Safety Assessment of *Helianthus annuus* (Sunflower)-Derived Ingredients as Used in Cosmetics

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All interested persons are provided 60 days from the above date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a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. Lillian J. Gill.

The 2015 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is Lillian J. Gill, D.P.A. This report was prepared by Lillian C. Becker, Scientific Analyst/Writer.

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INTRODUCTION

This is a review of the available scientific literature and unpublished data relevant to assessing the safety of *Helianthus annuus* (sunflower)-derived ingredients as used in cosmetics. The functions of these ingredients include skin-conditioning agents – miscellaneous, abrasives, and absorbents (Table 1).[1] The 13 ingredients in this safety assessment are:

Helianthus Annuus (Sunflower) Extract
Helianthus Annuus (Sunflower) Flower Extract
Helianthus Annuus (Sunflower) Leaf/Stem Extract
Helianthus Annuus (Sunflower) Sprout Extract
Helianthus Annuus (Sunflower) Seed Extract
Helianthus Annuus (Sunflower) Seed
Helianthus Annuus (Sunflower) Seed Butter
Helianthus Annuus (Sunflower) Seedcake
Helianthus Annuus (Sunflower) Seed Flour
Helianthus Annuus (Sunflower) Seed Wax
Hydrogenated Sunflower Seed Extract
Hydrolyzed Sunflower Seed Wax
Ozonized Sunflower Seed Oil

The ingredients in this report are grouped together because they are extracts, waxes, or powders (flour) derived from plant parts of *H. annuus*, the sunflower. Helianthus annuus (sunflower) seed oil, and other *H. annuus*-derived seed oils (with the exception of ozonized sunflower seed oil), are not covered in this review here because they were included in the Cosmetic Ingredient Review (CIR) safety assessment of plant-derived oils.[2]

In the safety assessment of plant-derived oils, the CIR Expert Panel (Panel) concluded that *H. annuus* (sunflower)-derived seed oils were safe as used (Table 2).[2] The Panel has also reviewed the safety of phytosterols, plant-derived sterols that includes phytosteryl sunflower sedate, as used in cosmetics and concluded that they were also safe as used.[3]

The seeds of *H. annuus* are consumed by humans, both raw and roasted, on a regular basis. The rest of the plant, as well as the seeds, are fed to farm animals and pets. Exposure from food use would result in much larger systemic exposures than those from use in cosmetic products because exposure through the skin has much less potential for systemic effects than from absorption through oral exposures. This is because the rates of absorption and metabolism of these ingredients in the skin are expected to be negligible compared to the corresponding rates in the digestive tract. Additionally, there are only a few cases of food allergies to the seeds and of inhalation allergies to the pollen.[4-12] Therefore, the oral toxicity of these ingredients will not be the focus of this safety assessment although oral information may be included here. The primary focus of this safety assessment of *H. annuus* (sunflower)-derived ingredients as used in cosmetics is on the potential for irritation and sensitization from dermal and inhalation exposure. It is noted that *H. annuus* is a member of the *Asteraceae* family; members of this family tend to be sensitizing.[6,10,13,14]

Botanicals such as *H. annuus* (sunflower)-derived ingredients contain hundreds of constituents, some of which have the potential to cause toxic effects. For example, sesquiterpene lactones may cause allergic reactions and toxicity if overdosed. In this assessment, CIR is reviewing information available to evaluate the potential toxicity of each of the *H. annuus* (sunflower)-derived ingredients as a whole, complex substance. Except for specific constituents of concern, CIR is not reviewing information that may be available to assess the potential toxicity of the individual constituents of which *H. annuus* ingredients are composed.

CHEMISTRY AND CHARACTERIZATION

Helianthus annuus

H. annuus is an annual plant in the family *Asteraceae* (synonym *Compositae*), daisy or sunflower family, sub family asteroideae.[15-18] The plant is a dicot annual with a height range of 0.7-3.5 m.[18] Sunflower leaves are rough, broad, coarsely toothed, and mostly alternate. What is often called the "flower" of the sunflower is actually a "flower head" called a pseudanthium or captulum, which is made up of numerous small individual five-petaled flowers ("florets"). The outer flowers, which resemble petals, are called ray flowers. These ray flowers consist of a ligule composed of fused petals of an asymmetrical ray flower. They are sexually sterile and may be yellow, red, orange, or other colors. The flowers in the center of the head are called disk flowers, and these are arranged spirally. If pollenated, usually by insects, the flowers mature into fruit (seeds). The taproot is strong and penetrates to a depth of 3 m and has large lateral spread of surface roots. Wild *H. annuus* is a widely branched annual plant with multiple flower heads that mature sequentially.

H. annuus seeds are achenes (or fruits) that consist of a kernel (true seed) and a pericarp (hull), which are 4-sided and flat.[17,19] They are approximately 0.6 cm long and 0.3 cm wide. Oil seeds (oil content >40% and 35%-38% protein) are usually have a black seed coat; edible seeds (oil content approximately 30%) usually have a hull that is dark brown or white. The kernel consists of an embryo, endosperm, and seed coat. The pericarp (maternal tissue) consists of several layers: cuticle (external layer), epidermis, hypodermis, phytomelanin layer, fibrose tissue, and parenchymal layers adjacent to the kernel.

The pseudanthium (flower head) may contain 1000–4000 florets, with the potential of as many seeds.[20] The average yield of seeds in a pseudanthium is 1200-1500.[19] The average yield of seeds range from 900–1,575 kg/ha; yields of over 3,375 kg/ha have been reported

H. annuus is native to western North America.[18] The plant was introduced to Europe and Russia in the 16th century and has spread to tropical and temperate countries including Russia, Argentina, the combined European Union, China, India,

Turkey, and South Africa.[21] Hybridization and selective breeding has increased oil production. The breeding resulted in the development of strains with high oleic acid content, referred to as oil-seed.[22]

Definition

The definitions and functions of the *Helianthus annuus* (sunflower)-derived ingredients included in this report are provided in Table 1. In some cases, the definition provides insight on the method(s) of manufacture.

The ingredients in this report are related by source, as each is a derivative of part or parts of the *H. annuus* plant. While the identity and concentrations of ingredient constituents may vary from plant part to plant part, and by extraction method, those constituents and their concentrations cannot be known until such information is provided. Differences in those components do not necessitate the regrouping of these ingredients, but instead warrant a comparison/contrast effort as to how those differences effect safety. Those differences are likely to be informative.

Physical and Chemical Properties

Helianthus annus (sunflower) extract is a brownish yellow powder with a characteristic odor (Table 3).

Helianthus annuus (sunflower) seed wax is a complex mixture consisting of long chain non-glyceride esters, and a small amount of free fatty alcohols and free fatty acids.[23]

The color of helianthus annuus (sunflower) seed flour changes with pH.[24] From pH 2-7, the color is cream white. At a pH of 8, it is grey; at pH of 9 it is yellowish grey, at pH of 10 it is light brown, and at pH of 10.5 it is dark brown.

Constituents and Components

H. annuus plant has a high amount of moisture at maturity.[25] The composition of *H. annuus* plant (minus the pseudanthium) varies with maturity level (Table 4).

H. annuus leaves are known to contain high levels of saponins, but have not been quantified.[25]

The fatty acid profile of *H. annuus* varies with selective breeding; an example is provided in Tables 5.[25] Overall, oleic acid (C18:1) may be present as low as 14%-39.4% in wild/conventional plant seeds and as high as 75%-90.7% in selectively bred plant seeds; palmitic acid (C16:0) may be present as low as 2.6%-5.0% in high oleic acid oil seeds or as high as 5.0%-7.6% in low oleic acid oil seeds. The phytosterols and tocopherols also vary with the oleic acid content in the seeds of wild and bred plants (Table 6).

The vitamin with the greatest content in *H. annuus* non-oilseed kernels is folate at 239.86 µg/100 g dry material (Table 7).

The amino acid content profile of *H. annuus* seed flour includes phenylalanine + tyrosine (8.2 g/100 g crude protein) and leucine (6.5 g/100 g crude protein; Table 8).[25] The fatty acid methyl esters detected in *H. annuus* seed flour were palmitate (12.04% of detected fatty acids), stearate (8.26%), oleate (31.14%), and linoleate (48.56%).[24] The unheated flour is reported to be made up of 6.80% moisture, 45.50% protein, 4.40% crude fat, 2.00% crude fiber, and 8.10% ash and the heated flour is reported to be made up of 8.56% moisture, 42.37% protein, 9.20% crude fat, 1.90% crude fiber, and 7.70% ash.

The composition (e.g., crude protein, fiber, and fat) of *H. annuus* seed meal (possible precursor to *H. annuus* seed extract and seed cake) may vary with the source and depending on whether or not the seed hull is included or the seeds are partially dehulled (Table 9).[25] This also applies to amino acids and crude protein contained in the meal (Table 10).

Electrophoresis showed that protein bands were similar among 3 *H. annuus* seed strain samples.[26] There were 3 polypeptides groups of helianthinin fraction detected. Of these, 2 were acidic (α , MW=36 800-42 900 and α', MW=31 000-35 300), and 1 was basic (β , MW=21 000-29 600). The molecular weight of the 2S albumin proteins ranged from 11 500-20 100. Sunflower proteins are rich in globulins (55%-60 %), albumins (17%-23 %), and glutelins (11%-17 %).[27]

Constituents of Concern

H. annuus plants are reported to contain sesquiterpene lactones, which may cause allergic reactions.[28]

The carcinogen benz[a]pyrene (3,4-benzpyrene) has been detected in unrefined sunflower seed oil.[29]

H. annuus petals were reported to contain saponins, helianthosides A, B, and C derived from echinocystic acid.[30]

A 14-amino-acid, backbone-cyclized protein (SFTI-12) has been reported in the seeds of *H. annuus*; it possesses potent trypsin inhibitory activity as well as weaker inhibitory activity against proteases such as thrombin.[31]

Sunflower kernels and hulls contain phenolic compounds, which include chlorogenic and caffeic acids; these are easily oxidized during common processing causing green to brown discoloration in protein isolates and/or concentrates.[32,33] These compounds have been studied both for their additive/synergistic effect on carcinogenesis and their anti-carcinogenic properties with no definitive result.[34]

Sunflower seeds have been found to contain an allergen, 2S albumin, which shows homology to the 2S albumins in other seeds.[35] The 2S albumin proteins in other seeds, such as rapeseed, castor beans, cottonseed, Brazil nuts, and walnuts, have been associated with allergenicity. Consequently, the 2S albumin proteins in sunflower seed may also be allergens.

Method of Manufacture

A scheme of the general manufacturing process of *H. annuus* oil, flour/protein, and meal is depicted in Figure 1.

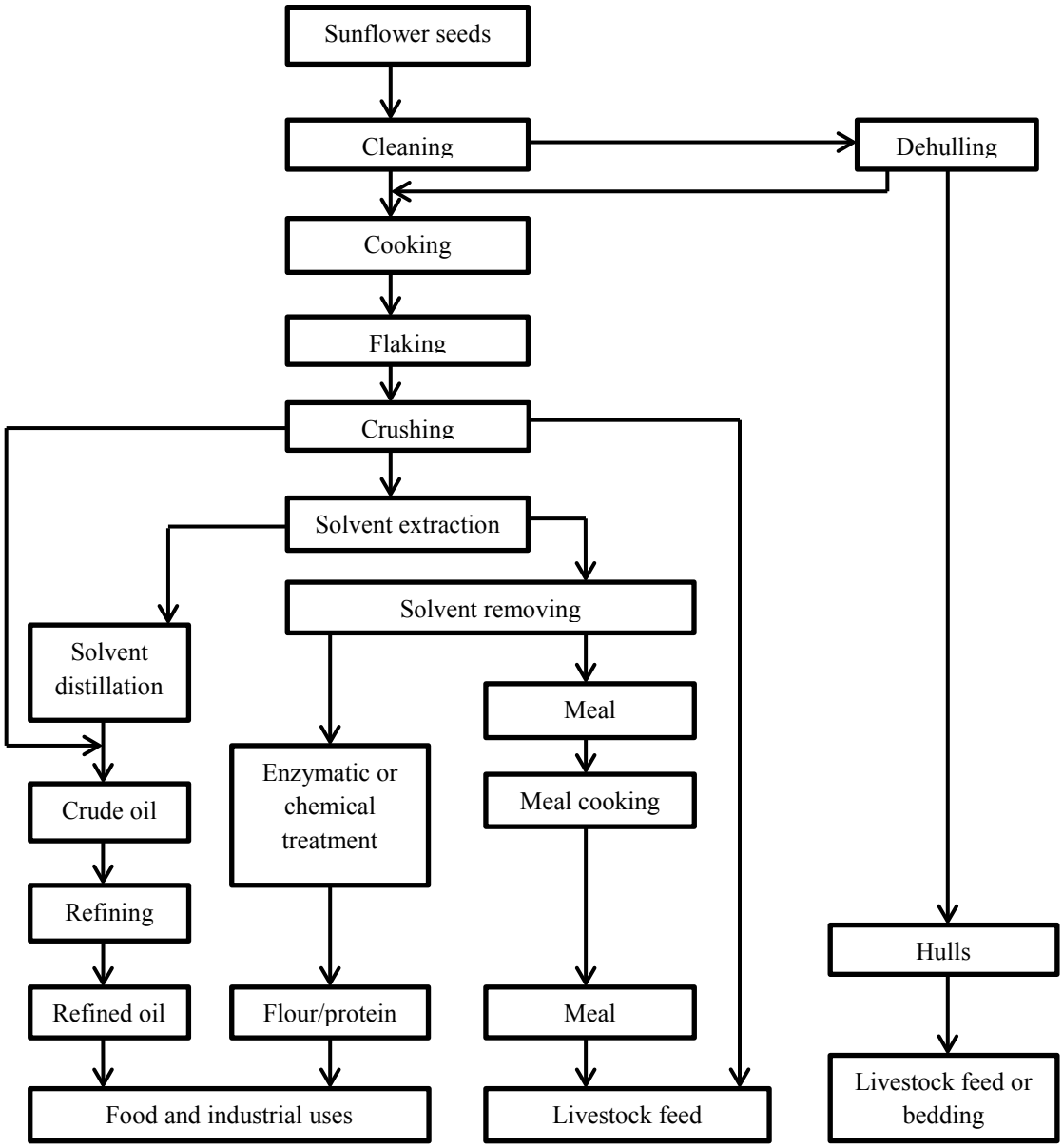

Figure 1. Method of manufacture of *H. annuus* (sunflower)-derived products.[25]

Helianthus annuus (sunflower) extract was reported to be a water/grain alcohol extraction of the macerated dried bark.[36]

Impurities

A supplier reported that helianthus annuus (sunflower) extract contained ≤5% ash or moisture; ≤1 ppm heavy metals and ≤1 ppm organic residues.[36] There were no pesticides detected and solvent (water/grain alcohol) residue was ≤0.01%. The total yeast and mold detected was ≤50 colony forming units (cfu)/g. The sample was negative for *Escherichia coli*, *Salmonella*, and *Staphyloccoccus*.

Commercial *H. annuus* seeds that have not been shelled were shown to be contaminated with pollen, a potential allergen.[10]

Aflatoxins or molds that produce aflatoxins have been detected in some dried sunflower seeds samples.[37-39] Not all samples are contaminated.[40]

USE

Cosmetic

The safety of the cosmetic ingredients included in this safety assessment is evaluated on the basis of the expected use in cosmetics. The Panel utilizes data received from the U.S. Food and Drug Administration (FDA) and the cosmetics industry in determining the expected cosmetic use. The data received from the FDA are those it collects from manufacturers on the use of individual ingredients in cosmetics by cosmetic product category in its Voluntary Cosmetic Registration Program (VCRP), and those from the cosmetic industry are submitted in response to a survey of the maximum reported use concentrations by category conducted by the Personal Care Products Council (Council).

According to 2015 VCRP data, helianthus annuus (sunflower) seed extract had the highest reported number of uses in this safety assessment in 380 formulations (Table 11).[41] Helianthus annuus (sunflower) extract had the next highest number of reported uses in 91 formulations. All other in-use ingredients are reported to be used in 70 or fewer formulations.

The results of the concentration of use survey conducted by the Council in 2015 indicate that hydrolyzed sunflower seed wax had the highest reported maximum concentration of use; it is used at up to 10% in skin cleansing formulations.[42] The highest maximum concentration of use reported for products resulting in leave-on exposure is 4% in helianthus annuus (sunflower) seed wax in mascara and 4% in hydrolyzed sunflower seed wax in lipstick.

The ingredients not in use according to the VCRP and industry survey are listed in Table 12.

In some cases, reports of uses were received in the VCRP, but no concentration of use data are available. For example, helianthus annuus (sunflower) flower extract is reported to be used in 5 formulations, but no use concentration data were available. In other cases, no reported uses were received in the VCRP, but use concentrations were provided in the industry survey. For example, helianthus annuus (sunflower) seed was not reported in the VCRP to be in use, but the industry survey indicated that it is used in 2 types of hair products and a suntan product. It should be presumed that helianthus annuus (sunflower) seed is used in at least one cosmetic formulation for which a concentration of use is reported.

Helianthus annuus (sunflower) extract (concentration not reported), helianthus annuus (sunflower) seed extract (up to 0.24%), helianthus annuus (sunflower) seedcake (up to 0.41%), helianthus annuus (sunflower) seed wax (up to 4%), and hydrolyzed sunflower seed wax (up to 4%) are used in products used near the eye. Helianthus annuus (sunflower) seed extract (up to 1%), helianthus annuus (sunflower) seedcake (up to 0.00012%), helianthus annuus (sunflower) seed wax (up to 3.9%), and hydrolyzed sunflower seed wax (up to 4%) are used in products that may be ingested. Helianthus annuus (sunflower) extract (0.075%), helianthus annuus (sunflower) flower extract (concentration not reported), helianthus annuus (sunflower) seed extract (up to 5%), helianthus annuus (sunflower) seedcake (up to 0.12%), helianthus annuus (sunflower) seed wax (up to 3.9%), and hydrolyzed sunflower seed wax (up to 4%) are used in products that may come in contact with mucus membranes. Products containing these ingredients may be applied as frequently as several times per day and may come in contact with the skin or hair for variable periods following application. Daily or occasional use may extend over many years.

Additionally, some of the *H. annuus* (sunflower)-derived ingredients are used in cosmetic sprays and could possibly be inhaled; for example, helianthus annuus (sunflower) seed extract is reported to be used at up to 0.05% in hair sprays and helianthus annuus (sunflower) seedcake is reported to be used at up to 0.0012% in spray face and neck products. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 µm, with propellant sprays yielding a greater fraction of droplets/particles <10 µm compared with pump sprays.[43,44] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[45,46]

All of the *H. annuus* (sunflower)-derived ingredients, except for helianthus annuus (sunflower) leaf/stem extract, named in the report are not restricted from use in any way under the rules governing cosmetic products in the European Union (EU).[47] Helianthus annuus (sunflower) leaf/stem extract was not listed in the EU database.

Non-Cosmetic

H. annuus is cultivated primarily for the seeds which yield the world's second most common source of edible oil.[18] Hulled seed press-cake is used as a high protein feed for livestock. The raw kernels are used as feed for poultry and cage birds. The stalks and leaves are used for fodder, silage and as a green-manure crop.[48,49] The seed hulls are used for filler in livestock feed and bedding. A yellow dye is extracted from the flowers.

Non-oilseed seeds are used for confectionary purposes.[25] De-hulled seeds (kernels) are eaten roasted and salted alone or in other foods (e.g., salads and cakes). Whole sunflower seeds (with hulls) are also eaten as a snack food. Such seeds contain less oil.

H. annuus seeds are used to make an alternative to peanut butter.[50] In the EU, sunflowers and seeds are not required to be labelled as allergens.[51]

In the EU, the flowers and seed oil from the seeds of *H. annuus* were on the market as food or food ingredients and were consumed to a significant degree before 15 May 1997.[52] Thus its access to the market is not subject to the Novel Food Regulation (EC) No. 258/97. However, other specific legislation may regulate the placing on the market of this product as a food or food ingredient in some Member States.

Medicinal uses of *H. annuus* seeds are reported to be as a diuretic, expectorant, and is used to treat colds, coughs, throat, and lung ailments.[20] The flowers and seeds are reported to be used in folk remedies for cancer in Venezuela. The

flowers and seeds are also reported to have multiple uses, including: antiseptic, aphrodisiac, bactericidal, diuretic, expectorant, and malaria preventative uses. *H. annuus* plants have multiple uses in folk remedies, including: bronchitis, carbuncles, cold, colic, cough, diarrhea, eye ailments, fever, flu, inflammations, rheumatism, urogenital ailments, and wounds.

Ozonized sunflower seed oil is used in topical medications to treat various foot fungi.[53]

Native Americans have been reported to use *H. annuus* in multiple ways.[54] The seed and root were used to ward off illness in neonates by feeding them to newly pregnant women. The ground seed flour was used for food; roasted and ground seeds were made into cakes and used to feed livestock. The flower head was used as a vegetable. The sap was chewed to ward off thirst.

The stalks have been used to make acoustic ceiling tiles, door cores (with flame suppressors, burn-resistant doors), deburring and polishing abrasives for metal, and plant starter material.[55]

H. annuus plants are used in photoremediation to extract heavy metals and other toxic substances from the soil (e.g., lead, arsenic and uranium).[56,57] This plant is also used in rhizofiltation to neutralize radionuclides and other toxic substances and to remove harmful bacteria from water.[58]

TOXICOKINETICS

Since these ingredients are complex mixtures, data on the toxicokinetics of *H. annuus* (sunflower)-derived ingredients would not be practical. However, since these ingredients are consumed as food and feed, exposure to the components of these ingredients in cosmetics is expected to be lower than dietary exposure.

TOXICOLOGICAL STUDIES

Dermal

Acute and repeated dose dermal toxicity data on *H. annuus* (sunflower)-derived ingredients were not found in the published literature and no unpublished data were provided.

Oral

Acute and repeated dose oral toxicity data on *H. annuus* (sunflower)-derived ingredients were not found in the published literature and no unpublished data were provided. However, as noted earlier, some of the ingredients reviewed in this safety assessment and various plant parts may be consumed as food and/or feed, and daily exposure from food use would result in much larger systemic exposures than those from use in cosmetic products. Therefore, the systemic toxicity potential of *H. annuus* (sunflower)-derived ingredients via oral exposure is not the focus of this safety assessment. The primary focus is the potential for irritation and sensitization reactions after dermal exposure to these ingredients.

Inhalation

Acute and repeated dose inhalation toxicity data on *H. annuus* (sunflower)-derived ingredients were not found in the published literature and no unpublished data were provided.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Reproductive and developmental toxicity data on *H. annuus* (sunflower)-derived ingredients were not found in the published literature and no unpublished data were provided.

GENOTOXICITY

Genotoxicity data on *H. annuus* (sunflower)-derived ingredients were not found in the published literature and no unpublished data were provided.

CARCINOGENICITY

Carcinogenicity data on *H. annuus* (sunflower)-derived ingredients were not found in the published literature and no unpublished data were provided.

IRRITATION AND SENSITIZATION

Irritation

Dermal

OZONIZED SUNFLOWER SEED OIL

A topical medication containing ozonized sunflower seed oil (measured as 8%-12% hydroxiperoxides of unsaturated triglycerides as active oxygen; amount not specified, assumed as needed to treat the skin disease) was dermally administered to human subjects (n=100) who had tinea pedis 2 times per day, for 6 weeks.[53] There were no adverse events reported including irritation, edema, and erythema. The ability to observe adverse events on the skin increased as the tinea pedis reduced.

Ocular

Ocular irritation data on *H. annuus* (sunflower)-derived ingredients were not found in the published literature and no unpublished data were provided.

Sensitization

Dermal – Human

HELIANTHUS ANNUUS (SUNFLOWER) EXTRACT

A patch test of helianthus annuus (sunflower) extract (1%) was performed in subjects (n=9) that were known to have developed allergies to chrysanthemums (another member of the *Asteraceae* family).[16] To make the extract, freshly cut sunflower plants were dipped whole into peroxide-free diethyl ether for 60 sec; the ether was then dried over Na_2SO_4 for 8 h to a dry residue. The residue was incorporated into white petrolatum. The test substance was administered using plaster strip and the test site was observed at 24, 48, and 72 h. Five of the subjects had positive reactions ranging from + to +++.

HELIANTHUS ANNUUS (SUNFLOWER) SEED EXTRACT

Patch tests and IgE tests of helianthus annuus (sunflower) seed extract (concentration not specified) were performed in subjects (n=17) with established fruit, nut, and/or legume allergies, including 2 subjects with a confirmed *H. annuus* seed allergy.[59] Negative and positive controls for skin testing were saline solution and histamine dihydrochloride, respectively. Seven (41%) of the subjects had a positive reaction by 1 or both of the allergy tests.

An *H. annuus* seed extract (1:100 w/v) was used in skin prick tests in atopic subjects (n=84; each positive for a common allergen).[60] A commercial radioallergosorbent test (RAST) was also performed. The *H. annuus* extract was prepared from hulled seed after pressing with a hydraulic press to remove the oil. The pressed seeds were extracted with physiologic saline overnight and centrifuged. The supernatant was ultracentrifuged and the middle fraction extracted and sterilized. There were 18 positive reactions for the skin prick test, of these 3 were also positive for the RAST. The positive reactions strongly correlated to owning a caged bird and a history of at least 1 food allergy.

A skin prick test and food-specific IgE assays were conducted in subjects (n=65 adults) with various fruit and or seed allergies, including 2 subjects with allergies to *H. annuus* seeds.[59] The 17 of 65 subjects had a positive reaction to *H. annuus* seeds in 1 or both of the assays; none of the subjects with positive reactions had a positive reaction to a double-blind placebo-controlled food challenge for *H. annuus* seeds.

Oral

There are cases of food allergies to *H. annuus* seeds reported in the literature (Table 13).[7,59,61-63] These allergies are confirmed with skin prick tests, RASTs, and/or double-blind, placebo-controlled food challenges. It has been shown that there is the possibility that during the harvesting process, the seeds are contaminated with pollen, which may be a cause of the allergic reaction.[10]

Inhalation

There are cases of people developing allergies to *H. annuus* pollen.[4,10,13,14,61,64-67] These tend to be people who live in areas that grow *H. annuus* or work in facilities that process these plants and handle the plant material. Some perceived allergies to the seeds have been found to be allergies to the pollen (Table 13).[10,64]

For example, subjects who worked in an animal feed processing plant (n=35) were administered skin prick tests of the components of the feed, which included helianthus annuus (sunflower) seeds.[67] The subjects had worked in the plant an average of 14 years (3-30 years) and were exposed to feed "aerosols" 8 h per shift. The skin prick tests were of aqueous preparations of the components of the feed (1:10 w/v dilution). Positive reactions to the helianthus annuus (sunflower) seeds were observed in 19 (54.3%) of the exposed subjects. There was only 1 positive reaction to sunflower seed in the control group of subjects who did not work in the plant (n=30).

CLINICAL USE

Case Reports

There are multiple case reports of children and adults who are allergic to *H. annuus* seeds (Table 13).[4-6,8-12,68] Contacts were by dermal, oral, and/or inhalation exposure.

SUMMARY

This is a review of the available scientific literature relevant to assessing the safety of *H. annuus* (sunflower)-derived ingredients as used in cosmetics. The functions of these ingredients include skin-conditioning agents – miscellaneous, abrasives, and absorbents.

The ingredients in this report are grouped together because they are extracts, waxes, or powders derived from plant parts of *H. annuus*, the sunflower.

The seeds of *H. annuus* are consumed by humans, both raw and roasted, on a regular basis. The remaining parts of the plant, as well as the seeds, are fed to farm animals and pets. Exposure from food use would result in much larger systemic exposures than those from use in cosmetic products. Therefore, the oral toxicity of these ingredients will not be the focus of this safety assessment though oral information may be included here. The primary focus of this safety assessment of *H. annuus* (sunflower)-derived ingredients as used in cosmetics is on the potential for irritation and sensitization from dermal exposure. It is noted that *H. annuus* is a member of the *Asteraceae* family; members of this family tend to be sensitizing.

According to the 2015 VCRP data, helianthus annuus (sunflower) seed extract had the highest reported number of uses in 380 formulations of the ingredients in this safety assessment. Helianthus annuus (sunflower) extract had the next highest number of reported uses in 91 formulations. All other in-use ingredients are reported to be used in 70 or fewer formulations.

In the 2015 Council survey, hydrolyzed sunflower seed wax had the highest reported maximum concentration of use; it is used at up to 10% in skin cleansing formulations. The highest maximum concentration of use reported for products resulting in leave-on exposure is 4% in helianthus annuus (sunflower) seed wax in mascara and 4% in hydrolyzed sunflower seed wax in lipstick.

Ozonized sunflower seed oil, at up to 12% hydroxiperoxides of unsaturated triglycerides as active oxygen, produced no adverse effects when administered to human subjects with tinea pedis twice daily for 6 weeks.

In a patch test of helianthus annuus (sunflower) extract in human subjects with known allergies to another member of the *Asteraceae* family, 5 of 9 subjects had positive reactions ranging from + to +++.

In a patch test in human subjects with known food allergies, 7 of 17 subjects had positive reactions to helianthus annuus (sunflower) seed extract in a patch test and/or an IgE test. The concentration was not specified.

In a skin prick of helianthus annuus (sunflower) seed extract (1:100 w/v) in human subjects with a common allergy, 18 of 84 subjects had a positive result; 3 of these were also positive in a RAST.

There are multiple case reports of people with food allergies to sunflower seeds. These allergies are confirmed with skin prick tests, RASTs, and/or double-blind, placebo-controlled food challenges

There are multiple cases of humans developing allergies to *H. annuus* plants and/or seeds, possibly from inhalation of the pollen. For example, 19 of 35 subjects who work in a facility processing animal feed, including *H. annuus*, had positive reactions in a skin prick test for and aqueous extract (1:10 w/v) of the plant.

DATA NEEDS

The CIR staff requests any data on the toxicity of *Helianthus annuus* (sunflower)-derived ingredients, including information on:

- Characterization of constituents of each of these ingredients
- Method of manufacture for cosmetics for each of these ingredients including methods for removing constituents of concern
- Dermal and inhalation toxicity data for each of these ingredients at or above the reported concentrations of use
- Reproductive and developmental toxicity, genotoxicity, and carcinogenicity data for each of these ingredients at or above the reported concentrations of use
- Dermal and ocular irritation data for each of these ingredients at or above the reported concentrations of use
- Irritation and sensitization data of each of these ingredients at or above the reported concentrations of use

TABLES AND FIGURES

Table 1. Definitions and functions of the *Helianthus annuuss*-derived ingredients in this safety assessment.[1]

Ingredient	Definition	Functions
Helianthus annuus (sunflower) extract	Helianthus annuus (sunflower) seed extract is the extract of the whole plant, *Helianthus annuus*.	Skin-conditioning agent – miscellaneous
Helianthus annuus (sunflower) flower extract	Helianthus annuus (sunflower) flower extract is the extract of the flowers of *Helianthus annuus*.	Skin-conditioning agent – miscellaneous
Helianthus annuus (sunflower) leaf/stem extract	Helianthus annuus (sunflower) leaf/stem extract is the extract of the leaves and stems of *Helianthus annuus*.	Skin-conditioning agent – miscellaneous
Helianthus annuus (sunflower) sprout extract	Helianthus annuus (sunflower) sprout extract is the extract of the sprouts of *Helianthus annuus*.	Skin-conditioning agent – miscellaneous
Helianthus annuus (sunflower) seed	Helianthus annuus (sunflower) seed is the seed of *Helianthus annuus*.	Abrasive; Skin-conditioning agent – miscellaneous
Helianthus annuus (sunflower) seed butter	Helianthus annuus (sunflower) seed butter is the fat obtained from the seeds of *Helianthus annuus*.	Skin-conditioning agent – emollient; skin-conditioning agent - occlusive
Helianthus annuus (sunflower) seedcake	Helianthus annuus (sunflower) seedcake is the residue from the expression of oil from the seeds of *Helianthus annuus*.	Abrasive; absorbent; bulking agent; Skin-conditioning agent – miscellaneous
Helianthus annuus (sunflower) seed extract	Helianthus annuus (sunflower) seed extract is the extract of the seeds of *Helianthus annuus*.	Skin-conditioning agent – miscellaneous; sunscreen agent
Helianthus annuus (sunflower) seed flour	Helianthus annuus (sunflower) seed flour is the flour obtained from the finely ground seeds of *Helianthus annuus*.	Abrasive; absorbent; bulking agent; viscosity increasing agent
Hydrolyzed sunflower seed wax	Helianthus annuus (sunflower) seed wax is the wax obtained from the seed of the sunflower, *Helianthus annuus*.	Skin-conditioning agent – miscellaneous
Hydrogenated sunflower seed extract	Hydrogenated sunflower seed extract is the end-product obtained by the controlled hydrogenation of helianthus annuus (sunflower) seed extract	Skin-conditioning agent – miscellaneous
Ozonized sunflower seed oil	Ozonized sunflower seed oil is the end-product of the controlled ozone treatment of helianthus annuus (sunflower) seed oil.	Skin-conditioning agent – miscellaneous
Helianthus annuus (sunflower) seed wax	Helianthus annuus (sunflower) seed wax is the wax obtained from the seed of the sunflower, *Helianthus annuus*.	Skin-conditioning agent – miscellaneous

Table 2. Previous safety assessment of ingredients related to the *H. annuus* ingredients in this report.

Ingedient(s)	Conclusion	Maximum concentration of use in safety assessment	Reference
Helianthus Annuus (Sunflower) Seed Oil, Helianthus Annuus (Sunflower) Seed Oil Unsaponifiables, Hydrogenated Sunflower Seed Oil, and Sunflower Seed Acid in Plant-Derived Fatty Acid Oils	Safe as used.	100%	[2]
Phytosteryl Sunflower Sedate, C10-40 Isoalkyl Acid Phytosterol Esters, Dihydrophytosteryl Octyldecanoate, Phytosteryl Buyrate, Phytosteryl Caprylate/Caprate, Phytosterol Hydroxystearate, Phytosteryl Isostearate, Phytostearyl Linoleate, Phytostearyl Linoleate/Linolenate, Phytosteryl Nopnanoate, Phytosteryl Oleate, Beta-Sitosterol, Beta-Sitosteryl Acetate, and Phytosterols in Phytosterols	Safe as used	8%	[3]

Table 3. Chemical and physical properties of *H. annuus* (sunflower)-derived ingredients.

Property	Value	Reference
Helianthus annuus (sunflower) extract		
Physical Form	Fine powder	[36]
Color	Brownish yellow	[36]
Odor	Characteristc	[36]
Water Solubility g/L @ ºC & pH	Soluble	[36]
Hydrolyzed sunflower seed wax		
Physical Form	Solid wax	[23]
Color	Yellow	[23]
Odor	Very low	[23]
Density/Specific Gravity @ 20 ºC	0.87-0.95	[23]
Melting Point ºC	74-77	[23]
Boiling Point ºC	>200	[23]
Water Solubility g/L @ ºC & pH	Insoluble	[23]

Table 4. Composition of *H. annuus* whole plant at different growth stages.[25]

	Mature		Before bloom	Beginning of bloom	In bloom	After bloom
	Source 1	Source 2	Source 3			
	g/100g fresh weight					
Dry matter	-	30	12	20	14	15
	g/100 g dry matter					
Crude protein	11-12	12.5	19.3	13.9	14.7	14.0
Crude fat	10.12	10.7	2.7	4.4	2.4	2.8
Acid-detergent fiber	32.0	39	-	-	-	-
Lignin	10-16	12.3	-	-	-	-

- = No data

Table 5. Sample comparison of oil content (g/100 g dry material) in oilseed and non-oilseed *H. annuus*.[25]

Acid	Oilseed	Non-oilseed
Myristic acid (C14:0)	0.02	0.05
Palmitic acid (C16:0)	2.84	2.95
Palmitoleic acid (C16:1)	0.03	0.05
Stearic acid (C18:0)	2.12	2.33
Oleic acid (C18:1)	8.48	9.89
Linoleic acid (C18.:2)	27.8	34.48
Linolenic acid (C18:3)	0.04	0.07
Arachidic acid (C20:1)	0.06	0.05

Table 6. Composition of phytosterols and tocopherols as a function of oleic acid content in *H. annuus* seeds.[25]

Sterol	Conventional/wild	Mid oleic acid	High oleic acid
Total sterols	240-500(mg/g)	NR	170-520(mg/g)
β-sitosterol[1]	50%-70%	56%-58%	42%-70%
Campesterol[1]	6.5%-13.0%	9.1%-9.6%	5%-13%
Stigmasterol[1]	6.0%-13.0%	9.0%-9.3%	4.5%-13%
Total tocopherols (mg/g)	44-152	50.9-74.1(mg/g)	45-112(mg/g)
α (vitamin E) (mg/g)	40.3-93.5(mg/g)	48.8-66.8(mg/g)	40-109(mg/g)
B (mg/g)	ND-4.5(mg/g)	1.9-5.2(mg/g)	1.0-3.5(mg/g)
γ (mg/g)	ND-3.4(mg/g)	0.2-1.9(mg/g)	0.3-3.0(mg/g)

[1] Percent of total sterols

Table 7. The vitamin content of non-oilseed seeds of *H. annuus*.[25]

Vitamin	Amount (/100 g dry materiala)
Vitamin C (mg)	1.48
Thiamine (mg)	2.42
Riboflavin (mg)	0.26
Niacin (mg)	4.75
Pantothenic acid (mg)	7.13
Vitamin B-6 (mg)	0.81
Folate (µg)	239.86
Vitamin A (IU)	52.84
Vitamin E (α tocopherol) (mg)	36.46
Vitamin K (µg)	2.85

Table 8. Amino acid content in *H. annuus* seed flour.[25]

Amino acid	Amount (g/100 g of crude protein)
Isoleucine	3.7
Leucine	6.5
Lysine	3.4
Methionine + cysteine	4.1
Triptophan	1.5
Phenylalanine + tyrosine	8.2
Valine	4.9
Threonine	3.3

Table 9. Composition of *H. annuus* meal derived from whole and part-dehulled seeds from different sources.[25]

	Whole seed meal		Part-dehulled seed meal		Hulls
	Source 1 (mean±sd)	Source 2 (mean)	Source 1 (mean)	Source 2 (mean)	Source 3 (mean (range))
g/100 g fresh weight					
Dry matter	88.7±1.4	-	89.7±1.2	92.0	87.8 (85.0-92.0)
g/100 g dry matter					
Crude protein	27.7±2.2	28.4	33.4±2.2	38.0	5.0 (3.5-9.0
Crude fiber	25.5±2.6	-	21.2±2.0	20.0	45.0 (40.0-50.0)
Crude fat	2.0±0.8	1.4	6.7±0.5	8.0	3.0 (0.5-3.0)
Minerals (ash)	6.2±0.6	7.7	6.7±0.5	8.0	
Neutral-detergent fiber	41.1±3.7	40.0	35.9±3.6	36.0	70.0 (65.0-75.0)
Acid-detergent fiber	29.3±3.0	30.0	24.7±2.4	24.0	56.0 (50.0-63.0)
Lignin	10.1±1.4	-	8.2±1.2	-	
Ash	-	-	-	-	2.7 (2.0-3.0)
Calcium	-	-	-	-	0.30 (0.25-0.35)
Phosphorus	-	-	-	-	0.15 (0.10-0.20)
Magnesium	-	-	-	-	0.20 (0.15-0.25)

- = No data
sd = standard deviation

Table 10. Amino acid and protein content of *H. annuus* meal derived from whole and part-dehulled seeds from 3 sources.[25]

	Non-dehulled sunflower meal			Dehulled sunflower meal	
Amino acid	**Source 1**	**Source 2**	**Source 3**	**Source 2**	**Source 3**
Arginine	2.32	2.64	2.56	3.15	3.17
Histidine	0.74	0.73	0.61	0.99	0.97
Isoleucine	1.16	1.43	1.11	1.55	1.59
Leucine	1.82	2.07	1.78	2.48	2.47
Lysine	1.01	1.12	1.11	1.29	1.38
Methionine	0.65	0.66	0.56	0.88	0.89
Cystine	0.50	0.53	0.56	0.71	0.71
Phenylalanine	1.31	1.37	1.28	1.78	1.85
Threonine	1.06	1.16	1.17	1.43	1.44
Tryptophan	0.34	0.42	0.50	0.47	0.46
Valine	1.41	1.66	1.78	1.87	1.94
Glycine	-	-	-	-	2.26
Tyrosine	-	0.84	-	1.11	1.01
Serine	-	-	1.11	-	1.66
Crude protein	28.4	29.8	25.9	45.4	41.0

- = No data

Table 11. Frequency of use according to duration and exposure of *H. annuus* (sunflower)-derived ingredients.[41,42]

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Helianthus Annuus (Sunflower) Extract		**Helianthus Annuus (Sunflower) Flower Extract**		**Helianthus Annuus (Sunflower) Seed Extract**		**Helianthus Annuus (Sunflower) Seed**	
Total/range	**91**	**0.0000015-0.075**	**5**	NR	**380**	**0.000015-5**	**NR**	**0.00002-0.01**
Duration of use[a]								
Leave-on	48	0.0003-0.05	2	NR	202	0.000015-1	NR	0.00091-0.01
Rinse-off	42	0.0000015-0.001	3	NR	177	0.000015-5	NR	0.00002
Diluted for (bath) use	1	0.075	NR	NR	1	0.0003-0.0016	NR	NR
Exposure type								
Eye area	1	NR	NR	NR	10	0.0003-0.24	NR	NR
Incidental ingestion	NR	NR	NR	NR	7	0.0002-1	NR	NR
Incidental Inhalation-sprays	7; 22[b]; 8[c]	0.0005[b]	1[b]	NR	26; 52[b]; 50[c]	0.000015-0.05; 0.00003-0.025[b]	NR	0.00091[b]
Incidental inhalation-powders	1;8[c]	0.0003[d]	NR	NR	50[c]	0.0025-0.032[d]	NR	NR
Dermal contact	34	0.0003-0.075	4	NR	128	0.0001-5	NR	0.01
Deodorant (underarm)	1[b]	NR	1[b]	NR	2[b]	NR	NR	NR
Hair-noncoloring	55	0.0000015-0.0025	1	NR	216	0.000015-5	NR	0.00002-0.00091
Hair-coloring	2	NR	NR	NR	29	0.00009-5	NR	NR
Nail	NR	NR	NR	NR	NR	NS0.0001	NR	NR
Mucous Membrane	5	0.075	2	NR	24	0.0002-5	NR	NR
Baby	NR	NR	NR	NR	NR	NR	NR	NR

Table 11. Frequency of use according to duration and exposure of *H. annuus* (sunflower)-derived ingredients.[41,42]

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Helianthus Annuus (Sunflower) Seedcake		**Helianthus Annuus (Sunflower) Seed Wax**		**Hydrolyzed Sunflower Seed Wax**			
Total/range	**70**	**0.000015-0.41**	**NR**	**0.0038-4**	**21**	**3.3-10**		
Duration of use								
Leave-on	59	0.000015-0.41	NR	0.19-4	21	3.3-4		
Rinse-off	11	0.000015-0.12	NR	0.0038	NR	10		
Diluted for (bath) use	NR	NR	NR	NR	NR	NR		
Exposure type								
Eye area	9	0.000015-0.41	NR	3.6-4	2	3.5		
Incidental ingestion	NR	0.00012	NR	3.9	9	3.3-4		
Incidental Inhalation-sprays	30[b]; 10[c]	0.0012; 0.000015[b]	NR	0.19[b]	5[b]; 2[c]	NR		
Incidental inhalation-powders	10[c]	0.41[d]	NR	0.52-0.75[d]	2[c]	NR		
Dermal contact	69	0.000015-0.41	NR	0.19-3.6	11	10		
Deodorant (underarm)	NR	NR	NR	NR	NR	NR		
Hair-noncoloring	NR	NR	NR	0.0038	NR	NR		
Hair-coloring	1	NR	NR	NR	NR	NR		
Nail	NR	NR	NR	NR	NR	NR		
Mucous Membrane	NR	0.00012-0.12	NR	3.9	9	3.3-4		
Baby	NR	NR	NR	NR	NR	NR		

NR = Not Reported; Totals = Rinse-off + Leave-on Product Uses.
Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.
[a] Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
[b] It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.
[c] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.
[d] It is possible these products may be powders, but it is not specified whether the reported uses are powders.

Table 12. *H. annuus* (sunflower)-derived ingredients with no reported uses.[41,42]

Helianthus Annuus (Sunflower) Leaf/Stem Extract	Helianthus Annuus (Sunflower) Sprout Extract
Helianthus Annuus (Sunflower) Seed Butter	Helianthus Annuus (Sunflower) Seed Flour
Hydrogenated Sunflower Seed Extract	Ozonized Sunflower Seed Oil

Table 13. Case reports of children and adults with oral and dermal allergic reactions to *H. annuus* seeds and plants.

Case History	Testing	Reference
Oral Exposure		
3-year-old boy presented with oral discomfort that developed after eating sunflower seeds for the first time. Treatment with diphenhydramine and rest resolved the reaction. A few weeks later, he had a similar reaction to a snack bar made with sunflower seed "butter". He was not treated but observed by his parents. In a subsequent episode, the boy had a similar reaction to a bread roll with poppy seeds; this required epinephrine and an emergency room visit. This child had a history of mild infantile atopic dermatitis. There was an older sibling with a confirmed peanut allergy and the home had been peanut-free for some time and alternatives, such as sunflower seed "butter" had been fed to the children.	A skin prick test of a slurry of fresh *H. annuus* seed resulted in a 1-mm wheal within 3-4 min and severe pruritus. A similar reaction was elicited from poppy seeds (>10 mm wheal) and a smaller reaction to pumpkin seeds (8 mm wheal).	8
5-year-old girl with a diagnosed peanut allergy (at 18 months of age) presented with generalized urticaria and angioedema of the lips. She had just eaten a few bites of sunflower seed butter (reportedly from a facility that does not process peanuts).	Skin prick tests at 18 months were positive for peanuts (6 mm wheal) and negative for *H. annuus* seed; at 5 years, the tests were positive for peanuts (21 mm wheal) and *H. annuus* seed (16 mm wheal).	68
11-year-old boy who presented with generalized urticaria/ angioedema and bronchospasm within 30 min of eating *H. annuus* seeds. Epinephrine relieved the symptoms. He had eaten *H. annuus* seeds at least once before without any reactions. He had a history of seasonal allergic rhinitis for the previous 2-3 years.	Scratch tests and RAST to *H. annuus* seed extract were positive as well as trees molds and grasses.	9

Table 13. Case reports of children and adults with oral and dermal allergic reactions to *H. annuus* seeds and plants.

Case History	Testing	Reference
A 22-year-old female, with a history of atopic dermatitis and Japanese cedar pollinosis, ate 5 pieces of sunflower seed chocolates. She experienced sudden nausea and dyspnea 5 min later, followed by development of wheals all over her body. In the emergency room, wheezing was heard in the region of her larynx. Her bulbar conjunctiva was hyperemic. She was treated with injections of epinephrine and corticosteroids. Later, although she again ate chocolate confections, no immediate allergic reactions occurred. She recalled having often eaten sunflower seeds as a snack during high school.	A skin prick test, CAP assay, ELISA, the ImmunoCAP® inhibition assay, immunoblot and immunoblot inhibition assays, and N-terminal sequence analysis. Skin prick tests were performed with the native protein extract from sunflower seeds and 7 other extracts from the *Asteraceae* family. There were positive reactions to the extracts of sunflower seeds in SPTs but not in other extracts. The level of serum IgE antibody for sunflower seed was high (35.1 UA/ml, class 4). There was a high titer of IgE antibody specific for Japanese cedar pollen (27.2 IU/ml, class 4). Her serum was negative for specific IgE antibodies against mugwort, birch, ragweed, dandelion, latex, chocolate, cacao, peanuts, almonds, Brazil nuts, and gelatin. ELISA of the extract from sunflower seeds showed higher absorbance than the controls ($P < 0.01$). There were no reactions to the 4 kinds of nuts. The ImmunoCAP® inhibition assay of the extract from sunflower seeds showed suppression that depended on the concentration of the inhibitor (sunflower seed). The same test for Japanese cedar pollen with sunflower seeds showed no suppression. Several IgE-binding protein bands on the immunoblot assay using the extract from sunflower seeds were identified. These IgE-binding protein bands were almost undetectable when using control sera. On the inhibition immunoblot assay using the *H. annuus* extract, the IgE-binding signal of one band (13 kDa) disappeared completely. The N-terminal amino acid sequence of the IgE-binding protein band (13 kDa) of *H. annuus* seed closely matched LTP from *H. annuus* seeds. The author concluded that LTP is able to induce severe and systemic symptoms and sensitization by the oral route in fruit allergic patients who do not have associated pollen allergy	12
A 22-year-old woman developed systemic allergic reactions comprising rhinitis, nasal congestion, tearing, and facial and generalized urticaria after eating shelled *H. annuus* seeds. The symptoms resolved in a few hours. She had no history of allergy to seed that she shelled herself.	Skin prick test-positive for *H. annuus* pollen and dust mites; negative for other pollens and foods. Open food challenge-positive for shelled *H. annuus* seeds. Analysis showed that the shelled seeds were contaminated with pollen.	10
A 37-year-old woman experienced anaphylaxis (diffuse pruritus, urticaria, angioedema, nausea and vomiting, chest tightness, and wheezing, followed by vascular collapse and loss of consciousness) within 20 min of ingesting *H. annuus* seeds. She was treated with epinephrine, intravenous fluids, diphenhydramine and steroids. Over the next week, she had several episodes of lip and facial swelling in the morning on awakening. She had a history of eating sunflower seeds without incident and she had no prior allergic reactions to foods. She had a history of anaphylactic reactions to fire ant venom. Her general health was good, and she was taking no medications.	P-K test- Heated and unheated serum from the subject was used. After injections of the serums, skin sites were challenged with intradermal injections of commercial *H. annuus* seed extracts (1:1000 w/v; 0.02 mL). The passive transfer recipient was strongly positive at the unheated serum site on challenge with *H. annuus* seed extract. The heated serum site challenged with sunflower seed extract was negative. Skin Prick Test-commercial sunflower seed extract resulted in a 12x16 mm wheal; causative seed extract resulted in a 16x16 mm wheal; cold-pressed sunflower oil was negative. RAST-Commercial sunflower seed extract (1:20 w/v in 50% glycerin) and an extract prepared from the causative seeds (extracted in diluent saline, 1 gm/100 mL, filtered) resulted in a class 4 reaction (a moderate reaction). Open challenge to the inner upper lip and oral mucosa-refined and cold-pressed oil had no reaction.	7
A 58-year-old man present with "tingling of his lips", a generalized itching sensation, and laryngeal edema that began within 5 min of ingesting 3 *H. annuus* seeds. He developed abdominal pain, generalized angioedema, and bronchospasm within 30 min of arriving at the hospital. Most of the symptoms were resolved with epinephrine, but he was hypotensive, so he was admitted for treatment with theophylline and steroids. He had a history of perennial rhinitis and reported sensitivity to walnuts. He had no known allergies to foods in the *Asteraceae* family.	Scratch tests and RASTs to a *H. annuus* seed extract were positive along with June grass and ragweed. The *H. annuus* seed extract was an aqueous paste made by emulsifying washed sunflower seeds in buffered saline.	9
Dermal Exposure		
A 23-year-old man, with a history of rhinoconjunctivitis, asthma, and hypersensitivity to grass pollens presented with contact urticaria from dermal contact with peeled *H. annuus* seeds. The symptoms (itching, erythema, and wheal-and-flare reactions) appeared 15 min after contact. He reported tolerating the consumption of sunflower seeds with occasional pruritus or the oral mucosa and mild obstruction of the pharynx after eating larger amounts of the seeds. He tolerated sunflower oil both dermally and orally.	Total serum IgE was 456 IU/mL (strongly positive). Local urticaria was observed after 30 min in a closed patch test of peeled sunflower seed; and open patch test showed only local erythema. An itchy wheal of 5 mm was observed in a prick test of sunflower seed.	5
A 50-year-old woman who presented with generalized urticaria, facial angioedema, laryngeal edema, wheezing, and dyspnea about 2 h after ingesting several *H. annuus* seeds. The symptoms were relieved by antihistamine. She had eaten these seeds in the past. She reported that when she handled *H. annuus* seeds that she used to feed	Scratch tests and RAST titers to the *H. annuus* seed extract were positive with mixed results to grass, ragweed, tree pollens walnut, and peanut	9

Table 13. Case reports of children and adults with oral and dermal allergic reactions to *H. annuus* seeds and plants.

Case History	Testing	Reference
birds, she developed pruritus of her hands. She had no other history of food sensitivity; she had a history of allergic rhinitis and occasional mild bronchospasm since childhood, for which she was not taking medication.		
A 62-year-old man presented with forehead dermatitis that had lasted for 2 months. It was resolved with topical corticosteroids but returned when treatment stopped. The man handled cattle fodder that was composed of *H. annuus* plants.	Patch tested with European standard series and *Asteraceae* plant series. Positive results were observed for *H. annuus* leaves and the cattle fodder.	6
Inhalation Exposure		
A 24-year-old man had developed rhinitis and conjunctivitis over 5 years of exposure to sunflower pollens and then developed asthma during the fifth year. All respiratory and ocular symptoms resolved when he discontinued exposure to *H. annuus* plants and pollen. He later had a food allergic reaction while eating honey containing 30% sunflower pollen.	Skin prick tests and RAST to an *H. annuus* pollen extract (1/20 w/v) showed that he had developed an occupational allergy; skin test results with *H. annuus* seed were negative. Bronchial provocation tests were performed after a rest period away from exposure to *H. annuus* pollens, but there was no nonspecific hyperactivity. It was found by RAST that *H. annuus* pollen does not cross-react with other members of the pollen from other pollens from the *Asteraceae* family or with *H. annuus* seed. The honey that elicited food intolerance was demonstrated to inhibit significantly *H. annuus* pollen RAST.	4
A 31-year-old man developed rhinochonjuctivitis and asthma when exposed to dried *H. annuus* seeds. After working as a baker for approximately 9 years, he started working in a bakery that used sunflower seeds. After 3 months, he developed rhinochonjuctivitis and asthma, even when his coworkers were handling the sunflower seeds. He reported having experienced an anaphylactic reaction after eating approximately half a *H. annuus* seed. The symptoms were increasing as he continued to work in the bakery. After changing jobs to another bakery, he still exhibited rhinitis and asthma at work and developed nocturnal asthma attacks. The subject stopped working at bakeries but still experienced symptoms, even with treatment of inhaled fluticasone propionate and salbutamol.	After 8 months without exposure to *H. annuus* seeds, a baseline lung function test was conducted showing FEV_1=3.17 (72% of predicted value) and FEV_1/forced vital capacity ratio of 62%. The subject had a 20% decrease in these scores after tipping lactose powder back and forth between 2 trays, indicating a marked nonspecific bronchial hyperresponsiveness. The next day, the tray experiment was repeated with sunflower seeds for 5 min. There was a 39% decrease in FEV_1. The next day, the same types of exposure to flour (assumed wheat) for 75 min resulted in a 42% decrease in FEV_1. Skin prick test - positive reactions to dust mites but not extracts of wheat, barley, rye, and oats. An extract of *H. annuus* seed dust was prepared by stirring the dust in phosphate-buffered saline (20% w/v) for 10 min; a 1/10 dilution of the seed extract was used, there was a 10-mm wheal reaction. Skin prick tests of *H. annuus* and other *Asteraceae* pollen were negative. *H. annuus* seed dust elicited positive reactions in inhalation challenges and immunologic tests (details not provided). The author suggested that the continued respiratory symptoms, even after months of avoidance, showed a probably sensitization to α-amylase and that sensitization can develop from the inhalation of sunflower seed dust.	11

CAP - cell-based antioxidant protection; ELISA - enzyme-linked immunosorbent assay; FEV - forced expiratory volume; K-P test - Prausnitz-Küstner; LTP – lipid transfer protein; RAST – radioallergosorbent test

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