Review article

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Solid Lipid Nanoparticle: UV Protection

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Abstract

Sunscreen formulation, safety is of high importance because of the diminishing ozone layer. Solid lipid nanoparticles are introduced as the new generation of carrier for cosmetics, especially for UV blockers. The efficiency of a cosmetic product depends not only on the active ingredients but also on the carrier systems involved, with the aim to improve its bioavailability, photoprotection and photostability. Thus the emergence of SLN has recently used in preparation of sunscreen and as an active carrier for organic and inorganic sunscreen agents to optimize UV protection and it acts as an active carrier for sunscreens since they represent physical sunscreen on their own. Thus the incorporation of molecular sunscreen into SLN has a synergistic photoprotection effect. The improving blocking activity allows reduction of concentration of UV blocker. While the benefits of regular use of sunscreen are undisputed, some adverse effects of these organic UV blockers have been reported due to penetration into particulate drug delivery system each as solid lipid nanoparticle while maintaining the protective level of conventional formulation.

Keywords: Sunscreen, Solid lipid nanoparticle, UV blockers

Introduction

Exposure to sunlight (UV radiation) prominently results in damage to the skin surface. The UV solar spectrum consists of three ranges:

UV A (315-400 nm): Long wave radiation and penetrates deeply into the skin and can lead to cancer and premature skin ageing.

UV B (280-315 nm): Medium wave radiation and is mainly involved in tanning and burning of skin.

UV C (100-280 NM): Shortwave radiation and is completely absorbed by the earth's atmosphere.

Effect of UV radiation on human skin can be dived into 2 categories:

Acute: Includes sunburn and production of the vitamin D (caused by UV B) and sun tanning (caused by UV A).

Chronic: Includes carcinoma melanoma and photoaging (caused by UV B).

Protection against above range of three radiations may result in advancement in sunscreen formulation success. This can be achieved by incorporation of UV A and UV B agents into solid lipid nanoparticles.

Factors affecting the nature of sunscreen product:

(1) Sun protection factor: Measure of sunscreen efficacy and is defined as the amount of UV radiation required to produce sunburn on protected skin relative to that of the unprotected skin.
(2) Ability to block UV A radiation
(3) Substantivity: Ability to remain effective under the adverse conditions such as water and sweat.
(4) Stability: Long lasting protection without photodegradation[1].

Conventional Sunscreen Ingredients

An optimal sunscreen formulation contains 2 types of sunscreen agents: Organic sunscreen agents and Inorganic sunscreen agents.

Organic sunscreen components

Organic sunscreens are conjugated systems that absorb UV light and release the absorbed energy in the form of heat.

Avobenzone: Oil soluble and use to absorb the full spectrum of UV A rays; as Avobenzone is highly degradable in the presence of sunlight and is often paired with a photostabiliser in sunscreen formulation[2,3].

Oxybenzone: Absorbs UV A radiation. Potentially harmful and is a likely photocarcinogen [4].

Ensulizole: Protects against UV B and minimally against UV A. Water soluble and is used in formulations for non-greasy feeling[5].

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Octinoxate: Absorbs UV B radiation. Reduces the appearance of scars. Water insoluble, making it useful in waterproof formulations[6].
Octisalate: Formed by condensation of salicylic acid with 2-ethylhexanol. The salicylate portion of the molecule absorbs UV whereas ethyhexanol adds water resistant property[7]. Favorable safety profile and are added to formulation in a relatively high concentration. They are highly photostable agents used to reduce photodegration of other sunscreen ingredients. They are hydrophobic and can serve as solvents for other sunscreen agents[8].
Octrylene: Weak UV absorber, improves photostability, it is costly and difficult to integrate into sunscreen product[4].
Para amino benzoic acid (PABA): It is one of the most potent UV B agent, ability to bind keratinocytes, increasing skin staining but allows it to withstand water immersion and perspiration[9], but it can cause contact allergies so Padimate O is less effective PABA derivatives and are used mostly[10].

Advantages and disadvantages of organic sunscreen components

Organic components used in sunscreen formulations are generally photostable, but all of them are not. They offer more coverage against UV A and UV B rays than physical sunscreens, but range of protection will depend on the particular active and its stability. They are colorless, odorless, and usually runny in texture. They are generally safe, however, some chemical filters generate free radicals, which can cause skin damage, irritation, and ageing[9].

Inorganic sunscreen components

Use of nanoparticles as a sunscreen ingredient over bulk form of sunscreen shows certain advancement such as when applied onto the skin they deflect or block the sun rays. Titanium dioxide is UV B reflector whereas zinc oxide is UV A reflector and has white tone because of its higher refractive index[11].

Advantages and disadvantages of inorganic sunscreen components

Inorganic components used in sunscreen are found to be more effective than organic because they absorb, reflect or scatter ultraviolet radiation rather absorption as inorganic. Transparency property of inorganic sunscreen formulation makes it the first choice[11]. Inorganic compounds require additional material for coating to show better dispersion[13]. Direct exposure of inorganic components with UV radiation can lead to oxidation and result in the release of free radicals, thus coating is essential for these components[7]. DNA, RNA and their bases pyrimidine and purine posses damage on exposure to UV A and UV B radiation in contact with inorganic agents[12].

Solid Lipid Nanoparticle:

At the beginning of the 1990's as an unconventional carrier system like solid lipid nanoparticle (SLN) was developed over the existing conventional carriers, such as emulsions, liposome and polymeric nanoparticles as a colloidal barrier for controlled drug delivery[13-15]. These particles are prepared from extremely purified triglycerides, complex glycerides mixtures or even waxes by replacing the liquid lipid (oil) of an o/w emulsion by 0.1% (w/w) to 30% (w/w) of solid lipid or a blend of solid lipid (i.e. lipids that are solid at room temperature and also at body temperature) and stabilized by surfactant(s) with a preferred concentration of 0.5% (w/w) to 5% (w/w). The mean particle size of SLN is in submicron range, ranging from 40 to 1000 nm[15-18].

Methods Used For Preparation:

There are different methods used for the preparation of SLN like:

Hot homogenization technique

In the hot homogenization method the drug is dissolved or dispersed in melted solid lipid for SLN or in a mixture of liquid lipid (oil) and melted solid lipid for nanostructure lipid carrier. This lipid melts containing drug is then mixed with high speed stirring in a solution of the hot surfactant at the same temperature (5– 10˚C above the melting point of the solid lipid or lipid blend). This pre-emulsion is then passed through a high pressure homogenizer adjusted to the same temperature, generally applying three cycles at 500 bar or two cycles at 800 bars[19-21].

Cold homogenization technique

In the cold homogenization method, the lipid micro particles are obtained by melting and subsequent cooling of drug containing lipid melt followed by crushing, grinding and diffusing in cold surfactant to

obtain a cold pre-suspension of micronized lipid particles. This suspension is then forced to pass through a high pressure homogenizer at room temperature applying typically 5–10 cycles at 1500 bar[21,22].

Microemulsion dilution technique

Lipids are heated above their melting point and an aqueous phase containing surfactants and cosurfactants is added at the same temperature in order to form a clear oil in water (o/w) microemulsion under stirring; lipophilic drug can be dissolved in the hot microemulsion. Multiple w/o/w microemulsion can be prepared, too, in order to encapsulate hydrophilic drugs within SLN [23, 24]. SLN with reduced mean particle size and narrow size distribution can be obtained after dilution in cool (2-10° C) water of the hot microemulsion.

The lipids employed can be triglycerides, fatty acids, fatty alcohols. Surfactants can be chosen among bile salts, phospholipids, polysorbates and cosurfactants among short chain alcohols and glycols (butanol, hexanol, hexanediol, propylene glycol), short chain fatty acids (butyric acid, hexanoic acid), phosphoric acid alkyl esters and benzyl alcohol [25]. Microemulsion can be diluted with a volume of water in ratio 1:10-1:200.

Microemulsion cooling technique

Recently, Mumper and Jay[26-28] patented a microemulsion based method for preparation of SLN. This method involves preparation of o/w microemulsion where an emulsifying wax is melted at 37-55°C and addition of water which heated at the same temperature with minimal stirring so as to form a homogenous milky slurry. Further, after addition of specified amounts of a suitable pharmaceutically acceptable polymeric surfactant in water, a stable and clear o/w microemulsion in a form of liquid matrix is produced. This o/w microemulsion are further cooled at room temperature or at 4°C so as to precipitate SLN from it. This method is reproducible, simple and easy to scale up.

Moreover, all the ingredients used are biocompatible; no organic solvents are used in the preparation method. SLN's are produced with particle size of 50 to 300 nm and with higher entrapment efficiencies [29].

Ultrasonication or High speed homogenization

SLNs can also be prepared by sonication or high speed stirring. This is very general and simple technique and can be beneficial over other methods like hot and cold homogenization, but with the drawback of distribution of larger particle size ranging between micrometer range leading to physical instability such as particle growth upon storage and also metal contamination due to ultrasonication[30,31].

SLNs preparation using supercritical fluid

This is a new technique for preparation of SLN giving the benefit of processing without solvent. Rapid growth of supercritical carbon dioxide (99.99%) solutions which is considered to be a good solvent is used in the formation of solid lipid nanoparticle. This method is known as RESS method[32-34].

SLNs prepared by solvent emulsification/evaporation

In this method, lipid precipitation in aqueous phase upon evaporation of water immiscible organic solvent is carried out by dispersion of nanoparticles in o/w emulsions[35,36].

Double emulsion method

It is a novel method of preparation of solid lipid nanoparticles loaded hydrophilic drug moiety and is based on solvent emulsification evaporation by drug encapsulation in the outer water phase of w/o/w double emulsion along with a stabilizer to avoid partitioning of the drug to outer water phase during solvent evaporation[37].

Spray drying method

It is a less costly method than lyophilisation. In this method, particle aggregation occurs due to elevated temperature, shear forces and partial melting of the particle. The most excellent outcome is obtained by the SLN concentration of 1% in a solution of trehalose in water or 20% trehalose in ethanol-water mixtures (10/90 v/v)[38].

Phase inversion method

The PIT concept was introduced in the last decade by Shinoda and Saito, using the specific ability of surfactants, usually nonionic (NS), such as polyethoxylated surfactants, to modify their affinities for water and oil in function of the temperature, and therefore to undergo a phase inversion. The so-called transitional emulsion phase inversion occurs, when, at

fixed composition, the relative affinity of surfactants for the different phases is changed, resulting in the gradual modification of the temperature. Within the transitional region between macro-emulsions, i.e. for the temperatures at which the nonionic surfactants exhibit a similar affinity for the two immiscible phases, the ternary system shows an ultra low interfacial tension and curvature, typically creating microemulsions, bicontinuous and nanoscale systems. Therefore, the PIT method consists of sudden dilution in water or oil. Nanoemulsions are immediately generated. Cooling of the system induces lipid nanaoparticle precipitation[39].

Evaluation of SLN:

Particle size and Zeta potential:
The physical stability of SLNs depends on their particle size. Photon correlation spectroscopy (PCS) and laser diffraction (LD) are the most powerful techniques for determination of particle size. PCS measures the fluctuation of the intensity of the scattered light, which is produced by particle movement. PCS detects the particle size in the range of 3 nm to 3 µm and by laser diffraction in the size range of 100 mm to 180 µm. Although PCS is a good tool to characterize nanoparticles, but is capable for the detection of larger microparticles[40].

Zeta potential measurement:
Zeta Potential can be carried out using a zeta potential analyzer or zetameter. Before measurement, SLN dispersions are diluted 50-fold with the original dispersion preparation medium for size determination and zeta potential measurement[41].

Electron microscopy:
Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are used to observe nanoparticles. TEM however, has a small limit of detection and hence SEM is better for morphological examination[42].

Atomic force microscopy (AFM):
This method involves a probe tip with atomic scale sharpness is rastered across a sample to produce a topological map based on the forces at play between the tip and the surface. The probe can be dragged across the sample (contact mode), or allowed to hover just above (non contact mode), with the exact nature of the particular force employed serving to distinguish among the sub techniques. This approach produces ultra- high resolution, which leads, ability to map a sample according to properties in addition to size[43].

Differential scanning calorimetry (DSC):
DSC and powder X-ray diffractometry (PXRD) is performed for the determination of the degree of crystallinity of the particle dispersion by comparing the melting enthalpy/g of the bulk material with the melting enthalpy/g of the dispersion[44].

Nuclear magnetic resonance (NMR):
NMR can be used to determine both the size and the qualitative nature of nanoparticles. The selectivity afforded by chemical shift to provides information on the physicochemical status of components within the nanoparticle[44].

SLN as a carrier of UV molecular absorbers

SLN can act as a UV blocker:
Highly crystalline solid lipid nanoaparticles can act as particulate UV blockers by scattering the light efficiently. Mulhen A. Zur et.al., described a UV scan of 10% cetyl palmitate SLN dispersion versus an o / w showed that the particles were physically long-term stable after nanoemulsion of identical lipid content and surfactant concentration. To enhance the UV protection by SLN further, a molecular sunscreen was incorporated into the solid lipid matrix. When measuring the UV absorption, it was surprisingly found that incorporation of the molecular sunscreen into SLN led to synergistic protective effect, i.e. the measured UV absorption was higher than the theoretically calculated values from the single effects of the molecular sunscreen and the particle dispersion itself. This means the total amount of molecular sunscreen in the formulation can be reduced. Thus, further minimizing the side effects in addition to already achieved reduction by firm incorporation of the sunscreen into the particle matrix [45,46].

SLN prolongs the release profile of UV molecular absorbers:
Incorporation of UV blockers in SLN was performed in a way that the release was prolonged, i.e. very little release increasing within the application time of 6–8

h[48]. Wissing S.A. et.al., studied *in vitro* release studies were performed to compare the release of sunscreen from o/w nanoemulsion and from the SLN dispersions. A membrane free release model was used, i.e. putting an oil phase above the aqueous nanoemulsion or aqueous SLN dispersion in a test tube. After 4 hrs, 6.5% sunscreen was released from the nanoemulsion, however, only 3.1% of the incorporated amount from the SLN dispersion. In this *in vitro* test, a membrane free model was used, thus *in vivo*, even less uptake is expected due to the membrane function of the stratum corneum. Stripping test on human skin was performed confirming this. The concentrations found on the strips were 2 – fold higher for the nanoemulsion compared to the SLN dispersion (6.2 vs. 3.2%)[47].

Thus the cumulative amount of UV molecular absorbers released is less leading to a higher amount to be retained superficially on the skin, they should penetrate as little as possible into the viable epidermis, the dermis and into systemic circulation, which has desired effect for the sunscreen preparations to be more efficacious [48].

SLN enhances the photostability:

Most of the UV molecular blockers are photounstable. The photostability of these blockers is enhanced by incorporation into lipid nanoparticles. Geun-Soo Lee et al., studied preparation and characterization of Bis-ethylhexyloxyphenolmethoxy-phenyltriazine (BEMT) loaded SLN, which increased the photochemical stability of BEMT in sunscreen products[49].

Conclusion

Solid lipid nanoparticle is the active carriers for the sunscreen products. SLNs are an effective means of delivering sunscreen agents to skin and localizing their effects. Improving the UV blocking activity allows reduction of the concentration of the UV blocker. Thus SLN act as an active carrier due to their particulate character, i.e. they represent physical sunscreen on their own.

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