Lipid Nanoparticles as Novel Carrier for Broad-spectrum Sunscreen Formulations

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ABSTRACT

The most widely used UVA absorber in broad-spectrum sunscreens is avobenzone. In the sunlight, however, it will be photolysised rapidly and its photoprotection against UVA will greatly decrease. A photoprotective formulation was developed with an increased sun protection factor(SPF), compared to a conventional formulations, but having the same concentration. In the present paper, the effectiveness of a sunscreen mixture, incorporated into the novel topical delivery systems, i.e. solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC), used as ultraviolet (UV) protector enhancers with a distinctly higher loading capacity has been developed and evaluated. After the production by hot high pressure homogenization, the NLC were analyzed in terms of particle size, physical state, particle shape, ultraviolet absorbance and stability. The determination of 3 organic UVfilters was performed by HPLC with UV spectrophotometric detection. The loading capacities for molecular sunscreens reported before now are in the range of 10–15%. It was possible to load NLC with up to 40% with molecular sunscreen. The particle size for all NLC was around 300 nm after production. In the sunlight, the retention rate of avobenzone was up to 90% .

Keywords: avobenzone, nanostructured lipid carriers(NLC), sunscreens, HPLC

1 INTRODUCTION

Solar ultraviolet radiation incident on the earth's surface can be divided into two parts: the UVB region (290–320nm) and the UVA region (320–400nm). The UVA component of sunlight is now believed to be the main cause of photoaging and photocarcinogenesis and is much more effective than UVB in inducing peroxidative damage[1]. Consequently, most skin care cosmetic products now include UVA filters in their formulations along with UVB filters. There are few chemical absorbers that provide protection in the UVAI (340–400nm) range. Of these avobenzone is the most widely used. However, a number of sunscreen products containing this filter are not sufficiently photoprotective because of the photoinstability of avobenzone. At the same time, potential undesired effects of molecular sunscreens are penetration into the skin leading to side effects such as photo allergies, phototoxicity and skin irritations[2; 3].

Therefore, there is an urgent need for the development of safer and more effective sunscreens delivery system. Lipid nanoparticles, SLN and NLC are innovative carrier systems derived from o/w emulsions, where the liquid lipid was replaced by a solid lipid or a blend of solid and liquid lipids that is solid at room and body temperature[4]. They have been shown to be able to enhance photoprotection by synergistically combining the advantages of organic and inorganic sun screening agents and without addition of other chemical entities. In addition, inclusion of the molecular sunscreens into the particle matrix leads to a delayed release and to reduced penetration of sunscreens into the skin and thus to decreasing side effects[5; 6].

The aim of the present study was to develop and optimize stable sunscreen formulations based on lipid nanoparticles with a high loading of molecular sunscreens. Three common organic UV filters, namely, 4-tert-butyl-4'-methoxydibenzoylmethane, 2-cyano-3,3-diphenyl-acrylic

acid, ethylhexyl methoxycinnamate were chosen as model UV filters. Preparation and their physicochemical properties of lipid nanoparticles were investigated using various analytical equipments such as SEM, sizing methods and HPLC.

2 MATERIALS AND METHODS

2.1 Materials

Three organic UV filters were used: Parsol® 1789 (4-tert-butyl-4'-methoxydibenzoylmethane, avobenzone; DSM, Basel, Switzerland), Parsol® MCX (ethylhexyl methoxycinnamate, OMC; DSM, Basel, Switzerland), Sunsafe-OCR (2-Cyano-3,3-diphenylacrylic acid, Octocrylene; Uniproma). SIMULSOL 165 and CORUM 2367 were purchased from ELGIN Corporation(Chongqing, China). All other chemicals and reagents were of commercial available from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Ultrapure water with conductivity of 18.2 MΩ cm was used in all the experiments.

2.2 Preparation

Preparation of the lipid nanoparticles suspensions was carried out by hot high pressure homogenization (HPH), as described elsewhere. Briefly, different amounts of the mixture of sunscreens Octocrylene (S1), OMC (S2), avobenzone (S3) in the ratio 10 : 20 : 12 ，forming the lipid phase，were melted at 75°C .The lipid phase was 42% of the formulation. The aqueous phase (58%), containing 4% of surfactant C2367 and 8% of surfactant S165, was heated to the same temperature. The hot lipid phase was dispersed in water and a premix was formed by homogenizing high speed stirring (1000 rpm for 5 min). Afterwards, the pre-emulsion was homogenized by HPH (ATS 100D, Canada). Two cycles were carried out at 600 bar and 80°C. The obtained hot nanoemulsion was cooled to room temperature leading to the lipid phase recrystallization and formation of the lipid nanoparticles dispersions.

2.3 Analysis of Particle size

Analysis of particle size was performed by photon correlation spectroscopy (PCS) with a Malvern Zetasizer ZS90 (Malvern Instruments, UK). PCS yields the mean particle size (Z-ave) and the polydispersity index (PDI) which is a measure of the width of the size distribution. The Z-ave and PDI values were obtained by averaging of 3 measurements at an angle of 90° at 25 °C. To detect the possible presence of microparticles, the laser diffractometry (LD) (Mastersizer 2000, Malvern Instruments, UK) was applied. The LD values obtained indicate the percentage of particles possessing a diameter equal or lower than the given value.

2.4 High-Performance Liquid Chromatography (HPLC)

Prepared samples were kept in glass vials away from light at three temperatures(4°C, 25°C and 40°C) and under the light at room temperature. The content of avobenzone was analyzed at certain time intervals using reverse-phase HPLC methods. The HPLC system was composed of a Shimadzu Corporation (Kyoto, Japan) model LC-20AD pump and model SPD-M20A Diode array detector. The analytical column was Global Chromatography C18 (250×4.6 mm, 5 μm) (Jiangsu, China). The injection volume was 10μL; the gradient liquid chromatographic system constituted of 70% mobile phase A [Methanol : Tetrahydrofuran (5 : 9 v/v)] and 30% mobile phase B [water:$HClO_4$ (300 : 0.2 v/v)]at a flow rate of 1.0 mL/min; the wavelength was 311 nm; the column temperature was 40 °C.

2.5 Scanning Electron Microscopy (SEM)

The morphological characteristics of the nanoparticles were observed by SEM. The NLC dispersion was diluted by 800 times; 5μL of sample was dropped on the chip and dried under a nitrogen gas stream. The sample was examined by field emission scanning electron microscope (S-4800, Hitachi, Tokyo, Japan) at 1.0 kV accelerating voltage.

3 RESULTS

3.1 Particle size analysis

Figure 1 shows the mean particle size and PDI of evaluated by PCS after production and after storage for 4 months at three temperatures(4°C, 25°C and 40°C).The figures show that the particle size remained almost constant with no significant growth during 120 days at 4 °C, 25 °C and 40°C.

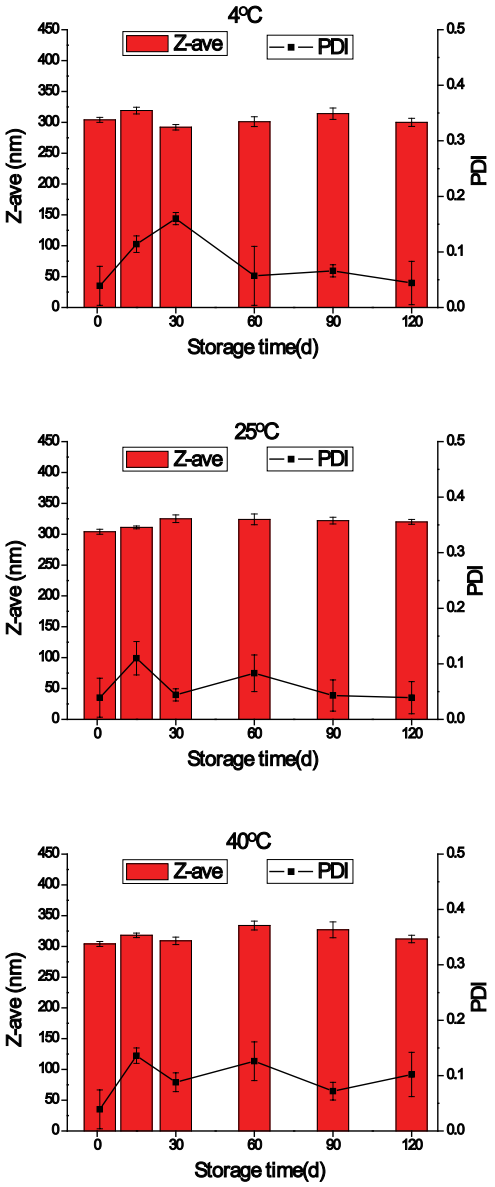

Figure 1: The particle size and PDI of NLC in the simulated formulation at different temperatures (4 ˚C, 25 ˚C and 40 ˚C). The particle size and PDI was the mean± SD (n = 3)

The average diameter of NLC stored at 4˚C was little smaller than that stored at 25 ˚C and 40˚C. That may be because liquid lipids solidify along with the change of temperature in surrounding circumstance. Meanwhile, PDI values of were lower than 0.2 in all the measurement, suggesting that the nanoparticles were in a state of good monodispersity. This observation indicated the prepared NLC had a good stability in the long-term storage.

3.2 Retention rate

The retention rate of active loaded in the NLC was a significant criterion judging the stability of NLC dispersion. Figure 2 shows that the retention rate of avobenzone loaded in the NLC changed during 60 days under the light(room temperature) and away from light(4˚C, 25˚C and 40˚C). In the first month, the retention rate of all storage conditions is relatively steady and keeping at about 99%. There was a slight decline phenomenon observed at light during the second month. This phenomenon was also observed and explained by Müller et al[7]. During the cooling of the produced O/W nanoemulsion, the solubility of the drug in the water phase decreased continuously with decreasing temperature of the water phase. This drug repatriated and concentrated in the still liquid outer shell of the NLC and/or on the surface of the particles. The amount of drug in the outer shell and on the particle surface was released in the form of a burst, while the drug incorporated into the particle core was released in a prolonged way. In the second month, the avobenzone was released from nanoparticles and the avobenzone stored under the light was photolysised.

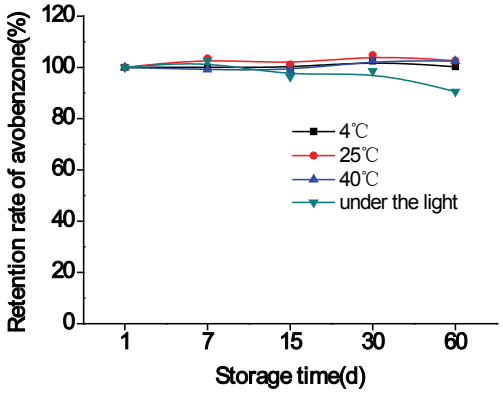

Figure 2: Retention rate of avobenzone stored under the light(room temperature) and away from light(4˚C, 25˚C and 40˚C). Testing interval was chosen respectively at one day, seven days, half a month, one month and two months after preparation.

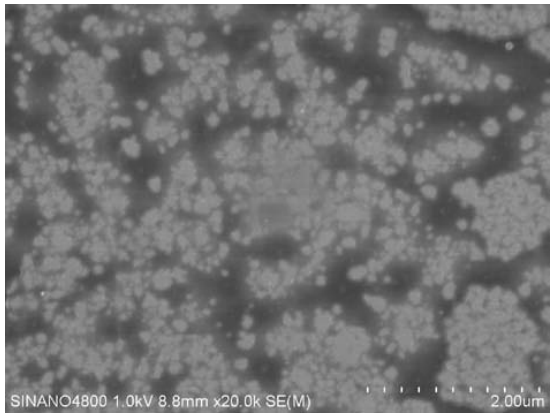

Figure 3:Scanning electron micrograph of NLC formulation

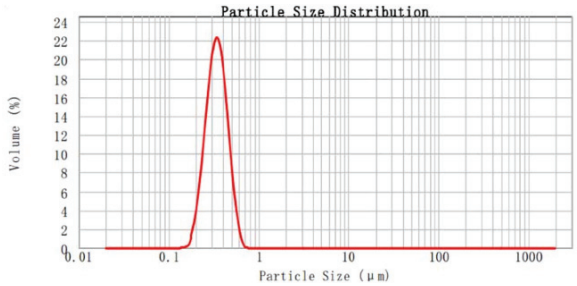

Figure 4:Particle size distribution NLC obtained by LD

3.3 Nanoparticle morphology analysis

Figure 3 shows the result of SEM measurement, we could see that the shape of NLC could be displayed as flat spheroid. The average diameter of NLC was smaller than the result from PCS. The reason may be the hydrodynamic diameter measured in aqueous circumstance by the PCS, while the sample prepared for SEM was dried by nitrogen. The loss of water would be considered as another significant reason for the different result in these two equipments. The particle size measured by LD (Figure 4 D0.1 =242nm, D 0.5= 343 nm and D0.9= 476 nm) , well in accordance with SEM data.

4 CONCLUSION

In general, incorporation of sunscreens into nanostructured lipid carriers enhances the photostability of avobenzone. Relevant data showed that samples were kept stable for at least 60 days. Furthermore, the preliminary study revealed that NLC be able to enhance photoprotection by synergistically combining the advantages of organic and inorganic sun screening agents. The loading capacity of up to 40% molecular sunscreen allows the production of creams and lotions with high SPF. The HPH technique, 600 bar 2 circles, was easily applied to produce sunscreens NLC dispersions in large scale. Conclusively, sunscreens NLC has very promising potential in cosmetic industry.

5 ACKNOWLEDGEMENTS

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