



EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL
Directorate C - Public Health and Risk Assessment
C7 - Risk assessment

SCIENTIFIC COMMITTEE ON CONSUMER PRODUCTS

SCCP

Opinion on

***Tagetes erecta, T. minuta and T. patula* Extracts and Oils
(phototoxicity only)**

Adopted by the SCCP
during the 4th plenary of 21 June 2005

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1. BACKGROUND

During the 18th Plenary meeting of 25 September 2001, the SCCNFP¹ adopted an opinion (SCCNFP/0392/00 final) on an initial list of perfumery materials to be included in Annex III to Directive 76/768/EEC.

Following a review of the list, the SCCNFP adopted an updated opinion (SCCNFP/0770/03) during the 26th plenary meeting of 9 December 2003. The SCCNFP asked for additional information to allow further evaluation of fragrance ingredients.

In June 2004, the European Flavour & Fragrance Association submitted additional information on the following fragrances:

- Methylhydrocinnamic aldehyde
- Tagetes absolute, Tagetes minuta absolute and Tagetes oil
- Opoponax
- Storax

2. TERMS OF REFERENCE

- *On the basis of currently available information, the SCCP is asked to assess the risk to consumers when Methylhydrocinnamic aldehyde, Tagetes absolute, Tagetes minuta absolute, Tagetes oil, Opoponax or Storax are present in cosmetic products, and if necessary, to revise the maximum concentration in fragrances used in cosmetic products considering the concentration limits or other restrictions suggested by industry.*
- *Does the SCCP recommend any further restrictions with regard to the presence of Methylhydrocinnamic aldehyde, Tagetes absolute, Tagetes minuta absolute, Tagetes oil, Opoponax or Storax as an ingredient of fragrances used in cosmetic products?*

¹ SCCNFP - Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumer

3. OPINION

3.1. Chemical and Physical Specifications

3.1.1. Chemical identity

3.1.1.1. Primary name and/or INCI name

This opinion concerns the following fragrance ingredients according to EU Inventory Names (*):

1. *Tagetes erecta* Flower Extract (EU Inventory Name)
2. *Tagetes erecta* Flower Oil (EU Inventory Name)
3. *Tagetes minuta* Flower Extract (EU Inventory Name)
4. *Tagetes minuta* Flower Oil (EU Inventory Name)
5. *Tagetes patula* Flower Extract (EU Inventory Name)
6. *Tagetes patula* Flower Oil (EU Inventory Name)

(*) The complete EU Inventory entries are given in the Appendix.

3.1.1.2. Chemical names

1. *Tagetes erecta* Flower Extract is the extract obtained from the flowers of the plant, *Tagetes erecta*, *Compositae*
 2. *Tagetes erecta* Flower Oil is the essential oil obtained from the flowers of the plant, *Tagetes erecta*, *Compositae*
 3. *Tagetes minuta* Flower Extract is the extract obtained from the flowers of the plant, *Tagetes erecta*, *Compositae*
 4. *Tagetes minuta* Flower Oil is the essential oil obtained from the flowers of the plant, *Tagetes minuta*, *Compositae*
 5. *Tagetes patula* Flower Extract is the extract obtained from the flowers of the plant, *Tagetes erecta*, *Compositae*
 6. *Tagetes patula* Flower Oil is the essential oil obtained from the flowers of the plant, *Tagetes erecta*, *Compositae*
- The above definitions include all types of extracts (Tinctures, Concretes, Resinoids, Pomades, Absolutes, Rectified extracts etc.) and all types of Essential Oils (obtained either by dry-distillation or by steam-distillation, flash pasteurization etc.).

3.1.1.3. Trade names and abbreviations

Tagetes Oil (synonym of *T. erecta*, *T. patula*, and *T. glandulifera* Schrank Flower Oils)
 Marigold Oil (synonym of *T. erecta*, and *T. patula* Flower Oils)
 Tagetes Minuta Absolute (synonym of *T. minuta*, and *T. glandulifera* Schrank Flower Extracts)
 Tagetes Minuta ext. (synonym of *T. minuta*, and *T. glandulifera* Schrank Flower Extracts)
 Tagetes Patula Absolute (for *T. patula* Flower Extract)
 Tagetes Minuta ext. (synonym of *T. patula* Flower Extract)

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3.1.1.4. CAS / EINECS number

1.	<i>T. erecta</i> Flower Extract	CAS	:	90131-43-4
		EINECS	:	290-353-9
2.	<i>T. erecta</i> Flower Oil	CAS	:	90131-43-4 (replacing 8016-84-0)
		EINECS	:	290-353-9
3.	<i>T. minuta</i> Flower Extract	CAS	:	91770-75-1 (replacing 8016-84-0)
		EINECS	:	294-862-7
4.	<i>T. minuta</i> Flower Oil	CAS	:	91770-75-1 (replacing 8016-84-0)
		EINECS	:	294-862-7
5.	<i>T. patula</i> Flower Extract	CAS	:	91722-29-1
		EINECS	:	294-431-3
6.	<i>T. patula</i> Flower Oil	CAS	:	91722-29-1 (replacing 8016-84-0)
		EINECS	:	294-431-3

3.1.1.5. Structural formula

/

3.1.1.6. Empirical formula

Formula : /

3.1.2. Physical form

/

3.1.3. Molecular weight

Molecular weight : /

3.1.4. Purity, composition and substance codes

/

3.1.5. Impurities / accompanying contaminants

/

3.1.6. Solubility

/

3.1.7. Partition coefficient (Log P_{ow})Log P_{ow} : /

3.1.8. Additional physical and chemical specifications
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Organoleptic properties	:	/
Melting point	:	/
Boiling point	:	/
Flash point	:	/
Vapour pressure	:	/
Density	:	/
Viscosity	:	/
pKa	:	/
Refractive index	:	/

3.2. Function and uses

The *Tagetes* spp. extracts and oils are widely used fragrance ingredients of many fragrance compounds used in perfumery.

Because of industry assessment that *Tagetes* spp. extracts and oils cause photo-toxicity, the IFRA standards recommend:

“For applications on areas of skin exposed to sunshine, excluding bath preparations, soaps and other products which are washed off the skin, oils and absolutes obtained from *Tagetes minuta* L., syn. *Tagetes glandulifera* Schrank and *Tagetes patula* L. should not be used such that the level in the consumer product exceeds 0.01% (see remark on phototoxic ingredients in the introduction to the IFRA Code of Practice).

This recommendation is based on test results of RIFM on the phototoxicity of oils and absolutes obtained from *Tagetes minuta* and *Tagetes patula* from Egypt and South Africa indicating similar phototoxic potential. A no-effect level of 0.05% for phototoxicity was determined on humans using Egyptian *Tagetes minuta* absolute (C.S. Letizia, A.M. Api (2000), *The Toxicologist*, 54 (1), 397”

In the updated EU Inventory, Section II: Perfume and Aromatic Raw Materials (doc. SCCNFP/0389/00), the above restriction (previously flagged with one asterisk) is summarized as follows:

“Maximum level 0.05 %^(*) in cosmetic products applied in skin areas likely to be exposed to sunshine, excluding rinse-off products. In the presence of other phototoxic ingredients, the sum of concentrations (expressed as % of the respective maximum levels) shall not exceed 100%.”

(*) The difference is apparently due to misinterpretation of the older IFRA standard, referring to concentration in “fragrance compounds” used at a maximum level of 20% in the final products.

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3.3. Toxicological Evaluation

3.3.1. Acute toxicity

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3.3.2 Irritation and corrosivity

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3.3.3. Skin sensitisation

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3.3.4. Dermal / percutaneous absorption
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/

3.3.5. Repeated dose toxicity

/

3.3.6. Mutagenicity / Genotoxicity

/

3.3.7. Carcinogenicity

/

3.3.8. Reproductive toxicity

/

3.3.9. Toxicokinetics

/

3.3.10. Photo-induced toxicity**3.3.10.1. Photo-toxicity****Human data****Test 1**

Material tested : *Tagetes minuta* Flower Extract
 Sample : *Tagetes minuta* absolute (Marigold abs. - Egypt)A-1235-84-0.01/0.05, B-91235-84-0.25
 Subjects : male and female volunteers
 Concentration : 0.01 %, 0.05% and 0.25% in 75% ethanol/25% diethyl phthalate

0.3 ml aliquots of the test material were applied to a pair of contact Parker-Davis Webril patches, which were then applied under occlusion to naive skin sites on the back under occlusion for 24-hours, together a vehicle control patch. After 24 hours one of each pair of patches was removed, any excess test material was wiped off with a moistened towel and the site was irradiated with 16-20 J/cm² of UVA (1000 W Xenon Arc Solar Simulator) within 10 minutes following patch removal. The duplicate patch was then removed. The irradiated site was used for evaluation of phototoxicity potential and the other to evaluate existing contact sensitization or primary irritation. Reactions were scored at 1, 24, 48 and 72 hours after patch removal.

Results

No reactions at 0.01 % (0/25).

No reactions at 0.05% (0/25).

2/25 reactions at 0.25%. According to authors, the test material is phototoxic at this concentration.

Ref.: 14, 15

Test 2

Material tested : *Tagetes minuta* Flower Extract
 Sample : *Tagetes minuta* absolute A-1235-84-0.5 Egypt
 Subjects : male and female volunteers
 Concentration : 0.5% in 75% ethanol/25% diethyl phthalate

The test was performed as described in the previous study above (ref. 14, 15) on individuals patched also with duplicate patches of another 4 test substances (identities not reported).

Results

27/28 reactions.

Ref.: 17

Animal data

Test 1

The experimental protocol and documentation is unclear, making interpretation impossible.

Ref.: 3

Test 2

Material tested : *Tagetes minuta* Flower Oil
 Sample : *Tagetes* oil (T. minuta - S. Africa) C-988-86
 Controls : Methanol (negative); 8-MOP on methanol (positive)
 Species/strain : male Skh: HR hairless mice (6/group)
 Concentration : 0.01%, 0.1%, 1% (range 1), 3.125%, 6.25%, 12.5% (range 2), 25% 50% and 100% (range 3). Solvent: methanol.

Dilution Assay with 3 decimal dilutions in each of 3 concentration ranges. A 20 µl aliquot of the test material was applied to a 5cm² area of dorsal skin of each mouse. Approximately 30 minutes after treatment, each animal was covered by an aluminium foil mask taped to the mouse and restraining tray, and then exposed to a bank of 11 fluorescent black light lamps (F40T1BL PUVA, Sylvania) (Phosphor type BL-O^(*)) providing a broad output band centered near 350nm, that was placed 0.27 meters from exposure trays. A measured intensity of 0.5 S.U/hr^(**) was delivered for 60 minutes. The area to be exposed to light was defined by a 1 cm diameter hole in the foil centered over the treatment area. Reactions were read 4 hours after irradiation and again at 1, 2, 3 and 4 days. The treatment areas were scored for presence or absence of erythema, oedema, scaling, ulceration or fissuring. Animals exhibiting one or more of these symptoms at any examination period were considered positive for phototoxicity if the response was confined to the light-exposed area.

(*) Forbes, F.D. et al, Emission spectrum differences in fluorescent blacklight lamps. Photochem. Photobiol.24: 613, 1976.

(**) Berger, D.S., The Sunburning Ultraviolet Meter: Design and Performance, Photochem Photobiol. 24: 587-593 (1976).

Results

Range 1 : No reactions at 0.01 % (0/6), 5/6 reactions at 0.1 %, 5/5 reactions at 1 %.

Range 2 : 6/6 reactions at 3.125%, 5/5 reactions at 6.25%, 6/6 reactions at 12.5%.

Range 3 : 6/6 reactions at 25%, 6/6 reactions at 50%, 6/6 reactions at 100%.

The test article induced a phototoxic response in all animals at a level of 1% or higher and in most animals at 0.1%, but no response at 0.01%. The positive control (8-MOP) was phototoxic at levels of 0.0025% (6/6), 0.00125% (4/6), 0.000625% (3/6), but not at 0.0003125% (0/6). The Phototoxic Index is > 62.5.

Ref.: 9, 10

Test 3

Material tested : *Tagetes minuta* Flower Oil
 Sample : *Tagetes minuta* Oil, South African (sample #C-998-86)
 Species/strain : male Skh: HR hairless mice
 Concentration : 100%

Phototoxicity Screen after epicutaneous application to Hairless Mice: The test is applicable if negative results are obtained from a preliminary irritation screening of the test substance under the same conditions but without irradiation (6 animals). A 20 µl aliquot of the test material was applied to a 5cm² area of dorsal skin (saddle region) of each mouse. Approximately 30 minutes after treatment, each animal was covered by an aluminium foil mask taped to the mouse and restraining tray, and then exposed to either stimulated sunlight (6.5 KW long-arc Xenon high pressure burner Model RM65) placed 1 meter from exposure trays or a bank of 11 fluorescent black light lamps (F40TIBL PUVA, Sylvania) (Phosphor type BL-O^(*)) providing a broad output band centered near 350nm, that was placed 0.27 meters from exposure trays. A measured intensity of 0.5 S.U/hr^(**) was delivered for 60 minutes. The area to be exposed to light was defined by a 1 cm diameter hole in the foil centered over the treatment area. Animals were individually examined 4 hours after treatment and again at 1, 2, 3 and 4 days. The treatment areas were scored for presence or absence of erythema, oedema, scaling, ulceration or fissuring. Animals exhibiting one or more of these symptoms at any examination period were considered positive for phototoxicity if the response was confined to the light-exposed area.

(*) Forbes, F.D. et al, Emission spectrum differences in fluorescent blacklight lamps. Photochem. Photobiol.24: 613, 1976.

(**) Berger, D.S., The Sunburning Ultraviolet Meter: Design and Performance, Photochem Phtbiol. 24: 587-593 (1976).

Results

12/12 reactions (6/6 in each of the Xenon Lamp and the Black Light groups). Severe response characterized by transient skin staining in irritancy area, not observed following irradiation, and rapid (4-hour) oedema followed by eschar formation.

Ref.: 8

Test 4

Material tested : *T. minuta* Flower Extract
 Sample : *Tagetes minuta* absolute - Egypt (sample # 1235-84-2)
 Controls : Methanol (negative); 8-MOP on methanol (positive)
 Species/strain : male Skh: HR hairless mice (6/group)
 Concentration : 0.098%, 0.2%, 0.39%, 0.78%, 1.56% and 3.125% in methanol

Dilution Assay with 6 decimal dilutions in the detection range of 0.098% - 3.125%. A 20 µl aliquot of the test material was applied to a 5cm² area of dorsal skin of each mouse. Approximately 30 minutes after treatment, each animal was covered by an aluminium foil mask taped to the mouse and restraining tray, and then exposed to a bank of 11 fluorescent black light lamps (F40TIBL PUVA; Sylvania) (Phosphor type BL-O^(*)) providing a broad output band centered near 350nm, that was placed 0.27 meters from exposure trays. A measured intensity of 0.5 S.U/hr^(**) was delivered for 60 minutes. The area to be exposed to light was defined by a 1 cm diameter hole in the foil centered over the treatment area. Reactions were read 4 hours after irradiation and again at 1, 2, 3 and 4 days. The treatment areas were scored for presence or absence of erythema, edema, scaling, ulceration or fissuring. Animals exhibiting one or more of these symptoms at any examination period were considered positive for phototoxicity if the response was confirmed to the light-exposed area.

(*) Forbes, F.D. et al, Emission spectrum differences in fluorescent blacklight lamps. Photochem. Photobiol.24: 613, 1976.

(**) Berger, D.S., The Sunburning Ultraviolet Meter: Design and Performance, Photochem Phtobiol. 24: 587-593 (1976).

Results

6/6 reactions were observed at all dose levels: The test article induced a phototoxic response in all animals (6/6) at all levels in the range 0.098% - 3.125%. The response at the lowest level (0.098%) was more severe than that produced by the reference 8-MOP solution at 0.005%. The positive control (8-MOP) was phototoxic at levels of 0.05% (6/6), 0.0025% (5/5), 0.00125% (5/6), 0.000625% (2/5). The Phototoxic Index is > 127. The appropriate classification of the test article is "severely phototoxic" with strong positive responses still observable following 32-fold further dilution.

Ref.: 16

Test 5

Material tested : *T. minuta* Flower Extract
 Sample : *Tagetes minuta* absolute- Egypt (sample # 1235-84-2)
 Controls : Methanol (negative); 8-MOP on methanol (positive)
 Species/strain : male Skh: HR hairless mice (6/group)
 Concentration : 100% and 3.125%, 6.25%, 12.5%, 25% and 50% in methanol

Test

Dilution Assay with 6 decimal dilutions in the detection range of 3.125% - 100%. The study was performed as described in the previous study above (ref. 16).

Results

6/6 reactions were observed at all dose levels. The test article induced a phototoxic response in all animals (6/6) at all levels in the range 3.125% to 100% in methanol. The positive control (8-MOP) was phototoxic at levels of 0.05% (6/6), 0.0025% (5/6), 0.00125% (3/6), 0.000625% (1/6) in methanol.

Ref.: 4

Test 6

Material tested : *T. minuta* Flower Extract
 Sample : *Tagetes minuta* absolute (sample 1235-84-2)
 Controls : Methanol (negative); 8-MOP on methanol (positive)
 Species/strain : male Skh: HR hairless mice
 Concentration : Undiluted (100%)

Phototoxicity Screen after epicutaneous application to Hairless Mice. The study was performed as described in the previous study above on *Tagetes patula* Flower Extract (ref. 8)

Results

12/12 reactions (6/6 in each of the Black Light and the Xenon Lamp groups). Strong response characterized by rapid (4-hour) oedema (6/6 in each group), persistent for at least 48 hours (3/6 in the Black Light group, 1/6 in the Xenon lamp group) and followed in some cases by flaking. The positive control (8-MOP) was phototoxic at 0.01% in methanol (6/6).

Ref.: 5

Test 7

Material tested : *T. minuta* Flower Extract
Sample : *Tagetes minuta* absolute -South African (Marigold abs. Lot # 548963)
Species/strain : 10 Himalayan white spotted guinea pigs/dose level
Concentration : 0.003%, 0.03% and 3% in ethanol

Test

A 0.025 ml aliquot of the test material was applied to 2 cm² test sites on the shaved flanks. Thirty minutes after application of the test material, the left flank was exposed to nonerythemogenic UV-A irradiation (20 J/cm²) from Westinghouse FS 40 Black Lamps. The test sites on the right flanks remain unexposed and serve as control sites. Test sites were examined at 4, 24 and 48 hours after application of the test material.

Results

No reactions at 0.003% (0/10)
8/10 reactions at 0.03%
10/10 reactions at 3%

Ref. 6

Test 8

Material tested : *T. minuta* Flower Extract
Sample : *Tagetes minuta* absolute (Egypt) (Marigold abs. Lot # 101076)
Species/strain : 10 Himalayan white spotted guinea pigs/dose level
Concentration : 0.001 %, 0.01% and 3% in ethanol

Test

A 0.025 ml aliquot of the test material was applied to 2 cm² test sites on the shaved flanks. Thirty minutes after application of the test material, the left flank was exposed to nonerythemogenic UV-A irradiation (20 J/cm²) from Westinghouse FS 40 Black Lamps. The test sites on the right flanks remain unexposed and serve as control sites. Test sites were examined at 4, 24 and 48 hours after application of the test material.

Results

No reactions at 0.001 % (0/10)
8/10 reactions at 0.01 %,
10/10 reactions at 3%

Ref. 7

Test 9

Material tested : *T. minuta* Flower Extract
 Sample : *Tagetes minuta* absolute (Lot A)
 Species/strain : Dunkin Hartley guinea pigs (10/sex)
 Concentration : 3% in methanol

A 0.5 ml aliquot of test material was applied to the clipped and depilated retro-scapular region of the guinea pig on a eight layer Codex hydrophilic gauze pad about 2 cm². The pad was kept in contact with the skin for 90 minutes with an adhesive and hypoallergenic patch (Neodermotest Roc) covered with a 25cm² aluminum sheet held in place with an allergenic microporous bandage. Irradiation was carried out using a system of two fluorescent lamps with continuous spectrum emission: 4000-3100 Å (Mazdafluor black light fluorescent lamp) or 3500-2850 Å (Westinghouse fluorescent sun lamp). The lamps were placed 10 cm from the back of the animals and irradiation was delivered for 5 minutes (energy flow liberated: 0.43 J/cm²). Animals were then irradiated with 2 Mazdafluor black light lamps placed at: 5 cm for 90 minutes (12 J/cm²). The total energy output was 12.5 J/cm² and the rate of UV-B., 1 %. Reactions were scored 6 and 24 hours; after irradiation.

Results

No reactions (0/20).

Comment

It is unclear whether the energy quantities described above refer to those emitted by the lamp. The actual doses received are not stated. Poorly designed and reported test.

Ref.: 11

Test 10

Material tested : *T. patula* Flower Extract
 Sample : *Tagetes patula* absolute, South African (sample #D-1245-86)
 Species/strain : male Skh: Hr hairless mice
 Concentration : Undiluted (100%)

Phototoxicity Screen after epicutaneous application to hairless mice. The study was performed as described in the previous study above on *Tagetes minuta* Flower Oil (ref. 8).

Results

12/12 reactions (6/6 in each of the Xenon Lamp and the Black Light groups). Strong response characterized by persistent non-localized residue seen in both irritancy and photosensitivity area, and rapid (4-hour) persistent oedema followed in some cases by flaking and peeling.

Ref.: 13

Test 11

Material tested : *T. patula* Flower Extract
 Sample : *Tagetes patula* absolute (sample #D-1245-86)
 Controls : Methanol (negative); 8-MOP on methanol (positive)

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Species/strain : male Skh: HR hairless 1 % in methanol mice (6/group)
 Concentration : 0.01%, 0.1% and 1%

Phototoxicity Screen after epicutaneous application to Hairless Mice. The study was performed as described in the previous study above on *Tagetes minuta* absolute (ref. 16).

Results

2/6 reactions at 0.01 %

6/6 reactions at 0.1 %

6/6 reactions at 1 %

The responses at levels 1% and 0.1% were more severe than that produced by the reference 8-MOP solution at 0.0025%. The positive control (8-MOP) was phototoxic at levels of 0.0025% (6/6), 0.00125% (4/6) and 0.000625% (2/6), but not at 0.0003125%. The Phototoxic Index is > 62.5.

Ref.: 12

Test 12

Material tested : *T. erecta* Extract
 Sample : *alpha* - Terthienyl isolated from *Tagetes erecta*
 Species/strain : *Candida utilis*
 Concentration : 2.0 mg

Test

Phototoxicity yeast assay. An emulsion of 2.0 mg of *alpha*-Terthienyl and 0.1 ml Tween 20 in 1 ml of water was added to a culture which was incubated with shaking in a water bath at 30 C while being irradiated with monochromatic light (19.5 W UVL-22 "Black Ray lamp").

Results

Phototoxic effects were observed.

Ref.: 2

Test 13

Material tested : *T. patula* Root Extract
 Sample : 5-(3-buten-1-ynyl)-2,2'- bithienyl and *alpha*-terthienyl, which were isolated from the roots of *Tagetes patula*
 Species/strain : *Candida albicans* (UBC 54)
 Concentration : N/A

In vitro yeast cell assay. Several small wells were cut in Sabouraud dextrose agar plates. The plates were each streaked with sterile cotton swabs in one direction and cross-wise in the other direction. About 1 µl of test material was added to 2 separate wells on one plate. Test plates were incubated at room temperature for at least 24 hours under illumination provided by a 2 Blacklite F 15Y8-BL fluorescent tubes (320-390 nm).

Results

Phototoxic effects were observed by the above test method on two intensely mauve UV

fluorescent compounds isolated from *Tagetes* root. The compounds were identified as 5-(3-buten-1-ynyl)-2,2'-bithienyl and alpha-terthienyl.

Ref.: 1

3.3.10.2. Photo-allergenicity

Human data

Material tested : *Tagetes minuta* flower extract
 Sample : *Tagetes minuta* absolute (Marigold abs. - Egypt)
 Subjects : 1 male and 24 female volunteers
 Concentration : 0.05% in 75% ethanol/25% diethyl phthalate

A 0.3 ml aliquot of the test material was applied to the Webril pad of Parker-Davis patches which were then applied to naive sites on the back for 24 hours under occlusion. After patch removal, a 1 cm² area in the patch test site was exposed to 2 MED UVB (290-320 nm), with some UVA, from a 1000 W Xenon Arc Solar Simulator with a WG320 filter (average irradiance 26-32 mW/cm²). This sequence was repeated six times over three consecutive weeks (2 exposures/week). All induction applications were made to the same site. Site responses were evaluated and scored at 24 (applications 1, 3 and 5) or 72 hours (applications 2, 4 and 6) after irradiation. After a 2-week rest period, a single application of duplicate patches was made to naive sites on the back for 24 hours under occlusion. One patch, from each pair of patches, was removed after approximately 24 hours and the entire patch test site was immediately exposed to 16-20 J/cm² UVA (320-400 nm) from a 1000 W Xenon Arc Solar Simulator with a WG345 filter and a UG-11 filter (average irradiance 0.156 W/cm²). The non-irradiated treated site and an irradiated vehicle treated site served as controls. Reactions were read at 1, 24, 48 and 72 hours after patch removal.

Results

No reactions (0/25)

Ref.: 15

3.3.11. Human data

See elsewhere in opinion

3.3.12. Special investigations

/

3.3.13. Safety evaluation (including calculation of the MoS)**CALCULATION OF THE MARGIN OF SAFETY**

Not applicable

3.3.14. Discussion

The data submitted demonstrate that *Tagetes* extracts and oils possess phototoxic potential. Some of the experiments indicate that this potential is severe.

There is information to suggest that the phototoxic agent in *Tagetes* oils and extracts is a α -Terthienyl-compound. However, the precise mechanism by which *Tagetes* oils and extracts exerts their phototoxic effects is not known.

The experimental data reviewed is old and largely poorly documented.

4. CONCLUSION

According to the data submitted, *Tagetes* extracts and oils are phototoxic.

As no safe limit of use in cosmetic products has been demonstrated, it is recommended that *Tagetes erecta*, *Tagetes minuta* and *Tagetes. patula* extracts and oils should not form part of cosmetic products.

5. MINORITY OPINION

Not applicable

6. REFERENCES

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3. RIFM (Research Institute for Fragrance Materials, Inc.), 1977. Phototoxicity testing of fragrance materials in hairless mice and miniature swine. RIFM report number 1814. July 17. (RIFM, Woodcliff Lake NJ USA)
4. RIFM (Research Institute for Fragrance Materials, Inc.), 1985. Phototoxicity dilution assay of *Tagetes minuta* absolute in hairless mice. RIFM report number 3824 August 24. (RIFM, Woodcliff Lake NJ USA)

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5. RIFM (Research Institute for Fragrance Materials, Inc.), 1985a. Phototoxicity screening of marigold absolute in hairless mice. RIFM report number 3822 August 12. (RIFM, Woodcliff Lake NJ USA)
6. RIFM (Research Institute for Fragrance Materials, Inc.), 1985b. Determination of phototoxicity of *Tagetes minuta* absolute in guinea pigs. RIFM report number 3361 December 17. (RIFM, Woodcliff Lake NJ USA)
7. RIFM (Research Institute for Fragrance Materials, Inc.), 1985c. Determination of phototoxicity of *Tagetes minuta* absolute in guinea pigs. RIFM report number 3362 December 17. (RIFM, Woodcliff Lake NJ USA)
8. RIFM (Research Institute for Fragrance Materials, Inc.), 1986. Phototoxicity screening of *Tagetes minuta* oil South African in hairless mice. RIFM report number 3827. June 6. (RIFM, Woodcliff Lake NJ USA)
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APPENDIX

- Common Name : **TAGETES ERECTA FLOWER EXTRACT**
 EINECS No. : 290-353-9
 CAS RN : 90131-43-4
 Chem. Name : Extract obtained from the flowers of the plant, *Tagetes erecta*,
Compositae.
 Restrictions : Maximum level 0.05 % in cosmetic products applied in skin areas likely to be exposed to sunshine, excluding rinse-off products. In the presence of other phototoxic ingredients, the sum of concentrations (expressed as % of the respective maximum levels) shall not exceed 100%.
- Common Name : **TAGETES ERECTA FLOWER OIL**
 EINECS No. : 290-353-9
 CAS RN : 90131-43-4
 Chem. Name : “Marigold Oil; Tagetes Oil”. Essential oil obtained from the flowers of the plant, *Tagetes erecta*, *Compositae*. It contains mainly *D*-limonene, ocimene, 2,6-dimethyl-7-octen-4-one.
 Restrictions : Maximum level 0.05 % in cosmetic products applied in skin areas likely to be exposed to sunshine, excluding rinse-off products. In the presence of other phototoxic ingredients, the sum of concentrations (expressed as % of the respective maximum levels) shall not exceed 100%.
- Common Name : **TAGETES MINUTA FLOWER EXTRACT**
 EINECS No. : 294-862-7
 CAS RN : 91770-75-1
 Chem. Name : Extract obtained from the flowers of the plant, *Tagetes minuta*,
Compositae.
 Restrictions : Maximum level 0.05 % in cosmetic products applied in skin areas likely to be exposed to sunshine, excluding rinse-off products. In the presence of other phototoxic ingredients, the sum of concentrations (expressed as % of the respective maximum levels) shall not exceed 100%.
- Common Name : **TAGETES MINUTA FLOWER OIL**
 EINECS No. : 294-862-7
 CAS RN : 91770-75-1
 Chem. Name : Essential oil obtained from the flowers of the plant, *Tagetes minuta*,
Compositae.
 Restrictions : Maximum level 0.05 % in cosmetic products applied in skin areas likely to be exposed to sunshine, excluding rinse-off products. In the presence of other phototoxic ingredients, the sum of concentrations (expressed as % of the respective maximum levels) shall not exceed 100%.

Opinion on *Tagetes erecta*, *T. minuta* and *T. patula* Extracts and Oils (phototoxicity only)

Common Name	:	TAGETES PATULA FLOWER EXTRACT
EINECS No.	:	294-431-3
CAS RN	:	91722-29-1
Chem. Name	:	Extract obtained from the flowers of the plant, <i>Tagetes patula</i> , <i>Compositae</i> .
Restrictions	:	Maximum level 0.05 % in cosmetic products applied in skin areas likely to be exposed to sunshine, excluding rinse-off products. In the presence of other phototoxic ingredients, the sum of concentrations (expressed as % of the respective maximum levels) shall not exceed 100%.
Common Name	:	TAGETES PATULA FLOWER OIL
EINECS No.	:	294-431-3
CAS RN	:	91722-29-1
Chem. Name	:	“Marigold Oil; Tagetes Oil”. Essential oil obtained from the flowers of the plant, <i>Tagetes patula</i> , <i>Compositae</i> . It contains mainly <i>D</i> -limonene, ocimene, 2,6-dimethyl-7-octen-4-one.
Restrictions	:	Maximum level 0.05 % in cosmetic products applied in skin areas likely to be exposed to sunshine, excluding rinse-off products. In the presence of other phototoxic ingredients, the sum of concentrations (expressed as % of the respective maximum levels) shall not exceed 100%.