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### Effect of UV Sunscreens Loaded in Solid Lipid Nanoparticles: A Combined SPF Assay and Photostability

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# Effect of UV Sunscreens Loaded in Solid Lipid Nanoparticles: A Combined SPF Assay and Photostability

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*The aim of this investigation was to obtain lipid nanoparticles loaded with different sunscreen agents in order to achieve enhanced photoprotection and to decrease the amount of UV – absorbers, with preserving at the same time a high sun protection factor. The developed formulations combined different types of additives including a mixture of non-ionic surfactant and lechitine with two lipids as solid matrix to obtain favourable stable lipid formulations. The research work could be concluded as successfully production of lipid nanoparticles loaded with UV-A and UV-B absorbers (with average size less than 100 nm) that may represent useful UV-blocking systems in sunscreen products for cosmetical purpose.*

**Keywords** High shear homogenisation; solid lipid nanoparticles; sun protection factor (SPF); sunscreen

## 1. Introduction

Solid lipid nanoparticle (SLN) technology represents a promising approach that may be used to develop new biocompatible carriers for various lipophile compounds (e.g., vitamins, peptides, proteins, oligonucleotides and other drugs) [1–6], with pharmaceutical, cosmetic and biochemical purposes. These nanoparticles have been suggested as more attractive new lipid-based delivery systems for lipophilic molecules than other colloidal delivery systems. Many researches compared these systems with traditional carriers, the results being the obvious advantages over other dispersed systems. Thus, SLNs manifest a good tolerability and biodegradation [7], have high bioavailability and targeting effect [8], avoid the use of organic solvents in some preparation processes, are amenable to large scale production, may protect the sensitive active components from the external environment (e.g., water) against chemical

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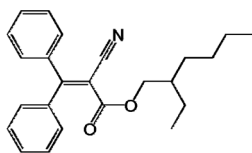
degradation [9], have the ability to modulate compound release and a wide potential application spectrum (dermal, peroral, intravenous) for controlled release of drugs [10]. The most remarkable advantage of SLN is the fact that the lipid matrix is made from physiological well-tolerable lipids (the solid lipid matrices can be composed of fats or waxes) which minimize the danger of acute and chronic toxicity and owing to the solid state of the lipid permit more controlled drug release due to increased mass transfer resistance [11]. The biocompatibility of lipids, self-assembly capabilities, particle size versatility, and low costs make lipid based delivery systems an attractive subject for many research topics. Among them, nanosized particles are of growing interest for topical treatment of skin diseases.

Due to the current ozone layer depletion in the stratosphere, radiation from the sun especially UVA and UVB can reach the earth in a higher extent leading to unwanted and harmful effects on human skin. These occur due to photochemical impact on the skin as a result of peroxidation reactions. Therefore, the researches based on sun protection have received a continuous interest for the specialists [12], being unanimous accepted that the impact of UV radiations represents a major threat on public health in the next decades, on both UVB (290 – 320 nm) and UVA domain (320–400 nm) [13]. The interest in developing of new sunscreens has been growing in the last years due to the harmful effects of UV radiation on the skin such as dryness, mottled pigment abnormalities, erythema, accelerated skin ageing (wrinkle, photoageing) and ultimately the induction of skin cancer [14]. As a consequence, the formulation of safe sunscreen products with enhancement of efficient UV protective effects, is a topic of high importance to avoid exposure to harmful UV light and counteract the damage induced by UV photons in the skin [15], simultaneously with minimization of local side effects.

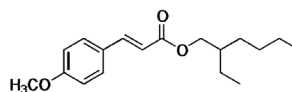
In this context, solid lipid nanoparticles (SLN) are introduced as a new generation of carrier systems for active cosmetic components [3], especially as UV blockers for the human use, mainly for skin. The SLNs have specific features which recommend them as promising carriers systems in cosmetic industry. Firstly, they can provide improved stability of sensitive active ingredients, as has been demonstrated for retinol and tocopherols [16,17]. Due to their ability to provide a controlled release, the solar screens persist longer on skin surface where it may action [12]. Moreover, they present a protective effect on skin by forming a thin film, manifest occlusive properties that lead to the increase of water content in skin [18]. SLN present a high potential of UV radiation blocking, e.g., they can themselves act as a physical UV blocker and are able to improve the UV photoprotection [19]; this last feature may lead to a significant decrease in amount of sunscreen used, with preserving a high sun protection factor (SPF).

The development of photoprotection has been stimulated by a change in the behaviour habits of human society. Photoprotection is an essential prophylactic and therapeutic element which is critical to avoid all the above mentioned undesired effects [15]. In the cosmetic field, the sunscreen agents have been widely used as photoprotective agents for long time ago, but the incorporation of them into lipid carriers with an increased SPF has not yet been fully accomplished. In this context, in this paper the effectiveness of three individual sunscreen agents incorporated into the novel topical delivery systems based on solid lipid nanoparticles (SLN), used as UV protective enhancers has been developed and evaluated.

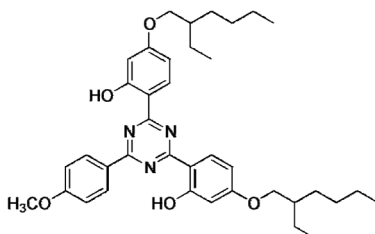
The UV absorbers (sunscreens) are conjugated aromatic molecules with a structure that allow them to absorb high-energy UV rays and release the energy as lower-energy



(a) 2-Ethylhexyl-2-cyano-3,3-diphenylacrylate (OCT)



(b) 2-Ethylhexyl trans-4-methoxycinnamate (OMC)



(c) Bis-Ethylhexyloxyphenol methoxyphenyl triazine (BEMT)

**Figure 1.** UV absorbers structure.

rays, thus preventing the skin damage by UV radiations [20]. From the class of organic sunscreen, we selected two molecular sunscreens with optimal screening for UVB wavelengths: 2-ethylhexyl trans-4-methoxycinnamate and 2-ethylhexyl-2-cyano-3,3-diphenylacrylate known as octocrylene), the latter with a blocking effect on a short UVA domain, and another with a large blocking spectrum on UVA and UVB (bis-ethylhexyloxyphenol methoxyphenyl triazine, known as bemotrizinol). The structures of selected molecular sunscreens are presented in Figure 1.

The purpose of this work is the designing and characterization of sunscreen loaded SLNs focusing on a potential application as an efficiently sunscreen delivery system. Consequently, it is desirable to avoid the side effects of a high amount of sunscreen, by reducing the effective sunscreen concentrations that could become harmful for human health, simultaneously with obtaining of an enhanced blocking effect. For this reason, SLN surface properties have been manipulated by concentration variation of two different types of nonionic surfactants in aqueous phase together with an amphiphilic lecithin, with two lipids (cetyl palmitate and glycerol stearate) as solid matrix, that have been explored to offer their inherent merits to improve the SPF properties of SLN dispersions and to obtain favourable stable SLNs systems. In order to explore the potential of SLNs in improving the topical delivery of molecular sunscreen agents, the photostability of some cosmetic formulations based on a combination between a cream base with OMC-SLN, OCT-SLN and BEMT-SLN, have been also developed and evaluated.

## 2. Experimental Part

### 2.1. Materials

Polyethylene glycol sorbitan monooleate (Tween 80) was purchased from Merck, Germany; Synperonic PE/F68 (block copolymer of polyethylene and polypropylene glycol), L- $\alpha$ -Phosphatidylcholine, 2-Ethylhexyl-2-cyano-3,3-diphenylacrylate (OCT), 97% and 2-Ethylhexyl trans-4-methoxycinnamate (OMC), 98% were obtained from Sigma Aldrich Chemie GmbH; n-Hexadecyl Palmitate (CP), 95% was purchased from Acros Organics, USA; Glycerol stearate (GS), Bis-Ethylhexyloxyphenol

methoxyphenyl triazine (BEMT) and the cream base (which contains stearats, glycerine, fatty alcohols, emulsifier, emollients and an antioxidant – butylhydroxyanisole) were supplied by Elmplant S.A., Romania.

## 2.2. Preparative Technique for Sunscreen Loaded SLNs Synthesis

The sunscreen loaded SLNs were prepared by a modified high shear homogenization method. The lipid mixture (1:1, w/w) formed by cetyl palmitate and glycerol stearate (10% from the total SLN dispersion) was melted at about 80°C and an appropriate amount of sunscreen was added (1%). An aqueous phase that contains a mixture of surfactants (between 2 ÷ 5%, with a mass ratio of Tween 80: Synperonic F68: Lecithin = 1:0.25:0.25) was heated to the same temperature. After 1 h of individual stirring of the lipid and aqueous phases, respectively, the hot lipid phase was gradually poured into the hot aqueous-surfactants solution. Before the mixing of the two phases, the aqueous surfactant solution was complied to a high speed stirring (15 000 rpm) for 3 minutes. Then, the resulted emulsion was stirred for 2 h at 80°C. This hot pre-emulsion was further processed by a high shear homogenization (by using a Lab High-Shear Homogenizer SAII-20 type; 0 ~ 28.000 rpm and power of 300 W, Shanghai Sower Mechanical & Electrical Equipment Co., Ltd., China), by applying 25 000 rpm for 15 minutes. The lipid dispersion was diluted with 50 mL deionised water and cooled to room temperature (while stirring), and solidified to obtain the aqueous sunscreen loaded-SLNs dispersions. In case of free-SLN, this was produced in the same manner as loaded-SLNs, by replacing the sunscreen amount with deionised water. The excess water is removed by lyophilisation in order to increase the SLN particle concentration, by using a Christ Delta 2–24 KD lyophilizer (Germany). The SLN dispersions with 1% sunscreen agent was cast in glass dishes and freeze-dried in the next conditions: 1. cooling to –40°C during 4 h, heating to –20°C within 4 h at 0.12 mbar and heating to 20°C within 20 h at the same pressure; 2. heating within 4 h to 30°C at 0.01 mbar and hold for 8 h. The lyophilised SLNs have contained an amount of 7% sunscreen. The cream formulations have been prepared by dispersing various amounts of lyophilised sunscreen-SLNs in a cream base. The final developed cream formulations have contained between 1% ÷ 4.5% sunscreen (w/w).

## 2.3. Physico-Chemical Characterization of Sunscreen-SLNs

Size analysis, measurement of the polydispersity index and zeta potential of the SLN dispersions were evaluated by the dynamic light scattering (DLS) technique on a Zetasizer Nano ZS (Malvern Instruments Ltd., U.K.), at a scattering angle of 90° and 25°C. All samples were diluted with deionised water to an adequate scattering intensity prior to the measurement. For each sample, the hydrodynamic radius was measured in triplicate. The particle size analysis data were evaluated using intensity distribution.

The morphology of sunscreen-SLNs was examined using a transmission electron microscope (Philips 208 S, Netherlands). After being diluted 50 times with distilled water, a drop of the resultant SLN dispersion solution was placed onto a carbon-coated copper grid and kept for 15 min. before the samples were viewed and then photographed. The TEM images were recorded after three months from the preparation.

The thermal analysis was used to investigate possible changes in the crystallinity of the lipid matrix. Thermograms were recorded with a differential scanning calorimeter Jupiter, STA 449C (Netzsch). Samples were heated at the scanning rate of 3°C/min over a temperature range between 30 and 100°C.

The determination of SPF indexes was realized by using UV-VIS V670 Spectrophotometer equipped with integrated sphere and the adequate soft. For SPF evaluation, an amount of 2 mg/cm<sup>2</sup> cream is applied onto Transpore<sup>TM</sup> 3 M support and the sample spectrum is registered on 290–400 nm, by using a reference support – Transpore<sup>TM</sup> 3 M whitout cream. The method for *in vitro* determination of sun protection factors (SPF) of sunscreens is based on Diffey and Robson theory [21]:

$$SPF = \frac{\sum_{(400-290)} E_{\lambda} \cdot B_{\lambda}}{\sum_{(400-290)} \frac{E_{\lambda} \cdot B_{\lambda}}{MPF_{\lambda}}}$$

where:  $E_{\lambda}$  – sun radiation extinction for Earth (between 20°– 40° N latitude);  $B_{\lambda}$  – relative extinction for each wavelength;  $MPF_{\lambda}$  – the monochromatic protection factor for selected wavelength (the difference between the spectrum of measured sample applied on support and support spectrum).

The information about the photostability of some cosmetic formulations that contain various content of sunscreen-SLN were obtained by UVA-UVB irradiation with the energy of 19.5 J/cm<sup>2</sup>, at two wavelengths: 365 nm (UVA) and 312 nm (UVB) on a short period (1 h on UVA and 2 h on UVB) and prolonged period of time (2 h on UVA and 4 h on UVB), with an Irradiation System BioSun, Vilver Lourmat, France. The sunscreen-loaded SLN formulations were irradiated with the same energy of 19.5 J/cm<sup>2</sup> to investigate the photostability. The extent of photodegradation was monitored by recording the absorption spectra in the wavelength range of 290–400 nm on a UV-VIS V670 Spectrophotometer (Jasco, Japan), by using the dispersive with integrated sphere.

### 3. Results and Discussion

#### 3.1. Particle Size, Zeta Potential and Thermal Evolution of the Sunscreen SLNs

The choice of the lipid matrix and the surfactant is essential in order to prepare a safe and stable formulation. The nature and amount of the surfactant used in the formulation can completely affect the chemical stability of the lipid matrix (e.g., differences in incorporation of the surfactant in the outer shell of the particles, different solubilizing capacities in the lipid phase and so on), the size distribution, structure and stability of the resulting nano-emulsions and nanoparticles [21]. In addition, it has been demonstrated that the combination of different surfactants [22] may lead to a greater stabilization of SLN rather than with a single surfactant (e.g., dispersions with more than two surfactants frequently yield to a more homogeneous appearance and lower tendency to form macroscopic particles). The steric hindrance provided by the non-ionic surfactants, especially block copolymers of polyethylene and polypropylene glycol, is another additional effect which increases the stability of colloidal dispersions and might prevent more efficiently the aggregation of the nanoparticles in the colloidal system [23]. Moreover, by adding phospholipids to a nonionic surfactant mixture, there is a surface modification that enables an electrostatic stabilization

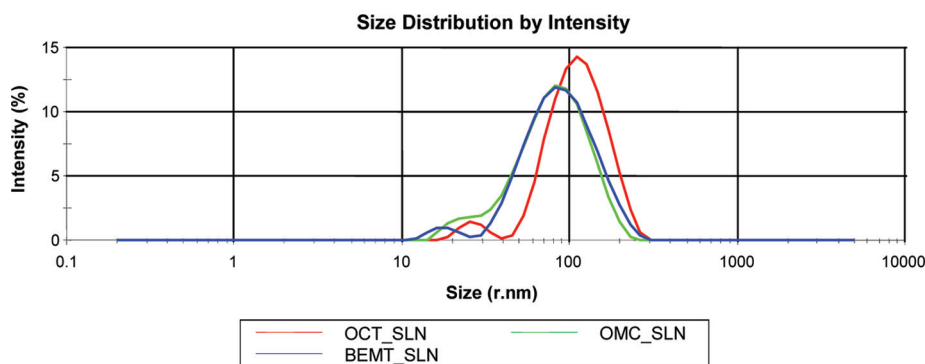


of colloidal particles, especially when synthesis of the colloidal particles is carried out in aqueous medium [24].

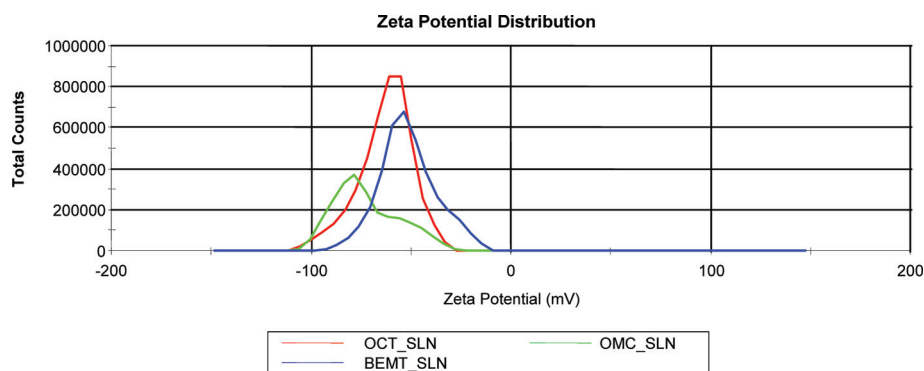
Based on all these aspects, we selected for sunscreen loaded SLNs preparation 2 types of emulsifiers including a mixture of non-ionic surfactants (Tween-80 and Synperonic F68) and Lecithin, in addition to a modified high sheer homogenization (HSH) technique, in order to obtain favorably stable SLN formulations. Solid lipid nanoparticles made from biodegradable solid lipids can be prepared by several methods. Even though the most popular preparation method involves the use of high-pressure homogenization to size down the particles to the submicron range, in this research a simple and efficient high sheer homogenization technique has been used. It is known that high shear homogenization method is usually accompanied by an ultrasound treatment. These combined methods are responsible for the problems that the SLNs obtained generally have leading to a broad particle size distribution, physical instabilities such as particle growth during storage and metal content of samples from ultrasound treatment. Some of these drawbacks may be avoided by using a higher surfactant concentration, but in this case the toxicological implications must be evaluated. In present study, during formation process of emulsion at 80°C, the surfactant concentration has not been increased, different amount of surfactants, varied from 2 to 5% surfactant mixture have been used as parts of the aqueous phase in order to increase the solubility of lipophylic sunscreen compounds.

An adequate characterization of the solid lipid nanodispersion is a necessity for the control of the quality of the final product. The particle size is an important parameter in the process control and particularly in quality assurance, since the physical stability of colloidal dispersions depends on particle size and particle size distribution. Therefore, the particle size parameters of developed SLN dispersions have been evaluated by photon correlation spectroscopy (PCS) based on laser light scattering, immediately after their production (Fig. 2) and these sizes had no significant changes after three months of preserving (at 4°C).

SLNs containing mixtures of individual sunscreens and the selected surfactants possessed a well size distribution (Fig. 2) and excellent particle stability, reflected by zeta potential distribution (Fig. 3). The particles were small and characterized by absence of micrometer particles. The experimental results of the mean diameters prepared using 1% molecular sunscreen with surfactant concentrations of 3% are presented in Figure 2. It was found that the particle sizes produced with different



**Figure 2.** Particle size analysis by dynamic light scattering.



**Figure 3.** The zeta potential distribution of sunscreens loaded-SLN.

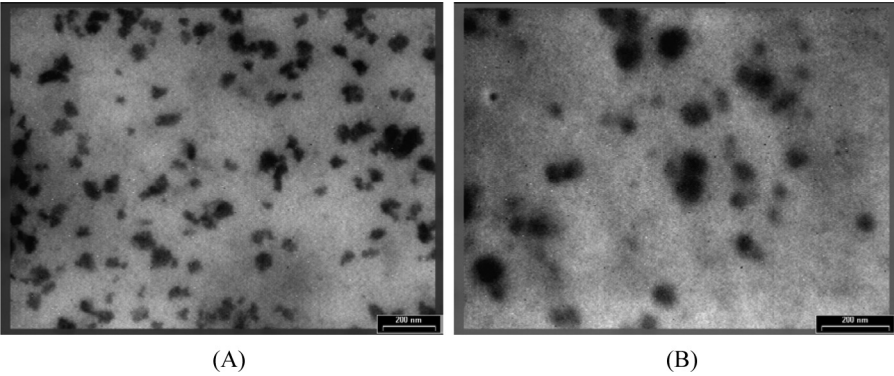
molecular sunscreens were not significantly different, being in the range of 20–250 nm, with good polydispersity indices (0.23 for OCT-SLN, 0.20 for OMC-SLN, 0.22 for BEMT-SLN). The average diameter sizes for OCT-SLN was 102 nm (95.4%), for OMC-SLN of 67 nm (96%) and 75 nm (96.5%) for BEMT-SLN, respectively, with a tail with average diameters between  $18 \div 26$  nm (<4.6%) (Fig. 2).

Zeta potential (ZP) reflects the electric charge on the particle surface, being a key factor to evaluate the physical stability of colloidal dispersions. When the absolute value of ZP is higher than  $\pm 30$  mV for colloidal formulation, the particles are electrochemically stable under the investigated conditions [26]. The physical stability of sunscreen loaded SLN suspensions was excellent. The zeta potential values were less than 30 mV, the mean zeta potentials of the loaded SLNs were  $-61$  mV for OCT-SLN,  $-72$  mV for OMC-SLN, and  $-52$  mV for BEMT-SLN, respectively (Fig. 3). These values demonstrated that the SLN dispersions obtained by modified-HSH method is a physically stable system. Moreover, after three month of preserving at  $4^{\circ}\text{C}$ , there were no visible aggregation in the nanoparticles suspension/system during storage and the size averages did not significantly change compared to the initial particle size. For instance, the particle size after three months of OMC-SLN was 67 nm (average size diameter), as comparing to the measurements after one day of preparation (74 nm) and 75 nm for BEMT-SLN, as comparing to 81 nm (the graphic not shown here).

In the Figure 4 the TEM images of the lipid nanoparticles loaded with OCT and BEMT sunscreen agents are shown. The diameters of the particles observed in the micrographs are in good agreement with the DLS results (Figs. 2 and 3). Figure 4A and B illustrate that almost all the particles have an average size less than 100 nm in each system and there is a low possibility for aggregation. Furthermore, in case of BEMT-SLN it is obviously that the particles investigated are round and homogeneous in their shape, the particle size ranging approximately from 50 to 80 nm.

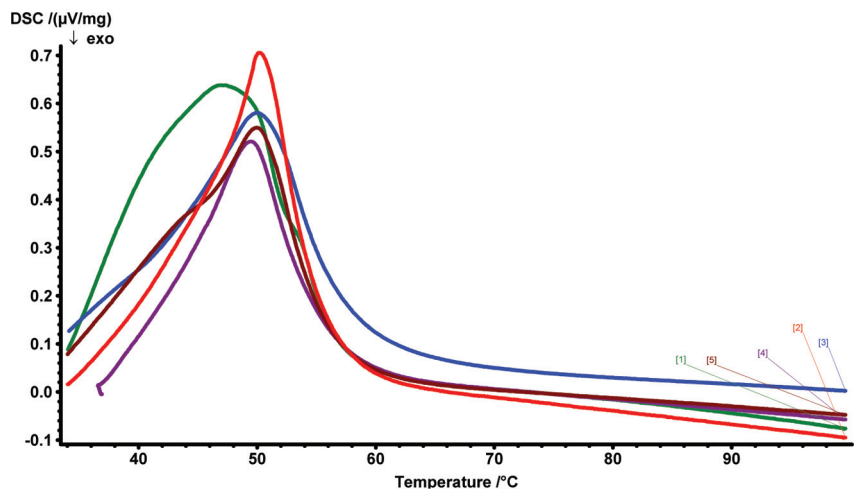
The phase behavior of a lipid matrix system is highly influenced by the presence of guest molecules and the related thermodynamic variables (melting temperature and enthalpy changes), are dependent on the nature of the interactions among the constituents. In this context, in order to evaluate the crystallinity degree of lipid mixture, DSC analysis was performed. Figure 5 shows an overview of the melting process of bulk lipid matrix (physical mixture of CP and GS), lyophilized unloaded SLN and sunscreen loaded SLNs. The bulk lipid material exhibits a broad melting





**Figure 4.** Transmission electron microscopy micrographs of lipid nanoparticles: (A) OCT loaded into SLN; (B) BEMT loaded into SLN.

range, while the SLNs samples have a maximum peak at 50.2°C (for unloaded SLN), 49.9°C (for OCT-SLN), 49.5°C (for OMC-SLN) and 50°C, with a weaker peak at about 44.3°C (for BEMT-SLN), respectively. From DSC curves (Fig. 5) it may be observed that the crystallinity was differed in the bulk lipid mixture, free-SLN and loaded-SLN, due to the presence of surfactants and organic sunscreens in their compositions. The surfactants presence confers a highly ordered arrangement of lipid network, as can be seen by the tightening of melting range, as compared with physical mixture of lipids. Moreover, by comparing the unloaded-SLN with loaded sunscreen SLNs, it may be observed that the incorporation of selected UV absorbers inside solid lipid matrix had lead to a decrease of crystallin arrangement, pointed by the decrease of endotherm peaks intensity.

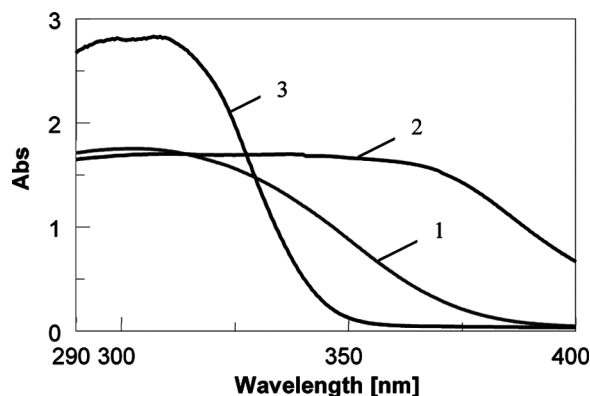


**Figure 5.** Thermal analysis of loaded SLN samples with sunscreen agents: 1. physical lipid mixture; 2. unloaded SLN; 3. OCT-SLN; 4. OMC-SLN; 5. BEMT-SLN.

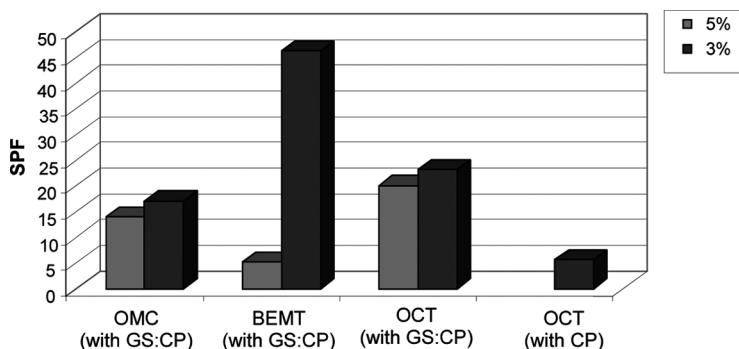
### 3.2. SPF Evaluation and Photostability of Potential Cosmetic Formulations with Sunscreen-SLNs

SPF is the most reliable indicator of the efficacy of sunscreen filters. In general, the SPF number approximately corresponds to the multiple of time during which the sunscreen will prevent obvious reddening of the skin, over the exposure time that causes unprotected skin to exhibit reddening [27]. There is some differences between the specific blocking action of various sunscreen agents. The fotoprotection substances act on two directions: by absorbtion of radiations (organic sunscreen) or by diffusion/dispersal of radiations (inorganic sunscreen) [28]. The use of only one type of sunscreen agent, does not assure a bloking effect of both UVA and UVB radiations. Most commercially available sunscreens provide excelent protection against UV-B, but not all of them are effective against UV-A. Usually, from commercial point of view, this drawback is eliminated by realization of some combinations between different organic and inorganic substances, that assure a protection on large UVA and UVB domain. High-SPF sunscreens always contain a physical filter and at least two organic filters: one with optimal screening for UVB wavelengths and the other for UVA photons [15]. In our study, the experimental researches were carried out in order to avoid the simultaneous use of inorganic and organic compounds. The UV-absorber loaded into SLNs contain only one type of active ingredient, in concentration lower than the maximum concentration (10%) admitted by International Agency of Food and Drug Administration (FDA) [29]. The UV spectra of the liophylized SLN formulation containing 7% molecular sunscreen agents incorporated in the lipid matrix are shown in Figure 6. In all the experiments, the inglobation of OMC, OCT and BEMT into SLN has lead to an over additive UV-bloking effect (synergistic UV-blocking behavior, determined by the presence of complex structural lipids), this demonstrating that the prepared sunscreen-SLNs are promising carrier systems for cosmetic formulations. Moreover, by using BEMT agent, the bloking effect is realized on a broad UV-A and UV-B spectrum and the concentration of the molecular sunscreen can be decreased by 30%, with maintaining at the same time of the absorption level.

The SPF values for liophylised SLNs prepared with two surfactant concentrations, are presented in Figure 7. The best results were obtained by using a lower



**Figure 6.** Wavelength scans of liophylised sunscreen-SLNs containing 7% sunscreen 1. OCT-SLN; 2. BEMT-SLN; 3. OMC-SLN.



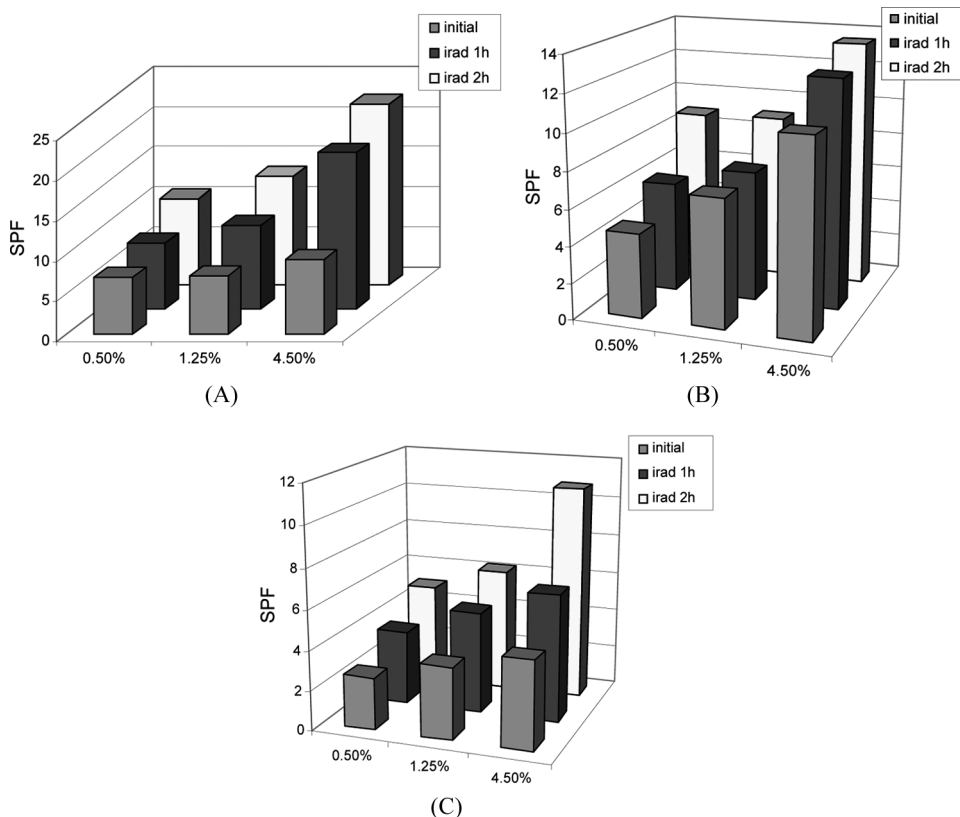
**Figure 7.** The SPF values for liophylized sunscreen SLNs, prepared by using 3% and 5% surfactant concentrations.

content of 3% surfactant for preparation of SLN dispersions. It was observed that for a maximum content of 7% active ingredient in liophylised SLNs samples, high SPF values were obtained:  $\text{SPF} = 23.1$  for OCT-SLN (that assures a blocking effect of 94% from UVB radiation),  $\text{SPF} = 46.2$  for BEMT-SLN SLN (that assures a blocking effect of 97%) and a lower value for OMC-SLN ( $\text{SPF} = 17$ ). A possible explanation for the decrease of SPF values of samples with high content of surfactant may be given by the fact that by increasing the surfactant amount from 3% to 5%, but keeping constant the lipid content (10%), the surface of SLNs will be too small to adsorb all the surfactant molecules and sunscreen micelles (without lipid contribution) can be formed, thus leading to a reduction of the incorporation efficiency of sunscreen into SLN.

While most published data presented the SLN preparation with glyceride lipids, little knowledge is reported on wax carriers. Thus, starting from the literature remarks [12] that underline the ability of cetyl palmitate SLN particles to reflect and scatter the UV radiation on their own, without the need of a molecular sunscreen, a comparative sample of SLN was prepared only by using cetyl palmitate as lipid matrix. In this case is more evident the role of a lipid mixture in preparation of loaded SLN with high photoprotection effect. The SPF value for the OCT-SLN prepared with only cetyl palmitate was significantly reduced ( $\text{SPF} = 5.6$ ). This decrease may be explained by the difficulty experimentally encountered at spreading of cream film on the support surface. On the other hand, it was confirmed [30] that by mixing some complex solid lipids with differently structured (sized) molecules can prevent the formation of a perfect crystalline network, thus providing a less ordered network with some imperfections appropriate to accommodate the active guest molecule inside the lipid matrix.

Photochemical stability of UV – radiations absorbers is in attention of the latest researches regarding the photoprotection action of new nanostructured carriers that may lead to a new generation of photoprotection agents with a larger action spectrum and a superior protection capacity. In order to determine the influence of sunscreen encapsulation on SPF properties and photostability, the advanced sunscreen-SLN activators prepared in this study (with different amounts of absorber) have been incorporated in an appropriate cosmetic carrier (a cream base). The photostability of developed cosmetic formulations based on sunscreen-SLNs has been evaluated by exposure to a photochemical UV irradiation at a low energy,

simultaneously with providing an improved safety profile by using a low sunscreen content (0.5 – 4.5%). The effect of irradiation conditions on the SPF properties of the cosmetic formulations (Fig. 8) was examined on wavelength range of 290–400 nm, by irradiation in simulated sun tanning conditions (encountered in the middle day). The results shown in Figure 8 have demonstrated that after UV irradiation, the photoprotective effect have been significantly increased in all the samples, as comparing to formulations before irradiation (more evident for a prolonged irradiation period). For instance, this increase in SPF index has reached a more than double value: in case of BEMT – SLN,  $\text{SPF} = 10.8$  ( $\text{SPF}_{\text{initial}} = 4.4$ ); for OCT – SLN,  $\text{SPF} = 22.5$  ( $\text{SPF}_{\text{initial}} = 9.4$ ), respectively. This increase of SPF after irradiation may be the consequence of a structural rearrangement based on the fact that screen molecules contain  $n/\pi$  conjugated electrons that are excited at a certain wavelength. Moreover, it is well known that most of the active ingredients manifest a good photostability [31], excepting azobenzenes and oxycinnamates derivatives that need a chemical stabilizer such as octocrylene or other photostabilisers [32]. Upon exposure to UV light the active ingredients from a sunscreen that are usually aromatic molecules conjugated with carbonyl groups, do not undergo significant chemical change, allowing these ingredients to retain the UV-absorbing potency without significant photodegradation [33].



**Figure 8.** The photostability of developed cream formulations with different sunscreen concentrations: (A) OCT-SLN; (B) OMC-SLN; (C) BEMT-SLN.

#### 4. Conclusion

The modified-HSH technique used for the production of solid lipid nanoparticles loaded with sunscreen products is an appropriate procedure to obtain small particles stabilized with non-ionic surfactants and phospholipid, without the need for a supplementary ultrasound treatment. All the colloidal systems of nanoparticles have presented zeta potential values less than  $-50$  mV, which indicated a high stability of prepared SLNs dispersions. The mean particle size was found to be less than  $100$  nm with a relatively narrow particle distribution of polydispersity index ( $PDI < 0.23$ ).

For a maximum content of 7% active ingredient in lyophilized SLNs samples, high SPF values were obtained ranging between 17 and 46. The crystallization of sunscreen inside the lipid core improved the SPF values by more than twice in lipid samples after irradiation. Thus, it is possible to obtain a good photoprotection effect, an improved photostability and a lower allergenic potential by using less than half of maximum admitted concentration imposed by FDA regulations (10%) and without being necessary a contribution of an inorganic UV blockers.

The inclusion of OMC, OCT and BEMT into solid lipid nanoparticles has led to an over additive UV blocking effect, this demonstrating that the prepared sunscreen-SLNs are promising carrier systems for cosmetic formulations. Moreover, in case of BEMT-SLNs, the concentration of molecular sunscreen from a cosmetic formulation can be significantly decreased thus avoiding the side effects on skin, with maintaining the protection level assured by the high SPF values.

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