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

Status: Draft Report for Panel Review
Release Date: March 14, 2014
Panel Meeting Date: June 9-10, 2014

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.

MEMORANDUM

To: CIR Expert Panel and Liaisons

From: Lillian C. Becker, M.S.
Scientific Analyst and Writer

Date: May 16, 2014

Subject: *Avena sativa*-Derived Ingredients as Used in Cosmetics

Attached is the draft report of *Avena sativa* (oat)-derived ingredients. This report does not include colloidal oatmeal because the definition does not restrict the source oats to the *A. sativa* species. However, if it was confirmed that the source plant was *A. sativa* for a tested colloidal oatmeal, the data was included in the report for the Panel's information.

The kernel oil was originally included in this report for the SLR. Since it was included in the plant-derived fatty acid oils report (2011) it was removed.

The Personal Care Products Council is requesting that the Panel consider including hydrolyzed oat protein (77 VCRP uses), hydrolyzed oat flour (7 VCRP uses) and hydrolyzed oats (38 VCRP uses) because some ingredients in the current report contain protein as do the suggested ingredients.

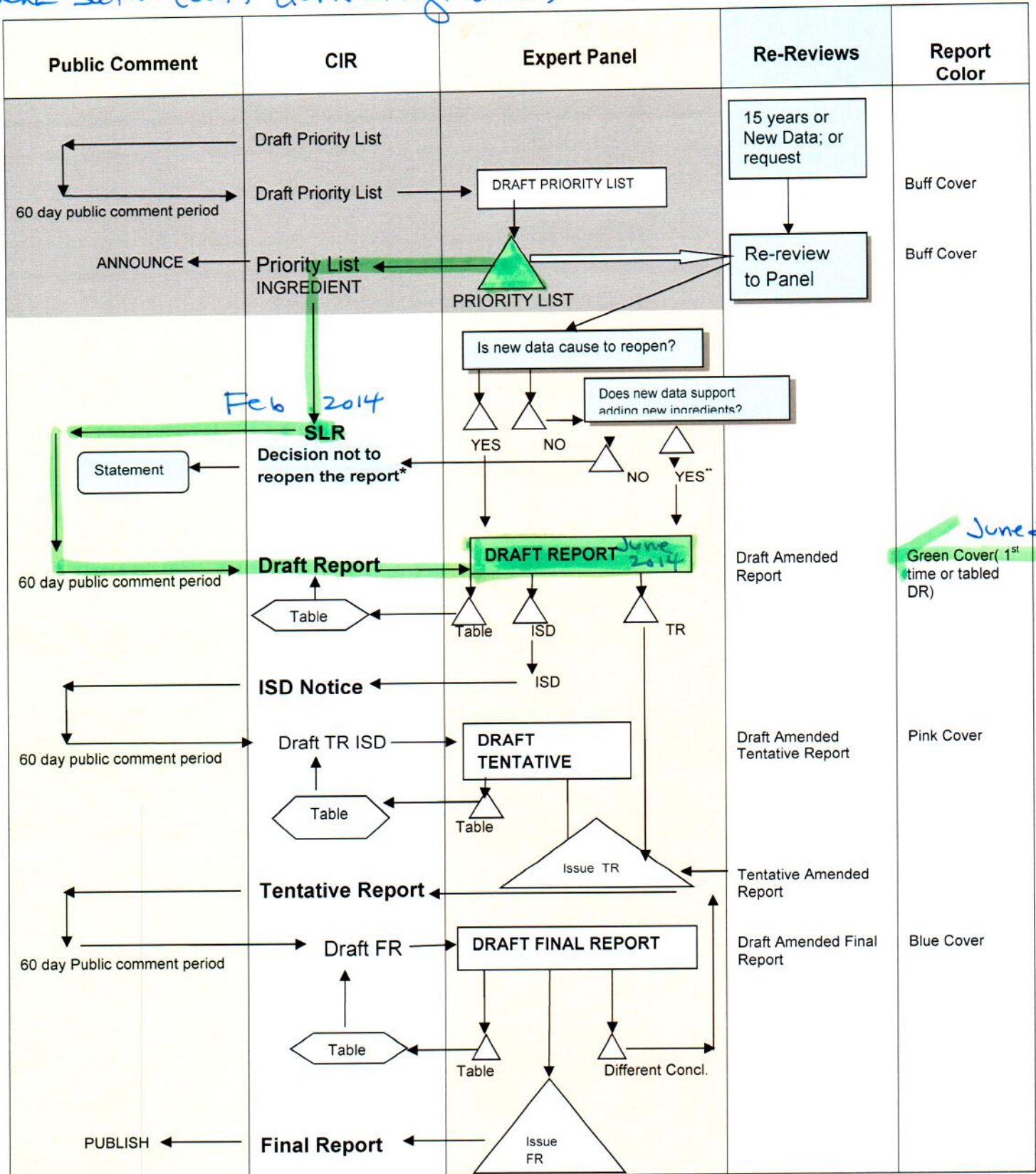
A substantial amount of the irritation and sensitization data is from several use studies of cosmetic products that contain *A. sativa*-derived colloidal oatmeal (Criquet et. al 2012). The article does not provide any concentrations of use for these products. Attempts have been made to contact the lead author asking for that information with no reply. Should staff receive a response, the data will be added to the report.

The Panel is to decide if the suggested ingredients should be added to this report. The Panel is to also determine if there is sufficient data to come to a conclusion for *Avena sativa* (oat)-derived ingredients. If not, then an insufficient data announcement is to be issued with a list of data needs. If so, then the Panel is to develop the basis for the Abstract, Discussion, and Conclusion. Then the Panel is to issue a tentative report.

SAFETY ASSESSMENT FLOW CHART

Avena Sativa (oat)-derived ingredients

June 2014



June 2014

*The CIR Staff notifies of the public of the decision not to re-open the report and prepares a draft statement for review by the Panel. After Panel review, the statement is issued to the Public.

**If Draft Amended Report (DAR) is available, the Panel may choose to review; if not, CIR staff prepares DAR for Panel Review.



History for *Avena sativa*-Derived Ingredients

March, 2014 – SLR posted for review

June, 2014 – Panel reviews draft report

Avena sativa-Derived Ingredients Data Profile for June, 2014. Writer - Lillian Becker

	ADME		Acute toxicity			Repeated dose toxicity			Irritation			Sensitization		Repro/Devel toxicity	Genotoxicity	Carcinogenicity	Phototoxicity
	Dermal Penetration	Log K _{ow}	Use	Oral	Dermal	Inhale	Oral	Dermal	Inhale	Ocular Irritation	Dermal Irr. Animal	Dermal Irr Human	Sensitization Animal				
Avena sativa (oat) bran			X														
Avena sativa (oat) bran extract			X														
Avena sativa (oat) flower/leaf/stem juice																	
Avena sativa (oat) kernel extract			X														
Avena sativa (oat) kernel flour			X														
Avena sativa (oat) kernel meal			X														
Avena sativa (oat) kernel protein			X														
Avena sativa (oat) leaf extract																	
Avena sativa (oat) leaf/stalk extract											P		P				
Avena sativa (oat) leaf/stem extract											P		P				
Avena sativa (oat) meal extract																	
Avena sativa (oat) meristem cell extract																	
Avena sativa (oat) peptide			X														
Avena sativa (oat) protein extract			X														
Avena sativa (oat) seed extract																	
Avena sativa (oat) seed water																	
Avena sativa (oat) sprout oil																	
Avena sativa (oat) starch			X														
Avena sativa (oat) straw extract			X														
Colloidal oatmeal										X		X		X			

X – Data on this ingredient is in the report

P – Data on plant parts that overlap/include this ingredient definition.

Search Strategy – *Avena sativa*-Derived Ingredients

SciFinder – CAS Nos., “*Avena sativa*”, oats. 354 hits. Refined with “toxicity”, “dermal”, “skin”. None useful.

ECHA – CAS Nos. 1 hit, not useful. “*Avena sativa*” 10 results, none useful.

PubMed - "*Avena sativa*" toxicity, 82 hits, none useful. "*Avena sativa*" dermal 3 hits.

("*AVENA SATIVA* (*OAT*)"[TW] OR "*AVENA SATIVA* (*OAT*)"[TW] OR "*AVENA SATIVA*"[TW] OR "*AVENA SATIVA* (*OAT*)"[TW] OR "*AVENA SATIVA*"[TW]), 2007 hits; AND tox*, 128 hits, 26 ordered; AND “derm*”, 34 hits, 16 ordered; AND “ocular” 1 hit; AND “sensitiz*”, 7 hits, 1 ordered.

FDA Poisonous Plant DB – “*Avena sativa*”. 88 hits. Ordered ~20

Canadian Biodiversity Information Facility – 1 reference ordered

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INTRODUCTION

This is a review of the available scientific literature, as well as unpublished data, provided by industry relevant for 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 19 ingredients included in this report are:

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

This safety assessment does not include colloidal oatmeal. The *International Cosmetic Dictionary and Handbook* defines colloidal oatmeal as finely ground oatmeal without specifying the species of oat from which it is derived.¹ Therefore, any oat species (i.e., *A. abyssinica*, *A. byzantine*, *A. nuda*, and *A. strigosa*) may be used. For this safety assessment, data on colloidal oatmeal are included when it is specified that the colloidal oatmeal is derived from *A. sativa*; that data are included for read across purposes.

The U.S. Pharmacopeia Convention (USP) defines colloidal oatmeal as derived from only *A. sativa* or *A. byzantina*; the USP definition does not include *A. nuda* or *A. strigosa*. The USP indicates that oats used to make colloidal oatmeal must meet U.S. standards for No.1 or 2 grade oats (97% or 94% undamaged oats) and may contain, singly or in combination, not more than 25% wild oats and other grains for which standards have been established under the U. S. Grain Standards Act.² [7CRF810.1001]

Avena sativa (oat) kernel oil was reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel (Panel) in 2011 and it was concluded that it was safe as used.³

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.⁴ 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 and green, with the sheaths rounded on the back. The cluster of flowers is a diffuse panicle with 2 to 3 florets which can be all bisexual or mostly bisexual with the distal one or two flowers reduced and male or sterile. The grain is tightly enclosed in the hard lemma and palea. The seed size varies with cultivar (plant strain) and commonly yields approximately 30 000 seeds per kilogram harvested plants.

CONSTITUENTS

Constituent groups found in *A. sativa* include:

Amino acids - Oats are rich in the amino acid lysine, approximately 4%.⁵ L-Threonine has also been identified.

Avenacins and Avenacosides – These are saponins. Avenacosides are biologically inactive until they are converted into antifungal monodesmosidic saponins (26-desglucoavenacosides A and B) in response to tissue damage.⁶ The stem and leaves contain bidesmosidic steroidal saponins (e.g., avenacosides A and B).⁶

Enzymes – The enzymes found in *A. sativa* include lipase, lipoxygenase, and superoxide dismutase.^{7,8}

Flavanoids – The following flavonoids have been isolated from *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; tricetin 7-O- β -D-glucopyranoside; tricetin; kaempferol; and luteolin.⁹

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

The stem and leaves are rich in apigenin and luteolin flavonoids (i.e., C-glycosylflavones), tricetin flavones, and flavonolignans.¹¹

Lipids – *A. sativa* contains 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.^{12,13} The lipid content depends on

genetic and environmental factors. The methods of extraction and analysis result in differences in lipid content of the extracts.

A. *sativa* starches contain lipids ranging from 1% to 3%, present in the starch possibly as amylose–lipid complexes.¹³

Phenolic compounds – At various growth stages, *A. sativa* has been found to contain a large number of phenolic compounds including all major classes in addition to avenanthramides: benzoic and cinnamic acids, quinones, flavones, flavonols, chalcones, flavanones, anthocyanidines, and aminophenolics.¹⁴ *A. sativa* oat flour contains the glyceryl esters of hydroxycinnamic, ferulic, *p*-coumaric, and caffeic acids.¹⁵ Antioxidant activity is attributed to the presence of phenolic esters.^{14,16} *A. sativa* also contains various compounds with antioxidant activity which protect the lipids from oxidation.¹⁴ Avenanthramides are soluble, phenolic compounds that are minor components of *A. sativa* (0.03% by weight).^{17,18,19} They have powerful anti-oxidative activity. They also have anti-inflammatory properties.²⁰ The stem and leaves contain phenolic compounds (e.g., avenanthramides).^{11,21,22}

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

Polysaccharides – these include starches and β -glucan.^{23,24} Carbohydrates mostly consist of araban and xylan gums.²⁵

Proteins – *A. sativa* has a high level of total protein compared other grasses.^{26,27} The stem and leaves contain proteins (including membrane proteins and soluble proteins of chloroplasts).⁶

Vitamins and minerals – *A. sativa* contains a variety of minerals and vitamins.²⁷ These include vitamin E, mostly as α -tocopherol.^{8,26}

CONSTITUENTS OF CONCERN

Quercetin – Quercetin has been reported to be in the hay of *A. sativa*. This constituent was positive for genotoxicity in an Ames assay.²⁸ It was also consistently positive in genotoxic in vitro tests and in some in vivo studies of i.p. injections in mice and rats, but was consistently negative in oral-exposure genotoxicity tests using mice and rats.²⁹

Physical and Chemical Properties

The flavonoids with phenolic structures strongly absorb ultra violet A (UVA) in the 320 to 370 nm range.¹⁴ Other phenolic esters, called avenacins (saponins structurally), have also been isolated.

The solid components of an alcohol extract of ground and macerated *A. sativa* seeds were reported to have a relative molecular mass of 1000 to 10 000 Da when measured by ultrafiltration.³⁰

Method of Manufacture

To produce extracts (information was unclear on the exact plant parts and the solvents) without detectable proteins, young (prior to earing) *A. sativa* plants are dried and crushed.³¹ 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 of enzyme-linked immunoassay [ELISA] less than 0.5 ppm protein) in an extract of young *A. sativa* plants.³¹

Fusarium avenaceum, *Pseudodiscosia avenae* and *Sclerospora macrospora* are among the species of fungi known to infect oat plants, including *A. sativa* (Table 2).⁵

Two of five oat-based cereals tested positive for the mycotoxin deoxynivalenol (DON) at 2.6 and 1.3 μ g/g.³² Three of these products tested positive for zearalenone (ZEA) at an average of 16 ng/g. Aflatoxin B₁ (AFB₁) was not detected in these samples.

The mycotoxins 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).³³ 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.³⁴

Cadmium content in fresh *A. sativa* grown in Finland ranged from 0.008 to 0.120 mg/kg dry weight.³⁵ There was no difference in cadmium content between conventionally and organically grown crops. Nitrogen fertilization increased cadmium content. Cadmium content may vary by strain and may exceed the safe levels for human consumption set by the European Commission of 0.1 mg/kg fresh mass.³⁶

USE

Cosmetic

Data on ingredient usage are provided to the Food and Drug Administration (FDA) Voluntary Cosmetic Registration

Program (VCRP; Table 3).³⁷ A survey was conducted by the Personal Care Products Council (Council) of the maximum use concentrations for these ingredients.³⁸

Avena sativa (oat) kernel extract has the most reported uses with 499 in cosmetic products. *Avena sativa* (oat) kernel extract has the highest reported use concentration of 25%.^{38,39}

There were no reported uses for:

Avena sativa (oat) flower/leaf/stem juice

Avena sativa (oat) leaf/stalk extract

Avena sativa (oat) leaf/stem extract

Avena sativa (oat) meristem cell extract

Avena sativa (oat) seed 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.⁴⁰ 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.^{18,19} 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.⁴¹⁻⁴⁶ Other indications for colloidal oatmeal products include prickly heat, hives, sunburn and rashes.

TOXICOKINETICS

Data on the toxicokinetics of A. sativa-derived ingredients were not found in the published literature nor were unpublished data provided.

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 the avenanthramides. These constituents have been shown to reduce oxazolone-induced contact hypersensitivity, resiniferatoxin-induced neurogenic inflammation, and induced histamine-mediated itch.⁴⁷ In vitro, avenanthramides reduced histamine release from mast cells stimulated by substance P. The buffering property of colloidal oatmeal (the pH of the skin surface is important for preservation of skin barrier function) was demonstrated when treatment with colloidal oatmeal reduced the elevated pH of diseased skin (e.g., eczematous or pruritic) and alkali-treated normal skin to within the normal range. Other reported skin-barrier related effects include the formation of a protective moisturizing barrier by the proteins and polysaccharides in colloidal oatmeal, which reduced measurements of transepidermal water loss (TEWL). Colloidal oatmeal has also been shown to act as an emollient, humectant and occlusive on the skin.⁴⁸ The application of *A. sativa* extracts to sodium lauryl sulfate (SLS)-treated skin has been reported to reduce irritation, demonstrating the anti-inflammatory effects of oats and suggesting potential benefits for the skin barrier.⁴⁹ *A. sativa* extracts reportedly inhibited the phospholipase A2 (PLA2)-dependent mobilization of arachidonic acid from phospholipids in cultured human keratinocytes.⁵⁰ This extract also inhibited the formation of eicosanoids, expression of cytosolic phospholipase PLA2, and formation of metabolites of roscyclin in keratinocytes, all of which are implicated in the regulation of inflammation. An *A. sativa* extract oligomer reduced vasodilation induced by vasoactive intestinal peptide (VIP) in human skin samples.⁵¹ Treatment with the oligomer reduced edema and mean surface of dilated vessels. It has also been reported that colloidal *A. sativa* extracts (both ethanol and phosphate buffer; with and without boiling) inhibited the activity of prostaglandin synthase of bull seminal vesicles.³⁰

Dermal Effects

In Vitro

When fibroblasts from cosmetic surgery patients were incubated with *A. sativa* whole-young-plant extract (0.05%; solvent not provided), there was an increase in the proliferation of the cells and extension of a neoepithelium compared to untreated cells.⁵² There were no differences in the number of basal layers up to day 20 post exposure, and then there were more layers observed in the treated cells on day 22. The dermal equivalent was created in a petri dish by combining the

dermal fibroblasts with collagen type I. A punch biopsy from skin left over from surgery was used as the source of epidermal cells which were then placed 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 biopsy punches 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 incisions were measured by tensile strength across the wound and the healing of the punches were 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), resulted in no adverse effects.⁵³ The group using colloidal oatmeal had reduced itchiness 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. Patients who had been admitted to intensive care were excluded from this study.

Complete or marked itch relief was reported by over 71% of the subjects (n = 139; aged 21 to 91) suffering from pruritic dermatoses when colloidal oatmeal was used as a bath and regular cleanser for 3 months.⁴⁴

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 exhibited improved soothing and cleansing effects with no irritation compared to standard therapy.⁴²

TOXICOLOGICAL STUDIES

Data on the toxicology of A. sativa-derived ingredients were not found in the published literature nor were unpublished data provided.

Anti-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 less than in the rats injected with estradiol alone.⁵⁴ This result was consistent when the extract 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.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Data on the reproductive and developmental toxicity of A. sativa-derived ingredients were not found in the published literature nor were unpublished data provided.

GENOTOXICITY

Data on the genotoxicity of A. sativa-derived ingredients were not found in the published literature nor were unpublished data provided.

CARCINOGENICITY

Data on the carcinogenicity of A. sativa-derived ingredients were not found in the published literature nor were unpublished data provided.

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/stalk extract and/or avena sativa (oat) leaf/stem extract; concentration, amount applied, and extract solvent not provided) was administered to female subjects (n = 16) with dry skin, there were no signs of irritation.³¹ 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 tape 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 subjects experienced any symptoms of a reaction.³¹

COLLOIDAL OATMEAL

In 12 use safety studies of various personal care products containing *A. sativa* colloidal oatmeal, there was a low percentage of subjects (0 – 10.9%) who had positive reactions and it was concluded that these products had a low potential for irritation (Table 4).⁵⁵ The concentrations of colloidal oatmeal were not provided. The products tested were a shower and bath oil, cream, moisturizing oil, shower gel, night cream, conditioning shampoo, body lotion, liquid hand wash, face and eye cleansing lotion (two products), facial exfoliating cleanser, intimate wash, and baby milk. Clinical efficacy was assessed by a dermatologist. Assessments included visual examination of skin dryness and appearance of the skin, as well as tactile evaluation of skin roughness. A 10 cm visual analog scale was used, where 0 represented “none” and 10 was “severe”. The subjects self-assessed using a questionnaire with a five-point scale. Measurements were made on the treated body areas (leg and inner forearm), as well as on an untreated area on the mid-thigh which served as a control site. Clinical assessments were performed only on the treated leg and on the control area.

Ocular - Human

COLLOIDAL OATMEAL

Two use studies of a face and eye cleansing lotion containing *A. sativa* colloidal oatmeal (concentration not provided), the products caused little or no ocular irritation (Table 4).⁵⁵

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-type hypersensitivity to the products after using them for 21 days.⁵⁶ 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 initiating the study, an open application test was conducted on all subjects. The *A. sativa* extracts (colloidal 5%, phenolic 5%, acetic 5%, enzyme-hydrolyzed phenolic 5%, acetic 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.⁵⁶

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 5).⁵⁷ Sixteen of 44 subjects tested positive at 5%, 6 each for 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 specified). 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 attributed 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).⁵⁷

There were no signs of irritation or sensitization in a human repeated insult patch test (HR IPT; n = 104) of a cream containing *A. sativa* (concentration not provided; 50 µL).³¹ 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 allergic reactions to two bath products containing *A. sativa* colloidal oatmeal at the expected use concentration (0.007% in water) or an elevated concentration (0.7% in water).⁵⁸ 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.⁵⁷ Of those sensitized, 15.6% (5 of 32) and 28% (7 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 suggested that topical creams containing *A. sativa* proteins should be avoided in infants with atopic dermatitis.

In 12 HRIPTs (total n = 2291) performed of 12 skin care products containing *A. sativa* colloidal oatmeal, the products did not produce signs of sensitization (Table 6).⁵⁵ These comprised 3 lotions, 2 face creams, 1 serum product, 2 cleansing lotions, 1 exfoliating cleanser, 2 baby products (1 cream and 1 cleanser), and 1 hand cream. The concentrations of colloidal oatmeal in the products were not provided. Overall, 23 subjects experienced a reaction. A total of 34 transient low-level grade ± reactions (i.e., faint minimal erythema) was observed, including 1 subject with 8 consecutive faint erythema readings), 6 transient low-level grade 1 reactions in 6 subjects, and mild erythema in 1 subject. In the challenge period, 17 subjects had the following reactions: 18 transient low-level grade ± reactions in 14 subjects, 9 transient low-level grade 1 reactions in 7 subjects, and 5 grade 1 reactions with edema in 3 subjects. Edematous reactions were not confirmed in subsequent patch tests for 2 subjects. The other subject's reactions were confirmed for the complete product.

Phototoxicity

A. sativa has been reported to cause photosensitization when consumed by cattle, goats, pigs, and sheep.⁵⁹ No further information was provided.

CLINICAL USE

Case Studies

A 4-month old infant with atopic dermatitis and allergy to cow's milk tested positive in patch-tests (++) for sensitization to oats (species not specified) and exhibited a sensitization to wheat, which the child had never ingested.⁶⁰ The authors suggested that, although sensitization to wheat in utero could not be eliminated, most likely the infant developed a cross-sensitization to wheat during exposure to a cream containing oats (Aderma®). At 1 year old, the child had results for the patch-test to wheat identical to the results at 4 months 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 specified).⁶¹ 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.⁶² IgE levels were elevated and a standard prick test was positive for *Dermatophagoides farinae* 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.⁶³ 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 (0.76 kU/L) 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.⁶⁴ 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 subsequent occasions.

A 33-year-old woman presented with atopic eczema and allergic rhinoconjunctivitis.⁶⁵ She had a history of type 1 hypersensitivity reactions to dust mites, cats, dogs, malassezia, nuts, shrimp, lobster, and asparagus. She had used a moisturizer made for atopic and very dry skin, and 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.⁶⁵

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 safety assessment does not include colloidal oatmeal as the definition does not restrict the species of oats used to *A. sativa*. However, data from colloidal oatmeal that were confirmed to be derived from this species were included for read-across purposes.

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 499 up to 25%. *Avena sativa* (oat) kernel flour is used in 122 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 tape stripped skin of human subjects for up to 5 days. In 12 use safety studies of various personal care products containing colloidal oatmeal (concentration not specified), there was a low percentage of subjects (0 – 10.9%) who had positive reactions and it was concluded that these products had a low potential for irritation.

Two use studies of a face and eye cleansing lotion containing colloidal oatmeal (concentration not specified) caused little or no ocular irritation.

The use of a cream and soap containing the extract of young *A. sativa* plants (12%, and 3%, respectively) for 21 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. In HRIPTs performed of skin care products containing *A. sativa* colloidal oatmeal (concentration not provided), the products did not yield signs of sensitization.

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

DISCUSSION

The Discussion will be developed at the June, 2014 Panel meeting.

CONCLUSION

The conclusion will be developed at the June, 2014 Panel meeting.

TABLES AND FIGURES**Table 1.** Definition and function of *A. sativa*-derived ingredients.¹

Ingredient	Definition	Function
Avena sativa (oat) bran	The broken coat of the kernels of oats, <i>Avena sativa</i> .	Abrasive, absorbent, bulking agent
Avena sativa (oat) bran extract	The extract of the bran of <i>Avena sativa</i>	Skin-conditioning agents – miscellaneous
Avena sativa (oat) flower/leaf/stem juice	The juice expressed from the flowers, leaves and stems of <i>Avena sativa</i> .	Skin-conditioning agents – miscellaneous
Avena sativa (oat) kernel extract 84012-26-0	The extract of the kernels of <i>Avena sativa</i> .	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, <i>Avena sativa</i> .	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, <i>Avena sativa</i>	Abrasive, absorbent, bulking agent
Avena sativa (oat) kernel oil	The fixed oil expressed from the kernels of the oat, <i>Avena sativa</i> .	Skin-conditioning agent – occlusive
Avena sativa (oat) kernel protein	A protein obtained from the kernels of oats, <i>Avena sativa</i> .	Film former; hair conditioning agent; skin-conditioning agent – miscellaneous
Avena sativa (oat) leaf extract	The extract of the leaves of <i>Avena sativa</i> .	Cosmetic astringent
Avena sativa (oat) leaf/stalk extract	The extract of the leaves and stalks of <i>Avena sativa</i> .	Skin-conditioning agent – miscellaneous
Avena sativa (oat) leaf/stem extract	The extract of leaves and stems of <i>Avena sativa</i> .	Skin-conditioning agent – miscellaneous
Avena sativa (oat) meal extract	The extract of the meal of <i>Avena sativa</i> .	Skin-conditioning agent – miscellaneous
Avena sativa (oat) meristem cell extract	The extract of the cultured meristem cells of <i>Avena sativa</i> .	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 extract	The extract of the seeds of the oat, <i>Avena sativa</i> .	Hair conditioning agent; skin-conditioning agent - miscellaneous
Avena sativa (oat) seed water	An aqueous solution of the steam distillates obtained from the seeds of <i>Avena sativa</i>	Solvent
Avena sativa (oat) sprout oil	The oil obtained from the sprouts of <i>Avena sativa</i> .	Skin-conditioning agent – miscellaneous
Avena sativa (oat) starch 9005-25-8 (generic)	A starch obtained from oats, <i>Avena sativa</i> .	Absorbent
Avena sativa (oat) straw extract	The extract of the straw of <i>Avena sativa</i> .	Skin-conditioning agent – miscellaneous

Table 2. Fungi that are known to attack *A. sativa*.⁵

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

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

Use type	Maximum Concentration (%)		Maximum Concentration (%)		Maximum Concentration (%)		Maximum Concentration (%)	
	Uses		Uses		Uses		Uses	
	Avena sativa (oat) bran		Avena sativa (oat) bran extract		Avena sativa (oat) flower/leaf/stem juice		Avena sativa (oat) kernel extract	
Total/range	35	0.0072-2.5	6	0.2	NR	NR	499	0.00001-25
<i>Duration of use</i>								
Leave-on	17	0.0072	4	0.2	NR	NR	411	0.000016-25
Rinse-off	18	2.5	1	NR	NR	NR	86	0.00001-1
Diluted for (bath) use	NR	NR	1	NR	NR	NR	2	NR
<i>Exposure type</i>								
Eye area	NR	0.0072	NR	NR	NR	NR	33	0.00006-0.13
Incidental ingestion	2	NR	NR	NR	NR	NR	NR	0.24
Incidental Inhalation-sprays	10 ^a	NR	3 ^a	NR	NR	NR	351 ^a	0.0006-0.14 ^a ; 0.0025 ^b
Incidental inhalation-powders	15 ^c	NR	3 ^c	NR	NR	NR	350 ^c	0.005-0.14 ^c
Dermal contact	27	0.0072-2.5	6	0.2	NR	NR	473	0.000016-25
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	6	NR	NR	NR	NR	NR	24	0.00001-0.05
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	0.00006
Nail	NR	NR	NR	NR	NR	NR	1	NR
Mucous Membrane	7	2.5	1	NR	NR	NR	26	0.0051-1
Baby	11	NR	NR	NR	NR	NR	10	NR
	Avena sativa (oat) kernel flour		Avena sativa (oat) kernel meal		Avena sativa (oat) kernel protein		Avena sativa (oat) leaf extract	
Total/range	122	0.001-20	21	1	29	0.001-5.2	3	NR
<i>Duration of use</i>								
Leave-on	84	0.01-20	4	NR	22	0.001	3	NR
Rinse-off	36	0.1-5	14	1	7	0.001-5.2	NR	NR
Diluted for (bath) use	2	NR	3	NR	NR	NR	NR	NR
<i>Exposure type</i>								
Eye area	NR	NR	NR	NR	4	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-sprays	41 ^a	0.01-3 ^a	2 ^a	NR	17 ^a	0.001 ^{b,d}	3 ^a	NR
Incidental inhalation-powders	61 ^c	NR	2 ^c	NR	15 ^c	NR	3 ^c	NR
Dermal contact	115	0.01-20	21	1	22	5.2	3	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	7	0.001-3.2	NR	NR	7	0.001	NR	NR
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	14	NR	11	1	1	5.2	NR	NR
Baby	7	NR	NR	NR	NR	NR	NR	NR

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Use type	Maximum Concentration (%)		Maximum Concentration (%)		Maximum Concentration (%)		Maximum Concentration (%)	
	Uses		Uses		Uses		Uses	
	Avena sativa (oat) leaf/stalk extract		Avena sativa (oat) leaf/stem extract		Avena sativa (oat) meal extract		Avena sativa (oat) meristem cell extract	
Total/range	NR	NR	NR	NR	22	0.0001-0.005	NR	NR
<i>Duration of use</i>								
Leave-on	NR	NR	NR	NR	13	0.001-0.0025	NR	NR
Rinse-off	NR	NR	NR	NR	9	0.0001-0.005	NR	NR
Diluted for (bath) use	NR	NR	NR	NR	NR	0.005	NR	NR
<i>Exposure type</i>								
Eye area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-sprays	NR	NR	NR	NR	12 ^a	NR	NR	NR
Incidental inhalation-powders	NR	NR	NR	NR	12 ^c	NR	NR	NR
Dermal contact	NR	NR	NR	NR	20	0.0001-0.005	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	NR	NR	NR	NR	2	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	4	0.001-0.005	NR	NR
Baby	NR	NR	NR	NR	NR	NR	NR	NR
	Avena sativa (oat) peptide		Avena sativa (oat) protein extract		Avena sativa (oat) seed water		Avena sativa (oat) sprout oil	
Total/range	5	0.0026-0.33	4	1.5	NR	NR	NR	NR
<i>Duration of use</i>								
Leave-on	2	0.013-0.33	2	1.5	NR	NR	NR	NR
Rinse-off	3	0.0026-0.013	2	NR	NR	NR	NR	NR
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	NR
<i>Exposure type</i>								
Eye area	1	0.33	NR	NR	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-sprays	1 ^a	0.013 ^a	2 ^a	1.5 ^a	NR	NR	NR	NR
Incidental inhalation-powders	NR	NR	2 ^c	NR	NR	NR	NR	NR
Dermal contact	3	0.013-0.33	4	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	2	NR	NR	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

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

Use type	Maximum Concentration (%)		Maximum Concentration (%)		Maximum Concentration (%)	
	Uses		Uses		Uses	
	Avena sativa (oat) starch		Avena sativa (oat) straw extract			
Total/range	5	NR	2	0.001		
<i>Duration of use</i>						
Leave-on	3	NR	2	0.001		
Rinse-off	2	NR	NR	NR		
Diluted for (bath) use	NR	NR	NR	NR		
<i>Exposure type</i>						
Eye area	NR	NR	NR	NR		
Incidental ingestion	NR	NR	NR	NR		
Incidental Inhalation-sprays	2 ^a	NR	2 ^a	NR		
Incidental inhalation-powders	3 ^c	NR	2 ^c	NR		
Dermal contact	5	NR	NR	0.001		
Deodorant (underarm)	NR	NR	NR	NR		
Hair-noncoloring	NR	NR	NR	NR		
Hair-coloring	NR	NR	NR	NR		
Nail	NR	NR	NR	NR		
Mucous Membrane	NR	NR	NR	NR		
Baby	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 Product(s) may or may not be a powder

^d Pump spray

Table 4. Use safety tests of personal care products containing colloidal oatmeal derived from *A. sativa*. The concentration of the colloidal oatmeal in these products was not provided.⁵⁵

Test material	Date/country	n;		Application	Results
		Skin/hair type, skin/eye sensitivity (if applicable)			
Dermal					
Shower and bath oil	December 2006, UK	53/60 completed; dry, very dry body skin. Skin sensitivity: 19% not sensitive, 47% a little sensitive, 23% sensitive, 11% very sensitive. Age 18–55 yrs. Female		Use product on 7 consecutive days instead of usual shower product	Adverse reaction: 3.8%. 2/53. 1 moderate, 1 slight.
Cream moisturizing oil	December 2006, UK	56/60 completed; dry, normal to dry body skin; Skin sensitivity: 23% not sensitive, 52% a little sensitive, 21% sensitive, 4% very sensitive. Age 18–55 yrs. Female		Use product once a day on 7 consecutive days instead of usual body moisturizer	Adverse reaction: 3.6%. 2/56. 1 severe, 1 moderate.
Shower gel	August 2006, UK	59/60 completed; dry, sensitive body skin. Skin sensitivity not indicated. Age 20–50 yrs. Female		Use product on 7 consecutive days instead of usual shower product	Adverse reaction: 3.4%. 2/59 (two moderate)
Night cream	April–May 2009, UK	64/70 completed; facial skin: normal, dry, normal to dry, normal to greasy, normal/dry/greasy. Skin sensitivity: 5% not sensitive, 61% a little sensitive, 30% sensitive, 5% very sensitive. Age 25–49 yrs. Female		Use product on 28 consecutive days instead of usual night-time moisturizer	Adverse reaction: 10.9%. 7/64. 5 subjects with slight to moderate reactions, 1 subject with moderate to severe reactions, and 1 subject with severe reactions.
Conditioning shampoo	January–February 2007, UK	55/60 completed (30/sex); all hair types. Age 18–55 yrs		Use product on 10 occasions, no use of conditioner	Adverse reaction: 3.6%. 2/55 (two moderate)
Body lotion	November–December 2006, UK	57/60 completed; dry, normal to dry body skin. Skin sensitivity: 12% not sensitive, 39% a little sensitive, 19% sensitive, 30% very sensitive. Age 18–55 yrs. Female		Use product on 7 consecutive days as frequently as required	Adverse reaction: 0%

Table 4. Use safety tests of personal care products containing colloidal oatmeal derived from *A. sativa*. The concentration of the colloidal oatmeal in these products was not provided.⁵⁵

Test material	Date/country	n; Skin/hair type, skin/eye sensitivity (if applicable)	Application	Results
Liquid hand wash	October 2006, UK	58/60 completed; dry, normal to dry, very dry hand skin. Skin sensitivity: 12% not sensitive, 55% a little sensitive, 22% sensitive, 10% very sensitive. Age 18–55 yrs. Female	Use product on 7 consecutive days as frequently as required instead of usual hand wash product	Adverse reaction: 5.2%. 3/58 (1 slight and 2 moderate)
Facial exfoliating cleanser	March–April 2009, Bulgaria	60/62 completed; normal, mixed oily, oily, mixed dry, dry skin. Sensitive skin 100%, history of atopy 32%. 2 withdrew consent. Age 18–60 yrs. Female	Use product 1x/day on face and neck for 3 weeks	Safety evaluation: Adverse reactions observed by dermatologist: 0/60. Adverse reaction reported by subjects: 3/60.
Intimate wash	January 2007, Germany	60/60 completed; 48% healthy skin, 17% dry skin, 2% sensitive skin, 33% atopic dermatitis/eczema-free interval. Age 18–58 yrs. Female	Use product at least 1 x/day for 4 weeks. Subsequent occlusive patch test with 1%, 2%, 5% dilutions, inner forearm for 24 hours	After 4 weeks: adverse reaction: 0. Patch test: no reaction at any concentration.
Baby milk	January 2007, Germany	20/20 adults (6 male, 14 female) completed; 25% normal skin, 20% dry skin, 20% sensitive skin, 35% atopic dermatitis/eczema free interval. Age 21–47 yrs. 30/30 children (11 male, 19 female) completed; 27% normal skin, 20% dry skin, 17% sensitive skin, 37% atopic dermatitis/eczema free interval. Age 8 months - 4 yrs.	Use product at least 2 x/day for 4 weeks. Subsequent occlusive patch test with adults only (undiluted), inner forearm for 24 h	After 4 weeks: adverse reaction: 0. Patch test: no reaction.
Ocular				
Face and eye cleansing lotion	September 2009, Poland	22/22 completed; normally sensitive eyes. Age 18–70 yrs. Female	Use product 2 x/day on face including eye area and neck for 3 weeks	Clinical signs: 0%
Face and eye cleansing lotion	September 2009, Poland	21/22 completed; normally sensitive eyes. Age 18–60 yrs. Female	Use product 2 x/day on face including eye area and neck for 3 weeks	Clinical signs: 14%. 3/21 (possibly attributable to product and for 2 subjects only on 1 eye)

Table 5. Results of atopy patch test and skin prick test of *A. sativa* extracts on children under 15 years old who were referred for allergy testing.⁵⁷

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. SPT – Skin prick test

Table 6. HRIPTs of personal care products that contain colloidal oatmeal derived from *A. sativa*. The concentration of the colloidal oatmeal in each product was not provided.⁵⁵

Test material	Date, country	n and description	Application	Results
Lotion	June–July 2005, US	207/245 completed. 66 male, 141 female. Age 18–70 years.	Occlusive	No reaction during induction phase or challenge phase. Conclusion: no potential for dermal irritation or sensitization
Lotion	December 2001–January 2002, US	209/226 completed. 55 male, 154 female. Age 18–69 years.	Occlusive	Induction phase: 1 transient low-level \pm reaction in 1 subject. Challenge phase: 3 low-level \pm reactions in one subject (48, 72, 96 h); 1 level 1+ edema reaction (72 h), 1 transient low-level reaction (1 ^a) in 1 subject (96 h). Remarks: test material did induce an edematous reaction indicative of dermal sensitization in 1 human subject. This reaction was not confirmed by a second patch testing. Conclusion: no potential of the product for dermal sensitization
Lotion SPF 15	July–August 2001, US	193/221 completed. 55 male, 138 female. Age 18–69 years.	Semi-occlusive	No reaction during induction phase or challenge phase. Conclusion: no potential for dermal irritation or sensitization
Cleansing lotion	February–April 2005, US	206/227 completed. 66 male, 140 female. Age 18–70 years.	Semi-occlusive	Induction phase: 2 transient low-level \pm reactions in 1 subject (readings 1, 2 ^a); 3 transient low-level \pm reactions in 1 subject (readings 7–9 ^a). Challenge: no reactions. Conclusion: no potential for dermal irritation or sensitization.
Cleansing lotion	February–April 2000, US	183/213 completed. 48 male, 135 female. Age 18–69 years.	Occlusive	Induction phase: 1 transient low-level \pm reaction in 2 subjects (readings 6, 8 h); 2 transient low-level \pm reactions in 2 subjects (readings 4, 5 ^a); 4 low level transient reactions (1 \times 1; 3 \times \pm) in 1 subject (readings 2–5 ^a). Challenge phase: 1 transient low-level reaction (\pm) in 4 subjects (24 h, 3 \times 48 h); 2 transient low-level reactions (1; \pm) in 1 subject (48, 72 h). Conclusion: no potential for dermal irritation or sensitization.
Cream	December 2005–January 2006, US	223/240 completed. 59 male, 165 female. Age 18–69 years.	Occlusive	No reaction during induction phase. Challenge phase: 1 transient low-level reaction (\pm) in 1 subject (48 h); 2 transient low-level \pm reactions in 1 subject (48, 72 h). Conclusion: no potential for dermal irritation or sensitization.
Night cream	July–August 2006, US	217/240 completed. 68 male, 149 female. Aged 18–70 years.	Semi-occlusive	Induction phase: 1 transient low-level \pm reaction in 2 subjects (readings 2 ^a). Challenge phase: 2 transient low-level \pm reactions in 1 subject (48, 72 h). Conclusion: no potential for dermal irritation or sensitization.
Serum	July–August 2006, US	217/240 completed 68 male, 149 female. Age 18–70 years.	Semi-occlusive	Induction phase: 1 transient low-level \pm reaction in 3 subjects (readings 2, 9, 9 ^a); one transient low-level reaction (1 ^a) in one subject (reading 5 ^a); 2 transient low-level reactions (1; \pm) in 1 subject (readings 5, 6 ^a). Challenge phase: 1 level 1 + edema reaction (48 h), 2 low-level transient reactions (1 ^a) in 1 subject (24, 72 h); 2 transient low-level reactions (1; \pm) in 1 subject (48, 72 h). Remark: test material did induce an edematous reaction indicative of dermal sensitization in 1 human subject; reaction not confirmed by a second patch test. Conclusion: no potential of the product for dermal sensitization
Baby cream	February–March 2009, Romania	109/114 completed. 13 male, 96 female. Age 18–70 years.	Semi-occlusive	Induction phase: 1 mild erythema (1 ^a) in 1 subject (reading 3 ^a). Challenge phase: no reaction. Conclusion: no potential for dermal irritation or sensitization.
Hand cream	May–June 2002, US	201/240 completed. 59 male, 142 female. Age 18–70 years.	Semi-occlusive	Induction phase: 2 transient low-level reactions (1 ^a ; \pm) in one subject (readings 3, 4 ^a); 8 low-level reactions (\pm) in 1 subject (readings 2–9 ^a). Challenge phase: 1 transient low-level reaction (\pm) in 1 subject (72 h); 3 level 1 + edema reactions in 1 subject (48, 72, 96 h). Remarks: test material did induce an edematous reaction indicative of dermal sensitization in 1 human subject; reaction confirmed with the finished product by a second patch testing but not with <i>Avena sativa</i> . Conclusion: doubtful.
Exfoliating cleanser	March–May 2009, Romania	109/114 completed. 23 male, 86 female. Age 18–68 years.	2% dilution; semi-occlusive	No reaction during induction phase or challenge phase. Conclusion: no potential for dermal irritation or sensitization
Wash (head-to-toe)	August–September 2007, US	216/245 completed. 59 male, 157 female. Age 18–70 years.	8% dilution; semi-occlusive	Induction phase: 1 transient low-level \pm reaction in 3 subjects (readings 2, 7, 7 ^a); 1 transient low-level reaction (1 ^a) in 1 subject (reading 2 ^a); 2 transient low-level reactions (1 ^a ; \pm) in 1 subject (readings 7, 8 ^a). Challenge phase: 2 transient low-level reactions (1 ^a ; \pm) in 2 subjects (48, 72 hours); three transient low-level reactions (2 \times 1; 1 \times \pm) in one subject (48, 72, 96 h). Conclusion: no potential for dermal irritation or sensitization.

^a 0 = no reaction; 10 = severe reaction.

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MEMORANDUM

To: CIR Expert Panel and Liaisons

From: Lillian C. Becker, M.S.
Scientific Analyst and Writer

Date: May 16, 2014

Subject: Data for *Avena sativa*-Derived Ingredients as Used in Cosmetics

Attached are the supplemental data for *Avena sativa*-derived ingredients. The data include:

- 1) Concentration of use survey from the Council
- 2) VCRP data for these ingredients
- 3) Data on the constituents of *A. sativa* from Dr. Duke's database



TO: Lillian Gill, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Halyna Breslawec, Ph.D.
Industry Liaison to the CIR Expert Panel

A handwritten signature in blue ink, appearing to read "H. Breslawec", is written over a horizontal line.

DATE: February 3, 2014

SUBJECT: Concentration of Use information: *Avena sativa*-Derived Ingredients

Concentration of Use by FDA Product Category*

Avena Sativa (Oat) Kernel Extract	Avena Sativa (Oat) Leaf/Stem Extract
Avena Sativa (Oat) Bran	Avena Sativa (Oat) Meal Extract
Avena Sativa (Oat) Bran Extract	Avena Sativa (Oat) Meristem Cell Extract
Avena Sativa (Oat) Flower/Leaf/Stem Juice	Avena Sativa (Oat) Peptide
Avena Sativa (Oat) Kernel Flour	Avena Sativa (Oat) Protein Extract
Avena Sativa (Oat) Kernel Meal	Avena Sativa (Oat) Seed Extract
Avena Sativa (Oat) Kernel Oil	Avena Sativa (Oat) Seed Water
Avena Sativa (Oat) Kernel Protein	Avena Sativa (Oat) Sprout Oil
Avena Sativa (Oat) Leaf Extract	Avena Sativa (Oat) Starch
Avena Sativa (Oat) Leaf/Stalk Extract	Avena Sativa (Oat) Straw Extract

Ingredient	Product Category	Maximum Concentration of Use
Avena Sativa (Oat) Kernel Extract	Eye lotion	0.0006-0.13%
Avena Sativa (Oat) Kernel Extract	Eye makeup remover	0.02-0.12%
Avena Sativa (Oat) Kernel Extract	Mascara	0.00006%
Avena Sativa (Oat) Kernel Extract	Hair conditioners	0.002-0.05%
Avena Sativa (Oat) Kernel Extract	Shampoos (noncoloring)	0.00001-0.003%
Avena Sativa (Oat) Kernel Extract	Tonics, dressings and other hair grooming aids	0.0006-0.015%
Avena Sativa (Oat) Kernel Extract	Hair tints	0.00006%
Avena Sativa (Oat) Kernel Extract	Face powders	5%
Avena Sativa (Oat) Kernel Extract	Lipstick	0.24%
Avena Sativa (Oat) Kernel Extract	Bath soaps and detergents	0.0051-1%
Avena Sativa (Oat) Kernel Extract	Other personal cleanliness products	0.15%
Avena Sativa (Oat) Kernel Extract	Aftershave lotions	0.1%
Avena Sativa (Oat) Kernel Extract	Skin cleansing	0.001-0.33%
Avena Sativa (Oat) Kernel Extract	Face and neck products not spray spray	0.001-25% 0.0025%
Avena Sativa (Oat) Kernel Extract	Body and hand products not spray	0.000016-1.3%
Avena Sativa (Oat) Kernel Extract	Moisturizing products not spray	0.01-0.24%
Avena Sativa (Oat) Kernel Extract	Night products not spray	0.005%
Avena Sativa (Oat) Kernel Extract	Paste masks and mud packs	0.005%
Avena Sativa (Oat) Kernel Extract	Skin fresheners	0.005-0.14%

Avena Sativa (Oat) Kernel Extract	Other skin care preparations	0.0025-0.04%
Avena Sativa (Oat) Kernel Extract	Suntan products not spray	0.5%
Avena Sativa (Oat) Bran	Eye lotion	0.0072%
Avena Sativa (Oat) Bran	Bath soaps and detergents	2.5%
Avena Sativa (Oat) Bran	Moisturizing products not spray	0.0072%
Avena Sativa (Oat) Bran Extract	Face and neck products not spray	0.02%
Avena Sativa (Oat) Kernel Flour	Hair conditioners	0.001-0.4%
Avena Sativa (Oat) Kernel Flour	Shampoos (noncoloring)	0.4-3.2%
Avena Sativa (Oat) Kernel Flour	Other hair preparations (noncoloring)	0.1%
Avena Sativa (Oat) Kernel Flour	Blushers (all types)	1%
Avena Sativa (Oat) Kernel Flour	Face powders	5%
Avena Sativa (Oat) Kernel Flour	Foundations	20%
Avena Sativa (Oat) Kernel Flour	Aftershave lotions	0.3-1%
Avena Sativa (Oat) Kernel Flour	Skin cleansing	0.2%
Avena Sativa (Oat) Kernel Flour	Face and neck products not spray	0.1%
Avena Sativa (Oat) Kernel Flour	Body and hand products not spray	0.1-1%
Avena Sativa (Oat) Kernel Flour	Moisturizing products not spray	0.01-3%
Avena Sativa (Oat) Kernel Flour	Pastes masks and mud packs	0.1-5%
Avena Sativa (Oat) Kernel Flour	Other skin care preparations	10%
Avena Sativa (Oat) Kernel Meal	Bath soaps and detergents	1%
Avena Sativa (Oat) Kernel Oil	Bath soaps and detergents	0.045%
Avena Sativa (Oat) Kernel Oil	Face and neck products not spray	0.001%
Avena Sativa (Oat) Kernel Oil	Body and hand products not spray	0.25%
Avena Sativa (Oat) Kernel Protein	Hair conditioners	0.001%
Avena Sativa (Oat) Kernel Protein	Hair sprays pump	0.001%

Avena Sativa (Oat) Kernel Protein	Bath soaps and detergents	5.2%
Avena Sativa (Oat) Meal Extract	Other bath preparations	0.005%
Avena Sativa (Oat) Meal Extract	Bath soaps and detergents	0.001%
Avena Sativa (Oat) Meal Extract	Skin cleansing	0.0001-0.005%
Avena Sativa (Oat) Meal Extract	Body and hand products not spray	0.001-0.0025%
Avena Sativa (Oat) Meal Extract	Moisturizing products not spray	0.001%
Avena Sativa (Oat) Meal Extract	Paste masks and mud packs	0.001%
Avena Sativa (Oat) Peptide	Eye lotion	0.33%
Avena Sativa (Oat) Peptide	Hair conditioners	0.013%
Avena Sativa (Oat) Peptide	Shampoos (noncoloring)	0.0026%
Avena Sativa (Oat) Peptide	Tonics, dressings and other hair grooming aids	0.013%
Avena Sativa (Oat) Peptide	Face and neck products not spray	0.22%
Avena Sativa (Oat) Peptide	Body and hand products not spray	0.013%
Avena Sativa (Oat) Protein Extract	Skin cleansing	1.5%
Avena Sativa (Oat) Straw Extract	Body and hand products not spray	0.001%

*Ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but not uses were reported.

Information collected in 2013-2014
Table prepared February 3, 2014

2014 VCRP Data for *Avena sativa*-Derived Ingredients

01A - Baby Shampoos	AVENA SATIVA (OAT) BRAN	4
01B - Baby Lotions, Oils, Powders, and Creams	AVENA SATIVA (OAT) BRAN	5
01C - Other Baby Products	AVENA SATIVA (OAT) BRAN	2
05F - Shampoos (non-coloring)	AVENA SATIVA (OAT) BRAN	2
09A - Dentifrices	AVENA SATIVA (OAT) BRAN	2
10A - Bath Soaps and Detergents	AVENA SATIVA (OAT) BRAN	4
10E - Other Personal Cleanliness Products	AVENA SATIVA (OAT) BRAN	1
11E - Shaving Cream	AVENA SATIVA (OAT) BRAN	3
12A - Cleansing	AVENA SATIVA (OAT) BRAN	1
12D - Body and Hand (exc shave)	AVENA SATIVA (OAT) BRAN	2
12F - Moisturizing	AVENA SATIVA (OAT) BRAN	8
12H - Paste Masks (mud packs)	AVENA SATIVA (OAT) BRAN	1
		35
	AVENA SATIVA (OAT) BRAN EXTRACT	1
02B - Bubble Baths	AVENA SATIVA (OAT) BRAN EXTRACT	1
12A - Cleansing	AVENA SATIVA (OAT) BRAN EXTRACT	1
12C - Face and Neck (exc shave)	AVENA SATIVA (OAT) BRAN EXTRACT	1
12F - Moisturizing	AVENA SATIVA (OAT) BRAN EXTRACT	1
12I - Skin Fresheners	AVENA SATIVA (OAT) BRAN EXTRACT	1
12J - Other Skin Care Preps	AVENA SATIVA (OAT) BRAN EXTRACT	1
		6
	AVENA SATIVA (OAT) KERNEL EXTRACT	5
01A - Baby Shampoos	AVENA SATIVA (OAT) KERNEL EXTRACT	5
01B - Baby Lotions, Oils, Powders, and Creams	AVENA SATIVA (OAT) KERNEL EXTRACT	3
01C - Other Baby Products	AVENA SATIVA (OAT) KERNEL EXTRACT	2
02B - Bubble Baths	AVENA SATIVA (OAT) KERNEL EXTRACT	1
02D - Other Bath Preparations	AVENA SATIVA (OAT) KERNEL EXTRACT	1
03C - Eye Shadow	AVENA SATIVA (OAT) KERNEL EXTRACT	1
03D - Eye Lotion	AVENA SATIVA (OAT) KERNEL EXTRACT	15
03E - Eye Makeup Remover	AVENA SATIVA (OAT) KERNEL EXTRACT	5

03F - Mascara	AVENA SATIVA (OAT) KERNEL EXTRACT	1
03G - Other Eye Makeup Preparations	AVENA SATIVA (OAT) KERNEL EXTRACT	11
05A - Hair Conditioner	AVENA SATIVA (OAT) KERNEL EXTRACT	7
05F - Shampoos (non-coloring)	AVENA SATIVA (OAT) KERNEL EXTRACT	10
05G - Tonics, Dressings, and Other Hair Grooming Aids	AVENA SATIVA (OAT) KERNEL EXTRACT	1
05I - Other Hair Preparations	AVENA SATIVA (OAT) KERNEL EXTRACT	1
07A - Blushers (all types)	AVENA SATIVA (OAT) KERNEL EXTRACT	1
07B - Face Powders	AVENA SATIVA (OAT) KERNEL EXTRACT	1
07C - Foundations	AVENA SATIVA (OAT) KERNEL EXTRACT	2
07I - Other Makeup Preparations	AVENA SATIVA (OAT) KERNEL EXTRACT	3
08G - Other Manicuring Preparations	AVENA SATIVA (OAT) KERNEL EXTRACT	1
10A - Bath Soaps and Detergents	AVENA SATIVA (OAT) KERNEL EXTRACT	14
10E - Other Personal Cleanliness Products	AVENA SATIVA (OAT) KERNEL EXTRACT	10
11A - Aftershave Lotion	AVENA SATIVA (OAT) KERNEL EXTRACT	1
11G - Other Shaving Preparation Products	AVENA SATIVA (OAT) KERNEL EXTRACT	1
12A - Cleansing	AVENA SATIVA (OAT) KERNEL EXTRACT	27
12C - Face and Neck (exc shave)	AVENA SATIVA (OAT) KERNEL EXTRACT	55
12D - Body and Hand (exc shave)	AVENA SATIVA (OAT) KERNEL EXTRACT	25
12F - Moisturizing	AVENA SATIVA (OAT) KERNEL EXTRACT	255
12G - Night	AVENA SATIVA (OAT) KERNEL EXTRACT	10
12H - Paste Masks (mud packs)	AVENA SATIVA (OAT) KERNEL EXTRACT	7
12I - Skin Fresheners	AVENA SATIVA (OAT) KERNEL EXTRACT	1
12J - Other Skin Care Preps	AVENA SATIVA (OAT) KERNEL EXTRACT	17
13B - Indoor Tanning Preparations	AVENA SATIVA (OAT) KERNEL EXTRACT	3
13C - Other Suntan Preparations	AVENA SATIVA (OAT) KERNEL EXTRACT	1
		499

01B - Baby Lotions, Oils, Powders, and Creams	AVENA SATIVA (OAT) KERNEL FLOUR	4
01C - Other Baby Products	AVENA SATIVA (OAT) KERNEL FLOUR	3
02B - Bubble Baths	AVENA SATIVA (OAT) KERNEL FLOUR	2
04C - Powders (dusting and talcum, excluding aftershave talc)	AVENA SATIVA (OAT) KERNEL FLOUR	7
05A - Hair Conditioner	AVENA SATIVA (OAT) KERNEL FLOUR	2
05B - Hair Spray (aerosol fixatives)	AVENA SATIVA (OAT) KERNEL FLOUR	1
05F - Shampoos (non-coloring)	AVENA SATIVA (OAT) KERNEL FLOUR	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	AVENA SATIVA (OAT) KERNEL FLOUR	2
05I - Other Hair Preparations	AVENA SATIVA (OAT) KERNEL FLOUR	1
07A - Blushers (all types)	AVENA SATIVA (OAT) KERNEL FLOUR	5
07B - Face Powders	AVENA SATIVA (OAT) KERNEL FLOUR	12
07C - Foundations	AVENA SATIVA (OAT) KERNEL FLOUR	3
07I - Other Makeup Preparations	AVENA SATIVA (OAT) KERNEL FLOUR	1
10A - Bath Soaps and Detergents	AVENA SATIVA (OAT) KERNEL FLOUR	11
10E - Other Personal Cleanliness Products	AVENA SATIVA (OAT) KERNEL FLOUR	1
11A - Aftershave Lotion	AVENA SATIVA (OAT) KERNEL FLOUR	4
11G - Other Shaving Preparation Products	AVENA SATIVA (OAT) KERNEL FLOUR	2
12A - Cleansing	AVENA SATIVA (OAT) KERNEL FLOUR	10
12D - Body and Hand (exc shave)	AVENA SATIVA (OAT) KERNEL FLOUR	20
12F - Moisturizing	AVENA SATIVA (OAT) KERNEL FLOUR	15
12G - Night	AVENA SATIVA (OAT) KERNEL FLOUR	3
12H - Paste Masks (mud packs)	AVENA SATIVA (OAT) KERNEL FLOUR	9
12J - Other Skin Care Preps	AVENA SATIVA (OAT) KERNEL FLOUR	3
		122

02A - Bath Oils, Tablets, and Salts	AVENA SATIVA (OAT) KERNEL MEAL	3
10A - Bath Soaps and Detergents	AVENA SATIVA (OAT) KERNEL MEAL	6
10E - Other Personal Cleanliness Products	AVENA SATIVA (OAT) KERNEL MEAL	2
12A - Cleansing	AVENA SATIVA (OAT) KERNEL MEAL	5
12C - Face and Neck (exc shave)	AVENA SATIVA (OAT) KERNEL MEAL	2
12H - Paste Masks (mud packs)	AVENA SATIVA (OAT) KERNEL MEAL	1
12J - Other Skin Care Preps	AVENA SATIVA (OAT) KERNEL MEAL	2
		21
01B - Baby Lotions, Oils, Powders, and Creams	AVENA SATIVA (OAT) KERNEL OIL	1
02B - Bubble Baths	AVENA SATIVA (OAT) KERNEL OIL	1
10A - Bath Soaps and Detergents	AVENA SATIVA (OAT) KERNEL OIL	1
10E - Other Personal Cleanliness Products	AVENA SATIVA (OAT) KERNEL OIL	1
12A - Cleansing	AVENA SATIVA (OAT) KERNEL OIL	1
12F - Moisturizing	AVENA SATIVA (OAT) KERNEL OIL	8
13C - Other Suntan Preparations	AVENA SATIVA (OAT) KERNEL OIL	1
		14
03D - Eye Lotion	AVENA SATIVA (OAT) KERNEL PROTEIN	1
03G - Other Eye Makeup Preparations	AVENA SATIVA (OAT) KERNEL PROTEIN	3
05A - Hair Conditioner	AVENA SATIVA (OAT) KERNEL PROTEIN	4
05B - Hair Spray (aerosol fixatives)	AVENA SATIVA (OAT) KERNEL PROTEIN	2
05H - Wave Sets	AVENA SATIVA (OAT) KERNEL PROTEIN	1
10A - Bath Soaps and Detergents	AVENA SATIVA (OAT) KERNEL PROTEIN	1
11A - Aftershave Lotion	AVENA SATIVA (OAT) KERNEL PROTEIN	1
12C - Face and Neck (exc shave)	AVENA SATIVA (OAT) KERNEL PROTEIN	2
12D - Body and Hand (exc shave)	AVENA SATIVA (OAT) KERNEL PROTEIN	1
12F - Moisturizing	AVENA SATIVA (OAT) KERNEL PROTEIN	11
12G - Night	AVENA SATIVA (OAT) KERNEL	1

12H - Paste Masks (mud packs)	PROTEIN AVENA SATIVA (OAT) KERNEL PROTEIN	1 29
12F - Moisturizing	AVENA SATIVA (OAT) LEAF EXTRACT	3
05A - Hair Conditioner	AVENA SATIVA (OAT) MEAL EXTRACT	1
05F - Shampoos (non-coloring)	AVENA SATIVA (OAT) MEAL EXTRACT	1
10A - Bath Soaps and Detergents	AVENA SATIVA (OAT) MEAL EXTRACT	2
10E - Other Personal Cleanliness Products	AVENA SATIVA (OAT) MEAL EXTRACT	2
12A - Cleansing	AVENA SATIVA (OAT) MEAL EXTRACT	3
12D - Body and Hand (exc shave)	AVENA SATIVA (OAT) MEAL EXTRACT	5
12F - Moisturizing	AVENA SATIVA (OAT) MEAL EXTRACT	7
12J - Other Skin Care Preps	AVENA SATIVA (OAT) MEAL EXTRACT	1 22
03D - Eye Lotion	AVENA SATIVA (OAT) PEPTIDE	1
05A - Hair Conditioner	AVENA SATIVA (OAT) PEPTIDE	1
05F - Shampoos (non-coloring)	AVENA SATIVA (OAT) PEPTIDE	1
12F - Moisturizing	AVENA SATIVA (OAT) PEPTIDE	1
12H - Paste Masks (mud packs)	AVENA SATIVA (OAT) PEPTIDE	1 5
12A - Cleansing	AVENA SATIVA (OAT) PROTEIN EXTRACT	2
12C - Face and Neck (exc shave)	AVENA SATIVA (OAT) PROTEIN EXTRACT	1
12G - Night	AVENA SATIVA (OAT) PROTEIN EXTRACT	1 4

04C - Powders (dusting and talcum, excluding aftershave talc)	AVENA SATIVA (OAT) STARCH	1
12F - Moisturizing	AVENA SATIVA (OAT) STARCH	2
12H - Paste Masks (mud packs)	AVENA SATIVA (OAT) STARCH	2
		5
12F - Moisturizing	AVENA SATIVA (OAT) STRAW EXTRACT	2

Chemicals listed in Dr. Duke's database.

Chemical	Part	Range (ppm)
Phytic-acid	Bran	
Selenium	Bran	
3'-hydroxyavenalamic-acid	Fruit	
Avenalamic-acid	Fruit	
Quercetin	Hay	310
1,3,4-pentane-tricarboxylic-acid-trimethyl-ester	Hull Husk	1.3
3,4-dimethoxy-acetophenone	Hull Husk	
Aegilopsin	Hull Husk	
Alpha-keto-glutaric-acid	Hull Husk	
Beta-hydroxy-beta-methyl-glutaric-acid	Hull Husk	
Cellulose	Hull Husk	350 000
Citric-acid	Hull Husk	
Dihydrohaematinic-acid	Hull Husk	
Dimethoxy-butyl-benzene	Hull Husk	
Furfural	Hull Husk	100 000-13 2000
Glucovanillin	Hull Husk	
Glutaric-acid	Hull Husk	
Isopropyl-tartaric-acid	Hull Husk	
Lignin	Hull Husk	100 000-150 000
Malic-acid	Hull Husk	
Malonic-acid	Hull Husk	
Methoxy-malic-acid	Hull Husk	
Pentane-1,3,4-tricarboxylic-acid	Hull Husk	
Pentosans	Hull Husk	320 000-360 000
Phytic-acid	Hull Husk	5600-8700
Tartaric-acid	Hull Husk	
2-carboxyarabinitol	Leaf	517
4,5-dihydroxy-7-methoxy-8-c-glucosyl-o-rhamnoside	Leaf	
5-dehydro-avenasterol	Leaf	
7-dehydro-avenasterol	Leaf	
Apigenin-6,8-di-c-glucoside	Leaf	
Apigenin-6-c-glucoside	Leaf	
Apigenin-6-c-glucosyl-o-arabinoside	Leaf	
Apigenin-8-c-arabinosylhexoside	Leaf	
Apigenin-8-c-glucosyl-o-rhamnoside	Leaf	
Apigenin-8-c-rhamnosylglucoside	Leaf	
Avenalumin-i	Leaf	
Beta-sitosterol	Leaf	
Campestanol	Leaf	
Cholest-7-en-3-beta-ol	Leaf	
Cholestanol	Leaf	
Hordenine	Leaf	

Chemicals listed in Dr. Duke's database.

Chemical	Part	Range (ppm)
Isoorientin	Leaf	
Isoorientin-2"-o-alpha-l-arabinoside	Leaf	
Isoswertisin-o"-rhamnoside	Leaf	16
Lophenol	Leaf	
Luteolin-6-c-glucoside	Leaf	
Luteolin-6-c-glucosyl-o-arabinoside	Leaf	
Putrescine	Leaf	1186
Silicic-acid	Leaf	
Spermidine	Leaf	14
Spermine	Leaf	13
Stigmast-7-en-3-beta-ol	Leaf	
Stigmastanol	Leaf	
Stigmasterol	Leaf	
Tricin	Leaf	
Tricin-4'-o-alpha-l-arabinoside	Leaf	
Tricin-4'-o-beta-d-glucoside	Leaf	
Tricin-7-o-beta-d-glucoside	Leaf	
Vitamin-a	Leaf	0.6
Vitexin-2"-rhamnoside	Leaf	
26-desglucoavenacosides	Plant	
Acetic-acid	Plant	
Aconitic-acid	Plant	
Aluminum	Plant	
Ascorbic-acid	Plant	26-120
Ash	Plant	18 040-210 000
Avenacin-a-1	Plant	
Avenacin-b-2	Plant	
Avenacosides	Plant	1000-15 000
Avenarin	Plant	
Beta-carotene	Plant	0-75
Beta-sitosterol	Plant	
Caffeic-acid	Plant	
Calcium	Plant	1300-14 300
Carbohydrates	Plant	265 000-861 000
Carotene	Plant	2.6-702
Cellulose	Plant	305 000
Chlorine	Plant	1000-5700
Chlorophyll-a	Plant	
Chlorophyll-b	Plant	
Chromium	Plant	0.9-3.9
Cobalt	Plant	0.03-1.7
Copper	Plant	4
Fat	Plant	1540-39 000
Fiber	Plant	122 000-417 000
Fiber (crude)	Plant	173 000

Chemicals listed in Dr. Duke's database.

Chemical	Part	Range (ppm)
Fiber (dietary)	Plant	62 0000
Fructose	Plant	
Glucose	Plant	
Glutamic-acid	Plant	19 000
Guanine	Plant	
Hypoxanthin	Plant	
Iodine	Plant	0.154
Iron	Plant	3-990
Isoleucine	Plant	13 000
Isovitexin	Plant	
Kilocalories	Plant	4529-4540
Leucine	Plant	18 000
Lignin	Plant	85 000
Lysine	Plant	14 000
Magnesium	Plant	300-14 800
Manganese	Plant	0.1-168
Methionine	Plant	2000
Niacin	Plant	17-99
Oxalic-acid	Plant	400
Pantothenic-acid	Plant	3.5-45.3
Pectin	Plant	800
Phosphorus	Plant	618-8800
Potassium	Plant	598-78 900
Protein	Plant	14 000-424 000
Pyridoxine	Plant	1.76-3.08
Riboflavin	Plant	0.4-26
Secalose	Plant	
Selenium	Plant	0.3-1.3
Silica	Plant	36 000
Silicon	Plant	4-183
Silicon-oxide	Plant	
Sodium	Plant	700-9400
Sucrose	Plant	
Sugars	Plant	93000
Sulfur	Plant	800-4100
Thiamin	Plant	0.9-4
Thiamine	Plant	0.4-2
Threonine	Plant	16 000
Tin	Plant	1.3-6
Tryptophan	Plant	2000
Uronic-acids	Plant	
Valine	Plant	12 000
Vanillin	Plant	
Water	Plant	780 000-792 000
Zinc	Plant	19
Graminine	Rhizome	
Avenacin-a-1	Root	

Chemicals listed in Dr. Duke's database.

Chemical	Part	Range (ppm)
Avenacins	Root	
Avenic-acid-a	Root	
Avenin	Root	
Betaine	Root	0.1
Choline	Root	0.2
Fructose	Root	
Proline	Root	2.4
Scopoletin	Root	10
2,2,6-trimethyl-cyclohexanone	Seed	
29-isofucosterol	Seed	
2-methyl-hept-2-en-6-one	Seed	
4-vinyl-guaiacol	Seed	
5-dehydro-avenasterol	Seed	
5-hydroxy-n-hentriacontan-14,16-dione	Seed	
6-hydroxy-n-hentriacontan-14,16-dione	Seed	
7-dehydro-avenasterol	Seed	
7-hydroxy-n-hentriacontan-14,16-dione	Seed	
Alanine	Seed	4000
Alpha-tocopherol	Seed	4.4-10.1
Arginine	Seed	3000-13 000
Ash	Seed	19 000-96 000
Aspartic-acid	Seed	7000
Avenacoside-a	Seed	
Avenacoside-b	Seed	
Avenanthramides	Seed	
Avenin	Seed	11 200-185 600
Benzaldehyde	Seed	
Beta-cyclocitral	Seed	
Beta-ionone	Seed	
Beta-sitosterol	Seed	
Biotin	Seed	0.132-1.4
Boron	Seed	2-7
Brassicasterol	Seed	
Butenyl-isothiocyanate	Seed	
Caffeic-acid-ester	Seed	
Calcium	Seed	400-4800
Campestanol	Seed	
Campesterol	Seed	
Carbohydrates	Seed	562 000-775 000
Carotene	Seed	0-0.22
Caryophyllene	Seed	
Chlorine	Seed	500-1900
Cholest-7-en-3-beta-ol	Seed	
Cholestanol	Seed	
Cholesterol	Seed	

Chemicals listed in Dr. Duke's database.

Chemical	Part	Range (ppm)
Choline	Seed	134-1712
Cobalt	Seed	0-0.32
Colamine	Seed	
Copper	Seed	2.4-25.7
Cystine	Seed	1000-5000
Daucosterol	Seed	
Dec-trans-2-en-1-al	Seed	
Delta-5-avenasterol	Seed	
Delta-7-avenasterol	Seed	
Delta-7-stigmasterol	Seed	
Ergothioneine	Seed	
Fat	Seed	11 000-97 000
Ferulic-acid	Seed	
Ferulic-acid-ester	Seed	
Fiber	Seed	10 000-289 000
Folic-acid	Seed	0-0.75
Formaldehyde	Seed	
Fur-2-aldehyde	Seed	
Gamma-murolene	Seed	
Geraniol-acetone	Seed	
Glutamic-acid	Seed	29 000-31 000
Gluten	Seed	
Glycine	Seed	2000
Heptan-1-al	Seed	
Heptanal	Seed	
Hexan-1-al	Seed	
Hexanal	Seed	
Hex-cis-3-en-1-ol	Seed	
Hex-trans-3-enyl-acetate	Seed	
Hexyl-acetate	Seed	
Histidine	Seed	1000-6000
Indole-3-acetic-acid-glucoprotein	Seed	
Iron	Seed	20-300
Isoleucine	Seed	4000-9000
Kilocalories	Seed	3740-4710
Leucine	Seed	6000-14 000
Lichenin	Seed	
Limonene	Seed	
Lophenol	Seed	
Lysine	Seed	2000-7000
Magnesium	Seed	300-2900
Manganese	Seed	20-204
Melatonin	Seed	
Methionine	Seed	1000-4000
Myrcene	Seed	
Niacin	Seed	6-44
Nonan-1-al	Seed	
Nonan-1-ol	Seed	

Chemicals listed in Dr. Duke's database.

Chemical	Part	Range (ppm)
Nona-trans-2-trans-4-dienal	Seed	
Nuatigenin	Seed	
Oct-1-en-3-ol	Seed	
Octan-1-al	Seed	
Octan-1-ol	Seed	
Octanal	Seed	
Oct-trans-2-en-1-ol	Seed	
Orgothionine	Seed	
Pantothenic-acid	Seed	4.4-28.3
<i>p</i> -Coumaric-acid	Seed	
Phenylalanine	Seed	4000-10 000
Phosphorus	Seed	500-10 200
<i>p</i> -Hydroxy-benzoic-acid	Seed	
Phylloquinone	Seed	0.1
Phytate	Seed	8970-10 000
Phytosterols	Seed	580
Potassium	Seed	2200-8900
Propanal	Seed	
Protein	Seed	74 000-232 000
Pyridoxine	Seed	0.22-2.4
Riboflavin	Seed	0.66-11.7
Salicylates	Seed	0
Salicylic-acid-methyl-ester	Seed	
Saponins	Seed	1000-13 000
Serine	Seed	4000
Sinapic-acid	Seed	
Sodium	Seed	100-1600
Starch	Seed	500 000-600 000
Stigmast-7-en-3-beta-ol	Seed	
Stigmasta-7,24(28)-dien-3-beta-ol	Seed	
Stigmastadienol	Seed	
Stigmastanediol	Seed	
Stigmastanol	Seed	
Stigmasterol	Seed	
Sugars	Seed	20 000-50 000
Sulfur	Seed	1500-3100
Thiamin	Seed	2.6-12.1
Threonine	Seed	3000-7000
Trans-hept-2-enal	Seed	
Trans-non-2-en-1-al	Seed	
Trigonelline	Seed	
Tryptophan	Seed	0-3000
Tyrosine	Seed	2000-14 000
Valine	Seed	4000-11 000
Vanillic-acid	Seed	
Vitamin-b-1	Seed	7
Vitamin-b-2	Seed	1.3

Chemicals listed in Dr. Duke's database.

Chemical	Part	Range (ppm)
Water	Seed	48 000-213 000
Wax	Seed	9000
Avenacoside-a	Shoot	
Avenacoside-b	Shoot	
Avenanthramide-g	Shoot	22.4
Betaine	Shoot	2
Choline	Shoot	0.3
Isoswertisin-2"-o-alpha-l-rhamnoside	Shoot	
Isovitexin-2"-o-alpha-l-arabinoside	Shoot	
Myoinositol-oxidase	Shoot	
Proline	Shoot	1.3
Vitexin-2"-o-alpha-l-rhamnoside	Shoot	
1,3-amino-propyl-pyrrolinium	Sprout Seedling	
7-o-methoxyvitexin-o-rhamno-glucoside	Sprout Seedling	
Avenein	Sprout Seedling	
Delta-amino-levulinic-acid	Sprout Seedling	
Diadenosine-tetraphosphoric-acid	Sprout Seedling	
Diamino-propane	Sprout Seedling	
Isovitexin	Sprout Seedling	
Isovitexin--o-arabinoside	Sprout Seedling	
Nicotianamine	Sprout Seedling	
O"-rhamnosyl-8-c-d-glucopyranosylgenkwanin	Sprout Seedling	
Phaeophorbide	Sprout Seedling	
Scopoletin	Sprout Seedling	
Scopolin	Sprout Seedling	
Vitexin-o-glucoside	Sprout Seedling	
Xanthophyll-epoxide	Sprout Seedling	

<http://sun.ars-grin.gov:8080/npgspub/xsql/duke/plantdisp.xsql?taxon=144>



Memorandum

TO: Lillian Gill, D.P.A.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Halyna Breslawec, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: April 24, 2014

SUBJECT: Comments on the Scientific Literature Review: Safety Assessment of *Avena sativa*-Derived Ingredients as Used in Cosmetics

The Council has no suppliers listed for *Avena Sativa* (Oat) Leaf Extract.

Key Issues

A number of ingredients in this report contain protein. Therefore, the CIR Expert Panel should consider adding Hydrolyzed Oat Protein (77 VCRP uses) to this report. A concentration of use survey for Hydrolyzed Oat Protein was completed in 2012. Hydrolyzed Oat Flour (7 VCRP uses) and Hydrolyzed Oats (38 VCRP uses) are also included in the Dictionary. Addition of these 2 ingredients would require a delay to complete a concentration of use survey.

The Introduction and Summary should also note the USP definition of Colloidal Oatmeal which refers to 7CFR810.1001, the definition of oats. This definition of oats only includes *Avena sativa* and *Avena byzantina*. It does not include *A. nuda* or *A. strigosa* as listed in the introduction of the CIR report. The USP also indicates that oats used to make Colloidal Oatmeal must meet U.S. standards for No.1 or 2 grade oats (97% or 94% sound oats) (see attached CFR).

Although Colloidal Oatmeal is not currently in this report, the following paper concerning personal care products (abstract attached) should be added to the CIR report:

Criquet M, Roure R, Dayan, et al. 2012. Safety and efficacy of personal care products containing colloidal oatmeal. Clin Cosmet Investig Dermatol 5: 183-193.

The extraction solvent should be stated for each extract studied (or the CIR report should state that the extraction solvent used was not stated).

Additional Comments

- p.1 - The Introduction should also note that Avena Sativa (Oat) Kernel Oil has been previously reviewed by CIR and found safe as used.
- p.1 - The following does not make sense: “the method extraction and analysis and also result in differences in lipid content.” Although the method of analysis may indicate differences in lipid content, it is not a factor that determines the lipid content of grains.
- p.1 - If Avena Sativa (Oat) Kernel Oil is left in the report, the composition of this oil should be added to the Constituents section.
- p.2 - What is the constituent of concern? It states: “Quercitrin - Quercetin”. These are two different compounds. In what species was “it” (based on the reference it is likely quercetin) genotoxic following i.p. exposure?
- p.2, Table 2 - A listing of fungi know to infect oats is not helpful. Which of the fungi species are associated with microtoxin production? A statement that x, y, fungi species that produce various micotoxins have been associated with oats would be sufficient for the CIR report.
- p.2 - The fact that oat straw bedding contaminated with a toxic mold caused skin lesions in cows is not relevant to the CIR report and should be deleted.
- p.2 - For what, in what media is 0.1 mg/kg fresh mass “the safe level set by the European Commission”? A reference (from the European Commission) should be provided for this value.
- p.2-3 - The text of the Cosmetic Use section should focus on the ingredients with the greatest number of reported uses. In the text, please use specific FDA product categories rather than the assumptions (which may not be correct) that products are either leave-on or rinse-off products.
- p.3, reference 37 - If the Physician’s Desk Reference for Nonprescription Drugs is going to be cited in the CIR report, please use a more recent edition. Reference 37 is for the 15th edition in 1994. The 35th edition was published in 2014.
- p.3, Toxicokinetics - It is not correct to state that no data on the toxicokinetics of the constituents of *A. sativa* ingredients were “discovered”. There are data on the kinetics of quercetin (the only constituent of concern noted in the CIR report) such as:
Boonpawa R, Spenkelin A, Rietjens IM. 2014. A physiologically based kinetic (PBK) model describing plasma concentrations of quercetin and its metabolites in rats. Biochem Pharmacol 89(2): 287-299.

Lin CF Leu YL, Al-Suwayeh SA, et al. 2012. Anti-inflammatory activity and percutaneous absorption of quercetin and its polymethoxylated compound and glycosides: the relationships to chemical structures. Eur J Pharm Sci 47(5): 857-864.

For the purposes of this CIR report, it is not necessary to include these studies, but the CIR report should not imply that this information does not exist.

- p.3 - Please check reference 44. This is a study of the anti-estrogenic effect of oat hay, and the abstract says that anti-estrogenic activity was demonstrated. Therefore, it does not make

sense to state that uterine weights of rats treated with oat straw extract and estradiol were greater than uterine weights of rats treated with estradiol alone.

- p.4 - Where there any controls used in the study in dermal fibroblasts (reference 51)?
- p.4 - Please revise the following sentence: "In a blind study of acute burn patients (n=35), a shower/bath oil containing colloidal oatmeal (5% in liquid paraffin), reported no adverse effect." Based on the structure of this sentence, the sentence is saying that the shower/bath oil reported no adverse effects. If available, please indicate the severity of the burns in the study subjects.
- p.5 - Searching the Dictionary for the trade names used in reference 28, indicates that the material tested was the leaf/stem and/or leaf/stalk extract.
- p.5 - It is not necessary to state "acetic 5%" twice in the second paragraph in the Sensitization section. Although "acetic" may be an uncommon word, it is an adjective and does not need [sic].
- p.5 - Why were the children in reference 53 referred for allergy testing?
- p.6 - Was there any discussion as to what compounds in oats were associated with photosensitization in livestock?
- p.8, Table 1 - Please add a footnote to this table that defines "meristem".
- p.9-11, Table 3 - In the title of Table 3, it does not make sense to state: "The Council conducted a survey or the concentration of use for the ingredients added to this report." This is a new report - so it does not make sense to state that some ingredients were added to the report.

For some product categories, the Council concentration of use survey reported that some products are "not spray" and that some products are "not powder". It does not make sense to include the "not spray" products in the row "Incidental inhalation-sprays" and then add footnote "Not spray product(s)". The "not spray" products should not be in the row "Incidental inhalation-sprays". It also does not make sense to include the "not powder" products in the row "Incidental inhalation-powders" and then add footnote "Not powder product(s)". The "not powder" products should not be in the row "Incidental inhalation-powders".

- p.12, Table 4 - Please provide a reference with this table. Why were these children tested?

§ 810.803

PRINCIPLES GOVERNING THE APPLICATION OF STANDARDS

§ 810.803 Basis of determination.

Each determination of damaged and heat-damaged kernels, and the percentage of each kind of grain in the mixture is made on the basis of the sample after removal of foreign material and fines. Other determinations not specifically provided for under the general provisions are made on the basis of the grain as a whole, except the determination of odor is made on either the basis of the grain as a whole or the grain when free from foreign material and fines.

GRADES AND GRADE REQUIREMENTS

§ 810.804 Grades and grade requirements for mixed grain.

(a) *U.S. Mixed Grain (grade)*. Mixed grain with not more than 15.0 percent of damaged kernels, and not more than 3.0 percent of heat-damaged kernels, and that otherwise does not meet the requirements for the grade U.S. Sample grade Mixed Grain.

(b) *U.S. Sample grade Mixed Grain*. Mixed grain that:

(1) Does not meet the requirements for the grade U.S. Mixed Grain; or

(2) Contains more than 16.0 percent moisture; or

(3) Contains 8 or more stones that have an aggregate weight in excess of 0.2 percent of the sample weight, 2 or more pieces of glass, 3 or more *Crotalaria* seeds (*Crotalaria* spp.), 2 or more castor beans (*Ricinus communis* L.), 8 more cockleburs (*Xanthium* spp.) or similar seeds singly or in combination, 4 or more pieces of an unknown foreign substance(s) or a recognized harmful or toxic substance(s), 10 or more rodent pellets, bird droppings, or an equivalent quantity of other animal filth per 1,000 grams of mixed grain; or

(4) Is musty, sour, or heating; or

(5) Has any commercially objectionable foreign odor except smut or garlic; or

(6) Is otherwise of distinctly low quality.

7 CFR Ch. VIII (1-1-13 Edition)

SPECIAL GRADES AND SPECIAL GRADE REQUIREMENTS

§ 810.805 Special grades and special grade requirements.

(a) *Blighted mixed grain*. Mixed grain in which barley predominates and that contains more than 4.0 percent of fungus-damaged and/or mold-damaged barley kernels.

(b) *Ergoty mixed grain*. (1) Mixed grain in which rye or wheat predominates and that contains more than 0.30 percent ergot, or

(2) Any other mixed grain that contains more than 0.10 percent ergot.

(c) *Garlicky mixed grain*. (1) Mixed grain in which wheat, rye, or triticale predominates, and that contains 2 or more green garlic bulblets, or an equivalent quantity of dry or partly dry bulblets in 1,000 grams of mixed grain; or

(2) Any other mixed grain that contains 4 or more green garlic bulblets, or an equivalent quantity of dry or partly dry bulblets, in 500 grams of mixed grain.

(d) *Smutty mixed grain*. (1) Mixed grain in which rye, triticale, or wheat predominates, and that contains 15 or more average size smut balls, or an equivalent quantity of smut spores in 250 grams of mixed grain, or

(2) Any other mixed grain that has the kernels covered with smut spores to give a smutty appearance in mass, or that contains more than 0.2 percent smut balls.

(e) *Treated mixed grain*. Mixed grain that has been scoured, limed, washed, sulfured, or treated in such a manner that its true quality is not reflected by the grade designation U.S. Mixed Grain or U.S. Sample grade Mixed Grain.

[52 FR 24418, June 30, 1987, as amended at 52 FR 24441, June 30, 1987]

Subpart G—United States Standards for Oats

TERMS DEFINED

§ 810.1001 Definition of oats.

Grain that consists of 50 percent or more of oats (*Avena sativa* L. and *A. byzantina* C. Koch) and may contain, singly or in combination, not more than 25 percent of wild oats and other

Grain Inspection, Packers and Stockyard Admin. (FGIS), USDA § 810.1005

grains for which standards have been established under the United States Grain Standards Act.

§ 810.1002 Definition of other terms.

(a) *Fine seeds.* All matter that passes through a $\frac{5}{64}$ triangular-hole sieve after sieving according to procedures prescribed in FGIS instructions.

(b) *Foreign material.* All matter other than oats, wild oats, and other grains.

(c) *Heat-damaged kernels.* Kernels and pieces of oat kernels, other grains, and wild oats that are materially discolored and damaged by heat.

(d) *Other grains.* Barley, corn, cultivated buckwheat, einkorn, emmer, flaxseed, guar, hull-less barley, nongrain sorghum, Polish wheat, popcorn, poulard wheat, rice, rye, safflower, sorghum, soybeans, spelt, sunflower seed, sweet corn, triticale, and wheat.

(e) *Sieves*—(1) $\frac{5}{64}$ triangular-hole sieve. A metal sieve 0.032 inch thick with

equilateral triangular perforations the inscribed circles of which are 0.0781 ($\frac{5}{64}$) inch in diameter.

(2) $0.064 \times \frac{3}{8}$ oblong-hole sieve. A metal sieve 0.032 inch thick with oblong perforations 0.064 inch by 0.375 ($\frac{3}{8}$) inch.

(f) *Sound oats.* Kernels and pieces of oat kernels (except wild oats) that are not badly ground-damaged, badly weather-damaged, diseased, frost-damaged, germ-damaged, heat-damaged, insect-bored, mold-damaged, sprout-damaged, or otherwise materially damaged.

(g) *Wild oats.* Seeds of *Avena sativa* L. and *A. sterilis* L.

PRINCIPLES GOVERNING THE APPLICATION OF STANDARDS

§ 810.1003 Basis of determination.

Other determinations not specifically provided for under the general provisions are made on the basis of the grain as a whole.

GRADES AND GRADE REQUIREMENTS

§ 810.1004 Grades and grade requirements for oats.

Grade	Minimum limits—		Maximum limits—		
	Test weight per bushel (pounds)	Sound oats (percent)	Heat-damaged kernels (percent)	Foreign material (percent)	Wild oats (percent)
U.S. No. 1	36.0	97.0	0.1	2.0	2.0
U.S. No. 2	33.0	94.0	0.3	3.0	3.0
U.S. No. 3 ¹	30.0	90.0	1.0	4.0	5.0
U.S. No. 4 ²	27.0	80.0	3.0	5.0	10.0

U.S. Sample grade—

U.S. Sample grade are oats which:

- (a) Do not meet the requirements for the grades U.S. Nos. 1, 2, 3, or 4; or
- (b) Contain 8 or more stones which have an aggregate weight in excess of 0.2 percent of the sample weight, 2 or more pieces of glass, 3 or more crotalaria seeds (*Crotalaria* spp.), 2 or more castor beans (*Ricinus communis* L.), 4 or more particles of an unknown foreign substance(s) or a commonly recognized harmful or toxic substance(s), 8 or more cocklebur (*Xanthium* spp.) or similar seeds singly or in combination, 10 or more rodent pellets, bird droppings, or equivalent quantity of other animal filth per $1\frac{1}{2}$ to $1\frac{1}{4}$ quarts of oats; or
- (c) Have a musty, sour, or commercially objectionable foreign odor (except smut or garlic odor); or
- (d) Are heating or otherwise of distinctly low quality.

¹Oats that are slightly weathered shall be graded not higher than U.S. No. 3.

²Oats that are badly stained or materially weathered shall be graded not higher than U.S. No. 4.

SPECIAL GRADES AND SPECIAL GRADE REQUIREMENTS

§ 810.1005 Special grades and special grade requirements.

(a) *Bleached oats.* Oats that in whole or in part, have been treated with sulfuric acid or any other bleaching agent.

(b) *Bright oats.* Oats, except bleached oats, that are of good natural color.

(c) *Ergoty oats.* Oats that contain more than 0.10 percent ergot.

(d) *Extra-heavy oats.* Oats that have a test weight per bushel of 40 pounds or more.

(e) *Garlicky oats.* Oats that contain 4 or more green garlic bulblets or an

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Clin Cosmet Investig Dermatol. 2012;5:183-93. doi: 10.2147/CCID.S31375. Epub 2012 Nov 8.

Safety and efficacy of personal care products containing colloidal oatmeal.

Criquet M¹, Roure R, Dayan L, Nollent V, Bertin C.

Author information

¹Johnson & Johnson Santé Beauté France, Issy les Moulineaux, France.

Abstract

BACKGROUND: Colloidal oatmeal is a natural ingredient used in the formulation of a range of personal care products for relief of skin dryness and itchiness. It is also used as an adjunctive product in atopic dermatitis. The safety of personal care products used on vulnerable skin is of particular importance and the risk of developing further skin irritations and/or allergies should be minimized.

METHODS: In a series of studies, we tested the safety of personal care products containing oatmeal (creams, cleansers, lotions) by assessing their irritant/allergenic potential on repeat insult patch testing, in safety-in-use and ocular studies using subjects with nonsensitive and sensitive skin. We also tested the skin moisturizing and repair properties of an oatmeal-containing skin care product for dry skin.

RESULTS: We found that oatmeal-containing personal care products had very low irritant potential as well as a very low allergenic sensitization potential. Low-level reactions were documented in 1.0% of subjects during the induction phase of repeat insult patch testing; one of 2291 subjects developed a persistent but doubtful low-level reaction involving edema during the challenge phase in repeat insult patch testing. No allergies were reported by 80 subjects after patch testing after in-use application. Sustained skin moisturizing was documented in subjects with dry skin that lasted up to 2 weeks after product discontinuation.

CONCLUSION: Our results demonstrate that colloidal oatmeal is a safe and effective ingredient in personal care products. No allergies were reported by consumers of 445,820 products sold during a 3-year period.

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Biochem Pharmacol. 2014 May 15;89(2):287-99. doi: 10.1016/j.bcp.2014.02.007. Epub 2014 Feb 19.

A physiologically based kinetic (PBK) model describing plasma concentrations of quercetin and its metabolites in rats.

Boonpawa R¹, Spenkelink A², Rietjens IM², Punt A².

Author information

Abstract

Biological activities of flavonoids *in vivo* are ultimately dependent on the systemic bioavailability of the aglycones as well as their metabolites. In the present study, a physiologically based kinetic (PBK) model was developed to predict plasma concentrations of the flavonoid quercetin and its metabolites and to tentatively identify the regiospecificity of the major circulating metabolites. The model was developed based on *in vitro* metabolic parameters and by fitting kinetic parameters to literature available *in vivo* data. Both exposure to quercetin aglycone and to quercetin-4'-O-glucoside, for which *in vivo* data were available, were simulated. The predicted plasma concentrations of different metabolites adequately matched literature reported plasma concentrations of these metabolites in rats exposed to 4'-O-glucoside. The bioavailability of aglycone was predicted to be very low ranging from 0.004%-0.1% at different oral doses of quercetin or quercetin-4'-O-glucoside. Glucuronidation was a crucial pathway that limited the bioavailability of the aglycone, with 95-99% of the dose being converted to monoglucuronides within 1.5-2.5h at different dose levels ranging from 0.1 to 50mg/kg bw quercetin or quercetin-4'-O-glucoside. The fast metabolic conversion to monoglucuronides allowed these metabolites to further conjugate to di- and tri-conjugates. The regiospecificity of major circulating metabolites was observed to be dose-dependent. As we still lack *in vivo* kinetic data for many flavonoids, the developed model has a great potential to be used as a platform to build PBK models for other flavonoids as well as to predict the kinetics of flavonoids in humans.

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KEYWORDS: Absorption distribution metabolism excretion (ADME), Bioavailability, Physiologically based kinetic (PBK) modeling, Quercetin

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Eur J Pharm Sci. 2012 Dec 18;47(5):857-64. doi: 10.1016/j.ejps.2012.04.024. Epub 2012 May 17.

Anti-inflammatory activity and percutaneous absorption of quercetin and its polymethoxylated compound and glycosides: the relationships to chemical structures.

Lin CF¹, Leu YL, Al-Suwayeh SA, Ku MC, Hwang TL, Fang JY.

Author information

Abstract

The potential of **quercetin**-related compounds for topical application has not previously been systematically investigated. To better elucidate relationships of the structure and activity with skin permeation, some **quercetin** compounds were used as permeants, including aglycone, a polymethoxylated compound (**quercetin** 3,5,7,3',4'-pentamethylether, QM), and seven glycosides. **Quercetin** and the glycoside with glucopyranuronic acid (Q4) at a dose of 30 μ M completely inhibited superoxide anion activated neutrophils. QM also potentially suppressed superoxide by 90%. Both **quercetin** and QM showed inhibitory activity on elastase release with respective IC(50) values of 6.25 and 15.76 μ M. Glycosylation significantly diminished this activity. Both an infinite concentration and saturated solubility in pH 7 buffer were used as permeant doses for the in vitro permeation experiments. The flux or permeability coefficient, which is the indicator for total absorption of **dermal** delivery due to the use of nude mouse skin, was the greatest for QM, followed by the glycosides and **quercetin**. QM showed 26 \times greater flux compared to **quercetin**. No **penetration** of **quercetin** occurred at the dose of saturated solubility. Rutin generally exhibited the highest skin permeation among the glycosides. It was found that the glycoside enantiomers (Q2 and Q3) revealed completely different permeation profiles. The stratum corneum was the principal **penetration** barrier for **quercetin** and its glycosides but not QM. Rutin provoked some skin redness and inflammation after a 5-day administration in nude mouse. QM caused no irritation, suggesting that it is a superior candidate for topical delivery.

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PMID: 22609526 [PubMed - indexed for MEDLINE]