

Oleic acid-based microemulsions for imiquimod skin delivery: an in vitro study

I.Telò, S. Nicoli, C. Padula, P.Santi

Dept. of Pharmacy, University of Parma, Parco Area delle Scienze, 27/A, 43124 Parma

isabella.telo@gmail.com

Purpose

Imiquimod (IMQ) is a toll-like receptor-7 agonist, approved for the treatment of actinic keratosis. The aim of this work was to develop a new formulation using microemulsion technology in order to increase IMQ skin retention and reduce the applied dose.

Methods

COMPONENTS	MICROEMULSION		
	1	2	3
OLEIC ACID	70	10	50
TRANSCUTOL	14	35	22,5
TWEEN 80	14	35	22,5
WATER	2	20	5

Table 1. Microemulsions composition (%v/v)

Microemulsions preparation: Transcutol and oleic acid were mixed under magnetic stirring, then Tween 80 was added. The mixture was then diluted with water (Table 1). Excess of IMQ was added to the final formulation and left under stirring overnight then centrifuged and analyzed.

IMQ skin accumulation: experiments were performed at 37°C using vertical diffusion cells. Porcine skin was used (full-thickness and tape stripped (ts)).

Different formulations were tested: Imunocare® at finite or infinite dose, saturated solutions in Transcutol, Tween 80, oleic acid, and saturated microemulsions. Cells were dismantled after 6h, skin was separated in epidermis and dermis and extracted overnight with a validated method.

Results

IMQ accumulation from Imunocare® (5%w/w) (Fig 1) was not influenced neither by the dose nor by the presence of stratum corneum. The results obtained show that IMQ has a high solubility in

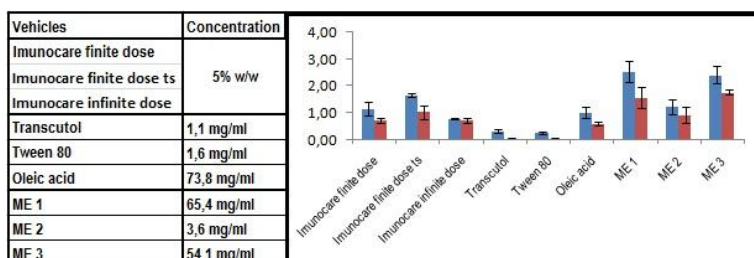


Fig 1. µg/cm² accumulated in epidermis and dermis from different vehicles.

oleic acid and from this vehicle skin retention is comparable to Imunocare®. The amounts of IMQ accumulated from microemulsions are higher than the ones recovered from

the single excipients. In particular, the amount

accumulated with ME2, despite the very low donor concentration, is comparable with the one obtained with Imunocare®. Higher amount were recovered from the application of ME1 and 3.

Conclusions

IMQ is characterised by very poor skin penetration properties. Stratum corneum seems not to act as a barrier for IMQ accumulation. From the results obtained, microemulsions seem to be able to increase IMQ skin retention and can be evaluated as an alternative vehicles for IMQ dermal application.