Spirulina for Skin Care

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Spirulina stands out as a sustainable bioactive microalga with health-promoting properties, and an important active ingredient of natural cosmetics products.

Spirulina microalga cyanobacteria natural cosmetics skin care skin health

1. Introduction

Since ancient times, botanical extracts have been extensively used in cosmetics and skin care products. In recent decades, researchers have turned their interest towards microalgae and cyanobacteria for the preparation of healthy and nutrient natural products, both as food and cosmetics [1][2].

Between the microalgae, *Spirulina* (Arthrospira) is one of the most promising species, due to its precious content of phytochemicals and its greener and more sustainable production chain. *Spirulina* is a unicellular cyanobacterial-type microalga, which grows at pH 10-12. The genus *Athrospira* includes a great variety of species (see, i.e., ref [3]), such as the most popular *Spirulina platensis* and *Spirulina maxima*. These two algae types differ in both ultrastructural and morphological characteristics, alongside in their geographic origin: the *Spirulina platensis* is mainly found in Africa and Asia, while *Spirulina maxima* is widespread in California and Mexico [4]. The safety of *Spirulina* utilization is well justified by its long history of use—this microalgae has been cultivated for centuries, and is still commonly consumed in Africa and in Chad—and by a plenty of in vivo/vitro studies [5][6][7][8].

Spirulina is considered also highly sustainable due to a multiplicity of synergic factors [9]: (i) it is easily grown in “bioreactors” under solar light with considerable savings in water, soil and (ii) without the need of pesticide or herbicide. (iii) This pretty simple production process requires minimal operator training and technical supervision thus ensuring a high economic impact. (iv) After cultivation the whole microalgae is used, unlike other fruit and vegetable crops where root, stem and leaf systems are all byproducts, (v) helping to save energy, cutting greenhouse gas emissions and the overall environmental impact. All these advantages are furthermore strengthened by the fact that (iv) *Spirulina* is highly dense and rich of nutrients and of phytochemicals [10][11].

2. Benefits of *Spirulina* for Skin Care Formulations

To date, few research have aimed at studying and demonstrating the *Spirulina*’s healthy effect on the skin. The most of cosmetic actions, supported by the literature and claimed by the market, are firstly the antiage one, including moisturizing, antioxidant and brightening proprieties, and secondly the antiacne and wound healing properties.

2.1. Antiage

2.1.1. Moisturizing

Skin aging is a complex process that depends on both a genetic predisposition and external factors, and causes functional and structural skin damage. Water molecules play a pivotal role in maintaining the skin structural proprieties: indeed, water binds the dermal proteins, such as collagen, and ensures the tissue thickness. Therefore, aged skin is poor of bounded water and has weak hydration networks, which make skin look less and less glowy and firm. Typically, UV radiation, pollution, a poor diet and an unhealthy lifestyle are the main causes of skin aging, and therefore of the loss of moisture together with the decrease of skin barrier.

Currently, the increase in life expectancy and the growing interest in a youthful appearance have led the cosmetic market to formulate antiage products with moisturizing and wrinkle reduction effects. Considering that beauty companies are also involved in searching sustainable raw materials and active ingredients, the studies on the antiaging effects of algae, like *Spirulina*, aroused great interest in recent years [12][13].

2.1.2. Antioxidant

The antioxidant potential of blue-colored cyanobacteria is of great interest in the cosmesis. Pigments can be used as natural colorants in make-up products, like eyeliner and lipstick, and as antioxidant agents, which protect against UV radiation [14]. Indeed, *Spirulina* contains a lot of photosynthetic pigments like chlorophyll and especially phycocyanin, which determine a long-lasting green-blue coloration in cosmetic formulas.

In 2012 Dr. Lotan A. (Nidaria Technology Ltd., Israel) patented some biologic sunscreen formulas, which included a blend of algae as active ingredients [15]. The claimed activity was the synergistic effect of the simultaneous use of UV filters and algae, which absorb sunlight, “convert it in energy source”, protect the skin and improve its appearance. The patent argues that “the agent primarily responsible for the improved effect on the skin is the incorporation of the algae” and *Spirulina* was one of the tested algae (*Spirulina*, *Dunaliela*, *Hematococus*, *Nannochlorosis* and *Tetraselmis*). However, despite the importance of this statement, an undeniable scientific demonstration is missing. The patent proposed three formulations containing 10% *w/w* non-viable intact algae, a topical gel and both W/O and O/W emulsions.

Few years later, C. Souza et al., further developed a stable and effective sunscreen formulation containing a mixture of UV filters and antioxidants (using *Spirulina* between the others). As such it further encourages researchers to design more efficacious and reliable sunscreens [16]. As an antioxidant, *Spirulina* may reduce skin hyperpigmentation and protect skin against sun-induced damages (e.g., photoaging) by inhibiting ROS-induced damage to the dermis. Both visual and rheological analyses revealed that the sunscreen formulations were stable during the study period. Therefore, the inclusion of UV filters Tinosorb® S, Tinosorb® M, Uvinul® APlus and Uvinul®

T150, along with *Spirulina* dry extract and dimethylmethoxy chromanol-loaded solid lipid nanoparticles (DMC-loaded SLN) did not alter the physical stability of the cream. Such formulations were characterized by a pH range between 5.3 and 5.8, suitable for topical application. DMC-loaded SLN were successfully produced with a high inclusion rate (approximately 96%, after 24 h) and stability (54 days). These formulations exhibited a non-Newtonian and pseudoplastic behavior and, in terms of safety, according to the sensorial analyses, they did not irritate the skin.

Table 1. Composition of the sunscreen cream based on UV filters and antioxidants. Published by Ref. [16].

Composition [a]	**Concentration (% *w*/*w*)**		
	Formulation Codes		
	F1	**F2**	**F3**
Oil phase [b]	12.6	12.6	12.6
Preservative	0.8	0.8	0.8
Aqueous phase	3.1	3.1	3.1
Bis-ethylhexyl methoxyphenyl triazine—Tinosorb® S	-	4.0	4.0
Diethylamino hydroxybenzoyl hexyl benzoate—Uvinul® APlus	-	1.0	1.0
Ethylhexyl triazone—Uvinul® T150	-	4.0	4.0
Methylene bis-benzotriazolyl tetramethylbutylphenol—Tinosorb® M	-	6.0	6.0
Spirulina dry extract	-	-	0.1
DMC-loaded SLN [c]	-	-	10.0

Water solvent q.s.	100 g	100 g	100 g

[a] Qualitative composition was reported in accordance with INCI (International Nomenclature of Cosmetic Ingredient). [b] Quantitative composition of oil and aqueous phases were previously reported by ref. [17] [c] DMC final concentration into F3 formulation was 0.05% (*w*/*w*). DMC-loaded SLN: dimethylmethoxy chromanol-loaded solid lipid nanoparticles.

The C. Souza's research team examined the photoprotective effects of the developed formulations, both in vitro and in vivo, and highlighted the pivotal contribution of the addition of *Spirulina*. The in vitro UVA protection of formula F2 and F3 was evaluated by the UVA/UVB ratio and by the critical wavelength. The in vivo SPF values of both formulations were nearly 30 while the in vitro SPF values of formulations F2 and F3 were respectively around 2.5-times and 3.0-times higher than those obtained in vivo. Therefore, in vitro results suggest that the combination of *Spirulina* and SLN loaded DMC with UV filters improve the SPF value. However, in vivo tests did not adequately confirm this result. It has been observed that, while in vitro experiment measures the formulation transmittance, the in vivo procedure determines the effective ability to prevent inflammatory reaction (erythema) triggered by solar radiation. This means that *Spirulina* increase the light scattering properties without furnishing enough anti-inflammatory activity.

To further clarify the benefit of using *Spirulina* into the formulations, a 3-month single-blind clinical study has been carried out with 44 healthy participants (30–50 years old), during which the water content of stratum corneum, TEWL, dermis echogenicity and skin elasticity and pigmentation were measured. The results showed that *Spirulina*-supplemented sunscreen significantly improves both the health of the dermis and the skin elasticity after 84 days of the treatment, with respect to the sunscreen itself. Moreover, as previously stated by Delsin et al. [18], topically applied *Spirulina* regenerates the skin barrier and reduces the loss of water.

2.1.3. Brightening

Skin hyperpigmentation is an aesthetic issue, which raises a growing concern in the current cosmetic market. Currently, whitening products are pivotal in the antiage skin care routine, since they reduce spots and skin dyschromia caused by UV exposure. The pigmentogenesis begins inside melanocytes, which are a type of cell located between the keratinocytes in the basal layer of epidermis. During the mentioned process, tyrosinase plays an important role in controlling the production of melanin and then in coloring hair, skin and eyes. In fact, this multicopper enzyme facilitates the transformation of L-tyrosine in L-dihydroxyphenylalanine (L-DOPA), which in turn oxidizes itself and becomes DOPA-quinone. A set of spontaneous cascade reactions leads to the creation of a pigment polymer, called melanin, which is released to the surrounding keratinocytes [19]. Both the abnormal loss and the overproduction of melanin may generate serious esthetical and dermatological skin disorders in humans, such as *Acanthosis nigricans*, melasma, Cervical poikiloderma, Lentigines, Periorbital hyperpigmentation, neurodegeneration associated with skin cancer risk and Parkinson's disease. The most reliable strategy to treat such pigmentary disorders so far is to use inhibitors of the tyrosinase.

2.2. Wound Healing

Skin wound is a disruption of intact tissue, which leads to a loss in functional and anatomic continuity. Environmental conditions, accidents but also skin issues, like dryness and dermatitis, might be some of the trigger factors. Wound healing is, instead, a complex process involving inflammatory system, synthesis of structural proteins, migration and proliferation of both parenchymal and connective tissue cells. Full recovery is complex and, sometimes, chronic diseases or bacterial infections may further undermine the healing process.

In 2011, *Spirulina* was investigated for its effectiveness in wound healing, due to its flavonoids and triterpenoids, which act as astringent and antimicrobial agents [20]. The *Spirulina* wound healing effect of dry extracts, obtained in petroleum ether, chloroform and methanol was tested on rats and monitored for 16 days. Specifically, the wound contraction—as the percentage reduction in wound area—and its closure time were controlled. A significant improvement in the wound healing activity was noticed with the three extracts aforementioned. The best result was obtained in the ointment with *Spirulina* petroleum ether-based extract at 10% *w/w*. In 2013, Gur et al. studied the impact of the crude *Spirulina* extract and the phycocyanin isolated from the crude *Spirulina* extract on cultures of human keratinocyte, by using in vitro and in vivo models of wound healing [21]. They observed that *Spirulina* extract showed the best growth stimulation at 33.5 µg/mL dose of treatment, which declared a cell activity ranging from 100% to 270% after 72 h. Cell viability has also improved with phycocyanin and it was measured, even up to 213%. Cell activity and proliferation difference between *Spirulina* extract and phycocyanin were noted not to be important ($p > 0.05$) at the range of doses (33.5–0.0335 µg/mL) examined. It was also discovered that 1.25% of C-phycocyanin has a superior effect on the in vivo efficiency, compared to other preparations with *Spirulina* extract, on the 7th day. Overall, the proliferation and growth stimulation activities of *Spirulina* extract seem to be directly connected to the presence of both phycocyanin and carotenoids, which synergistically contribute to the wound healing and tissue regeneration. A few years later, Gunes et al. developed natural skin creams enriched with bioactive *S. platensis* extract, and studied its wound healing, genotoxic and immunoreactive effects in vitro to evaluate the potential use of *Spirulina* in biomedical and pharmaceutical sector [22]. The in vitro cell culture tests demonstrated that *Spirulina* extracts showed significant effects on fibroblast cell proliferation and migration. Fibroblasts are mesenchymal cells that enable tissue preservation by secreting extracellular matrix, and they are in charge of the inflammation and scar formation, during the wound healing process. A skin-care cream, which incorporates 1.125% of *Spirulina* extract, presented the biggest proliferative effect on skin cells with an increase of Type 1 collagen immunoreactivity. The micronucleus assay, which shows DNA damage, demonstrated that *Spirulina* based cream had no genotoxic effect on human peripheral blood cells. Additionally, *Spirulina platensis* also revealed a strong antioxidant property, due to its superoxide dismutase (SOD) activity with values up to 8.0 U/mL of SOD in *Spirulina* extract. All these features lead the blue-green microalga to be suitable for biomedical and cosmetic applications, particularly for wound dressings as well as sunburns, erythema and photoaging.

More recently a Korean research team absorbed *Spirulina* in an engineered-tissue, to evaluate its wound healing potential [23][24]. They selected nanofibers of polycaprolactone (PCL) as a supporting material suitable for tissue regeneration. PCL, which is an FDA-approved polymer, is also biocompatible, biodegradable and known to favor the oxygen absorptivity, the drainage capability and the water evaporative control, which are critical factors for the skin regeneration. In a study, *Spirulina* aqueous extract was absorbed on the nanomaterial and the wound regeneration was evaluated using an in vivo wound model [23]. In this specific regard and from a bioethical view, we contest such use of an animal for analysis in the cosmetic field and we strongly recommend the stakeholders to find other cruelty free alternatives to perform efficiency tests. In general, *Spirulina*-PCL helped to regenerate wounds and enhanced skin regeneration, by improving the antioxidant mechanism against the reactive oxygen species (ROS) of fibroblast under oxidative stress (Figure 1). Nevertheless, the developed nanofibers had a restricted capability to moisturize wounded skin because of the hydrophobicity of PCL.

Figure 1. Schematic design of the *Spirulina*-PCL nanofibers application to cutaneous wound. Published by Ref. [23].

To resolve the issue of the hydrophobic behavior of *Spirulina*-PCL nanofibers, the alginate was added in a following step due to its high hydrophilicity and absorbing capability [24]. Alginate (Alg) has a hydrophilic structure that consists of alpha-L- guluronic acid and beta-D-mannuronic acid, which can accommodate large amounts of water. The study revealed that *Spirulina* extract-alginate saturated polycaprolactone nanofibers (*Spirulina*-Alg/PCL) effectively accelerated the tissue regeneration in a rat model (3.7% *w*/*v* of *Spirulina* extract). When this patch was applied to the animal's wounds, the extracellular matrices were rearranged faster than those treated with the simple patch support without *Spirulina*. In comparison to the earlier developed *Spirulina*-PCL nanofibers, alginate improved the moisture preservation and adhesiveness of the *Spirulina*-Alg/PCL nanofibers, in addition it accelerated the regeneration of full-thickness wounded skin in the rat model.

2.3. Antiacne

Acne is an epidermis disorder correlated to a sebum hypersecretion in deformed follicles, which implies inflammation and comedones formation. The anaerobic *Cutibacterium* acnes (also known as Propionibacteriumacnes) plays a role in the inflammation process because it hyperproliferates in the sebaceous lipid environment and produces reactive oxygen species (ROS) and proinflammatory compounds. This cytokine cascade also induces the follicular wall rupture of sebaceous glands and a consequently variation in the sebum composition. Acneic skins are low in linoleic acid and, therefore, their barrier skin function is compromised. Such a lesion pathway may also help the colonization of other bacteria like the *Staphylococcus epidermis* (*S. epidermis*). Indeed, although this *Staphylococcus* is a commensal skin microbiome bacterium, it was found in acne as well [25].

Acne disorder affects several people, mostly during adolescence, and it may lead to a lack of the self-confidence, resulting in body shame. Since acne-inducing bacteria shown side effects and an increasing resistance towards the synthetic drugs like tetracycline, many alternative approaches have been explored in the last decades. Among them, the topical applications of cosmetic formulas containing botanicals as safer active ingredients are the more suitable [26].

Currently, the cosmetic market is strongly interested in formulating antiacne products with a special focus on natural active ingredients, in addition to topical medication [27]. With this purpose, in 2018 Nihal et al. developed a topical antiacne formulation using *Spirulina* extract rich in phycocyanin protein [28]. The latter protein, as already mentioned, is known to be responsible for most of the natural *Spirulina* benefits. The phycocyanin was successfully extracted from the alga by using sonication and the cold-maceration process and then it was purified by the dialysis method. The authors thus studied its antimicrobial and anti-inflammatory activities. In particular, the antioxidant activity was found to be dependent on phycocyanin concentration in the range between 0.05 and 0.3 mg*mL^{-1}.

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