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Amended Safety Assessment of Sesamum Indicum (Sesame) Seed Oil, Hydrogenated Sesame Seed Oil, Sesamum Indicum (Sesame) Oil Unsaponifiables, and Sodium Sesameseedate

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Abstract

Sesamum indicum (sesame) seed oil and related cosmetic ingredients are derived from *Sesamum indicum*. Sesamum indicum (sesame) seed oil, sesamum indicum (sesame) oil unsaponifiables, and hydrogenated sesame seed oil function as conditioning agents. Sodium sesameseedate functions as a cleansing agent, emulsifying agent, and a nonaqueous viscosity increasing agent. These ingredients are neither skin irritants, sensitizers, teratogens, nor carcinogens at exposures that would result from cosmetic use. Both animal and human data relevant to the cosmetic use of these ingredients were reviewed. The CIR Expert Panel concluded that these ingredients are safe in the present practices of use and concentration as described in this safety assessment.

Keywords

cosmetics, hydrogenated sesame seed oil, safety, sesamum indicum (sesame) oil unsaponifiables, sesamum indicum (sesame) seed oil and related cosmetic ingredients derived from *Sesamum indicum*

Introduction

The Cosmetic Ingredient Review (CIR) Expert Panel previously evaluated the safety of sesame oil with the conclusion that this cosmetic ingredient is safe in the practices of use at that time.[1]

Sesame oil is primarily composed of oleic, linoleic, palmitic, and stearic acids and is used in a variety of cosmetics that come into contact with skin, eyes, hair, and mucous membranes. The oral median lethal dose (LD_{50}) of a lipstick containing sesame oil (10%-11%) was greater than 5 g/kg. The dermal LD_{50} was greater than 2 g/kg. The acute intravenous LD_{50} of sesame oil for rabbits was 0.74 mL/kg. This ingredient is neither a primary skin nor ocular irritant. A formulation containing sesame oil was neither a sensitizer nor a photosensitizer. Although not teratogenic, sesame oil increased resorptions and deciduomas in mice. Extracts of sesame seeds were not mutagenic with metabolic activation.

Because the available safety test data in that safety assessment, combined with newly available data on the oil, are considered adequate to address the safety of the hydrogenated oil, the oil unsaponifiables, and the sodium salt of the fatty acid components of the oil, the Expert Panel has amended the original conclusion to include additional ingredients.

Accordingly, the amended safety assessment includes the following:

Sesamum indicum (sesame) seed oil,
Hydrogenated sesame seed oil,
Sesamum indicum (sesame) oil unsaponifiables, and
Sodium sesameseedate.

Only the newly available data are addressed in this report.

In other previous safety assessments, the Expert Panel has assessed the safety of 6 fatty acid components of sesame oil: oleic acid, lauric acid, palmitic acid, myristic acid, stearic acid,[2] and arachidonic acid.[3]

Although sesamum indicum (Sesame) seed is listed in the *International Cosmetic Ingredient Dictionary and Handbook*, its safety is not reviewed in this safety assessment.

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Chemistry

Sesamum Indicum (Sesame) Seed Oil

Sesamum Indicum (Sesame) Seed Oil (CAS No. 8008-74-0) is the oil obtained from the seeds of *Sesamum indicum*.[4] Other names for this ingredient include gingilli oil, sesame oil, sesame seed oil, and sesami oleum.

Sesamum indicum (sesame) seed oil has also been defined as the refined fixed oil obtained from the seed of one or more cultivated varieties of *Sesamum indicum* L. (Family Pedaliaceae; Welch, Holme, and Clark Co, Inc 2008).[5] Chen et al[6] have described the oil bodies of plant seeds as containing a triacylglycerol matrix surrounded by a monolayer of phospholipids embedded with alkaline proteins termed oleosins.

Sesamum Indicum (Sesame) Oil Unsaponifiables

Sesamum Indicum (Sesame) Oil Unsaponifiables (no CAS No.) is the fraction of sesame oil that is not saponified in the refining recovery of sesame oil fatty acids.[4] Other names for this ingredient include sesame oil unsaponifiables; sesamum indicum unsaponifiables; unsaponifiables, sesame oil; and unsaponifiables, sesamum indicum.

Hydrogenated Sesame Seed Oil

Hydrogenated Sesame Seed Oil (no CAS No.) is the end product of the controlled hydrogenation of sesamum indicum (sesame) seed oil.[4]

Sodium Sesameseedate

Sodium Sesameseedate (no CAS No.) is the sodium salt of the fatty acids derived from sesamum indicum seed oil.[4]

Chemical and Physical Properties

Sesamum indicum (sesame) seed oil. The chemical and physical properties of different samples of sesame oil vary slightly. However, the description of sesame oil used in cosmetics is representative of the oil in general. As specified for use in cosmetics, sesame oil must have a characteristic odor with no suggestion of rancidity. The infrared absorption spectrum of the oil must be a close match to the Cosmetic, Toiletry and Fragrance Association (CTFA) spectrum. Sesame oil must contain no cottonseed oil. The specific gravity of the oil at 25°C must be 0.916 to 0.921. The acid value must not exceed 2.0. The unsaponifiable matter must not exceed 2.0%. The saponification value must be between 187 and 195. The iodine value must be between 103 and 116. The titer of fatty acids must be 20°C to 25°C.[7] Sesame oil absorbs neither in the ultraviolet A (UVA) nor ultraviolet B (UVB) wavelength range.[8]

Sesame oil does not cloud at temperatures greater than or equal to 0°C (Swern 1979).[9] It becomes solid at about –5°C.[10] Sesame oil is soluble in chloroform, ether, petroleum ether, hexane, and carbon disulfide. It is slightly soluble in alcohol and is insoluble in water.[7,10]

According to the Agricultural Marketing Resource Center,[11] commercially, the 2 basic types of sesame oil are as follows: one type is a pale, yellow liquid (high in polyunsaturated fat; used as a frying oil) with a pleasant grainlike odor and somewhat nutty taste. The other type of oil is amber-colored and aromatic (in cooking, used as a flavoring agent) and is made from pressed and toasted sesame seeds. It is not used as a cooking oil, because the flavor is too intense and it burns easily, but is normally added as a flavoring agent in the final stages of cooking. The outstanding characteristic of sesame oil is its long shelf life, a quality that makes it applicable for use in the manufacture of margarine in many parts of the world with inadequate refrigeration.

Composition

Sesamum indicum (sesame) seed oil. The monounsaturated, diunsaturated, and triunsaturated triglycerides of sesame oil consist principally of oleic acid, linoleic acid, and other fatty acids in smaller amounts. Table 1 includes the CIR review status of fatty acid components of sesamum indicum (sesame) seed oil.

Sesame oil contains nonsaponifiable substances that are not removed by refining. Sesamol, sesamin, and sesamolin have been detected in sesame oil but have not been detected in other fats. The structures of these compounds are included in Figure 1. Sesame oil contains 0.4% to 1.1% sesamin, 0.3% to 0.6% sesamolin, and traces of sesamol.

The heavy metals specification for refined sesame oil is less than 0.001% max.[13]

Method of Manufacture

Sesamum indicum (sesame) seed oil. Oil is extracted from sesame seeds by mechanical pressing.[11] The seed may be cold pressed to produce an aromatic salad oil or hot pressed to produce a lower grade product. The oil yield varies from 50% to 57%, depending on the growing conditions and seed variety. Sesame oil is extracted by pressure in a mechanical expeller and is tolerant of only minimal heating by the extraction process.

Sesamum Indicum (Sesame) Oil Unsaponifiables

The refining recovery of sesame oil fatty acids from sesamum indicum (sesame) seed oil yields a fraction that is not saponified, that is, sesamum indicum (sesame) oil unsaponifiables.[4]

Hydrogenated Sesame Seed Oil

Hydrogenated sesame seed oil results from the controlled hydrogenation of sesamum indicum (sesame) seed oil.[4]

Impurities

Sesamum indicum (sesame) seed oil. The following chlorinated benzene residues have been reported in crude sesame oil (from China): 1,4-dichlorobenzene (0.15 μg/g); 1,3,5-trichlorobenzene (0.005 μg/g); 1,2,3-trichlorobenzene (0.15 μg/g); and 1,2,4,5-tetrachlorobenzene and/or 1,2,3,5-tetrachloro

Table 1. Ranges of Fatty Acid Distributions Tentatively Adopted by the Food and Agriculture Organization/World Health Organization Codex Alimentarius Committee on Fats and Oils for Sesame Oil[9] (Swern 1979) and the CIR Review Status of These Fatty Acids

Fatty Acid	Wt (%)	CIR Review Status
<14	<0.1	Published final report with conclusion stating that Lauric Acid (12:0) is safe in the present practices of use and concentration in cosmetics.[2]
14:0 (myristic)	<0.5	Published final report with conclusion stating that Myristic Acid is safe in the present practices of use and concentration in cosmetics.[2]
16:0 (palmitic)	7.0-12	Published final report with conclusion stating that Palmitic Acid is safe in the present practices of use and concentration in cosmetics.[2]
16:1 (palmitoleic)	<0.5	Not reviewed
18:0 (stearic)	3.5-6.0	Published final report with conclusion stating that Stearic Acid is safe in the present practices of use and concentration in cosmetics.[2]
18:1 (oleic)	35-50	Published final report with conclusion stating that Oleic Acid is safe in the present practices of use and concentration in cosmetics.[2]
18:2 (linoleic)	35-50	Not reviewed
18:3 (linolenic)	<1.0	Not reviewed
20:0 (arachidonic)	<1.0	Published final report with conclusion stating that the safety of this ingredient has not been documented and substantiated for cosmetic product use, and that the CIR Expert Panel cannot conclude whether Arachidonic Acid is safe for use in cosmetic products until the appropriate safety data have been obtained and evaluated. The types of data required included (1) Dermal absorption data. Based on the results of the absorption studies, the Panel indicated there may be a need for the following data: (2) Immunomodulatory data, (3) Carcinogenicity and photocarcinogenicity data, and (4) Human irritation, sensitization, and photosensitization data.[3]
20:1 (gadoleic)	<0.5	Not reviewed
22:0 (behenic)	<0.5	Not reviewed

benzene (0.005 μg/g).[14] Traces of 1,2,4-trichlorobenzene; 1,2,3,4-tetrachlorobenzene; and pentachlorobenzene were also reported.

A survey of aflatoxin B_1, B_2, G_1, and G_2 contamination in various foods on the retail market was conducted in Japan in 2004 and 2005.[15] The mycotoxins were analyzed by high-performance liquid chromatography, liquid chromato graphy-mass spectrometry, or high-performance thin-layer chromatography. Aflatoxin contamination was not found in sesame oil.

A survey of 69 vegetable oils sampled from the Danish market was conducted.[16] Sesame oil was included. The level of benzo[a]pyrene (BaP) in the oils was considered low. The average BaP concentrations in sesame oil were 1.0 μg/kg (range = <0.2 to 1.8 μg/kg.

Various foods were analyzed for BaP levels to estimate dietary intake levels of BaP for the assessment of BaP-related cancer risk in Koreans.[17] Sesame oil contained BaP at a level of 0.36 μg/kg.

Use

Purpose in Cosmetics

Sesame indicum (sesame) seed oil functions as an occlusive in cosmetic products.[4] Hydrogenated sesame seed oil functions in cosmetics as a binder, emulsion stabilizer, hair-conditioning agent, emollient, slip modifier, and nonaqueous viscosity-increasing agent. Sesamum indicum (sesame) oil unsaponifiables function as hair-conditioning agents and skin-conditioning agents in cosmetics. Sodium sesameseedate functions as a cleansing agent, emulsifying agent, and nonaqueous viscosity-increasing agent.[4]

According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 1987, sesamum indicum (sesame) seed oil was being used in 253 cosmetic products at concentrations ranging from ≤1% to greater than 50%. Voluntary Cosmetic Registration Program data provided by FDA in 2009 indicated that sesamum indicum (sesame) seed oil was being used in 402 products and that sesame indicum (sesame) oil unsaponifiables was being used in 6 products. The results of a 2008 industry survey[18] indicated that sesamum indicum (sesame) seed oil was being used in cosmetic products at concentrations ranging from 0.0001% to 73% and that sesamum indicum (sesame) oil unsaponifiables was being used in cosmetic products at concentrations ranging from 0.01% to 0.03%. Hydrogenated sesame seed oil and sodium sesameseedate were not reportedly used.[19] Use concentration data on hydrogenated sesame seed oil or sodium sesameseedate were not provided in the industry survey. Use frequency/use concentration data on sesamum indicum (sesame) seed oil and sesamum indicum (sesame) oil unsaponifiables are included in Table 2.

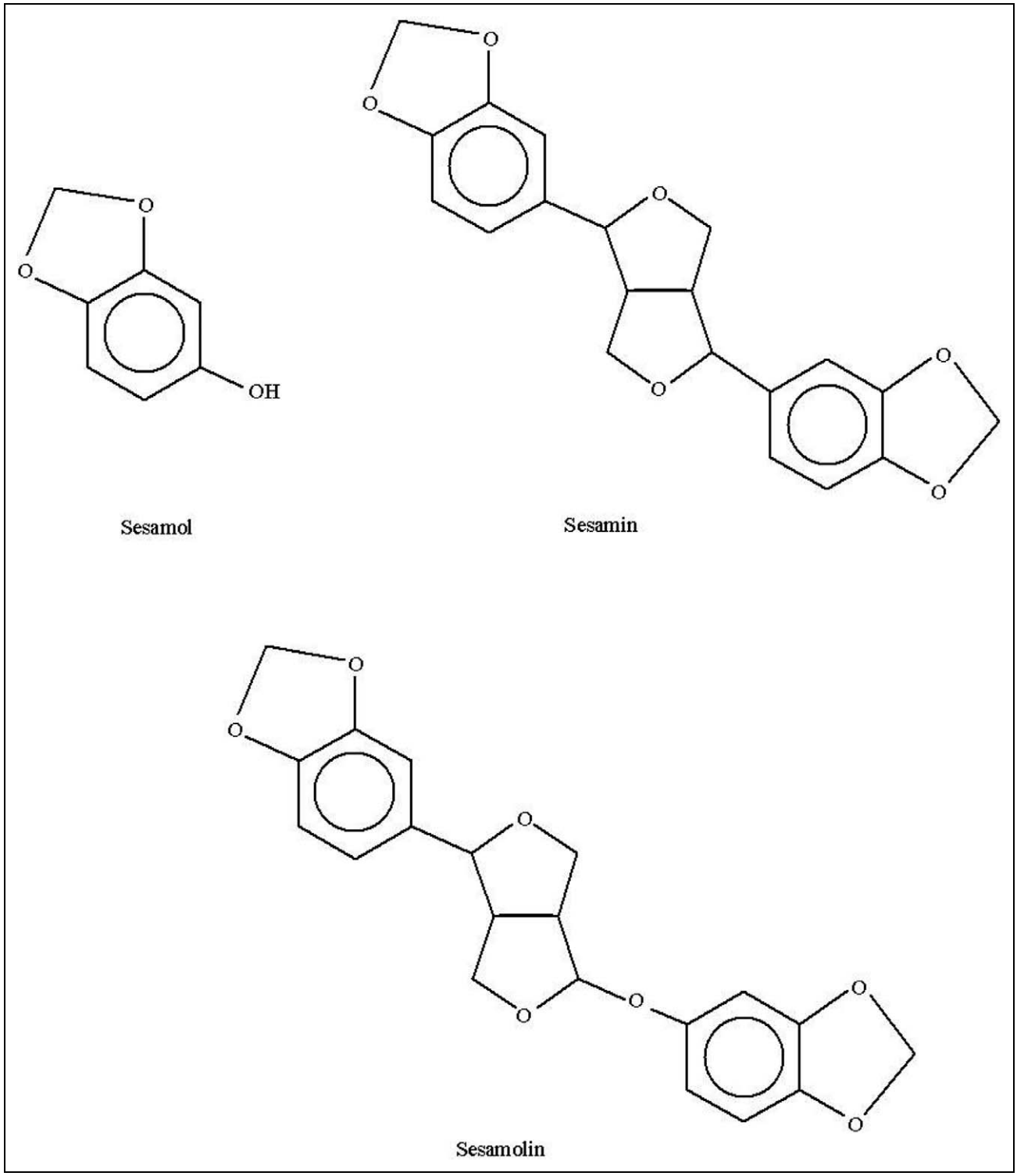

Figure 1. Structures of sesame oil components: sesamol, sesamin, and sesamolin (Swern 1979).[9,12]

Cosmetic products containing sesamum indicum (sesame) seed oil may be applied to or may come in contact with skin, eyes, hair, nails, and mucous membranes. Those containing sesamum indicum (sesame) oil unsaponifiables may come in contact with the skin, eyes, and mucous membranes. Product formulations containing sesamum indicum (sesame) seed oil or sesamum indicum (sesame) oil unsaponifiables may be applied as frequently as several times per day and may remain in contact with the skin for variable periods following application. Daily or occasional use may extend over many years.

The potential adverse effects of inhaled aerosols depend on the specific chemical species, the concentration, the duration of

the exposure, and the site of deposition within the respiratory system.[21] In general, the smaller the particle, the farther into the respiratory tree the particle will deposit and the greater the impact on the respiratory system.[22]

Anhydrous hair spray particle diameters of 60 to 80 μm have been reported, and pump hair sprays have particle diameters of 80 μm or larger.[23] The mean particle diameter is around 38 μm in a typical aerosol spray.[24] In practice, aerosols should have at least 99% of particle diameters in the 10- to 110-μm range. This means that most aerosol particles are deposited in the nasopharyngeal region and are not respirable.

None of the ingredients included in this safety assessment is included on the list of substances that must not form part of the composition of cosmetic products marketed in the European Union (European Commission 2009).[25]

Noncosmetic Use

Sesamum indicum (sesame) seed oil. Sesame (seed or oil not specified) is a generally recognized as safe (GRAS) food additive permitted for direct addition to food for human consumption (21 CFR 182.10). Sesame oil may be used as an indirect food additive; it can be used in the production of resinous polymeric coatings used as the food-contact surfaces of articles intended for producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food (21 CFR 175.300).

Sesame oil has been used in the manufacture of soap. It has also been used as a synergist for pyrethrum pesticides (Swern 1979).[9]

Sesame oil is being evaluated in the FDA over-the-counter (OTC) drug review program for its use in the topical treatment of fever blister.[26] The Miscellaneous External OTC Drug Advisory Review Panel is responsible for evaluating sesame oil, and both external analgesic and skin protectant reports on sesame oil relating to this use have been developed and final rules are pending.

General Biology

Absorption and Distribution

Sesamum indicum (sesame) seed oil. Groups of young adult albino rats were dosed, either subcutaneously (SC) or intraperitoneally (IP), with sesame oil, and killed after approximately 1 year on test.[27] One female rat in the 62-mL IP group had a massive deposition of sesame oil within the parenchyma of the lung, which was considered evidence of systemic distribution of sesame oil after IP dosing. Overall, there was a tendency for sesame oil to migrate within the body of the rat following IP or SC injection. Following SC injection, the test substance tended to pool in the SC tissue of the ventral abdomen. A similar pattern of distribution in the SC tissue was noted in all groups of rats dosed IP with sesame oil.

Metabolism and Excretion

Sesamum indicum (sesame) seed oil—humans. In a study by Moazzami,[28] 6 participants (3 males, 3 females; 22 to 32 years old) took a single dose of Sesame oil (508 μmol sesamin, major sesame oil lignan) and their urine was collected for four 12-hour periods. The urine samples were treated with β-glucuronidase/sulfatase and extracted with chloroform. The major urinary sesamin metabolite in the chloroform extract was characterized as (1R,2S,5R,6S)-6-(3,4-dihydroxyphenyl)-2-(3,4-methylenedioxyphenyl)-3,7-dioxabicyclo[3,3,0]octane using nuclear magnetic resonance (NMR) and mass spectroscopy. The excretion of the sesamin catechol metabolite ranged from 22.3% to 38.6% (mean ± SD, 29.3 ± 5.6) of the ingested dose and happened mainly in the first 12 hours after ingestion.

Animal Toxicology

Acute Toxicity

Sesamum indicum (sesame) seed oil. The acute oral toxicity of sesame oil (water extract; dose = 10 g/kg) was evaluated using 5 ICR female mice (5 weeks old; weight = 25 g). [29] The LD_{50} was greater than 10 g/kg, and there was no apparent acute toxicity.

Repeated-Dose Toxicity

Sesamum indicum (sesame) seed oil. Dow Corning Corporation conducted a study on the effects of sesame oil in rats following IP or SC dosing.[27] Results relating to distribution of the test substance after dosing are included in the section on Absorption and Distribution earlier in the report text. Young adult albino rats (Sherman strain) were used. Each test group consisted of 10 rats (5 males, 5 females). The test animals were dosed either SC or IP. The 3 IP groups were dosed with 5, 20, and 62 mL sesame oil. The 2 SC groups were dosed with 5 and 20 mL sesame oil. The 2 untreated control groups consisted of 20 and 10 rats, respectively. The SC injections were administered in the lower back area, with high-dose animals receiving 2 injections of equal amounts on each side. The injection sites of all (SC and IP) middle- and high-dose animals were closed with stainless steel suture clips to prevent leakage of the test material. The clips were removed at 1 week postadministration. All groups were killed after approximately 1 year on test. At the conclusion of the experiment, complete gross necropsy was performed and select tissues were examined microscopically. Only the lesions related to test substance administration were discussed.

There were no significant differences in the number of rats that died between test and control groups. However, there was a trend suggesting that 62 mL of Sesame Oil IP increased mortality.

Compared with controls, the erythrocyte counts in the 5-mL IP and 5-mL SC dose groups were significantly different ($P < .05$). Because these changes were not dose-related, they did not appear to be associated with treatment. Abnormal erythrocytes were not observed in smears of peripheral blood made monthly and at the end of the experiment. Vacuoles were not observed in these smears. For urinalysis findings, there were no significant differences between test and control groups.

Table 2. Historical and Current Cosmetic Product Uses and Concentrations for Sesamum Indicum (Sesame) Ingredients

Product Category[20]	1987 Uses (Total Number of Products in Category[1])	2009 Uses (Total Number of Products in Category)[19]	1987 Concentrations[1] (%)	2008 Concentrations[17] (%)
Sesamum Indicum (Sesame) Seed Oil				
Baby products				
Lotions, oils, powders, and creams	2 (39)	1 (132)	>1 to 50	6
Bath products				
Oils, tablets, and salts	3 (180)	5 (257)	>1 to 50	—
Soaps and detergents	—	18 (1329)	—	0.09 to 0.3
Bubble Baths	1 (335)	1 (262)	≤1	10
Other	—	3 (239)	—	68
Eye makeup				
Eyebrow Pencil		—		—
Eyeliners	[a] (407)[C]	1 (384)	≤1 to 50[C]	—
Eye shadow		1 (1196)		3
Eye lotion		2 (177)		0.1 to 10
Eye makeup remover		1 (131)		—
Mascara		—		—
Other		6 (288)		0.0008
Fragrance products				
Powders	—	1 (278)	—	—
Other	—	1 (399)	—	2 (in fragranced body rinse)
Noncoloring hair care products				
Conditioners	3 (544)	10 (1249)	≤1	0.01 to 2
Sprays/aerosol fixatives	—	3 (371)	—	—
Permanent waves	—	—	—	30 (15 after dilution)
Rinses	—	—	—	0.1
Shampoos	5 (798)	14 (1403)	≤1	0.001 to 0,01
Tonics, dressings, etc.	—	8 (1097)	—	0.0001 to 2
Other	3 (533)	15 (716)	≤1 to 50	—
Hair coloring products				
Dyes and colors	—	—	—	0.8 (0.4 after dilution)
Bleaches	—		—	0.03 (0.1 after dilution)
Makeup				
Blushers	7 (451)	2 (539)	≤1 to 50	—
Face powders	3 (331)	2 (613)	≤1	—
Foundations	15 (430)	13 (635)	≤1 to 50	0.1 to 5
Lipsticks	59 (1494)	57 (1912)	≤1 to 10	0.1 to 16
Makeup bases	4 (215)	27 (164)	≤1 to 10	0.2 to 0.3
Rouges	2 (103)	—	>1 to 50	—
Other	4 (265)	2 (406)	>1 to 10	3
Nail care products				
Basecoats and undercoats	3[a] (214)[c]	—	≤1 to 10[c]	—
Cuticle softeners		1 (18)		—
Creams and lotions		2 (17)		—
Extenders		—		—
Nail polish and enamel		—		—
Nail polish and enamel removers		—		—
Other		3 (124)		8
Oral hygiene products				
Dentifrices (aerosol, liquid, pastes, and powders)	—	—	—	7
Personal hygiene products				
Feminine deodorants	—[a]	—[a]	—[a]	32
Other	—	4 (514)	—	0.8 to 10 (10 in a body exfoliating product)

(continued)

Table 2 (continued)

Product Category[20]	1987 Uses (Total Number of Products in Category[1])	2009 Uses (Total Number of Products in Category)[19]	1987 Concentrations[1] (%)	2008 Concentrations[17] (%)
Shaving products				
Aftershave lotion		6 (395)		—[b]
Preshave lotions	1 (35)[c]	1 (27)	≤1[c]	—
Shaving cream		4 (162)		2
Other		1 (107)		
Skin care products				
Skin cleansing creams, lotions, liquids, and pads	16 (707)	13 (1368)	≤1 to > 50	0.6 to 2
Face and neck lotions	—	22 (1195)	—	0.06 to 73 (face and neck creams, lotions, and powders)
Body and hand lotions	—	60 (1513)	—	0.04 to 44 (body and hand creams, lotions, and powders)
Moisturizers	84 (2030)	57 (2039)	≤1 to > 50	0.005 to 6 (moisturizing creams, lotions, and powders)
Night creams and lotions	—	11 (343)	—	0.8 to 3
Paste masks (mud packs)	—	3 (418)	—	1 to 16
Other	21 (941)	14 (1244)	≤1 to 50	1 to 8 (8 in a massage oil)
Suntan products				
Suntan gels, creams, and liquids	11 (240)[c]	6 (156)	>1 to 50[c]	1
Indoor tanning preparations		3 (200)		0.1
Other		2 (62)		—
Total uses/ranges for Sesamum Indicum (Sesame) Seed Oil	253	402	≤1 to >50	0.0001 to 73
Sesamum Indicum (Sesame) Oil Unsaponifiables				
Eye makeup				
Other	—	—	—	0.01
Makeup				
Lipstick	—	—	—	0.03
Skin care products				
Face and neck lotions	—	3 (1195)	—	—
Body and hand lotions	—	1 (1513)	—	—
Moisturizers	—	1 (2039)	—	0.01
Night	—	1 (343)	—	—
Total uses/ranges for Sesamum Indicum (Sesame) Oil Saponifiables	—	6	—	0.01 to 0.03

[a] In FDA's voluntary reporting system, no uses/use concentrations reported for this category in 1987; no uses reported for this category in 2007.
[b] In industry survey, no use concentrations reported for this category.
[c] This category was combined when the original safety assessment was performed and is now more than one category.

Compared with controls, brain weights were decreased in rats in the 20-mL SC dose group. This finding does not appear to be associated with treatment because the effect was not dose-related.

There was gross evidence of sesame oil in the peritoneal cavity of rats dosed at 20- and 62-mL IP. Although not extensive, the inflammatory reaction in the peritoneal cavity of the sesame oil–treated rats consisted mainly of macrophages and some fibrous tissue proliferation. Deposits of sesame oil in the ventral subcutaneous tissues were observed in rats from all 3 IP dose groups. Rats in the 20-mL IP group had focal areas of steatitis in the omentum, whereas rats in the 5-mL IP group had no microscopic lesions that were associated with the deposition of sesame oil.

For the 5-mL SC and 20-mL SC dose groups, multifocal yellow cysts were observed in the subcutaneous regions of the dorsal tail head, the site of oil deposition. There were various adjacent inflammatory reactions, varying from none to focal collections of plasma cells, macrophages, and a few lymphocytes, comprising a focal steatitis.[27]

Reproductive and Developmental Toxicity

Sesamum indicum (sesame) seed oil. A 42-week 2-generation reproductive toxicity study on lewisite (chemical warfare agent) using parental male and female Sprague-Dawley rats and their offspring.[30] Vehicle control animals were given an

unstated volume of sesame oil. No adverse effects on the offspring were reported following intragastric dosing with the sesame oil vehicle control.

Several internal and external malformations induced by etretinate (long-acting vitamin A analogue) in C57BL/6 mice were examined.[31] For the sesame oil vehicle control group, the fetal survival rate was 95.5% (21 of 22 mice) following the administration of a single intragastric dose on day 9 of gestation.

The teratogenicity of EV.EXT 33 (a patented Zingiber officinale extract; vehicle: sesame oil), using groups of pregnant female SPF rats, was evaluated.[32] The rats were dosed once daily by gastric intubation. Doses of EV.EXT 33 or vehicle oil (sesame oil) were administered on days 6 through 15 of gestation. The dose volume was 10 mL/kg, based on daily body weight. In the vehicle control group (oral dosing), a value of 95% was reported for both the fertility index and the pregnancy index. Neither embryotoxic nor teratogenic effects were associated with the control group.

The effects of sesame oil on weights of the uterus and ovaries of immature female rats and the testes, prostate, and seminal vesicles of male rats were examined.[33] Groups of 10 rats (pregnant females, at gestation day 14) of the Crj:CD (SD) IGS strain were used. Untreated control groups of male and female rats were also established. Sesame oil was administered (SC injection; 5 mL/rat per day) to female rats, on postnatal day (PND) 21 for 3 or 7 days, and to male rats, from PND 21 for 7 and 10 days. The rats were killed approximately 24 hours after the last dose.

There were no significant differences in body weights of male or female rats between the group treated with sesame oil and the untreated control group.

Genotoxicity

Sesamum indicum (sesame) seed oil. The genotoxicity of vegetable oils were evaluated in the wing spot test using *Drosophila melanogaster*.[34] The following 2 types of crosses were used: (1) the standard (STD) cross with $flr^3/TM3, BD^S$ females mated to *mwh/mwh* males and (2) the NORR cross with *NORR/NORR*; $flr^3/TM3, Bd^S$ females mated to *NORR/NORR*; *mwh/mwh* males. The oils tested include 5 seed oils including sesame oil. Larvae of the standard and highly bioreactive crosses of *Drosophila melanogaster* were fed medium containing 6% and 12% of each of the oils. Sesame oil showed some genotoxic activity. Compared with the negative control (medium made with distilled water alone), the higher concentration of sesame oil (12%) produced higher frequencies of spots in the STD cross and the NORR cross (significance level = .05 in both) and was classified as genotoxic. Results for the lower concentration of sesame oil (6%) in the STD cross and the NORR cross were classified as either inconclusive or negative.

Carcinogenicity

Sesamum indicum (sesame) seed oil. Sprague-Dawley rats (n = 72 of each sex) were divided into 6 groups (12/sex per group) and gavaged with 0, 0.003, 0.01, 0.03, 0.1, or 0.3 mg/kg sulfur mustard (in sesame oil) 5 days per week for 13 weeks.[35] A small number of papillomas (benign) of the nonglandular stomach were observed in 8 of 94 of the intermediate and 10 of the 94 of the high-dose groups. There were relatively few other neoplastic lesions in the control (sesame oil, dose volume not stated) and no lesions involving the genital tract of either sex was observed. There was also no indication that neoplasms were associated with the administration of sesame oil.

Cocarcinogenicity

Sesamum indicum (sesame) seed oil. Bischoff[36] evaluated the cocarcinogenic activity of cholesterol oxidation products and sesame oil using Marsh-Buffalo male and female mice. Groups of 30 Marsh-Buffalo mice (males and females, either castrated or intact) per compound were used. When injections were made in sesame oil, the first injection was made at 3 months of age, and 1 or 2 subsequent injections were made at 2-month intervals. The total amount of steroid administered in sesame oil per mouse was 15 to 20 mg. The sesame oil solution was heated on the water bath for 10 minutes and consisted of sesame oil (7 mL), steroid (350 mg), and ethanol (1 mL). In all cases, the injections were SC dorsal injections and were made as far as possible from the mammary gland areas. The mice were killed at 18 months of age.

Three batches of sesame oil, obtained from 3 sources, were tested as controls for sesame oil alone at various times throughout the period of experimentation and tests for carcinogenic activity of cholesterol derivatives were made simultaneously. The residue of a bottle of sesame oil that had been in the laboratory for 15 years were also tested. An experiment with sesame oil that had air bubbled through it for 44 hours at room temperature was also included. This procedure formed a product that gave a positive test for peroxide with potassium iodide (KI). The original oil gave a negative test. Tumor incidence data are presented in Table 3. These data, for 355 mice carried to the age of 17 to 18 months, were on the effect of subcutaneous dosages of 3 different batches of sesame oil; the incidence of fibrosarcoma was 1.4%. There is no indication from these data that sex or castration affected the response to sesame oil nor is there any evidence that the incidence for Sesame Oil is greater than that of untreated mice. In 40 undosed males carried to 18 months of age, there was no evidence of fibrosarcoma. In 126 castrated males carried to 17 to 18 months, 2 developed fibrosarcoma (tissue/organ not specified). When the dregs of old sesame oil or sesame oil that had been aerated to produce peroxide were tested, the incidence of fibrosarcomas (tissue/organ not specified) was 9% for 63 mice. These series were sufficiently large to warrant the definite conclusion that sesame oil injected SC is not carcinogenic to Marsh-Buffalo mice but that aerated sesame oil is mildly carcinogenic.

The authors noted that if the incidence of fibrosarcoma, 1.2% $\pm$ 0.7% in 248 mice carried to 18 months of age, is taken as the sesame oil control incidence for the colony,

Table 3. Tumor Incidence of Marsh-Buffalo Mice Injected with Cholesterol Oxidation Products and Oil Vehicles[34]

Vehicle	No. of mice and Sex	Accumulative Incidence to Age 18 Months (%)			
		Adenocarcinoma	Lymphoid Tumors	Fibrosarcoma	Death, Other Causes
Sesame Oil	79 intact males	0	5	0	33
Sesame Oil	31 castrated males	0	6	0	12
Sesame Oil	66 castrated females	13	9	1.5	15
Sesame Oil	72 intact females	64	7	3[a]	7
Sesame Oil, 15 years old	31 castrated males	0	3	12	9
Sesame Oil, aerated	32 castrated females	0	3	6	9
Lard, peroxide #8	32 intact males	0	3	0	25

[a] Two percent fibrosarcoma in an additional 107 females taken to age 17 months.

an incidence below 9% in a group of 32 mice would clearly be without significance. Figures between 9% and 15% would have doubtful significance. Figures above 25% would be highly significant.

All of the results of this study can be summarized as follows: (1) Sesame oil or purified cholesterol dissolved in sesame oil is not carcinogenic following injection SC into Marsh-Buffalo mice. (2) A number of oxidation products of cholesterol, when administered with sesame oil and the vehicle, are carcinogenic. The most potent found to date are 4-cholestene-3,6(dione; 5α,6α-epoxy-3β-cholestanol; and 6β-hydroperoxy-4-cholesten-3-one. The latter compounds have an oxygen linkage at carbon 6 in common. (3) Oxidation products of cholesterol that were carcinogenic when administered in a sesame oil vehicle were noncarcinogenic when administered as aqueous colloids.[36]

Clinical Assessment of Safety

Nasal Exposure

Sesamum indicum (sesame) seed oil. In a randomized crossover study, 2 different treatments for nasal dryness were compared in 79 participants (25 males, 54 females; median age: 60 years).[37] Half of the participants received pure sesame oil for 14 days, followed by isotonic sodium chloride solution (ISCS) for 14 days. The remaining half received ISCS for 14 days, followed by pure sesame oil for 14 days. Both treatments were administered with 1 to 3 sprays in each nostril 3 times daily.

During the study, 6 participants (8%) in the pure sesame oil group and 4 (5%) in the ISCS group reported adverse events (no difference between groups [$P = .30$]). Adverse effects included respiratory tract infection, rhinitis, sinusitis, and nose bleeds.

Skin Irritation

Sesamum indicum (sesame) seed oil. The cumulative skin irritation potential of a massage oil containing 32% sesamum indicum (sesame) seed oil was evaluated using 34 healthy participants, 31 (7 males, 24 females; ages: 19 to 68 years) of whom completed the study.[38] The reason why 3 participants discontinued the study was not stated. A semiocclusive patch containing approximately 0.2 g or 1 cm^3 of the test substance was applied to the back of each participant. Applications of the test substance to the same patch test sites were made 3 times per week over a 14-day period (total of 6 applications). At approximately 48 hours postapplication (at 72 hours postapplication on weekends), the patches were removed and reactions were scored according to the following scale: 0 (no visible reaction) to 4 (severe reaction with erythema, induration, vesicles [may be weeping], pustules). A grand total score for the test substance was obtained by summing the 14-day totals for all of the participants (maximum grand total possible = 600). The grand total cumulative irritation score for a massage oil containing 32% sesamum indicum (sesame) seed oil in this study was 0. The skin sensitization potential of a cologne containing 54% sesame seed oil was evaluated in a repeated-insult patch test (RIPT) using 121 healthy participants (18 to 70 years old).[39] The cologne was tested as received; volatiles were allowed to evaporate from the patch before skin application. Of the 121 participants, 110 (27 males, 83 females) completed the study; 11 participants withdrew for reasons unrelated to test substance application. A semiocclusive patch containing 0.2 g of the test substance was applied to the left side of the back, and the site was wiped prior to subsequent patch applications. Each participant was instructed to allow each patch (must remain dry) to remain in place for approximately 24 hours and then remove it. Patch removals were followed by a 24- to 48-hour rest period. A series of 9 induction patch applications (occlusive patches, same test site) was completed over a period of approximately 3 weeks. The induction phase was followed by a nontreatment period of approximately 2 weeks. During the challenge phase, 0.2 g of the test substance was applied (semiocclusive patch) to a new test site on the right side of the back. Challenge reactions were scored at 24, 48, 72, and 96 hours after removal. Participants were scored for any reactions (at induction or challenge) that were observed on a 0 (no visible reaction) to 4 (severe reaction) scale.

Three participants reported faint, minimal erythema during induction. During the challenge phase, 1 participant had a ± reaction at 48, 72, and 96 hours and the same participant had a 1 reaction at 24 hours. It was concluded that the cologne containing 54% sesame seed oil did not induce dermal sensitization.[39]

The skin sensitization potential of a massage oil containing 32% sesamum indicum (sesame) seed oil was evaluated using 240 participants, 200 (45 males, 155 females; ages: 18 to 69 years) of whom completed the study.[40] A series of 9 induction patch applications was made over a period of approximately 3 weeks. During induction, a semiocclusive patch containing 0.2 g of the test substance was applied to the left side of the back of each participant, and the participants were instructed to remove the patch at 24 hours postapplication. Patch removals were followed by a 24- to 48-hour rest. Reactions were scored as above. Induction was followed by a 2-week nontreatment period.

During the challenge phase, a semiocclusive patch containing 0.2 mg of the test substance was applied to the right side of the back (new site) of each participant. Patches were removed at 24 hours postapplication; reactions were scored at the time of patch removal and at 48, 72, and 96 hours. Reactions were not observed during the induction phase and a low-level transient reaction (faint, minimal erythema) was observed in 1 participant during the challenge phase. It was concluded that a massage oil containing 32% sesamum indicum (sesame) seed oil did not induce skin sensitization in human participants.[40]

The skin sensitization potential of a body oil containing 66.55% sesame seed oil (tested as supplied) was evaluated using the maximization test.[41] The study was conducted using 26 healthy adult volunteers (21 females, 5 males; 18 to 64 years old). Initially, approximately 0.05 mL of 25% aqueous sodium lauryl sulfate (SLS) was applied (occlusive patch) to the volar forearm or back of each participant for 24 hours. The SLS patch was then removed and 0.05 mL of the test substance was applied (occlusive induction patch) to the same site. The induction patch remained in place for 48 hours (or for 72 hours, when placed over a weekend), after which it was removed and the site examined for skin irritation. If skin irritation was not observed, a patch containing 0.25% aqueous SLS was reapplied to the same site for 24 hours. Sodium lauryl sulfate patch application was then followed by reapplication of a new induction patch containing the test substance. This patch application sequence (24-hour SLS patch application followed by 48-hour induction patch [test substance]) was repeated for a total of 5 induction exposures.

If there was any evidence of skin irritation during the induction phase, SLS patch application was discontinued and only the test substance was reapplied to the same site following a 24-hour nontreatment period. The challenge phase was initiated following a 10-day nontreatment period at the end of induction. Prior to the challenge phase, the challenge site (new site on opposite arm, forearm, or side of back) was pretreated with 0.5 mL of 5% aqueous SLS (occlusive patch) for 1 hour. After SLS patch removal, a single 48-hour application of the test substance (occlusive patch) was made to the same site. Patches were then removed and each site was graded 15 to 30 minutes later and, again, 24 hours later using the following scale: 0 (not sensitized) to 3 (strong sensitization: large vesiculo-bullous reaction).

At the end of the challenge phase, contact allergy was not observed at 24 or 72 hours after challenge patch application. It was concluded that the body oil containing 66.55% sesame seed oil does not possess a detectable contact-sensitizing potential, and, hence, is not likely to cause contact sensitivity reactions under normal conditions of use.[41]

Skin Sensitization

The increased reporting of sesame allergy during the past 5 decades, with reports mostly from developed countries, was reviewed. [42] Clinically, most sesame allergy presented in 2 major forms: (1) immediate hypersensitivity (often expressed as systemic anaphylaxis) associated with positive SPT and/or immunoglobulin (Ig) E antibody test results to sesame proteins, with some cross-reactivity with other foods and (2) delayed hypersensitivity to lignin-like compounds in sesame oil, clinically expressed as contact allergic dermatitis. The authors concluded that sesame allergy is a significant, serious, and growing problem. They suggested that there is evidence of the ability of protein and oil components of sesame to trigger immediate hypersensitivity via IgE and delayed hypersensitivity via cell-mediated immune responses, respectively.

Phototoxicity and Photoallergenicity

Sesamum indicum (sesame) seed oil. The phototoxicity of an oil massage formula containing 32% sesamum indicum (sesame) seed oil was evaluated using 10 healthy participants (1 male, 9 females; ages 43 to 68 years).[43] Only fair-skinned participants with the following skin types participated in the study: type I (always burns easily; never tans), type II (always burns easily; tans minimally), or III (burns moderately; tans gradually). Ultraviolet A (irradiation was produced by custom-made light sources using 4 Philips F40BL fluorescent tubes with a peak output at 369 nm and a half-power bandwidth of 15 to 16 nm. The UVA intensity was 3.3 to 4.4 mW/cm^2, and the exposure duration was 17 minutes (total dose = 4.0 $\pm$ 0.4 J).

Semiocclusive patches (duplicate patches) containing 0.2 g of the test substance were applied to the back (on each side) of each participant, and the participants were instructed to keep the patches dry and allow them to remain in place for 24 hours. At approximately 24 hours postapplication, patch removal, and the scoring of the reaction site to be irradiated were conducted. The following grading scale was used: 0 (no visible reaction) to 4 (wheal-flare blister [vesicles]). The designated test site was then irradiated with UVA light, and reactions were scored immediately after irradiation (17-minute exposure).

Because the dosage of UVA light was not erythemogenic, a control site was not delineated on each participant's back. Thus, the entire back served as the irradiated control. The nonirradiated test site, located on the opposite side of each participant's back, which had been patch tested, was protected from the light source by the participant's clothing or by the patch. The participants were cautioned to protect the nonirradiated test site from exposure to sunlight throughout the test period. Patches were removed from nonirradiated sites at 24 hours and reactions were scored. At approximately 48 and 72 hours

postapplication, reactions at the irradiated and nonirradiated test sites were scored. Because a 2-level or greater reaction was not observed at any of the test sites, the phototoxicity test was said to have been complete.

Reactions were not observed at irradiated or nonirradiated patch test sites, and the same was true for irradiated sites that had not been patch tested (control sites). It was concluded that an oil massage formula containing 32% sesamum indicum (sesame) seed oil did not induce a dermal phototoxic response in human participants.[43]

The photoallergenicity of a massage oil formula containing 32% sesame indicum (sesame) seed oil using 32 healthy participants was evaluated.[44] Of the 32 participants, 28 (8 males and 20 females; ages: 18 to 70 years) completed the study. Participant selection and UVA irradiation are described above.

UVB irradiation was produced by a custom-made light source, which had a peak output at 313 nm and a half-power band width of 30 nm. The UVB intensity was 1.0 ± 0.2 mW/cm^2, and UVB irradiation was based on each participant's skin type and minimal erythema dose (MED). The MED was determined prior to the first irradiation, and UVB irradiation was at 2 MEDs (the time required to achieve a 1.0 erythema). The UVB exposure per dose rate was at 1.0 ± 0.2 mW/cm^2.

For the first 3 weeks, patches were applied twice per week to identical sites, for a total of 6 induction applications. For each application, a semiocclusive patch containing 0.2 g of the test substance was applied to the upper back of each participant. The participants were instructed to keep the patches dry and allow them to remain in place for 24 hours. The following grading scale was used: 0 (no visible reaction) to 4 (erythema [fiery color], substantial vesiculation (far beyond patch margins).

The designated test site was then irradiated with UVA and UVB light at 24 hours postapplication (time of patch removal), and reactions were scored immediately after irradiation. An additional site on each participant's back served as the irradiated control site (no test substance). A site on the opposite side of each participant's upper back served as the nonirradiated test site, which was protected from the light source. Following a 2-week rest period, a semiocclusive challenge patch was applied to a new site (irradiated challenge test site) on the lower back of each participant, with the same controls noted previously. Reactions were scored 24 hours postapplication and following first, second, and third challenge visits or postirradiation, respectively.

During the induction phase, low-level, transient $\pm$/1 (minimal erythema/erythema within patch margins) reactions were observed at the irradiated (no test substance) control site. Slight tanning responses at irradiated sites (with and without test substance) were also observed during the induction phase. During the challenge phase, reactions were not observed at irradiated or nonirradiated sites to which the test substance had been applied. The same was true for irradiated control (no test substance) sites. It was concluded that a massage oil formula containing 32% sesame indicum (sesame) seed oil did not induce photoallergy or dermal sensitization in human participants.[44]

Case Reports

Sesamum Indicum (Sesame) Seed Oil

A case of a 46-year-old male with recurrent bouts of severe food reactions over the preceding 18 years was reported.[45] He found that many of the reactions could be attributed to the ingestion of sesame products, particularly sesame oil. A pin-and-needle sensation on the face, followed by the onset of chills, shakiness, and abdominal cramps, were reported after eating. His complete blood cell count, erythrocyte sedimentation rate, and total hemolytic complement were all normal, and his IgE value was 130 IU/mL. Skin testing revealed a 4+ multitest response to whole commercial seed oil and only a 2+ intracutaneous response to commercial sesame seed antigen at a concentration of 1:1000. The radioallergosorbent test (RAST) was only marginally positive to sesame seed oil, commercial sesame seed antigen, and whole sesame seed.

Basophil histamine release revealed significant histamine release with sesame seed antigen (90%), cooked sesame seed extract (80%), commercial seed oil (40%), and intact sesame seed (70%), but only minimally with commercial sesame seed antigen. No histamine release was found in whole blood of the 4 control participants, including 2 participants with moderately strong skin test reactions to commercial sesame seed antigen.[45]

Nine cases (ages 4 to 51; most older than 30) of allergy to sesame seed flour and/or Sesame Seed Oil were reported.[46] Histamine release assays were positive in 3 of 4 cases tested with sesame seed flour and in 1 of 3 cases tested with sesame seed oil. The labial provocation test was positive in 1 of 3 cases tested with sesame seed flour and in 2 of 2 cases tested with sesame seed oil. The oral provocation test was positive in 7 of 9 cases tested with sesame seed flour (up to 10 g) and in 1 of 2 cases tested with sesame seed oil at a dose of 3 mL. The oral provocation test with 10 g of sesame seed flour was negative in 5 controls.

A case of a 45-year-old female with recurrent anaphylactic reactions after ingestion of food containing sesame was reported.[47] Prick and scratch tests performed with native sesame oil (cold pressed and heat extracted) and raw, peeled, crushed, and unpeeled sesame seeds did not show any skin reaction.

A 30-year-old man had a 3-year history of attacks of generalized urticaria when eating hamburgers made with sesame buns. Occupationally, his hands came in contact with a body oil (contained sesame seed oil) and an extensive contact urticaria appeared immediately. Open test results for sesame oil were positive (++).[48]

A case of an 18-year-old female patient with anaphylaxis to sesame was reported.[49] A year earlier, the patient presented with 2 severe systemic reactions after eating food containing sesame. The first episode involved facial erythema, pruritus, and conjunctivitis a few minutes after eating food containing sesame, and a second episode, which involved generalized itching and laryngeal edema, occurred 1 week later. Prick-by-prick tests (test procedure not included) performed with sesame seeds and sesame oil did not reveal any skin reaction.

A case of allergic contact dermatitis caused by sesame oil in a topical Chinese medicine, shi-un-ko, was reported.[50] Shi-un-ko is composed of sesame oil as a solvent and of *Angelica acutiloba*, *Lithospermum erythrorhizon*, beeswax, and lard. A 51-year-old female presented with severe pruritic erythematous macules, vesicles, pustules, and crusts on the soles and palms where she had applied the topical Chinese medicine, shi-un-ko. The pruritic erythemas, papules, and vesicles spread to the extremities, and the patient also had a fever and a painful, swollen and erythematous macule on the right lower leg. Closed patch test results indicated the following reactions to Sesame Oil: day 2 (+), day 3 (+), day 4 (+), and day 11 (+). The results were identical to those for shi-un-ko. Patch test results for the other ingredients and petrolatum were negative. Results for control patch testing (20 healthy volunteers) with pure sesame oil (as is) and petrolatum were negative, that is, no allergic or irritation reactions were observed.

Summary

Sesamum indicum (sesame) seed oil is the oil obtained from the seeds of *Sesamum indicum* by a mechanical pressing process, and hydrogenated sesame seed oil is the end product of the controlled hydrogenation of sesamum indicum (sesame) seed oil. Sesamum indicum (sesame) seed oil is extracted from sesame seeds by mechanical processing. The oil yield varies from 50% to 75%, depending on the growing conditions and seed variety. Sesame oil is composed primarily of oleic, linoleic, palmitic, and stearic acids; 3 trace constituents—sesamol, sesamin, and sesamolin—are unique to this oil. Residues of chlorinated benzenes, pesticides, ochratoxin, and benzo[a]pyrene are some of the impurities that have been detected in sesame oil.

Sesamum indicum (sesame) oil unsaponifiables is the fraction of sesame oil that is not saponified in the refining recovery of sesame oil fatty acids. Sodium sesameseedate is the sodium salt of the fatty acids derived from sesamum indicum (sesame) seed oil.

Of the cosmetic ingredient functions reported, conditioning agent (skin/hair) is associated with sesamum indicum (sesame) seed oil, sesamum indicum (sesame) oil unsaponifiables, and hydrogenated sesame seed oil. Sodium sesameseedate functions as a surfactant-cleansing agent, surfactant—emulsifying agent, and a viscosity-increasing agent—nonaqueous.

Data provided by the FDA in 2009 indicated that sesamum indicum (sesame) seed oil was being used in 402 products and that sesame indicum (sesame) oil unsaponifiables was being used in 6 products. Uses of hydrogenated sesame seed oil and sodium sesameseedate were not reported in this database. The results of a 2008 industry survey conducted by the Personal Care Products Council indicated that sesamum indicum (sesame) seed oil was being used in cosmetic products at concentrations ranging from 0.0001% to 73% and that sesamum indicum (sesame) oil unsaponifiables was being used in cosmetic products at concentrations ranging from 0.01% to 0.03%. Neither use concentration data on hydrogenated sesame seed oil nor sodium sesameseedate were provided in the industry survey.

Sesame oil is included in FDA's OTC drug review, and is being evaluated by both the miscellaneous external analgesic and miscellaneous external skin protectant advisory review panels for topical treatment of fever blisters. A final rule from each panel is pending.

Sesame oil is systemically distributed after IP dosing.

The acute oral LD_{50} of sesame oil (water extract) was greater than 10 g/kg, and the acute oral LD_{50} of a lipstick containing 10% to 11% sesame oil was greater than 5 g/kg (rats). The acute dermal LD_{50} was greater than 2 g/kg (rabbits), and the acute intravenous LD50 of sesame oil was 0.74 mL/kg (rabbits).

No treatment-related changes were observed in groups of rats following IP (up to 62 mL) or SC (up to 20 mL) dosing with sesame oil. All groups were killed at approximately 1 year on test.

Data presented in the previous safety assessment showed that sesame oil was neither a primary skin nor ocular irritant.

Newer data reviewed was consistent with the previous conclusion that sesame oil is not teratogenic. Sesame oil is commonly used as a control vehicle in teratogenicity studies.

Sesame oil produced small, single wing spots (1 to 2 cells) and large single wing spots (more than 2 cells) in the *Drosophila* wing spot genotoxicity test.

The cocarcinogenic activity of cholesterol oxidation products and sesame oil was evaluated using mice. Three batches of sesame oil, obtained from 3 sources, were tested as controls for sesame oil alone at various times throughout the period of experimentation and tests for the carcinogenic activity of cholesterol derivatives were made simultaneously. Additionally, the dregs of a bottle of sesame oil that had been in the laboratory for 15 years and sesame oil (air bubbled through it for 44 hours) were also tested. It was noted that the numbers of animals tested in experiments were sufficiently large to warrant the definite conclusion that sesame oil itself (7 mL in solution, SC injections) was not carcinogenic, but that aerated sesame oil was mildly carcinogenic.

New clinical skin irritation studies confirm previous data showing that sesame oil is not a skin irritant. The skin sensitization potential of a cologne containing 54% sesame oil was evaluated in an RIPT using 110 healthy participants. The product was essentially nonirritating during induction and was classified as a nonsensitizer. Similar results were reported for a massage oil containing 32% sesame oil in another RIPT involving 200 healthy participants. The maximization test was used to evaluate the skin sensitization potential of a body oil containing 66.55% sesame oil.

An oil massage formula containing 32% sesame oil did not induce a dermal phototoxic response in any of the 10 participants (all healthy) tested. This formulation also did not induce photoallergy or dermal sensitization in any of the 28 participants (all healthy) tested.

In a number of other case reports, individuals with sesame food allergies had positive prick test, scratch test, patch test, and so forth, reactions to sesame oil. However, this was not the case in all reports. A patient with allergic contact dermatitis

after using a medication containing sesame oil had a positive patch test reaction to this ingredient; patch test results were negative in 20 healthy control participants.

Discussion

The CIR Expert Panel recognized that there are data gaps regarding uses and concentrations of sesamum indicum (sesame) seed oil and sesamum indicum (sesame) oil unsaponifiables. However, the overall information available on the types of products in which these ingredients are used and at what concentrations indicated a pattern of use, which was considered by the Expert Panel in assessing safety. There was no evidence that either hydrogenated sesame seed oil or sodium sesameseedate is being used in cosmetic products.

Sesamum indicum (sesame) seed oil is being used in noncoloring hair products (sprays/aerosol fixatives). In the absence of inhalation toxicity data on this ingredient, the Panel determined that sesamum indicum (sesame) seed oil can be used safely in hair sprays, because the ingredient particle size is not respirable. The Panel reasoned that the particle size of aerosol hair sprays ($\sim$38 μm) and pump hair sprays (>80 μm) is large, compared with respirable particulate sizes ($\leq$10 μm).

The Expert Panel considered the high-use concentrations of sesame oil (ie, up to 73%) and the need for data supporting such use. The results of clinical studies indicated that a cologne containing 54% sesame oil was a nonsensitizer in an RIPT involving 110 participants and that a body oil containing 66.55% sesame oil was a nonsensitizer in a maximization test involving 25 participants.

The Panel reviewed its previous assessment on sensitization and irritation and concluded that the previous data (which included testing on 100% sesame oil) supported high concentrations of use.

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 sesamum indicum (sesame) seed oil, hydrogenated sesame seed oil, sesamum indicum (sesame) oil unsaponifiables, and sodium sesameseedate are safe as cosmetic ingredients in the practices of use and concentration as described in this safety assessment. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in the group.

Author's Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, 1101 17th St., Suite 412, Washington, DC 20036, USA.

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