

OPINION OF THE SCIENTIFIC COMMITTEE ON COSMETIC PRODUCTS AND NON-FOOD
PRODUCTS INTENDED FOR CONSUMERS

CONCERNING

THE USE OF ALPHA-TOCOPHEROL ACETATE
IN COSMETIC PRODUCTS

adopted by the SCCNFP during the 18th Plenary meeting
of 25 September 2001

1. Review

1.1. Background

The antioxidant alpha-Tocopherol acetate is the most common form of vitamin E in commercial sunscreen and skin care products.

Studies in mice on the photo-protective effect of topically applied vitamin E compounds indicate that alpha-tocopherol prevents the formation of pre-mutagenic DNA changes, known to be important in skin carcinogenesis.

However, comparative studies with other forms of vitamin E (thermostable esters of vitamin E, alpha-tocopherol acetate or alpha-tocopherol succinate) revealed that neither alpha-Tocopherol acetate nor alpha-Tocopherol succinate prevent photo-carcinogenesis, but may even enhance skin cancer development and growth.

1.2. Terms of Reference

Alpha-Tocopherol and its derivatives are not subject to particular regulation in any of the annexes to Directive 76/768/EEC concerning cosmetic products. Their use falls under Article 2 of the Directive, which says that 'A cosmetic product put on the market within the Community must not cause damage to human health when applied under normal or reasonable foreseeable conditions of use'.

The SCCNFP was asked to review the use of alpha-tocopherol acetate in cosmetic products and to respond to the following questions :

- Does the safety profile documented in the attached submissions support the statement that the use of alpha-tocopherol acetate poses a significant threat to the health of the consumer?
- Does the SCCNFP propose any restrictions or conditions of the use of alpha-tocopherol acetate in cosmetics products.

1.3. Scientific evidence

The effects induced after exposure to UV radiation may differ according to the mode of exposure and include sunburn, immuno-suppression, photo-ageing and photo-carcinogenesis. At the molecular level, UV radiation is responsible for pre-mutagenic damage including the formation of Reactive Oxygen Species (ROS), cyclobutyl rings in adjacent pyrimidines (thymidine dimers) and photo-products. They may also enhance the binding of DNA single strand breaks (SSB) to nuclear proteins and/or contribute to the activation of proto-oncogenes.

In order to reduce and minimise the effects of UV radiation, sunscreen products and other cosmetic products contain UV filters and may contain Vitamin E derivatives.

Vitamin E compounds, that prevent or minimise lipid peroxidation, may cause photo-protection. However, due to the limited stability at room temperature of the native compound alpha-tocopherol, alpha-tocopherol acetate and alpha-Tocopherol succinate are used in cosmetic products.

A recent study in animals has claimed that, following topical application in acetone, alpha-tocopherol acetate and alpha-Tocopherol succinate failed to prevent photo-carcinogenesis and may have enhanced the incidence of squamous cell carcinoma.

Ref. : 1

The following comments are made about this study :

- * absence of a dose-effect relationship;
- * concern about the statistical methodology used, and
- * the results have not been repeated or obtained in independent trials.

These lead to the conclusion that experimental shortcomings may be responsible for the positive results mentioned above. Direct extrapolation to human cannot be made regarding carcinogenicity. The same authors have also pointed that most of the Vitamin E applied to the skin in the ester form accumulates in the skin with little hydrolysis to the free alpha-tocopherol.

A study conducted in human volunteers showed that topically applied alpha-tocopherol acetate is less absorbed by the epidermal and dermal layer of human skin than alpha-tocopherol and that there was little conversion of alpha-tocopherol acetate to its unesterified form : free alpha-tocopherol.

Ref. : 2

As McVean and Liebler have clearly demonstrated, the inhibition of UVB induced thymidine dimers - in a dose-dependent manner - by the free alpha tocopherol, their results also showed a similar effect with alpha-tocopherol acetate and other derivatives (gamma- and delta-tocopherol, alpha-tocopherol methyl ether) qualitatively.

Quantitatively, alpha-tocopherol acetate is about 10 times less potent than free alpha-tocopherol for the prevention of cyclopyrimidine dimers (CPDs) formation from UVB but also UVC radiation.

Ref. : 3

A recent paper demonstrated the variability in the degree of photo-protection of various vitamin E compounds when applied in a 5 % dispersion in a neutral cream vehicle.

Ref. : 4

The photo-protective properties of Vitamin E compounds lead them to be of relevance in the prevention of UV induced skin carcinogenesis. One of them, the free alpha-tocopherol has been shown to reduce significantly the tumour incidence in mice when topically applied whereas one of the naturally transformed thermostable esters, the alpha-tocopherol acetate, did not. The biological relevance in terms of human health of such an animal experiment is questionable due to the experimental shortcomings. The prevention of DNA photodamage by vitamin E compounds and sunscreens are related to the form of topical vitamin E. In this sense, alpha-tocopherol acetate behaves as a less potent inhibitor of cyclopyrimidine dimers formation than the free alpha-tocopherol.

Presently, on the basis of the available literature, the safety profile of alpha-tocopherol acetate is not questionable and no other toxicological data support the animal findings of Gensler, Aickin, Peng and Xu (ref. 1).

2. Opinion of the SCCNFP

On the basis of current knowledge, the SCCNFP is of the opinion that alpha-tocopherol acetate does not pose a threat to the health of the consumer and therefore does not propose any restrictions or conditions on the use of alpha-tocopherol acetate in cosmetic products.

3. References

1. Gensler HL, Aickin M., Peng YM, Xu M, Importance of the form of topical vitamin E for prevention of photocarcinogenesis. *Nutrition and Cancer* 1996; 26(2), 183-191.
2. Alberts DS et al, Disposition and metabolism of topically administered alpha-tocopherol acetate : a common ingredient of commercially available sunscreens and cosmetics. *Nutrition and Cancer* 1996; 26(2) : 193-201
3. McVean M., Liebler DC, Inhibition of UVB induced DNA photodamage in mouse epidermis by topically applied alpha-tocopherol. *Carcinogenesis* 1997 Aug; 18(8) : 1617-1622
4. McVean M., Liebler DC, Prevention of DNA photodamage by Vitamin E compounds and sunscreens : roles of ultraviolet absorbance and cellular uptake. *Molecular Carcinogenesis* 1999 Mar; 24 (3) : 169-176