commerce [2]. Consequently, the market size of cosmetic ingredients, evaluated USD 22.89 billion in 2016, is forecasted to increase at a compound annual growth rate (CAGR) of 4.6% until 2025, amounting to roughly USD 33.8 billion by 2025 [3]. Moreover, by the

awareness today of waste and dangerous pollution, the growing inclination towards natural cosmetics and the increasing prevalence of age and life-style related diseases, consumers have become more conscious of their personal appearance and healthcare measures [2]. Therefore, the increasing necessity for the regular use of cosmetics and diet supplements have ignited the worldwide interest of consumers [4–7]. These products are useful to obtain a personalized and tailor-made beauty “from within” and should be characterized for their effectiveness and safeness for both humans and the environment [4–7]. Therefore, the current situation led to the development of environmentally-friendly multifunctional cosmeceuticals and nutraceuticals (i.e., nutritional cosmetics) made by natural ingredients, including botanical extracts, biopolymers, enzymes, aminoacids and other active compounds [2–7]. Thus, despite their higher cost in comparison to synthetic materials, natural or organic ingredients are increasingly preferred by consumers, due to a focus on maintaining human health and the environmental ecosystem, with a crossover between skin care and cosmetic dermatology [5]. Moreover, due to the central concern of consumers towards beauty and health, the skin care supplement market is notably increasing, which is also sustained by the concept of “beauty from within” with the modern and worldwide perception of a global beauty value [7,8]. Nutraceuticals, therefore, account for the largest share of more than 35% of the global beauty supplements market, being projected to grow from USD 71.81 billion in 2021 to USD 128.64 billion in 2028 at a CAGR of 8.68 during the 2021–2028 period [9]. Moreover, the positive outlook of both the cosmeceuticals and nutraceuticals market is encouraging manufacturers to focus on R&D initiatives for developing innovative and sustainable products based on collaborations with universities and research centers as requested from scientists and consumers [10].

Consequent to the above, innovation and sustainability are considered the key business strategy to drive a new economic growth focused on the interdependent relationship between the three pillars of sustainability: Environment, economy and society [11]. There are, in fact, interconnections between environment, society and economy: “Economy depend on, and within the Environment, while human existence and society are dependent on, and within the Environment” [11]. However, there is a need to discover and study innovative, natural-oriented ingredients that are skin and environmentally friendly and maintain human health and the planet eco-systems and respect the scientists and consumers’ requirements [9,10]. Consumers, in fact, show a growing interest in the product formulation and the ingredients used to understand the relative obtainable benefits [7,9]. Consequently, they are looking for botanicals and nutra-cosmeceutical products. Moreover, they are aware of the dangers for themselves and the environment due to the continuous use of the man-made chemicals utilized in conventional personal care cosmetics and diet supplements [2,4–6,12]. Thus, they are searching for more clarity, transparency and flexibility on the purchased products, wishing to also know more about their efficacy. They want to be sure that nutritional eco-cosmetics—cosmeceuticals and nutraceuticals—and their ingredients, obtained by the use of the latest biotechnologies may really deliver the selected active ingredients at the level of the promised skin and mucous layers and cells, thus resulting in more effective treatments [12–14]. However, nutritional eco-cosmetics, which claim to produce skin health benefits from outside and inside, should strive to stimulate the imagination and produce emotions by combining exciting images and sensual fragrances, conveying the sensations of a total beauty effect (Figure 1) [7–9].



**Figure 1.** Total beauty and health effect from outside and inside.

However, which kind of effectiveness are consumers searching for in their purchased cosmetics? They think the beauty products, applied on the skin and taken contemporary by oral route, should possess functional properties such as the ability to slow down the skin fine lines and wrinkles, thus bettering the aging appearance [15,16]. Consequently, nutritional eco-cosmetics should improve the skin barrier function, ameliorating and strengthening its tone and texture. Additionally, these innovative products should increase the hydration level, enhancing collagen production and therefore reducing fine lines with a consequent increase in skin firmness [16,17]. Thus, they should promote smoother, healthier and younger looking skin, also increasing its immunological properties [11–16]. In conclusion, to obtain all the consumers' expectations, it will be necessary not only to find and use active ingredients with a higher effectiveness and safeness, but also to control their outsourcing that have to be of natural origin, respectful of the environment and obtainable from waste material to avoid impoverishing the planet's natural resources [17–19]. Agro-food, marine-based, breeding-based [20–23] or forestry waste can be examples of attractive sources of valuable compounds. However, the cascade valorization of natural resources is one of the fundamentals of a circular economy [24]. The latter is aimed at considering waste as a resource, dissociating economic growth from the consumption of limited resources.

## 2. Active Ingredients of Bio-Nanotechnology

As previously reported, the market for active ingredients for both cosmetics and beauty diet supplements is increasing year by year [1,2]. Thus, consumers and companies, looking for the best way to address a younger appearance try to find more effective formulations that are able to restore a healthy prematurely aged or altered skin [25,26]. As a result, it is essential to focus more studies on recovering active ingredients that can be used to make innovative cosmeceuticals and nutraceuticals, which are effective and safe for both skin health and the environment [27–29]. To this end, many scientific research studies have been oriented to the use of nano biotechnology-derived ingredients. With bio-nanotechnology, it seems possible to develop innovative compounds, new delivery systems and tools, which are able to control the product effectiveness and safeness at the level of the cell biology through new smart techniques, including the molecular biology, recombinant DNA, and gene and microbiome regulations [27–29]. New active micro-nano ingredients were, therefore, recovered and applied to different biological systems, including skin and mucous membranes, for overcoming the various biological barriers by the use, for example, of dermal and transdermal delivery systems [30–33]. Some active ingredients, such as chitin nanofibrils(CN) and nanolignin (NL), may be diffused by nanocarriers, such as liposomes, niosomes, innovative nanovesicles, matrices, nanocomposites and nanoparticles applied to biological systems, for example by electromagnetic fields [30–33].

However, what does bio-nanotechnology mean? It "is the branch of nanotechnology with biological and biochemical applications", including the use of biomolecules as part

of nanotechnological devices, supported by mathematic, physic, engineering, computer science and information technology [34]. This new branch of science, therefore, is currently developing environmentally-friendly processes that produce zero waste and low consumption of water and energy, which are requirements for obtaining a cleaner and healthier planet. Thus, in the sector of nutritional eco-cosmetics (used topically or by oral route), bio-nanotechnology is playing an important role, ameliorating performance and bioavailability of the active ingredients, which, for example, encapsulated or adsorbed on the surface of nanoparticles, might enhance their penetration through skin or mucous membranes [35]. Naturally, it is necessary to know how the skin/mucous penetration may be influenced by different physiological factors, including age, ethnicity, gender and disorders as well as by the physicochemical properties of the selected ingredients and vehicles (carriers) [35,36]. However, the contribution of biotechnological processes toward the nutritional cosmetics is huge, owing to the production and use of safe and efficacious active ingredients obtained at low-cost and by contamination-free methods [35]. Typical examples of bio-cosmetics and nutritional eco-cosmetics, used for skin and hair care, might be realized by the use of natural ingredients, derived from plants, crops and animals, always free of pathogenic microorganisms, pesticides, chemical fertilizers and parasiticide treatments [37]. They could include extracts from marine and vegetable origin rich of antioxidant and antibacterial compounds [37,38], as well as ingredients made by fermentation processes and plant-cell culture [39], including antimicrobial protective peptides (AMPs), which also act on the human skin as immune modulators [40]. AMPs, because of their specific activities, seem to be suitable candidates for pharmaceutical and cosmeceutical products, due to their specific effectiveness, shown at different ranges on pathogenic dermatological diseases caused, for example, from gram-negative bacteria [41].

There are many natural active ingredients that may be used for nutritional eco-cosmetics. These might form the basis of a green policy of growth, based on zero waste and zero greenhouse gas [GHG] emissions [4,7,41,42].

### 3. Natural Ingredients Used in the Medical, Cosmetic and Diet Supplement Field

As examples, among the ingredients of more common use are: Ascorbic acid (vitamin C), utilized for its antioxidant properties in the pigment-lightening formulations together with alpha lipoic acid, arbutin and Kojic acid [42]; aloe vera, which finds applications for its antibacterial, antiviral and immune modulating effectiveness [43]; grape seed oil, used as anti-aging agent thanks to its antioxidant and healing properties [44]; and green and black tea rich in antioxidant and antibacterial molecules, which are also able to inhibit the virus entry [45]. Some selected natural ingredients of common use in the cosmetic field and obtained from waste, micro algae and bacteria are reported in Table 1 as an example [46–56], while the more used ones, such as hyaluronic acid, oligopeptides, biomimetic peptides and collagen, are described reporting their supposed mechanism of action.

**Table 1.** Natural active ingredients of cosmetic use obtained from waste, microalgae, fungi and bacteria.

Bioingredients	Source	References
Flavonoids, polyphenols	fruits, vegetables, cereals (Coffee, tomato, rice, etc.)	[47–49]
Salicylic/cinnamic acid	Aloe vera plant	[50]
Tocopherols/FFA	Argania Spinosa oil	[51]
Chitin	Crustaceans, fungi, insects	[52]
Lignin	Agro and forestry waste	[52]
Vitamin b and C, minerals	Potato	[53]
Cannabinoids, terpenes	Cannabis sativa	[54]
Minerals, proteins	Microalgae	[55,56]

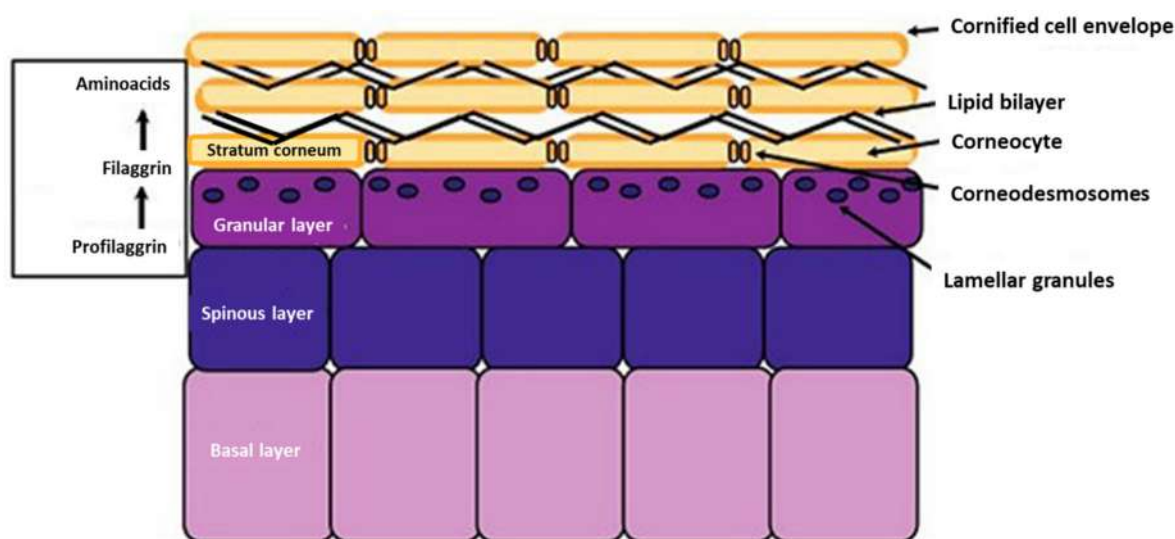
### 3.1. Hyaluronic Acid

Hyaluronic acid [HA] is an important ingredient of great interest used as a component of cosmetics, diet supplements and injected medical fillers for its moisturizing and anti-wrinkle effectiveness [46,57,58]. It is, in fact, a linear polysaccharide that plays multifaceted roles in regulating different biological functions, such as anti-inflammatory [59], immunomodulatory [60], antiaging [61] and skin repairing activities [62,63]. Due to its very high molecular weight, the polymer is able to take up a great quantity of water, thus being of great utility as a moisturizing and anti-aging agent, also for the capacity shown to entrap water molecules into the stratum corneum, when applied on the skin by emulsions or nonwoven tissues [63,64]. However, the HA effectiveness seems to be associated with the ability to stimulate collagen synthesis via fibroblasts induction at the level of dermis [63,64].

### 3.2. Oligopeptides

Of more recent medical and cosmetic interest, there are various oligopeptides, consisting of linked amino acids used as active ingredients, biodegradable carriers and packaging compounds for pharmaceutical and cosmetic use [65,66]. Many of these oligopeptides have shown to possess different effectiveness when used as active ingredients to make cosmeceuticals and nutraceuticals. On the one hand, they seem to find it difficult to penetrate through the skin layers because of the large molecular size and the various hydrogen intermolecular bonds, surface charges and hydrophilicity that characterize their molecules [67]. On the other hand, it should be remembered that many oligopeptides, organized by short chains of macromolecules made up of amino acids from 2 to 20 units with molecular weight under 3 kDa, occur normally in the human body as fragments of proteins carrying out important biological functions [68]. Thus, the natural bio-polymers for their specific and biochemical and therapeutic features play several biological roles as signaling/regulating molecules in many physiological processes, including cell immunity, growth, reproduction and homeostasis. Additionally, they are also components of the natural moisturizing factor [NMF], a mixture of ingredients fundamental to prevent the skin water loss [38,40,69–71].

For skin moisture loss, it is useful to remember that NMF is a collection of water-soluble low molecular weight compounds (i.e., amino acids) which, found in the outmost skin layer, i.e., the Stratum Corneum (SC), are able to retain water, acting as an important source of moisturizing agents [72]. This mixture of ingredients, generated from filaggrin, originates from the continuous keratinocytes' turnover and corneocytes degradation, contributing to skin hydration and its healthy appearance (Figure 2) [73].



**Figure 2.** Skin turnover and NMF generation (i.e., amino acids and other compounds) through the corneocytes degradation.



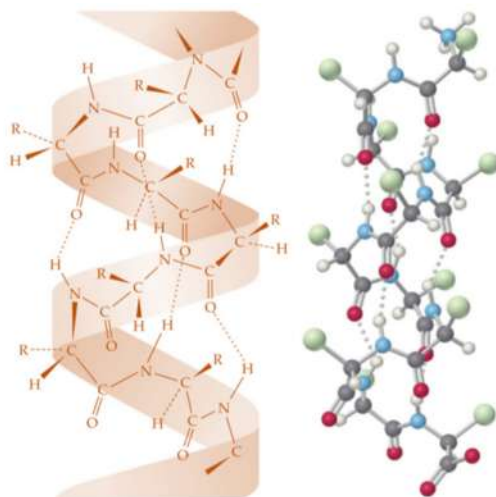
However, due to their specific amino acids sequence and 3D conformation, the biopeptides are capable of interacting with a huge number of biological macromolecules and biochemical compounds, modulating the many functions previously reported [67–69,73].

### 3.3. Biomimetic Peptides

Among the physiological oligopeptides, the so-called biomimetic peptides [74] should be mentioned. They are biotechnological synthetic compounds consisting of modified amino acids chains which, having an identical amino acid sequence to physiological peptides and being able to interact with the cell receptors, improve many natural biological functions, including skin permeability and barrier function [74,75]. Thus, for example, some biomimetic peptides find application as rejuvenating agents as an alternative to botulinum neurotoxin, due to the capacity they have to regulate the extracellular matrix production [ECM], stimulating the synthesis of both collagen and elastin [76–78].

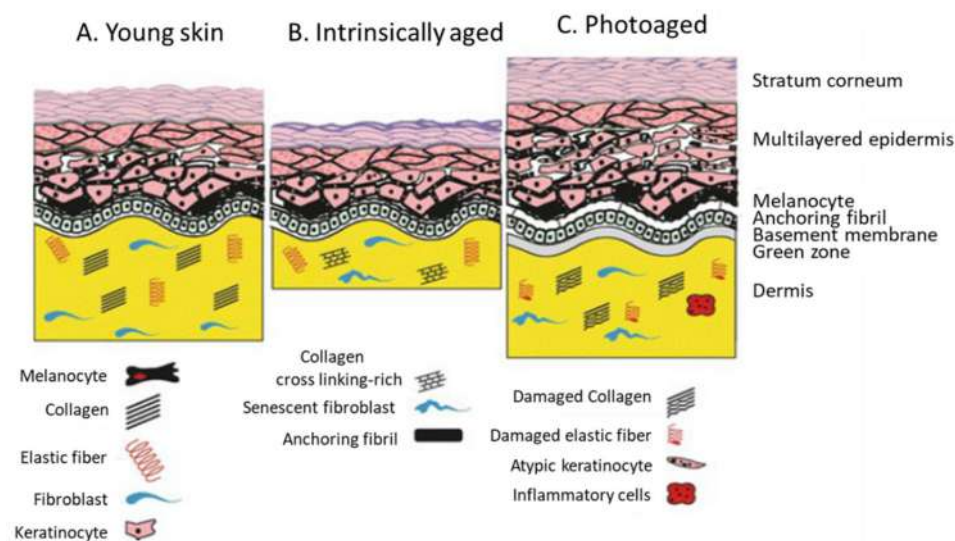
### 3.4. Collagen

Coming back to the natural biopeptides, collagen (CG) is a natural polymer made by a primary structure consisting of amino acids represented mostly by glycine (33%), proline and hydroxyproline (22%) with a secondary structure. This structure is formed by alpha chains which, composed singularly by 1014 amino acids with a molecular weight of around 100 kDa, are twisted around each other's and bundled up by hydrogen bridges into a triple helix (Figure 3) [78,79].



**Figure 3.** Partial structure of collagen alpha helix with its hydrogen bridges.

This natural polymer, representing 25% of the dry weight of all the body tissues including skin, is synthesized under the influence of diet, environment and age. However, its synthesis depends also on the state of hormonal background, the inherent genetic sequences and the epigenetic regulation of the gene's activity, which encode key proteins and enzymes during the collagen formation [80,81]. To this end, it is important to remember the many essential roles played by the previously reported ECM which, produced principally from fibroblasts, provides structural support for cells and tissues, modulating cell morphology, proliferation, migration and also gene expression [82,83]. Moreover, it should not be forgotten that, during the aging process, the collagen fibers become more disorganized, change their diameters (Figure 4) and increase their rigidity with a consequential decrease in elasticity, caused by the increasing in the inter- and intra-fibers cross links. In conclusion, the skin also loses part of its normal functions due to oxidative stress and modification of the metalloproteinase's activity [83–87].



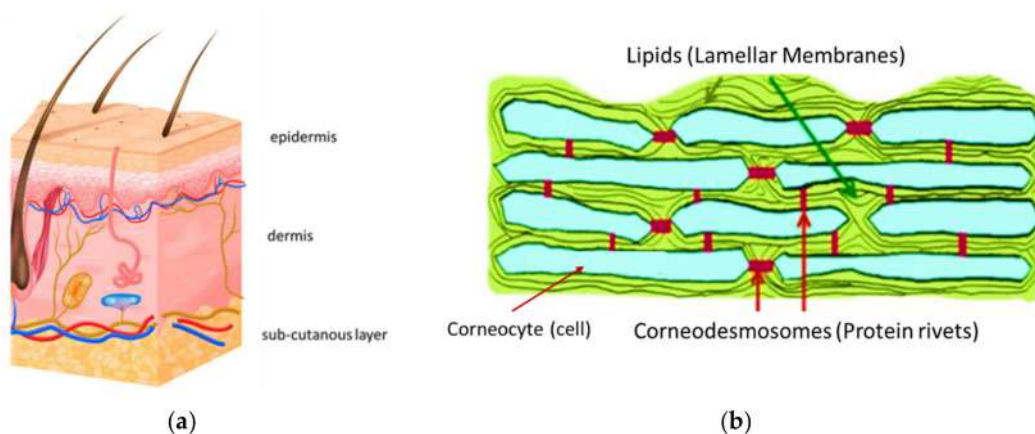
**Figure 4.** Collagen fibers and other cellular structures during aging: (A) Young skin; (B) Intrinsically aged; (C) Photoaged.

Among the 29 types of collagen identified, encoded by 45 genes with structures varying according to their alpha-chain, type I is the most common found in the skin and other tissues and organs [87] and performs mechanical and signaling functions. Moreover, collagen I is also involved in the organization of the extracellular matrix [ECM], which, in turn, affects the organized structures of both the epidermis and dermis [88]. Due to its regenerative properties shown at the level of ECM, this interesting polymer is frequently used in cosmeceutical, nutraceutical and medical formulations for aged skin [89]. The collagen synthesis, in fact, decreases by about 75% during the aging processes in comparison to that of young adults, representing the most important protein of the body [88,89].

Moreover, the reported specific use of collagen I is also due to its stable structure possessing interesting capacity of interactions with other compounds. In fact, the intramolecular hydrogen bonds, present between the amino acid glycine in the alpha helix present in its chains, have the ability to give the molecule exceptional mechanical resistance to tensile forces with a further capacity to bind a plethora of different compounds [86,88–90]. For this purpose, the activity shown by the low molecular weight peptides obtained from the hydrolyzed collagen should be remembered [90,91]. Films and non-woven tissues made by these polymers, in fact, have been shown to reinforce the skin barrier property, acting as support for cell adhesion and proliferation as well as increasing the skin water uptake capacity [92–95]. However, for trying to better understand the skin activity of cosmeceuticals and nutraceuticals, a short description of the skin structure is considered important [96].

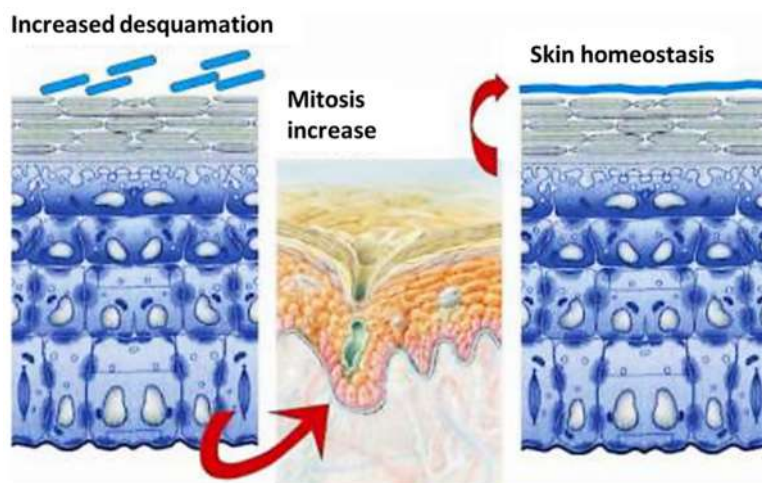
#### 4. Structure of Skin

On the surface of our body, the skin provides a protective barrier offering thermal insulation, preventing water loss and repairing against the external aggressions, including toxic and irritant micro-nanoparticles, microorganisms, ultraviolet [UV] irradiation and allergens [96]. This organ, generally less than 2 mm thick, is divided into three anatomically distinct viable layers—epidermis, dermis and hypodermis—covered by the non-viable stratum corneum (SC) that plays an important role in skin protection and hydration (Figure 5) [96].

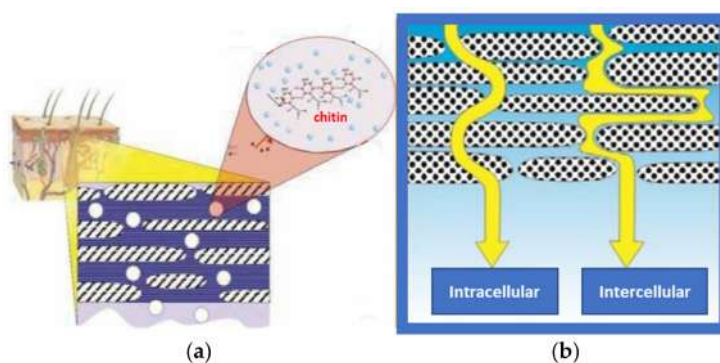


**Figure 5.** Skin structure (a) and corneocytes organized by lipid lamellae (b).

The major cellular component of the epidermis includes keratinocytes, which, at the end of the skin turnover, forms an overlapping structure made by non-living cells, the corneocytes, bridged together by specialized junctions, named corneodesmosomes (Figure 6) [96–98]. However, keratinocytes, held together by desmosomes, provide cell-to-cell adhesion while corneocytes enveloped together by lipid layers (i.e., Lipid lamellae) contribute to the structure and function of SC (Figure 7) [96–98]. Therefore, the SC thick layer is able to adsorb three times its weight in water, is basically represented by a two-compartment system composed of vertically stacked cells, the corneocytes, which, filled with keratin filaments and enclosed in a membrane envelop of protein and lipids, are released from lamellar bodies within the epidermis during the skin turnover (Figure 6) [96–98].



**Figure 6.** Skin turnover.



**Figure 7.** (a) skin penetration of chitin through the SC of the epidermis; (b) intracellular and intercellular penetration paths through SC.



Thus, corneocytes, migrating on the top of the skin, extrude their lipidic surrounding content (i.e., the lipidic lamellae) which, degraded to the NMF compounds, contribute to make the hydro-lipidic and moisturizing barrier [97,98]. These lipid lamellae, being around 20% of SC, are present mostly in a solid crystalline or gel state. They consist of 10%–15% of the dry weight tissue and are mainly composed of fatty acids (10%–20%), cholesterol (25%) and ceramides (30%–50%). They are also responsible for the skin hydration and homeostasis [99]. The lamellae, in fact, located on top of each other, form a lipidic stack consisting of a repeating structure with alternating hydrophilic and lipophilic domains [100]. In conclusion, keratinocytes, multiplying themselves through cell division and migrating toward the skin surface for becoming corneocytes, continually remove the outmost hydrophilic/hydrophobic structure, thus modifying both the barrier and the skin appearance [96,98]. However, dermis composed of various amounts of glycoproteins (PGs) and glycosaminoglycans (GAGs) and prevalently made by the ECM network embedded by collagen fibers and secreted by fibroblasts, forms a three-dimensional scaffold surrounding the cells [95–97]. This important skin structure contains vessels, lymphatics, and nerve cells, in addition to skin appendages, while the hypodermis is formed from connective tissue and fat. A special mention must be reserved for the previously reported ECM which, mainly composed of GAGs and PGs, negatively charged saccharide chains, includes collagens, elastin, fibronectin and laminin. This complex structure, which is necessary for giving the skin elasticity and adhesiveness [97,99], acts not only as a simple and mechanical scaffold for the cells, but also represents a dynamic environment that mediates the skin functions [100]. It is involved, in fact, in signaling events, and inhibiting many biochemical pathways by its hydrogel network, acts as a supporting material for tissue regeneration and cell delivery of the active ingredients' payload [101,102].

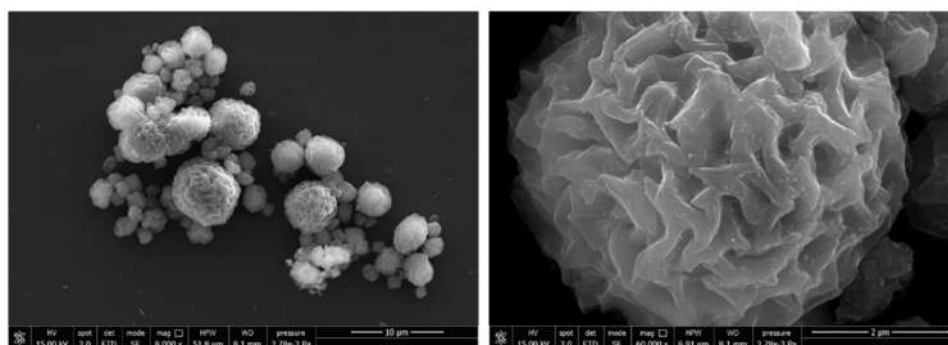
For all these reasons, the SC, 10–20 millimicrons thick, represents the primary barrier opposed to skin penetration of active ingredients, applied on its structure by the cosmetic products. Therefore, to obtain the required cosmetic effectiveness and safeness, it is necessary to overcome the skin barrier. Thus, the need to develop the right formulations made by specific carriers which, loading and transporting the selected active ingredients, should result in being able to penetrate the SC, releasing them at the deigned skin layers.

### 5. Skin Penetration and Supposed Mechanism of Action of Carriers/Active Ingredients

As previously reported, there are many active ingredients used for formulating cosmetics and nutraceuticals which should be skin- and environmentally-friendly together with the different materials utilized for packaging purpose. Worldwide consumers, in fact, are looking for nutritional eco-cosmetics that supplying multiple benefits, should have the capacity to give a global health and wellbeing for humans and the environment [2,4,103,104]. Additionally, young generations are also searching for more quality, credibility, authenticity and transparency of the products, also discovered frequently via social media [4,26,103,104]. It should not be forgotten, in fact, that younger generations will be the key market for future innovations because of their own desire to change the world with products that are made with zero waste, consume low amounts of energy and show respect for the environment [4,103,104]. Consequently, there is an industrial necessity to search and select appropriate carriers and active ingredients for realizing efficacious cosmetic and nutraceutical formulations. Thus, there is a need to know how the selected molecules move from the carrier through the different skin layers and mucous membranes. It is necessary, in fact, to predict their solubility and diffusion within the ingredients and the SC skin surface lipids or/and the mucin polymers of mucous membranes [105–108]. However, it is necessary to remember the different skin penetration modalities, achievable through three pathways -intercellular, intracellular and trans-follicular. They depend on the barrier disruption area and frequency of application, the degree of friction or rubbing of the product onto its surface and naturally to the composition of carrier and the selected active ingredients (Figure 7) [105–107]. The primary purpose of the carrier, in fact, is to enable the cosmetic active ingredients to be conveniently spread upon the skin for their

better penetration through its layers. Consequently, composition and physicochemical characteristics of the carriers represent an important instrumental role of the products' activity, which depends principally on the scaffold porous material used to make the carrier structure. The product effectiveness and safeness, in fact, are determined by the intrinsic activity of the selected active ingredients and the capacity of the carrier to deliver them at the right skin or mucous membrane layers [105–107].

The carrier, mimicking the skin ECM, may perform its essential functions, such as anchorage, proliferation and migration of the cells [108–110]. Thus, for example, the right porosity of the carrier-tissue permits growth and migration of the cells, which, through its pores, may have not only the necessary oxygen and nutrients but also the possibility to eliminate the waste materials [108]. This is the reason why many scientific research studies have been published during the last years on the topic of carriers and nanocarriers, including micro/nano emulsions, liposomes, lipid nanoparticles and polymeric nanocomposites, all realized with the aim to overcome the skin' penetration problems [101,106–112]. In particular, nanoparticles and polymeric nanocomposites have the capacity to deliver a wide range of ingredients. These particular delivery systems, in fact, have shown to optimize the skin penetration because of their modifiable physicochemical properties, including size, surface charge and physical morphology [113–115]. Therefore, the possibility to make innovative biodegradable carrier-tissues which, capable of maximizing the efficacy index of active ingredients encapsulated into or linked over their structures, are specifically designed and realized to obtain a controlled release of optimal dosing and enhanced effectiveness [116]. For trying to understand the mechanism of action of these new carriers, different modalities have been proposed. Some studies have supposed an interaction between carrier and SC, which is able to alter the lipid lamellae structure [106–108]. As a consequence, the lipid chains' polarity could be improved by the disorganization of the skin layers' tight arrangement [106–108]. Thus, the skin barrier weakens, encouraging the active ingredients' penetration, meanwhile mobility and permeability of the SC lipids are affected reversibly [106–108]. By other studies, it has been shown that charged nanoparticles (NPs), such as chitin nanofibrils (CN), may increase the skin penetration creating electrostatic interactions with negatively charged elements of the ECM matrix, including collagen and GAGs [117–121]. In addition, these NPs can be spray dried as micrometric round particles (Figure 8) by adding polyethylene glycols [122,123]. This corona, providing to the nanoparticles steric stabilization and conferring stealth properties, may affect their interaction with the skin environment [121,124–126].



**Figure 8.** Microparticles of chitin nanofibrils spray dried using poly(ethylene glycol).

Therefore, by all these techniques, it seems possible to make innovative cosmeceuticals, nutraceuticals and advanced medications, capable of increasing the effective percutaneous penetration of many active ingredients [108–111].

Thus, the reason to realize and use the proposed new smart tissues as innovative cosmeceutical carriers is because of their appropriate mechanical strength, physicochemical characteristics, biocompatibility and modulated properties [63,127,128]. They, in fact, may be embedded by nanoparticles encapsulating various active ingredients, having the capacity

not only to protect the ingredients from environmental aggressions, but also to load, carry and release them, at the level of the skin or mucous membranes layers, at the designed dose and time [63,127,128].

Regarding the delivery of nutraceuticals, they can be administered by the same water-soluble carrier-tissues through the trans-mucosal sublingual route [129]. The oral mucosa, in fact, is characterized by a high permeability and capability to bypass the first-pass metabolism of liver. Thus, the active ingredients may slowly diffuse into the systemic circulation in a relatively short time, avoiding their distraction by the gastric juices [130–132]. Therefore, the necessity to realize specialized nano-carriers able to traverse this thick web, evading adhesion to the sticky mucin fibers [133–135]. Just for trying to better understand the problem, it is interesting to remark that mucosa, covered by an adhesive gel, the mucus, is composed of a density network of natural mucin polymers [128–131]. These macromolecules, interspersed with a variety of glycoproteins made by about 10 carbohydrate side chains, create a selective barrier to the diffusion of other macromolecular systems across mucosal surfaces [105,134]. As a consequence, there is the need to better understand the different carriers to be used for cosmeceutical and nutraceutical formulations, because of the different delivery route of penetration existing between skin and mucous membranes, characterized by different structures and properties.

## 6. Skin and Mucous Membrane: Penetration, Safeness and Effectiveness and the Ambiguity of the Rules

The outmost layer of skin, as previously discussed, is made by a compact keratinized layer of cells covered by a thin hydro-lipidic film [71,96,97], while mucosal surface is made by less keratinized layers covered by a protective lubricant film of mucus rich of mucins' polymers [104,129,130,136,137]. However, both skin and mucous membranes are characterized by a daily turnover rate of cells produced mainly by the respective basal layers [135]. Moreover, all the different mucous membranes, but specifically the oral ones, are made by permanently and maximally hydrated tissues, showing an increased permeability to water compared to body skin, also if the mucus acts as an efficient barrier against the entrance of many substances [136–138]. Thus, the reported necessity to formulate specialized carriers which, made by selected macromolecules and specialized particulates, should have the ability to load and release the active ingredients to the skin and mucous membranes' layers, being compatible with both the structures.

In conclusion, nutritional eco-cosmetics, designed and formulated for their effectiveness and safeness should be able to remodel and remove the cellular dysfunctions of skin and mucous membranes of people affected, for example, by premature aging processes [139]. Therefore, they might be formulated by selected active ingredients embedded, for example, into emulsions and/or the proposed tissue-carriers made by the complex chitin nanofibrils-nanolignin (CN-NL) [139]. For this purpose, some active ingredients, such as vitamins A, C and E have shown to be cell regulators in both the carriers, acting as important antioxidant compounds capable to delay different skin aging processes [12,43,44]. They, in fact, may be applied on the skin by cosmetic emulsions or innovative tissues and/or taken by oral route as nutritional supplements. However, it has been shown that their penetration and effectiveness through skin and mucous membranes is enhanced, when active ingredients and carriers are used at their micro/nano dimensions [i.e., nanoparticles and nano emulsions] [140–144]. Moreover, it is important to remember the effectiveness of both cosmeceuticals and nutraceuticals may be obtained, only when the selected active ingredients have the possibility to be delivered to the designed site of action at right concentration and time [143]. Consequently, the product effectiveness depends directly to the penetration of the active ingredients through the skin/mucous membranes because, loaded and carried by the right vehicles and released at level of the viable tissues and cells, may achieve their function [144–146]. For this purpose and as previously reported and discussed, smart non-woven tissues, made by natural polymers and embedded by

chitin-lignin (CN-NL) nanoparticles encapsulating selected active ingredients, seem to be particularly useful carriers to achieve this goal [128,141–149].

Unfortunately, the skin/mucous membranes penetration seems to represent a problem not yet solved, also because of the ambiguity of the rules, which arise in the definition of the activity of cosmetics products vs medical devices and drugs [150–154]. Cosmetics, in fact, should have a preventive action only, “acting without modifying the skin physiology”, in comparison with drugs and medical devices which may modify the skin structure by its pharmacological activity. It is difficult, therefore, to understand how it may be possible for the cosmetic products to “protect (the skin), keeping it in good condition” [154]. The cosmetic active ingredients, in fact, should not penetrate through the skin structures, so they can't carry their biological activities at the designed and necessary skin layers, as necessary. For these reasons dermatologists and consumers are looking for the so-called cosmeceuticals and nutraceuticals, hoping and thinking on their supposed increased effectiveness [152–155]. In our opinion nutritional eco-cosmetics (cosmeceuticals and nutraceuticals) have been shown to possess an interesting bio-physiological effectiveness and, acting differently from drugs, might be used not only in healthy skin and mucous membranes, but also in the treatment of minor disorders and or abnormalities as reported many years ago from a paper of our group [154].

Thus, for example, it was proposed that it might be possible to distinguish between skin redness, a slow inflammation process, and skin erythema, represented by a high inflammation process. However, both have to be considered inflammatory processes. Thus, the former case may be treated by the supposed biological activity of cosmeceuticals, having not yet reached a pathological level, while the second one has to be cured by the pharmacological activity of medical devices or drugs [154].

In any case, it is important to underline that if (and where official rules allow) the cosmetic products are able to penetrate through the skin and mucous layers, exerting the activities reported by the relative claims, then naturally [151–155].

## 7. Future Trends: Biopolymers as Substrates

As previously discussed, Beauty and Personal care products are represented by a particular market, increasing day by day for the major consumption of young people and the growing aged population. Both the consumers desire to maintain and/or obtain a healthy mind and body with a juvenile appearance [2,8,15,24,25,156–158]. Consequently, being aware about waste and pollution, considered the main cause of the worldwide disasters, they wish to live in a happy Planet. Thus, preserving clean air and water of our environment, it will be possible to maintain natural raw materials and biodiversity for future generations [25,159]. The future smart nutritional eco-cosmetics requested from the consumers' majority, could be formulated by the recovery and use of innovative, effective and safe ingredients of natural origin obtained by innovative bio nanotechnologies. People plan to spend more on natural-derived products and cosmetic' rejuvenation procedures to prevent or minimize the signs of skin aging, improving wellness and wealth [25,158–160]. Consumers, in fact, are conscious about the possibility to obtain a better physical and mental health, by the use of the right cosmeceuticals and nutraceuticals possibly at low cost, considered necessary for maintaining better nutrition and sleeping, to ameliorate their health and the natural appearance [159,160]. Thus, due also to the COVID-19 pandemic, the consumers' habits have been forced to change while the companies' business model have been transformed and governments have adjusted many of their regulations [9,15,161,162]. Therefore, the need to formulate innovative nutritional eco-cosmetics by the use of natural bio-ingredients and bio-carriers, possibly obtained from food and agricultural waste, as the reported cosmeceutical-tissues [9,10,13,16–18]. On the one hand the reduction of waste has become a necessity to reduce pollution, diseases and the many worldwide environmental disasters, changing the way of producing and consuming [4,13,15–19,163]. On the other hand, the production of smarter nutritional cosmetics by applying circular economy principles became a necessity for recycling products, thus protecting the Earth biodiversity for



the future generations [164]. As a consequence, the need to use biomaterials obtained from waste to make natural carriers, such as micro-nanoparticles and nano-emulsions/gels or engineered innovative non-woven tissues as well as active ingredients, including natural extracts and juices [43,45,100,164]. Naturally all the different materials and manufacturing technologies have to be accurately selected and differentiated, for obtaining an optimized release with the best effectiveness of the selected ingredients at level of the skin and mucous membranes' layers [165–167]. Therefore, the final product has to be designed to achieve the necessary functions request from consumers, including stability, availability, effectiveness and safeness [165–167]. At this purpose and as previously underlined, the efficiency of carries represents a fundamental option to load, carry, deliver, release and diffuse the active ingredients at the designed site by the necessary dose and time [122,146–149,168–170]. Moreover, it is not to forget the importance of biomaterials used for making beauty films and tissues for beauty masks [64,171–175] or for biodegradable packaging also, thus contributing to maintain a clean environment at zero waste. This should be the goal of the actual nutritional eco-cosmetics made possibly by the use of ingredients obtained from waste materials [176]. An example of nutritional eco-cosmetic application is given by the electrospun tissue based on pullulan loaded by dry powder impregnation with CN-NL complexes containing glycyrrhetic acid (from liquorice), produced to obtain an innovative and effective beauty mask by Teno et al. [177]. Compression moulded beauty masks releasing starch in water [178–189] modified on the surface with CN-NL, CN and CN-NL containing Vitamine E [180] were also prepared and studied as biopolymeric substrates for developing new nutritional cosmetics. Moreover, CN from shrimps exoskeletons and polyphenols from watermelon peels were simply deposited, by formulating a liquid coating, on cellulose tissues for personal care applications [181]. Their permanence onto cellulose is granted by hydrogen bonds due to the similar chemical structures of molecules and substrates, bearing a high concentration of -OH groups. Nevertheless, on the wet skin, the functional molecules can be released to exert their anti-microbial and anti-oxidant actions. In Table 2 the three described examples of nutritional cosmetics are schematized, indicating the biopolymers used as substrates and the active molecules applied on them to be successively released on wet skin.

**Table 2.** List of three different nutritional eco-cosmetics.

Nutritional Eco-Cosmetics	Substrate	Active Molecules	Loading Method	References
electrospun beauty mask	Pullulan, nanostructured tissue	CN-NL-glycyrrhetic acid	Dry powder impregnation	[177]
Compression moulded beauty mask	polyhydroxyalcanoate/starch, film	CN+CN-NL+ CN-NL-Vitamine E, starch	spray	[178–180]
Cellulose wipe	Cellulose, tissue	CN and polyphenols from watermelon	spray	[181]

However, the future perspective of these innovative cosmetics, based on nano-science and nanotechnologies, go towards the use of natural active ingredients which, characterized for their nano size, might be diffused by micro-nano-carriers such as the proposed chitin nanofibril-nanolignin-based nanoparticles [121] and the smart biodegradable tissues, free of emulsifiers, preservatives, fragrances, colors and other chemicals [182–185]. These smart and innovative carriers, in fact, seem able to easily deliver the loaded ingredients, being skin- and environmentally-friendly [183], also for the packaging materials used for them [171–173,186–189], that can be cellulosic.

## 8. Conclusions

Cosmetic and nutritional cosmetics should give benefits and advantages to both skin and mucous membranes, thus resulting in being highly efficacious for human health and the environment, according to the consumers and the scientists' expectations for a greener

world. The proposed cosmeceutical-tissues seem to go in this direction. Moreover, peoples global awareness regarding sustainability must be increased through effective campaigns useful to make public the necessity of changing the way of producing and consuming goods and nutritional cosmetics without creating waste, to obtain a greener and pleasant world.

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