Effect of hydroxypropyl-β-cyclodextrin on butyl methoxydibenzoylmethane skin permeation from lipid microparticles

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Rationale

Butyl methoxydibenzoylmethane (BMDBM), the most widely used UVA absorber, has been shown to be photo-unstable and to exhibit appreciable permeation into human stratum corneum and viable epidermis. In earlier investigations we demonstrated that complexation of BMDBM with hydroxypropyl-β-cyclodextrin (HP-β-CD) reduced the sunscreen degradation under simulated sunlight, although no significant influence on the percutaneous penetration of the UVA filter was observed. However, the photostabilizing effect on BMDBM produced by its complexation with HP-β-CD decreased following its incorporation in an emulsion vehicle, probably due to the competitive displacement of the UV filter from the cyclodextrin cavity by the formulation excipients. This drawback was overcome by incorporation of the BMDBM/HP-β-CD complex in lipid microparticles, particles in the micrometer size-range consisting of a solid fat core stabilized by a layer of surfactant molecules at the surface.
The purpose of this study was to evaluate whether the encapsulation of the BMDBM/HP-β-CD complex into lipid microparticles could also affect the skin permeation of the sunscreen agent. The lipoparticles loaded with the complex between BMDBM and the cyclodextrin were incorporated in a model emulsion formulation and their influence on the UV filter percutaneous penetration was assessed \textit{in vivo} by the tape-stripping technique. For comparison purposes formulations containing the non-encapsulated BMDBM/HP-β-CD complex or lipoparticles loaded with uncomplexed BMDBM were also prepared and examined.
Lipoparticle preparation

Melt emulsification technique (80°C)

Phosphate buffer (0.1 M, pH 7.4 + 2% (w/v) hydrogenated soybean phosphatidylcholine

Tristearin (3.6 g) + BMDBM (1.2 g) or BMDBM/HP-β-CD complex (2.4 g)

13500 rpm for 3 min
Lipoparticle morphology and size
BMDBM physical state, loading and distribution

BMDBM was found in a nearly molecular dispersion (Differential Scanning Calorimetry) and homogeneously distributed inside the lipoparticle structure (optical videomicroscopy coupled with epifluorescence, magnification: X 100)

Loading level: 20.40 ± 1.2 % (w/w) for BMDBM alone
3.85 ± 0.6 % (w/w) for BMDBM/HP-β-CD complex
BMDBM

*in vitro* release

Release medium: Miglyol 812

![Graph showing in vitro release of BMDBM lipoparticles and BMDBM/HP-β-CD lipoparticles](image-url)
Tape-stripping test (1)

In vivo penetration studies were performed on creams (oil-in-water emulsions) containing BMDBM (0.5%, w/w) or its complex with HP-β-CD, non-encapsulated or loaded in lipoparticles. The emulsion excipients were: sorbitan monostearate (2%), polyoxyethylene sorbitan monostearate (4.5%), butylated hydroxyanisole (0.02%), isopropyl istostearate (9.0%), cetearyl isononanoate (8.0%), cetearyl alcohol (7.0%) for the internal phase and sodium benzoate (0.1%), glycerin (2.0%), dehydroacetic acid (0.1%), EDTA (0.1%) and water (66%) for the external phase.

- Volunteer number: 6
- Application area: 2 x 5 cm, volar forearm
- Dose: 2 mg/cm²
- Application time: 30 min
- Strip number: 10
- BMDBM analysis: extraction with methanol-acetonitrile and HPLC
Tape-stripping test (2)

![Graph showing penetration of BMDBM and its combinations across different strips.]

- **BMDBM**
- **BMDBM/HP-beta-CD**
- **BMDBM/lipoparticles**
- **BMDBM/HP-beta-CD/lipoparticles**

The graph displays the percentage of applied dose (%) penetrated into the BMDBM across different strips (2-4, 5-7, 8-10). The data is represented with error bars indicating variability.
Conclusions

From the data reported in this study it can be deduced that the incorporation of BMDBM as HP-β-CD complex into lipid microparticles decreases the sunscreen penetration into the stratum corneum. Since the concentration present in the stratum corneum is related to the fraction that reaches the deeper viable skin tissues and the systemic circulation, the obtained results suggest that lipoparticles loaded with complexed BMDBM reduce the percutaneous absorption of the sunscreen agent. This effect not only enhances the protective power of the UVA filter by retaining it at the skin surface, but also limits potential toxic reactions. The latter factor is particularly relevant for BMDBM, since this sunscreen agent generates free radicals when exposed to sunlight.

References


