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

Lillian C. Becker*, Ivan J. Boyer, Wilma F. Bergfeld***, Donald V. Belsito***, Ronald A. Hill****, Curtis D. Klaassen***, Daniel C. Liebler****, James G. Marks, Jr****, Ronald C. Shank****, Thomas J. Slaga***, Paul W. Snyder***, Lillian J. Gill*****, and Bart Heldreth†**

Abstract

This is a review of the scientific literature and unpublished data that are relevant for assessing the safety of 12 *Helianthus annuus* (sunflower)-derived ingredients as used in cosmetics. Because final product formulations may contain multiple botanicals, each containing similar constituents of concern, formulators are advised to be aware of these constituents and to avoid levels that may be hazardous to consumers. *Helianthus annuus* (sunflower)-derived ingredients may contain allergens, including 2S albumins and sesquiterpene lactones. Industry should use current good manufacturing practices (cGMP) to limit impurities and constituents of concern. The Expert Panel for Cosmetic Ingredient Safety (Panel) concluded that 9 *Helianthus annuus* (sunflower) seed- and flower-derived ingredients are safe as used in cosmetics in the present practices of use and concentration described in this safety assessment. The data are insufficient to evaluate the safety of 3 ingredients that are derived from other plant parts.

Keywords

sunflower, safety, cosmetics, helianthus annuus

Introduction

This is a review of the scientific literature and unpublished data that are relevant for assessing the safety of *Helianthus annuus* (sunflower)-derived ingredients as used in cosmetics. According to the *International Cosmetic Ingredient Dictionary and Handbook* (*Dictionary*), the functions of these ingredients include skin-conditioning agent – miscellaneous, abrasive, and absorbent (Table 1).[1] The 12 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

The ingredients in this report are grouped together because they are extracts, waxes, or powders (flour) derived from plant parts of *Helianthus annuus*, commonly called the sunflower. Helianthus Annuus (Sunflower) Seed Oil, and other

*Cosmetic Ingredient Review Former Scientific Analyst/Writer
**Cosmetic Ingredient Review Former Toxicologist
***Expert Panel for Cosmetic Ingredient Safety Member
****Expert Panel for Cosmetic Ingredient Safety Former Member
*****Cosmetic Ingredient Review Former Director
†Cosmetic Ingredient Review Executive Director

Corresponding Author:
Bart Heldreth, Executive Director, Cosmetic Ingredient Review, 1620 L Street, NW, Suite 1200, Washington, DC 20036, USA.
Email: cirinfo@cir-safety.org

Helianthus annuus (sunflower)-derived seed oils, were included in the Panel's safety assessment of plant-derived oils and are therefore not included in this review.[2]

In the safety assessment of plant-derived oils, the Panel concluded that Helianthus Annuus (Sunflower) Seed Oil, Helianthus Annuus (Sunflower) Seed Oil Unsaponifiables, Hydrogenated Sunflower Seed Oil, and Sunflower Seed Acid are safe as used.[2] The Panel has also reviewed the safety of phytosterols, plant-derived sterols that include Phytosteryl Sunflower Seedate, and concluded that they are also safe as used in cosmetics.[3]

The seeds of *Helianthus annuus* (sunflower), both raw and roasted, are consumed by humans on a regular basis. The rest of the plant, as well as the seeds, are fed to farm animals and pets. Because the rates of absorption and metabolism of these ingredients in the skin at the concentrations used are expected to be negligible compared to the corresponding rates in the digestive tract, exposure from food use is expected to result in much greater systemic exposures than those from use in cosmetic products. Additionally, there are only a few reported cases of food allergies to the seeds and of inhalation allergies to the pollen.[4-12] Although oral data may be included in this safety assessment, the primary focus is on the potential for irritation and sensitization from dermal and inhalation exposure, and the systemic toxicity potential of *Helianthus annuus* (sunflower)-derived ingredients via oral exposure is not addressed further in this report.

In this assessment, the Panel is reviewing information available to evaluate the potential toxicity of each of the *Helianthus annuus* (sunflower)-derived ingredients as a whole, complex substance. Except for specific constituents of concern, the Panel is not reviewing information that may be available to assess the potential toxicity of the individual constituents derived from *Helianthus annuus* (sunflower). Botanical cosmetic ingredients, such as *Helianthus annuus* (sunflower)-derived ingredients, contain hundreds of constituents, some of which have the potential to cause toxic effects. For example, sesquiterpene lactones may cause Type IV allergic reactions (cell-mediated, delayed-type hypersensitivity) and toxicity when present in sufficient amounts, and 2S albumins may cause Type I allergic reactions (IgE-mediated, immediate hypersensitivity).[13-15] It is noted that *Helianthus annuus* (sunflower) is a member of the *Asteraceae* family; members of this family are known to contain potential sensitizing constituents.[6,10,15-17]

The ingredient names, according to the *Dictionary*, are written as listed above, capitalized without italics and without abbreviations. When referring to the plant from which these ingredients are derived, the taxonomic practice of using *italics* will be followed (e.g., *Helianthus annuus*).

Chemistry and Characterization

Definition

The definitions and functions of the *Helianthus annuus* (sunflower)-derived cosmetic 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 to each other by source, because each is a derivative of a part, or parts, of the *Helianthus annuus* (sunflower) plant. The identities and concentrations of the constituents of botanical ingredients typically vary widely from plant part to plant part, by extraction method, and many other factors. Although some information on the exact constituents and their concentrations can be found in the literature, the actual manufacture and characterization of these ingredients, and their use in cosmetic formulations are best determined from composition information provided by Industry.

Plant Identification

Helianthus annuus is an annual plant in the family *Asteraceae* (synonym *Compositae*), daisy or sunflower family, subfamily *Asteroideae*.[18-21] The plant is a dicot ranging in height range from .7 to 3.5 m.[21] *Helianthus annuus* (sunflower) leaves are rough, broad, coarsely toothed, and mostly alternate. What is often called the "flower" of the *Helianthus annuus* (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 in an asymmetrical pattern. 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, penetrates to a depth of 3 m, and has large lateral spread of surface roots. Wild *Helianthus annuus* (sunflower) is a widely branched annual plant with multiple flower heads that mature sequentially.

Helianthus annuus (sunflower) seeds are achenes (or fruits) each of which consists of a kernel (true seed) and a pericarp (hull); the pericarp is four-sided and flat.[20,22] The seeds are approximately .6 cm long and .3 cm wide. *Helianthus annuus* (sunflower) oil seeds (seeds having high oleic acid content; oil content >40% and 35 - 38% protein) usually have a black seed coat; seeds grown for consumption (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 to 4000 florets, with the potential of as many seeds.[23] The average yield of seeds in a pseudanthium is 1200 to 1500.[22] The average yield of seeds ranges from 900 to 1575 kg/ha; yields of over 3375 kg/ha have been reported.

Helianthus annuus (sunflower) is native to western North America.[21] The plant was introduced to Europe and Russia in the 16th century and has spread to tropical and temperate

Table 1. Definitions and Reported Functions of the *Helianthus annuus*-Derived Ingredients.[1]

Ingredient	Definition	Functions
Helianthus Annuus (Sunflower) Extract	Helianthus Annuus (Sunflower) 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	Hydrolyzed Sunflower Seed Wax is the hydrolysate of Helianthus Annuus (Sunflower) Seed Wax derived by acid, enzyme or other method of hydrolysis.	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
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

countries, including Argentina, China, India, Turkey, and South Africa, as well as Russia and the combined European Union.[24] Hybridization and selective breeding has increased oil production. Breeding resulted in the development of strains with high oleic acid content, referred to as oil-seed.[25]

Physical and Chemical Properties

Helianthus Annuus (Sunflower) Flower Extract is a solid powder, and Hydrolyzed Sunflower Seed Wax is a yellow or white wax (Table 2).[26]

The color of Helianthus Annuus (Sunflower) Seed Flour changes with pH.[27] 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.

Method of Manufacture

A scheme of the general manufacturing process of *Helianthus annuus* (sunflower) oil, flour/protein, and meal is depicted in Figure 1. A scheme of the method of manufacture for Helianthus Annuus (Sunflower) Seedcake is depicted in Figure 2. A scheme of the method of manufacture for Helianthus Annuus (Sunflower) Seed Wax is depicted in Figure 3.

Several methods of manufacture of Helianthus Annuus (Sunflower) Seed Extract have been reported. One supplier reported that Helianthus Annuus (Sunflower) Seed Extract is a methanol extract of *Helianthus annuus* seeds, followed by filtration, purification, and drying.[28]

Another supplier reported that Helianthus Annuus (Sunflower) Seed Extract is manufactured from the fresh or dry seed, which is extracted with a specified eluent under appropriate temperature conditions (not specified) to yield a concentrate.[29] The concentrate, containing phytochemical constituents, is then blended with a diluent and preservatives to produce the final product. Each batch is analyzed for compliance to specifications, contaminants, and physiochemical properties.

A third supplier reported that Helianthus Annuus (Sunflower) Seed Extract is manufactured by aqueous extraction of the Helianthus Annuus (Sunflower) Seedcake produced by the method depicted in Figure 2.[30] Soluble and insoluble phases are separated by filtration and then the extract is sterilized. The final product consists of water (97.25 - 98.15%), Helianthus

Table 2. Chemical Properties of *Helianthus annuus* (sunflower)-Derived Ingredients.

Property	Value	Reference
Helianthus Annuus (Sunflower) Seed Extract		
Physical Form	Powder	26
Helianthus Annuus (Sunflower) Seed Extract		
Physical Form	Liquid	29
Color	Colorless or pale yellow	29
Odor	Characteristic	29
pH (@ 25°C)	4.0-7.5	29
Specific Gravity (@ 25°C)	.99-1.02	29
Water Solubility	Soluble	29
Helianthus Annuus (Sunflower) Seed Flour		
Color		
pH 20-7	Cream white	27
pH 8	Gray	27
pH 9	Yellowish gray	27
pH 10	Light brown	27
pH 10.5	Dark brown	27
Helianthus Annuus (Sunflower) Seed Wax		
Melting Point (°C)	74-80	36
Hydrolyzed Sunflower Seed Wax		
Physical Form	Solid wax	26
Color	Yellow	26
	White[a]	99
Odor	Very low	26
Specific Gravity (@ 20°C)	.87-.95	26
Melting Point (°C)	74-77	26
	67-75[a]	99
Boiling Point (°C)	>200	26
Water Solubility	Insoluble	26

[a]Wax extracted from seed hulls.

Annuus (Sunflower) Seed Extract (1.4 - 2.2%), and preservatives (.45 - .55%).

Composition

Helianthus annuus Plants. The *Helianthus annuus* (sunflower) plant has a high amount of moisture at maturity.[31] The composition of the *Helianthus annuus* (sunflower) plant (minus the pseudanthium) varies with maturity level (Table 3).

Helianthus annuus (sunflower) leaves are known to contain high levels of saponins, but they have not been quantified.[31]

The fatty acid profile of *Helianthus annuus* (sunflower) varies with selective breeding; a specific example is provided in Table 4.[31] Overall, oleic acid (C18:1) may be present as low as 14% to 39.4% in wild/conventional (edible) plant seeds and as high as 75 - 90.7% in selectively bred plant (oil) 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 cultivated plants (Table 5).

The hulls are difficult to remove from the oilseed strains of *Helianthus annuus* (sunflower) seed and thus, the data on oilseed includes the hulls (Table 4, Table 5, and Table 6). Hulls are easily separated from the non-oilseed strains of *Helianthus annuus* (sunflower), and thus, the non-oilseed data does not include the hull.

The amino acid content profile of *Helianthus annuus* (Sunflower) Seed Flour includes phenylalanine + tyrosine (8.2 g/100 g crude protein) and leucine (6.5 g/100 g crude protein; Table 7).[31] The fatty acids in *Helianthus annuus* (Sunflower) Seed Flour were palmitate (12.04% of detected fatty acids), stearate (8.26%), oleate (31.14%), and linoleate (48.56%).[27] The unheated flour is reported to be made up of 6.80% moisture, 45.50% protein, 4.40% crude fat, and 2.00% crude fiber; the heated flour is reported to be made up of 8.56% moisture, 42.37% protein, 9.20% crude fat, and 1.90% crude fiber. Residual ash content following pyrolization is 7.70%.

The composition (e.g., crude protein, fiber, and fat) of *Helianthus annuus* (sunflower) seed meal (possible precursor to *Helianthus 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 8).[31] This also applies to amino acids and crude protein contained in the meal (Table 9).

Electrophoresis showed that protein bands were similar among 3 *Helianthus annuus* (sunflower) seed strain samples.[32] There were 3 polypeptides groups of helianthinin fraction detected. Of these, 2 were acidic (α, MW = 36,800 - 42,900 Da and α', MW = 31,000 - 35,300 Da), and one was basic (β, MW = 21,000 - 29,600 Da). The molecular weight of the 2S albumin proteins varied 11,500 - 20,100 Da. Another analysis characterized the 2S albumin fractions from inbred lines and cultivars as single chain proteins with relative molecular masses 10,000 - 18,000 Da, some with intra-chain disulphide bonds.[33] *Helianthus annuus* (sunflower) proteins are rich in globulins (55 - 60%), albumins (17 - 23%), and glutelins (11 - 17%).[34]

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.[26] The seed hull contains most of the wax found in a seed (Table 10).[35]

Helianthus Annuus (Sunflower) Seed Wax mainly contains: esters of C16-24 fatty acids and C26-32 alcohols (approximately 90%), free alcohols (approximately 1% to 5%), and hydrocarbons (approximately 1%) with no glycerol and other polyalcohol esters.[36]

Constituents of Concern. *Helianthus annuus* (sunflower) plants are reported to contain sesquiterpene lactones, which may cause dermal Type IV (*delayed-type*) *hypersensitivity reactions* following *dermal exposure* (i.e., allergic contact dermatitis).[13,15]

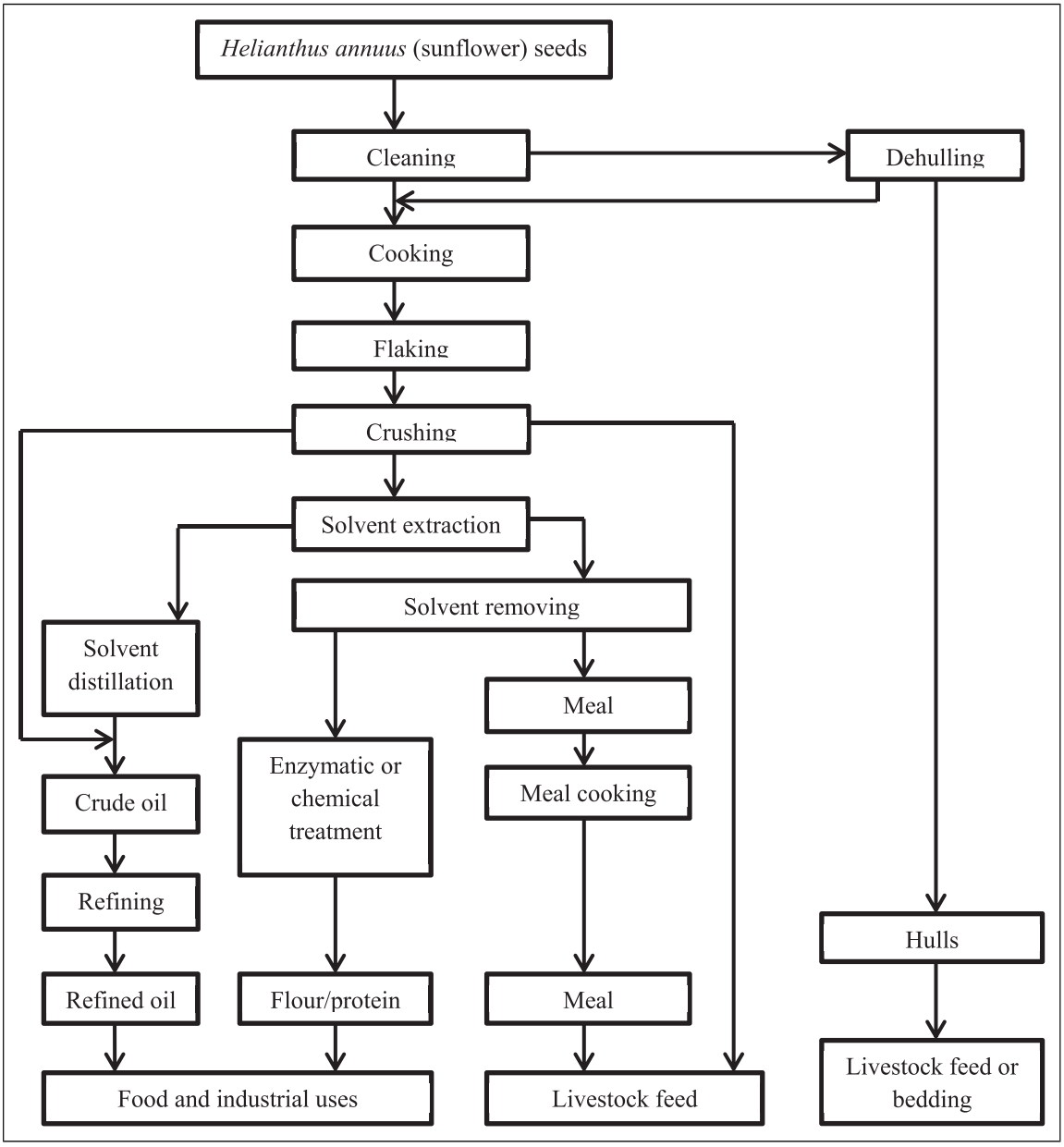

Figure 1. Method of manufacture of some *Helianthus annuus* (sunflower) seed-derived products.[31]

Helianthus annuus (sunflower) petals were reported to contain saponins, and helianthosides A, B, and C derived from echinocystic acid.[37]

A 14-amino-acid, backbone-cyclized peptide (SFTI-12) has been reported in the seeds of *Helianthus annuus* (sunflower); it is a potent trypsin inhibitor and a relatively weak inhibitor of thrombin and other proteases.[38]

Helianthus annuus (sunflower) kernels and hulls contain phenolic compounds, which include chlorogenic and caffeic acids; these are readily oxidized during common processing causing green to brown discoloration in protein isolates or concentrates.[39,40] These compounds have been studied both for their additive/synergistic effect on carcinogenesis and their anti-carcinogenic properties, with no definitive result.[41]

Helianthus annuus (sunflower) seeds contain a 2S-protein fraction that, in other seeds and nuts, includes albumins known to induce IgE-mediated allergies.[14,42] The characteristics of 2S albumins include relatively low molecular weight, high solubility in water, and high nitrogen and cysteine contents.[43-46] On the other hand, the compactness and rigidity of 2S albumins, resulting from their disulfide bond arrangement and electrostatic interactions, confers high stability against thermal or surfactant-induced denaturation and digestion by proteolytic enzymes.[45,47,48] Resistance to denaturation and digestion is a key factor for

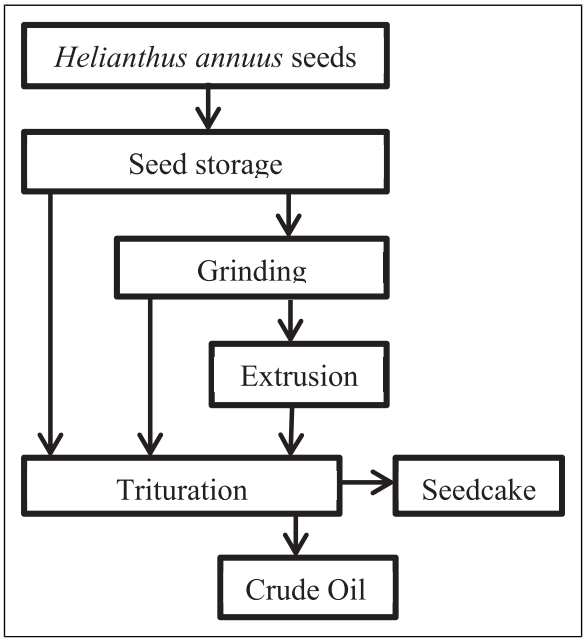

Figure 2. Method of manufacture for Helianthus Annuus (Sunflower) Seedcake.[30]

the allergenicity of food components. This property would allow 2S albumins to reach the gastrointestinal tract almost intact.[48] The resistance of allergenic 2S proteins to food processing, cooking, and proteolytic attack may help explain their potential to cause severe food allergies.[45,48]

The protein content was approximately .52% in a product mixture that contained Helianthus Annuus (Sunflower) Seed Extract (10%).[29] Analysis of a product mixture that contained Helianthus Annuus (Sunflower) Seed Extract (1.4% to 2.2%) showed that a total of 87.0% of the proteins were <243 Da (1.35 g/l).[30] This product mixture was reported to be mainly composed of peptides with a molecular weight lower than 2000 Da (99% of total proteins); 1.1% of the proteins were >2000 Da and there were no proteins >10,000 Da (Table 11).

Impurities

Analysis of 3 product mixtures that contained Helianthus Annuus (Sunflower) Seed Extract showed that heavy metal, pesticide, and other impurity content (i.e., formaldehyde) were below the limits of detection (Table 12).[29,30,49]

The carcinogen benzo[*a*]pyrene has been detected as a contaminant in unrefined and cooking seed oil from *Helianthus annuus* (sunflower).[50,51] While the source may be atmospheric pollution or contamination from the soil, there is also evidence that levels of benzo[a]pyrene increase in plant products as a result of processing.

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

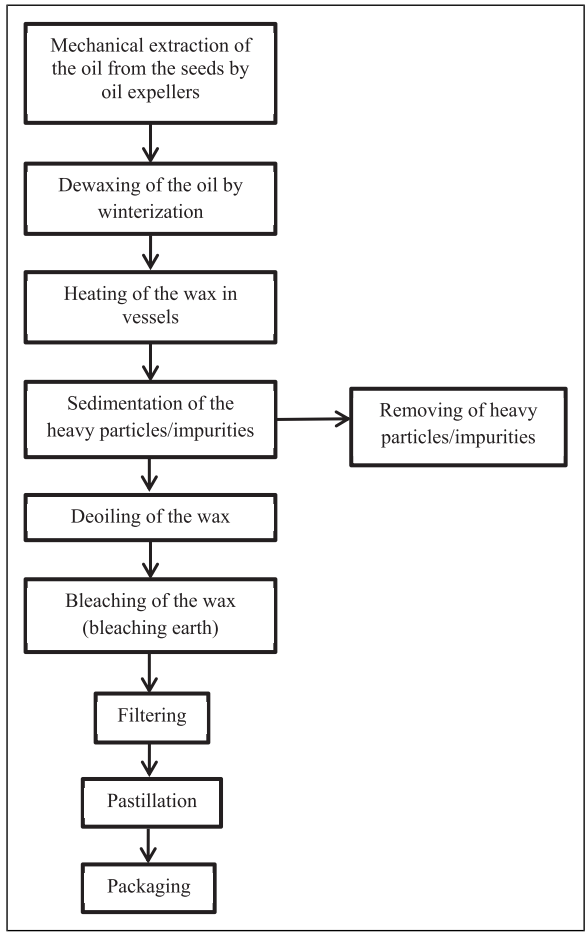

Figure 3. Method of manufacture of some Helianthus Annuus (Sunflower) Seed Wax.[100]

Aflatoxins or molds that produce aflatoxins have been detected in some dried *Helianthus annuus* (sunflower) seed samples.[52-54] Not all samples were contaminated.[55]

USE

Cosmetic

The safety of the cosmetic ingredients included in this safety assessment is evaluated based on the data the Panel receives from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected cosmetic use of ingredients. The data 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). Those received from the cosmetic industry are submitted in response to a survey conducted by the Personal Care Products Council (Council) of the maximum reported use concentrations by category.

According to 2016 VCRP data, Helianthus Annuus (Sunflower) Seed Extract had the highest number of reported

Table 3. Composition of *Helianthus annuus* (Sunflower) Whole Plant at Various Growth Stages.[31]

	Mature		Before Bloom	Beginning of Bloom	In Bloom	After Bloom
	Source 1	Source 2	Source 3			
g/100 g 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 4. Sample Comparison of Oil Content (g/100 g dry Seed Material) in Oilseed (High in Oleic Acid Content) and Non-oilseed Strains *Helianthus annuus* (Sunflower) Seeds.[31]

Acid	Oilseed (Includes hulls)[1]	Non-oilseed (no hulls)
Myristic acid (C14:0)	.02	.05
Palmitic acid (C16:0)	2.84	2.95
Palmitoleic acid (C16:1)	.03	.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)	.04	.07
Arachidic acid (C20:1)	.06	.05

[1]The hulls are difficult to remove from the oilseed strains of *Helianthus annuus* (sunflower) seed, so the data on oilseed includes the hulls. Hulls are easily separated from the non-oilseed strains of *Helianthus annuus* (sunflower), and thus, the non-oilseed data does not include the hull.

Table 5. Composition of Phytosterols and Tocopherols as a Function of Oleic Acid Content in *Helianthus annuus* (Sunflower) Seeds.[31]

Sterol	Conventional/Wild	Mid Oleic Acid	High Oleic acid[a]
Total sterols	240-500 mg/g	ND	170-520 mg/g
β-Sitosterol[b]	50%-70%	56%-58%	42%-70%
Campesterol[b]	6.5%-13.0%	9.1%-9.6%	5%-13%
Stigmasterol[b]	6.0%-13.0%	9.0%-9.3%	4.5%-13%
Total tocopherols (mg/g)	44-152	50.9-74.1	45-112
α (vitamin E) (mg/g)	40.3-93.5	48.8-66.8	40-109
β (mg/g)	ND-4.5	1.9-5.2	1.0-3.5
γ (mg/g)	ND-3.4	.2-1.9	.3-3.0

ND = Not detected.
[a]The hulls are difficult to remove from the oilseed strains of *Helianthus annuus* (sunflower) seed, so the data on oilseed includes the hulls. Hulls are easily separated from the non-oilseed strains of *Helianthus annuus* (sunflower), and thus, the non-oilseed data does not include the hull.
[b]Percent of total sterols.

uses in this safety assessment at 389 formulations (Table 13).[56] Helianthus Annuus (Sunflower) Extract had the next highest number of reported uses in 96 formulations. All other in-use ingredients are reported to be used in 76 or fewer formulations.

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 rinse-off skin cleansing formulations.[57,58] The highest maximum concentration of use reported for leave-on products is 4% in Helianthus Annuus (Sunflower) Seed Wax in mascara and 4% Hydrolyzed Sunflower Seed Wax in lipstick.

The ingredients not in use according to the VCRP and industry survey are listed in Table 14.

In some cases, reports of uses were received in the VCRP, but no concentration-of-use data were provided. For example,

Table 6. The Vitamin Content of Seeds of Non-oilseed Strains of *Helianthus annuus* (Sunflower).[31]

Vitamin	Amount (/100 g dry materials)[1]
Vitamin C (mg)	1.48
Thiamine (mg)	2.42
Riboflavin (mg)	.26
Niacin (mg)	4.75
Pantothenic acid (mg)	7.13
Vitamin B-6 (mg)	.81
Folate (μg)	239.86
Vitamin A (IU)	52.84
Vitamin E (α tocopherol) (mg)	36.46
Vitamin K (μg)	2.85

[1]Hulls are easily separated from the non-oilseed strains of *Helianthus annuus* (sunflower), so the non-oilseed data does not include the hull.

Table 7. Amino Acid Content in *Helianthus annuus* (Sunflower) Seed Flour.[31]

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

Helianthus Annuus (Sunflower) Flower Extract is reported to be used in 5 formulations, but no use concentration data were provided. 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 in each use category for which a concentration of use is reported.

These ingredients are reported to be used in products used near the eye (e.g., 4% Helianthus Annuus (Sunflower) Seed Wax in mascara), in products that may be ingested (e.g., 4% Hydrolyzed Sunflower Seed Wax in lipstick) and in products that may come in contact with mucous membranes (e.g., 5% Helianthus Annuus (Sunflower) Seed Extract in bath soaps and detergents). 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 *Helianthus 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 .05% in hair sprays and Helianthus Annuus (Sunflower) Seedcake is reported to be used at up to .0012% in spray face and neck products. In practice, most of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μm, with propellant sprays yielding a greater

Table 8. Composition of *Helianthus annuus* (Sunflower) Meal Derived From Whole and Part-Dehulled Seeds From Different Sources.[31]

	Whole Seed Meal		Part-Dehulled Seed Meal		Hulls
	Source 1 (mean ± SD)	Source 2 (mean)	Source 1 (mean ± SD)	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 (.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	—	—	—	—	.30 (.25-.35)
Phosphorus	—	—	—	—	.15 (.10-.20)
Magnesium	—	—	—	—	.20 (.15-.25)

— = No data
SD = standard deviation

Table 9. Amino Acid and Protein Content (g/100 g dry Matter) of *Helianthus annuus* (Sunflower) Meal Derived From Whole and Part-Dehulled Seeds From 3 Sources.[31]

	Non-dehulled *Helianthus annuus* Meal			Dehulled *Helianthus annuus* 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	.74	.73	.61	.99	.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	.65	.66	.56	.88	.89
Cystine	.50	.53	.56	.71	.71
Phenylalanine	1.31	1.37	1.28	1.78	1.85
Threonine	1.06	1.16	1.17	1.43	1.44
Tryptophan	.34	.42	.50	.47	.46
Valine	1.41	1.66	1.78	1.87	1.94
Glycine	—	—	—	—	2.26
Tyrosine	—	.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 10. Wax Distribution in the Whole Seed, Hull, and Dehulled Seed of Two Samples of *Helianthus annuus* (Sunflower) Seeds.[35]

	Sample 1			Sample 2		
Wax (Carbon Number	Hull (wt%)	Whole Seed (wt%)	Dehulled Seed (wt%)	Hull (wt%)	Whole Seed (wt%)	Dehulled Seed (wt%)
36	2.7	8.5	14.5	1.5	11.6	16.1
37	1.7	7.0	11.1	0.6	8.5	11.2
38	1.9	2.9	4.6	0.7	3.4	4.9
39	0.8	2.6	4.2	0.2	3.0	4.2
40	3.6	10.0	16.5	2.3	12.5	18.0
41	2.2	11.5	19.4	0.8	13.7	18.8
42	10.0	7.1	6.6	7.7	7.0	6.3
43	1.9	3.5	5.3	1.1	4.3	4.9
44	24.4	14.1	3.4	26.6	10.9	1.9
45	2.5	2.3	1.8	2.2	2.0	1.7
46	26.6	15.9	4.6	30.0	11.9	3.1
48	23.9	14.6	8.0	26.3	11.2	8.9
Total wax content (mg/kg)	14,250	1254	759	14,955	1008	580

Table 11. Distribution and Quantity of Proteins in a Product Containing 1.4%-2.2% Helianthus Annuus (Sunflower) Seed Extract.[30]

Molecular Weight Range (Da)	Distribution (%)	Quantity of Proteins (g/L)
Fraction 1: 10,000 < MW	0.0	.00
Fraction 2: 3500 < MW <10,000	0.4	.01
Fraction 3: 2000 < MW <3500	0.7	.01
Fraction 4: 243 < MW <2000	11.9	.18
Fraction 5: MW <243	87.0	1.35

Table 12. Impurities in Product Mixtures That Contain Helianthus Annuus (Sunflower) Seed Extract.[29,30,49]

Impurity	Helianthus Annuus (Sunflower) Seed Extract at 10%	Helianthus Annuus (Sunflower) Seed Extract at 20%	Helianthus Annuus (Sunflower) Seed Extract at 1.4%-2.2%
Protein	Approximately .52%	.02%	Detected
Allergens	<2 ppm[a]	None[a,b]	None[b]
Formaldehyde	<2.5 ppm[a]	NR	NR
Pesticides	<.03 ppm	None	None
Methanol	<10 ppm[a]	NR	NR
Nonylphenol	<500 ppm[a]	NR	NR
Microbial count	NR	<100 organisms/g	NR
Heavy metals	<2.5 ppm	NR	NR
Antimony	NR	<.25 mg/L[a]	NR
Arsenic	NR	<.050 mg/L[a]	<1 ppm[a]
Cadmium	NR	<.010 mg/L[a]	<1 ppm[a]
Chromium	NR	<.050 mg/L[a]	None
Iron	NR	<5.0 mg/L[a]	NR
Lead	NR	<.050 mg/L[a]	None
Mercury	NR	.0040 mg/L[a]	None
Nickel	NR	.050 mg/L[a]	<1 ppm[a]

NR = Not reported.
[a]Limit of detection.
[b]None of the 26 allergens defined by the 7th Amendment to the EU Cosmetic Directive were detected (detection limit <10 ppm).

fraction of droplets/particles <10 μm compared with pump sprays.[59,60] 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.[61,62] Helianthus Annuus (Sunflower) Extract is reported to be used in powders (concentration not reported). Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400- to 1000-fold less than protective regulatory and guidance limits for inert airborne particles in the workplace.[63-65]

None of the *Helianthus annuus* (sunflower)-derived ingredients named in the report are restricted from use in any way under the rules governing cosmetic products in the European Union (EU).[66]

Non-Cosmetic

Helianthus annuus (sunflower) is cultivated primarily for the seeds which yield the world's second most common source of edible oil.[21] 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.[67,68] 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.[31] De-hulled seeds (kernels) are eaten roasted and salted alone or in other foods (e.g., salads and cakes). Whole *Helianthus annuus* (sunflower) seeds (with hulls) are also eaten as a snack food. Such seeds contain less oil.

Helianthus annuus (sunflower) seeds are not listed as a major allergen by the Food Allergen Labeling and Consumer Protection Act.[69]

Helianthus annuus (sunflower) seeds are used to make an alternative to peanut butter.[70] In the EU, foods containing *Helianthus annuus* (sunflower) sunflowers and seeds are not required to be labelled as allergens.[71]

In the EU, the flowers and seed oil from the seeds of *Helianthus annuus* (sunflower) were on the market as food or food ingredients and were consumed to a significant degree before 15 May 1997.[72] 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.

Traditional medicinal uses of *Helianthus annuus* (sunflower) seeds are reported to be as a diuretic, expectorant, and to treat colds, coughs, throat, and lung ailments.[23] 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. *Helianthus annuus* (sunflower) plants have multiple uses in folk remedies, including: bronchitis, carbuncles, cold, colic, cough, diarrhea, eye ailments, fever, flu, inflammations, rheumatism, urogenital ailments, and wounds.

Native Americans have been reported to use *Helianthus annuus* (sunflower) in multiple ways.[73] The seed and root

Table 13. Frequency of Use According to Duration and Exposure of *Helianthus annuus* (sunflower)-Derived Ingredients.[56-58]

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	96	.0000015-.075	5	NR	389	.000015-5	NR	.00002-.00091
Duration of use[a]								
Leave-on	54	.0003-.05	2	NR	210	.000015-1	NR	.00091
Rinse-off	41	.0000015-.001	3	NR	177	.000015-5	NR	.00002
Diluted for (bath) use	1	.075	NR	NR	2	.0003-.0016	NR	NR
Exposure type								
Eye area	4	NR	NR	NR	11	.0003-0.1	NR	NR
Incidental ingestion	NR	NR	NR	NR	7	.0002-1	NR	NR
Incidental Inhalation-sprays	7; 25[b]; 9[c]	.0005[b]	1[b]	NR	25; 54[b]; 56[c]	.000015-.05; .00003-.025[b]	NR	.00091[b]
Incidental inhalation-powders	1; 9[c]	.0003[d]	NR	NR	56[c]	.0025-.032[d]	NR	NR
Dermal contact	41	.0003-.075	4	NR	143	.0001-.24	NR	NR
Deodorant (underarm)	1[b]	NR	1[b]	NR	2[b]	NR	NR	NR
Hair-noncoloring	53	.0000015-.0025	1	NR	209	.000015-5	NR	.00002-.00091
Hair-coloring	2	NR	NR	NR	29	.00009-5	NR	NR
Nail	NR	NR	NR	NR	NR	.0001	NR	NR
Mucous Membrane	5	.075	2	NR	26	.0002-5	NR	NR
Baby	NR	NR	NR	NR	NR	NR	NR	NR
Total/range	76	.000015-.41	28	.0038-4	NR	3.3-10		
Duration of use								
Leave-on	65	.000015-.41	28	.19-4	NR	3.3-4		
Rinse-off	11	.000015-.12	NR	.0038	NR	10		
Diluted for (bath) use	NR	NR	NR	NR	NR	NR		
Exposure type								
Eye area	10	.000015-.41	2	3.6-4	NR	3.5		
Incidental ingestion	NR	.00012	16	3.4	NR	3.3-4		
Incidental Inhalation-sprays	32[b]; 12[c]	.0012; .000015[b]	4[b]; 2[c]	.19[b]	NR	NR		
Incidental inhalation-powders	12[c]	.41[d]	2[c]	.52-.75[d]	NR	NR		
Dermal contact	75	.000015-.41	11	.19-3.6	NR	10		
Deodorant (underarm)	NR	NR	NR	NR	NR	NR		
Hair-noncoloring	1	NR	NR	.0038	NR	NR		
Hair-coloring	NR	NR	NR	NR	NR	NR		
Nail	NR	NR	NR	NR	NR	NR		
Mucous Membrane	NR	.00012-.12	16	3.9	NR	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 14. *Helianthus annuus* (sunflower)-Derived Ingredients With No Reported Uses.[56-58]

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

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.[74]

Helianthus annuus (sunflower) plants are used in phytoremediation to extract heavy metals and other toxic substances from the soil (e.g., lead, arsenic, and uranium).[75,76] This plant is also used in rhizofiltation to neutralize radionuclides and other toxic substances and to remove harmful bacteria from water.[77]

Toxicokinetic Studies

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

Toxicological Studies

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 those *Helianthus annuus* (sunflower)-derived ingredients which are normal components of the human and animal diet is not the focus of this safety assessment. The primary focus is the potential for irritation and sensitization reactions after topical exposure to these ingredients.

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

Developmental and Reproductive Toxicity (DART) Studies

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

Genotoxicity Studies

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

Carcinogenicity Studies

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

Irritation and Sensitization Studies

Irritation

Animal. A trade name mixture containing Helianthus Annuus (Sunflower) Seed Extract (1.4 - 2.2%; maximum concentration of 2.2%) was administered neat to the undamaged skin of rabbits (n = 3) under occlusion for 4 h.[30] There were no signs of cutaneous reactions at 1, 24, 48, and 72 h after removal of the patch. It was concluded that this mixture was not dermally irritating.

Human. Human irritation studies are summarized in Table 15.

In a 4-wk use study of a moisturizer containing Helianthus Annuus (Sunflower) Seed Extract (.0335%) in humans with sensitive skin and a 2-wk use study of a lipstick containing Helianthus Annuus (Sunflower) Seed Wax (4%), there were no signs of the potential for dermal irritation.[78,79] A trade name mixture containing Helianthus Annuus (Sunflower) Seed Extract (effective concentration 10%) was well tolerated in a 48-h patch test.[28]

Sensitization

Animal. In a guinea pig sensitization study using the Buehler protocol, a trade name mixture containing Helianthus Annuus (Sunflower) Seed Extract (12%) was tested at 10% (in petrolatum).[80] The final concentration of Helianthus Annuus (Sunflower) Seed Extract was 1.2%. There were no skin reactions observed and the sensitization rate at 24 and 48 h after challenge was 0%. It was concluded that the mixture was not sensitizing at 1.2%.

In a guinea pig maximization test, a trade name mixture (tested at 12.5, 25, 50, or 100%) containing Helianthus Annuus (Sunflower) Seed Extract (1.4 - 2.2%; maximum concentration of 2.2%) was administered to albino guinea pigs (n not specified).[30]

No significant reactions were observed at any concentration. There were no signs of a reaction under macroscopic examination during the challenge phase of the experiment. It was concluded that this trade name mixture was probably not sensitizing.

Human. Human sensitization studies are summarized in Table 15.

A human repeated insult patch test (HRIPT) of a face cream containing Helianthus Annuus (Sunflower) Seed Extract (.238%) resulted in low-level reactions; it was concluded that it was not irritating and not sensitizing.[81] A trade name mixture containing 12% Helianthus Annuus (Sunflower) Seed Extract was not sensitizing to human subjects when tested at 10% (1.2% Helianthus Annuus (Sunflower) Seed Extract) in an HRIPT.[80] A trade name mixture containing 10% Helianthus Annuus (Sunflower) Seed Extract was not sensitizing to human subjects at 100% in an HRIPT.[82] In HRIPTs, a moisturizer containing Helianthus Annuus (Sunflower) Seed Extract (.0335%) and 2

Table 15. Human Irritation and Sensitization Studies on Products/Mixtures Containing *Helianthus annuus* (sunflower)-Derived Ingredients.

Ingredient	Product; Concentration	Study; n	Results	Reference
		Irritation		
Helianthus Annuus (Sunflower) Seed Extract	Moisturizer; .0335%	4-week use study; 34	No signs of the potential for dermal irritation	[79]
Helianthus Annuus (Sunflower) Seed Extract	Trade name mixture; 10%, .2 mL	Patch test in approximately 50 mm^2 Finn chambers for 48 h. Examination 30 min after removal; 10	Very slight erythema in 2 subjects and clear erythema in 1 subject. Well tolerated.	[28]
Helianthus Annuus (Sunflower) Seed Wax	Lipstick; 3.34%	2-week use study in humans with sensitive skin; 26	Not irritating or sensitizing	[78]
		Sensitization		
Helianthus Annuus (Sunflower) Seed Extract	Face cream; .238%	HRIPT; 53	2 + level reactions and 11 ? level reactions during induction. 2 + level reactions and 5 ? level reactions at 48, 72, and/or 96 h after challenge. Not irritating or sensitizing. ("+" = definite erythema, no edema; "?" = minimal or doubtful response)	[81]
Helianthus Annuus (Sunflower) Seed Extract	Moisturizer; .0335%	HRIPT; 102	Not irritating or sensitizing	[83]
Helianthus Annuus (Sunflower) Seed Extract	(12% in a trade name mixture tested at 10%) tested at 1.2%	HRIPT; 50	1 marginal reaction during induction. Not irritating or sensitizing.	[80]
Helianthus Annuus (Sunflower) Seed Extract	10% in a trade name mixture, tested at 100%	HRIPT; 48	Not irritating or sensitizing.	[82]
Helianthus Annuus (Sunflower) Seed Wax	Lipstick; 4%	HRIPT; 114	There were no adverse events. It was concluded that this product was not a potential dermal irritant.	[85]
Helianthus Annuus (Sunflower) Seed Wax	Lipstick; 3.34%	HRIPT; 107	Not irritating or sensitizing	[84]

different lipsticks containing Helianthus Annuus Seed Wax (3.34 and 4%) were not irritating or sensitizing.[83-85]

Type I and IV Hypersensitivity

Helianthus annuus (sunflower) seeds have been reported to cause anaphylactic reactions after ingestion and rhinitis and asthmatic reactions after occupational exposure to the seed dust in susceptible people.[14,42] Clinical reports indicated that exposure to *Helianthus annuus* (sunflower) seeds can cause allergic reactions in *Helianthus annuus* (sunflower) seed-sensitized individuals.[32] Some of the 2S albumins from sunflower seeds were first suspected to be allergens based on their degree of homology (34%) with the allergenic mature 2S albumins of Brazil nuts.[14,42] 2S albumins in *Helianthus annuus* (sunflower), sesame, and mustard seeds are considered major allergens.[86] Other seeds, nuts, grains, and cereals contain related allergens, including peas, soy beans, castor beans, rapeseeds, cotton seeds, Brazil nuts, walnuts and peanuts.[42,48,86] However, not all the 2S albumins should be considered major allergens,[45] and those that are allergenic are not necessarily cross reactive.[45,48,87] In fact, cross-reactivity seems to be uncommon in this protein family.[45,47] The 2S albumin seed-storage proteins have been described as "universal allergens" and "inherently allergenic" or "intrinsically allergenic" proteins in seeds in which they occur.[47,48,86,87] This view is consistent with observations that, in general, proteins with a similar folds are not necessarily cross-reactive.[48,88] The incidence of these reactions appears to be low, based on published reports, and reactions were generally associated with atopic populations (pers comm. Dr. Stefano Luccioli, Senior Medical Advisor, FDA Office of Food Additive Safety (OFAS)).

Ocular Irritation Studies

In a hen's egg chorion-allantoic membrane (HET-CAM) assay for predicting ocular irritation, the mean irritation index was 3 for a product mixture containing Helianthus Annuus (Sunflower) Seed Extract (effective concentration 10%), and it was concluded that the product mixture was slightly irritating.[28]

Clinical Studies

Retrospective and Multicenter Studies

Provocative Assays

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).[19] To make the extract, freshly cut *Helianthus annuus* (sunflower) plants were dipped whole into peroxide-free diethyl ether for 60 sec; the ether was then dried over sodium sulfate 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 both performed in subjects (n = 17) with established fruit, nut, and/or legume allergies, including 2 subjects with a confirmed *Helianthus annuus* (sunflower) seed allergy.[89] Negative and positive controls for skin testing were saline solution and histamine dihydrochloride, respectively. Seven (41%) of the subjects had a positive reaction in one or both of the allergy tests; it was not specified whether the 2 subjects with the *Helianthus annuus* (sunflower) seed allergy had positive results.

A *Helianthus annuus* (sunflower) seed extract (1:100 w/v) was used in skin prick tests (SPT) in atopic subjects (n = 84; each positive for a common allergen).[90] A commercial radioallergosorbent test (RAST) was also performed on these subjects. The *Helianthus annuus* (sunflower) seed 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 SPT, of these 3 were also positive for the RAST. The positive reactions strongly correlated to owning a cage bird and a history of at least one food allergy.

A SPT 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 *Helianthus annuus* (sunflower) seeds.[89] Seventeen of 65 subjects had a positive reaction to *Helianthus annuus* (sunflower) seeds in one 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 *Helianthus annuus* (sunflower) seeds.

Case Reports

There are multiple case reports of children and adults who are allergic to *Helianthus annuus* (sunflower) seeds (Table 16).[4-6,8-12,91] Contacts were by dermal, oral, and/or inhalation exposure.

Cases of food allergies to *Helianthus annuus* (sunflower) seeds have also been reported in the literature (Table 16).[7,89,92-94] These allergies are confirmed with SPTs, 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]

There are cases of people developing allergies to *Helianthus annuus* (sunflower) pollen.[4,10,16,17,92,95-98] These tend to be people who live in areas where *Helianthus annuus* (sunflower) is grown or work in facilities that process these

Table 16. Case Reports of Children and Adults With Oral, Dermal, and Inhalation Allergic Reactions to *Helianthus annuus* (Sunflower) Seeds and Plants.

Case History	Testing	Reference
Oral Exposure		
3-year-old boy presented with oral discomfort that developed after eating *Helianthus annuus* (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 *Helianthus annuus* (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 *Helianthus annuus* (sunflower) seed "butter" had been fed to the children.	A SPT of a slurry of fresh *Helianthus annuus* (sunflower) 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 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 *Helianthus annuus* (sunflower) seed butter (reportedly from a facility that does not process peanuts).	SPT at 18 months were positive for peanuts (6 mm wheal) and negative for *Helianthus annuus* (sunflower) seed; at 5 years, the tests were positive for peanuts (21 mm wheal) and *Helianthus annuus* (sunflower) seed (16 mm wheal).	[91]
11-year-old boy who presented with generalized urticaria/angioedema and bronchospasm within 30 min of eating *Helianthus annuus* (sunflower) seeds. Epinephrine relieved the symptoms. He had eaten *Helianthus annuus* (sunflower) 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 *Helianthus annuus* (sunflower) seed extract were positive as well as tree molds and grasses.	[9]

(continued)

Table 16. (continued)

Case History	Testing	Reference
A 22-year-old female, with a history of atopic dermatitis and Japanese cedar pollenosis, ate 5 pieces of *Helianthus annuus* (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 *Helianthus annuus* (sunflower) seeds as a snack during high school.	SPT, CAP assay, ELISA, the ImmunoCAP® inhibition assay, immunoblot and immunoblot inhibition assays, and N-terminal sequence analysis. SPT were performed with the native protein extract from *Helianthus annuus* (sunflower) seeds and 7 other extracts from the *Asteraceae* family. There were positive reactions to the extracts of *Helianthus annuus* (sunflower) seeds in SPTs but not in other extracts. The level of serum IgE antibody for *Helianthus annuus* (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 *Helianthus annuus* (sunflower) seeds showed higher absorbance than the controls ($P < .01$). There were no reactions to the 4 kinds of nuts. The ImmunoCAP® inhibition assay of the extract from *Helianthus annuus* (sunflower) seeds showed suppression that depended on the concentration of the inhibitor (*Helianthus annuus* (sunflower) seed). The same test for Japanese cedar pollen with *Helianthus annuus* (sunflower) seeds showed no suppression. Several IgE-binding protein bands on the immunoblot assay using the extract from *Helianthus annuus* (sunflower) seeds were identified. These IgE-binding protein bands were almost undetectable when using control sera. On the inhibition immunoblot assay using the *Helianthus annuus* (sunflower) seed 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 *Helianthus annuus* (sunflower) seed closely matched LTP from *Helianthus annuus* (sunflower) 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 *Helianthus annuus* (sunflower) seeds. The symptoms resolved in a few hours. She had no history of allergy to seed that she shelled herself.	SPT-positive for *Helianthus annuus* (sunflower) pollen and dust mites; negative for other pollens and foods. Open food challenge-positive for shelled *Helianthus annuus* (sunflower) seeds. Analysis showed that the shelled seeds were contaminated with pollen.	[10]
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 *Helianthus annuus* (sunflower) seeds. The symptoms (itching, erythema, and wheal-and-flare reactions) appeared 15 min after contact. He reported tolerating the consumption of *Helianthus annuus* (sunflower) seeds with occasional pruritus or the oral mucosa and mild obstruction of the pharynx after eating larger amounts of the seeds. He tolerated *Helianthus annuus* (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 *Helianthus annuus* (sunflower) seed; and open patch test showed only local erythema. An itchy wheal of 5 mm was observed in a prick test of *Helianthus annuus* (sunflower) seed.	[5]

(continued)

Table 16. (continued)

Case History	Testing	Reference
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 *Helianthus annuus* (sunflower) 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 *Helianthus annuus* (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 *Helianthus annuus* (sunflower) seed extracts (1:1000 w/v; .02 mL). The passive transfer recipient was strongly positive at the unheated serum site on challenge with *Helianthus annuus* (sunflower) seed extract. The heated serum site challenged with *Helianthus annuus* (sunflower) seed extract was negative. SPT-commercial *Helianthus annuus* (sunflower) seed extract resulted in a 12 × 16 mm wheal; causative seed extract resulted in a 16 × 16 mm wheal; cold-pressed *Helianthus annuus* (sunflower) oil was negative. RAST-Commercial *Helianthus annuus* (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 50-year-old woman who presented with generalized urticaria, facial angioedema, laryngeal edema, wheezing, and dyspnea about 2 h after ingesting several *Helianthus annuus* (sunflower) seeds. The symptoms were relieved by antihistamine. She had eaten these seeds in the past. She reported that when she handled *Helianthus annuus* (sunflower) seeds that she used to feed 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.	Scratch tests and RAST titers to the *Helianthus annuus* (sunflower) seed extract were positive with mixed results to grass, ragweed, tree pollens walnut, and peanut	[9]
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 *Helianthus annuus* (sunflower) 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 *Helianthus annuus* (sunflower) seed extract were positive along with June grass and ragweed. The *Helianthus annuus* (sunflower) seed extract was an aqueous paste made by emulsifying washed *Helianthus annuus* (sunflower) seeds in buffered saline.	[9]
Dermal Exposure		
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 *Helianthus annuus* (sunflower) plants.	Patch tested with European standard series and *Asteraceae* plant series. Positive results were observed for *Helianthus annuus* (sunflower) leaves and the cattle fodder.	[6]

(continued)

Table 16. (continued)

Case History	Testing	Reference
Inhalation Exposure		
A 24-year-old man had developed rhinitis and conjunctivitis over 5 years of exposure to *Helianthus annuus* (sunflower) pollens and then developed asthma during the fifth year. All respiratory and ocular symptoms resolved when he discontinued exposure to *Helianthus annuus* (sunflower) plants and pollen. He later had a food allergic reaction while eating honey containing 30% *Helianthus annuus* (sunflower) pollen.	SPTs and RAST to a *Helianthus annuus* (sunflower) pollen extract (1/20 w/v) showed that he had developed an occupational allergy; skin test results with *Helianthus annuus* (sunflower) seed were negative. Bronchial provocation tests were performed after a rest period away from exposure to *Helianthus annuus* (sunflower) pollens, but there was no nonspecific hyperactivity. It was found by RAST that *Helianthus annuus* (sunflower) pollen does not cross-react with other pollens from the *Asteraceae* family or with *Helianthus annuus* (sunflower) seed. The honey that elicited food intolerance was demonstrated to inhibit significantly *Helianthus annuus* (sunflower) pollen RAST.	[4]
A 31-year-old man developed rhinoconjunctivitis and asthma when exposed to dried *Helianthus annuus* (sunflower) seeds. After working as a baker for approximately 9 years, he started working in a bakery that used *Helianthus annuus* (sunflower) seeds. After 3 months, he developed rhinoconjunctivitis and asthma, even when his coworkers were handling the *Helianthus annuus* (sunflower) seeds. He reported having experienced an anaphylactic reaction after eating approximately half a *Helianthus annuus* (sunflower) 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 *Helianthus annuus* (sunflower) 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 hyper-responsiveness. The next day, the tray experiment was repeated with *Helianthus annuus* (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. SPT-positive reactions to dust mites but not extracts of wheat, barley, rye, and oats. An extract of *Helianthus annuus* (sunflower) 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. SPTs of *Helianthus annuus* (sunflower) and other *Asteraceae* pollen were negative. *Helianthus annuus* (sunflower) 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 probable sensitization to α-amylase and that sensitization can develop from the inhalation of *Helianthus annuus* (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; SPT-skin prick test

plants and handle the plant material. Some perceived allergies to the seeds have been found to be allergies to the pollen (Table 16).[10,95] For example, subjects who worked in an animal feed processing plant (n = 35) were administered SPTs of aqueous preparations of the components of the feed (1:10 w/v dilution), which included *Helianthus annuus* (sunflower) seeds.[98] The subjects had worked in the plant an average of 14 yr (3 - 30 yr) and were exposed to feed "aerosols" 8 h per shift. 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 *Helianthus annuus* (sunflower) seeds in the control group of subjects who did not work in the plant (n = 30).

Summary

This is a review of the available scientific literature relevant to assessing the safety of *Helianthus annuus* (sunflower)-derived ingredients as used in cosmetics. The reported functions of these ingredients in cosmetics 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 *Helianthus annuus*, the sunflower plant.

The seeds of *Helianthus annuus* (sunflower) 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. Instead, the primary focus of this safety assessment of *Helianthus annuus* (sunflower)-derived ingredients as used in cosmetics is on the potential for irritation and sensitization from topical exposure. *Helianthus annuus* (sunflower) is a member of the *Asteraceae* family; members of this family are known to comprise, in part, sensitizers.

In an analysis of a product mixture that contained Helianthus Annuus (Sunflower) Seed Extract (10%), the protein content was approximately .52%. In an analysis of a product mixture that contained Helianthus Annuus (Sunflower) Seed Extract (20%), the protein content was .02%.

In an analysis of a product mixture that contained Helianthus Annuus (Sunflower) Seed Extract (1.4% to 2.2%), a total of 87.0% of the proteins were <243 Da (1.35 g/l). This product is mainly composed of peptides with a molecular weight lower than 2000 Da (99% of total proteins); 1.1% of the proteins were >2000 Da and there were no proteins >10,000 Da.

According to the 2016 VCRP data, Helianthus Annuus (Sunflower) Seed Extract had the highest reported number of uses of the ingredients in this safety assessment; it is used in 389 formulations. Helianthus Annuus (Sunflower) Extract had the next highest number of reported uses (96) in formulations. All other in-use ingredients are reported to be used in 76 or fewer formulations.

In the 2015 Council survey, Hydrolyzed Sunflower Seed Wax had the highest reported maximum concentration of use at up to 10% in skin cleansing formulations. The highest maximum concentration of use reported for leave-on products is 4% Helianthus Annuus (Sunflower) Seed Wax in mascara and 4% Hydrolyzed Sunflower Seed Wax in lipstick.

A trade name mixture containing Helianthus Annuus (Sunflower) Seed Extract (1.4 - 2.2%) was not irritating to the undamaged skin of rabbits at 100%.

In a 4-wk use study of a moisturizer containing Helianthus Annuus (Sunflower) Seed Extract at .0335% in humans with sensitive skin and a 2-wk use study of a lipstick containing Helianthus Annuus (Sunflower) Seed Wax at 4%, there were no signs of dermal irritation. A trade name mixture containing Helianthus Annuus (Sunflower) Seed Extract at 10% was well tolerated in a patch test.

In a HET-CAM assay for predicting ocular irritation of a product mixture containing Helianthus Annuus (Sunflower) Seed Extract (10%), it was concluded that the product mixture was slightly irritating.

In a guinea pig sensitization study of a trade name mixture containing Helianthus Annuus (Sunflower) Seed Extract there were no skin reactions observed and it was concluded that the mixture was not sensitizing at 1.2%. In a guinea pig maximization test, a trade name mixture containing Helianthus Annuus (Sunflower) Seed Extract (1.4 - 2.2%) was not sensitizing to albino guinea pigs at up to 100%.

An HRIPT of a face cream containing Helianthus Annuus (Sunflower) Seed Extract at .238% resulted in low-level reactions; it was concluded that it was not irritating and not sensitizing. A lipstick containing Helianthus Annuus (Sunflower) Seed Wax at 3.34% was non-sensitizing in a 2-wk use study in subjects with sensitive skin. A trade name mixture containing Helianthus Annuus (Sunflower) Seed Extract at 10% was not sensitizing to human subjects at 100% in an HRIPT. In HRIPTs of cosmetic products, a moisturizer containing Helianthus Annuus (Sunflower) Seed Extract at .0335% and 2 lipsticks containing Helianthus Annuus Seed Wax at 3.34% and 4% were not irritating or sensitizing.

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 test of human subjects with known food allergies, 7 of 17 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 SPT 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 *Helianthus annuus* (sunflower) seeds. These allergies were confirmed with SPTs, RASTs, and/or double-blind, placebo-controlled food challenges.

There are multiple cases of humans developing allergies to *Helianthus annuus* (sunflower) 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 *Helianthus annuus* (sunflower), had positive reactions in a SPT for and aqueous extract (1:10 w/v) of the plant.

Discussion

The Panel examined irritation and sensitization data on *Helianthus annuus* (sunflower)-derived ingredients. The Panel also considered data linking food allergies and 2S albumins, along with the methods of manufacture and impurity data. *Helianthus annuus* (sunflower) seeds contain 2S albumins similar to those of other seeds. Some 2S albumins in other seeds, such as rapeseed, castor beans, cottonseed, Brazil nuts, and walnuts, have been associated with allergenicity. Consequently, the 2S albumin proteins in *Helianthus annuus* (sunflower) seed are potential allergens. These proteins are generally known to be quite stable against enzymatic or chemical treatment. Two studies indicated that *Helianthus annuus* (sunflower) seeds are likely to be allergenic in some people and that the 2S proteins of *Helianthus annuus* (sunflower) seeds may be cross-reactive with the allergens in other foods. However, the incidence of persons with sensitivity to *Helianthus annuus* (sunflower)-derived ingredients is low, and the Panel noted that reactions attributable to contact with products containing such ingredients have not been observed in their clinical experience. The Panel agreed with Dr. Luccioli (Senior Medical Advisor, FDA OFAS) that the evidence does not warrant a heightened level of public concern or a warning label for seed or tree nut allergic individuals. However, the Panel emphasized that persons with sensitivity to 2S albumins from seeds, nuts, or legumes should be cautious when using formulations that contain *Helianthus annuus* (sunflower)-derived ingredients.

Further, *Helianthus annuus* (sunflower) seeds are not considered a high risk by the EU and are not listed as a major allergen by the Food Allergen Labeling and Consumer Protection Act.

Type I immediate hypersensitivity reactions could possibly occur following exposure to a protein-derived ingredient. Traditional HRIPTs and related tests do not detect Type I reactions. The Panel noted that these ingredients may be used in aerosolized products, however, and incidental inhalation of allergenic peptides has the potential to cause Type I reactions in sensitized individuals. Thus, the Panel recommends that people with known allergies to *Helianthus annuus* seed proteins avoid using personal care products that contain these ingredients and may be incidentally inhaled during use (e.g., spray or loose powder products).

Because final product formulations may contain multiple botanicals, each possibly containing similar constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. For *Helianthus annuus* (sunflower)-derived ingredients, the Panel was concerned about the presence of 2S albumin and sesquiterpene lactones, which could result in Type I and Type IV hypersensitivity reactions, respectively. Therefore, when formulating products, manufacturers should avoid reaching levels of plant constituents that may cause sensitization or other adverse health effects.

The Panel expressed concern about pesticide residues, heavy metals, and substances from plants of other species (weeds) that may be present in botanical ingredients. To address these concerns, the cosmetics industry should continue to use cGMPs to limit impurities.

Aflatoxins have been detected in some samples of *Helianthus annuus* (sunflower) seeds. The Panel recognizes the United States Department of Agriculture (USDA) designation of ≤15 ppb as corresponding to "negative" aflatoxin content and believes that aflatoxins will not be present at levels of toxicological concern in *Helianthus annuus* (sunflower)-derived ingredients.

The Panel concluded that the data were sufficient to come to a conclusion of safe as used for all of the ingredients that are derived from the seeds and the flower. However, the data were insufficient for the ingredients that are derived from other plant parts. The additional data needed are:

- Method of manufacture
- Composition of these ingredients, especially protein content (including 2S albumins)
- Impurities

The Panel discussed the issue of incidental inhalation exposure from hair sprays, face and neck products, and face powders. There were no inhalation toxicity data available. These ingredients are reportedly used at concentrations up to .05% in cosmetic products that may be sprayed; there was no reported concentration of use for the face powder. The Panel noted that droplets/particles from spray and loose-powder cosmetic products would not be respirable to any appreciable amount. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

Conclusion

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 9 *Helianthus annuus* (sunflower)-derived ingredients are safe as used in cosmetics in the present practices of use and concentration described in this safety assessment:

Helianthus Annuus (Sunflower) Seed Extract

Helianthus Annuus (Sunflower) Flower 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

**Not reported to be in current use. 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 this group.*

and that the data are insufficient to come to determine safety for the following 3 ingredients:

Helianthus Annuus (Sunflower) Extract

Helianthus Annuus (Sunflower) Leaf/Stem Extract†

Helianthus Annuus (Sunflower) Sprout Extract†

†Not reported to be in use.

Author Contributions

Becker, L. contributed to conception and design, contributed to acquisition, analysis, and interpretation, drafted manuscript, and critically revised manuscript; Boyer, I. contributed to conception and design, contributed to analysis and interpretation, drafted manuscript, and critically revised manuscript; Bergfeld, W., Belsito, D., Hill, R., Klaassen, C., Liebler, D., Marks, J., Shank, R., Slaga, T., Snyder, P., and Gill, L. contributed to conception and design, contributed to analysis and interpretation, and critically revised manuscript; Heldreth, B. contributed to design, contributed to analysis and interpretation, and critically revised manuscript. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Author's Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, 1620 L Street, NW, Suite 1200, Washington, DC 20036, USA.

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