

In Vitro Absorption Guidelines for Cosmetic Ingredients

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ABSTRACT SUMMARY

In vitro skin absorption studies are designed to measure the penetration (to the skin) and subsequently the permeation (through the skin) of a compound applied topically. This abstract will review the current available guidelines published by three organizations, the OECD (1), the CTFA (2) and the WHO (3).

INTRODUCTION

The evaluation of dermal penetration of compounds from cosmetic and skin care formulation is highly recommended for safety and efficacy assessment. Safety studies are required to assure deposition of the compound in the skin and its minimal further absorption into the blood circulation. Efficacy can be addressed for active compounds that are expected to interact with biological entities in skin sub-tissues.

The *in vitro* method has been shown as appropriate for prediction of human dermal penetration. It saves time; cost and resources in the product design process and is highly reproducible. Understanding the potential absorption of an ingredient can also prevent skin adverse reactions. It can also allow for a better design of the carrier formula, as its effect on skin barrier properties is assessed.

EXPERIMENTAL METHODS

The test compound in the chosen carrier is applied to the surface of a skin sample (cadaver or fresh) that is fixed between two chambers of a diffusion cell. The excised skin is mounted as a barrier between donor and receptor compartments. The amount of test compound and/or its metabolites permeating from the carrier applied to the skin and through

it to the receptor is determined as a function of time.

The carrier formulation remains on the skin for a specified time under precise conditions such as temperature and mixing rate.

For cosmetic preparation a “finite dose” system is utilized. Finite dose studies mimic “in use, real time” situations where a fixed dose of a compound is applied for a specified period of time. Using this regimen, dose depletion is likely to occur. Depending on the vehicle/delivery system, a study protocol can be tailored to determine skin absorption from cosmetic/personal care products to illustrate penetration. During the experiment, the skin needs to be maintained at a physiological temperature of $32\pm 1^{\circ}\text{C}$.

When a semi-solid formulation is tested, $2\text{-}5\text{mg}/\text{cm}^2$ is applied to the surface of the skin; when a liquid is tested, $5\text{-}10\mu\text{l}/\text{cm}^2$ is applied. The donor compartment can be left un-occluded or can be capped or covered to simulate occlusion or semi-occlusion conditions, or when the formulation contains volatile ingredients.

RESULTS AND DISCUSSION

When a finite dose is tested, the mean maximum amount of the applied compound absorbed is determined. This requires a complete recovery of the test substance: 90-110% or 85-115%, according to OECD and SCCNF guidelines, respectively. The protocol requires quantification of the following:

- Quantity washed from the skin
- Quantity associated with the skin
- Amount present in the receptor compartment

Test compound and/or its metabolites should be determined in the following:

- Applicator used for spreading the formulation
- Donor chamber: amount removed following the rinse procedure
- Dose removed from the skin surface
- Stratum corneum when tape stripping is utilized
- Remaining skin sample
- Receptor fluid and receptor chamber
- Volatile compound trap (if present)

When extracting the skin at the end of the experiment, the quantity in the entire epidermal tissue is determined. Separation of the stratum corneum from the viable epidermis can be achieved by tape stripping which will determine the amount deposited in the upper layer of the skin. This can be advantageous for cosmetic formulations or delivery systems that are designed to create a reservoir in the stratum corneum, such as moisturizing agents.

The amount of compound remaining in the skin should be considered as absorbed unless demonstrated that absorption can be determined from receptor fluid alone. The amount absorbed can be expressed in an absolute form such as mg/cm^2 of the skin surface area. For cosmetic product testing, amounts that are retained by the stratum corneum at the time of sampling are not considered to be dermally absorbed and therefore do not contribute to the systemic dose.

CONCLUSION

Skin absorption studies are part of various international regulatory requirements for safety assessment of exposure to chemicals. For topically applied formulations, when the skin is the target of action, assessment of penetration can allow for better product design. Studies can vary significantly with the choice of skin, diffusion chamber, sampling regimen, receptor fluid and more. It is therefore essential to determine the appropriate objective, to integrate physical and chemical properties of the product tested, to design the appropriate study and to correctly interpret the results.

REFERENCES

1. OECD Guidelines for dermal in vitro absorption testing. #428, 2004 (Organization for Economic Cooperation and Evaluation, 2004)
2. CTFA Safety evaluation guidelines, 127-134, 2007 (Cosmetic, Toiletry and Fragrance Association, recently renamed: Personal Care Council, 2007)
3. Environmental Health Criteria 235 on Dermal absorption, WHO, 38-58, 2006 (World Health Organization, 2007)