ENCAPSULATION OF ETHYLHEXYL METHOXYCINNAMATE, A LIGHT-SENSITIVE UV FILTER, IN SOLID LIPID NANOPARTICLES

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INTRODUCTION

Among the different UVB filters acceptable in topical formulations, Ethylhexyl Methoxycinnamate (EMC) is one of the most commonly used in sunscreen products. Its maximum absorption wavelength is 320 nm. However, the major problem regarding the use of EMC in sunscreen products is its relatively fast degradation under UV radiation. The original conformation of EMC is the "trans" isomer but a cis-isomerisation appears after light exposition. This isomer is characterized by a lower level of absorption in UVB range than the "trans" configuration, thereby decreasing its effectiveness. This phenomenon constitutes a non-negligible drawback to insure suitable protection against UV radiations for long exposition times. In order to decrease its photoinstability, EMC was encapsulated in a nanoparticular solid lipid matrix system. Three lipids were investigated: glyceryl behenate (Compritol® 888 ATO, Gatefossé), a mineral wax (Ozokerite Wax no.7726, Poth Hille) and rice bran wax (vegetal wax: Rice Bran Wax # 224P, Koster Keunen Holland bv)). These lipids possessed different HLB values and were characterized by a relative high melting temperature. The aqueous lipid suspensions were prepared with different emulsifiers depending on the nature of the lipid matrix.

MATERIALS AND METHODS

Formulations

Formulations	Lipids	EMC	Surfactant
SLN 1	Glyceryl behenate (HLB2; 69-74°C) 6%	14%	Poloxamer 188 1%
SLN 2	Ozokerite (HLB 9; 63-68°C) 6%	14%	Span60 +Tween60 1.35%+0.65%
SLN 3	Rice Bran Wax (HLB 10; 77-82°C) 6%	14%	Sodium cocoamphoacetate 2.5%

The lipid suspensions contained 70% of EMC (w/w, related to the lipid mass). The lipid-EMC blends were analyzed by differential scanning calorimetry (DSC) and hot stage microscopy (HSM) in order to evaluate their cristallinity and melting point value.

Preparation and characterization of formulations

Preparation: Aqueous phase + Lipid phase + Surfactant

↓ Melt dispersion technique: Ultra-Turrax (T-25 Basic, IKA-Werk)

↓ Agitation: 20500 RPM Duration:1min. Temperature: 75-80°C

Microparticles suspension (SLM)

↓ High Pressure Homogenizer (HPH) (Emulsiflex C5 Avestin) 3 cycles at 500 bars

↓ Temperature: 85°C, then quick cooling with ice

Nanoparticles suspension (SLN)

Characterization:

The particle size and the size distribution of the nanoparticles were measured with a Mastersizer Laser Diffractometer (Hydro 2000, Malvern Instrument, UK).

The level of protection of EMC was evaluated by exposing the suspensions to UV light using a Suntest CPS plus (Atlas, Germany), equipped with an IR-block filter to avoid unwanted thermal effects (parameters: 2 hours, 250W/m², 30°C). UV spectra were analyzed before and after UV-light exposition using an UV-Visible HP 8453 spectrophotometer (Agilent, Germany).

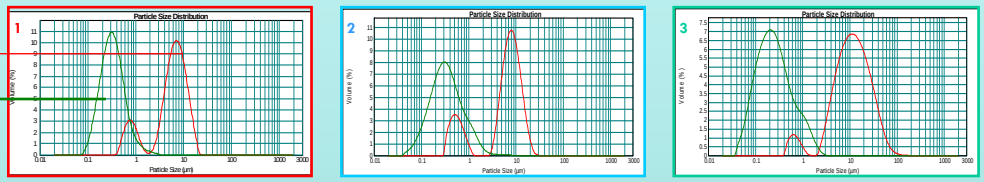
EMC loading was estimated by HPLC analysis after a centrifugation/filtration step.

RESULTS AND DISCUSSION

Particle size and size distribution

Ultra-Turrax

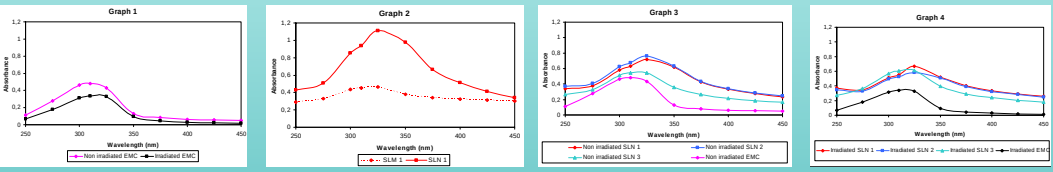
HPH



1-Glyceryl behenate
2-Ozokerite Wax
3- Rice Bran Wax

The particle size was reduced using the HPH method. An unimodal distribution was obtained. The nanoparticles were characterized by a mean size of about 300 nm when encapsulated with Glyceryl Behenate and Ozokerite Wax, while the suspension made with Rice Bran wax presented a mean particle size of about 200 nm. The lipid mixtures being melted during the entire formulation process, aggregation of the lipid nanoparticles, appearing during the size reduction step, seemed to depend only on the chemical nature of the surfactant. According to the data obtained with laser diffraction, the association of Rice Bran Wax and sodium cocoamphoacetate should be selected to avoid the agglomeration phenomenon.

Protection level of EMC



Loss of absorbance after irradiation at 310nm:

SLN1: 12.8%

SLN2: 21,0%

SLN3: 10,0%

EMC: 30,0%

As we can see (Graphs1 and 2), compared to microparticles and free product, EMC showed an important shift to higher absorption values when encapsulated in nanoparticles. Indeed, the nanoparticles presented an important capacity to scatter the UV-light due to their smaller size. Before irradiation (Graph 3), each formulation presented different absorbance in UVB range : using the same EMC concentration (2.8 mg/mL), the absorbance values at 310nm were 0.64, 0.62 and 0.58 for SLN2, SLN1 and SLN3, respectively. This variability was due to the cristallinity of each lipid mixture: the UV-blocking ability increased with the theoretical cristallinity index of the SLN (this was determinated using the ratio between the melting enthalpy (J/g) of raw lipid and EMC-lipid mixture present in the nanosuspension). Moreover, in each case, UV protection was effective (Graph 4): while free EMC presented a 30,0% loss of its efficiency after two hours of irradiation, the three other SLN formulations showed a loss of absorbance less than 21,0%. The best protection was obtained with the SLN 3 containing Rice Bran Wax (10,0%) and Glyceryl behenate (SLN 2) (12.8%).

EMC loading

The EMC loading was of 87±4%, 92±6% and 93±4% for SLN 1, SLN2 and SLN3, respectively. Therefore, each formulation presented high capacity of encapsulation. This was due to the high melting point value of the selected lipids and to the homogenous mixing of EMC with these lipids in the matrix system.

CONCLUSION

The encapsulation by solid lipids seems to be effective to protect EMC against UV light degradation. The evaluated nanosuspensions may be useful in sunscreen formulations as they permit to decrease the final concentration of EMC, while the same Sun Protection Factor is preserved. Further *in vitro* penetration tests should be conducted to make sure that nanosuspensions are safe to use.

Skin and Formulation 3rd Symposium – Palais des Congrès Versailles, France – March 9-10, 2009