

Poster: skin models as alternatives to animal testing

## Phototoxicity of essential oils intended for cosmetic use

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The phototoxic potential of chemicals, cosmetics, dietary supplements and pharmaceuticals is a growing concern in the consumer products industry. The determination of phototoxicity in the 3T3 Neutral Red Uptake Phototoxicity Test (3T3-NRU-PT), an *in vitro* test accepted in the EU Member States since 2000 and in the OECD Member States since 2004, is the first step in the sequential phototoxicity testing strategy. The reconstructed human skin model assays represent an important supplement to the 3T3-NRU-PT which may be used in order to obtain additional information on bioavailability of the chemical in human skin and phototoxicity risk related to topical exposure. The 3D human skin models overcome many of the limitations of the 3T3-NRU-PT, as they employ multi-layer tissues that closely parallel human skin morphology instead of a fibroblast monolayer, the human primary keratinocyte-based tissues are a more relevant model than a mouse tumor cell line, and non-aqueous soluble formulations can be tested. However, further investigations are needed in the extrapolation of *in vitro* results to the human situation.

The aim of this study, linked-up with a previous study on bergamot oils (Kejlová et al., 2007), was the evaluation of phototoxic potential of a group of essential oils used as cosmetic ingredients. The applied tiered testing strategy included chemical analysis of the substances (by means of capillary gas chromatography/mass spectrometry), the *in vitro* 3T3 NRU Phototoxicity Test and the EpiDerm™ Skin Phototoxicity Assay, performed according to the pre-validated phototoxicity test design (Liesch et al., 1999). In order to clarify the situation in man, the negative results or the first non-phototoxic concentrations determined by the EpiDerm skin model were confirmed *in vivo* by means of the human skin photopatch test in a limited group of volunteers.

The study revealed, that phototoxicity of the selected essential oils was dependent on the content of photoactive substances (namely geraniol and nerol) and the solvent used. Using aqueous dilutions, a phototoxic classification was obtained *in vitro* and experienced also *in vivo* in the human photopatch test. In higher concentrations, the phototoxic effect was in some cases accompanied by skin irritation reactions.

The 3D human skin model test seems to be a useful tool for consideration of initial concentrations for confirmatory human photopatch tests to prove product safety, however, a safety factor of 10 might be considered for extrapolation.

### References

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