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Unveiling novasomes as a novel carrier approach for enhanced photoprotection

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Abstract
Pharmaceutical research has developed many new innovative drug delivery forms. Advances in current drug delivery methods have led to the development of many new revolutionary technologies that support drug formulations that are safer and more effective than existing formulations. Novasome technology is a novel microencapsulation-based drug delivery method that is more efficient than standard liposome systems. It consists of a mixture of surfactants, cholesterol, and free fatty acids, creating vesicles with superior drug delivery properties. Numerous studies have scrutinized the ideal combination of type of surfactant, type of free fatty acid along with their ratios as well as formulation parameters which can notably influence the properties of vesicles. Novasome technology is one of the most recent innovations that serves as an encapsulation process for the efficient delivery of a variety of substances in foods, cosmetics, personal care, chemicals, agrochemicals, and pharmaceuticals. Due to their deep penetration ability, novasomes are one of the most popular skin cosmetics. They are continuously being researched to achieve improved release properties. The anticipation of drug targeted delivery utilizing novasomes is an essential area of research and development. This study highlights different aspects of Novasomes and their abilities for promoting enhanced photoprotection activity.

Keywords: Novasomes, photoprotectants, novel technology, enhanced permeation

Introduction
Scientists continue to explore new strategies to enhance the absorption of substances through the skin [1], such as active (micro-needling and electroactive activators) and passive (activators and penetration vectors) techniques [2]. Vesicular drug encapsulation systems are a delivery method to facilitate transdermal penetration [3]. Repeated exposure to sunlight can cause short-term and long-term changes to the structure of the skin. In the short term, repeated exposure results in erythema (redness) of the skin, commonly known as sunburn [4]. The erythema then activates melanocytes to increase melanin production (hyperpigmentation) resulting in darkening of the skin, also known as tanning. Long-term effects of repeated exposure include irreversible loss of skin elasticity and can lead to the development of melanoma and non-melanoma skin cancers [5].
The use of sunscreens as photoprotectants has become more prevalent in recent decades [6].With increasing awareness of the protective properties of sunscreens against sunburn, skin aging and melanoma, the demand for sunscreen formulations is set to continue to grow and there is a significant opportunity for the pharmaceutical industry to meet this demand by producing quality, effective, safe and aesthetically appealing sunscreen formulations. [7]. The first generation of vesicle technology was conventional liposomes (CLs). They can encapsulate lipophilic or hydrophilic drugs and facilitate skin penetration. However, there is evidence that CLs have difficulty penetrating deeper layers of the skin due to confinement and reduced ability to increase systemic drug absorption. In addition, low encapsulation capacity and drug leakage potential are significant [2].
Scientists have discovered new vesicle technologies to enhance the capacity of CL, such as niosomes, transfersomes, ethosomes, fitosomes, ufasomes, and novasomes, each of which has its own advantages and limitations [1]. Novasome technology is a new microcapsule-based delivery method that is more efficient than standard liposome systems [8]. The Novasomal drug delivery technique is a patented encapsulation technology for targeted

delivery of substances. This technology was initially developed by Novavax. IGI laboratories, Inc [9]. Novasomes are bilayer vesicles with high nuclear capacity within a narrow size range, allowing them to transport large amounts of active chemicals [10]. Novasomes consist of paucillamellar vesicles with diameters ranging from 200 to 700 nm, consisting of 2 to 7 bilayer membranes, each containing an amorphous core and an amphipathic molecule. Novasomes are considered one of the most effective treatments for skin disorders, with virtually no side effects and no cytotoxicity [11]. Novasomal Technique is a permeation promoting technology for delivery of many substances efficiently. This article emphasize the use of novasome in sunscreen technology to enhance the photoprotection activity by increased permeability and stability [12]. The main component of novasome is polyoxyethylene fatty acid monoesters, cholesterol and free fatty acids. The composition may vary in type and concentration for different formulations.

Basis of sunscreen use

Cosmetics are defined as "articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance" [13]. Among the most commonly used cosmetics is sunscreen. These are compounds that are applied to the surface of the skin to protect against the harmful effects of ultraviolet (UV) rays. Skin recurrence is associated with a high risk of skin cancer. Sunrays consist of an array of wavelengths ranges that vary in frequency and their energy profiles.

The UV spectrum is further divided into three classes as UVA, UVB, UVC. The corresponding wavelengths are 320-400 nm, 290-320 nm, 100-290 nm [14]. However, it has no medicinal value because it is filtered by the ozone layer. UVB creates the melanin pigment and stimulates skin cells to produce a thicker epidermis, resulting in a long-lasting tan and is also the major cause of sunburn. UVA light activates melanin in the epidermis to produce a short-lived tan. Penetrating the skin deeper than UVB can cause long-term skin damage including skin aging due to loss of elasticity and wrinkles [15]. UV filters, also known as sunscreens, are elements of photo protection models that directly interfere with the sun's radiation through absorption, reflection, or electronic scattering [16].

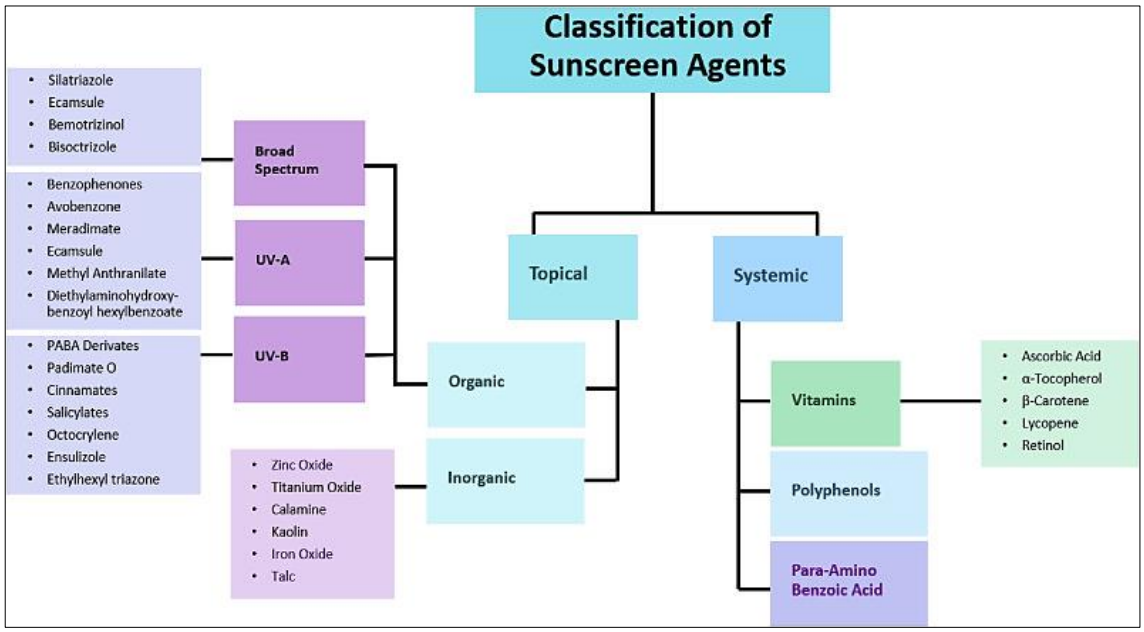

Fig 1: Classification of sunscreen

Organic sunscreen

These are aromatic compounds that are attached to an organic group. It is generally divided into three categories based on the extent of protection. UVB (290-320 nm) and UVA (320-400 nm) sun protection with a broad spectrum that covers the entire spectrum (290-400 nm) [18].

Examples

UVB Filters - octisalate, cinoxate,
UVA filters - benzophenones, oxybenzone
Broad spectrum Filters - besoctrizole, silatriazole [19].

Inorganic sunscreen

The inorganic sunscreens are also referred to sunblocks, a term coined from their mechanism of photoprotection [20]. They act as a physical barrier to indent ultraviolet and UV light [21]. They are considered broad spectrum as they cover the entire ultraviolet spectrum [20].

Examples

Titanium dioxide and Zinc oxide [21].

Systemic Sunscreens

These are sunscreens that are absorbed by the body, absorbed into the skin, and protect against UV rays. The use of systemic sunscreens for daily routine is usually minimal [17].

Examples

Ascorbic acid, beta carotene, retinol [17].

Mechanism of photoprotection

Sunscreens work by blocking and reducing the harmful effects of the sun's ultraviolet rays after exposure to the sun. Sunscreen has been shown to increase the skin's tolerance to UV rays. Photoprotectants works mainly by two mechanisms.

(a)Scattering and reflection of UV energy from the skin surface. Inorganic photoprotectants mainly work by this mechanism. They provide a coating that blocks sun rays from penetrating through the skin [20].
(b)Initial Absorption of the UV energy and converting it to heat energy so as to reduce its detrimental effects and to reduce the depth through which it can penetrate the skin. Organic sunscreens work primarily through this mechanism [22, 23].

Many organic molecules are usually assimilated into chemical photoprotectants to attain maximum protection against a range of the UV spectrum. Inorganic particulates may scatter.
the micro-particles in the skin epidermis, thereby enhancing the optical pathway of photons, which leads to absorption of more photons and to amplify the sun protection factor (SPF), this results in high efficiency of the compound.

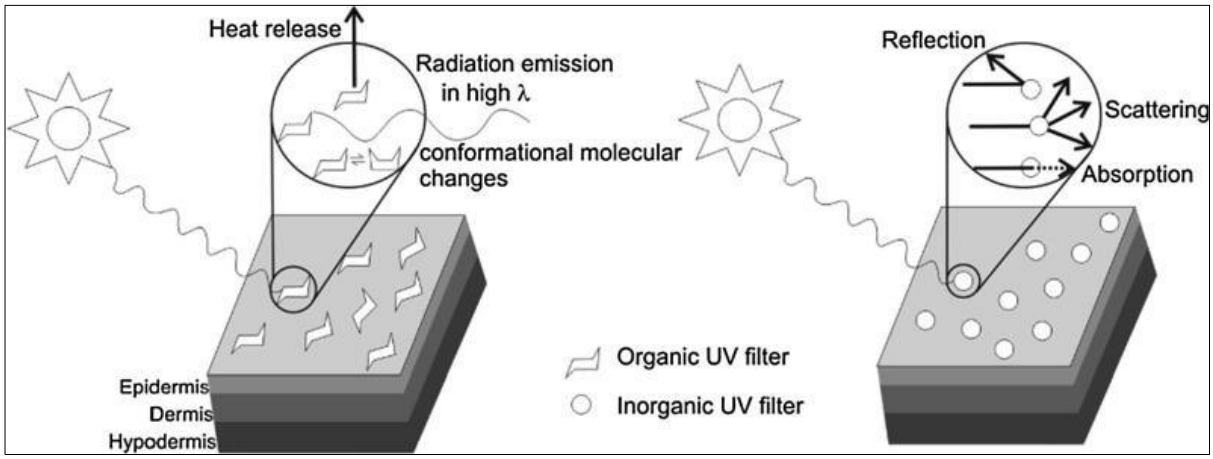

Fig 2: Mechanism of sun protection [24]

Properties of an ideal sunscreen
The desired chemical properties are:
- Inertness, non-irritating, light clarity and compatibility with other foods.

Physical properties include:
- Low viscosity to promote good spreading, attractive appearance, low particle size, water resistance, good solubility and odour.

Functional attributes include
- The ability to protect against a wide range of wavelengths and low systemic absorption into the skin to reduce sensitivity. Products should be easily accessible, cheap and uncontaminated [25].

Benefits of Novasomes
Novasomes, as innovative vesicular drug delivery systems, offer several advantages over other vesicles. Let's explore these benefits:

Enhanced Drug Delivery Efficiency
- Novasomes combine features of ufasomes (fatty acid vesicles) and niosomes (surfactant vesicles).
- Their unique composition-mixing surfactants, cholesterol, and free fatty acids results in superior vesicle characteristics.
- Novasomes efficiently encapsulate drugs, enhancing their delivery to target sites [35].

Improved Skin Penetration
- The multilayer structure of novasomes facilitates better penetration through skin layers.
- This property is especially advantageous for topical drug delivery, allowing substances to reach deeper tissues [35].

Controlled and Predictable Release
- Novasomes provide consistent and predictable drug release kinetics.
- This predictability ensures sustained efficacy and reduces the need for frequent re-application [36].

High Encapsulation Capacity
- Novasomes can encapsulate a significant amount of active ingredients.
- Despite their small size, they efficiently carry a substantial drug payload [36].

Safety and Minimal Side Effects
- Novasomes are generally safe for skin applications.
- They have minimal side effects and are well-tolerated by most individuals [35].

Characteristics [1]
- It is a multi bilayered vesicle with a large central core.
- Its surface can be negatively, positively, or neutrally charged.
- It may be stable over a broad pH range between 2 and 13.
- It is stable at a temperature between 0 and 100ºC.
- The amorphous core inside can be loaded with up to 80-85% of the drug product.
- It can be manufactured in a variety of specific sizes.
- It has the ability to adhere to the skin or hair shaft depending on the different conditions of the vesicle surface charge as well as the skin surface.
- It has the advantage of containing more active ingredients in a small amount.
- It has the feature of predictable release of active ingredients, thus reducing the frequency of use.
- It is capable of transporting and releasing large volumes of water-soluble components.

Structural organization

Novasomes represent an exciting advancement in vesicular drug delivery systems.

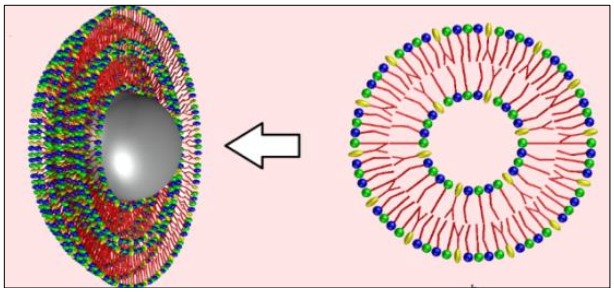

Fig 3: Structure of Novasomes [26]

Composition and Design

- Novasomes are vesicles designed to enhance drug delivery efficiency.
- Their unique composition combines features of ufasomes (fatty acid vesicles) and niosomes (surfactant vesicles).

Novasomes typically consist of

- **Cholesterol:** Provides stability and influences membrane fluidity.
- **Free Fatty Acids (FFAs):** Enhance vesicle characteristics and drug encapsulation.
- **Polyoxyethylene Fatty Acids:** Contribute to the overall structure [1].

Multi-layered Structure

- Novasomes exhibit a multi-lamellar structure, resembling concentric lipid bilayers.
- This multilayer arrangement allows for efficient drug entrapment and sustained release.
- The layers protect the encapsulated drug, preventing premature degradation [1].

Formulation

Ethanol injection method [27]

This process involves mixing an edge activator with a fixed amount of non-ionic surfactant. The medication is first dissolved in span-infused ethanol to get it ready for encapsulation. The following five minutes are spent sonicating the lipid solution. Currently, an edge activator (like Tween-80)-containing heated aqueous phase is continuously injected with this solution. For the last 30 minutes, this phase has been agitated on a magnetic stirrer at temperatures between 70 and 80 ºC and at speeds between 800 and 1600 rpm.

Sonication method [27]

In this case, the mixture of surfactant and cholesterol is first distributed in the liquid phase. The mixture was sonicated at 60 °C for ten minutes. It helps in the synthesis of multilamellar vesicles (MLV). MLVs are also sonicated using a probe and a sonicator bath to produce unilamellar vesicles.

Ether injection [27]

A 14-gauge needle is used to inject the surfactant into an aqueous phase that has been heated to 600ºC at a rate of 25ml per minute. The surfactant needs to be dissolved in 20ml of ether in order to use this procedure. A rotating evaporator will be used to remove the ethanol from the ether solution. Vesicles with a single layer will occur as a result of the procedure once the organic solvent has been totally eliminated.

Micro-fluidization technique [27]

A new technique for creating unilamellar vesicles with a defined size distribution is called microfluidization. This method is usually used based on the submersible jet principle, which involves fluid flows in micro-channels defined in the interaction chamber. To keep the energy supplied to the system within the region of the desired molecular pattern, a thin sheet of water is inserted into the front. As a result, the tumors that appear are more uniform and smaller.

Handshaking method [27]

Another name is thin film hydration method. Here vesicle forming substances like cholesterol and surfactant combined with inert organic solvents such as diethyl ether, methanol or chloroform in a rotary evaporator set at room temperature (20 °C), leaving a thin layer of it. The solid mixture on the bottle wall of the removed surfactant layer and the ability to rehydration form distinct multi-layered novasomes.

Multiple membrane extrusion method [27]

Evaporation creates a thin layer of a mixture of diacetyl phosphate and cholestrol surfactant in chloroform. Hydrated drug polycarbonate integument are used to hydrate the film. The solution and resulting suspension are passed through the membranes arranged in a series of up to eight channels. This is an effective way to adjust the size of the particles produced.

Evaluation

Physical analysis [28]

Includes organoleptic tests to observe changes in the colour, and presence of phase separation in the product.

Stability tests [28]

Colour, phase separation and liquefaction. There should be no colour changes nor separation of phases in sunscreen formulations in the stability tests if they are to pass the quality tests.

pH determination over time [29]

The formulated Sunscreen is evaluated for optimum pH using Digital pH meter. The tests are replicated for multiple samples after definite storage period. The ideal pH is around 6.0 which is similar to that of skin pH. The changes in pH stipulate the eventuality of chemical reactions which may affect the quality of the product.

Determination of SPF

Sun Protection Factor (SPF) refers to the ability of the sunscreen to prevent the development of erythema upon exposure to UV radiation [30].

***In-vivo* SPF determination [31]**

SPF is expressed as the ratio of the minimal erythemal dose (MED) that is required to induce erythema on the protected skin to the dose required to induce the same on the unprotected skin of the same individual.

The mathematical expression is shown in Formula

$$\text{SPF} = \frac{\text{MED of protected skin}(2\ \text{mg/cm}^2)}{\text{MED of unprotected skin}}$$

(MED = minimal erythemal dose)

***In-vitro* SPF determination**

There is a global shift to minimize animal testing in the development of medicines and related products with recent guidelines prohibiting use of animals in experimental studies [32]. Method proposed by Mansur *et al* in 1986 involve spectrophotometric measurement of the absorption characteristics of the sunscreen products may be used with accurate SPF determination [33].

$$\text{SPF}_{in\ vitro} = \text{CF} \times \sum_{290}^{320} \text{EE}(\lambda) \times I(\lambda) \times \text{abs}(\lambda)$$

Where,
EE - Erythemal Effect spectrum
I - Solar intensity spectrum
Abs - Absorbance of the product
CF - Correction Factor

Entrapment Efficiency (EE) [27]

It is defined as the percentage amount of drug which is entrapped by the novasomes. Entrapment efficiency is calculated by using the formula:

EE = Amount of entrapped drug / Total amount added × 100

The substance that has not been entrapped is first separated using an appropriate technique (such as centrifugation) in order to determine the entrapment efficiency. After that, the resultant solution is divided, and the liquid supernatant is gathered. Following collection, the supernatant is diluted as directed and calculated using a suitable technique as detailed in the monograph of that particular drug.

Table 1: Marketed formulations

Product	Action	Reference
MPA Hydra-Pearls	Humectant	[38]
MPA Benzoyl-Plus	Keratolytic, Antibacterial, Degreasing, Follicular Flushing, Humectant	[37]
MPA Dermal-Soothe	Antipruritic, Cellular Repair, Humectant	[34]
MPA Miconazole Shampoo	Antifungal, Humectant	[34]
MPA Seba-Hex	Antibacterial, Antifungal, Keratolytic, Keratoplastic, Humectant	[34]
MPA Dermal-Soothe Cream Rinse	Antipruritic, Cellular Repair, Humectant	[37]
MPA Dermal-Soothe Spray	Antipruritic, Cellular Repair, Humectant	[38]
Novasome®	Small pox	[37]
Novasome I	Novasome I showed great levels of drug compared with liposomes	[39]
AcneWorx®	Reduce acne blemishes, prevent new pimples before appearing	[34]
Nova Pearls™	Deodorant for pet skin care	[38]

Microscopic evaluation [27]

Transmission electron microscopy (TEM) was used for microscopic evaluation of novasomal dispersions. TEM is used for the evaluation of size, shape and structure of the vesicles.

Conclusion

Novasomes were discovered to boost product stability, extend shelf life from weeks to years, prevent oxidation and emulsification, and allow antagonistic components to be separated inside the formulation until usage. Novasomes also allow for the controlled release of active substances by heat, pressure, and time. The incremental cost of developing items with novasomes is negligible. It has numerous applications in foods, cosmetics, medicines, chemicals, agrochemicals, personal care, and other industries. The technology of novasomes is constantly evolving. Many novasomes-based products are being developed for commercialization. Novasome technology is being improved on a regular basis. Many Novasome-based products are being developed for market release.

References

1. Ntimenou V, Fahr A, Antimisiaris SG. Elastic vesicles for transdermal drug delivery of hydrophilic drugs: A comparison of important physicochemical characteristics of different vesicle types. J Biomed Nanotechnol. 2012;8(4):613-623.
2. Varia U, Joshi D, Jadeja M, Katariya H, Detholia K, Soni V. Development and evaluation of ultradeformable vesicles loaded transdermal film of boswellic acid. Future J Pharm Sci., 2022, 8(1).
3. Lin HW, Xie QC, Huang X, Ban JF, Wang B, Wei X, *et al*. Increased skin permeation efficiency of imperatorin via charged ultra-deformable lipid vesicles for transdermal delivery. Int J Nanomedicine. 2018;13:831-842.
4. Moore C, Cevikbas F, Pasolli HA, Chen Y, Kong W, Kempkes C, *et al*. UVB radiation generates sunburn pain and affects skin by activating epidermal TRPV4 ion channels and triggering endothelin-1 signaling. Proc. Natl Acad Sci USA, 2013 Aug 20, 110(34).
5. Harrison SC, Bergfeld WF. Ultraviolet light and skin cancer in athletes. Sports Health. 2009 Jul;1(4):335-340.
6. Jansen R, Osterwalder U, Wang SQ, Burnett M, Lim HW. Photoprotection: part II. Sunscreen: development, efficacy, and controversies. J Am Acad Dermatol. 2013 Dec;69(6):867-e1.
7. Tuchinda C, Lim HW, Osterwalder U, Rougier A. Novel emerging sunscreen technologies. Dermatol Clin. 2006 Jan;24(1):105-117.
8. Singh A, Malviya R, Sharma PK. Novasome: A breakthrough in pharmaceutical technology. Adv Biol Res. 2011;5(4):184-189.

9. Lasic DD. Liposomes and Niosomes. In: Rieger MM, Rhein LD, editors. Surfactants in Cosmetics. New York: Marcel Dekker; c1997. p. 263-83.
10. Chambers MA, Wright DC, Brisker J, Williams A, Hatch G, Gavier-Widén D, *et al*. A single dose of killed Mycobacterium bovis BCG in a novel class of adjuvant (Novasome™) protects guinea pigs from lethal tuberculosis. Vaccine. 2004;22(8):1063-71.
11. Kaur M, Upadhyay PA. Review on novasome technology. IJPPR Human. 2020;17(4):93-101.
12. Abd-Elal RMA, Shamma RN, Rashed HM, Bendas ER. Trans-nasal zolmitriptan novasomes: *In vitro* preparation, optimization and *in vivo* evaluation of brain targeting efficiency. Drug Deliv. 2016;23(9):3374-86.
13. FDA. Federal Food Drug and Cosmetic Act. 2018a.
14. Moyal DD, Fourtanier AM. Broad-spectrum sunscreens provide better protection from solar ultraviolet-simulated radiation and natural sunlight-induced immunosuppression in human beings. J Am Acad Dermatol. 2008 May;58(5):54.
15. D'Orazio J, Jarrett S, Amaro-Ortiz A, Scott T. UV radiation and the skin. Int J Mol Sci. 2013 Jun 7;14(6):12222-48.
16. Schalka S, Steiner D, Ravelli FN, Steiner T, Terena AC, Marçon CR, *et al*. Brazilian consensus on photoprotection. An Bras Dermatol. 2014;89(6 Suppl 1):1-74.
17. Latha MS, Martis J, Shobha V, Shinde RS, Bangera S, Krishnankutty B, *et al*. Sunscreening agents: A review. J Clin Aesthet Dermatol. 2013 Jan;6(1):16.
18. Geoffrey K, Mwangi AN, Maru SM. Sunscreen products: rationale for use, formulation development and regulatory considerations. Saudi Pharm J. 2019 Nov;27(7):1009-18.
19. Tuchinda C, Lim HW, Osterwalder U, Rougier A. Novel emerging sunscreen technologies. Dermatol Clin. 2006 Jan;24(1):105-17.
20. Dransfield GP. Inorganic sunscreens. Radiat Prot Dosimetry. 2000 Sep;91(1-3):271-3.
21. Serpone N, Dondi D, Albini A. Inorganic and organic UV filters: Their role and efficacy in sunscreens and suncare products. Inorganica Chim Acta. 2007 Feb 15;360(3):794-802.
22. Lademann J, Schanzer S, Jacobi U, Schaefer H, Pflücker F, Driller H, *et al*. Synergy effects between organic and inorganic UV filters in sunscreens. J Biomed Opt. 2005 Jan;10(1):014008.
23. Manaia EB, Kaminski RC, Corrêa MA, Chiavacci LA. Inorganic UV filters. Braz J Pharm Sci. 2013;49:201-9.
24. Trivedi M, Murase J. Titanium dioxide in sunscreen. In: Janus M, editor. Appl Titan Dioxide. InTech; 2017.
25. Donglikar MM, Deore SL. Sunscreens: A review. Pharmacognosy J. 2016;8(3).
26. Rosalina A, Sagita E. Placenta extract-loaded novasome significantly improved hair growth in a rat *in vivo* model. Int J Appl Pharm. 2023 May 1;15(3):138-145.
27. Novasomes: A novel nano vesicular carrier. J Xi'an Univ Arch Technol. 2023 Dec;15(11):166-74.
28. Abdassah M, Aryani R, Surachman E, Muchtaridi M. *In vitro* assessment of effectiveness and photostability of avobenzone in cream formulations by combination of ethyl ascorbic acid and alpha tocopherol acetate. J Appl Pharm Sci. 2015 Jun 27;5(6):70-4.
29. Smaoui S, Hlima HB, Chobba IB, Kadri A. Development and stability studies of sunscreen cream formulations containing three photo-protective filters. Arab J Chem. 2017 Feb 1;10-22.
30. Mbanga L, Mulenga M, Mpiana PT, Bokolo K, Mumbwa M, Mvingu K. Determination of sun protection factor (SPF) of some body creams and lotions marketed in Kinshasa by ultraviolet spectrophotometry. Int J Adv Res Chem Sci. 2014 Oct;1(8):7-13.
31. Osterwalder U, Herzog BS. Sun protection factors: Worldwide confusion. Br J Dermatol. 2009 Nov;161(S3):13-24.
32. Smith R. Core EU legislation 2015-16. Macmillan International Higher Education; 2015 Aug 7.
33. Dutra EA, Oliveira DA, Kedor-Hackmann ER, Santoro MI. Determination of sun protection factor (SPF) of sunscreens by ultraviolet spectrophotometry. Rev Bras Cienc Farm. 2004;40:381-5.
34. Pinsky MA. Materials and methods for delivering antioxidants into the skin. U.S. Patent 20,100,098,752. 2010.
35. Aslam Abdul Rahiman CA, Krishnan K, Sreelekshmi AS, Arjun KK, Nair SC. Novasome: A pioneering advancement in vesicular drug delivery. Int J Appl Pharm. 2021;13(1):59-64.
36. Rosalina A, Sagita E, Iskandarsyah I. Novasome: Combining Ufasome and Niosome for excellent vesicular drug delivery system. Sci Pharm. 2023;2(1):26-36.
37. Singh A, Malviya R, Sharma PK. Novasome: A breakthrough in pharmaceutical technology. Adv Biol Res. 2011 Jan;5(4):184-9.
38. Waghmare S, Patil A, Patil P. Novasome: Advance in liposome and niosome. The Pharma Innovation. 2016 May 1;5(5, Part A):34.
39. Niemiec SM, Ramachandran C, Weiner N. Influence of nonionic liposomal composition on topical delivery of peptide drugs into pilosebaceous units: An *in vivo* study using the hamster ear model. Pharm Res. 1995 Aug;12:1184-8.