International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 14, Issue 4, 2022

Review Article

NOVEL COSMECEUTICAL FORMULATIONS: A BETTER APPROACH TO PHOTOPROTECTION

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Received: 08 Mar 2022, Revised and Accepted: 04 May 2022

ABSTRACT

Using photoprotection, it is possible to prevent UV-induced skin damage and skin cancers. Radiation that falls between visible light and X-rays is defined as ultraviolet. By biological consequences, UVR is classified into five types, UVA, UVB, UVC, Far UV, and Vacuum UV. However, sunscreen functions as an essential device in our accessories of photo protective action, whose goal is to protect us from sunburn and from the harmful effects of ultraviolet radiation. Sunscreens are categorized as systemic and topical, depending on how they are administered. Again, topical sunscreen divides into organic and inorganic sunscreen. Despite the main objective of sunscreen is to be secure, chemically inert, non-toxic and protected against wide-ranging radiation so as to combat photo aging and photocarcinogenesis. But chemical and synthetic sunscreen causes several undesirable effects, which is a matter of concern. Therefore, a better and safer photoprotective agent is needed in sunscreen. In this regard, nanoparticles, or nanoparticulate systems, are becoming increasingly popular as a form of sunscreen for many different reasons, such as boosting SPF and stability, customizing the release profile, and minimizing adverse effects. In this review, the nanoformulation approach of sunscreen has been described, which has more demand than conventional sunscreen, including liposomes, ethosomes, microemulsions, nano-emulgel, solid-lipid nanoparticles, nano-transferosomes, and niosomes which received a lot of attention worldwide. In short, this review provides an outline of novel advent to sunscreen formulations.

Keywords: Photoprotection, UVA, UVB, Inorganic sunscreen, Organic sunscreen, Conventional sunscreen

DOI: https://dx.doi.org/10.22159/ijap.2022v14i4.44602. Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

The earth is continuously uncovered to radiation from the solar, that's crucial for life. Visible, infrared, and ultraviolet light are examples of such types of emitted radiation. Radiation that falls between visible light and x-rays is defined as ultraviolet (UV). It is characterized by wavelengths between 40 and 400 nm. It is important to note that ultraviolet radiation (UVR) plays a significant role in influencing human health. Ultraviolet electromagnetic radiation was first discovered in the early 19th century by Johann Wilhelm Ritter. UVR has been proven to be effective in the treatment of vitamin D deficiencies, sarcoid (general), mycosis fungoides, psoriasis, and a variety of other epidermal diseases [1]. UVR (40-400 nm) is categorized into five types according to the biological consequences where UVA range lies between 320-400 nm, UVB between 280-320 nm, UVC between 220-280 nm, Far UV between 190-220 nm and Vacuum UV lies in the range of 40 nm to 190 nm respectively [2].

UVC is the most harmful UV radiation since the ozone layer absorbs it almost completely. UVB radiation is an efficient sunburn inducer, accounting for around 5 to 10% of the total spectrum of UV light emitted from the earth's surface and responsible for the most powerful biological consequences (like pigmentation, sunburn, carcinogenesis, diet D3 synthesis, and immunosuppression), ultraviolet B is captured by chromophores inside the stratum corneum of the skin. There are two types of UVA radiation: UVA2 (wavelengths from 320 to 340 nm) and UVA1 (wavelengths from 340 to 400 nm) [2]. UltravioletA1 belongs to the lowest-energy group of UV radiation. UVA1 is able to reach the epidermis' deeper layers, affecting blood vessels, collagen fibers and impairing the ordinary functioning of cells. Although it is now widely recognized that ultraviolet A light may harm human skin [3].

Additionally, UVR aging contributes to human pores and skin, as well as the development of photodermatoses, which have different characteristics according to wavelengths (table 1) [4]. UV-induced erythema and tanning although, they have almost similar action spectrums but UVA appears to play a larger role in long-term solar harm (fig. 1) than it does in acute effects like Vitamin D production or sunburn, which are primarily caused by UVB [5]. Fig. 1(a) represents erythema nodosum which is a form of inflammatory skin condition that affects the fatty layer of the skin. [6,7]. On the other hand, fig. 1(b) shows SCLE (subacute cutaneous lupus erythematosus), a photosensitive dermatosis that does not leave scars or cause atrophy; hence, it affects solar-exposure regions like the shoulders, upper chest, neck, upper back, extensor arms. Fig. 1(c) shows extensive nuchal elastosis results from many years of sun exposure and fig. 1(d) represents Erythematous pruritic plaque on the cheek [4, 8].

Sunscreen

In 1938, a Swiss student called Franz Greater produced the first commercially viable sunscreen in the USA market. In the United States, sunscreens containing benzyl salicylate and benzyl cinnamate have been available since 1928 [9]. The aim of sunscreen products is to save us from sunburns and to defend us from various detrimental effects of solar UV, which may result in a compromised immune system, photoaging, and irregular pigmentation. Such items are particularly popular among outside workers and individuals who spend a lot of time outdoors participating in recreational and athletic activities [10].

Table 1: Wavelengths of ultraviolet light and their impacts on body of human

	190-280 nm (UVC)	280-320 nm (UVB)	320-400 nm (UVA)	Reference
Acute effect	Filtered by the ozone layer in the stratosphere	Erythema, Edema, Darkening of pigment, tanning delayed synthesis of vitamin D and thickening of the epidermis	Instant darkening of pigments (spread within 2h)	[4]
Chronic effect	Na	Photocarcinogenesis immunosuppression Photo aging	Photo aging immunosuppression photocarcinogenesis (weak)	[4]

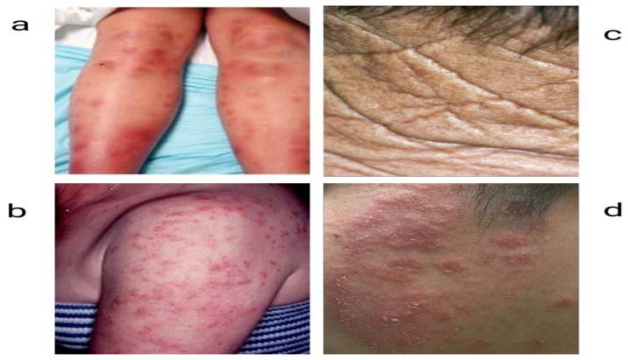

Fig. 1: (a)Erythema nodosum(b) Subacute cutaneous lupus erythematosus(c) Extensive nuchal elastosis resulting from many years of sun exposure(d) Erythematous pruritic plaque on the cheek

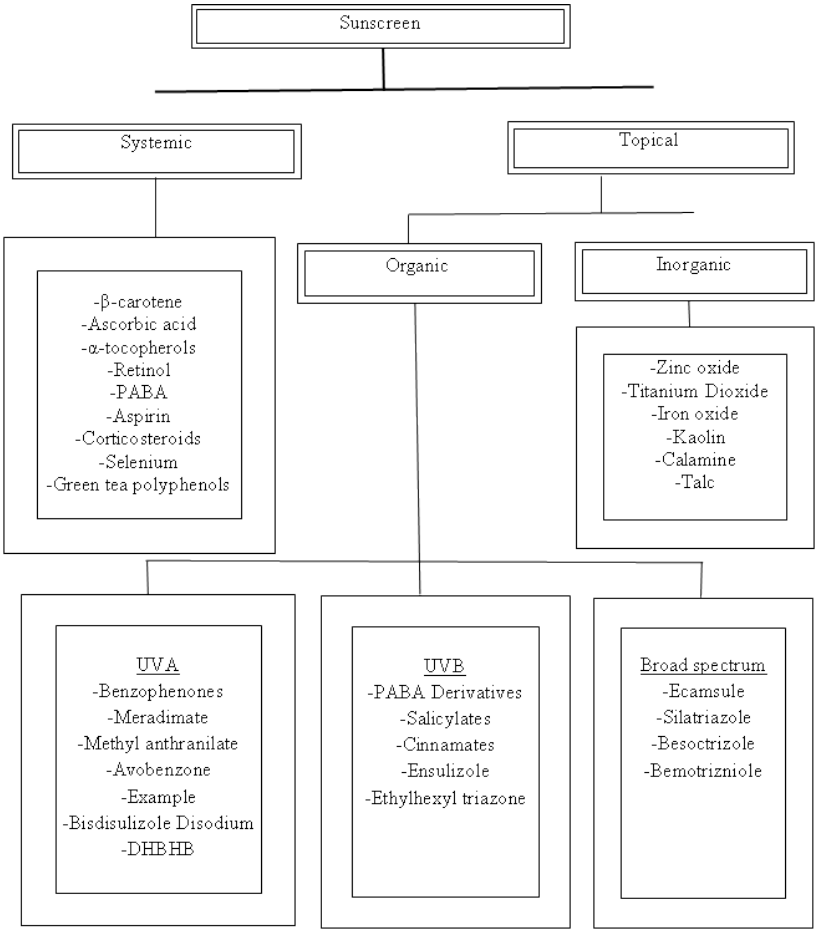

Fig. 2: Classification of sunscreen

Classification of sunscreen

In general, sunscreens are categorized as either systemic or topical, depending on how they are administered. The materials used in topical sunscreen are also split into two groups depending on their safety feature: inorganic materials and organic materials. Solar blockers are a term used to describe inorganic sunscreen (fig. 2). Organic blockers capture high-energy UV light, whereas inorganic blockers absorb and diffract [11].

Systemic sunscreen

Sunscreens that may be consumed into the human body and accumulated in the skin to protect against UV rays are referred to as systemic sunscreens [12].

Organic sunscreen

Organic sunscreens are regarded as chemical sunscreens. Aromatic compounds containing a carbonyl group are most commonly used. Because of its shape, high-energy UV radiation may be absorbed, causing the molecule to get excited. UVB, UVA, and broad-spectrum sunscreens are the three most common classifications depending on the range of protection they provide. Broad-spectrum sunscreen covers the entire spectrum. UVA (anthranilates, dibenzoyl methane, and benzophenones) and UVB (camphor derivatives, para-aminobenzoic acid (PABA) derivatives, salicylates, and cinnamates) organic blockers help in the absorption of sunscreen (fig. 2). As compared to inorganic UV filters, organic agents have superior safety and cosmetic features, such as being non-photo sensitizing,

non-irritant, non-volatile, and non-staining to human skin. Some organic filter (such as PABA derivatives, benzophenones, and PABA), have a significant negative influence, such as the elevated risk of skin cancer, burning sensations, and eczematous dermatitis [12].

Inorganic sunscreen

Ultra-violet filters such as compounds like iron, zinc, and titanium are used in conventional inorganic sunscreens. A sunscreen from this older generation blocks a wide spectrum of UV radiation and is more photoprotective than other agents like octyl cinnamate. However, because of their poor texture and unappealing aesthetic look, their usage has been restricted. UV rays are scattered and absorbed by inorganic sunscreen particles. Indent UV and UV light are physically blocked by them. Zinc oxides, as well as Titanium dioxide, are the two most often utilized particles in sunscreens. Zinc, iron, and titanium are hard to maintain in non-greasy transportation in their bulk form. On the skin, they normally leave a powdery, thick white residue. Since the early 1990s, this type of metal oxides has been produced as nanoscale and microparticles of range 10 to 50 nm [12].

Sun protection factor (SPF)

An SPF measured by the difference between UV energy necessary to create MED (minimal erythemal dose) in protected skin and the Ultraviolet energy required to generate MED in unprotected skin is what characterizes an effective sunscreen. In general, sunscreen with high SPF value is having the capability to prevent erythema upon exposure to UV radiation [13]. The formula for calculating the minimal erythematous dosage of sun protection factor may be found below:

$$\text{SPF} = \text{MED protected skin/MED Unprotected skin}$$

The length of time duration spent in the sun is widely misunderstood as a factor in SPF. It is proportionate to the amount of UV exposure, not the amount of time spent in the sun. Thus, this is not accurate. The preceding is how protection levels are represented in various places. Low sun protection SPF is less than 15; whereas SPF between 15-29 is considered medium protection; SPF 30-49 represents high protection and SPF over 50 provides excellent protection [14].

Conventional sunscreen

Sunscreens that block UVB and UVA emissions are known as broad-spectrum sunscreens, while conventional sunscreens or chemical sunscreens only block a very small amount of UVA emissions, similar to the nominal SPF. Two types of sunscreens are there, Chemical sunscreens and Mineral sunscreens. Each category uses an extraordinary mechanism to protect the skin from harm. Natural chemical substances like carotenoids, polyphenols (flavonoids, tannins), a few vitamins, anthocyanidins, volatile oils from natural products, medicinal plant components (leaves, flowers, end result, berries), lichens, and algae are more effective than artificial chemical compounds, due to their long duration useful outcomes, especially in case of free radical in conjunction with UV-rays blocking [15].

The common element in conventional or chemical sunscreens includes Octinoxate, oxybenzone, octocrylene, avobenzone, octisalate, homosalate. Chemical sunscreen is made up of inorganic and natural elements. Chemical sunscreens are captured by our skin and stored in the innermost layers. They consume UV rays and convert the UV rays into heat, then discharge the heat from the skin. Because UV rays are absorbed by the skin to reach these chemicals into the skin's inner surface, chemical sunscreens cannot protect in case of all UVA rays, which still cause injury to the deeper layers of the skin. Several drawbacks of chemical sunscreen include: It Starts working after about 20 min of application. In order to achieve a broad range of UVB and UVA protection, chemical ingredients in sunscreens may cause side effects, including oedema, erythematic patches, and irritation (People who have a compromised moisture barrier are more likely to experience this.). This is because of the combination of different elements in chemical sunscreens. Those with sensitive skin may be more likely to experience irritation with SPFs of 50 or higher. Since direct UV light accelerates the depletion of its protection, reapplication should be more frequent in this case. There is a greater likelihood of redness or flushing in skin types prone to rosacea because UV rays are transformed into heat. Increased chance of clogging pores for oily skin types. However, when we need a sunscreen that is water-resistant and absorbs quickly into our skin, or when we play sports or sweat a lot during the day, chemical sunscreen is better [16].

Mineral sunscreen is also known as physical sunscreen. It contains titanium dioxide or zinc oxide and frequently feels going on the skin. These are stored on top of the skin layers, acting like a physical blocker by diverting and separating UV rays apart from the skin. Hence, provides protection against UVB as well as UVA radiation as they block UV rays at the skin's surface. Mineral sunscreen provides more moisture to the skin, which is why it can feel heavy on the skin. It is low irritating, good for sensitive skin, and moisturizes rough skin. It is difficult to completely fuse into the skin, but nowadays, there are some brands that can fuse into the skin completely; you can find a matte or tinted version that can blend into the skin very easily. Problems associated with physical sunscreens: During outdoors, they can be easily rubbed off by sweat, washed off by rain, and reapplied as necessary. Physical sunscreen agents provide the external preparations with high transparency, making the formation of the prepared creams unattractive and leaving a white coating on the skin surface. This makes some formulae unsuitable for medium to black skin tones. UV light could penetrate between the sunscreen molecules and penetrate the skin if not applied and reapplied generously and accurately [17].

Therefore, sunscreens should be protective, chemically inert, non-toxic, non-irritating, and well protected against wide-ranging radiation in order to prevent photoaging and Photocarcinogenesis. However, conventional sunscreen creams are ineffective against UVA radiation because they are unstable, harmful, and only moderately efficient. It doesn't absorb or prevent all UV rays; some go through. They are as also not good at blocking UVA radiation, leading to long solar exposure and more solar harm. It only has an effect in the places where it is applied. It's difficult to implement and is sticky, which makes it uncomfortable to use. A number of unwanted effects can be caused by chemical and synthetic sunscreen agents. Therefore, a better and safer photoprotective agent is needed in sunscreen. Vitamin A, E, C, flavonoids, polyphenols, and plant oligosaccharides act as scavengers of free radicals, avoiding UV-induced immunosuppression and other negative consequences [15-17].

Nano-formulation approach for sunscreen

The pharmaceutical and cosmetic industries are interested in developing sunscreen formulations using nanoparticulate systems because of the many potential benefits, such as boosting SPF and stability, customizing the release profile, and minimizing adverse effects. Research and development of nanotechnology focus on the study of materials with unique characteristics on a very tiny scale, with most categories spanning from 1-100 nm [18]. The benefits of using nanoparticles in cosmetics products are to increase the stability of different cosmetic components contained inside nanoparticles, such as unsaturated fatty acids, vitamins, or antioxidants; Next is to increase the absorption of specific substances, including vitamins and antioxidants; also, UV filters on the surface of the skin have improved safety and efficacy which increase the aesthetic appeal of the product [19, 20]. Liposomes, ethosomes, microemulsions, nano-emulgel, solid-lipid nanoparticles, nano-transferosomes, and niosomes have proven greater potential in recent years since they may provide a greater potential for adherence to biological membranes while allowing for the controlled delivery of therapeutic medicines [21, 22].

Liposome

In 1960, liposome was discovered by Alec D Bangham at Babraham Institute, University of Cambridge. Microparticles and nanoparticles containing bilayers of lipids made up of charged phospholipids and cholesterol are called liposomes. Phospholipids with amphipathic properties usually contain a polar head linked to two fatty acids with carbon chains ranging from 10 to 24 and 0 to 6 double bonds. In this lipid bilayer, cholesterol is interspersed. Liposomes are biodegradable in nature ranging from 20 to 1000 nanometres and categorized as multilamellar, unilamellar, and oligolamellar [23].

However, disadvantages associated with liposomes include stability and the slow-release profile of encapsulated compounds during long-term storage. Liposomes can absorb a wide range of hydrophobic and hydrophilic substances, allowing for better drug metabolism at the administration site and decreased adverse effects. Further, it has the capacity to hold bio-active molecules on the skin's surface for a longer period of time [24].

Elastic liposome (ELs)

In 1992, Cevc and Blume first described modified liposomes, such as elastic liposomes. They are made up of a single-chain surfactant and phospholipids like Tween 80 or Span 80, sodium cholate, and deoxycholate, which can damage lipid bilayers and give more flexibility than the liposome itself [25]. ELs are biodegradable bilayer vesicular structures capable of delivering a wide range of substances for pharmacological, biochemical, and cosmetic applications. Ultra-deformable liposomes, deformable liposomes, ultra-flexible liposomes, flexible liposomes, and transferosomes are some of the terms that have been used to describe ELs. Because of their superior pharmacokinetic and physicochemical characteristics, ELs can overcome the barriers that traditional delivery of drugs vehicles face [26].

Niosomes

Niosomes, commonly known as non-ionic surfactant vesicles, have recently been employed as carriers in a range of pharmaceutical and cosmetic applications. Niosomes were discovered in 1979; developed into a drug delivery system in the pharmaceutical industry. Niosomes have a lot in common with liposomes in terms of physical characteristics, manufacturing techniques, and structure. But, niosomes offer other benefits in the transdermal administration of drugs, including prolonged drug release, greater penetration, and skin retention. These are more stable and less expensive to prepare, having a size range of 100 to 200 nanometres. Biodegradable and biocompatible materials are used to make niosomes. The benefits of niosomes are, that they are more stable and have a longer shelf life as compared to liposomes, have good compatibility with biological systems, and are biodegradable and non-immunogenic with low toxicity [27].

Ethosome

In 1997, ethosome was developed by Touitou *et al.*, using water, ethanol, and phospholipids as additional novel lipid carriers. Liposomes are reported to have enhanced drug delivery to the skin. Drugs can be delivered to inner skin layers and/or the systemic circulation *via* ethosomes, which are non-invasive delivery carriers. Because ethanol is well known for disrupting the structure of skin lipid bilayers, the ethosomes have a high concentration of ethanol. As a result, when it is absorbed by the membrane of a vesicle, the vesicle is able to infiltrate the epidermis. Ethosomes are drug delivery systems that may contain a large range of medicines (protein molecules, peptides). The delivery of a fluorescent probe to the skin *via* ethosomal systems is significantly more efficient in terms of quantity and depth. The toxicological characteristics of the ethosome components have a low-risk profile. Because ethosome medications are given in a semisolid form (cream or gel), patient compliance is high. Products with patented technology have a high market appeal, but ethosomes are rather easy to make, and they don't involve any expensive technological investments. The ethosomes system is both passive and active, and it can be commercialized immediately [28].

Solid-lipid nanoparticle (SLN)

The first efforts in the creation of lipid nanoparticles were carried out in university labs in 1990. They were followed in 1991 by two separate patent applications, with the first publications released shortly afterward. Gasco M. R. in Turin (Italy), Müller R. H. in Berlin (Germany) and Lucks J. S. in Kiel (North Germany) produced lipid nanoparticles simultaneously [29]. These are colloidal carriers made up of solid lipid cores combined with water or an aqueous surfactant in certain proportions. Biocompatible, non-toxic, and biodegradable, these lipids are perfect for cosmetics and cosmeceutical formulations. Because of their compact size, they have a high occlusivity, reduce trans-epidermal water loss, pack securely, and promote skin hydration. They're simple to make, expand, and purify, and they don't even require the use of special solvents. Some SLN has intrinsic photoprotective properties, such as crystalline cetyl palmitate nanoparticles (CCP-NP). When compared to typical emulsions, native CCP-NP has around a 2-3fold higher UV-absorbing capacity. This action has been found to offer sunscreen ingredients additive and synergistic photoprotective benefits. Colloidal carriers known as SLNs (solid-lipid nanoparticles) are created as a replacement for conventional carriers. Because of their uniform size, high drug loading capacity, and smaller surface area, SLNs are becoming increasingly popular [30].

Nanostructured lipid carrier (NLC)

NLCs are a new generation of SLNs. As a hybrid carrier, nanostructured lipid carriers are made up of a mixed combination of solid and liquid lipids. The solid lipid contains a long-chain fatty acid, whereas the liquid lipid contains a short-chain fatty acid. Unfavorable SLNs tendencies like unexpected drug/active ingredient or gelation evacuation during storage, low drug/active ingredient loading, and particle development are addressed using nanostructured lipid carriers. Stearic acid, API file, Dynasty, precifac, beeswax, carnauba wax, and Cucina CP are examples of common solid lipids. Whereas miglyol, oleic acid, Cetiol V, olive oil, davana oil, palm oil, and castor oil are examples of liquid lipids. NLC was developed in 2000 because of the poor use of SLN. The purpose of these carriers is to find the better off to the SLN challenges. One difference between solid lipid nanoparticles and Nanostructure lipid carriers is that SLN is made up entirely of solid lipids, whereas NLC is made up of both liquid and solid lipids. Nanostructure lipid carriers are one sort of nanocarrier that plays a bigger part in topical therapy than other types of carriers. Because a larger proportion of medicines are soluble in liquid lipids, the structural component of NLC that results in better loading capacity can be justified, and when a combination of solid and liquid lipids is produced, Solid lipids surround liquid lipids in the core space, as a consequence of which medications are precisely encapsulated. (i)Imperfect NLCs, (ii) Amorphous NLCs, and (iii) Multiple NLCs are the identified structures of NLCs generated by matching various compositions and characteristics [31].

Transferosomes

Cevc *et al.* introduced transferases, a novel form of carrier system, in the 1990s. Transfersomes are ultra-deformable due to phospholipids and edge activators (EAs) which soften membranes (such as sodium cholate Tween 80 and Span 80). When transfersomes approach the skin pores, their membrane flexibility changes, allowing them to pass through the pores on their own. They are modified liposomes containing edge activators and phospholipids (such as sodium cholate and sodium deoxycholate) that effectively enhance drug penetration through the skin. Transfersomes can successfully protect drugs from unwanted penetration into cutaneous blood vessels, in addition to permitting them to be stored in the skin. The advantages of transferosomes include high penetrating ability with high lipophilic drug entrapment efficiency. Corticosteroids, anesthetic, anticancer, sex hormone, insulin, albumin, and gap junction protein are some examples of big molecular drugs that act as carriers. Furthermore, chemical instability and expensive nature are the drawbacks associated with this type of drug delivery [32].

Nanogel

In 1999, the term nanogel was first introduced by Kabanov and his group. Nanogels are nanoscale particles made up of chemically or physically crosslinked polymer networks that grow when in contact with a suitable solvent. The word "nanogel" was initially used to describe a crosslinked dual-functional system comprising a non-ionic surfactant polymer and a polyion for polynucleotide distribution (crosslinked polyethyleneimine and polyethylene glycol) or PEG-cl-PEI) [33]. Nanogels are a better medication conveyance framework than others since it avoids quick clearance by Phagocyte cells. Furthermore, particle size and surface characteristics can be modified, allowing both passive and active

drug targeting. Drug release that is sustained and controlled at the target region increases treatment efficacy and reduces side effects. Due to biodegradable and biocompatible nature, it is having the ability to access the tiniest capillary veins, thus permeate tissues *via* paracellular or transcellular routes. Nanogels, with a size range of 20-200 nanometers, are effective in avoiding rapid renal exclusion while remaining small enough, yet to escape reticuloendothelial system absorption. Because of its small size, it has great penetration capabilities [34].

Nano-emulgel

The benefits of emulgel include greaseless nature with easily spreadable capacity, thixotropic, emollient, a long shelf life, along with a nice look, and having good skin penetration properties. Emulgel allows drug release from both the emulsion and the gel to be controlled simultaneously. Nanoemulsion has a droplet size of 20-500 nm, which is smaller than emulsion, which has a droplet size of 0.1-100 m and is more stable than emulsion. If a thickening agent is available, the nanoemulgel preparation stability will be improved owing to a drop in surface tension and also an improvement in viscosity and adhesion when applied topically. Nanoemulgel also has the advantages of being easy to distribute, clean, and non-greasy [35].

Nanoparticles (NPs)

A nanoparticle is any particle of matter with size within 1 to 100 nm. According to the general shape, these substances can be 3D, 2D, 1D, or 0D. Researchers revealed that it's the size of a product's physicochemical properties, like its optical capabilities, may be affected by its size. Recent years have seen an increase in interest in nanoparticles owing to their overarching application in various fields. They are ideal for many applications due to their small particle size and high surface area and are useful as active ingredient carriers. Typically, zinc oxide and titanium dioxide nanoparticles are used in sunscreens. Before being added to the sunscreen, these substances are made up of ultrafine material. In the 1980s, nanoparticle sunscreens first appeared, but it wasn't until the 1990s that they gained popularity. Sunscreens aren't the only things that contain nanoparticles. NPS is present in many cosmetics and skincare products, including shampoo, toothpaste, and foundation [36, 37].

Table 2: Novel sunscreen formulation approaches using a single drug/extract

S. No.	Extract/drug	Result/outcome	Method	Novel approach	Reference
1	Safranal	Showed greater SPF value and increased the skin hydration properties	High-shear homogenization and ultrasound methods	Solid-lipid nanoparticles	[38]
2	All-Trans retinoic acid	Increased the photostability and decrease skin irritation	High-pressure homogenization method	Nanostructured lipid carriers	[39]
3	Mangosteen pericarp extract (*Garcinia mangos-tana)*	MPE-containing SLNs are promising because they can be used as an alternative to synthetic sunscreen on the market, and they are stable in storage.	Ultrasonication method	Solid-lipid nanoparticles	[40]
4	Tocopherol acetate	Due to SLN's UV-Blocking properties and the synergistic effect of tocopherol acetate, a new sunscreen formulation without synthetic UV-blockers is possible.	High-pressure homogenization	Solid-lipid nanoparticles	[41]
5	Fucoxanthin	Increasing action of sunscreen in SLN formulation	High-speed homogenizer	Solid-lipid nanoparticles	[42]
6	Silymarin	It gives excellent photoprotective action	Probe sonication	Solid-lipid nanoparticles	[43]
7	Green tea leaves (Camellia sinensis)	In the presence of UVA and UVB radiation, ethanol extract of green tea leaves can be improved the photostability using the SLN system	High-speed homogenization method	Solid-lipid nanoparticles	[44]
8	Aloe vera	There was no skin irritation, excellent SPF value, and photoprotective action increased.	Micro-emulsification technique	Solid-lipid nanoparticles	[45]
9	Oxybenzone	Increased UV protection and reduced skin irritability	Solvent-diffusion method	Solid-lipid nanoparticles	[46]
10	Naringin	a high level of sun protection provides antioxidant activity	Hot method and mechanical dispersion method	Ethosomes	[47]
11	Naringenin	After three months of storage, the elastic liposome with naringenin-loaded remained stable and caused less skin irritation.	-	Elastic liposomes	[26]
12	Safranal	In 1 and 4 percent concentrations, Lip-Safranal may be a superior antisolar substance than homosalate, although it has no moisturizing effect.	Fusion-method and homogenization	Liposomes	[48]
13	Moringa oleifera leaves	It can be used to defend skin from UV rays as an active substance in a sunscreen nanoemulgel composition.	-	nanoemulgel	[49]
14	Black tea extract	Niosomes will deliver BTE to the skin as a sunscreen agent.	Lipid hydration films	Niosomes	[50]
15	Organosolv lignin	There is a rise in the SPF and UVA PF values, which blocks the UV rays of the sunscreen.	Solvent shifting method	Nanoparticles	[51]
16	Bemotrizinol	Modifying bemotrizinol using novel drug delivery systems that maintain its photostability while being highly SPF-effective could be an excellent option.	-	Nanoemulsion	[52]

Table 3: Novel sunscreen formulation using a combination of drugs/extracts

S. No.	Drug/extract	Result/outcome	Method	Approach	Reference
1	B. Orellana oil (urucum oil) and octyl methoxycinnamate	*In vitro* experiments revealed that replacing 20% of the OMC with urucum oil had no effect on SPF, but it has a more antioxidant effect due to urucum.	-	Solid-lipid nanoparticles	[53]
2	Octocrylene and butyl-methoxydibenxoylmethane	Increased UV protection, photostability, and reduced skin penetration	Melt emulsification method	Solid-lipid Nanoparticles	[54]
3	Diethylamino hydroxy benzoyl hexyl benzoate and 2-Ethylhexyl salicylate	Increased antioxidant activity and UV protection	High shear homogenization and high-pressure homogenization	Nanostructured lipid carriers	[55]
4	OMC, OCT, and BEMT	The good photoprotective effect increased photostability and also reduced allergenic potential	the modified Melt homogenization method	Lipid Nanoparticles	[56]
5	Avobenzone and Octocrylene	Increased UV protection	High-pressure homogenization	Nanostructured lipid carriers	[57]
6	4-methoxy-cinnamic acid-2-Ethylhexyl ester, phenyl ketone-3, and avobenzone	Better UV blocking capacity	High-speed homogenization method	Nanostructured lipid carriers	[58]
7	butyl methoxydibenxoylmethane and octyl methoxycinnamate, and titanium dioxide	Increase the SPF value	Classical method of preparation	Solid-lipid Nanoparticles	[59]
8	Diflucortolone valerate and Titanium dioxide	Increased UV blocking activity, Increased SPF value, and improved patient compliance	High shear homogenization and ultrasonication techniques	Nanostructured lipid carriers	[60]
9	Octyl-methoxy cinnamate (OMC)and butyl methoxy-dibenzoyl methane (BMBM)	BMBM controlled the calorimetric behavior of SLN by interacting with OMC.	phase inversion temperature (PIT) method	Solid-lipid nanoparticles	[61]
10	polyhydroxy butyrate (PHB)and coffee extracts	Newly synthesized paired PHB-liposomes could be securely used as effective and persistent carriers of organic UV filters for external sunscreens due to PHB's additional UV-scattering capability.	-	Liposomes	[62]
11	L-ascorbic acid (Vc) and 4-cholestero carbonyl-49-(N, N'-Diethyl amino butyloxy) azobenzene (CDBA)	Due to CDBA's UV-vis absorption capabilities, CDBA-liposome was a good sunscreen product, suggesting that it could be used as a sunscreen cosmetic.	Standard sonication method	Liposomes	[63]
12	Avobenzone and octilmetoxicinnamato	Avobenzone photodegradation is reduced when it is encapsulated in liposomes using isolecitine, regardless of the presence of octilmetoxicinnamato.	_	Liposomes	[64]
13	TiO2/Zn2TiO4/Ag	The nanocomposite TiO2/Zn2TiO4/Ag might be useful in the formation of high-protection sunscreen creams.	Sol-gel method	Nanoparticles	[65]
14	Brazilian red propolis extract and polyprenylated benzophenones	Nanoemulgel carrying BZP from BRP could be a viable option for preventing UVA/UVB-induced oxidative damage.	Spontaneous emulsification	Nanoemulgel	[66]
15	grapeseed oil and anisotriazine	The sunscreen nanoemulgel preparation using anisotriazine and grape seed oil was more stable than emulgel preparations.	High-energy emulsification method	Nanoemulgel	[67]
16	C-methylcalix [4] resorcinaryl octabenzoate and C-phenylcalix [4] resorcinaryl octacinnamate	The nanoemulgel sunscreen products were effective in generating high *in vivo* SPF values and might possibly be developed as organic sunscreens in the future due to their non-toxicity in culture cells.	_	Nanoemulgel	[68]
17	Epigallocatechin-3-gallate and hyaluronic acid	It aims to improve UV radiation protection along with anti-aging and antioxidant properties and high penetration of the skin	Thin film hydration technique	Transfersomes	[69]
18	octyl methoxy cinnamate (OMC)and melatonin (MEL)	High antioxidant activity was shown when OMC Pickering emulsions were combined with lyophilized MEL-loaded elastic niosomes, and investigations in cell cultures validated the formulation's safety.	Thin-film hydration method	Elastic Niosomes	[70]
19	Diethylzinc (Zn (Et)2), titanium (IV) isopropoxide (TTIP),	A long-term stability study of nanoparticles showed good particle size and UV absorption.	Flash Nano-Precipitation (FNP) technique	Nanoparticle	[71]

CONCLUSION

The current review was focused on an attempt to discuss the various novel drug delivery approaches in the cosmetic world, especially sunscreen formulations, and their future perspective. Although nano-carrier systems like liposome, ethosome, nanoparticles, transferosome, SLNs, NLC and nano-emulgel studied over last couple of years, seems utmost promising in the revolutionizing fields of biomedical applications, cosmetic applications and dermatology. Yet, there is the scarcity of conclusive evidences for the demands of its effectiveness and the popular industries are working on that part too. Tremendous controversies as regards to safety and toxicity of these nanomaterials have risen. Hence, precise researches on the safety profile of these sunscreen nano-products are needed. Furthermore, clinical trials are not required for these cosmeceuticals/sunscreen formulations, but strict law/amendment is recommended for its proper long-lasting effect in today's global market with increased stability.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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