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Note

The development of an improved carrier system for sunscreen formulations based on crystalline lipid nanoparticles

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Abstract

The aim of this study was the in vitro evaluation of the efficacy of two different carrier systems for the molecular sunscreen benzophenone-3. One carrier system was a conventional o/w emulsion, the other consisted of highly crystalline lipid nanoparticles (CLN). It was observed that CLN act as physical sunscreens themselves and show improved photoprotection compared with a placebo emulsion with the same lipid content. Incorporation of a molecular sunscreen further improves the protection level in a synergistic way. This in vitro study based on the Transpore™ test by Diffey showed that the amount of molecular sunscreen can be decreased by up to 50% while maintaining the UV protection efficacy. Therefore, the use of CLN as an active carrier for sunscreens is a promising innovation.

Keywords: Lipid nanoparticles; Sunscreens; Photoprotection

Photoprotection has become an essential topic in daily life due to the worldwide decrease of the ozone layer and the resulting increase of skin cancer incidents (Finlay-Jones and Hart, 1998). Sunscreens are used on a regular basis by millions of people. Regarding long-term and frequent use, particular attention has to be paid to their efficiency and safety.

Many molecular sunscreens penetrate into the skin causing photoallergies, phototoxic reactions and skin irritations (Wolf, 1999). Therefore, there is an urgent need for the development of safer sunscreen systems. This can be achieved by formulations that penetrate less into the skin or by formulations with a reduced amount of potentially dangerous molecular UV blocker while maintaining the sun protection factor by other means, e.g. carriers with sunblocking characteristics (Mariani et al., 1998).

Solid lipid nanoparticles have been introduced as carriers for various pharmaceutical and cosmetic actives (Müller et al., 1995). It has been found that these lipid nanoparticles act as physical sunscreens on their own, i.e. they have the ability of scattering/reflecting incoming UV radia-

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tion (Wissing and Müller, 2001). Their scattering properties depend strongly on the degree of crystallinity of the lipid matrix (unpublished data). Therefore, it is desirable to incorporate a molecular sunscreen in a highly crystalline lipid matrix.

In this in vitro investigation the effectiveness of a highly crystalline nanoparticulate carrier for the molecular sunscreen benzophenone-3 was investigated. Benzophenone-3 is a widely used lipophilic wide-band sunscreen. The well known Transpore™ test by Diffey (Diffey and Farr, 1991) served as a valuable tool to analyze by what percentage the amount of benzophenone-3 can be decreased compared with a reference emulsion while maintaining the same protection level.

Tripalmitate (Dynasan 116, Condea, Germany) and medium chain triglycerides (Miglyol 812 Beiersdorf, Germany) were used as lipid bases. Tyloxapol (Sigma, Germany) was used as emulsifiers for the formulations. The molecular sunscreen benzophenone-3 was obtained from Merck, Germany. Water was supplied by a Millipore MilliQ-Plus. Transpore™ tape was purchased from 3 M Medica, Germany.

Crystalline lipid nanoparticles (CLN) and emulsion systems were produced by the hot homogenization technique (500 bar, 3 cycles, 85 °C) on a Micron Lab 40 (APV Gaulin, Germany) as described by Müller et al. (1997). The formulations contained 20% Dynasan 116 (D) or Miglyol 812 (M) as lipid phase, 5% tyloxapol (T) and up to 20% benzophenone-3 (B) with regard to the lipid phase.

Particle size was analyzed by photon correlation spectroscopy (PCS) using a Zetasizer 4 (Malvern, Germany) and by laser diffraction (LD) using a Coulter LS230 (Coulter, Germany). The average size (z-ave) and polydispersity index (PI) are shown in Table 1. Fig. 1 shows LD50, LD95, LD99-values which were also used as quality parameters. LD50 means that 50% of the particles are smaller than the given size. It can be seen that benzophenone-3 was successfully incorporated into physically stable CLN dispersions and emulsions with a narrow size distribution in concentrations up to 20% with respect to the lipid matrix. Particle size in the CLN dispersions was clearly smaller than in the emulsions as can be seen in Fig. 1. The CLN dispersion contains only nanoparticles whereas some microparticles can be found in the emulsion suggesting decreased long term stability. However, incorporation of benzophenone-3 has a stabilizing effect on the emulsions (reduced content of micrometer droplets).

Table 1
PCS data of investigated CLN (DT) dispersions and emulsions (MT)

Formulation	z-ave (nm)	PI
DT	155 ± 2	0.168
DTB5%	154 ± 2	0.181
DTB10%	166 ± 2	0.198
MT	193 ± 2	0.229
MTB10%	152 ± 2	0.191
MTB20%	152 ± 2	0.173

Parameters shown are the average PCS size (z-ave) and polydispersity index (PI).

For the Transpore in vitro assay, samples were evenly applied on Transpore™ tape (2 mg/cm^2) which was mounted on quartz cuvettes. After a 15 min drying period, the samples were scanned from 450 to 280 nm using a Uvikon 940 double-beam spectrophotometer (Kontron, Germany).

Fig. 2 shows the results of the Transpore™ assay performed with the placebo formulations. As expected, the CLN are stronger scatterers/reflectors of UV radiation and thus show higher absorption values than the emulsion.

Wavelength scans of the formulations containing benzophenone-3 acquired with the Trans-

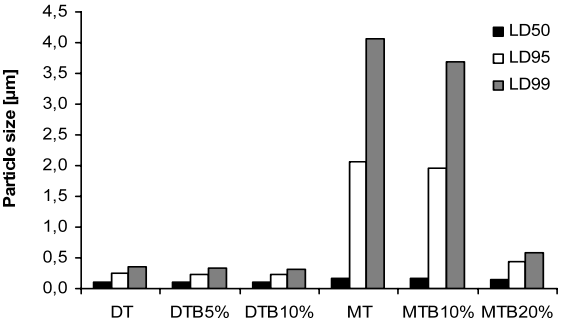

Fig. 1. Laser diffraction (LD) data of investigated CLN formulations (DT) and emulsions (MT) containing up to 20% benzophenone-3 (B). LD50 means that 50% of the particles are below the given size.

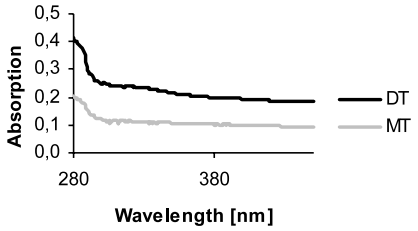

Fig. 2. Wavelength scans of placebo CLN (DT) dispersion and emulsion (MT) obtained by the Transpore™ assay.

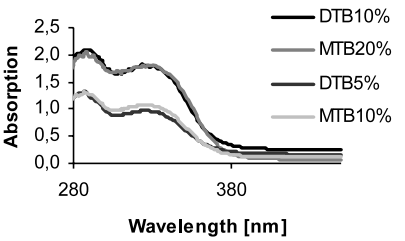

Fig. 3. Wavelength scans of CLN (DT) dispersions and emulsions (MT) containing up to 20% benzophenone-3 (B) obtained by the Transpore™ assay.

pore™ assay are shown in Fig. 3. In all formulations, the characteristic absorption pattern of benzophenone-3 is clearly visible. Comparison of the emulsion scans with the CLN scans shows that incorporation into a CLN formulation leads to improved, synergistic photoprotection.

Incorporation of 5% (10%) benzophenone-3 into the CLN dispersion leads to the same absorption values as 10% (20%) benzophenone-3 in the emulsion. The amount of benzophenone-3 can be reduced by 50% while maintaining the protection level.

Concluding, it can be remarked that in vitro investigations have shown that the use of highly crystalline lipid nanoparticles as carriers for molecular UV blockers offers the possibility of creating more effective and safer sunscreen formulations with reduced UV blocker content. This is due to the fact that CLN act as physical sunscreens (i.e. reflectors/scatterers) and, therefore, represent an active carrier for molecular sunscreens. The results obtained with this study are promising for future in vivo studies and for the development of innovative, better tolerated sunscreen products for the consumer market.

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