Safety Assessment of Avena Sativa-Derived Ingredients as Used in Cosmetics

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on this Scientific Literature Review and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a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

The 2014 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Ronald A Hill, Ph.D. James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is Lillian J. Gill, D.P.A. This report was prepared by Lillian C. Becker, Scientific Analyst/Writer.

1620 L Street, NW, Suite 1200 ♢ Washington, DC 20036-4702 ♢ ph 202.331.0651 ♢ fax 202.331.0088 ♢ cirinfo@cir-safety.org

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INTRODUCTION

This is a review of the available scientific literature and unpublished data provided by industry relevant to assessing the safety of *Avena sativa* (oat)-derived ingredients as used in cosmetics. The functions in cosmetics of these ingredients include: abrasives, antioxidant, skin-conditioning agents, absorbents, and bulking agents. The 18 ingredients included in this report are:

- Avena sativa (oat) bran
- Avena sativa (oat) bran extract
- Avena sativa (oat) flower/leaf/stem juice
- Avena sativa (oat) kernel extract
- Avena sativa (oat) kernel flour
- Avena sativa (oat) kernel meal
- Avena sativa (oat) kernel oil
- Avena sativa (oat) kernel protein
- Avena sativa (oat) leaf extract
- Avena sativa (oat) leaf/stalk extract
- Avena sativa (oat) leaf/stem extract
- Avena sativa (oat) meal extract
- Avena sativa (oat) meristem cell extract
- Avena sativa (oat) peptide
- Avena sativa (oat) protein extract
- Avena sativa (oat) seed water
- Avena sativa (oat) sprout oil
- Avena sativa (oat) starch
- Avena sativa (oat) straw extract

This safety assessment does not include colloidal oatmeal. Colloidal oatmeal is defined as finely ground oatmeal.[1] The definition of this ingredient does not specify the species of oat from which it is derived. Therefore, any oat species (i.e., *A. abyssinica*, *A. byzantine*, *A. nuda*, and *A. strigosa*) may be used. However, data on colloidal oatmeal that specifies that it is derived from *A. sativa* are included in this safety assessment for read across purposes.

CHEMISTRY

Definition and Description

The definitions and functions of *avena sativa*-derived ingredients are provided in Table 1.

A. sativa is a member of the Gramineae (grass) family.[2] The plant is an annual grass that grows up to 1.5 meters high. The stems may be tufted or solitary, erect or bent at the base, and smooth. The leaves are non-auriculate, green and the sheaths rounded on the back. The cluster of flowers is a diffuse panicle with 2 – 3 florets which are either all bisexual or the distal one or two may be reduced and male or sterile. The grain is tightly enclosed by the hard lemma and palea. The seed size varies with cultivar and commonly yields approximately 30 000 seeds per kilogram.

CONSTITUENTS

Constituent groups found in *A. sativa* include:

Amino acids - Oats are rich in the limiting amino acid lysine, approximately 4%.[3] L-Threonine has also been identified.

Avenanthramides – Soluble, phenolic compounds are a minor component of *A. sativa* (0.03% by weight).[4,5] They have powerful anti-oxidative activity. They also have anti-inflammatory properties.[6]

Enzymes – The enzymes found in *A. sativa* include lipase, lipoxygenase, and superoxide dismutase.[7,8]

Flavanoids – The following flavonoids have been isolated in A. sativa bran: kaempferol 3-O-(2",3"-di-E-p-coumaroyl)-α-L-rhamnopyranoside; kaempferol 3-O-(3"-E-p-coumaroyl)-α-L-rhamnopyranoside; kaempferol 3-O-(2"-O-E-p-coumaroyl)-β-D-glucopyranoside; kaempferol 3-O-β-D-glucopyranoside; kaempferol 7-O-α-L-rhamnopyranoside; linarin; tilianin; myricitrin; quercitrin; kaempferol 3-O-rutinoside; rutin; tricin 7-O-β-D-glucopyranoside; tricin; kaempferol; and luteolin.[9]

The total flavonoid content of the n-hexane extract of an *A. sativa* whole plant extract is 40.72 ± 4.81 mg/g, 77.59 ± 6.71 mg/g for an ethyl acetate extract.[10] No flavonoids were detected in an ethanol or a water extract.

Lipids – *A. sativa* contain higher levels of lipids, particularly those containing a high-content of unsaturated fatty acids, than other cereal type grains. The most abundant lipids are unsaturated triglycerides.[11,12] The lipid content depends on genetic and environmental factors; the method extraction and analysis and also result in differences in lipid content.

A. sativa starches contain lipids ranging from 1% to 3%, present in the starch possibly as an amylose–lipid complexes.[12]

Phenolic compounds – At various growth stages, *A. sativa* has been found to contain a large number of phenolic compounds including all major classes: benzoic and cinnamic acids, quinones, flavones, flavonols, chalcones, flavanones, anthocyanidines, and aminophenolics.[13] *A. sativa* oat flour contains the glyceryl esters of hydroxycinnamic, ferulic, *p*-coumaric, and caffeic acids.[14] Antioxidant activity is attributed to the presence of phenolic esters.[13,15] *A sativa* also contains various compounds with antioxidant activity that protect the lipids from oxidation.[13] One type of phenolic compound, called avenanthramides are found in oat extracts.[16]

The total phenol content of the n-hexane extract of an *A. sativa* whole plant extract is 26.10 ± 2.31 mg/g, 75.79 ± 4.02 mg/g for an ethyl acetate extract, 39.34 ± 0.78 mg/g for an ethanol extract, and 46.02 ± 0.07 mg/g for a water extract.[10]

Polysaccharides – these include starches and β-glucan.[17,18] Carbohydrates mostly consist of araban and xylan gums.[19]

Proteins – *A. sativa* has a high level of total proteins compared other grasses.[20]

Vitamins and minerals – *A. sativa* contains a variety of minerals and vitamins.[21] These include vitamin E, mostly as α-tocopherol.[8,20]

STEM AND LEAVES

The stem and leaves are rich in apigenin and luteolin flavonoids (i.e., C-glycosylflavones), tricin flavones, and flavonolignans. They also contain bidesmosidic steroidal saponins (e.g., avenacosides A and B), proteins (in particular, membrane proteins and soluble proteins of chloroplasts), and various phenolic compounds (e.g., avenanthramides).[22-25]

CONSTITUENTS OF CONCERN

Quercitrin – Quercetin has been reported to be in the hay of *A. sativa*. This constituent was positive for genotoxic effect in an Ames assay.[26] It is also consistently genotoxic in in vitro tests and in some in vivo studies of i.p. exposures, but was consistently nongenotoxic in oral exposure studies using mice and rats.[27]

Physical and Chemical Properties

The flavonoids with phenolic structures have strong absorption of ultra violet A (UVA) in the 320 to 370 nm range.[13] Other phenolic esters, called avenacins (saponins structurally), have also been isolated.

Method of Manufacture

To produce extracts (information was unclear on the type of extract, e.g., not clear if this would be avena sativa (oat) leaf extract, avena sativa (oat) leaf/stalk extract, and/or avena sativa (oat) leaf/stem extract) without detectable proteins, young (prior to earing) *A. sativa* plants are dried and crushed.[28] An extraction is performed under stirring for 1 hour. The extract is filtered and the residue is rinsed. The filtrate is then concentrated, delipidated, and dried. This yields an extract in powder form containing 2% to 15% flavonoids, and 0.2% to 2% avenacosides A and B.

Impurities

There were no detectable proteins (limit of detection for the enzyme-linked immunoassay [ELISA] technique less than 0.5 ppm of protein) in an extract of young *A. sativa* plants.[28]

Fusarium avenaceum , *Pseudodiscosia avenae* and *Sclerospora macrospora* are among the species of fungi known to infect oat plants, including *A. sativa* (Table 2).[3]

Two of five oat-based cereals tested positive for the micotoxin deoxynivalenol (DON) at 2.6 and 1.3 µg/g.[29] Three of these products tested positive for zearalenone (ZEA) at an average of 16 ng/g. Aflatoxin B_1 (AFB_1) was not detected in these samples.

The micotoxins DON, 3-acetyl DON (3AcDON), nivalenol, neosolaniol, T-2 triol, T-2 toxin, and HT-2 toxin (HT-2) were detected in samples of recently harvested oats (species/varieties not provided).[30] Samples were made from both conventional and organic farms.

ZEA (17%), DON (17%), and OTA (20%) were detected in *A. sativa* bran samples (n = 30) collected from grocery stores and health food stores in Spain.[31]

Oat straw bedding contaminated with *Fusarium sporotrichiodes*, a toxic mold, was the cause of raised, plaque-like and cracked skin lesions on the udders, hind quarters, lips, and muzzles of cows when the straw was used as bedding.[32]

Cadmium content in fresh *A. sativia* grown in Finland ranged from 0.008 to 0.120 mg/kg dry weight.[33] There was no difference between conventionally and organically grown crops. Nitrogen fertilization increased cadmium content. Cadmium content may vary by strain and may exceed safe levels.[34] The safe level set by the European Commission is 0.1 mg/kg fresh mass.

USE

Cosmetic

Data on ingredient usage are provided to the Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP; Table 3).[35] A survey was conducted by the Personal Care Products Council (Council) of the maximum use concentrations for these ingredients.[36]

Ingredients that had both frequency and concentration of use data were:

Avena sativa (oat) bran was reported to be used in 18 leave-on and 18 rinse-off products including baby shampoos; baby lotions, oils powders, and creams; dentifrices, shaving cream; and personal cleanliness products. This ingredient was reported to be used up to 0.0072% in leave-on products and up to 2.5% in leave-on eye lotion.

Avena sativa (oat) bran extract was reported to be used in 5 leave-on products and 1 rinse-off product. This ingredient was reported to be used up to 0.2% in leave on face and neck products.

Avena sativa (oat) kernel extract was reported to be used in 352 leave-on products including eye and makeup products. It was also reported to be used in 81 rinse-off products and 2 products diluted for the bath. This ingredient was reported to be used up to 25% in leave-on products and up to 1% in leave-on products. There were no concentrations of use reported for products diluted for the bath.

Avena sativa (oat) kernel flour was reported to be used in 92 leave-on products, 37 rinse-off products, and 2 products diluted for the bath. This ingredient was reported to be used up to 20% in leave-on products (up to 20% in foundations) and up to 5% in rinse-off products (up to 5% in paste masks and mud packs).

Avena sativa (oat) kernel meal was reported to be used in 7 leave-on products, 15 rinse-off products, and 3 products diluted for the bath. This ingredient was reported to be used up to 1% in bath soaps and detergents.

Avena sativa (oat) kernel oil was reported to be used in 39 leave-on products, 5 rinse-off products, and 1 diluted for the bath. This ingredient was reported to be used up to 0.25% in leave-on products (up to 0.25% in body and hand products) and up to 0.45% in bath soaps and detergents.

Avena sativa (oat) kernel protein was reported to be used in 24 leave-on products and 8 rinse-off products. This ingredient was reported to be used up to 0.001% in leave-on products (up to 0.001% in hair conditioners and pump hair sprays) and up to 5.2% 5.2% in bath soaps and detergents.

Avena sativa (oat) meal extract was reported to be used in 13 leave-on products and in 11 rinse-off products. This ingredient was reported to be used up to 0.0025% in leave-on products including body and products and moisturizing products. It was also reported to be used up to 0.005% in rinse-off products, and up to 0.005% products diluted for the bath.

Avena sativa (oat) peptide was reported to be used in 2 leave-on products and 3rinse-off products. It was reported to be used up to 0.33% in leave-on products and up to 0.013% in rinse-off products.

Avena sativa (oat) protein extract was reported to be used in 2 leave-on and 2 rinse-off products. This ingredient was reported to be used up to 1.5% in skin cleansing products.

Avena sativa (oat) straw extract was reported to be used in 1 moisturizing product. It was reported to be used in body and hand products up to 0.001%.

Frequency of use data only were available for:
Avena sativa (oat) starch was reported to be used in 4 leave-on products and 2 rinse-off products.

There were no reported uses for:
Avena sativa (oat) flower/leaf/stem juice
Avena sativa (oat) leaf extract
Avena sativa (oat) leaf/stalk extract
Avena sativa (oat) leaf/stem extract
Avena sativa (oat) meristem cell extract
Avena sativa (oat) seed water
Avena sativa (oat) sprout oil

Non-Cosmetic

A. sativa-containing products are used as a moisturizer and to treat itchy skin due to dryness, chicken pox, poison ivy/oak/sumac, and insect bites.[37] It is also used to treat acne.

Colloidal oatmeal, including oatmeal derived from *A. sativa*, is used to treat atopic dermatitis and other inflammatory dermal diseases.[5] It is regulated for this use by the FDA as an over the counter drug, and can be included in tub baths at a minimum concentration of 0.007% if alone, or at a minimum concentration of 0.003% when combined with mineral oil (30%, 35%). The monograph defines a skin protectant as a "drug product that temporarily protects injured or exposed skin or mucous membrane surfaces from harmful or annoying stimuli, and may help provide relief to such surfaces.[68 FR 33362] Products that contain colloidal oatmeal may be used for temporary protection and relief from minor skin irritation and itching.[21 CFR347.10(f)] The oatmeal product may be used in the bath or as a compress or wet dressing (minimum of 0.25% colloidal oatmeal).[21 CFR347.10(o)]

Colloidal oatmeal, including that derived from *A. sativa*, is used in dermatological practice as an adjunctive therapy to treat many pruritic skin conditions such as cercarial dermatitis (swimmer's itch), chicken, pox, poison ivy, oak and sumac, insect bites, winter itch, atopic dermatitis, dry skin, allergic or irritant contact dermatitis, and ichthyosis.[38-43] Other indications for colloidal oatmeal products include prickly heat, hives, sunburn and rashes.

TOXICOKINETICS

There were no data discovered or submitted on the toxicokinetics of the constituents of A. sativa *ingredients.*

Estrogenic Activity

When 23-24-day-old female rats (n = 5-10) were subcutaneously injected with avena sativa hay extract (0.15 mL in olive oil) and 0.05 µg estradiol, uterine weights were greater than in the rats injected with estradiol alone.[44] This result was

true when the solvent was ether, the chloroform extract fraction of the ether extract, or the fraction obtained from an alumina column of the ether extract using chloroform.

Overview of Dermal Effects

The dermal effects of colloidal oatmeal derived from *A. sativa* have been attributed to the anti-inflammatory and antipruritic properties of avenanthramides. This constituent has been shown to reduce oxazolone-induced contact hypersensitivity, resiniferatoxin-induced neurogenic inflammation, and induced histamine-mediated itch.[45] In vitro, avenanthramides reduced histamine release from mast cells stimulated by substance P. The buffering property of colloidal oatmeal, important for preservation of skin barrier function was shown when treatment with colloidal oatmeal reduced the elevated pH of pathologic skin (e.g., eczematous or pruritic) or alkali-treated skin to within the normal range. Other skin barrier effects include the formation of a protective moisturizing barrier by the proteins and polysaccharides in colloidal oatmeal, reducing transepidermal water loss (TEWL). Colloidal oatmeal has also been shown to act as an emollient, humectant and occlusive.[46] The application of *A. sativa* extracts to sodium lauryl sulfate (SLS)-treated skin has been shown to reduce irritation compared to vehicle demonstrating the anti-inflammatory effects of oats and suggesting potential benefits for the skin barrier as well.[47] It has been reported that *A. sativa* extracts inhibited the phospholipase A2 (PLA2)-dependent mobilization of arachidonic acid from phospholipids in cultured human keratinocytes.[48] This extract also inhibited the formation of eicosanoids, expression of cytosolic phospholipase PLA2 and formation of metabolites of rostacyclin, all of which are implicated in the regulation of inflammation. In a separate study, an *A. sativa* extract oligomer reduced vasodilation induced by vasoactive intestinal peptide in human skin samples.[49] Treatment with the oligomer reduced edema and mean surface of dilated vessels. It has also been reported that colloidal oat extracts (ethanol and phosphate buffer) had inhibitory activity toward prostaglandin synthase of bull seminal vesicles.[50]

Dermal Effects

In Vitro

When fibroblast cells obtained from cosmetic surgery were incubated with *A. sativa* whole young plant extract (0.05%), there was increase proliferation of cells and an extension of a neoepithelium.[51] There were no differences in the number of basal layers up to day 20, and then there were more layers on day 22. A dermal equivalent was created in a petri dish by combining dermal fibroblasts with collagen type I. A punch biopsy from skin left over from surgery was used as a source of epidermal cells which were implanted on the dermal equivalent, where a multilayered epidermis developed.

In Vivo

AVENA SATIVA WHOLE PLANT EXTRACT

In a wound-healing experiment using the *n*-hexane, ethyl acetate, ethanol, and water extracts of whole *A. sativa* plants, there were no adverse effects to Sprague-Dawley rats (n = 6+) and Swiss albino mice (n = 6+) when the extracts (1%, 0.5 g in an ointment base) were administered to wounds daily for 9 days.[10] The ethanol extract increased wound healing activity, the other extracts did not.

The rats and mice were anesthetized and either two incisions along either side of the backbone or a biopsy punch were performed. The extracts were administered to the wounds once per day for 9 days. The rats and mice were killed and the wounds excised. The healing of the incision was measured by tensile strength across the wound and the healing of the punch was measured by area of healing.[10]

COLLOIDAL OATMEAL

In a blind study of acute burn patients (n = 35), a shower/bath oil containing colloidal oatmeal (5% in liquid paraffin), reported no adverse effects.[52] The group using colloidal oatmeal had a reduction in itch compared to the group using paraffin oil alone. The subjects showered or bathed with the test material or the same product without the colloidal oatmeal for 30 days.

Complete or marked itch relief was reported by over 71% of subjects (n = 139; aged 21 to 91) suffering from various pruritic dermatoses when colloidal oatmeal was used as a bath and regular cleanser for 3 months.[41]

Pediatric subjects (n = 152) presenting with atopic dermatitis, contact dermatitis, fungus infections, or seborrheic dermatitis who were administered baths with colloidal oatmeal in an oil showed improved soothing and cleansing with no irritation compared to standard therapy.[39]

TOXICOLOGICAL STUDIES

No acute or repeated dose toxicity studies were discovered or submitted.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

No published reproductive or developmental toxicity studies were discovered and no unpublished data were submitted.

GENOTOXICITY

No published genotoxicity studies were discovered and no unpublished data were submitted.

CARCINOGENICITY

No published carcinogenicity studies were discovered and no unpublished data were submitted.

IRRITATION AND SENSITIZATION

Irritation

Dermal – Human

When a cream containing an extract of young *A. sativa* plants (information not clear on the type of extract, e.g., avena sativa (oat) leaf extract, avena sativa (oat) leaf/stalk extract, and/or avena sativa (oat) leaf/stem extract; concentration and amount applied not provided) was administered to female subjects (n = 16) with dry skin, there were no signs of irritation.[28] The cream was administered to one or other elbow fold twice daily for 4 days, then once more on day 5. The cream was also applied to one side of the face once daily. Sixty-three percent of the subjects had sensitive skin and 81% had sensitive eyes.

In another study of the same product, no irritation was observed when the cream was administered to the stripped skin of subjects (n = 19). Both elbow folds were stripped 6 times and the test material administered 72 h later to one of the stripped sites. The test material was administered twice per day for 4 days and once on the fifth day. The sites were examined for erythema, pruritus, heat, tingling, and burning on days 4, 5, 6, and 7. All subjects exhibited moderate to intense erythema after stripping. There was no erythema observed in 14 subjects by day 4 and in no one by day 8. No patients experienced any subjective signs of a reaction.[28]

Sensitization

Dermal – Human

In a use study of a cream and soap containing an extract of young *A. sativa* plants using subjects (n = 8 females, 4 males) with a history of cereal-sensitized atopic dermatitis, none of the subjects developed immediate or delayed hypersensitivity to the products after using them for 45 days.[53] The extract is from entire young plants so it is not clear if this would be avena sativa (oat) leaf extract, avena sativa (oat) leaf/stalk extract, and/or avena sativa (oat) leaf/stem extract. The cream contained 12 % and the soap contained 3% of the extract. Before and after the use study, none of the subjects displayed positive reactions in patch tests and skin prick tests of five fractions of the extract used in the products or the study cream. Total serum *A.sativa* IgE analyzed before and after the use study did not change.

Before the experiment started, an open application test was conducted on all subjects. The *A. sativa* extracts (colloidal 5%, phenolic 5%, acetonic 5%, enzyme-hydrolyzed phenolic 5%, acetonic [sic] 5%) and the cream were administered to the forearm for 15 min and observed for a reaction.

The subjects used their own cream for 10 days, during which they were administered a patch test and a prick test, which was repeated after the use part of the experiment. The patch tests consisted of 2 sets of 3 negative controls (patch only, petrolatum, saline); 1 positive control (sodium lauryl sulfate, 0.5%); and 5 *A. sativa* extracts in 11 mm Finn chambers. One set of chambers was removed after 30 min and observed immediately. The second set was removed after 48 h and observed 30 min and 48 h later. The prick tests of the same test materials were administered to the anterior left forearm. The test sites were observed after 30 min.

Before and after the use experiment, total IgE and *A. sativa*-specific IgE were measured.

On the first day, the test cream was administered to one half of the subjects' bodies. The vehicle cream, without the *A. sativa* extract, was administered to the other half of the subjects' bodies. The subjects showered 4 h later using the test soap. The subjects then used the cream with the extract twice per day and showered with the soap once per day for 21 days.[53]

In a group of children (under 15 years of age) referred for allergy testing (n = 150 females, 152 males), 14.6% had positive results in a patch test of the *A. sativa* young plant extract described above (1%, 3%, 5%; Table 4).[54] Sixteen of 44 subjects tested positive at 5%, 6 for both 3% and 5%, and 22 for all three concentrations.

In a skin prick test of the same subjects, 19.2% had positive reactions to a standardized oat extract (solvents not provided). Sensitization was observed in a total of 32.5% of the subjects. Only four subjects tested positive in both tests. Sensitization decreased as age increased.

The authors concluded that the prevalence of sensitivity to *A. sativa* was higher than expected and could possibly be due to the prevalent use of cosmetics that contain some form of *A. sativa*. In a history survey of 67 of the subjects, there was no connection between sensitization and clinical signs (asthma, hay fever, atopic dermatitis severity); home location; proximity of cereal production; consumption of oats; skin prick test results to grass, cereal pollen or wheat pollen; or oat- or wheat-specific IgE. In the patch test, 100% of the subjects that had not used products containing *A. sativa* tested negative; only 66.7% of those that had used product containing *A. sativa* had negative results (p-value = 0.0068).[54]

There were no signs of irritation or sensitization in a human repeated insult patch test (HRIPT; n = 104) of a cream containing *A. sativa* (concentration not provided; 50 µL).[28] The test material was administered in a Finn chamber on days 1,

3, 5, 8, 10, 12, 15, 17, and 19 for 48 or 72 h. After 2 weeks, the challenge was left in place for 48 h on a naïve site.

COLLOIDAL OATMEAL

Children (n = 65; 6 months to 2 years) that were atopic or nonatopic with and without previous exposure to *A. sativa* colloidal oatmeal, did not show signs of immediate or urticarial or allergic reactions to two bath products containing *A. sativa* colloidal oatmeal at the expected use concentration (0.007% in water) or the elevated concentration (0.7% in water).[55] These subjects were also non-reactive to *A. sativa* colloidal oat flour (0.7%, 0.007% in water). The subjects were exposed to the bath products for 15 min. There were no reactions. Then a patch test using pairs of Finn chambers (50 µL) was conducted. One set of chambers was removed and observed after 24 h, the second after 48 h. Both sets were observed at 72 and 96 h.

Of children (n = 302) with atopic dermatitis, 14.6% and 19.2% tested positive in patch test and skin prick test for *A. sativa* colloidal oatmeal.[54] Of those sensitized, 15.6% (five of 32) and 28% (seven of 25) tested positive in an oral food challenge and a repeated open application test. Children with atopic dermatitis that were referred for allergy testing were administered patch tests and skin prick tests to oat proteins (1%, 3% and 5%) and the European standard series sensitization tests were performed. Subjects found to be sensitized to *A. sativa* colloidal oatmeal were administered an oral food challenge and repeated open application test. Children under 2 years of age were more likely to have positive patch test. Thirty-two percent that used *A. sativa* creams had oat-positive patch tests, while none of the nonusers were sensitized. The authors noted that A. sativa sensitization in children with atopic dermatitis was higher than expected. This may be the result of repeated applications of cosmetics containing A. sativa on a damaged epidermal barrier. The authors suggest that topical creams containing *A. sativa* proteins should be avoided in infants with atopic dermatitis.

Phototoxicity

A. sativa has been reported to cause photosensitization when consumed by cattle, goats, pigs, and sheep.[56]

CLINICAL USE

Case Studies

A 4-month old infant with atopic dermatitis and allergy to cow's milk tested positive in patch-tests (++) for the sensitization to oats and showed a sensitization to wheat, that the child had never ingested.[57] The authors suggested that in utero wheat sensitization cannot be eliminated but most likely, the infant developed a cross-sensitization to wheat after being sensitized by a cream containing oats (Aderma®). At 1 year old, the child had identical results for the patch-test to wheat and remained on an eviction diet.

Three children (14 months, 2 years, and 14 years) with atopic dermatitis had positive patch tests for oatmeal extract (species not provided).[58] The children all had histories of bathing with a product that contained an oatmeal extract. The eczema worsened after such baths. None of the subjects had a history of consuming oats.

A 3-year-old girl presented with an atopic dermatitis event on her arm and hands after using a moisturizer cream containing the young *A. sativa* plant extract mentioned earlier.[59] IgE levels were elevated and a standard prick test was positive for *Dermatophagoides farina* and *D. pteronyssinus*. The subject had a family and personal history of other atopic maladies such as hay fever and rhinitis. Standard patch testing was positive for the cream at days 2 and 3 (++, ++). She was patch tested further with the ingredients of the cream (provided by the manufacturer) and was positive for the plant extract at days 2 and 3 (++, ++) but not for the zinc oxide and Vaseline oil. The atopic dermatitis did not reoccur when she no longer used the product.

A 7-year-old girl presented with swollen lesions where an oat cream had been applied after bathing.[60] The lesions appeared 15 min after application. She had a history of IgE-mediated allergic rhinoconjunctivitis, allergic asthma, and atopic dermatitis syndrome from the age of 3. The lesions were only on the application sites and resolved in less than 1 h without treatment. Skin tests were positive for grass, rice and oat pollens, and were negative for the other pneumoallergens and foods. An open patch test was positive, and swollen lesions were apparent on the right forearm 10 min after the cream was administered which resolved 30 min after administration of oral cetirizine. The oat-specific IgE assay was positive, at 0.76 kU/1, and negative for the other cereals. The girl ate foods containing oats with no adverse effects.

A 33-year-old female presented with a persistent rash that had linear streaks of eczema, mostly on the forearm, the sides of her face and neck, and less so on her waist and ankles.[61] The rash started 3 weeks after beginning a job weighing bird feeds that included oats. Patch test of the seeds had a ++ reaction to crushed oats at 48 h and + at 96 h. She also had a ++ reaction to bran at 96 h. The rash resolved when the subject avoided working with oats and bran. The rash reoccurred when she measured out oats and bran on two occasions.

A 33-year-old woman presented with atopic eczema and allergic rhinoconjunctivitis.[62] She had a history of type 1 hyersensitivity reactions to dust mites, cats, dogs, malassezia, nuts, shrimp, lobster, and asparagus. She had used a moisturizer made for atopic and very dry skin that contained *A. sativa* extract for 1 year. The reaction began to appear approximately 6 months after she began using the moisturizer. The reaction faded a few hours after application. The subject noted that she experienced itching and swelling of the lips and pruritic, erythematous papules and patchy lesions on her trunk after eating breads containing oatmeal.

The patch test of the moisturizer was negative but the prick test was positive. Her total IgE was slightly elevated.

Further analysis of her serum revealed immunoreactivity to a "casual" *A. sativa* extract but not another *A. sativa* extract with the proteins removed. The sera of three other cereal-sensitized subjects were tested with five different *A. sativa* extracts, one without proteins. Two subjects reacted to all of the extracts; the third did not react to any.[62]

SUMMARY

This is a safety assessment of *A. sativa*-derived cosmetic ingredients. These ingredients function as abrasives, antioxidant, skin-conditioning agents, absorbents, and bulking agents. This report does not include colloidal oatmeal as the definition does not restrict the species of oats used.

Multiple fungi and their toxins have been reported in the plant, seed, dried hay, and/or in processed oat cereals.

These ingredients are used up to 25% in leave-on products and up to 5.2% in rinse-off products. Avena sativa (oat) kernel extract has the most reported uses at 436 up to 25%. Avena sativa (oat) kernel flour is used in 131 cosmetic products up to 20%.

Dermal anti-inflammatory and buffering effects have been attributed to *A. sativa*. Dermal cells incubated in an extract of the whole plant of *A. sativa* had increase proliferation. Dermal administration of a whole plant ethanol extract of *A. sativa* increased wound healing activity in rats and mice. There were no adverse effects when products containing colloidal oatmeal were used on subjects with damaged skin.

Creams containing an extract of the entire young *A. sativa* plant were not irritating when administered to the intact and stripped skin of human subjects for up to 5 days.

The use of a cream and soap containing the extract of young *A. sativa* plants (12%, and 3%, respectively) for 45 days did not result in hypersensitivity. In a patch test of children referred for allergy testing, 14.6% tested positive for a young plant extract of *A. sativa* at 1%, 3% or 5%. In a skin prick test of the same subjects, 19.2% had positive reactions. An HRIPT of a cream containing an extract of the entire *A. sativa* plant was negative in 104 subjects.

Two bath products containing *A. sativa* colloidal oatmeal did not show signs of immediate or urticarial or allergic reactions when tested on children with and without atopic dermatitis. Of a group of children with atopic dermatitis, 14.6% and 19.2% tested positive in patch test and skin prick test for *A. sativa* colloidal oatmeal.

There are several reported cases of atopic dermatitis as a result of using products containing *A. sativa* ingredients.

DATA NEEDS

The CIR staff requests the following data and any other data that would be informative to this report:

- Characterization of all the ingredients in this report
- Method of manufacture for all ingredients except whole plant extract
- Reproductive and developmental toxicity studies
- Genotoxicity studies
- Carcinogenicity studies
- Irritation/sensitization studies for the avena sativa (oat) kernel protein, meristem cell extract, peptide, protein extract, and straw extract
- Phototoxicity studies

TABLES AND FIGURES

Table 1. Definition and function of avena stavia-derived ingredients.[1]

Ingredient	Definition	Function
Avena sativa (oat) bran	The broken coat of the kernels of oats, *Avena sativa*.	Abrasive, absorbent, bulking agent
Avena sativa (oat) bran extract	The extract of the bran of *Avena sativa*	Skin-conditioning agents – miscellaneous
Avena sativa (oat) flower/leaf/stem juice	The juice expressed from the flowers, leaves and stems of *Avena sativa*.	Skin-conditioning agents – miscellaneous
Avena sativa (oat) kernel extract 84012-26-0	The extract of the kernels of *Avena sativa*.	Antioxidant; skin-conditioning agent – emollient; skin-conditioning agent – miscellaneous
Avena sativa (oat) kernel flour 134134-86-4	A powder obtained by the fine grinding of the kernels of oats, *Avena sativa*.	Abrasive, absorbent, bulking agent; viscosity increasing agent – aqueous
Avena sativa (oat) kernel meal	A coarse meal obtained by the grinding of the kernels of oats, *Avena sativa*	Abrasive, absorbent, bulking agent
Avena sativa (oat) kernel oil	The fixed oil expressed from the kernels of the oat, *Avena sativa*.	Skin-conditioning agent – occlusive
Avena sativa (oat) kernel protein	A protein obtained from the kernels of oats, *Avena sativa*.	Film former; hair conditioning agent; skin-conditioning agent – miscellaneous
Avena sativa (oat) leaf extract	The extract of the leaves of *Avena sativa*.	Cosmetic astringent
Avena sativa (oat) leaf/stalk extract	The extract of the leaves and stalks of *Avena sativa*.	Skin-conditioning agent – miscellaneous
Avena sativa (oat) leaf/stem extract	The extract of leaves and stems of *Avena sativa*.	Skin-conditioning agent – miscellaneous
Avena sativa (oat) meal extract	The extract of the meal of *Avena sativa*.	Skin-conditioning agent – miscellaneous
Avena sativa (oat) meristem cell extract	The extract of the cultured meristem cells of *Avena sativa*.	Skin-conditioning agent – humectant
Avena sativa (oat) peptide 151661-87-9	The peptide fraction isolated from Avena Sativa (Oat) Protein Extract by ultra-membrane filtration.	Film former; hair conditioning agent; skin-conditioning agent – miscellaneous
Avena sativa (oat) protein extract	The extract of Avena Sativa (Oat) Kernel Protein.	Skin-conditioning agent – miscellaneous
Avena sativa (oat) seed water	An aqueous solution of the steam distillates obtained from the seeds of *Avena sativa*	Solvent
Avena sativa (oat) sprout oil	The oil obtained from the sprouts of *Avena sativa*.	Skin-conditioning agent – miscellaneous
Avena sativa (oat) starch 9005-25-8 (generic)	A starch obtained from oats, *Avena sativa*.	Absorbent
Avena sativa (oat) straw extract	The extract of the straw of *Avena sativa*.	Skin-conditioning agent – miscellaneous

Table 2. Fungi that are known to attack *A. sativa*.[3]

Alternaria sp.	*Aphanomyces camptostylus*	*Ascochyta graminicola*	*Botrytis cinerea*
Cercosporella herpotrichoides (resistant)	*Cladosporium graminum*	*Claviceps purpurea* (Ergot)	*Colletotrichum graminicola*
Erysiphe graminis	*Fusarium avenaceum*	*F. culmorum*	*F. graminearum*
F. moniliforme	*F. oxysporum*	*F. pose*	*F. roseum*
F. scirpi	*Fusicladium destruens*	*Giberella zeae*	*Helminthosporium avenae* (Stripe disease)
H. sativum	*H. victoriae*	*Heterosporium avenae*	*Leptosphaeria avenaria*
Marasmius tritici	*Pholiota praecox*	*Phyllosticta avenophila*	*Polymyxa graminis*
Pseudodiscosia avenae	*P. striaefaciens*	*Puccinia coronate*	*P. graminis*
P. rubigo-vera	*Pyrenochaeta terestris*	*Pyrenophora avenae*	*Pythium debaryanum*
P. aristosporum	*P. irregulare*	*P. rostratum*	*P. ultimum*
Rhizoctonia solani	*Sclerospora macrospora*	*Sclerotium rolfsii*	*Scoloectrichum graminis*
Septoria tritici	*Ustilago avenae* (Loose smut)	*Wojnowicia graminis*.	

Table 3. Frequency of use according to duration and exposure of *A. sativa*-derived ingredients. The Council conducted a survey or the concentration of use for the ingredients added to this report.

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Avena sativa (oat) bran		**Avena sativa (oat) bran extract**		**Avena sativa (oat) flower/leaf/stem juice**		**Avena sativa (oat) kernel extract**	
Total/range	**36**	**0.0072-2.5**	8	**0.2**	NR	NR	436	**0.00001-25**
Duration of use								
Leave-on	18	0.0072	5	0.2	NR	NR	352	0.000016-25
Rinse-off	18	2.5	1	NR	NR	NR	81	0.00001-1
Diluted for (bath) use	NR	NR	2	NR	NR	NR	2	NR
Exposure type								
Eye area	NR	0.0072	NR	NR	NR	NR	30	0.00006-0.13
Incidental ingestion	2	NR	NR	NR	NR	NR	NR	0.24
Incidental Inhalation-sprays	11	NR	4	NR	NR	NR	296	0.0006-0.14[a]; 0.0025[b]; 0.000016-25[c]
Incidental inhalation-powders	16	NR	4	NR	NR	NR	297	0.005-0.14d; 5[e]; 0.000016-25[f]
Dermal contact	28	0.0072-2.5	8	0.2	NR	NR	414	0.000016-25
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	6	NR	NR	NR	NR	NR	20	0.00001-0.05
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	0.00006
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	7	2.5	2	NR	NR	NR	25	0.0051-1
Baby	11	NR	NR	NR	NR	NR	10	NR

Table 3. Frequency of use according to duration and exposure of *A. sativa*-derived ingredients. The Council conducted a survey or the concentration of use for the ingredients added to this report.

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Avena sativa (oat) kernel flour		**Avena sativa (oat) kernel meal**		**Avena sativa (oat) kernel oil**		**Avena sativa (oat) kernel protein**	
Total/range	**131**	**0.001-20**	**25**	**1**	**35**	**0.001-0.45**	**32**	**0.001-5.2**
Duration of use								
Leave-on	92	0.01-20	7	NR	39	0.001-0.25	24	0.001
Rinse-off	37	0.1-5	15	1	5	0.45	8	0.001-5.2
Diluted for (bath) use	2	NR	3	NR	1	NR	NR	NR
Exposure type								
Eye area	NR	NR	NR	NR	NR	NR	4	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR	NR	
Incidental Inhalation-sprays	40	0.01-3[a]; 0.01-1[c]	5	NR	23	NR	19	0.001[b,g]
Incidental inhalation-powders	66	NR	4	NR	27	NR	18	NR
Dermal contact	122	0.01-20	25	1	33	0.001-0.45	26	5.2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	9	0.001-3.2	NR	NR	2	NR	6	0.001
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	14	NR	12	1	3	0.45	2	5.2
Baby	7	NR	NR	NR	7	NR	NR	NR

	Avena sativa (oat) leaf extract		**Avena sativa (oat) leaf/stalk extract**		**Avena sativa (oat) leaf/stem extract**		**Avena sativa (oat) meal extract**	
Total/range	**1**	NR	**NR**	NR	**NR**	NR	**24**	**0.0001-0.005**
Duration of use								
Leave-on	1	NR	NR	NR	NR	NR	13	0.001-0.0025
Rinse-off	NR	NR	NR	NR	NR	NR	11	0.0001-0.005
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	0.005
Exposure type								
Eye area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-sprays	1	NR	NR	NR	NR	NR	12	NR
Incidental inhalation-powders	1	NR	NR	NR	NR	NR	12	NR
Dermal contact	1	NR	NR	NR	NR	NR	22	0.0001-0.005
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	NR	NR	NR	NR	NR	NR	2	NR
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	6	0.001-0.005
Baby	NR	NR	NR	NR	NR	NR	NR	NR

Table 3. Frequency of use according to duration and exposure of *A. sativa*-derived ingredients. The Council conducted a survey or the concentration of use for the ingredients added to this report.

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Avena sativa (oat) meristem cell extract		**Avena sativa (oat) peptide**		**Avena sativa (oat) protein extract**		**Avena sativa (oat) seed water**	
Total/range	**NR**	NR	**5**	**0.0026-0.33**	**4**	**1.5**	**NR**	NR
Duration of use								
Leave-on	NR	NR	2	0.013-0.33	2	1.5	NR	NR
Rinse-off	NR	NR	3	0.0026-0.013	2	NR	NR	NR
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure type								
Eye area	NR	NR	1	0.33	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-sprays	NR	NR	1	0.013[a]; 0.013-0.22[c]	2	1.5[a]	NR	NR
Incidental inhalation-powders	NR	NR	NR	NR	2	NR	NR	NR
Dermal contact	NR	NR	3	0.013-0.33	4	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	NR	NR	2	NR	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	NR	NR	NR	NR	NR	NR
Baby	NR	NR	NR	NR	NR	NR	NR	NR

	Avena sativa (oat) sprout oil		**Avena sativa (oat) starch**		**Avena sativa (oat) straw extract**		
Total/range	**NR**	NR	**6**	NR	**1**	**0.001**	
Duration of use							
Leave-on	NR	NR	4	NR	1	0.001	
Rinse-off	NR	NR	2	NR	NR	NR	
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	
Exposure type							
Eye area	NR	NR	NR	NR	NR	NR	
Incidental ingestion	NR	NR	NR	NR	NR	NR	
Incidental Inhalation-sprays	NR	NR	3	NR	1	NR	
Incidental inhalation-powders	NR	NR	4	NR	1	NR	
Dermal contact	NR	NR	6	NR	NR	0.001	
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	
Hair-noncoloring	NR	NR	NR	NR	NR	NR	
Hair-coloring	NR	NR	NR	NR	NR	NR	
Nail	NR	NR	NR	NR	NR	NR	
Mucous Membrane	NR	NR	NR	NR	NR	NR	
Baby	NR	NR	NR	NR	NR	NR	

NR = Not Reported; NS = Not Surveyed; 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] Product(s) may or may not be a spray

[b] Spray product(s)

[c] Not spray product(s)

[d] Product(s) may or may not be a powder

[e] Powder product(s)

[f] Not powder product(s)

[g] Pump spray

Table 4. Results of atopy patch test and skin prick test of *A. sativa* extracts on children under 15 years old.

Test	0–2 (n = 55)	2–6 (n = 160)	6–15 (n = 87)	Total (n = 302)
APT+ SPT-	24	13	3	40 (13.2%)
APT- SPT+	0	31	23	54 (17.8%)
APT- SPT-	30	114	60	204 (67.5%)
APT+ SPT+	1	2	1	4 (1.5%)
APT +	25 (45.5%)	15 (9.3%)	4 (4.6%)	
SPT +	1 (1.8%)	33 (20.6%)	24 (27.6%)	

APT – atopy patch test. STP – Skin prick test

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