
Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics

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All interested persons are provided 60 days from the above release date (November 23, 2021) to comment on this safety assessment, and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available for review by any interested party, and may be cited in a peer-reviewed scientific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 Executive Director, Dr. Bart Heldreth.

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Lisa A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Christina L. Burnett, Senior Scientific Analyst/Writer, CIR.

ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 16 barley-derived ingredients, most of which are reported to function as skin-conditioning agents in cosmetic products. Industry should continue to use good manufacturing practices to minimize impurities that could be present in botanical ingredients. The Panel reviewed the available data to determine the safety of these ingredients. The Panel concluded that 4 barley-ingredients are safe in cosmetics in the practices of use and concentration described in this safety assessment. However, the Panel also concluded that the available data are insufficient to make a determination that the remaining 12 barley-derived ingredients are safe under the intended conditions of use in cosmetic formulations.

INTRODUCTION

The assessment of the safety of the following 16 barley-derived ingredients, as used in cosmetics, is based on the data contained in this report:

Hordeum Distichon (Barley) Extract	Hordeum Vulgare Leaf/Stem Powder
Hordeum Distichon (Barley) Seed Flour	Hordeum Vulgare Powder
Hordeum Vulgare Extract	Hordeum Vulgare Root Extract
Hordeum Vulgare Flower/Leaf/Stem Juice	Hordeum Vulgare Seed Extract
Hordeum Vulgare Juice	Hordeum Vulgare Seed Flour
Hordeum Vulgare Leaf Extract	Hordeum Vulgare Seed Water
Hordeum Vulgare Leaf Juice	Hordeum Vulgare Sprout Extract
Hordeum Vulgare Leaf Powder	Hordeum Vulgare Stem Water

Hordeum distichon and *Hordeum vulgare* are two species of barley that are cultivated as a cereal grain. These two species mainly vary by the arrangement of spikelets along the central stem of the plant.^{1,2} Most of barley-derived ingredients detailed in this safety assessment are reported to function in cosmetics as skin conditioning agents, while some are reported to have other functions, such as abrasives, antioxidants, and bulking agents, according to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*; see Table 1).³

The Expert Panel for Cosmetic Ingredient Safety (Panel) has reviewed the safety of Hydrolyzed Barley Protein.⁴ In 2017, the Panel concluded that this ingredient is safe in cosmetics in the present practices of use and concentration in cosmetics (as described in that safety assessment). The full report on this ingredient can be accessed on the Cosmetic Ingredient Review (CIR) website (<https://www.cir-safety.org/ingredients>).

Botanicals, such as barley-derived ingredients, may contain hundreds of constituents. Thus, in this assessment, the Panel is evaluating the potential toxicity of each of the barley-derived ingredients as a whole, complex substance; toxicity from single components may not predict the potential toxicity of botanical ingredients.

Many of the barley-derived seed and malt ingredients in this safety assessment may be consumed as food, and daily exposure as such would result in much larger systemic exposures than possible from use of these ingredients in cosmetic products. Therefore, the primary focus of this safety assessment is on the potential for local effects from topical exposure to these ingredients as used in cosmetics. Proteins from barley in the diet, specifically gluten, are associated with adverse health conditions (such as celiac disease) in a portion of the general population.⁵ Since the concentration of gluten in cosmetics is low, it is unlikely that enough gluten could be absorbed by the percutaneous route or by inadvertent ingestion from cosmetic products to precipitate a flare-up of either gastrointestinal or cutaneous symptoms.⁶

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that Panel typically evaluates, is provided on the CIR website (<https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites>; <https://www.cir-safety.org/supplementaldoc/cir-report-format-outline>). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

The cosmetic ingredient names, according to the *Dictionary*, are written as listed above, without italics and without abbreviations. When referring to the plant from which these ingredients are derived, the standard scientific practice of using italics will be followed (i.e., *Hordeum vulgare*). Often in the published literature, the general name "barley" is used, and it is not known how the substance being tested compares to the cosmetic ingredient. Therefore, if it is not known whether the material being discussed is a cosmetic ingredient, the generic terminology, in all lowercase (e.g., barley extract or barley flour), will be used. However, if it is known that the material is a cosmetic ingredient, the naming convention provided in the *Dictionary* (e.g., Hordeum Vulgare Extract or Hordeum Vulgare Seed Flour) will be used.

CHEMISTRY

Definition and Plant Identification

The definitions of the ingredients included in this review are provided in Table 1.³ The generic CAS number for the barley ingredients in this report is 85251-64-5. Barley is the 4th most widely produced cereal grain in the world after wheat, rice, and corn.^{7,8} Barley is one of the most ancient and most cultivated grains, and is more productive and stable against seasonal variations and poor soil conditions than other grains.^{1,8} The origin of *Hordeum vulgare* is uncertain, but it is believed to have been domesticated in the Fertile Crescent or in east Asia nearly 10,000 - 13,000 years ago.^{1,9,10} In present day, it is cultivated on all continents, except Antarctica, in temperate and tropical areas.¹¹

Table 2 lists the generic definitions of the parts of plants that are most pertinent to the ingredients in this report.³ The barley plant is an annual grass that may be either planted in the fall (winter annual variety) or in the spring (spring annual variety).^{1,12} Barley sprouts are the young leaves of barley harvested approximately 10 d after sowing seeds.¹⁰ Stems may vary in length from 1 to 4 ft, depending on variety and growing conditions. Stem are round, hollow between nodes, and develop 5 to 7 nodes below the head. At each node, a clasping leaf develops. The spike, which contains the flowers and later the mature seeds, consists of spikelets attached to the central stem or rachis. Three spikelets develop at each node on the rachis. The barley kernel consists of the caryopsis (internal seed), the lemma (the lower bract of the floret), and palea (the upper bract of the floret). The barley kernel is generally spindle-shaped.

Hordeum vulgare L. is a 6-rowed barley with a tough rachis (spike stem) that has all florets fertile with normal kernels (i.e. all three of the spikelets at each node develop a seed).^{1,2} Within this species, there are two main subgroups: a typical 6-rowed group where the lateral kernels are only slightly smaller than the central ones, and an intermedium group, where the lateral kernels are markedly smaller than the central ones.²

Hordeum distichon L. is a 2-rowed barley with a tough rachis comprised of a central spikelet containing a fertile flower, and lateral spikelets with male or sexless flowers (i.e. central spikelet develops a fertile flower and seed).^{1,2} This species also has two main subgroups: a typical 2-rowed group with lateral florets consisting of lemma, palea, rachilla, and reduced sexual parts; and a *deficiens* group with reduced lateral florets consisting of lemma, palea (rarely) and rachilla, and no sexual parts.²

Chemical Properties

Hordeum Vulgare Seed Extract

A supplier has reported that a product that is a milky preparation of the liposoluble fraction and the water-soluble fraction of *Hordeum vulgare* seeds is an opaque, ivory-colored solution with a pH of 3.5 - 4.7.¹³ A 10% diluted solution is miscible in water and alcohol 50% (v/v) and non-miscible in mineral and vegetal oils.

Another supplier has reported that Hordeum Vulgare Seed Extract is a white, odorless lyophilized powder that is stable at room temperature.¹⁴

Method of Manufacture

Hordeum Distichon (Barley) Extract

A supplier has reported that Hordeum Distichon (Barley) Extract is produced by extracting barley with specified eluent(s) under "appropriate temperature conditions" to yield a concentrate.¹⁵ Typical eluents include water, butylene glycol, safflower seed oil, glycerin, and propylene glycol. The concentrate is then blended with the desired diluent(s) and preservative system to produce the final ingredient. The final ingredients are evaluated for physiochemical properties and contaminants.

Hordeum Distichon (Barley) Seed Flour and Hordeum Vulgare Seed Flour

Barley flour is milled from pearled, blocked or hull-less barley.¹⁶ The milling system for barley is similar to that of wheat flour milling by utilizing roller mills with fluted and smooth rolls, and plansifters. Barley flour may also be a by-product of pearling and polishing processes. The methods described here are general to the processing of barley flour, and it is unknown if they apply to cosmetic ingredient manufacture.

Hordeum Vulgare Seed Extract

A supplier has reported that a tradename mixture of Hordeum Vulgare Seed Extract is obtained by decocting barley seeds with demineralized water, which is then filtered and combined with xanthan gum.¹⁷ The same supplier reported that a product containing Hordeum Vulgare Seed Extract was obtained by combining crushed barley seeds with crushed wheat and oat seeds and performing a warm aqueous co-extraction. The resulting mixture was then combined with xanthan gum.¹⁸

Another supplier has reported that Hordeum Vulgare Seed Extract is produced by harvesting hydroponically cultivated barley seeds, then drying and milling them.¹⁹ The milled seeds are then extracted with standard protein extraction buffers, containing buffering ions and sodium chloride at the appropriate pH. During this step, water-soluble barley proteins are pulled to the aqueous phase. The extract is then centrifuged to separate the slurry from the aqueous phase, which is collected for further clarification to eliminate further insoluble and unwanted particles. After clarification, the extract undergoes buffer exchange. The final steps are protein analysis, sterile filtration, and lyophilization.

Hordeum Vulgare Seed Water

A supplier has reported that Hordeum Vulgare Seed Water is obtained from dry barley seeds by steam distillate.²⁰ The steam distillation is carried out up to a ratio dry seed/distillate of 40%.

Composition/Impurities

Yields of constituents in barley have been found to be dependent on extraction methods and growing conditions, such as soil composition, climate, duration of growth period, and cultivar (i.e. specific genotypes, including those of different grain colors).²¹⁻²³ Additionally, different plant parts have different constituent compositions. For example, the composition of the water-soluble flavonoid, anthocyanin, varies depending on the grain color of barley (purple, black, or yellow) and on the location of the barley grain; e.g., the anthocyanin content in the outer 10% of the bran-rich kernel layers can be as much as 6 times greater than that found in the whole kernel flour.²⁴ Table 3 describes the phenolic composition of three different parts of two different barley cultivars.²⁵ Table 4 describes the available composition information of barley-derived ingredients that is mentioned below.

In general terms, barley grain contains about 64% starch, 11% protein, and 5% β -glucan, but variation can occur through types of grain processing (e.g. pearling, milling, etc.) and plant genotype.^{7,22} Phytochemicals in barley grain include phenolic acid, flavonoids (flavanols, anthocyanins, proanthocyanidins), lignans, tocals, phytosterols, and folates.²⁶

Mold, yeast, and bacterial infections are the main sources of microbial contaminants in barley that may adversely affect livestock and humans that consume the harvests.⁸ The main species affecting harvests are *Alternaria* spp., *Helminthosporium* spp., *Fusarium* spp., *Cladosporium* spp., *Aspergillus* spp., and *Penicillium* spp.⁸ Mycotoxins produced by these fungi and bacteria may also affect barley crops; for example, barley grain can be contaminated with trichothecene 2 toxin (T-2) and its metabolite, HT-2, which are type A mycotoxins produced by fungi belonging to the genus *Fusarium*, with aflatoxins from *Aspergillus*, and naphthoquinones from *Penicillium*.^{8,27,28}

Hordeum Distichon (Barley) Extract

A supplier has reported that a concentrate of Hordeum Distichon (Barley) Extract in an alcohol base had no detectable heavy metals or residual pesticides.¹⁵ This supplier also reported that the 26 fragrance allergens defined by the European Union Cosmetic Regulations were below threshold levels for this concentrate.

Hordeum Distichon (Barley) Seed Flour and Hordeum Vulgare Seed Flour

In an analysis of whole grain flour from 12 barley cultivars, protein content ranged from 12.4% to 16.5%, free lipid content ranged from 2.0% to 2.8%, β -glucan content ranged from 4.1% to 7.4%, and polyphenols (as gallic acid) ranged from < 0.10% to 0.45%.²⁹ Fatty acids of barley grain flours primarily include palmitic acid (19.0% - 22.0%), stearic acid (1.1% - 1.3%), eladic acid (14.9% - 18.4%), oleic acid (0.7% - 0.8%), linoleic acid (53.6% - 57.1%), linolenic acid (4.7% - 5.7%), and eicosenoic acid (0.8% - 1.0%). Barley grain flour was determined to contain 26 volatile compounds comprising aldehydes, ketones, alcohols, and a furan (2-pentylfuran). Total volatile content was 953 - 3339 μ g/l. Phenolic acids in whole grain barley flour include *p*-coumaric acid, ferulic acid, *p*-hydroxybenzoic acid, vanillic acid, caffeic acid, chlorogenic acid, protocatechuic acid, gallic acid, and syringic acid.³⁰

Hordeum Distichon (Barley) Seed Flour

Acetone extracts of *Hordeum distichon* grains contain 5-*n*-alkylresorcinols.²¹ Specifically, 1,3-dihydroxy-5-*n*-heneicosylbenzene (~40%); 1,3-dihydroxy-5-*n*-nonadecylbenzene (~29%); 1,3-dihydroxy-5-*n*-pentacosylbenzene (~19%); and 1,3-dihydroxy-tricosylbenzene were the predominant alkylresorcinols.

Hordeum Vulgare Juice

Phytochemical analysis of barley grass juice (15 d post-germination) was used to determine the presence of flavonoids, saponins, and terpenoids.³¹ The total phenolic and flavonoid content was 225.33 mg gallic acid equivalents (GAE)/g and 203 mg quercetin equivalents/g of extract, respectively.

Hordeum Vulgare Seed Extract

Constituents of a water extract of *Hordeum vulgare* seeds included phenolics, flavonoids, anthocyanins, flavanols, tannins, triterpenoids, and vitamin C.³² Phenolic constituents of this *Hordeum vulgare* seed extract include vanillic acid, syringic acid, vanillin, *p*-coumaric acid, ferulic acid, and ellagic acid.

In another constituent analysis of a methanol extract of *Hordeum vulgare* seeds (referred to synonymously as *Hordeum sativum*), total polyphenol content was 3.67 mg/g dry weight and total flavonoid content was 2.56 mg/g dry weight.³³ In a study of extract yields in three varieties of *Hordeum vulgare*, the total phenolic content of 100% methanol extract ranged from 88.1 to 118.5 mg/100 g extract.³⁴ Extracts with 80% methanol had total phenolic content ranging from 98.0 to 145.7 mg/100 g extract.

One supplier reported a tradename mixture was comprised of 3.0% Hordeum Vulgare Seed Extract, 94.9% water, 1.5% phenoxyethanol, 0.3% xanthan gum, and 0.3% potassium sorbate.³⁵ The same supplier reported the composition of another tradename mixture that was comprised of a 3.0% blend of Hordeum Vulgare Seed Extract, Triticum Vulgare (Wheat) Seed

Extract, and Avena Sativa (Oat) Kernel Extract; 94.9% water; 1.5% phenoxyethanol; 0.3% xanthan gum; and 0.3% potassium sorbate.³⁶

Another supplier has reported that the composition of a *Hordeum Vulgare* Seed Extract tradename mixture also contains sodium chloride and tromethamine.¹⁴ At 1 ppm of the seed extract, there is approximately 0.038% tromethamine. No further detail on the amount of constituents was provided. Levels of the pesticides avermectin and pirimicarb were below level of detection.³⁷

Hordeum Vulgare Seed Flour

Phenolic acid content of whole grain *Hordeum vulgare* flour includes caffeic acid, ferulic acid, sinapic acid, protocatechuic acid, vanillic acid, *p*-coumaric acid, *p*-hydroxybenzoic acid, syringic acid, and ferulic acid dehydrodimers.³⁸ The main phenolic acids were ferulic acid (250 mg/kg), ferulic acid dehydrodimers (130 mg/kg), and *p*-coumaric acid (40 mg/kg).

Hordeum Vulgare Sprout Extract

Analysis of *Hordeum vulgare* spring seedlings reported 152 phenolic secondary metabolites.³⁹ Flavonoids with various glycosylation and acylation, hydroxycinnamic acid glycosides, esters, and amides were identified in methanolic extracts of the leaves of nine *Hordeum vulgare* varieties. Specific derivatives included those from hordatines, hydroxyferulic acid, and flavones acylated directly on aglycone. Composition of constituents were dependent on variety, with one variety containing derivatives of flavonols, quercetin, and isorhamnetin.

An ethanol extract of *Hordeum vulgare* sprouts included the flavonoid saponarin (14.74 µg/mg), policosanol polyphenol series, various minerals (not specified), and free amino acids.¹⁰

The chlorophyll content of an acetone extract (10% w/v of 80%) of *Hordeum vulgare* sprouts was dependent on the age of the sprouts, with total chlorophyll content on days 7, 10, and 16 measured as 247.01 mg/100 g dry material (DM), 364.65 mg/100 g DM, and 625.20 mg/100 g DM, respectively.⁴⁰ Carotenoid content of the same extract also was dependent on the age of the sprouts, with total carotenoid content on days 7, 10, and 16 measured as 21.56 mg/100 g DM, 31.98 mg/100 g DM, and 56.08 mg/100 g DM, respectively.

Total polyphenols and total flavonoids of barley sprouts had a range of 1047.8 - 1263.2 mg GAE/100 g and 443.7 - 550.7 mg (+)-catechin hydrate equivalents/100 g DM, respectively, in four different *Hordeum vulgare* cultivars.⁴¹ Lutonarin and saponarin were reported to be major compounds in barley sprouts, with quantities varying at different harvest times.

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2021 VCRP survey data, *Hordeum Vulgare* Extract has the most reported uses in cosmetic products, with a total of 167 formulations; the majority of the uses are in leave-on makeup preparations and skin care products (Table 5).⁴² *Hordeum Vulgare* Seed Extract has the second greatest reported number of uses in this safety assessment with 36 formulations; the majority of the uses are in leave-on skin care products. The remaining 3 in-use ingredients are reported to be used in much smaller numbers. The results of the concentration of use survey conducted by the Council in 2018 indicate that the highest concentration of use for *Hordeum Vulgare* Extract is 1.5% in leave-on body and hand skin care products.⁴³ According to a Council survey conducted in 2020, *Hordeum Distichon* (Barley) Extract is reported to be used at up to 1.8% in leave-on moisturizing products.⁴⁴ No concentrations of use were reported for any of the other barley-derived ingredients in this report. The 11 ingredients not in use, according to the VCRP and industry survey, are listed in Table 6.⁴²⁻⁴⁴

Barley-derived ingredients may be used in products that can be incidentally ingested, come in contact with mucous membranes, or be used near the eye; for example, *Hordeum Vulgare* Extract is reported to be used in lipsticks at 0.15% and eye makeup preparations at up to 0.075%, and *Hordeum Distichon* (Barley) Extract is used at up to 0.3% in eye makeup preparations.^{43,44} Additionally, some of the ingredients are used in cosmetic sprays and powders and could possibly be inhaled; for example, *Hordeum Vulgare* Extract is reported to be used at up to 0.03% in body and hand spray preparations, and at concentrations up to 0.015% in face powders.⁴³ 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.^{45,46} 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.^{47,48} Conservative estimates of inhalation exposures to respirable particles

during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.⁴⁹⁻⁵¹

The barley-derived ingredients described in this report are not restricted from use in any way under the rules governing cosmetic products in the European Union.⁵²

Non-Cosmetic

According to the US FDA, under 21 CFR 582.20, malt extract from *Hordeum vulgare* L. (or other grains) is a substance generally recognized as safe (GRAS) in animal drugs, feeds, and related products. Roughly half of the barley grown in the US is used for livestock feed, and another quarter to a third is used for malting.^{1,12} Barley for human consumption is made into pearl barley by using abrasive disks to grind the hulls and bran off the kernels.

Worldwide, barley grain is mostly used as feed for animals, malt, and food for human consumption.⁸ Malt is the second largest use for barley. Barley is also grown as a hay crop in Asia, parts of the Middle East, and in northern and central Africa.^{1,8}

Barley has been used in traditional medicine to treat various inflammatory and cardiovascular diseases.⁵³ Barley seed extract has been studied for antioxidant properties and therapeutic benefits in kidney stone and nephrotoxicity management, hepatoprotective activity against ethanol, and diabetes mellitus control and management.^{32,33,54,55} Barley seed flour applied topically has been studied for therapeutic benefits in infants with jaundice.⁵⁶ Young barley grass water and juice extracts have been studied for obesity inhibition³¹ and chemopreventative potential in human colon and lung cancer cell lines,^{57,58} while young green *Hordeum vulgare* leaves have been studied for anti-stress properties that could be beneficial in treating psychiatric disorders such as depression.⁵⁹ Barley sprout “essence” and extract has been studied for its effects on blood cholesterol and treatment for chronic alcohol-induced liver injury.^{10,60-62}

TOXICOKINETIC STUDIES

No relevant toxicokinetics studies on barley-derived ingredients were found in the public literature, and unpublished data were not submitted. In general, toxicokinetics data are not expected to be found on botanical ingredients because each botanical ingredient is a complex mixture of constituents.

TOXICOLOGICAL STUDIES

Many of the barley-derived seed and malt ingredients that are addressed in this safety assessment are found in the foods that are consumed daily, and daily exposure from food use would result in much larger systemic exposures than those from use in cosmetic products. The potential for systemic exposure from absorption of these ingredients through the skin is much less than the potential for systemic exposure 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. Thus, the potential for systemic effects, other than sensitization, is not discussed in detail in this report.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

No DART studies for barley-derived ingredients were found in the published literature, and unpublished data were not submitted.

GENOTOXICITY STUDIES

No genotoxicity toxicity studies for barley-derived ingredients were found in the published literature, and unpublished data were not submitted.

CARCINOGENICITY STUDIES

No carcinogenicity studies for barley-derived ingredients were found in the published literature, and unpublished data were not submitted.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Dermal irritation and sensitization studies on barley-derived ingredients are summarized in Table 7. In human irritation tests, a product containing 0.005% *Hordeum Vulgare* Extract was not irritating in a 48-h patch test, while a mascara containing 0.3% *Hordeum Distichon* (Barley) Extract had “negligible” irritation potential in a 14-d cumulative irritation assay.^{63,64} A mascara product containing 0.3% *Hordeum Distichon* (Barley) Extract was determined to not be sensitizing in a human repeated insult patch test (HRIPT), but low-level (\pm) reactions were observed in the induction and challenge phases.⁶⁵ No dermal sensitization was observed with a lotion containing 1.8% *Hordeum Distichon* (Barley) Extract in a HRIPT; however a slight potential for dermal irritation was noted.⁶⁶ *Hordeum Distichon* (Barley) Extract also was not irritating or sensitizing in an eye cream at 1.8%;⁶⁷ however, one subject had mild-moderate reactions in an HRIPT of a facial moisturizer containing

2.76% *Hordeum Distichon* (Barley) Extract, which may have been due to prior exposure to one of the ingredients in the test material.⁶⁸ No dermal irritation or sensitization were observed in HRIPTs of a pressed powder, a facial moisturizer, or a facial mask each containing 0.005% *Hordeum Vulgare* Extract, or in a skin serum formulation containing 0.1% *Hordeum Vulgare* Seed Extract.⁶⁹⁻⁷²

OCULAR IRRITATION STUDIES

No ocular irritation studies for barley-derived ingredients were found in the published literature, and unpublished data were not submitted.

CLINICAL STUDIES

Ocular In-Use Studies

Hordeum Distichon (Barley) Extract

The ocular irritation potential of a mascara containing 0.3% *Hordeum Distichon* (Barley) Extract was evaluated in an in-use study of 62 subjects.⁷³ Approximately a quarter of the subjects had self-perceived sensitive eyes, and more than half of the panel (47) were contact lens wearers. Subjects were instructed to apply the mascara twice daily for 4 wk. An ophthalmologist conducted slit lamp examinations at the baseline, at the 2-wk interim, and final visits. Visual acuity was measured at the initial and final visits. Questionnaires seeking subject-perceived effects were completed by the subjects at the end of each 2-wk use period. No visible clinical irritation was observed related to the use of the test material and none of the subjects reported perceived discomfort or irritation during the study period.

Hordeum Vulgare Extract

The ocular irritation potential of an eye cream containing 0.005% *Hordeum Vulgare* Extract was evaluated in an in-use study of 27 female subjects.⁷⁴ Approximately half of the panel had self-perceived sensitive eyes, and approximately half of the panel were contact lens wearers. After completion of a preliminary ophthalmic examination, the subjects received the test material and were instructed to use it once a day for 4 wk. At the end of the 4-wk period, the subjects underwent a comprehensive ocular examination. During the course of the exposure period, no adverse events were reported. All ophthalmologic examinations were within normal parameters. The study authors concluded that the eye cream containing 0.005% *Hordeum Vulgare* Extract was neither an ophthalmologic irritant in contact or non-contact lens wearers, nor in individuals with normal or self-perceived sensitive eyes.

Case Reports

Contact urticaria was reported in a 20-yr-old woman after contact with beer while working in a bar.⁷⁵ The patient presented with wheals on her hand and forearms. The wheals would appear within 15 min of exposure and would disappear after a couple hours. The patient was able to drink beer without any reactions. Skin-prick tests with wheat flour and beer were strongly positive for beer. A provocative test with beer was also positive. Specific immunoglobulin E (IgE) antibodies were detected against barley (4.33 kU/l), malt (5.13 kU/l), grass pollen (40.8 kU/l), pet dander (35 - 36 kU/l), and dust mites (> 100 kU/l). Lower levels of specific IgE antibodies (< 0.1 kU/l) were detected against wheat, rye, and oats.

A 54-yr-old malt worker at a silo presented with eczema on the fingers of both hands.⁷⁶ The patient reported that the eczema would worsen and spread to his trunk and limbs when he cleaned barley silos. Patch tests with the Portuguese standard series, fragrances, a food series, and barley and malt residues were positive (++) for barley residues (as is and in 10% petrolatum), malt radicle (as is and in 10% petrolatum), and malt residues (as is and in 10% petrolatum). A prick test to barley was negative. Serum IgE was 97.9 IU/ml.

A 23-yr-old farm laborer presented with eczema on the hands and arms.⁷⁷ A patch test of the patient was positive to barley dust. A scratch test to barley dust was negative.

OCCUPATIONAL EXPOSURES

Work-related sensitization (IgE-mediated) to barley flour and other grain dusts has been reported in bakery workers.⁷⁸⁻⁸¹ Commonly known as baker's asthma, reactions are often preceded by rhinitis and other respiratory symptoms, with concomitant skin symptoms such as contact urticaria and hand eczema. Atopy and sensitization to grain flour and/or enzyme (e.g., α -amylase of fungal origin) occur frequently.^{78,80,81} Aside from cereal grains, baker's asthma may also be caused by molds, yeast, eggs, sesame seeds, nuts, and insects. Skin-prick testing, skin biopsies, and radioallergosorbent tests (RAST) have been utilized to identify and analyze the reactions observed in bakery workers.^{78,80,81} In bakery workers with occupational asthma, RAST have shown strong associations between the levels of specific IgE to wheat flour and those of barley flour, and competitive RAST inhibition showed wheat and barley contain cross-reacting proteins.⁷⁹ Barley flour contains proteins of similar molecular weights as those in wheat (10, 52, and 69 kDa). Results of Western blotting also suggest that the cross-reacting allergens in barley have molecular weights which are similar to proteins identified as cereal α - and β -amylase, α -amylase inhibitors, trypsin and trypsin inhibitors, and protease and protease inhibitors.

EPIDEMIOLOGY OF IMMUNE-MEDIATED GLUTEN AND BARLEY REACTIONS

Celiac disease affects approximately 1% of the population worldwide, including the US, with variations between countries.⁸²⁻⁸⁴ Food allergy to barley has been reported; in Korean children, evidence of cross-reactivity or co-sensitization with wheat has been found.^{85,86}

SUMMARY

Hordeum distichon and *Hordeum vulgare* are two species of barley, an annual grass, that is cultivated as a cereal grain. Most of the 16 barley-derived ingredients detailed in this safety assessment are reported to function in cosmetics as skin conditioning agents, while some are reported to have other functions, such as abrasives, antioxidants, and bulking agents. The Panel has reviewed the safety of Hydrolyzed Barley Protein, and concluded that this ingredient is safe in cosmetics in the present practices of use and concentration.

Barley is the 4th most widely produced cereal grain in the world after wheat, rice, and corn. Barley is one of the most ancient and most cultivated grains, and is more productive and stable against seasonal variations and poor soil conditions than other grains. Yields of constituents in barley have been found to be dependent on extraction methods and growing conditions such as soil composition, climate, duration of growth period, and cultivar. Additionally, different plant parts have different constituent compositions. Barley grain may be contaminated by mycotoxins, such as aflatoxins, trichothecenes, and naphthoquinones.

According to 2021 VCRP survey data, *Hordeum Vulgare* Extract has the most reported uses in cosmetic products, with a total of 167 formulations; the majority of the uses are in leave-on makeup preparations and skin care products. *Hordeum Vulgare* Seed Extract has the second greatest reported number of uses in this safety assessment with 36 formulations; the majority of the uses are in leave-on skin care products. The remaining 3 in-use ingredients are reported to be used in much smaller numbers. The results of the concentration of use survey conducted by the Council indicate that the highest concentration of use for *Hordeum Vulgare* Extract is 1.5% in leave-on body and hand skin care products. *Hordeum Distichon* (Barley) Extract is reported to be used at up to 1.8% in leave-on moisturizing products. No concentrations of use were reported for the remaining 11 barley-derived ingredients in this report.

Malt extract from *Hordeum vulgare* L. or other grains is considered GRAS in animal drugs, feeds, and related products, according to the US FDA. Barley is a food grain consumed by humans and animals, and is used to malt beverages. Barley has been used in traditional medicine to treat various inflammatory and cardiovascular diseases, and its various part have been studied for treatment of numerous ailments.

Many of the barley-derived seed and malt ingredients that are reviewed in this safety assessment are found in foods consumed daily the world over. The potential for systemic exposure from the absorption of these ingredient through the skin is much less than the potential for systemic exposure 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; and, the systemically available dose of these ingredients, even with theoretically complete absorption from cosmetic use, would be very small compared to that available from consumption.

In human irritation tests, a product containing 0.005% *Hordeum Vulgare* Extract was not irritating in a 48-h patch test, while a mascara containing 0.3% *Hordeum Distichon* (Barley) Extract had “negligible” irritation potential in a 14-d cumulative irritation assay. A mascara product containing 0.3% *Hordeum Distichon* (Barley) Extract was determined to not be sensitizing in a HRIPT, but low-level (+) reactions were observed in the induction and challenge phases. No dermal sensitization was observed with a lotion containing 1.8% *Hordeum Distichon* (Barley) Extract in a HRIPT; however a slight potential for dermal irritation was noted. *Hordeum Distichon* (Barley) Extract also was not irritating or sensitizing in an eye cream at 1.8%; however, one subject had mild-moderate reactions in an HRIPT of a facial moisturizer containing 2.76% *Hordeum Distichon* (Barley) Extract, which may have been due to prior exposure to one of the ingredients in the test material. No dermal irritation or sensitization were observed in HRIPTs of a pressed powder, a facial moisturizer, or a facial mask each containing 0.005% *Hordeum Vulgare* Extract, or in a skin serum formulation containing 0.1% *Hordeum Vulgare* Seed Extract.

No visible clinical ocular irritation was observed related to the use of a mascara containing 0.3% *Hordeum Distichon* (Barley) Extract. In another in-use study, an eye cream containing 0.005% *Hordeum Vulgare* Extract was determined not to be an ocular irritant.

Case reports of contact urticaria and eczema have been described in patients that have been exposed to barley. Work-related sensitization has been reported in bakery workers. Celiac disease affects approximately 1% of the population worldwide. Food allergy to barley has been reported with evidence of cross-reactivity or co-sensitization with wheat.

No relevant DART studies, genotoxicity studies, carcinogenicity studies, or ocular irritation studies were found in the published literature; and unpublished data were not submitted. No relevant toxicokinetic studies were found in the published literature; however, in general, toxicokinetics data are not expected to be found on botanical ingredients because each botanical ingredient is a complex mixture of constituents.

DISCUSSION

The Panel reviewed the safety of 16 botanical ingredients derived from the barley plants *Hordeum distichon* and *Hordeum vulgare*. The Panel concluded that the available data are sufficient for determining safety of 4 ingredients, i.e., those derived from barley seeds, as reportedly used in cosmetics. The Panel noted that the barley seed-derived ingredients that are reviewed in this safety assessment are found in foods that may be consumed daily, and daily exposure from food use would result in much larger systemic exposure compared to that resulting from use in cosmetic products. Additionally, the potential for systemic exposure from the absorption of these ingredient through the skin is much less than the potential for systemic exposure from absorption through oral exposures. This fact, coupled with negative findings in human dermal irritation and sensitization studies on whole plant extracts and seed extracts, led the Panel to determine that barley seed-derived ingredients are safe for use in cosmetic products.

The Panel noted that constituent yields can greatly vary between species cultivars, and even between parts of the same plant. While seeds of barley are generally recognized as safe (GRAS) for food use, other barley plant parts are not GRAS for food use, and safety test data are lacking. Thus, the Panel also concluded that data are insufficient for determining the safety for the non-seed ingredients. The additional data needed to determine safety of these ingredients as used in cosmetics are:

- 28-day dermal toxicity data on the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
 - If positive, developmental and reproductive toxicity and genotoxicity data maybe needed
 - Alternatively, acceptable evidence of use as a food for ingredients derived from the flower, leaf, stem, and root.

The Panel expressed concern about pesticide residues, heavy metals, and other plant species that may be present in botanical ingredients, and stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities. While aflatoxin has been detected in barley grain and flour, the Panel believes that aflatoxin should not be present in barley-derived cosmetic ingredients that are derived from *Hordeum distichon* or *Hordeum vulgare*. The Panel has adopted the United States Department of Agriculture (USDA) designation of ≤ 15 ppb as corresponding to “negative” aflatoxin content.

Some barley-derived ingredients were reported to be used in spray and powder products that could possibly be inhaled. For example, Hordeum Vulgare Extract is reported to be used at up to 0.03% in body and hand spray preparations, and at concentrations up to 0.015% in face powders. The Panel noted that in aerosol products, 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns for these ingredients. 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 4 barley-derived ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment:

Hordeum Distichon (Barley) Seed Flour*
Hordeum Vulgare Seed Extract

Hordeum Vulgare Seed Flour
Hordeum Vulgare Seed Water*

**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.*

However, the Panel also concluded that the available data are insufficient to make a determination that the following 12 barley-derived ingredients are safe under the intended conditions of use in cosmetic formulations:

Hordeum Distichon (Barley) Extract
Hordeum Vulgare Extract
Hordeum Vulgare Flower/Leaf/Stem Juice**
Hordeum Vulgare Juice**
Hordeum Vulgare Leaf Extract
Hordeum Vulgare Leaf Juice**

Hordeum Vulgare Leaf Powder**
Hordeum Vulgare Leaf/Stem Powder**
Hordeum Vulgare Powder**
Hordeum Vulgare Root Extract**
Hordeum Vulgare Sprout Extract**
Hordeum Vulgare Stem Water**

***There are currently no uses reported for these ingredients.*

TABLES

Table 1. Definitions and functions of the ingredients in this safety assessment.³

Ingredient/CAS No.	Definition	Function
Hordeum Distichon (Barley) Extract 85251-64-5; 94349-67-4	Hordeum Distichon (Barley) Extract is the extract of the whole plant, <i>Hordeum distichon</i> .	Skin-conditioning agent – misc.
Hordeum Distichon (Barley) Seed Flour	Hordeum Distichon (Barley) Seed Flour is the flour obtained from the finely ground seeds of <i>Hordeum distichon</i> .	Abrasives; bulking agent
Hordeum Vulgare Extract 85251-64-5	Hordeum Vulgare Extract is the extract of the whole plant, <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.
Hordeum Vulgare Flower/Leaf/Stem Juice 85251-64-5	Hordeum Vulgare Flower/Leaf/Stem Juice is the juice expressed from the flowers, leaves and stems of <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.
Hordeum Vulgare Juice 85251-64-5	Hordeum Vulgare Juice is the liquid expressed from <i>Hordeum vulgare</i> .	Not reported
Hordeum Vulgare Leaf Extract 85251-64-5	Hordeum Vulgare Leaf Extract is the extract of the leaves of <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.
Hordeum Vulgare Leaf Juice 85251-64-5	Hordeum Vulgare Leaf Juice is the juice expressed from the leaf of <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.
Hordeum Vulgare Leaf Powder 85251-64-5	Hordeum Vulgare Leaf Powder is the powder obtained from the dried, ground leaves of <i>Hordeum vulgare</i> .	Skin-conditioning agent – humectant
Hordeum Vulgare Leaf/Stem Powder 85251-64-5	Hordeum Vulgare Leaf/Stem Powder is the powder obtained from the dried, ground leaves and stems of <i>Hordeum vulgare</i> .	Antioxidant
Hordeum Vulgare Powder 85251-64-5	Hordeum Vulgare Powder is the powder obtained from dried and ground whole plant, <i>Hordeum vulgare</i> .	Abrasive
Hordeum Vulgare Root Extract 85251-64-5	Hordeum Vulgare Root Extract is the extract of the roots <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.
Hordeum Vulgare Seed Extract 85251-64-5	Hordeum Vulgare Seed Extract is the extract of seeds of <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.
Hordeum Vulgare Seed Flour 85251-64-5	Hordeum Vulgare Seed Flour is the flour obtained from the finely ground seeds of <i>Hordeum vulgare</i> .	Abrasive; bulking agent
Hordeum Vulgare Seed Water 85251-64-5	Hordeum Vulgare Seed Water is the aqueous solution of the steam distillates obtained from the seeds of <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.
Hordeum Vulgare Sprout Extract 85251-64-5	Hordeum Vulgare Sprout Extract is the extract of the sprouts of <i>Hordeum vulgare</i> .	Antioxidant; skin-conditioning agent - humectant
Hordeum Vulgare Stem Water 85251-64-5	Hordeum Vulgare Stem Water is the aqueous solution of the steam distillates obtained from the stems of <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.

Table 2. Generic plant part definitions as they apply to barley-derived ingredients.³

Plant Part	Definition
Bran	The outer hard layers of the grain formed by the fused fruit and seed wall in grains and cereals.
Flower	The reproductive shoot in flowering plants, usually with sepals, petals, stamens and pistil(s)
Grain	Dry one-seeded fruits produced by grasses, e.g. cereals such as barley.
Hull	A dry outer covering of a fruit or seed.
Juice	The liquid contained in the vegetative parts or fruits.
Kernel	The grain of a grass.
Leaf	Flattened photosynthetic organs, attached to stems.
Root	Organ of a plant that absorbs and transports water and nutrients, lacks leaves and nodes, usually underground
Seed	A propagating sexual structure resulting from the fertilization of an ovule, formed by embryo, endosperm, or seed coat.
Sprout	Seedling; germinating seed; any new growth of a plant from a stem such as a new branch or a bud
Stem	A slender or elongated structure that supports a plant or a plant part or plant organ.

Table 3. Phenolic composition (mg/kg) of barley plant parts in 2 different *Hordeum vulgare* cultivars.²⁵

Phenolic Compounds	Cultivar 1			Cultivar 2		
	Leaves	Seeds	Stems	Leaves	Seeds	Stems
3- <i>O</i> -feruloylquinic acid	39.8	NR	5.8	4.3	NR	5.1
chlorogenic acid	NR	NR	1.1	NR	NR	0.8
luteonarin	2150.8	1.5	NR	760.8	NQ	NR
<i>p</i> -coumaric acid	NR	6.2	5.3	NR	3.4	18.6
isoorientin-7- <i>O</i> -rutinoside	208.4	NR	NR	68.5	NR	NR
luteolin-6- <i>C</i> -arabinoside-8- <i>C</i> -glucoside	80.5	0.3	0.9	24.6	0.2	0.4
ferulic acid	33.6	2.4	2.5	25.2	1.0	5.9
saponarin	145.3	2.0	0.3	56.4	2.4	1.2
isoorientin-7- <i>O</i> -[6-feruloyl]-glucoside-4'- <i>O</i> -glucoside AND apigenin-6- <i>C</i> -arabinoside-8- <i>C</i> -glucoside	30.9	7.3	3.4	14.2	6.4	5.4
isovitexin-7- <i>O</i> -rutinoside AND isoscoparin-7- <i>O</i> -glucoside	217.5	29.3	8.8	70.5	26.4	15.3
apigenin-6- <i>C</i> -glucoside-8- <i>C</i> -arabinoside AND isovitexin-7- <i>O</i> -[6-sinapoyl]-glucoside-4'- <i>O</i> -glucoside	14.3	0.4	NQ	7.9	0.2	NQ
isoscoparin-7- <i>O</i> -rutinoside AND isoorientin	87.6	1.7	1.1	52.3	4.5	1.5
isovitexin-7- <i>O</i> -[6-feruloyl]-glucoside-4'- <i>O</i> -glucoside	3.1	NR	NR	3.1	NR	NR
isoorientin-7- <i>O</i> -glucoside-4'- <i>O</i> -[6-feruloyl]-glucoside AND isoorientin-7- <i>O</i> -[6-caffeoyl]-glucoside AND chrysoeriol-6- <i>C</i> -glucoside-8- <i>C</i> -arabinoside AND isoscoparin-7- <i>O</i> -[6-sinapoyl]-glucoside-4'- <i>O</i> -glucoside	32.6	NR	NR	23.1	NR	NR
isoorientin-7- <i>O</i> -[6-sinapoyl]-glucoside	167.3	NR	NR	47.8	NR	NR
isoorientin-7- <i>O</i> -[6-feruloyl]-glucoside-2''- <i>O</i> -glucoside AND isoscoparin-2''- <i>O</i> -glucoside AND isovitexin	3.2	NR	NR	2.0	NR	NR
isoorientin-7- <i>O</i> -[6-feruloyl]-glucoside	494.6	NR	NR	74.8	NR	NR
isovitexin-7- <i>O</i> -[6-sinapoyl]-glucoside	18.2	NR	NR	2.5	NR	NR
isovitexin-7- <i>O</i> -[6-sinapoyl]-glucoside	27.7	NR	NR	6.0	NR	NR
Total	3740.6	50.0	28.4	1232.9	44.4	51.1

Table 4. Composition of barley-derived ingredients

Constituent	Barley Seed Flour (generic) ^{29,30}	Hordeum Distichon (Barley) Seed Flour ²¹	Hordeum Vulgare Juice ³¹	Hordeum Vulgare Seed Extract ³²⁻³⁴	Hordeum Vulgare Seed Flour ³⁸	Hordeum Vulgare Sprout Extract ^{10,40,41}
Protein	12.4% - 16.5%					
Free amino acids						√
Free lipids	2.0% - 2.8%					
β-glucan	4.1% - 7.4%					
Fatty acids						
palmitic acid	19% - 22.0%					
stearic acid	1.1% - 1.3%					
eladic acid	14.9% - 18.4%					
oleic acid	0.7% - 0.8%					
linoleic acid	53.6% - 57.1%					
linolenic acid	4.7% - 5.7%					
eicosenoic acid	0.8% - 1.0%					
Vitamin C				√		
Minerals (unspecified)						√
Chlorophyll						247.01 - 625.20 mg/100 g DM (acetone)
Aldehydes	√					
Ketones	√					
Alcohols	√					
Furans	√					
Alkylresorcinols		√				
Polyphenols	<0.10% - 0.45%		Total phenolic content – 225.33 mg GAE/g	Total phenolic content – 98.0-145.7 mg/100 kg (80% methanol); 88.1- 118.5 mg/100 kg (100% methanol)		Total content – 1047.8 -1263.2 mg GAE/100 g
flavonoids			Total content – 203 mg quercetin equivalents/g	Total content – 2.56 mg/g dry weight (methanol)		Total content – 443.7-50.7 mg (+)-catechin hydrate equivalents/100 g DM
tannins				√		
tannic acid				√		
ellagic acid				√		
caffeic acid	√				√	
ferulic acid	√			√	250 mg/kg	
ferulic acid dehydrodimers					130 mg/kg	
sinapic acid					√	
protocatechuic acid	√				√	
vannilic acid	√			√	√	
vanillin				√		
p-coumaric acid	√			√	40 mg/kg	
p-hydroxybenzoic acid	√				√	
syringic acid	√			√	√	
gallic acid	√					
chlorogenic acid	√					
Terpenoids			√			
triterpenoids				√		
carotenoids						21.56 - 56.08 mg/100 g DM (acetone)
Saponins			√			

√ denotes component presence, but quantification was not available.

Table 5. Frequency (2021)⁴² and concentration (2018;⁴³ 2020⁴⁴) of use according to duration and type of exposure for barley-derived ingredients

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Hordeum Distichon (Barley) Extract		Hordeum Vulgare Extract		Hordeum Vulgare Leaf Extract		Hordeum Vulgare Seed Extract	
Totals†	30	0.005-1.8	167	0.000015-1.5	4	NR	36	NR
Duration of Use								
Leave-On	20	0.005-1.8	138	0.000015-1.5	4	NR	32	NR
Rinse Off	10	0.1	29	0.0015-0.15	NR	NR	4	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	4	0.005-0.3	4	0.005-0.075	1	NR	1	NR
Incidental Ingestion	NR	NR	16	0.15	NR	NR	NR	NR
Incidental Inhalation-Spray	8 ^a ; 5 ^b	NR	7; 79 ^a ; 15 ^b	0.03; 0.03-0.038 ^a ; 0.03 ^b	3 ^b	NR	12; 5 ^a ; 14 ^b	NR
Incidental Inhalation-Powder	5 ^b	0.005 ^c	15 ^b ; 2 ^c	0.015; 0.03 ^b ; 0.001-1.5 ^c	3 ^b	NR	14 ^b	NR
Dermal Contact	20	0.005-1.8	148	0.000015-1.5	4	NR	36	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	10	NR	3	0.0015-0.038	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	35	0.15	NR	NR	NR	NR
Baby Products	NR	NR	2	NR	NR	NR	NR	NR
	Hordeum Vulgare Seed Flour*							
Totals†	2	NR						
Duration of Use								
Leave-On	1	NR						
Rinse Off	1	NR						
Diluted for (Bath) Use	NR	NR						
Exposure Type								
Eye Area	NR	NR						
Incidental Ingestion	NR	NR						
Incidental Inhalation-Spray	NR	NR						
Incidental Inhalation-Powder	NR	NR						
Dermal Contact	2	NR						
Deodorant (underarm)	NR	NR						
Hair - Non-Coloring	NR	NR						
Hair-Coloring	NR	NR						
Nail	NR	NR						
Mucous Membrane	NR	NR						
Baby Products	NR	NR						

NR = Not reported

[†] 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.

* Includes one use in the VCRP data that was listed generically as barley flour and did not distinguish species.

^a. It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.

^b. Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

^c. It is possible these products may be powders, but it is not specified whether the reported uses are powders.

Table 6. Ingredients not reported in use.⁴²⁻⁴⁴

Hordeum Distichon (Barley) Seed Flour
 Hordeum Vulgare Flower/Leaf/Stem Juice
 Hordeum Vulgare Juice
 Hordeum Vulgare Leaf Juice
 Hordeum Vulgare Leaf Powder
 Hordeum Vulgare Leaf/Stem Powder
 Hordeum Vulgare Powder
 Hordeum Vulgare Root Extract
 Hordeum Vulgare Seed Water
 Hordeum Vulgare Sprout Extract
 Hordeum Vulgare Stem Water

Table 7. Dermal irritation and sensitization studies for barley-derived ingredients.

Test Article	Dose	Test Population	Procedure	Results	Reference
IRRITATION					
HUMAN					
Mascara containing 0.3% Hordeum Distichon (Barley) Extract	0.05 ml applied	25 subjects	14-d cumulative irritation assay; test article applied via occlusive patches to the same site on the upper back; patches were 15 mm diameter Webril™ discs; 0.25% sodium lauryl sulfate and a plain Webril cotton were positive and negative controls, respectively; a comparator mascara product was also tested	Test product had “negligible” irritation potential; mean cumulative irritation score was 0.24 and the cumulative irritation index was 0.01; no adverse effects of any kind were observed	⁶⁴
Product containing 0.005% Hordeum Vulgare Extract	Amount applied not reported	20 subjects	48-h patch test; test article applied via occlusive patches on back; test sites examined at 15 min and 24 h post-patch removal; use of controls not reported	Not irritating; 2 subjects had an erythema score of 1 at 15 min, with 1 subject continuing with the same score at 24 h; average irritation index was 0.1 at 15 min and 0.05 at 24 h	⁶⁵
SENSITIZATION					
HUMAN					
Mascara containing 0.3% Hordeum Distichon (Barley) Extract	0.05-0.10 g	111 subjects	HRIPT; test article applied via occlusive Webril™ patches; 9 induction patches were completed over a 3-wk period and followed by a 2-wk rest period; challenge patches on previously untested sites were read 24, 48, 72, and 96 h after application	Not sensitizing; 1 subject in the induction phase and 4 other subjects in the challenge phase exhibited low-level (±) reactions	⁶⁵
Lotion containing 1.8% Hordeum Distichon (Barley) Extract	Amount applied not reported	102 subjects	HRIPT conducted in a similar manner as described above; semi-occlusive patch on the upper back	Not a dermal sensitizer, but slight potential for eliciting dermal irritation; erythema noted during induction in several subjects and in 2 subjects during challenge phase	⁶⁶
Eye cream containing 1.8% Hordeum Distichon (Barley) Extract	0.2 ml	54 subjects	HRIPT conducted in a similar manner as described above; occlusive 2 cm ² Parke-Davis Readi-Bandage®	Not irritating or sensitizing; transient, barely perceptible (0.5 level) patch responses in 10 subjects observed during either the induction or challenge phases, reactions were considered neither evidence of clinically meaningful irritation nor allergic in nature	⁶⁷

Table 7. Dermal irritation and sensitization studies for barley-derived ingredients.

Test Article	Dose	Test Population	Procedure	Results	Reference
Facial moisturizer containing 2.76% Hordeum Distichon (Barley) Extract	0.1-0.15 g (25-38 mg/cm ²)	49 subjects	HRIPT conducted in a similar manner as described above; occlusive Parke-Davis Read-Bandage® patches	Not irritating or sensitizing; one subject had mild-moderate reactions during the first 3 induction patches and during challenge up to 144 h after application, response by subject was determined to be idiosyncratic and may have been due to prior exposure/sensitization to one or more components of the test material	⁶⁸
Facial moisturizer containing 0.005% Hordeum Vulgare Extract	0.2 g	101 subjects	HRIPT conducted in a similar manner as described above; semi-occlusive 2 cm ² Webril™ patches	Not irritating or sensitizing; total irritation score at induction was 0	⁷¹
Facial mask containing 0.005% Hordeum Vulgare Extract	0.2 g	110 subjects	HRIPT conducted in a similar manner as described above; semi-occlusive 2.54 cm ² patch	Not irritating or sensitizing	⁷²
Pressed powder containing 0.005% Hordeum Vulgare Extract	Amount applied not reported; however, patches were moistened with several drop of water to ensure adherence of test material	107 subjects	HRIPT conducted in a similar manner as described above; semi-occlusive patches	Not a dermal irritant or sensitizer	⁶⁹
Skin serum formulation containing 0.1% Hordeum Vulgare Seed Extract	Amount applied not reported	50 subjects	HRIPT conducted in a similar manner as described above; occlusive patches	Not a dermal irritant or sensitizer; no adverse reactions were induced	⁷⁰

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