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A review of the emerging role of cyanobacteria-based nanoformulations for skin care: Opportunities and challenges

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ABSTRACT

Use of nanomaterials (NMs) is a promising feature in skin care products. Nanotechnology offers several advantages such as tolerance, stability, efficacy, and improved delivery systems which make NMs suitable drug carriers for the skin. Cyanobacteria are prokaryotes that have various bioactive compounds used as natural ingredients in cosmetics as well as cosmeceuticals, and can help in the maintenance of skin structure and function. Cyanobacterial metabolites such as alkaloids, peptides, terpenes, polysaccharides, and lipids possess various beneficial bioactivities. In this review, we attempt to present new perspectives on cyanobacterial-based formulations with beneficial activity for the skin. New formulations present on the market are reported and also discussed the rules, regulations, toxicity, and safety assessments to determine the fate of nanotechnology and its commercialization. We estimate the global nanotechnology market for skin care and future growth. This review is focused on different cyanobacterial nanoformulations and the challenges in their development and commercialization.

1. INTRODUCTION

Cyanobacteria are able to produce secondary metabolites with significant bioactivity, including ultraviolet (UV) protective, cytotoxic, antitumor, anti-bacterial, anti-viral, antifungal, anti-inflammatory, antimalarial, antiprotozoal, and antituberculosis. Cyanobacteria existed billions of years ago on Earth when there was no oxygen in the atmosphere. They were exposed continuously to UV radiation to combat its effects; cyanobacteria developed various mechanisms like the production of UV protecting compounds, antioxidants, and proteins. Cyanobacterial metabolites have various applications in pharmaceutical and biotechnology companies. Natural extracts of plants, pigments, proteins, and flavonoids are widely used for the synthesis of nanoparticles [1,2].

Mankind is becoming more aware that prolonged exposure to UV rays causes a variety of skin problems such as sunburn, wrinkles, skin ageing, hyperpigmentation, and can even lead to skin cancer. The good news is that one can reduce the effects of UV radiation by taking simple protective measures. Blue green algae, or cyanobacteria, contain some of the hottest beauty ingredients, so it's set a ruffle of beauty feathers. According to the intelligence agency Mintel, blue green showed the biggest skin care trends in 2019 [3]. Cyanobacteria have the ability to retain water and produce UV protective compounds, allowing them to be used as natural UV filters and moisturisers [4]. They are also a rich source of antioxidants that can neutralise free radicals [5]. Nanotechnology offers wondrous, remarkable, innovative solutions for product delivery. New lipid carrier vehicles such as solid lipid, liquid lipid, non-ionic surfactant niosomes, nanoemulsions, and microemulsions possess highly penetrating power, high stabilization and entrapment efficiency, site-targeted drug delivery, and controlled and sustained drug release [5]. Cyanobacterial derived nanoparticles have shown better results due to less time consumption, slow kinetics, low cost, and eco-friendly [6]. Liposomes are suitable for the delivery of various cosmetic creams such as anti-ageing, moisturising cream, beauty, and sunscreen [7]. Lipid carrier and nanoemulsion systems are nanovehicles for moisturising agents. They have the property of retaining moisture, renewing collagen, rejuvenating, and lifting the skin [8]. Nanostructured lipid carriers (NLC) are considered to be the improved version of solid lipid nanoparticles (SLN). NLC offers increased skin hydration and penetration, sustained drug stability, and helps to improve the UV protection system with lesser side effects [5]. This review presents a detailed study on cyanobacterial nanoformulations, improved drug delivery, toxicity assessment rules and regulations, and further determines the beneficial role of these formulations in the cosmeceutical and pharmaceutical industries, as shown in Figure 1.

2. ROLE OF NANOFORMULATION IN DRUG DELIVERY FOR SKIN

Various new formulations have been synthesized for improved drug delivery systems such as nanogels, colloidal systems, nanoparticles,

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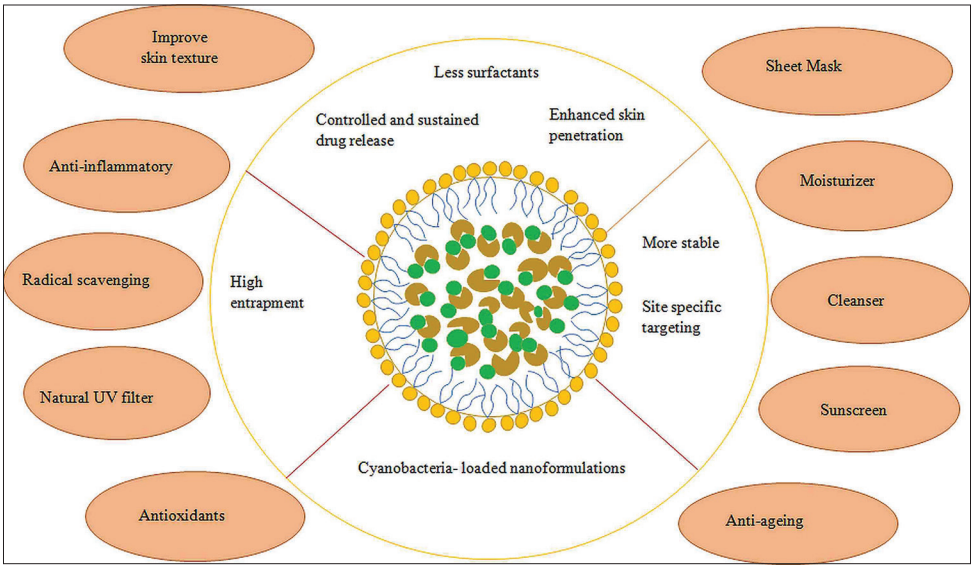

Figure 1: Pictorial presentation of various properties and beneficial roles of cyanobacterial nanoformulations for skin care.

and nanogels [9]. For several skin care problems, numerous methodologies are being developed. Natural ingredients are being used as nanoformulations and act as an efficient delivery system for the skin. These new generation nanoformulations have improved stability, drug delivery, and showed strong interactions [10] and lipid nanoparticles showed a controlled drug release pattern [11]. The natural nanomaterial (NM) loaded topical formulations are acceptable for topical delivery and offer a safer alternative with good efficacy for the treatment of diseases [10]. Different types of injectable nanoparticles have come on the market such as liposomes, polymeric nanoparticles, micelles, albumin, and a coreshell nanoparticle that avoids excessive drug circulation. Because of their ability to entrap both lipophilic and hydrophilic drugs, nanoformulations loaded with drugs should carry a large number of drugs for UVB-induced skin cancer [12]. Drug delivery nanocarriers such as nanoemulsions, microemulsions, SLN, NLC, liposomes, and niosomes have the advantages of controlled and sustained drug release, site specific targeting, high stability, and penetration power [5]. The properties of nanoparticles affect the skin permeation such as size, shape, coating, toxicity, and purity, and they are efficiently transported to the blood vessels through intercellular and transappendageal routes. Liposomes can be taken orally or applied topically. Liposomes can attain optimum therapeutic efficacy by continuous release of bioactive components, whereas the efficacy of NLCs is dependent on the temperature, percentage of oil incorporated into the lipid layer and the composition of the emulsifier [13].

3. CYANOBACTERIA UNIQUENESS FOR THE NANOFORMULATIONS SYNTHESIS

In recent years, synthesis of nanoparticles using cyanobacteria has become a growing area of interest due to its wide applications in the field of biomedical sciences. Furthermore, it is economical and environment-friendly. Several cyanobacterial genera have been investigated as a possible resource for the synthesis of nanoparticles. Several cyanobacterial species have been used to synthesize nanoparticles such as *Anabaena, Plectonema boryanum*, *Spirulina platensis, Lyngbya majuscula, Calothrix spp., S. platensis, Phormidium valderianum, and Microcoleus chthonoplastes*. The gold nanoparticles were synthesized using *P. Boryanum* [14]. Some scientists report the production of metal nanoparticles from the culture supernatant [15]. The extract, containing bioactive compounds, helped in the stabilization of the nanoparticles [16]. Silver nanoparticles have been made by N2-fixing cyanobacterium [17], whereas; the gold nanoparticles have been synthesized using *S. Platensis* [18]. To make nanoparticles, phycoerythrin is extracted from *Phormidium tenue* and combined with cadmium sulfide. Mycosporine-like amino acids (MAAs) and scytonemin formed the conjugated nanoparticles [16,19]. Hence, cyanobacteria could be used for the synthesis of metal nanoparticles. Zinc oxide nanoparticles (ZnONPs) in conjugation with MAAs have been synthesized to reduce free radicals and improve UV protective activity [19]. Another MAAs shinorine extracted from *Anabaena* strain L31 conjugated with ZnONPs also showed a reduction in reactive oxygen species (ROS). ZnONPs-shinorine conjugate is collectively used as a biological sunscreen. They are ecofriendly. Scytonemin and other MAAs are also used as photoprotectants as well as antioxidants [20,21]. *Scytonema sp.* showed antibacterial activity against human pathogenic bacteria, suggesting that it could be a promising treatment option for microbial skin infections [6,22].

4. CHARACTERIZATION OF NANOFORMULATIONS

Nanoformulations have been given tremendous consideration as quickly developing materials for an assortment of uses. Investigation of nanoparticles is a difficult task because of its versatile nature, lacking reference sources for the standardization of tools, sample preparation, estimate of their concentration, and explanation of the data. Nanoparticles can be characterized using different techniques. Nanoparticles were characterized on the basis of particle dispersion, distribution, shape, surface properties, and crystalline. The single property of nanoparticles can be assessed by more than one technique. The size distribution of nanoparticles is an important aspect in maintaining the relationship between the structure and materials that are utilized in nanoparticles, and this can be assessed by the dynamic light scattering technique and electron microscopy. Scanning electron microscopy is a technique that examines the surface of a sample and produces an image through a beam of electrons. Similarly, in transmission electron microscopy an electron beam is transmitted through the sample and produces an image. The sample section should be ultra thin, or less than 100 nm thick, and then the image is magnified and focused on the photographic plate. Atomic force

microscopy generates images by the interaction between the probe and sample. This measures the mechanical properties of a sample, like stiffness [23]. Dynamic light scattering is the general method of analysis of the hydrodynamic particle size and distribution over a range of sizes, dependent on Brownian motion and correlated with the velocity and size of the particle using the Stokese Einstein equation. The size of nanoparticles is depicted as the poly dispersity index. Dispersity is the major limiting factor and, thus, there needs to be an accurate size determination [23]. Infrared spectroscopy (IR spectroscopy or vibrational spectroscopy) gives data on the absorption, emission, and reflection of infrared radiation interactions with molecular species. It determines the functional groups in solid, liquid, and as well as gaseous forms [24]. In nanoparticles, different ligands attached may be easily identified [25]. Circular Dichorism spectroscopy is used when we make hybrid nanoparticles, that is, the aggregation of nanoparticles with photosensitizer molecules. It is basically used in organic/inorganic hybrid nanoparticles. This new creation must create new challenges. The fundamental need is to determine the presence of these aggregates [26].

5. VARIOUS TYPES OF CYANOBACTERIAL FORMULATIONS USED FOR SKIN CARE

5.1. Moisturizers

The outer layer is called the stratum corneum, and it serves as a barrier between the body and its surroundings. This layer gets easily dehydrated, leading to the dryness of the skin. Moisturizers are extensively used to retain water content in the skin [27]. It has been reported earlier that cyanobacterial exopolysacchride has strong moisture retention capacity as well as antioxidant activity. So, MAA and scytonemin could be used as moisturising agents [4]. Marine ingredients have been mixed to make a moisturizer which helps in collagen production, therefore increasing the moisture level. Skin remains hydrated for a long time. Zelens marine complex is a deep restorative, skin moisturizing skin care product [3]. Face Gym Training Sticks are a unique face gym complex that releases all the ingredients upon body heating to fight against free radicals. It is commercially available and infused with *Spirulina* to improve skin tightness and firmness [76] and Sunday Riley A+ High-Dose Retinoid Serum, is a commercial product which improves the texture and renews the new cells. It is a blend of 5% retinoid ester, 1% liposomal-encapsulated retinol blend, and 0.5% blue-green alga [77]. *Spirulina* is also used as a sheet mask to retain moisture and accelerate skin turnover (Origins by all greens mask, Nannette de Gaspe Bio-Stimulant Techstile Infusing Dry Masque Neck [3]. *Nostoc commune* has significant moisturizing, anti-inflammatory, and whitening properties. Hydro Algae formulated with the unique properties of blue green algae, has been used as a moisturizing cream [28].

5.2. Sunscreens

It has been suggested that sunscreens derived from natural sources such as cyanobacteria could be safer cosmetics in comparison to synthetically produced cosmetics [29]. UV protective compounds from cyanobacteria are the best natural UV filters [4]. Scytonemin 3a-imine, a reddish-mahogany colored pigment, is used as a novel sunscreen isolated from the cyanobacteria *Scytonema hoffmani* and *Scytonema spp*. [30]. Cyanobacterium *Synechocystis* produces an MAA called shinorine, which has been used a sunscreen [31]. MAAs extracted from *P. Umbilicalis* offer natural protection against sunburn under the name Helionori® [28]. 1-alkyl- 3-alcanoyl-1, 4, 5, 6-tetrahydropyridines, a synthetic analogue of MAAs, have been commercially used as sunscreen [32]. The sunscreen was incorporated into lipid nanoparticles due to its high loading capacity [33]. Supergoop! superscreen daily moisturizer sun protection factor (SPF) 40 is a cyanobacterial derived sunscreen present on the market.

5.3. Anti-ageing Products

Prolonged exposure to the sun is the main cause of loss of elasticity, rough skin, wrinkles, and hyperpigmentation. MAAs isolated from the cyanobacteria porphyra-334, shinorine, and mycosporine-glycine has anti-inflammatory and antioxidant properties [34]. Mycosporine-2-glycine extracted from *Aphanothece halophytic* showed a markable anti-ageing property [34]. Some products on the market have been used as anti- ageing products [35]. Methanolic extract of exopolysacchrides of the cyanobacteria *Arthrospira platensis* used as an antioxidant [36]. *Nostoc flagelliforme* produces ß-1, 3-glucan, which has anti-inflammatory and free radical scavenging properties [37,38]. It was reported earlier that lycopene isolated from *Anabaena vaginicola* has oxidant, anti-ageing and other properties [39]. *S. platensis* is also reported to be formulated into anti-ageing cosmetic products [38]. Cyanobacteria “In Eminence Organics Marine Flower Peptide Collection” is used to reduce lines and wrinkles [39].

5.4. Skin Cleanser

It is reported that UV radiation exposure and other pollutants create stress and therefore decrease the antioxidant defence system, which causes activation of ROS [40]. An effective anti-pollution skin care product that rich is in antioxidants should be used to fight against free radicals. *Spirulina* extract is a rich source of methyl-cobalamin and porphyrins, so they are used as facial cleansers to detoxify the dirt and pollutants from the skin [41,42]. Phycocyanin-C is the active form of *Aphanizomenon flos-aquae* which has the ability to defend against exogenous and endogenous pollution and could be used as a skin cleanser [42]. These are the various cyanobacterial formulated marketed products as shown in [Table 1].

6. RECENT PATHS OF PROTECTION FROM CYANOBACTERIA

Cyanobacteria are the most primitive organism on earth, and they depend on solar radiation for their normal life cycle. Increased solar radiation causes serious damaged to various physiological and biochemical process in the cyanobacteria. UV radiation caused direct effects by damaging the DNA or indirectly by producing ROS. To combat UV radiation, cyanobacteria developed various protective mechanisms like production of antioxidants, UV protective compounds such as MAAs, scytonemin, and protein resynthesis as shown in Figure 2.

6.1. Role of Cyanobacteria in Photoprotection

The level of anthropogenic chemical has increased due to ozone depletion this give rise to a serious issue with harmful effects on the earth’s ecosystem [43]. Cyanobacteria are more susceptible to UV stress; therefore, various UV protective mechanisms have been developed against the damaging effects of UV radiation on cyanobacterial cells. Various physiological and biochemical processes are effected either directly or indirectly [44]. Cyanobacteria in response to ROS generation produced protective and adaptive mechanisms by regulating gene expression in a variety of cellular signalling pathways. They produce antioxidants such as superoxide dismutase, catalase, and peroxidase

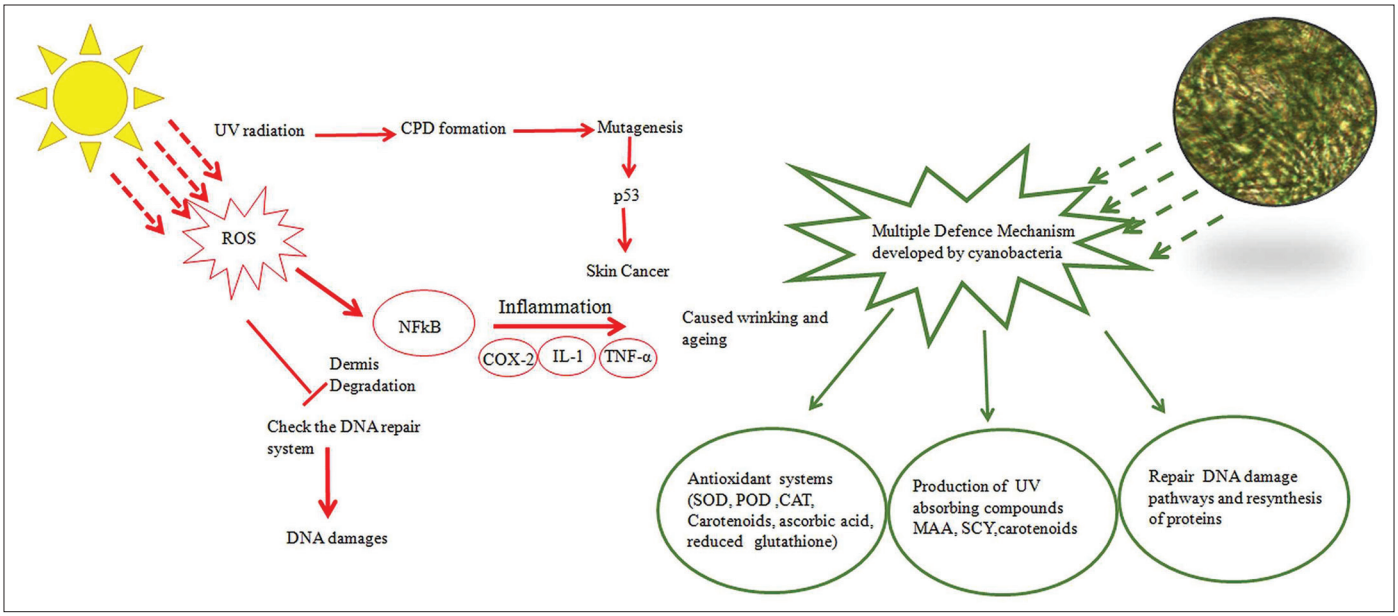

Figure 2: Effects of ultraviolet radiation on skin and multiple defence mechanism system developed by cyanobacteria against the damaging effect of UV.

Table 1: Various cyanobacterial marketed formulation used for skin care.

S. No.	Formulation Name	Cyanobacterial species	Application	References
1.	Iraya algae body serum	*Spirulina*	It moisturizes the skin, making it soft.	[3]
2.	Zelens marine complex deep restorative cream	*Spriulina maxima*	Skin moisturizer	[73]
3.	Face gym training stick serum	*Spirulina*	It improves the elasticity of the skin	[3,76]
4.	Sunday Riley A+High-Dose Retinoid Serum	*Spirulina*	It improve skin texture and boost skin cell renewal	[3,77]
5.	Origins by all greens mask sheet	*Spirulina*	Retain moisture in the skin and to speed up the skin turnover	[3]
6.	Hydro Algae	*Nostoc commune*	Moisturizing, anti-inflammatory and whitening properties	[28]
7.	Scytonemin3a-imine	*Scytonema hoffmani* and *Scytonema spp.*	Used as sunscreen	[30]
8.	Shinorine	*Synechocystis*	Used as sunscreen	[27]
9.	Helioguard® 365 formulation of shinorine and porphyra	*Porphyra umbilicalis*	Provide natural protection against the sunburn	[28,75]
10.	Supergoop! super screen daily moisturizer SPF 40	*Aphanizomenon Flos-Aquae Extract*	Used as sunscreen	[74]
11.	Mycosporine-2-glycine	*Aphanothece halophytic*	Anti-ageing properties	[29,32]
12.	Methanolic extract of exopolysacchrides	*Arthrospira platensis*	Used as antioxidants	[47]
13.	ß-1,3-Glucan	*Nostoc flegelliforme*	Used as free radical scavenging and anti-inflammatory activity	[37,38]
14.	Lycopene	*Anabaena vaginicola*	Used as antioxidant and anti-ageing agent	[39,62]
15.	In eminence organics marine flower peptide collection	*Aphanizomenon flos-aquae*	Used as to reduced the line and wrinkles	[63]
16.	*Spirulina* extract face cleanser	*Spirulina*	Detoxify the dirt and pollutants from the skin.	[28]
17.	Phycocyanin-C face cleanser	*Aphanizomenon flos-aquae*	Defend against exogenous and endogenous pollution	[28]

which convert ROS into nontoxic products. UV radiation causes breakage in the DNA and lipid peroxidation. Exopolysacchrides is outer layer plays a significant role in providing protection in cyanobacteria against UVR. They have the ability to fix the damaged DNA and protect it against lipid peroxidation by removing ROS produced due to UV radiation [45,46]. UV protecting compounds MAAs and scytonemin

produced by cyanobacteria have the ability to reduced toxicity. UV induced DNA lesions in cyanobacteria can be repaired through a variety of methods like photo, excision, recombination, and repair mechanisms. In cyanobacteria, the SOS response and apoptosis have a role in stress tolerance. It was reported that *P. Murrayi* grew linearly as UV-A levels increased and the UV-B inhibition balanced the damage and repair process when grown under white light and in combination with UV-A and UV-B [47]. Collectively, it appears that cyanobacteria have a stress tolerance mechanism that makes cyanobacteria the most ecologically successful prokaryotes on the planet.

6.2. Radical Scavenging Activity in Cyanobacteria

Scytonemin exhibited good free radical scavenging activity as well as photoprotective potential, suggesting that it could be used as a natural antioxidant [48]. Scytonemin extracted from *Lyngbya* sp. showed good radical scavenging activity at different concentrations. The free radical helped to cope with UV radiation [46]. Scytonemin has good radical scavenging activity, so it could be used as an antioxidants and UV protective cream [49,50].

6.3. Role of Cyanobacteria in Inducing Apoptosis

Abiotic (nutrient, light, temperature) and biotic (virus, bacterial, and fungal infection) stress in cyanobacteria due to generated cell death mechanisms [51]. Morphological changes, cell shrinkage, thylakoid degradation, vacuole formation in the cytoplasm, decreased ATP content, photosynthetic activity, and mitochondrial membrane disruption. Caspase-3 like activities is also a hallmark of cyanobacterial apoptosis. UV-induced apoptosis results in direct DNA damage (intrinsic), death receptor clustering on the cell surface (extrinsic), and the production of ROS [52]. Cyanobacterial filaments exposed to UV radiation cells were damaged, filament breakdown, degradation of proteins [51,52]. In the intrinsic pathway of apoptosis, heat shock protein expression plays a significant role in DNA repair mechanisms.

Table 2: Experimental techniques for the characterization of nanoformulations.

S. No.	Techniques for characterization	Parameter characterized
1.	Ultraviolet-visible spectroscopy	Optical properties, concentration
2.	Fourier transform infrared spectroscopy	Surface composition, mass, arrangements, density
3.	Transmission electron microscopes	Size, shape, aggregation, localization
4.	Scanning electron microscope	Morphology, dispersion of nanoformulations in the cells
5.	Zeta potential	Surface charge
6.	Zeta potential	Agglomeration state
7.	X-ray diffraction	Crystal structure, composition, crystalline size
8.	Nuclear magnetic resonance	Arrangement of particles, atomic composition and size
9.	Circular Dichorism	Symmetry and the magnetic moments of the particles
10.	Dynamic light scattering	Hydrodynamic size
11.	Atomic force microscopy	Formulation size and shape

Scytonemin pigment extracted from cyanobacteria is responsible for autophagic cell death by increasing ROS, forming multiple vacuoles and DNA fragmentation [50].

6.4. Anti-inflammatory Activity in Cyanobacteria

Cyanobacterial bioactive compounds play an important role in the treatment of inflammation by reducing immunogenic reactions to pathogens and toxic compounds. They act as promising anti-inflammatory agents in treatment of various diseases. Large scale production of these compounds is needed [46]. Inflammation is caused by the release of chemicals from the migrating cells and tissue. Various mechanisms are involved in cyanobacteria defending against inflammation: Chemokine activation via cyclooxygenase-2 decreased the expression of pro-inflammatory cytokines, decreased the expression of intercellular cell adhesion molecules, inhibited nitric oxide and nuclear factor kappa B, and increased the activity of antioxidant enzymes and peroxisome proliferator-activated receptors [45].

7. THE ADVANTAGE OF USING NANOFORMULATIONS FOR SKIN CARE

Current advancements in nanomedicine have occurred in the technological advancements in the distribution and delivery methods of drugs, as well as new methods of diagnosis. The efficacy of drug delivery has increased through formulated drugs with metals together with various nanovehicles such as solid lipid, liquid lipid, and liposomes. Novel natural biomaterials have remained in high demand due to their lower cytotoxic activity, being easily recyclable, and easily available [53]. Through crosslinking techniques, researchers have been able to make natural biomolecules more stable. Hence, polymeric nanoparticles have also been widely in use. Recently, integration therapy has been used to detect cancer like a natural biopolymer conjugated with metal nanoparticles for the detection methods. Nanotechnology available in the cosmetics is the latest area of research. Cosmetic companies use NMs for enhanced UV protection, improved skin penetration, and texture. Micellar nanoparticle-containing cosmetics are becoming increasingly popular in both domestic and international markets [54]. Small micelles formed from nanoemulsion have a high surface area, allowing bioactive compounds to be actively transported into the skin. Nanoemulsion was used extensively in a variety of cosmetic products [55]. Nanoscale emulsions have sparked a lot of interest in recent decades due to their unique characteristics, such as high reliability, esthetic appearance, and high efficiency. Hence, it has been widely used as a minute droplet size in cosmetics [56]. Micellar nanoparticles contain a hydrophobic head and a hydrophilic tail, formed from the aggregation of surfactant molecules. They are formed to encapsulate the hydrophobic drug [53,54]. Micellar nanoemulsion-based cosmetics have been in great demand due to their potential to deliver the bioactive compounds efficiently. They also possess good penetration power to deliver on the skin quickly. Low and high energy techniques have been used to form micelles in nanoemulsion systems [54]. The Malaysian brand contains the micellar nanoparticle in the cosmetic. They launched various cosmetic products such as cleanser and mist. In addition, Loreal, a French cosmetic company, received two patents to form micellar-based cosmetics [54].

8. POSSIBILITIES AND FACTS RELATED TO NANO-FORMULATED DRUG DEVELOPMENT

Microorganisms can be used to make a variety of inorganic and organic nanoparticles. Inorganic nanoparticles have low cytotoxic activity, are

hydrophilic and highly stable as compared to organic nanoparticles. Magnetic nanoparticles come under inorganic nanoparticles [53]. Nanoparticles are good targets for drug delivery because of their biocompatibility, ease of preparation on a large-scale, ease of use, and functional efficiency. Nanoparticles are used in a variety of industries, including cosmeceuticals and pharmaceuticals. Nanotechnology offers the fastest platform for developing nanoformulations [57].

Many researchers have developed safe nonmaterials using metals, lipids, polysaccharides, proteins, peptides, and natural products for therapeutics [58]. The bioavailability, stability, and solubility of nanoformulations have resulted in larger particle sizes and larger surface areas. In addition, they can be used in the treatment and diagnosis of biological systems, as well as in the monitoring and management of them. In recent years, cyanobacterial derived nanoformulations have been reported. Nanoformulation derived from cyanobacteria is a growing area of concern [59]. Thus, bioactive compounds found in cyanobacteria have been used for the synthesis of nanoparticles with a wide variety of biomedical applications. Recently, a huge demand for marine natural resources has been used in nanotechnology [59]. Cyanobacteria contain macromolecules such as proteins, amino acids, poysacchrides, vitamins, and minerals [55]. Cyanobacteria have applications in the food and medicine industries. However, there is a scarcity of published data on the production of nano-formulated medicines from microalgal resources. Pharmaceutical and cosmetic companies need to produce a variety of effective nanoformulations for skin health care [37]. Cyanobacterial bioactive and UV protective compounds have been formulated into anti-ageing, antioxidant, and anti-inflammatory creams [39,42]. The microalgal species that contain anticancer compounds have been used by pharmaceutical companies for commercialization. Some aquatic members of green algae, brown algae, red algae, blue green algae, have taken major steps forward in skin cancer treatment, but only a few types of algal nanoformulations are available commercially [60]. Non-melanoma skin cancer incidences have increased in recent years; use of sunscreen is an effective nanocarrier in this case. For example, MAAs and scytonemin loaded nanoformulations have been used to protect against UV radiation and are ultimately used in the treatment of skin cancer [61].

9. MARKET REGULATION AND THE REALITY OF NANOFORMULATED PRODUCTS

NM-based cosmetics have certain distinct advantages as compared to micro-scale cosmetics. The cosmetic industry uses NMs to achieve long-lasting effects and enhanced stability. NMs have a large surface area, which enables more efficient substance delivery through the skin. The efficient penetration into the skin for increased delivery of the product's ingredients, new color elements, transparency, and long-lasting effects are some of the key goals of employing NMs in cosmetics. When it comes to cosmetics, the ultimate goal is to make us look good [64,65]. The unique feature of NMs that have been present in cosmetic products gives rise to a serious issue, regarding the health of consumers. For this, a standard safety evaluation is necessary, such as the penetration into viable skin layers as well as inhalation [66]. Nanoformulations should be evaluated on the basis of physicochemical features such as aggregate, size distribution, shape, solubility, density, porosity, stability, and contaminants [67]. Cosmetic products should have validated efficacy as well as a rigorous safety investigation. A number of alternatives have been developed, like 2D cell culture models to reduce and bock the anti-inflammation and predict skin sensitization potency, whereas 3D human skin equivalent models have been developed to evaluate common skin dermatitis, and dermal absorption [68]. In European countries, there are certain NMs for example, colloidal silver, styrene acrylate polymer, and sillicates for which the Scientific Committee on Consumer Safety (SCCS) has expressed different opinions due to a lack of information regarding their toxicities [67]. Sprays and powders containing nanoparticles develop a platform for aerosol delivery, so precaution needs to be taken because inhalation can occur. The SCCS guidelines 1602/18 select a list of parameters that are required for an exposure [67]. NM concentrations are given in terms of weight, particle number and surface area and also, in the form of any accumulation, disintegration and dissipation are reported during exposure. Besides NMs in contact with skin, NMs are also present in toothpastes, mouthwashes, and lipsticks [67].

9.1. Regulations

Regulation 1223/2009 of the European Community (EU) is the fundamental regulatory guideline for cosmetic items in Europe. According to these rules, all customers should have access to a list of all NMs used in cosmetics [69,70]. The most recent catalogue was updated in October, 2019. It contains a list of 29 NMs. The EC amended the guidelines with the assistance of SCCS (SCCS/1611/19). The SCCS provides advice for industry and the general public on the use of cosmetic substances and ingredients in EC No. 1223/2009. It should be emphasised that, according to the SCCS/1484/12 guideline, animal testing of NMs was required [68,71]. According to the EU, all cosmetic products, before being placed on the market, must go through the Cosmetic Products Notification Portal (CPNP), for the purposes of market monitoring and proper medical treatment [67]. NMs were found to be <1.5% in cosmetic products at the end of 2018, according to the CPNP report. Regulation (EC) No 1223/2009 makes it essential to declare whether a cosmetic product contains any NMs [67]. NMs that employ nano-based colorants, UV filters, and preservatives are likewise subjected to a particular process before they can be used. The EC can also ask the SCCS to conduct further research. It is recommended by the European Commission that nano-ingredients should be labelled in cosmetic products [72]. Till now, the EC has recommended the use of titanium dioxide, zinc oxide, methylene bis-benzotriazolyl tetramethylbutylphenol, and tris-biphenyl triazine in UV filters and allowed the nanoform of carbon black to be used as colorant in cosmetic products [64]. In 2017, the EC published a catalogue containing a list of NMs used in cosmetics, and it was last updated in 2019. New areas such as immunotoxicity, NM encapsulation, and, nanovehicles have been updated for safety assessment [5,64]. To provide sufficient information for products, the European Union Observatory for NMs announced at the beginning of 2020 that all companies that manufacture cosmetics must have a Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) registration [68]. NMs that do not follow the guidelines of REACH are considered illegal. The Food and Drug Administration (FDA) in the United States keeps an eye on the usage of NMs in cosmetics. The FDA proposed a safe and effective NMs list in its 2007 Nanotechnology Task Force Report [67]. The Task Force raised an issue regarding the safety of cosmetics regarding which the FDA published guidelines in 2014 in Final Guidance for Industry—Safety of NMs in Cosmetic Products [68]. In 2007, Brazil, Canada, the European Union, Japan, and the United States formed the International Cooperation on Cosmetics Regulation to investigate the issue of safety, rules, and regulations in the use of NMs in cosmetics [67].

10. CONCLUDING REMARKS AND FUTURE PERSPECTIVES

Various bioactive compounds, including antioxidants, carotenoids, UV protective pigments, polysaccharides, steroids, have been present in cyanobacteria with wide application in pharmaceuticals, nutraceuticals, and biomedical. Certainly, our understanding of algal bioactive compounds regarding NMs has improved, but still more emphasis is needed on their use as medicine and commercialization needed. Nanoformulations containing cyanobacterial secondary metabolites have the potential to enhance UV radiation protection mechanisms, which will contribute to the advancement of skin health care.

In the review, we highlighted the lack of studies and commercialization using microalgal bioactive compounds for drug development. Furthermore, additional technologies and knowledge are required to investigate the efficacy of secondary metabolites to formulate the nanoformulations. A Cyanobacterial nanoformulation uses nano-fusion technology and green technology for drug development. Large scale production and cost effectiveness should be a major task to make cyanobacterial loaded nanoformulation. Novel functions of cyanobacterial secondary metabolites need to be explored.

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12. CONFLICT OF INTERESTS

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14. ETHICAL APPROVALS

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15. DATA AVAILABILITY

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