**Tentative Safety Assessment**

# Cucumis Sativus (Cucumber) -Derived Ingredients as Used in Cosmetics

**March 16, 2012**

*All interested persons are provided 60 days from the above date to comment on this Tentative Safety Assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Director, Dr. F. Alan Andersen.*

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## ABSTRACT

*The Expert Panel assessed the safety of six* Cucumis sativus *(cucumber)-derived ingredients and found them safe in the present practices of use and concentration. These ingredients are reported to function in cosmetics as skin conditioning agents. Cucumber is a commonly consumed food and generally recognized as safe. The focus of this assessment was the dermal exposure to the low concentrations of these ingredients as used in cosmetics. Many of the components of these* Cucumis sativus *(cucumber)-derived cosmetic ingredients have been previously assessed for safety as cosmetic ingredients.*


## INTRODUCTION

This document is a safety assessment of the following six *Cucumis sativus* (cucumber) derived ingredients as used in cosmetic formulations:

Cucumis Sativus (Cucumber) Fruit Extract
Cucumis Sativus (Cucumber) Extract
Cucumis Sativus (Cucumber) Fruit
Cucumis Sativus (Cucumber) Fruit Water
Cucumis Sativus (Cucumber) Juice
Cucumis Sativus (Cucumber) Seed Extract

All of the ingredients included in this safety assessment are reported to function in cosmetics as skin conditioning agents.

Cucumis Sativus (Cucumber) Seed Oil is not included in this safety assessment because it was previously reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel. In 2011, in the Safety Assessment of Plant-Derived Fatty Acid Oils as Used in Cosmetics, it was concluded that Cucumis Sativus (Cucumber) Seed Oil is safe as used in cosmetics.[1]

The chemical composition of cucumber is provided in this safety assessment. Some of the components of cucumber are cosmetic ingredients for which a CIR safety assessment is available. Others, such as the phytosterols, are compounds that have been discussed in other CIR safety assessments, such as the PEG Soy Sterols report.[2] Published toxicity data were not readily available. However, according to the Food and Drug Administration (FDA), cucumbers are one of the 20 most frequently consumed raw vegetables (21CFR101.44). The fact that cucumbers are a commonly consumed food suggests that these ingredients pose no significant safety issue following oral exposure and argues against the need for oral safety data. Irritation, sensitization, and phototoxicity data were available and are included in this assessment.

## CHEMISTRY

### Definition

The definition, chemical class, and reported functions of these ingredients are provided in Table 1.

### Chemical and Physical Properties

Chemical and physical properties are listed in Table 2.

### Composition

Cucumber fruit is composed mostly of water; more than 96% of edible unpeeled fruit is water.[3] Other constituents of *Cucumis sativus* L, according to one source, are vitamins, minerals, amino acids, phytosterols, phenolic acids, fatty acids, and cucurbitacins.[4] According to another source, traces of essential oil, amino acids, pectins, starch, sugars, vitamin C, and curcurbitacin are found in cucumbers.[5] Glycosides, steroids, flavonoids, carbohydrates, terpenoids, and tannins were identified in an aqueous extract of the cucumber fruit.[6] A comprehensive list of chemical constituents by plant part is presented in Table 3.

Liquid chromatography–mass spectrometry that incorporated $^{13}C_3$-labelled standards determined that cucumber contained 12-13 μg phytoestrogens/100 g wet wt cucumber.[7] In the breakdown of the phytoestrogen composition, the content was primarily the lignan secoisolariciresinol; the lignan matairesinol, the isoflavones daidzein, genistein, glycitein, biochanin A, and formononetin, and coumestrol, comprised <1 μg/100 g wet wt of the fruit. Another source reports the following phytosterols in cucumber fruit: 3800 μg β-sitosterol/100 g edible portion, 200 μg campesterol/100 g edible portion, 2900 μg stigmasterol/100 g edible portion, 300 μg β-sitostanol/ 100g edible portion, and 100 μg campestanol/100 g edible portion, giving a total plant sterol content of 7300 μg/100 g edible portion.[8]

The lipid fatty acid content of *Cucumis sativus* (cucumber) has been described. Table 4 provides information on cucumber lipids and their fatty acid composition. The major fatty acids in cucumbers are palmitic acid (23.6-27.5%), linoleic acid (22.7-26.3%), and linolenic acid (40-46%).[9,10]

The mixed fatty acid and triterpene alcohol composition of *Cucumis sativus* seeds is presented in Table 5. For extrapolation purposes, according to the CIR Safety Assessment on Plant-Derived Oils as Used in Cosmetics, the fatty acid composition of Cucumis sativus (cucumber) seed oil is 9-13% palmitic acid, 6-9% stearic acid, 14-20% oleic acid, 60-68% linoleic acid, and <1% linolenic acid.[1]

Table 6a provides the conclusions from safety assessments that exist for some of the constituents of cucumber. Table 6b references information on the safety of some components of cucumber that were discussed in previous CIR reports.

### Preparation/Extraction

Cucumis Sativus (Cucumber) Fruit Extract is reported to be manufactured by extracting cucumber fruit in mixtures of glycerin and water,[11] water and butylene glycol, or water and propylene glycol.[12] The fresh fruit is extracted peeled or unpeeled. A cucumber peel powder extract is prepared by a hydro-alcoholic extraction of the macerated fresh fruit; grain alcohol is used as the solvent.[13] The extract ratio is approximately 10:1.

## USE

### Cosmetic

The *Cucumis sativus*-derived ingredients included in this safety assessment are reported to function in cosmetics as skin conditioning agents.[14] Voluntary Cosmetic Registration Program (VCRP) data obtained from the FDA in 2011 indicate that Cucumis Sativus (Cucumber) Fruit Extract is used in 534 cosmetic formulations, 350 of which are leave-on.[15] VCRP data indicate that the other *Cucumis sativus* derived ingredients are used in less than 10 cosmetic formulations. A Personal Care Products Council (Council) survey of the maximum reported use concentrations found that the Cucumis Sativus (Cucumber) Fruit Water had the highest concentration of use, 3% in foundations, and that Cucumis Sativus (Cucumber) Fruit Extract was used in eye lotions and face and neck products at up to 1%.[16] The concentrations used in rinse-off products and products diluted for (bath) use were ≤0.4% and 0.005%, respectively.

Frequency and concentration of use data categorized by exposure and duration of use are provided in Table 7. In some cases, reported use was received by the VCRP, but no concentration of use data were reported in the Council survey. For example, Cucumis Sativus (Cucumber) Juice is reported to be used according to VCRP data, but no concentration of use data were submitted in response to the Council survey. In other cases, no reported uses were reported in the VCRP, but a use concentration was provided in the industry survey. For example, Cucumis Sativus (Cucumber) Fruit Water is not reported to be used in the VCRP, but the industry survey indicates that it is used at 3% in foundations and at 0.05% in baths soaps and detergents and in body and hand product formulations. It should be presumed that Cucumis Sativus (Cucumber) Fruit Water is used in at least one formulation in each of these categories.

Products containing Cucumis Sativus (Cucumber) Fruit Extract are reported to be used on baby skin, may be applied to the eye area or mucous membranes, or could be incidentally ingested. Additionally, Cucumis Sativus (Cucumber) Fruit Extract is used in cosmetic spray products such as face and neck and body and hand sprays, and could possibly be inhaled. This ingredient is reportedly used at concentrations up to 0.2% in these cosmetic sprays. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μm.[17-20] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[17,20] There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[17] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays.

All of the Cucumis sativus derived ingredients named in this safety assessment are listed in the European Union inventory of cosmetic ingredients.[21]

## TOXICOKINETICS

Published toxicokinetics data were not found.

## TOXICOLOGICAL STUDIES

Published toxicity studies were not found.

## REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Published reproductive and developmental toxicity studies were not found.

## GENOTOXICITY

*Cucumis Sativus (Cucumber) Fruit Extract*

An Ames test was performed with Cucumis Sativus (Cucumber) Fruit Extract composed of 54.8% water, 45% butylene glycol, and 0.2% cucumber.[22] Doses of 156-5000 μg/plate were assayed using *Salmonella typhimurium* strains TA100 and TA98 with and without metabolic activation. Negative and positive controls gave valid results. Cucumis Sativus (Cucumber) Fruit Extract was not mutagenic in this assay.

The mutagenic potential of an extract of cucumber was evaluated in an Ames test using *S. typhimurium* TA98 and TA100 with and without metabolic activation.[23] Cucumber was not mutagenic in this assay.

## CARCINOGENICITY

### Anti-Tumor Promotion

The effect of *Cucumis sativus* (cucumber) on tumor promotion was examined in Swiss Webster albino mice.[24] The test article was prepared by homogenization of the fruit and expressing the juice. Ten mice (sex not specified) were used per group. The mice were shaved, and 6 days later 0.2 ml of 410 µg of dimethylbenz[*a*]anthracene (DMBA) in acetone was applied to the back of each mouse. Four days after DMBA application, 0.2 ml of 0.03% croton oil in acetone was applied to the shaved back of each animal; this application was made three times per wk for 20 wks. Three protocols were used for the application of the cucumber extract. In Protocol 1, the extract was applied for 5 days prior to application of DMBA and 1 h before the croton oil. In Protocol 2, the extract was applied 1 h before the croton oil. In Protocol 3, the extract was applied immediately after the croton oil dried. Initially, a dose of 5.0 mg cucumber extract/0.2 ml acetone was "splashed on" the back of each animal. However, this reportedly caused 60-80% mortality prior to tumor development. (This unexplained outcome was observed with the three other test articles, i.e., sugar beet roots, New Zealand spinach leaves, and turmeric rhizomes, as well. It was the opinion of the Panel that the observed mortality was due to flaw in the study and not the test article.) As a result, the dose was changed to 2.5 mg cucumber extract/0.2 ml acetone. The positive control group was exposed to DMBA + croton oil, and the negative control group was untreated.

In the positive control group, none of the mice died before developing tumors (0% mortality), and the first tumor appeared at wk 9. The tumor incidence was 100%, and the average number of tumors/mouse was 4.7 ± 3.3. The time for the first tumor to appear in all three test groups was delayed, appearing at wk 12, for all 3 protocols using cucumber extract. Also, the tumor incidence was lower in all three groups exposed to cucumber extract. Using Protocol 1, mortality was 0%, the tumor incidence was 70%, and the average number of tumors per mouse was 2.3 ± 1.1 (using Kruskal-Wallis analysis of variance by ranks, statistical difference from positive control, $\alpha$=0.20). Using Protocols 2 and 3, mortality was 10% for both, the tumor incidence was 55.6% and 66.7%, respectively, and the average number of tumors/mouse was 4.2 ± 0.8, and 3.8 ± 1.3, respectively (statistical difference from positive control, $\alpha$=0.70 and 0.90, respectively). No tumors were reported in the negative control group.

## IRRITATION AND SENSITIZATION

### Skin Irritation/Sensitization

#### Human

*Cucumis Sativus (Cucumber) Fruit Extract*

A single insult patch test was performed on 20 subjects with Cucumis Sativus (Cucumber) Fruit Extract composed of 54.8% water, 45% butylene glycol, and 0.2% cucumber.[22] The extract was diluted in water to 1%, and 15 µl were applied for 24 h under an occlusive patch. No erythema or edema was observed at 24 or 48 h.

To test for dermal irritation, cosmetic formulations containing 0.5-2.5% ethanol extract of *Cucumis sativus* were prepared as oil-in-water emulsion-based creams, with stearic acid as the emulsifier.[25] The pH of the seven formulations that were prepared ranged from 6.4-6.9. The irritancy was evaluated by applying the creams to a 1 sq. cm. area on the dorsal surface of the hand and observing signs of irritation for 24 h. (The number of subjects tested was not stated.) No irritation, erythema, or edema were observed.

The irritation and sensitization potential of two formulations containing 0.00055% Cucumis Sativus (Cucumber) Fruit Extract was evaluated in a modified occlusive human repeat insult patch test (HRIPT). A 21-day induction phase, 10-24 day non-treatment period, and 4-day challenge phase was used. Distilled water was the negative control and sodium lauryl sulfate (SLS) was the positive control in both studies. In the first study, a moisturizer containing 0.00055% Cucumis Sativus (Cucumber) Fruit Extract was applied neat to 101 subjects.[26] The standardized cumulative irritation score was 0 for both the test material and distilled water and was 2430 for 0.5% SLS. (The scoring scale was not defined.) The formulation containing 0.00055% Cucumis Sativus (Cucumber) Fruit Extract was not predicted to be a significant skin irritant, and it was not a sensitizer.

In the second study, a facial cleanser containing 0.00055% Cucumis Sativus (Cucumber) Fruit Extract was applied to 104 subjects at a concentration of 1%.[26] The standardized cumulative irritation index was 96.15 for the test material, 58.65 for distilled water, and 1659.62 for 1% SLS. (The scoring scale was not defined.) The formulation containing 0.00055% Cucumis Sativus (Cucumber) Fruit Extract, tested at 1%, was not predicted to be a significant skin irritant, and it was not a sensitizer.

An HRIPT was completed in 103 subjects to determine the dermal irritation and sensitization potential of an eye lotion containing 1% Cucumis Sativus (Cucumber) Fruit Extract.[27] The test article was applied neat. During induction, a 24-h semi-occlusive patch was applied to the upper back of each subject three times per wk for 3 wks. Challenge patches were applied after a 2-wk non-treatment period, and the test sites were evaluated upon patch removal and at 48 and 72 h. No reactions were observed during induction. Five subjects (2 at 48 h, 2 at 72 h, and 1 at 48 and 72 h) had a ± reaction (barely perceptible erythema) and one subject had a 1+ reaction (mild diffuse erythema) observed at 24 h, which subsided to a ± reaction at 48 h

and no reaction at 72 h. The researchers concluded that the eye lotion containing 1% Cucumis Sativus (Cucumber) Fruit Extract demonstrated no potential for eliciting dermal irritation or sensitization.

The irritation and sensitization potential of an eye treatment mask containing 1% Cucumis Sativus (Cucumber) Fruit Extract was evaluated in a modified HRIPT that was completed in 600 subjects.[28] (It is not stated whether the product was tested neat or if it was diluted prior to application.) During induction, which consisted of ten 48-h occlusive patches on the back of each subject, the test sites were scored for immediate reactions and then 1-2 h after patch removal for delayed reactions. Challenge patches (48 h) were applied after a 2-wk non-treatment period and again 1 wk later. During challenge, the test sites were evaluated for immediate and delayed reactions. No reactions were observed, and an eye formulation containing 1% Cucumis Sativus (Cucumber) Fruit Extract was not a dermal irritant or a sensitizer.

Another HRIPT was performed in 108 subjects to determine the irritation and sensitization potential of an eye lotion containing 1% Cucumis Sativus (Cucumber) Fruit Extract.[29] Approximately 0.2 ml of the test material was applied neat to a 1 in. x 1 in. semi-occlusive patch, and the induction patches were applied for 24 h to the upper back of each subject three times per wk for 3 wks for a total of nine applications. Challenge patches were applied after a 2-wk non-treatment period. Two subjects had reactions at challenge. One had a mild response 24 h, but not 72 h, post-challenge; this was considered a transitory response and therefore clinically insignificant. The second subject had a moderate to mild response 24 and 72 h post-challenge. A re-challenge was performed and included an open repetitive application to the forearm for 4 consecutive days. No reactions were observed at rechallenge. An eye lotion containing 1% Cucumis Sativus Fruit Extract was not considered a dermal irritant or sensitizer.

Summary data from an HRIPT that was completed in 100 subjects to examine the irritation and sensitization potential of an eye hydrogel containing 5% Cucumis Sativus (Cucumber) Fruit Extract were provided to the CIR.[30] The undiluted test material was applied to the upper backs of subjects using an occlusive patch. Mild erythema with or without edema was observed in 6 subjects; these responses either decreased from the 48 h to the 96 h evaluation or were not confirmed at both challenge sites. The responses were considered irritant responses, and the formulation did not induce clinically identifiable evidence of contact hypersensitivity. (No other details or raw data were provided).

Summary data from a 21-day use study in which 21 subjects applied an eye gel containing 5% Cucumis Sativus (Cucumber) Fruit Extract 1-2 times daily were also provided to the CIR.[31] Eight subjects reported sensations of discomfort (primarily stretching) after application, but no clinically significant cutaneous reactions were observed. Dermal and ophthalmological assessments were performed, and it was concluded that the eye gel was well tolerated. (No other details or raw data were provided).

## Phototoxicity

*Cucumis Sativus (Cucumber) Fruit Extract*

Summary data from a study that was initiated in 11subjects to examine the phototoxicity potential of an eye gel containing 5% Cucumis Sativus (Cucumber) Fruit Extract were provided to the CIR.[32] Duplicate 24 h occlusive patches were applied to the mid-back of each subject. Upon patch removal, one site was irradiated with 2/3 of the minimal erythema dose of ultraviolet A (UVA) and UVB, supplemented with 10 J/cm$^2$ UVA. Both sites were evaluated for erythema at 10 min and 24, 48, and 72 h after irradiation. Nine subjects completed the study; two withdrew for reasons not related to the study. An eye gel containing 5% Cucumis Sativus (Cucumber) Fruit Extract was not phototoxic. (No other details or raw data were provided).

## Cross-Allergenicity

Cross-allergenicity among cucumber, celery, carrot and watermelon was investigated.[33] The pooled sera of 6 individuals that had demonstrated allergy to one or more of these foods in an enzyme-linked immunosorbent assay (ELISA) was used. At least two of the subjects were symptomatic and also skin test- or radioallergosorbent test- (RAST) positive to cucumber, celery, carrot and watermelon as index foods. A strong allergenic cross-reactivity among these four foods was demonstrated by both ELISA inhibition and immunoblot inhibition studies.

Researchers have studied the relationship between ragweed allergens and allergens found to the gourd family (including cucumber) in patients with sensitization to ragweed.[34] The researchers found that most oropharyngeal symptoms associated with these foods are mediated in part by an IgE mechanism, and that ragweed most likely shares allergens with the entire gourd family.

A case of cross-reactivity of cucumber with latex has been reported.[35] Details are provided in the section on 'Case Studies' below.

## Case Studies

A male greenhouse employee who worked with cucumber plants developed severe eczema 5 mos after starting work.[36] Patch testing was performed with cucumber leaves, stem, and peel, and with a cucumber ethanol extract. A positive reaction (++) to the upper and under side of the cucumber leaf was reported on days 2, 3, and 7. A follicular reaction to the stem and

ethanol extract was reported on days 3 and 7. No reaction was reported with the cucumber peel. In follow-up testing with cucumber leaves in 10 healthy subjects, slight redness was reported for two subjects.

Cucumber anaphylaxis, demonstrated by dizziness, vomiting, dyspnea, thoracic erythema, and vaginal itching, was reported in a female patient within 5 min of eating an incompletely peeled cucumber.[35] Three months prior to this reaction the patient had presented with an episode of papaya urticaria and a sensitization to latex was found. Prick-by–prick skin test results were positive for cucumber (peel and pulp), as well as for papaya and some other fruits and vegetables. Immunoblot inhibition confirmed latex-cucumber (and latex-papaya) cross-reactivity.

### Ocular Irritation

#### In Vitro

*Cucumis Sativus (Cucumber) Fruit Extract*

The ocular irritation potential of a moisturizer containing 0.00055% Cucumis Sativus (Cucumber) Fruit Extract was evaluated in a chorioallantoic membrane vascular assay (CAMVA) and a bovine corneal opacity and permeability test (BCOP).[26] The material was tested undiluted in both assays. In the CAMVA, the $RC_{50}$ was 66%. In the BCOP, the in vitro score was 2.62, the opacity score was 2.6, and the permeability score was 0.001. (No details were provided). The results of both of these assays predict the test material is not to irritating to the eye.

The potential ocular toxicity of an eye lotion containing 1% Cucumis Sativus (Cucumber) Fruit Extract was determined in a screening assay using the EpiOcular human cell construct.[37] The test material was tested as supplied. Sterile deionized water served as the negative control and 0.3% triton-X-100 served as the positive control. The $ET_{50}$ (duration of exposure resulting in a 50% decrease in 3[4,5-dimetylthiazol-2-yl]-2,5-diphenlytetrazolium bromide (MTT) conversion) was >1440 min. (The $ET_{50}$ of the positive control was 27.5 min).

#### Human

*Cucumis Sativus (Cucumber) Fruit Extract*

An use study was performed to determine the ocular irritation potential of an eye lotion containing 1% Cucumis Sativus (Cucumber) Fruit Extract.[38] Thirty female subjects, half of which were contact lens wearers, were instructed to apply the test material to the eye area, avoiding the eyelid, up to two times daily for 4 wks. An ophthalmic examination was made prior to and at the termination of testing. The skin in the eye area was also evaluated for dermal effects. One subject reported slight itching on the eyelids almost daily. Trace increases in redness of the palpebral conjunctivae were observed in two subjects and of the bulbar conjunctivae were observed one subject; these observations were not attributed to the test product. The eye lotion containing 1% Cucumis Sativus (Cucumber) Fruit Extract did not demonstrate a potential for eliciting ophthalmic (or dermal) irritation.

## SUMMARY

This assessment pertains to the safety of the following six ingredients as used in cosmetic formulations: Cucumis Sativus (Cucumber) Fruit Extract; Cucumis Sativus (Cucumber) Extract; Cucumis Sativus (Cucumber) Fruit; Cucumis Sativus (Cucumber) Fruit Water; Cucumis Sativus (Cucumber) Juice; and Cucumis Sativus (Cucumber) Seed Extract. These ingredients are reported to function in cosmetics as skin conditioning agents. Cucumis Sativus (Cucumber) Fruit Extract is used in 534 cosmetic formulations, 350 of which are leave-on type products. All the other *Cucumis sativus* (cucumber) ingredients are used in less than 10 formulations. The highest reported use concentrations were 3% Cucumis Sativus (Cucumber) Fruit Water in foundations and 1% Cucumis Sativus (Cucumber) Fruit Extract in eye lotions and face and neck products; all other reported use concentrations (in leave-on, rinse-off, and diluted for (bath) use formulations) were less than 0.4%.

*Cucumis sativus* contains, among other constituents, fatty acids, vitamins, amino acids, phytosterols, phenolic acids, and cucurbitacins. Glycosides, steroids, flavonoids, carbohydrates, terpenoids, and tannins were isolated in an aqueous extract. The major fatty acids in cucumbers are palmitic acid (23.6-27.5%), linoleic acid (22.7-26.3%), and linolenic acid (40-46%). Several of the chemical constituents have previously been assessed for safety as used in cosmetics.

Cucumbers are one of the 20 most frequently consumed raw vegetables; therefore, this assessment focused on the dermal exposure to these ingredients.

Results of a dermal application study with *Cucumis sativus* (cucumber), prepared by homogenization of the fruit and expressing the juice, suggested that the exposure to cucumber delayed the onset and decreased the incidence of tumors in a tumor promotion assay using DMBA and croton oil in mice. However, this study also reported a high unexplained mortality rate.

Cucumis Sativus (Cucumber) Fruit Extract was not mutagenic in an Ames assay when tested at doses of 156-5000 µg/plate with and without metabolic activation.

Cucumis Sativus (Cucumber) Fruit Extract, containing 0.2% cucumber, was not an irritant in a single insult patch test when tested as a 1% aq. dilution and cosmetic formulations containing 0.5-2.5% ethanol extract of *Cucumis sativus*, prepared as

oil-in-water emulsion based creams, were not irritants when applied for 24 h. Cosmetic formulations containing up to 1% Cucumis Sativus (Cucumber) Fruit Extract were not dermal irritants or sensitizers in clinical testing. In an HRIPT with a formulation containing 5% Cucumis Sativus (Cucumber) Fruit Extract, reactions that were observed during challenge were considered an irritant response, but the formulation did not induce clinically identifiable evidence of contact hypersensitivity. A 21-day use study concluded that an eye gel containing 5% Cucumis Sativus (Cucumber) Fruit Extract was well-tolerated. In a clinical phototoxicity study completed in 9 subjects, a formulation containing 5% Cucumis Sativus (Cucumber) Fruit Extract was not phototoxic. Cross-allergenicity among cucumber, celery, carrot, and watermelon has been demonstrated, as has a correlation between the ragweed pollen-specific IgE and the *Cucurbitaceae*-specific IgE and the specific IgE to *Cucurbitaceae* and to banana. A case of cross-reactivity of cucumber with latex has been reported.

In vitro ocular irritation testing predicted that Cucumis Sativus (Cucumber) Fruit Extract would not be an ocular irritant, and an eye lotion containing 1% Cucumis Sativus (Cucumber) Fruit Extract did not demonstrate a potential for eliciting ocular irritation.

## DISCUSSION

The Panel affirmed that cucumber is a commonly consumed food and generally recognized as safe; this fact suggested that these ingredients pose no significant safety issue following oral exposure and argued against the need for an extensive review of oral toxicity data. Therefore the focus of this safety assessment was on the dermal exposure to these *Cucumis sativus* (cucumber)-derived ingredients. The Panel noted that many of the constituent chemicals previously have been assessed for safety as used in cosmetics.

Skin sensitization and phototoxicity testing of a formulation containing 5% Cucumis Sativus (Cucumber) Fruit Extract (which is greater than the highest reported use concentration of 1%) demonstrated an absence of sensitization and phototoxicity potential. An irritant response to the formulation containing 5% Cucumis Sativus (Cucumber) Fruit Extract was observed in some subjects, but no irritation was observed with cosmetic formulations containing up to 2.5% of an ethanol extract of *Cucumis sativus* prepared as an oil-in-water emulsion-based cream or with a formulation containing 1% Cucumis Sativus (Cucumber) Fruit Extract.

Because Cucumis Sativus (Cucumber) Fruit Extract can be used in products that may be aerosolized, including face and neck sprays and body and hand sprays, the Panel discussed the issue of incidental inhalation exposure. In the absence of inhalation data, the Panel noted that Cucumis Sativus (Cucumber) Fruit Extract caused no irritation at concentrations up to 2.5% or sensitization or phototoxicity at concentrations up to 5%. Further, this ingredient is reportedly used at concentrations of ≤0.2% in cosmetic products that may be aerosolized. The Panel noted that 95% – 99% of droplets/particles produced in cosmetic aerosols would not be respirable to any appreciable amount. However, the potential for inhalation toxicity is not limited to respirable droplets/particles deposited in the lungs. Inhaled droplets/particles deposited in the nasopharyngeal and bronchial regions of the respiratory tract may cause toxic effects depending on their chemical and other properties. Nevertheless, coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects.

*Cucumis sativus*, and therefore derived extracts, contains a variety of phytochemicals, all present at relatively low concentrations. Whereas certain components of these extracts could exert significant biological effects (e.g., isoflavones), the low levels that are present preclude significant effects. Also, although no dermal absorption data were available, it is the experience of the Panel that phytosterols and phytosterol esters are not significantly absorbed and do no result in systemic exposure. Additionally, the Panel noted that diacylglycerols are present as components of the lipids of cucumber fruit, but in an amount that is below the threshold for toxicological concern.

The Panel discussed the published tumor promotion study that reported a high level of mortality in mice after a dose of 5.0 mg cucumber extract in 0.2 ml acetone was applied to the skin, noting that the high mortality also was observed with other test articles that were tested. After extensive evaluation, the Panel stated that this study had sufficient methodological flaws to render the results not relevant to assessing the safety of cucumber extract in cosmetics.

Finally, the Expert Panel expressed concern regarding pesticide residues and heavy metals that may be present in botanical ingredients. They stressed that the cosmetics industry should continue to use the necessary procedures to limit these impurities in the ingredient before blending into cosmetic formulation.

## CONCLUSION

The CIR Expert Panel concluded that Cucumis Sativus (Cucumber) Fruit Extract, Cucumis Sativus (Cucumber) Extract, Cucumis Sativus (Cucumber) Fruit, Cucumis Sativus (Cucumber) Fruit Water, Cucumis Sativus (Cucumber) Juice, and Cucumis Sativus (Cucumber) Seed Extract are safe in the present practices of use and concentration.

# TABLES

**Table 1. Definitions, Functions, and Chemical Class**

| Ingredient (CAS No.) | Definition | Reported Function(s) | Chemical Class |
|---|---|---|---|
| Cucumis Sativus (Cucumber) Fruit Extract (89998-01-6) | the extract of the **fruit**, *Cucumis sativus* | skin conditioning agent – emollient; skin conditioning agent – misc. | biological product |
| Cucumis Sativus (Cucumber) Extract | the extract of the **whole plant**, *Cucumis sativus* | skin conditioning agent – misc. | biological product |
| Cucumis Sativus (Cucumber) Fruit | the **crushed fruit** of the cucumber, *Cucumis sativus* | skin conditioning agent – misc. | biological product |
| Cucumis Sativus (Cucumber) Fruit Water (89998-01-6) | an aq. solution of the steam distillate obtained from the **fruit** of *Cucumis sativus* | skin conditioning agent – misc. | essential oils and waters |
| Cucumis Sativus (Cucumber) Juice (8024-36-0; 89998-01-6) | the liquid expressed from the **fresh pulp** of the cucumber, *Cucumis sativus* | skin conditioning agent – misc. | biological product |
| Cucumis Sativus (Cucumber) Seed Extract | the extract of the **seeds** of *Cucumis sativus* | skin conditioning agent – misc. | biological product |

Reference[14]

**Table 2. Chemical and Physical Properties**

| Property | Description | Reference |
|---|---|---|
| | **Cucumis Sativus (Cucumber) Fruit Extract** | |
| appearance | pale yellow to yellow liquid | 39 |
| specific gravity | 0.772 to 0.786 (25°C) | 39 |
| refractive index | 1.31 to 1.36 (20°C) | 39 |
| | **Cucumber Sativus (Cucumber) Extract** | |
| appearance | fine light greenish powder | 13 |
| solubility | soluble in water and alcohol solutions | 13 |

**Table 3. Chemical constituents by plant part**

| Constituent | Amount (ppm) | Constituent | Amount (ppm) |
|---|---|---|---|
| ***Plant*** | | ***Sprout Seedling*** | |
| stigmasterol | NS | cucurbitacin-D | NS |
| 24(R)-14-α-methyl-24-ethyl-5-α-cholest-9(11)-en-3-β-ol | NS | cucurbitacin-I | NS |
| 24-ethyl-5α-cholesta-7,22-dien-3β-ol | NS | cladochromes | NS |
| 24-ethylcholesta-5-en-7β-ol | NS | | |
| 24-methylenepollinasterol | NS | ***Seed*** | |
| 7,22-stigmastadien-3β-ol | NS | avensterol | NS |
| nona-trans-2,cis-6-dien-al | NS | campesterol | NS |
| phylloquinone | 0.2 | gramisterol | NS |
| | | stellasterol | NS |
| ***Fruit*** | | isomultiflorineol | NS |
| water | 944,000-971,000 | multiflorineol | NS |
| phytosterols | 14-3544 | obtusifoliol | NS |
| β-sitosterol | NS | taraxerol | NS |
| α-tocopherol | 0.4-38 | cycloartenol | NS |
| β-carotene | 0.3-8 | 2,4-methylene-cholesterol | NS |
| β-amyrin | NS | 22-dihydrobrassicasterol | NS |
| squalene | NS | 24-β-ethyl-25(27)-dehydrolathosterol | NS |
| mevalonic acid | 3 | 24-ε-ethyl-25(27)-dehydrolophenol | NS |
| cucurbitacin-A | NS | 24-methyl-25(27)-dehydrocycloartanol | NS |
| cucurbitacin-B | NS | 24-methyl-cholest-7-en-3-β-ol | NS |
| cucurbitacin-C | NS | 24-methyl-lathosterol | NS |
| cucurbitacin-E | NS | 24-methylene-24-dihydro-lanosterol | NS |
| alanine | 180-4557 | 24-methylene-24-dihydro-parkeol | NS |
| arginine | 340-8608 | 24-methylene-cycloartenol | NS |
| aspartic acid | 320-8101 | 25(27)-dehydro-chondrillasterol | NS |
| citruliine | 146 | 25(27)-dehydro-fungisterol | NS |
| cystine | 30-7259 | 25(27)-dehydro-poriferasterol | NS |
| glycone | 190-4810 | 7-dehydro-avenasterol | NS |
| histidine | 80-2025 | 7-stigmasten-3β-ol | NS |
| isoleucine | 170-4303 | stigmast-7,22,25-trien-3-β-ol | NS |
| leucine | 230-5822 | stigmast-7,25-dien-3-β-ol | NS |
| lysine | 220-5570 | cycloeucanlenol | NS |
| methionine | 40-1012 | euphol | NS |
| proline | 120-3038 | lupeol | NS |
| serine | 160-4051 | tirucallol | NS |

**Table 3. Chemical constituents by plant part**

| Constituent | Amount (ppm) | Constituent | Amount (ppm) |
|---|---|---|---|
| ***Fruit (con't)*** | | ***Seed (con't)*** | |
| threonine | 150-3797 | α-amyrin | NS |
| tryptophan | 40-1012 | cucurbitin | NS |
| tyrosine | 90-2278 | spermidine | NS |
| valine | 170-4304 | β-pyrazol-1-yl-alanine | NS |
| glutamic acid | 1540-38987 | γ-glutamyl-γ-pyrazol-1-yl-alanine | NS |
| hexanal | NS | 1,3-diaminopropane | NS |
| hexen-(2)-al-(1) | NS | stearic acid | 11,100-69,785 |
| non-trans-2-en-al | NS | linoleic acid | 66,900-170,468 |
| nonadien-2,6-al-1 | NS | oleic acid | 116,100-180,000 |
| nonen-2-al-1 | NS | palmitic acid | 12,420-20,400 |
| pentadec-cis-8-en-1-al | NS | phosphatidylcholine | NS |
| propanal | NS | phosphatidylethanolamine | NS |
| nonadien-2,6-ol-2 | NS | phosphatidylglycerol | NS |
| monounsaturated fatty acids | 30-759 | phosphyatidylinositol | NS |
| oleic acid | 20-506 | lysolecithin | NS |
| polyunsaturated fatty acids | 510-12,911 | fat | 300,000-425,000 |
| linoleic acid | 220-5570 | butyric acid | 1200-1700 |
| α-linolenic acid | 290-7342 | phosphatidic acid | NS |
| saturated fatty acids | 330-8354 | | |
| myristic acid | 10-253 | ***Seed Oil*** | |
| palmitic acid | 270-6835 | 24-ε-ethyl-31-norlanosta-8,25(27)-dien-3-β-ol | 11 |
| stearic acid | 30-759 | | |
| folacin | 0.12-4 | ***Cotyledon*** | |
| niacin | 3-76 | stearic acid | 28,880-59,100 |
| pantothenic acid | 2.5-63 | linoleic acid | 35,100-486,700 |
| riboflavin | 0.2-5.12 | linolenic acid | 312,200 |
| thiamin | 0.3-7.6 | oleic acid | 55,200-241,000 |
| vitamin B6 | 0.5-13 | palmitic acid | 213,200-504,700 |
| fiber | 6000-151,896 | | |
| protein | 5120-142,772 | ***Leaf*** | |
| carbohydrates | 29,100-736,709 | 22-dihydro-spinasterol | NS |
| sugar | 10,000 | α-spinasterol | NS |
| fat | 900-43037 | stigmast-7-en-3-β-ol | NS |
| aluminum | 340-8608 | isoorientin | NS |
| arsenic | 0.003-0.25 | meloside-A | NS |
| ash | 3670-140,000 | | |
| barium | 2-70 | ***Petiole*** | |
| boron | 1-46 | d-glucose | NS |
| cadmium | 0.001-0.56 | sulfoquinovosyl-diacyl-glycerol | NS |
| calcium | 129-10,000 | | |
| chromium | 0.002-0.98 | | |
| cobalt | 0-0.14 | | |
| copper | 0.3-42 | | |
| iron | 2.6-420 | | |
| lead | 0.002-2.8 | | |
| lithium | 0.236-0.56 | | |
| magnesium | 101-7000 | | |
| manganese | 0.5-98 | | |
| mercury | 0-0.5 | | |
| molybdenum | 0.1-2.8 | | |
| nickel | 0.01-1.25 | | |
| phosphorus | 158-12600 | | |
| potassium | 120-3038 | | |
| rubidium | 0.4-19 | | |
| selenium | 0.001-2.8 | | |
| silicon | 10-1000 | | |
| silver | 0.01-0.14 | | |
| sodium | 16-714 | | |
| strontium | 4-98 | | |
| sulfur | 140-5250 | | |
| titanium | 0.3-18 | | |
| zinc | 2-157 | | |
| zirconium | 1.18-2.8 | | |
| fluorine | NS | | |
| nitrogen | 1400-80,000 | | |
| caffeic acid | NS | | |
| chlorogenic acid | NS | | |
| ferulic acid | NS | | |

NS – not specified
Reference[40]

**Table 4. Cucumis sativus (cucumber) lipids, and their fatty acid composition**

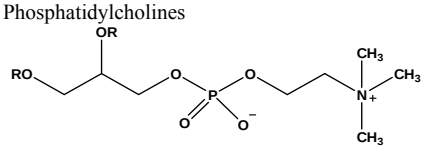
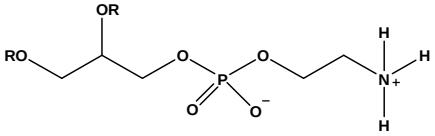
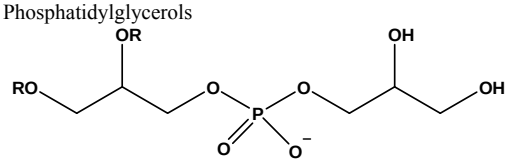
| | Percentage | Reference |
|---|---|---|
| **Fruit** | | |
| Lipid Class | (% of total lipid by weight) | [9] |
| phosphatidylcholines | 23.1 | |
| phosphatidylethanolamines | 16.6 | |
| phosphatidylglycerols | 2.0 | |
| phosphatidylinositols | 2.0 | |
| monogalactosyl diglycerides | 5.5 | |
| digalactosyl diglycerides | 6.1 | |
| cerebrosides | 6.5 | |
| sterol glucosides | 8.3 | |
| sterol acylglucosides | 4.9 | |
| sterols | 9.25 | |
| triacylglycerols | 3.8 | |
| 1,3-diacylglycerols | 2.2 | |
| 1,2-diacylglycerols | 2.2 | |
| Lipid Fatty Acid Class Profile | | |
| Phosphatidylcholines | | |
|  | | |
| : | | |
| wherein R is composed of the following fatty acid residues | (as % peak areas) | |
| 14:0 | 0.5 | |
| 16:0 | 19.6 | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | 0.4 | |
| 18:0 | 2.6 | |
| 18:1 | 2.1 | |
| 18:2 | 32.7 | |
| 18:3 | 40.8 | |
| 20:0 | 0.5 | |
| Phosphatidylethanolamines | | |
|  | | |
| : | | |
| wherein R is composed of the following fatty acid residues | | |
| 14:0 | 0.6 | |
| 16:0 | 40.8 | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | - | |
| 18:0 | 2.1 | |
| 18:1 | 1.8 | |
| 18:2 | 28.7 | |
| 18:3 | 24.6 | |
| 20:0 | 0.4 | |
| Phosphatidylglycerols | | |
|  | | |
| wherein R is composed of the following fatty acid residues: | - | |
| 14:0 | 62.4 | |
| 16:0 | trace | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | 6.5 | |
| 18:0 | 7.1 | |
| 18:1 | 11.8 | |
| 18:2 | 11.8 | |
| 18:3 | 0.1 | |
| 20:0 | | |

**Table 4. Cucumis sativus (cucumber) lipids, and their fatty acid composition**

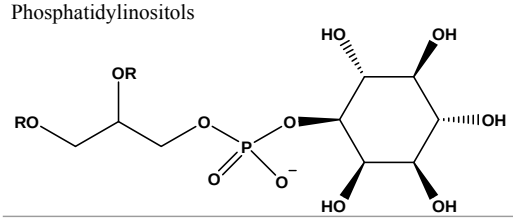
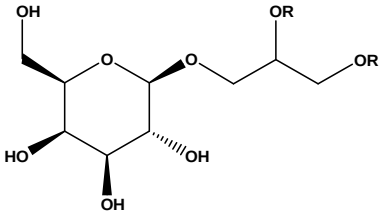
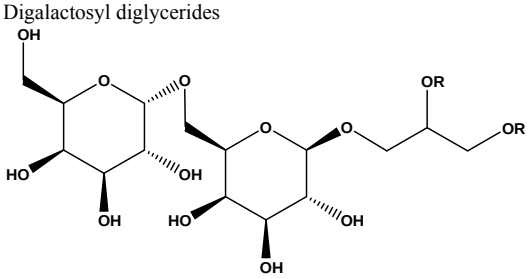
| | Percentage | Reference |
|---|---|---|
| Phosphatidylinositols  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 14:0 | - | |
| 16:0 | 50.6 | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | trace | |
| 18:0 | 4.0 | |
| 18:1 | 3.7 | |
| 18:2 | 22.6 | |
| 18:3 | 18.5 | |
| 20:0 | 0.4 | |
| Monogalactosyl diglycerides  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 14:0 | 2.4 | |
| 16:0 | 8.4 | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | 0.4 | |
| 18:0 | 1.5 | |
| 18:1 | 1.3 | |
| 18:2 | 11.4 | |
| 18:3 | 71.7 | |
| 20:0 | 2.0 | |
| Digalactosyl diglycerides  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 14:0 | 0.4 | |
| 16:0 | 20.6 | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | 0.4 | |
| 18:0 | 4.5 | |
| 18:1 | 2.6 | |
| 18:2 | 13.5 | |
| 18:3 | 53.2 | |
| 20:0 | 3.9 | |

**Table 4. Cucumis sativus (cucumber) lipids, and their fatty acid composition**

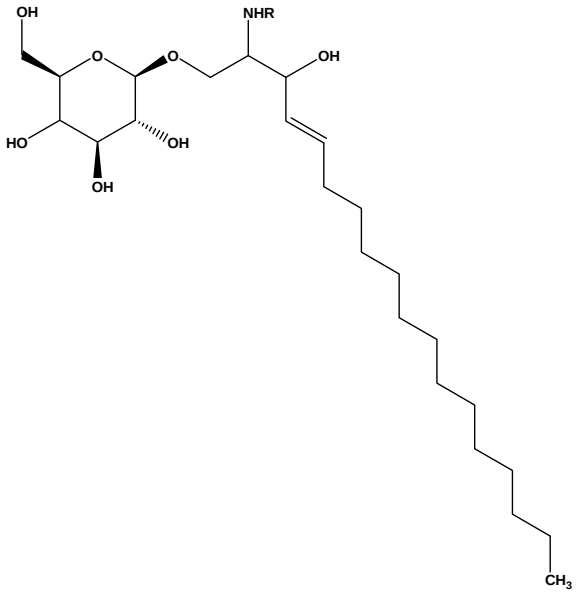
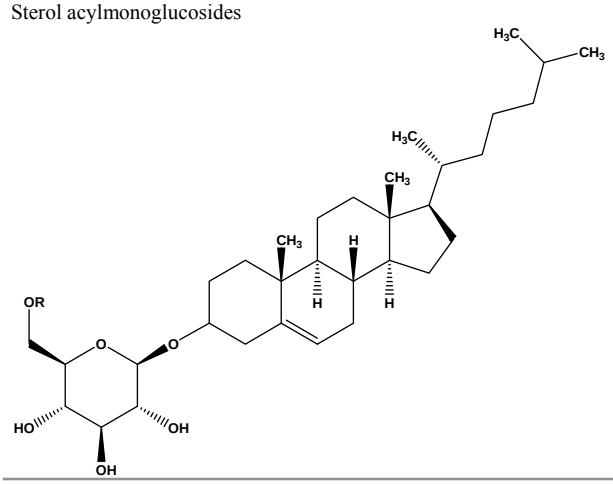
| | Percentage | Reference |
|---|---|---|
| Cerebrosides | | |
|  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 14:0 | 1.8 | |
| 16:0 | 7.0 | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | - | |
| 18:0 | 2.5 | |
| 18:1 | 1.9 | |
| 18:2 | 8.5 | |
| 18:3 | 9.7 | |
| 20:0 | - | |
| Sterol acylmonoglucosides | | |
|  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 14:0 | 3.7 | |
| 16:0 | 29.6 | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | 6.8 | |
| 18:0 | 6.9 | |
| 18:1 | 2.8 | |
| 18:2 | 24.7 | |
| 18:3 | 21.9 | |
| 20:0 | 3.5 | |

**Table 4. Cucumis sativus (cucumber) lipids, and their fatty acid composition**

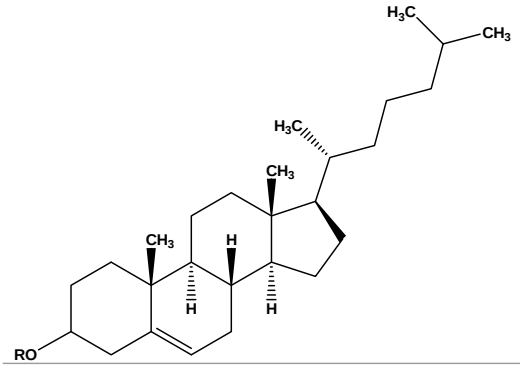
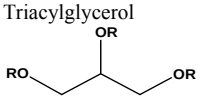
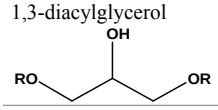
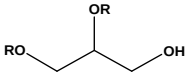
| | Percentage | Reference |
|---|---|---|
| Sterol esters   | | |
| wherein R is composed of the following fatty acid residues: | | |
| 14:0 | 1.2 | |
| 16:0 | 79.0 | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | 3.4 | |
| 18:0 | 1.8 | |
| 18:1 | 1.4 | |
| 18:2 | 23.8 | |
| 18:3 | 57.7 | |
| 20:0 | - | |
| Triacylglycerol   | | |
| wherein R is composed of the following fatty acid residues: | | |
| 14:0 | 0.4 | |
| 16:0 | 10.0 | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | 1.1 | |
| 18:0 | 1.7 | |
| 18:1 | 2.5 | |
| 18:2 | 27.6 | |
| 18:3 | 55.8 | |
| 20:0 | 0.2 | |
| 1,3-diacylglycerol   | | |
| wherein R is composed of the following fatty acid residues: | | |
| 14:0 | 1.7 | |
| 16:0 | 13.2 | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | 0.6 | |
| 18:0 | 1.8 | |
| 18:1 | 2.0 | |
| 18:2 | 21.4 | |
| 18:3 | 52.0 | |
| 20:0 | - | |
| 1,2-diacylglycerol   | | |
| wherein R is composed of the following fatty acid residues: | | |
| 14:0 | 1.8 | |
| 16:0 | 28.5 | |
| 16:1 (16:1(*cis*-9 and *trans*-3) | 1.3 | |
| 18:0 | 4.5 | |
| 18:1 | 4.0 | |
| 18:2 | 25.4 | |
| 18:3 | 29.7 | |
| 20:0 | 0.3 | |

**Table 4. Cucumis sativus (cucumber) lipids, and their fatty acid composition**

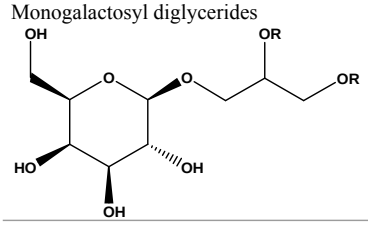
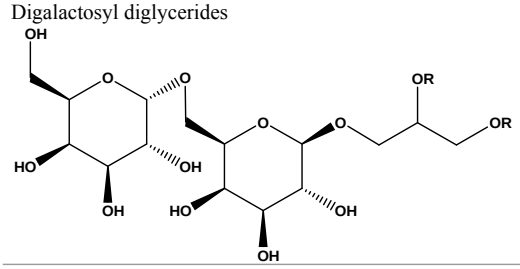
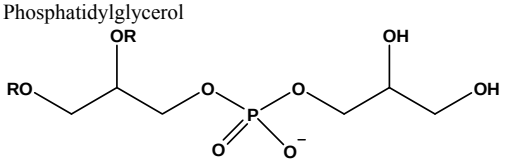
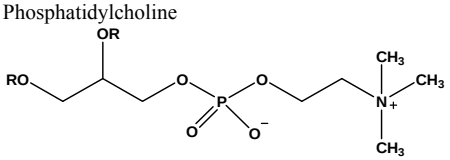
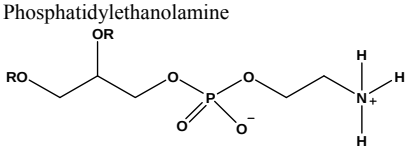
| | Percentage | Reference |
|---|---|---|
| Galactolipid Fatty Acids (as % of total fatty acids in the individual galactolipids) | | [41] |
| Monogalactosyl diglycerides  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 16:0 | 1.6 | |
| 16:1 | 0.3 | |
| 18:0 | 0.3 | |
| 18:1 | 1.2 | |
| 18:2 | 20.4 | |
| 18:3 | 76.2 | |
| Digalactosyl diglycerides  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 16:0 | 9.1 | |
| 16:1 | 0.2 | |
| 18:0 | 1.5 | |
| 18:1 | 1.6 | |
| 18:2 | 12.8 | |
| 18:3 | 74.8 | |
| Phospholipid Fatty Acids (as % of total fatty acids in the individual phospholipids) | | |
| Phosphatidylglycerol  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 16:0 | 47.4 | |
| *t*-16:1(3) | - | |
| *c*-16:1(3) | - | |
| 18:0 | 11.3 | |
| 18:1 | 19.0 | |
| 18:2 | 12.7 | |
| 18:3 | 9.6 | |
| Phosphatidylcholine  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 16:0 | 36.9 | |
| 16:1 | - | |
| 18:0 | 3.6 | |
| 18:1 | 5.0 | |
| 18:2 | 36.7 | |
| 18:3 | 17.8 | |
| Phosphatidylethanolamine  | | |

**Table 4. Cucumis sativus (cucumber) lipids, and their fatty acid composition**

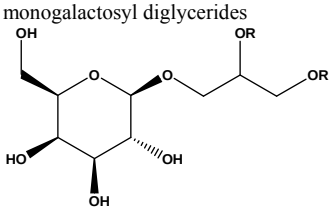
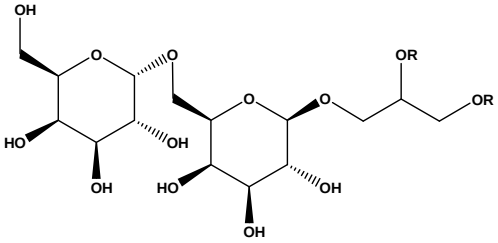
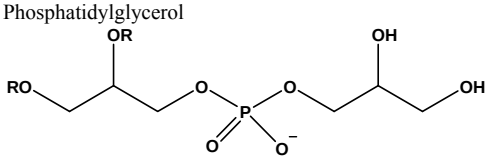
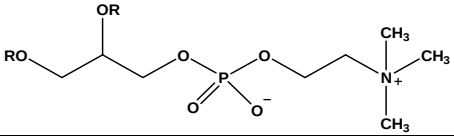
| | Percentage | Reference |
|---|---|---|
| wherein R is composed of the following fatty acid residues: | | |
| 16:0 | 32.7 | |
| 16:1 | 0.1 | |
| 18:0 | 1.2 | |
| 18:1 | 2.4 | |
| 18:2 | 47.5 | |
| 18:3 | 16.1 | |
| **Leaf (Chloroplasts)** | | |
| Galactolipid Fatty Acids (as % of total fatty acids in the individual galactolipids) | | 41 |
| monogalactosyl diglycerides  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 16:0 | 1.0 | |
| 16:1 | 0.4 | |
| 18:0 | 0.1 | |
| 18:1 | 0.8 | |
| 18:2 | 2.5 | |
| 18:3 | 95.2 | |
| digalactosyl diglycerides  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 16:0 | 9.5 | |
| 16:1 | 0.5 | |
| 18:0 | 0.9 | |
| 18:1 | 1.2 | |
| 18:2 | 2.3 | |
| 18:3 | 85.6 | |
| Phospholipid Fatty Acids (as % of total fatty acids in the individual phospholipids) | | |
| Phosphatidylglycerol  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 16:0 | 30.0 | |
| *t*-16:1(3) | 19.4 | |
| *c*-16:1(3) | 1.5 | |
| 18:0 | 12.0 | |
| 18:1 | 19.0 | |
| 18:2 | 5.0 | |
| 18:3 | 13.1 | |
| Phosphatidylcholine  | | |

**Table 4. Cucumis sativus (cucumber) lipids, and their fatty acid composition**

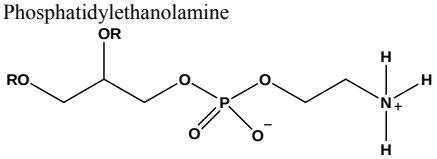
| | Percentage | Reference |
|---|---|---|
| wherein R is composed of the following fatty acid residues: | | |
| 16:0 | 27.2 | |
| 16:1 | 0.1 | |
| 18:0 | 6.9 | |
| 18:1 | 1.1 | |
| 18:2 | 15.8 | |
| 18:3 | 48.9 | |
| Phosphatidylethanolamine  | | |
| wherein R is composed of the following fatty acid residues: | | |
| 16:0 | 30.0 | |
| 16:1 | 0.1 | |
| 18:0 | 3.1 | |
| 18:1 | 1.2 | |
| 18:2 | 21.4 | |
| 18:3 | 44.2 | |

**Table 5. Cucumber seed composition**

| | | |
|---|---|---|
| Mixed Fatty Acids (excluding non-saponifiables) | (% by weight) | [42] |
| saturated acids | 13.23 | |
| unsaturated acids | | |
| conjugated triene (expressed as α-eleostearic) | - | |
| linoleic | 52.43 | |
| oleic | 34.78 | |
| Triterpene Alcohols from the unsaponifiable matter of the seed lipids (triterpene alcohols comprise 0.002% of the seeds) | (%) | [43] |
| isomultiflorenol | 52 | |
| multiflorenol | 5 | |
| α-amyrin | 2 | |
| β-amyrin | 5 | |
| taraxerol | trace | |
| lupeol | trace | |
| cycloartenol | 10 | |
| 24-methylenecycloartanol | 13 | |
| 24-methyl-25(27)-dehydrocycloartanol | 1 | |
| 24-methylene-24-dihydrolanosterol | 7 | |
| 24-methlenene-24-dihydroparkeol | 1 | |
| euphol | 2 | |
| tirucallol | 1 | |
| seed kernels | 42% oil<br>42% protein | [3] |

**Table 6a. Conclusions of CIR safety assessments on ingredients that are constituents of cucumber**

| Component Reviewed | Conclusion | Reference |
|---|---|---|
| Myristic Acid | safe as used (≤10% in leave-ons; ≤19% in rinse-offs) | 44 |
| Oleic Acid | safe as used (≤20% in leave-ons; ≤19% in rinse-offs) | 45,46 |
| Palmitic Acid | safe as used (≤16% in leave-ons; ≤20% in rinse-offs) | 45,46 |
| Stearic Acid | safe as used (≤22% in leave-ons; ≤43% in rinse-offs) | 45,46 |
| Niacin | safe as used (≤0.1% in leave-ons) | 47 |
| Pantothenic Acid | safe as used (≤0.01% in leave-ons: 0.00001% in rinse-offs) | 46,48 |
| Squalene | safe as used (≤97% in leave-on products; ≤5% in rinse-offs)) | 49,50 |
| Tocopherol | safe as used (≤2% in leave-ons; ≤0.4% in rinse-offs; ≤0.8% in products diluted for use) | 51 |

**Table 6b. Toxicity information on some components of cucumber as discussed in previous CIR reports**

| Component | Toxicity information | Reference |
|---|---|---|
| Caffeic Acid<br>Ferulic Acid | these acids are reported to penetrate skin and have UV photoprotective activity; an IARC report stated that there was evidence for carcinogenicity in animals, but the effect in humans was not conclusive | 52 |
| Chlorogenic Acid | an antioxidant that inhibited tumor promotion by phorbol esters in mice; some controversy exists over allergic reactions in green coffee beans, but it was accepted that chlorogenic acid was not the allergen | 52 |
| Phytosterols | oral studies demonstrate that phytosterols and phytosterol esters are not significantly absorbed and do not result in systemic exposure; small amounts did appear in the ovaries; well-defined phytosterols and phytosterol esters are not estrogenic and do not pose a hazard to reproduction; phytosterols were not mutagenic in bacterial and mammalian systems | 2 |
| Tannins | IARC has concluded that tannins are not classifiable to their carcinogenicity | 52 |
| Triterpene Alcohols | hepatoprotective and anti-carcinogenic activity has been suggested for lupeol; no toxicity data were available; triterpene alcohols were considered to have intermediate risk | 52 |

**Table 7. Frequency and concentration of use according to duration and type of exposure**

| | Cucumis Sativus (Cucumber Fruit Extract | | Cucumis Sativus (Cucumber) Extract | | Cucumis Sativus (Cucumber) Fruit | |
|---|---|---|---|---|---|---|
| | *# of Uses*[15] | *Max. Conc. of Use (%)*[16] | *# of Uses*[15] | *Max. Conc. of Use (%)*[16] | *# of Uses*[15] | *Max. Conc. of Use (%)*[16] |
| **Totals*** | **534** | **0.0000001-1** | **9** | **0.0002-0.003** | **3** | **NR** |
| ***Duration of Use*** | | | | | | |
| *Leave-On* | *350* | *0.00005-1* | *9* | *0.008-0.002* | *2* | *NR* |
| *Rinse Off* | *177* | *0.0000001-0.4* | *NR* | *0.0002-0.003* | *1* | *NR* |
| *Diluted for (Bath) Use* | *7* | *0.0005* | *NR* | *NR* | *NR* | *NR* |
| ***Exposure Type*** | | | | | | |
| Eye Area | 96 | 0.002-1 | NR | NR | NR | NR |
| Incidental Ingestion | NR | 0.01-0.1 | NR | NR | NR | NR |
| Incidental Inhalation-Spray | 13 | 0.002-0.2 | NR | NR | NR | NR |
| Incidental Inhalation-Powder | 2 | 0.002 | | 0.0008 | | NR |
| Dermal Contact | 512 | 0.0000001-1 | 9 | 0.0002-0.003 | 3 | NR |
| Deodorant (underarm) | 1[a] | NR | NR | NR | NR | NR |
| Hair - Non-Coloring | 19 | 0.0002-0.2 | NR | NR | NR | NR |
| Hair-Coloring | NR | NR | NR | NR | NR | NR |
| Nail | 2 | 0.01 | NR | NR | NR | NR |
| Mucous Membrane | 59 | 0.0000001-0.1 | NR | 0.002-0.003 | NR | NR |
| Baby Products | 7 | 0.001 | NR | NR | NR | NR |

| | Cucumis Sativus (Cucumber) Fruit Water | | Cucumis Sativus (Cucumber) Juice | | Cucumis Sativus (Cucumber) Seed Extract | |
|---|---|---|---|---|---|---|
| | *# of Uses*[15] | *Max. Conc. of Use (%)*[16] | *# of Uses*[15] | *Max. Conc. of Use (%)*[16] | *# of Uses*[15] | *Max. Conc. of Use (%)*[16] |
| **Totals*** | **NR** | **0.05-3** | **5** | **NR** | **6** | **0.01-0.08** |
| ***Duration of Use*** | | | | | | |
| *Leave-On* | *NR* | *0.05-3* | *4* | *NR* | *4* | *0.08* |
| *Rinse Off* | *NR* | *0.05* | *1* | *NR* | *2* | *0.01* |
| *Diluted for (Bath) Use* | *NR* | *NR* | *NR* | *NR* | *NR* | *NR* |
| ***Exposure Type*** | | | | | | |
| Eye Area | NR | NR | NR | NR | 1 | NR |
| Incidental Ingestion | NR | NR | NR | NR | NR | NR |
| Incidental Inhalation-Spray | NR | NR | NR | NR | NR | NR |
| Incidental Inhalation-Powder | NR | NR | NR | NR | NR | NR |
| Dermal Contact | NR | 0.05-3 | 5 | NR | 6 | 0.01-0.08 |
| Deodorant (underarm) | NR | NR | 1[a] | NR | NR | NR |
| Hair - Non-Coloring | NR | NR | NR | NR | NR | NR |
| Hair-Coloring | NR | NR | NR | NR | NR | NR |
| Nail | NR | NR | NR | NR | NR | NR |
| Mucous Membrane | NR | NR | NR | NR | NR | NR |
| Baby Products | NR | NR | NR | NR | NR | NR |

* Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types my not equal the sum of total uses
NR – not reported
[a] It is not known whether or not the product is a spray

## REFERENCES


1. Burnett, CL, Fiume MM, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Leibler DC, Marks JG, Shank RC, Slaga TJ, Snyder PW, and Andersen FA. Safety assessment of plant-derived fatty acid oils as used in cosmetics. Washington, D.C., Cosmetic Ingredient Review. 2011. http://cir-safety.org/staff_files/oils032011final.pdf.

2. Andersen FA (ed). Final report of the amended safety assessment of PEG-5, -10, -16, -25, -30, and -40 Soy Sterol. *Int J Toxicol*. 2004;23:(Suppl 2):23-47.

3. van Luijk MN. Cucumis sativus L. http://database.prota.org/dbtw-wpd/exec/dbtwpub.dll?AC=GET_RECORD&XC=/dbtw-wpd/exec/dbtwpub.dll&BU=http%3A%2F%2Fdatabase.prota.org%2Fsearch.htm&TN=Protabase&SN=AUTO26581&SE=565&RN=0&MR=20&TR=0&TX=1000&ES=0&CS=1&XP=&RF=Webreport&EF=Basic+Record+Form&DF=Webdisplay&RL=0&EL=1&DL=0&NP=3&ID=&MF=&MQ=&TI=0&DT=&ST=0&IR=402&NR=0&NB=0&SV=0&SS=0&BG=&FG=&QS=Search&OEX=ISO-8859-1&OEH=ISO-8859-1. Wageningen, Netherlands. 2004. Date Accessed 7-25-2011.

4. D'Amelio FS Sr. Botanicals. A Phytocosmetic Desk Reference. Boca Raton, FL: CRC Press, 1999.

5. Patri F and Silano V. Plants in cosmetics. Plants and plant preparations used as ingredients for cosmetic products. Strasbourg: Council of Europe Publishing, 2002.

6. Kumar D, Kumar S, Singh J, Rashmi N, Vashistha BD, and Singh N. Free radical scavenging and analgesic activities of *Cucumis sativus* L. fruit extract. *J Young Pharm*. 2010;2:(4):365-368.

7. Kuhnle GGC, Dell'Aquila C, Aspinall SM, Runswick SA, Joosen AMCP, Mulligan AA, and Bingham SA. Phytoestrogen content of fruits and vegetables commonly consumed in the UK based on LC-MS and 13C-labelled standards. *Food Chemistry*. 2009;116:(2):542-554.

8. Han J-H, Yang Y-X, and Feng M-Y. Contents of phytosterols in vegetables and fruits commonly consumed in China. *Biomedical and Environmental Sciences*. 2008;21:(6):449-453.

9. Fishwick MJ, Wright AJ, and Galliard T. Quantitative composition of the lipids of cucumber fruit (Cucumis sativus). *Journal of the Science of Food and Agriculture*. 1977;28:(4):394-398.

10. Peng AC and Geisman JR. Lipid and fatty acid composition of cucumbers and their changes suring storage of fresh-pack pickles. *J Food Sci*. 1976;41:859-862.

11. MakingCosmetics.com. Cucumber Fruit Extract. Fact sheet [pamphlet]. 7-17-2011.

12. Personal Care Products Council. 10-26-2011. Preparation Methods for Cucumis Sativus (Cucumber) Fruit Extract. Unpublished data submitted by Personal Care Products Council. 1 pages.

13. New Directions Aromatics. Materials Safety Data Sheet - Cucumber Peel Powdered Extract (INCI name - Cucumis sativus (cucumber) extract) [pamphlet]. 10-12-2008.

14. Gottschalck TE and Breslawec HP. International Cosmetic Ingredient Dictionary and Handbook. 14 *ed*. Washington, DC: Personal Care Products Council, 2012.

15. Food and Drug Administration (FDA). Frequency of use of cosmetic ingredients. *FDA Database.* 2011. Washington, DC: FDA.Updated Feb 25.

16. Personal Care Products Council. 1-10-2012. Concentration of use by FDA Product Category: *Cucumis sativus*-derived ingredients. Unpublished data submitted by Personal Care Products Council. 3 pages.

17. Bremmer HJ, Prud'homme de Lodder LCH, and Engelen JGM. Cosmetics Fact Sheet: To assess the risks for the consumer; Updated version for ConsExpo 4. 2006. Report No. RIVM 320104001/2006. pp. 1-77.

18. Johnsen MA. The influence of particle size. *Spray Technology and Marketing*. 2004;November:24-27.

19. Rothe H. Special Aspects of Cosmetic Spray Evalulation. 9-26-2011. Unpublished data presented at the 26 September CIR Expert Panel meeting. Washington, D.C.

20. Rothe H, Fautz R, Gerber E, Neumann L, Rettinger K, Schuh W, and Gronewold C. Special aspects of cosmetic spray safety evaluations: Principles on inhalation risk assessment. *Toxicol Lett*. 2011;205:(2):97-104.

21. European Commission. European Commission Health and Consumers Cosmetics - Cosing - Database. http://ec.europa.eu/consumers/cosmetics/cosing/. 2010. Date Accessed 2011.

22. Personal Care Products Council. 10-17-2011. Summaries of Studies of Cucumis Sativus (Cucumber) Fruit Extract. Unpublished data submitted by Personal Care Products Council. 1 pages.

23. Stoltz DR, Stavric B, Stapley R, Klassen R, Bendall R, and Krewski , D. Mutagenicity screening of foods. 2.Results with fruits and vegetables. *Environ Mutagen*. 1984;6:343-354.

24. Villasenor IM, Simon, MK, and Villanueva AMA. Comparative potencies of nutraceuticals in chemically induced skin tumor prevention. *Nutrition and cancer*. 2002;44:(1):66-70.

25. Rajvanshi A, Sharma S, Khokra SL, Sahu RK, and Jangde R. Formulation and evaluation of *Cyperus rotundus* and *Cucumis sativus* based herbal face cream. *Pharmacologyonline*. 2011;2:1238-1244.

26. Personal Care Products Council. 9-19-2011. Summaries of Studies of Products Containing Cucumis Sativus (Cucumber) Fruit Extract. Unpublished data submitted by Personal Care Products Council. 3 pages.

27. Clinical Research Laboratories Inc. 1995. Repeated insult patch test of an eye lotion containing 1% Cucumis Sativus (Cucumber) Fruit Extract. Unpublished data submitted by the Personal Care Products Council.

28. Orentreich Research Corporation. 2012. Predictive patch test study of an eye treatment mask containing 1% Cucumis Sativus (Cucumber) Fruit Extract. Unpublished data submitted by the Personal Care Products Council.

29. Consumer Product Testing Co. 2005. Final report on the repeated insult patch test on an eye lotion containing 1% Cucumis Sativus (Cucumber) Fruit Extract. Experiment Ref. No. C05-0363.01. Unpublished data submitted by the Personal Care Products Council on Jan. 24, 2012. (15 pp).

30. Hill-Top Research Inc. 1995. Summary of a human repeat insult patch test of an eye hydrogel containing 5% Cucumis Sativus (Cucumber) Fruit Extract. Unpublished data submitted by Personal Care Products Council. 1 pages.

31. EviC-CEBA. 1992. Summary of a clinical safety assessment of the cutaneous tolerance to a daily repeated application of an eye gel containing 5% Cucumis Sativus (Cucumber) Fruit Extract. Unpublished data submitted by Personal Care Products Council. 1 pages.

32. Clinical Science Research International Ltd. 1992. Summary of a dermal phototoxicity study of an eye gel containing 5% Cucumis Sativus (Cucumber) Fruit Extract. Unpublished data submitted by Personal Care Products Council. 1 pages.

33. Jordan-Wagner DL, Whisman BA, and Goetz DW. Cross-allergenicity among celery, cucumber, carrot, and watermelon. *Annals of allergy*. 1993;71:(1):70-79.

34. Enberg RN, Leickly FE, McCullough J, Bailey J, and Ownby DR. Watermelon and ragweed share allergens. *J Allergy Clin Immunol*. 1987;79:(6):867-875.

35. Vlaicu PC, Rusu LC, Ledesma A, Vicente M, Cuevas M, Zamorano M, Antolin D, Alvarez E, and DeLa H. Cucumber anaphylaxis in a latex-sensitized patient. *Journal of investigational allergology & clinical immunology : official organ of the International Association of Asthmology (INTERASMA) and Sociedad Latinoamericana de Alergia e Inmunologia*. 2011;21:(3):236-239.

36. Zachariae COC. Cucumber contact dermatitis. *Contact Dermatitis*. 2000;43:240-241.

37. Institute for In Vitro Sciences, Inc. 8-19-2005. Final report on the topical application ocular irritation screening assay using the EpiOcular™ human cell construct of an eye lotion containing 1% Cucumis Sativus (Cucumber) Fruit Extract. Study No. 05AC89, 03AA04.015001. Unpublished data submitted by the Personal Care Products Council on Jan. 24, 2012. (11 pp).

38. Clinical Research Laboratories, Inc. 7-29-2005. Final report of the safety in-use study to determine the ocular and dermal irritation potential of a dark circles eye area product containing 1% Cucumis Sativus (Cucumber) Fruit Extract. CRL Study No. CRL63405. Unpublished data submitted by the Personal Care Products Council on Jan. 24, 2012. (7 pp).

39. The Good Scents Company. Cucumber Extract [pamphlet]. 2011.

40. Dr. Duke's Phytochemical and Ethnobotanical Database. http://sun.ars-grin.gov:8080/npgspub/xsql/duke/plantdisp.xsql?taxon=325. 2011. Date Accessed 7-25-2011.

41. Whitaker BD. Fatty-acid composition of polar lipids in fruit and leaf chloroplasts of "16:3"- and "18:3"-plant species. *Planta*. 1986;169:(3):313-319.

42. Chakrabarty MM, Chowdhury DK, and Mukherji BK. Seed fats of Cucurbitaceae. *Naturwissenschaften*. 1955;42:344-345.

43. Itoh T, Shigemoto T, Shimizu N, Tamura T, and Matsumoto T. Triterpene alcohols in the seeds of two Cucumis species of Cucurbitaceae. *Phytochemistry (Elsevier)*. 1982;21:(9):2414-2415.

44. Becker LC, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Marks JG, Shank RC, Slaga TJ, Snyder PW, and Andersen FA. Final report of the amended safety assessment of myristic acid and its salts and esters as used in cosmetics. *Int J Toxicol*. 2010;29:(Suppl 3):162S-186S.

45. Elder RL (ed). Final report on the safety assessement of oleic acid, lauric acid, palmitic acid, myrisitic acid, and stearic acid. *J Am Coll Toxicol*. 1987;321:(401).

46. Andersen FA. Annual review of cosmetic ingredient safety assessements - 2004/2005. *Int J Toxicol*. 2006;25:(Suppl 2):1-89.

47. Andersen FA (ed). Final report on the safety assessement of niacinamide and niacin. *Int J Topxicol*. 2005;24:(Suppl 5):1-31.

48. Elder RL (ed). Final report on the safety assessment of panthenol and pantothenic acid. *J Am Coll Toxicol*. 2011;6:(1):139-162.

49. Elder RL (ed). Final report on teh safety assessment of squalane and squalene. *J Am Coll Toxicol*. 1982;1:(2):37-56.

50. Andersen FA. Annual review of cosmetic ingredient safety assessments - 2001/2002. *Int J Toxicol*. 2003;22:(Suppl 1):1-35.

51. Andersen FA (ed). Final report on the safety assessment of tocopherol, tocopheryl acetate, tocopheryl linoleate, tocopheryl linoleate/oleate, tocopheryl nicotinate, tocopheryl succinate, dioleyl tocopheryl methylsilanol, potassium ascorbyl tocopheryl phospate, and tocophersolan. *Int J Toxicol*. 2011;21:(3):51-116.

52. Andersen FA, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Leibler DC, Marks JG, Shank RC, Slaga TJ, and Snyder PW. Final report of the Cosmetic Ingredient Review Expert Panel. Amended safety assessment of Calendula officinalis-derived cosmetic ingredients. *Int J Toxicol*. 2010;29:(4):221S-243S.