BENZOPHENONE-3 AND RETINYL ACETATE SKIN PERMEATION AND ACCUMULATION

C. Padula, N. Campana, P. Santi

Department of Pharmacy, University of Parma, Italy

Introduction

Chronic exposure to the sun accounts for 80% of facial photoageing (1); despite the controversy, photoprotection, including both sun avoidance and broad-spectrum UVA/UVB sunscreen use, remains an important part of photoageing prevention (2).

Benzophenone-3 (BP3) is a broad-band UV filter widely used in sunscreen preparations alone or in combination with other UV filters. It can also be used in cosmetic products to ensure stability (concentration range between 0.05-0.5%) and in day creams and lipsticks to prevent premature ageing in particular in association with retinoids. Retinoids are natural or synthetic vitamin A derivatives and represent the most effective non surgical treatment approach for photoaged skin. Although retinol and its esters are less effective than retinoic acid, they have a better tolerance profile and can be easily metabolized to retinoic acid, the biologically active form of vitamin A (3).

Aim of the work

The aim of this work was to evaluate **skin permeation** of benzophenone-3 (**BP3)** and retinyl acetate (**RA**) and their accumulation in **stratum corneum**, **epidermis** and **dermis** of pig ear skin from different formulations.

Methodology

Permeation experiments

- Franz type diffusion cells
- Membrane: pig ear skin
- Receptor: PBS pH 7.4 + 5% (w/w) DMβCD
- Temperature: 37°C
- Time: 6 hours
- Donor: 1 ml Pluronic® F127 10% (w/w) solution(BP3 0.15%, RA 0.06%)
  1 ml Formulation 1
  1 ml Formulation 2

Components	Formulation 1 (F1)	Formulation 2 (F2)
Phase A		
Caprylic-Capric triglyceride	4.90	4.90
Cetearyl isononanoate	4.90	4.90
Liquid paraffin	9.80	9.80
Tween 80	0.18	0.18
Benzophenone-3	0.15	0.15
Retinyl acetate	0.24	0.24
Phase B		
Water	70.92	-
Pluronic F127 10% water solution	-	70.92
EDTA disodium salt	0.1	0.1
Pemulen	0.24	0.24
Carbomer	6.12	6.12
Phase C		
Polysorbate-20	0.98	0.98
Liquapar PE	0.98	0.98
Phase D		
Triethanolamine	0.49	0.49

At the end of permeation experiments, the excess of formulation was removed and the skin surface cleaned with isopropyl alchool.
Sixteen strips were taken in correspondence of the treated area. After stripping, the epidermis was heat separated from the dermis.

Extraction conditions

- **Stratum corneum**:
  1 ml of methanol @ room temp. for 60 min
- **Epidermis**:
  1 ml of methanol @45°C for 60 min
- **Dermis**:
  1 ml of acetone @ 45°C for 60 min

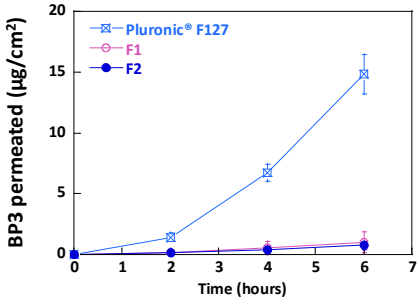
HPLC analysis

- NovaPak® C18 column
- Flow rate: 1 ml/min
- UV detection @ 325 nm
- Gradient elution:
  0-7 min A-B (60:40, v/v)
  7-10 min linear change to A-B (85:15, v/v)
  22-25 min linear change to A-B (60:40, v/v)

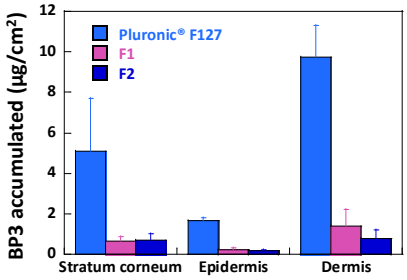
  A: H_2O containing 1% v/v of CH_3COOH
  B: acetonitrile

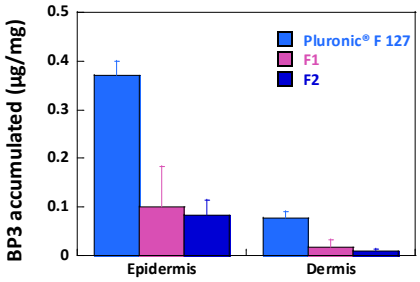
Results

BP3 permeated
(mean values±DS)

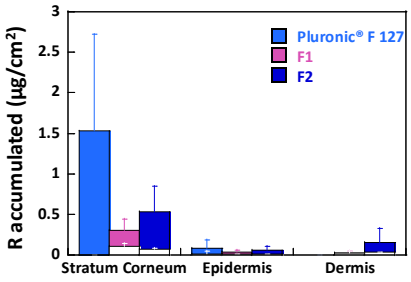


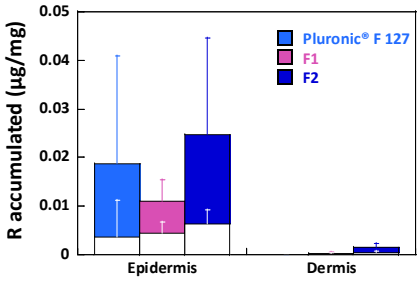
BP3 accumulated
(mean values±DS)





RA accumulated
(mean values±DS)





The colored portion of the column represents the amount of RA recovered, while the white pert indicates the amount of R originated after metabolism.

Conclusions

✓BP3 was found in the receptor compartment. The amount permeated was higher from Pluronic® F127 solutions than from emulsions.

✓The sunscreen was found in the stratum corneum, epidermis and dermis: the amount accumulated was higher in the case of Poloxamer solution compared to the emulsions.

✓In the case of emulsions, the presence of Pluronic® F127 did not influence the permeation of BP3 nor the accumulation in the skin.

✓RA was not found in the receptor compartment.

✓RA was found in the stratum corneum and in the epidermis and, in the case of emulsions also in the dermis.

✓In almost all tissues RA was accompanied by retinol, derived from enzymatic hydrolysis.

References

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3. Connor MJ and Smit MH. *Biochem. Pharmacol.* 1987; 36: 919-924.

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