Hexamidine dihydrochloride – what is it?

It is the result of the in-house purification of hexamidine disethionate (HEX D), a commercially available ingredient present in personal care formulations.

Traditionally used as a biocide in topical preparations since 1950

Recent evidence of effects in skin homeostasis

- Inhibitory effect on inflammatory proteases
- Role in skin ageing
- In vivo studies showed improvement in skin barrier function (with other ingredients)

Topical delivery profile has not been studied

Interaction with different CPEs remains unexplored

Which salt is more appropriate for skin delivery?

I. Introduction & Objectives

II. Methods

Single solvent systems

- PG
- PEG
- GLY

Binary solvent systems

- PG:PGML
- PEG-200:PGML

Infinite dose (250 µL)

32 ºC WATER BATH

TC

Skin surface

Extraction

Donor residual + 3x Washing

HPLC analysis

Total recovery (%)

32 ºC WATER BATH

Solvent systems 50:50 (PG:PGML, PEG-200:PGML, GLY:PGML)

No permeation was observed for the solutions of HEX H, and more than 85% of the applied dose was recovered from the skin.

Fig. 1. Mass balance of 0.1% HEX H after 48h permeation for single solvent systems, expressed in % recovery. 4<n<5

Skin total recovery was not statistically different from skin surface recovery. There was no statistical difference either among the three solvents for the skin extraction of the active (individual samples t-test, p > 0.05)

II. Methods

In vitro permeation and mass balance studies with single solvents

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2. In vitro permeation and mass balance studies with binary solvents

   - PG:PGML
   - PEG-200:PGML
   - GLY:PGML

   PGML enhanced skin extraction to up to 70% of the applied dose!

   Fig. 2. Mass balance of 0.1% HEX H after 48h permeation for binary solvent systems 50:50 (PG:PGML, PEG-200:PGML, GLY:PGML), expressed in % recovery. 4<n<5

   PGML is currently used in topical formulations as an emulsion stabiliser, ingredient solubiliser and has shown synergistic enhancing effects with other vehicles such as PG.

   PROPYLENEGLYCOL MONOLAURATE (PGML)

   - Significantly higher skin extraction (up to 75% of the applied HEX H)
   - Specific skin targeting (no permeation was observed)

III. Results

Unsuccessful CPEs in binary systems

- TRANSCUTOL P (TC)
  - Single solvent systems delivered a higher amount of active than binary systems with TC.
  - Widely used CPE with reported excellent solubilising properties and safety records. It was expected to promote topical delivery

- ISOPROPYL ALCOHOL (IPA)
  - Present in many formulations for topical and transdermal delivery
  - Low boiling point – capable of increasing the thermodynamic activity of the compounds
  - IPA did not improve HEX H skin extraction.

- 1,2-PENTANEDIOL (1,2-PENT)
  - Enhancement of delivery for a model hydrophilic compound and dependent to the enhancer’s concentration
  - In this case 1,2-PENT did not improve the topical delivery of HEX H

IV. Conclusions

HEX H did not permeate through the skin.

Only 1 out of 5 sets of binary systems significantly improved the skin extraction compared to the single solvent system, setting PGML as the best option for HEX H skin targeting.

HEX H can be delivered topically more effectively than HEX D using PGML as chemical permeation enhancer

It is key to elucidate the permeation enhancer’s mechanism of action for rational formulation development in the future.

References


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