Safety Assessment of *Saccharum officinarum* (Sugarcane)-Derived Ingredients as Used in Cosmetics

Status:	Draft Report for Panel Review
Release Date:	November 13, 2020
Panel Meeting Date:	December 7 - 8, 2020

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

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Cosmetic Ingredient Review

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Priya Cherian, Scientific Analyst/Writer, CIR
Date: November 13, 2020
Subject: Safety Assessment of *Saccharum officinarum* (Sugarcane)-Derived Ingredients as Used in Cosmetics

Enclosed is the Draft Report of the Safety Assessment of *Saccharum officinarum* (Sugarcane)-Derived Ingredients as Used in Cosmetics (*sugarc122020rep*). This is the first time the Panel is reviewing the safety assessment on these 4 ingredients. The Scientific Literature Review (SLR) was announced on September 17, 2020.

Comments provided by the Council on the SLR were received and addressed (*sugarc122020pcpc*). The 2019 survey concentration of use data for the two ingredients (*sugarc122020data1*), and 2020 concentration of use data for two additional ingredients (*sugarc122020data2*), are attached. In addition, manufacturing and physiochemical properties data on Saccharum Officinarum (Sugarcane) Extract were received, and are included in the packet as *sugarc122020data3*.

Also included in this package for your review are the 2020 VCRP frequency of use data (*sugarc122020FDA*), report history (*sugarc122020hist*), data profile (*sugarc122020prof*), search strategy (*sugarc122020strat*), and flow chart (*sugarc122020flow*).

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an Insufficient Data Announcement (IDA), specifying the data needs therein.

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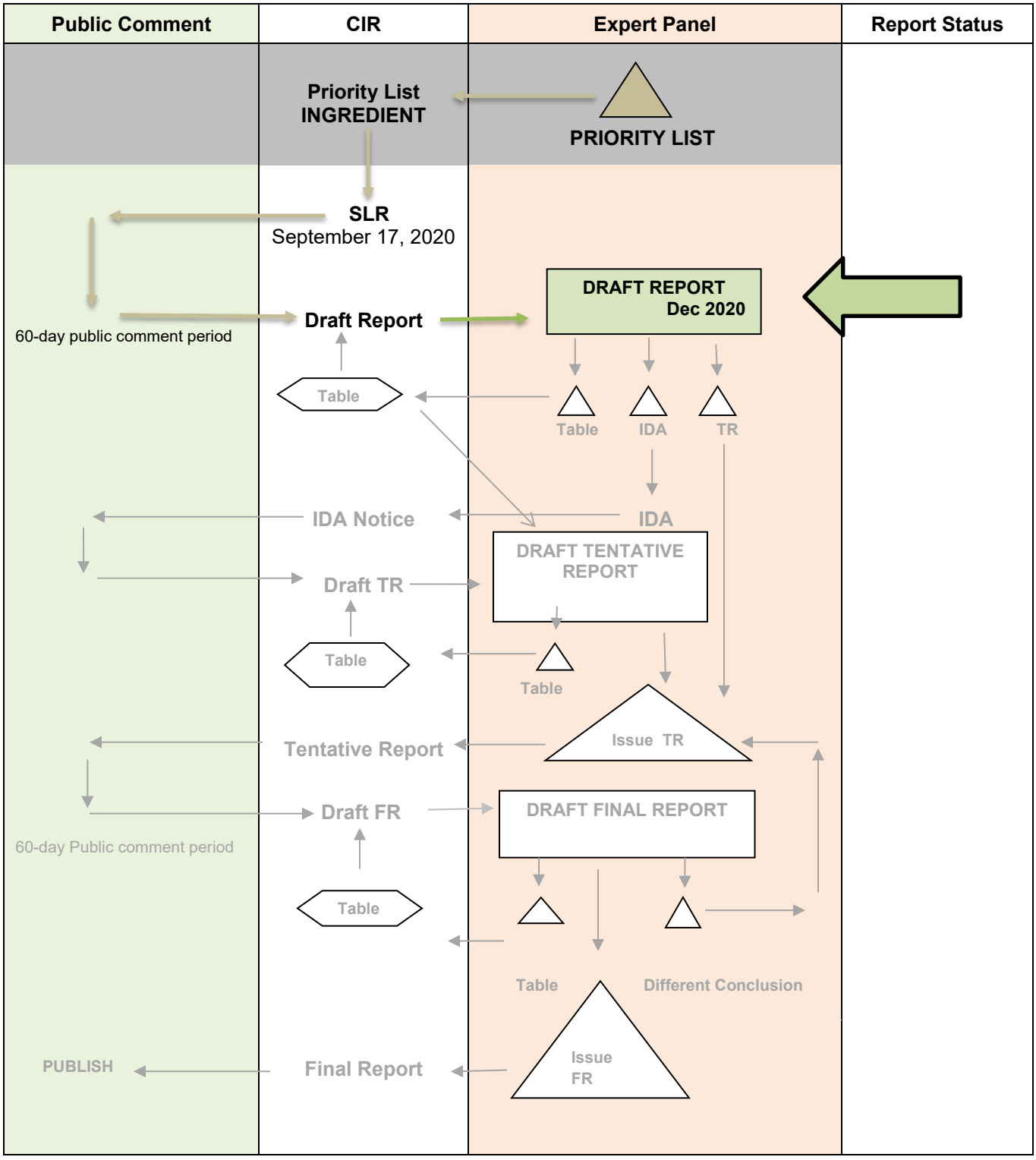
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY *Saccharum officinarum* (Sugarcane)-derived ingredients

MEETING December 2020



Saccharum officinarum (sugarcane) – derived ingredients – History

March 2019

- 2 new additional ingredients added to report: Saccharum Officinarum (Sugarcane) Bagasse Powder and Saccharum Officinarum (Sugarcane) Juice Extract

July 2019

- Concentration of use data received for Saccharum Officinarum (Sugarcane) Extract and Saccharum Officinarum (Sugarcane) Wax

September 2020

- SLR posted
- Comments on SLR received from PCPC

October 2020

- Manufacturing and physiochemical properties data on Saccharum Officinarum (Sugarcane) Extract received
- Concentration of use information received for the 2 additional ingredients (Saccharum Officinarum (Sugarcane) Juice Extract and Saccharum Officinarum (Sugarcane) Bagasse Powder)

December 2020

- The Expert Panel on Cosmetic Ingredient Safety (Panel) reviews the Draft Report

***Saccharum officinarum* (Sugarcane)-Derived Ingredients Data Profile – December 2020 – Priya Cherian, Scientific Analyst/Writer**																														
						Toxico-kinetics		**Acute Tox**			**Repeated Dose Tox**			**DART**		**Genotox**		**Carci**		**Dermal Irritation**			**Dermal Sensitization**				**Ocular Irritation**		**Clinical Studies**	
	Reported Use	**GRAS**	**Method of Mfg**	**Constituents**	**Impurities**	**Dermal Penetration**	**ADME**	**Dermal**	**Oral**	**Inhalation**	**Dermal**	**Oral**	**Inhalation**	**Dermal**	**Oral**	**In Vitro**	**In Vivo**	**Dermal**	**Oral**	**In Vitro**	**Animal**	**Human**	**In Vitro**	**Animal**	**Human**	**Phototoxicity**	**In Vitro**	**Animal**	**Retrospective/ Multicenter**	**Case Reports**
Saccharum Officinarum (Sugarcane) Extract	X		X	X																									
Saccharum Officinarum (Sugarcane) Bagasse Powder				X																									
Saccharum Officinarum (Sugarcane) Juice Extract	X		X	X	X				X																				
Saccharum Officinarum (Sugarcane) Wax	X		X	X																									
Saccharum Officinarum (Sugarcane) higher aliphatic primary acids*									X			X			X		X		X										
Saccharum Officinarum (Sugarcane) long chain primary alcohols*				X								X							X										

"X" indicates that data were available in a category for the ingredient

* data provided are on major components of sugarcane wax (higher aliphatic primary acids or long-chain primary alcohols), however, they are not a specified ingredient being reviewed in this report

Sugarcane-derived Ingredients Search Strategy

Ingredient	CAS #	InfoB	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Saccharum Officinarum (Sugarcane) Bagasse Powder		✓	✓			✓													✓
Saccharum Officinarum (Sugarcane) Extract	91722-22-4	✓	✓			✓													✓
Saccharum Oficinarum (Sugarcane) Juice Extract	91722-22-4	✓	✓			✓													✓
Saccharum Officinarum (Sugarcane) Wax	142583-61-7	✓	✓			✓													✓

Search Strategy

[*document search strategy used for SciFinder, PubMed, and Toxnet*]

Saccharum officinarum
Sugarcane toxicity
Sugarcane dermal
Sugarcane extract
Sugarcane wax
Sugarcane penetration
Sugarcane composition
Sugarcane cosmetic
Bagasse
Sugarcane pesticides
Sugarcane impurities
D-003 toxicity
Policosanol toxicity
CAS numbers
Sugarcane metabolism
Sugarcane carcinogenicity
Sugarcane tumor
Sugarcane cancer

LINKS

Search Engines

- Pubmed (- http://www.ncbi.nlm.nih.gov/pubmed)
- Toxnet (https://toxnet.nlm.nih.gov/); (includes Toxline; HSDB; ChemIDPlus; DART; IRIS; CCRIS; CPDB; GENE-TOX)

appropriate qualifiers are used as necessary
search results are reviewed to identify relevant documents

Pertinent Websites

- wINCI - http://webdictionary.personalcarecouncil.org
- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;,
- EAFUS: http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting&displayall=true
- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOGS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM135688.pdf
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- OTC ingredient list: https://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm135688.pdf
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/
- HPVIS (EPA High-Production Volume Info Systems) - https://ofmext.epa.gov/hpvis/HPVISlogon
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) - http://www.femaflavor.org/search/apachesolr_search/
- EU CosIng database: http://ec.europa.eu/growth/tools-databases/cosing/
- ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- IUCLID (International Uniform Chemical Information Database) - https://iuclid6.echa.europa.eu/search
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- SCCS (Scientific Committee for Consumer Safety) opinions: http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- NICNAS (Australian National Industrial Chemical Notification and Assessment Scheme)- https://www.nicnas.gov.au/
- International Programme on Chemical Safety http://www.inchem.org/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/
- www.google.com - a general Google search should be performed for additional background information, to identify references that are available, and for other general information

Botanical Websites, if applicable

- Dr. Duke's - https://phytochem.nal.usda.gov/phytochem/search
- Taxonomy database - http://www.ncbi.nlm.nih.gov/taxonomy
- GRIN (U.S. National Plant Germplasm System) - https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx
- Sigma Aldrich plant profiler- http://www.sigmaaldrich.com/life-science/nutrition-research/learning-center/plant-profiler.html
- American Herbal Products Association Botanical Safety Handbook (database) - http://www.ahpa.org/Resources/BotanicalSafetyHandbook.aspx
- European Medicines Agency Herbal Medicines - http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/herbal_search.jsp
- National Agricultural Library NAL Catalog (AGRICOLA) https://agricola.nal.usda.gov/
- The Seasoning and Spice Association List of Culinary Herbs and Spices
- http://www.seasoningandspice.org.uk/ssa/background_culinary-herbs-spices.aspx

Fragrance Websites, if applicable

- IFRA (International Fragrance Association) – http://www.ifraorg.org/
- Research Institute for Fragrance Materials (RIFM)

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INTRODUCTION

This is a safety assessment of the following 4 *Saccharum officinarum* (sugarcane)-derived ingredients as used in cosmetic formulations:

Saccharum Officinarum (Sugarcane) Bagasse Powder
Saccharum Officinarum (Sugarcane) Extract
Saccharum Officinarum (Sugarcane) Juice Extract
Saccharum Officinarum (Sugarcane) Wax

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), reported functions of these ingredients include, collectively, skin-conditioning agents, surfactants, exfoliants, solvents, deodorant agents, binders, skin protectants, and emulsion stabilizers.[1] (Table 1)

In 2019, the Expert Panel for Cosmetic Ingredient Safety (Panel) published a safety assessment on mono- and disaccharides (including sucrose, a major component of sugarcane), with the conclusion that those ingredients are safe in the present practices of use and concentration (as described in that safety assessment).[2] The full report on those ingredients can be accessed on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/ingredients).

Botanicals, such as sugarcane-derived ingredients, may contain hundreds of constituents. Thus, in this assessment, the Panel will assess the safety of each of the botanical ingredients as a whole, complex mixture.

Some of the ingredients reviewed in this safety assessment may be consumed as food, and daily exposure as such would result in much larger systemic exposures than possible from use of these ingredients in cosmetic products. Therefore, although oral studies are included herein, the primary focus of this safety assessment is on the potential for local effects from topical exposure to these ingredients as used in cosmetics.

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

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

CHEMISTRY

Definition and Plant Identification

All ingredients reviewed in this report are derived from the sugarcane plant (*Saccharum officinarum*). The definitions of the *Saccharum officinarum* (sugarcane)-derived ingredients included in this review are provided in Table 1; the generic CAS number for the majority of these ingredients is 91722-22-4.[1] Sugarcane is a perennial grass, indigenous to tropical south and southeast Asia.[3] The plant is currently cultivated in many regions, namely Brazil and India, the largest producers of sugarcane. The plant has a thick, longitudinal stalk, which ranges from 3 - 5 m in height, and approximately 5 cm in diameter. When stalks are crushed, the remaining fibrous matter is known as bagasse.[4] The stems of the sugarcane plant vary in color (green, pink, purple), and can reach 5 cm in length. The leaves are elongated and green, with thick midribs and saw-toothed edges that grow to a length of about 30 – 60 cm, and width of 5 cm. The wax of the sugarcane plant is a whitish to dark yellow powdery deposit on the surface of the stalks and leaves, which appears as a cuticle layer.

Chemical Properties

According to a supplier, a tradename mixture with Saccharum Officinarum (Sugarcane) Extract is prepared in glycerin and water is a colorless to yellow liquid, with a pH ranging from 1.5 – 5.0.[5] This tradename mixture is also soluble in water, has a refractive index of 1.3920 – 1.5000 (at 25°C), and a specific gravity of 1.20 – 1.50.

Method of Manufacture

Saccharum Officinarum (Sugarcane) Extract

According to a manufacturer, sugarcane is extracted with an eluent (water, butylene glycol, glycerin, or propylene glycol) under appropriate temperature conditions, to yield a concentrate (i.e., Saccharum Officinarum (Sugarcane) Extract).[5] The concentrate containing the phytochemical constituents is then blended with the desired diluent(s) and preservation

system to produce a final tradename mixture. The tradename mixture is evaluated for chemical properties according to specification requirements. The concentrate is also evaluated for contaminants and chemical properties, as needed. In a separate study, a sugarcane extract was produced by first crushing the sugarcane (4.36 kg) and exhaustively extracting with ethyl acetate at room temperature, yielding 72 g of the crude extract.[6]

Saccharum Officinarum (Sugarcane) Juice Extract

In order to produce a sugarcane juice, the sugarcane is washed and passed through a roller mill.[7] Fresh sugarcane juice is collected in sterilized screw-capped containers and processed. The juice is then filtered by muslin cloth and pasteurized at 90 °C for five minutes. The pH of the pasteurized juice is adjusted with citric acid.

Saccharum Officinarum (Sugarcane) Wax

Press mud, which is produced during the clarification of sugarcane juice, is a source of sugarcane wax.[8] Approximately 36 - 40 kg press mud is obtained after crushing 1 ton of sugarcane. The press mud contains sugar, fiber, and coagulated colloids including cane wax, albuminoids, inorganic salts, and soil particles. In order to extract the sugarcane wax from the press mud, a Soxhlet extractor is used with different solvents, such as toluene or benzene. The extract is filtered under a mild vacuum and the solvent is removed by distillation. After removing the solvent, the solid mass containing the wax and resin is dissolved in hot isopropyl alcohol and filtered. The remaining resin is separated, and the total sugarcane wax portion obtained is yellow or light cream in color.

Composition and Impurities

Saccharum Officinarum (Sugarcane) Bagasse Powder

Crushed sugarcane stalk is composed of a sugarcane powder: cellulose (45 - 55%), hemicellulose (20 - 25%), lignin (18 - 24%), and pectin (0.6 - 0.8%), as well as extractives (1.5 - 9%).[4] Pyrolization results in 1 - 4% ash by weight.

Saccharum Officinarum (Sugarcane) Extract

Sugarcane tops were extracted with ethyl acetate (thus a *Saccharum officinarum* extract), purified, and evaluated by nuclear magnetic resonance and electrospray ionization mass spectra.[9] The phenolic compounds were identified as caffeic acid, *cis*-*p*-hydroxycinnamic acid, quercetin, apigenin, albanin A, australone A, moracin M, and 5'-geranyl-5,7,2',4'-tetrahydroxyflavone. The amount of sterols in different sugarcane extract samples was evaluated by direct saponification followed by reversed-phase-high-performance liquid chromatography (RP-HPLC).[10] Both green- and red-rind sugarcane piths, nodes, and tips were evaluated. The results exhibited that stigmasterol (varied from 883.3 ± 23.5 to 1823.9 ± 24.5 µg/g dry weight (DW)) and β-sitosterol (varied from 117.6 ± 19.9 to 801.4 ± 33.5 µg/g DW) were the major phytosterols in the sugarcane extract samples. In addition, among other parts of the sugarcane, the tips contained the greatest amount of phytosterols.

Saccharum Officinarum (Sugarcane) Juice Extract

Sugarcane juice contains 75 - 85% water, 10 - 21% sucrose, 10 - 15% fiber, 0.3 - 3% reducing sugars (glucose and fructose), and other inorganic compounds.[11] Sugarcane juice contains phytochemicals such as phenolics, sterols, terpenoids, lignins, and mixtures of long chain primary alcohols.[12] HPLC with diode-array detection (HPLC-DAD) analysis of phenolic compounds from sugarcane juice showed the presence of phenolic acids such as hydroxycinnamic acid, sinapic acid, and caffeic acids, along with flavones such as apigenin, luteolin, and tricin.[3] Among the flavones, tricin derivatives accounted for the highest concentration.

The amount of minerals and heavy metals in 12 fresh sugarcane juice samples from Multan, Pakistan were examined via furnace atomic absorption spectroscopy.[13] Mean concentrations of microelements and heavy metals were reported to be 0.352 mg/l iron, 0.129 mg/l zinc, 0.265 mg/l manganese, 0.150 mg/l copper, 0.167 mg/l lead, 0.052 cadmium, 0.085 nickel, and 0.400 mg/l cobalt.

During harvesting season, most sugarcane plantations are burnt, causing the emission of polycyclic aromatic hydrocarbons (PAHs), and thus, contamination in sugarcane products.[14] A study was performed evaluating the presence of four PAHs (benz[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, and benzo[a]pyrene) in 80 samples of sugarcane juice collected from two Brazilian cities. Samples were collected in two different periods (during harvesting season and between harvests). The samples collected between harvests presented mean sums of PAHs of 0.013 µg/kg and 0.012 µg/kg, while samples collected during harvest presented mean sums of 0.053 µg/kg and 0.055 µg/kg. The most representative PAH was benzo[b]fluoranthene, which was detected in 39% of the samples.

Saccharum Officinarum (Sugarcane) Wax

The amount of wax in sugarcane plants ranges from 0.1 – 0.3%.[3] The sugarcane wax contains long chain fatty alcohols, acids, esters, aldehydes, and ketones. Aliphatic alcohols, long chain aliphatic fatty acids, steroids, and terpenoids have also been identified from sugarcane wax. Octacosanol constitutes 50 – 80% of the total aliphatic alcohols in sugarcane wax. Other such alcohols in sugarcane wax include triacontanol, hexacosanol, tetracosanol, heptacosanol, nonacosanol, dotriacontanol, and tetratriacontanol.[15]

USE

Cosmetic

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

According to 2020 VCRP survey data, Saccharum Officinarum (Sugarcane) Extract is reported to be used in 466 formulations (245 of which are leave-on formulations; Table 2).[16] The results of concentration of use surveys conducted by the Council in 2019[17] and 2020[18] indicate Saccharum Officinarum (Sugarcane) Extract also has the highest concentration of use in leave-on formulations; it is used at up to 2.4% in foot powders and sprays.[17] Use concentration data were reported for Saccharum Officinarum (Sugarcane) Wax[17] and Saccharum Officinarum (Sugarcane) Juice Extract,[18] but no uses were reported in the VCRP; it should be presumed there is at least one use for the category in which the concentration is reported. No uses were reported for Saccharum Officinarum (Sugarcane) Bagasse Powder.

Saccharum Officinarum (Sugarcane) Extract is reported to be used in products that may result in incidental eye or mucous membrane exposure. For example, this ingredient is reported to be used in eye lotions (concentration not reported), other eye makeup preparations (concentration not reported), bubble baths (concentration not reported), and bath soaps and detergents (at up to 0.00093%).

Additionally, Saccharum Officinarum (Sugarcane) Extract is used in cosmetic sprays and could possibly be inhaled; for example, this ingredient is reported to be used hair sprays (at up to 0.023%) and spray body and hand products (at up to 0.12%). In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 μm, with propellant sprays yielding a greater fraction of droplets/particles < 10 μm compared with pump sprays.[19,20] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[21,22] Saccharum Officinarum (Sugarcane) Extract was reportedly used in foot powders and sprays at concentrations up to 2.4% and could possibly be inhaled. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the air.[23-25]

None of the sugarcane ingredients named in the report are restricted from use in any way under the rules governing cosmetic products in the European Union.[26]

Non-Cosmetic

Food

Sugarcane juice is the first material used for the production of table sugar and other various products, such as raw sugar/brown sugar, jaggery (traditional, concentrated sugarcane juice), and molasses.[3,27] In some regions, the sugarcane is chewed raw, or crushed, and the resulting fresh juice is consumed.[13,28] In addition, chopped sugarcane stalks and tops are reported to be used as cattle feed.[29]

Industrial

Sugarcane bagasse is used as a fuel source in sugarcane mill furnaces.[4] Other industrial purposes for bagasse includes alcohol production and papermaking.[4]

Medicine

Sugarcane juice is used in holistic medicine.[11] In Indian Ayurveda, sugarcane juice is used as a diuretic, for hiccup relief, laxative, coolant, demulcent, and antiseptic. Sugarcane juice has also been recommended in ayurvedic medicine for patients suffering from low blood pressure, gastrointestinal issues, and jaundice. In Cambodia, sugarcane juice is an integral component of medicines used to treat ulcers of the skin and mucous membranes. Aliphatic alcohols and long chain aliphatic fatty acids, commonly isolated from sugarcane wax, are pharmacologically active substances used for their anti-inflammatory, anti-hypercholesterolemic, and anti-thrombotic effects.[3]

TOXICOKINETIC STUDIES

Toxicokinetics studies were not found in the published literature, and unpublished data were not submitted. In general, toxicokinetics data are not expected to be found on botanical ingredients because each botanical ingredient is a complex mixture of constituents.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Oral

Saccharum Officinarum (Sugarcane) Juice

Adult male Wistar rats (1 rat/group) were given 1600, 2900, or 5000 mg/kg sugarcane juice via gavage.[30] Animals were observed for 24 h. No deaths were observed, therefore, the LD_{50} of the test substance was considered to be greater than 5000 mg/kg.

Saccharum Officinarum (Sugarcane) Wax

The acute oral toxicity potential of a mixture of higher aliphatic primary acids purified from *Saccharum officinarum* wax was evaluated in Wistar rats (3 rats/sex/group).[31] Animals were dosed with this mixture suspended in acacia gum and distilled water (10 mg/ml water), via gastric gavage, in doses of either 50, 20, or 2000 mg/kg. Control animals were given similar volumes of acacia gum-water by the same route. No deaths occurred during the study, and clinical observations did not show evidence of test substance-related toxicity. No gross histopathological alterations were found at necropsy.

Subchronic and Chronic Toxicity Studies

Details of the subchronic and chronic oral toxicity studies summarized below are described in Table 3.

A 90-d oral toxicity assay was performed using Sprague-Dawley rats (3 animals/sex/group).[31] Animals were dosed with a mixture of higher aliphatic primary acids purified from sugarcane wax suspended in acacia gum and distilled water, via gastric gavage, in doses of either 50, 500, or 1250 mg/kg/d. Control animals were given similar volumes of acacia gum-water by the same route. After treatment period, necropsies were completed and animals were evaluated. No hematological or clinical signs of toxicity attributable to the test substance were observed.

The potential oral toxicity of a mixture of higher aliphatic primary acids purified from sugarcane wax was evaluated in Sprague-Dawley rats (20 rats/sex/group) for 6 mo.[32] Each group was given this mixture suspended in acacia gum in distilled water via gavage at doses of either 250, 500, or 1000 mg/kg/d. A control group was given the vehicle only (acacia gum/water). All evaluated parameters were similar between control and treated groups. A similar long-term toxicity study was performed in Sprague-Dawley rats (60/sex/group).[33] Animals were given either 50, 500, or 1500 mg/kg a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum water via gavage, 5 d/wk, for 24 mo. A control group was treated with the vehicle only. Mortality, clinical symptoms, weight gain, food consumption, organ weight, and tumor incidence were evaluated. (Carcinogenicity results from this study can be found in the Carcinogenicity section of this report.) Serum cholesterol levels in groups treated with 500 and 1500 mg/kg this mixture were lower than controls. All other toxicity results were similar among control and treated groups.

Beagle dogs (4 animals/sex/group) were used in a one-year study evaluating the potential toxicity of a mixture of long-chain primary alcohols purified from sugarcane wax.[15] Treated groups dosed by gavage with either 30 or 180 mg/kg/d of this mixture in a vehicle consisting of acacia gum and water. No clinical, hematological, or histopathological evidence of toxicity were observed throughout the study, however, lipid profile determinations showed that treatment with 30 mg or 180 mg/kg/d of this mixture decreased total cholesterol by 20% on wk 8 to 52 of treatment. The potential toxicity of a mixture of long-chain primary alcohols purified from sugarcane wax was also evaluated in male *Macaca artoides* monkeys (6 animals/ group).[34] This mixture (0.25, 2.5, or 25 mg/kg/d), was combined with a piece of banana and fed to the monkeys daily, for 54 wk. No signs of toxicity were observed, however a significant reduction in serum total cholesterol and low-density lipoprotein cholesterol was observed in alcohol mixture-treated animals when compared with controls.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

Details of the oral DART studies summarized below are described in Table 4.

Saccharum Officinarum (Sugarcane) Wax

A sperm morphology assay was performed in CEN/NMRI mice (8 animals/group).[35] Mice were treated with a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum/water via gavage at 5, 50, or 500 mg/kg/d for 90 d, and sacrificed 24 h after the last administration. A control group was left untreated. Results were similar in both the control and treated groups. In a study involving rats, pregnant Sprague-Dawley rats (25 rats/group) were given a mixture of higher aliphatic primary acids purified from sugarcane wax in an acacia gum solution via gavage at up to 1000 mg/kg/d.[36] Administration occurred on days 6 - 15 of gestation. No signs of maternal or developmental toxicity were observed. Similarly, no signs of maternal or fetal toxicity were observed in a different study in which pregnant Sprague-Dawley rats (25 rats/group) were given the same test substance via gavage on day 15 of pregnancy, through gestation, until day 21 post-partum.[37] The potential reproductive toxicity of a mixture of higher aliphatic primary acids purified from sugarcane wax was also evaluated in both male and female Sprague-Dawley rats (30 females and 15 males/group).[38] Females were treated via gavage with 500 or 1000 mg/kg/d before mating, through mating and gestation, to day 21 of lactation. Males were treated with the same doses for 4 wk before and during mating. No signs of developmental or reproductive toxicity were observed.

The reproductive toxicity of a mixture of higher aliphatic primary acids purified from sugarcane wax was also evaluated in New Zealand White rabbits (27 females/group). Pregnant rabbits were given this mixture in an acacia gum solution at doses of either 500 or 1000 mg/kg/d on days 6 - 18 of gestation. Administration occurred via gavage. A control group consisting of 27 pregnant female rabbits were given the vehicle only. No evidence of embryotoxicity or teratogenicity was observed.

GENOTOXICITY STUDIES

In Vitro

No in vitro genotoxicity studies were found in the published literature, and unpublished data were not submitted.

In Vivo

Saccharum Officinarum (Sugarcane) Wax

A bone marrow micronucleus test was performed in CEN/NMRI mice (6 - 8 animals/sex/group).[35] Animals were given a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum/water via gastric gavage at 5, 50, or 500 mg/kg for 90 d, and sacrificed 24 h after the last administration. Control animals were left untreated. Only female mice were evaluated for effects on bone marrow micronucleus. The test substance did not increase the frequency of micronucleated polychromatic erythrocytes, nor the ratio of polychromatic to normochromatic erythrocytes, compared with the controls. (Results regarding sperm morphology can be seen in the DART section of this report.) In a second series of the same study, a micronucleus assay was performed in CEN/NMRI mice of both sexes given 2000 mg/kg a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum/water via gastric gavage for 6 d. No genotoxic effects were observed.

An alkaline comet assay was performed with five male Sprague-Dawley rats.[35] Animals were treated with the vehicle (acacia gum/water) or with a mixture of higher aliphatic primary acids purified from sugarcane wax at 1250 mg/kg via gavage for 90 d. Positive control groups were treated with an injection of 50 mg/kg cyclophosphamide. Sampling time was 24 h after the last administration for all groups, and responses of rat liver cells to the test substance were assessed. No single-strand breaks or alkali-labile site induction on DNA was observed.

CARCINOGENICITY STUDIES

Saccharum Officinarum (Sugarcane) Wax

The carcinogenic potential of a mixture of long-chain primary alcohols purified from sugarcane wax was evaluated for carcinogenicity in male and female Swiss mice (80 animals/sex/ group).[39] Animals were administered the test substance (50 mg/kg or 500 mg/kg of this mixture in acacia gum and water) at a volume of 5 ml/kg, daily, via gavage, for 18 mo. Control mice were given similar volumes of acacia gum and water. The frequency of neoplastic lesions was similar in control and treated groups. Since no drug-related increased in the occurrence of malignant of benign neoplasms were found, nor acceleration in tumor growth in any specific group observed, the test substance was considered to be non-carcinogenic in Swiss mice.

In a different study, a mixture of higher aliphatic primary acids purified from sugarcane wax was evaluated in OF1 mice (50 mice/sex/group).[40] This mixture, in a vehicle of acacia gum and water, was administered to mice via gavage at doses of 50, 500, and 1500 mg/kg. Treatments were given 6 d/wk, for 18 mo. A control group was treated with the vehicle only. The test substance did not increase the frequency of neoplastic or non-neoplastic lesions with respect to controls. Lesions observed in this study were consistent with spontaneous lesions reported for this species.

A similar study was performed using Sprague Dawley rats (60/sex/group).[33] Animals were given either 50, 500, or 1500 mg/kg a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum water via gavage, 5 d/wk, for 24 mo. A control group was treated with the vehicle only. Mortality, clinical symptoms, weight gain, food consumption, organ weight, and tumor incidence were evaluated. (Toxicity results can be found in the Chronic Toxicity section of this report.) The frequency of neoplastic and non-neoplastic lesions was similar in control and treated groups. The occurrence of mammary tumors in females treated with this mixture was lower than in controls. The test substance was considered to be non-carcinogenic.

ANTI-CARCINOGENICITY STUDIES

In Vitro

Saccharum Officinarum (Sugarcane) Extract

The cytotoxic activity of a sugarcane extract (0.25 - 250 µg/ml; ethyl acetate) against 8 human tumor cell lines (U251 (glioma), MCF-7 (breast), NCI-ADR/RES (multiple drug-resistant ovary cells), 786-0 (kidney), NCI-H460 (lung, non-small cells), PC-3 (prostate), OVCAR-03 (ovary), and HT29 (colon)), was evaluated.[6] The extract was tested at concentrations ranging from 0.25 to 250 µg/ml. In general, the ethyl acetate extract showed cytostatic activity in the human tumor cell lines in concentrations ranging from 25.8 to 61.8 µg/ml.

OTHER RELEVANT STUDIES

Sensitization to Sugarcane Pollen in Children

Specific immunoglobin E (IgE) antibodies to sugarcane pollen were investigated by a radioallergosorbent test (RAST) in 74 children from Okinawa, Japan who suffer from allergic disorders.[41] Forty-seven of the patients were found to have asthma, 8 had atopic dermatitis, 9 had asthma and atopic dermatitis, 6 had asthma and allergic rhinitis, and 4 had atopic dermatitis and allergic rhinitis. The mean of the serum IgE levels for the group was 962.6 ± 1237.1 IU/ml. RAST results were scored by comparison to serially diluted reference sera from patients with sensitivity to pollen of *Betula platyphylla*. RAST scores of 2+, 3+, and 4+ were considered positive. Of all the patients tested, only 2 reacted to sugarcane pollen, both being asthmatic patients.

Allergic Potential of Airborne Sugarcane Pollen

The potential allergenic effect of airborne pollen grains of different plant species was evaluated in West Bengal, India.[42] When performing a 2-year volumetric aerobiological survey, 31 pollen types were identified, and sugarcane pollen showed maximum frequency. Clinical investigations by skin prick tests were carried out to detect the allergenic potential of the crude pollen extracts. Patients (n = 350) with respiratory disorders were evaluated. Ninety percent pure pollen was defatted with diethyl ether and extracted in sodium phosphate buffer. Wheal responses to the test substance (20 ml sugarcane pollen extract) were evaluated 20 minutes after skin prick test, and graded on a scale of 1+ to 3+. A positive control of 1 mg/ml histamine diphosphate was used. Fifty-four percent of patients elicited a positive response to the sugarcane pollen extract, while 15% of patients had a reaction rated a 2+ or more.

DERMAL IRRITATION AND SENSITIZATION STUDIES

No dermal irritation or sensitization studies were found in the published literature, and unpublished data were not submitted.

OCULAR IRRITATION STUDIES

No ocular irritation studies were found in the published literature, and unpublished data were not submitted.

SUMMARY

The safety of 4 *Saccharum officinarum* (sugarcane)-derived ingredients as used in cosmetics is reviewed in this safety assessment. All ingredients reviewed in this report are derived from the sugarcane plant. According to the *Dictionary*, collectively, these ingredients are reported to function as skin-conditioning agents, surfactants, exfoliants, solvents, deodorant agents, binders, and skin protectants, in cosmetic products.

According to 2020 VCRP data, the ingredient with the most reported uses is Saccharum Officinarum (Sugarcane) Extract, which is reported to be used 466 formulations (245 of which are leave-on formulations). The results of concentration of use surveys conducted by the Council indicate Saccharum Officinarum (Sugarcane) Extract also has the highest concentration of use; it is used at up to 2.4% in foot powders and sprays.

An oral LD_{50} of greater than 5000 mg/kg was determined in an acute toxicity assay involving Wistar rats given up to 5000 mg/kg sugarcane juice via gavage. The acute toxicity potential of a mixture of higher aliphatic primary acids purified from sugarcane wax was evaluated in Wistar rats. Animals were given this mixture in acacia gum and water via gavage at doses of up to 2000 mg/kg. No deaths or signs of toxicity were observed.

No hematological or clinical signs of toxicity were observed when Sprague-Dawley rats were given a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum and water (up to 1000 mg/kg/d), via gavage, for 90 d. The same test substance was also evaluated in Sprague-Dawley rats for 6 mo. The test substance was given via gavage at doses of up to 1000 mg/kg/d. All evaluated parameters were similar between control and treated groups. A similar long-term toxicity assay was performed using a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum and water (up to 1500 mg/kg/d), via gavage, for 24 mo. Serum cholesterol levels in groups treated with 500 and 1500 mg/kg of this mixture were lower than controls. All other toxicity results were similar among control and treated groups. The chronic toxicity of a mixture of long-chain primary alcohols purified from sugarcane wax was studied in beagle dogs. A mixture of higher aliphatic primary acids purified from sugarcane wax, in a vehicle of acacia gum and water, was given to the animals, via gavage, in doses of either 30 or 180 mg/kg/d, for one year. No signs of toxicity were observed, however treatment with the test substance resulted in a decrease in total cholesterols on wk 8 to 52 of treatment. The potential toxicity of a mixture of long-chain primary alcohols purified from sugarcane was also evaluated in male *Macaca artoides* monkeys. The test substance was fed to the monkeys, wrapped in banana, for 54 wk. No signs of toxicity were observed, however, a significant reduction in serum total cholesterol and low-density lipoprotein cholesterol was observed in treated animals compared to controls.

A sperm morphology assay on a mixture of higher aliphatic primary acids purified from sugarcane wax was performed in CEN/NMRI mice. This mixture in acacia gum and water was given to the animals at doses of up to 500 mg/kg/d, for 90 d.

A control group was left untreated. Results were similar in the control and treated groups. In a different study, pregnant Sprague-Dawley rats were given a mixture of higher aliphatic primary acids purified from sugarcane wax in an acacia gum solution (up to 1000 mg/kg/d), via gavage, on days 6 - 15 of gestation. No signs of developmental or maternal toxicity were observed. Similarly, no signs of maternal or fetal toxicity were observed in a different study in which female Sprague-Dawley rats were given the same test substance, on day 15 of pregnancy, until day 21 post-partum. The potential reproductive toxicity of a mixture of higher aliphatic primary acids purified from sugarcane wax was also evaluated in both male and female Sprague-Dawley rats. Females were treated via gavage with up to 1000 mg/kg/d before mating, through mating and gestation, to day 21 of lactation. Male rats were treated for 4 wk, before and during mating. No signs of developmental or reproductive toxicity were observed. In a different study, pregnant New Zealand White rabbits were given a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum solution at doses of up to 1000 mg/kg/d, via gavage, on days 6 - 18 of gestation. No evidence of embryotoxicity or teratogenicity was observed.

The potential genotoxicity of a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum/water was evaluated in CEN/NMRI mice. Animals were given the test substance, at doses of up to 500 mg/kg, for 90 d. The test substance did not increase the frequency of micronucleated polychromatic erythrocytes, nor the ratio of polychromatic to normochromatic erythrocytes, compared with the controls. In a second series of the same study, a micronucleus assay was performed in CEN/NMRI mice of both sexes given 2000 mg/kg of this mixture in acacia gum/water via gastric gavage for 6 d. No genotoxic effects were observed. An alkaline comet assay was performed using five male Sprague-Dawley rats. Rats were treated with a mixture of higher aliphatic primary acids purified from sugarcane wax in an acacia gum/water vehicle (1250 mg/kg) for 90 d. No single-strand breaks or alkali-labile site induction on DNA was observed.

In a carcinogenicity assay, no signs of carcinogenicity were observed in an assay involving Swiss mice. Animals were administered up to 500 mg/kg of the test substance (a mixture of long-chain primary alcohols purified from sugarcane wax in acacia gum and water), via gavage, for 18 mo. Similarly, a mixture of higher aliphatic primary acids purified from sugarcane wax, in acacia gum and water, was administered to OF1 mice, via gavage, at doses of up to 1500 mg/kg. Treatment lasted for 18 mo. The test substance did not increase the frequency of neoplastic or non-neoplastic lesions with respect to controls. A similar study was performed using the same test substance and concentrations in Sprague-Dawley rats. Animals were treated via gavage for 24 mo. The test substance was considered to be non-carcinogenic.

The cytotoxic potential of a sugarcane extract (0.25 - 250 µg/ml; ethyl acetate) against 8 human cancer cell lines was evaluated in an in vitro assay. In general, the ethyl acetate extract showed cytostatic activity in the human tumor cell lines in concentrations ranging from 25.8 to 61.8 µg/ml.

Specific IgE antibodies to sugarcane pollen were investigated using a RAST in 74 children from Okinawa, Japan who suffer from allergic disorders. Of all the patients tested, only 2 reacted to sugarcane pollen, both being asthmatic patients. In a different study, the potential allergic effect of airborne pollen grains of different plant species was evaluated in West Bengal, India. Clinical investigations by skin prick tests were carried out to determine the allergenic potential of these crude pollen extracts, including a crude sugarcane pollen extract. Fifty-four percent of patients (n = 350) elicited a positive response to the sugarcane pollen extract, while 15% of patients had a reaction rated a 2+ or more.

DISCUSSION

To be developed.

CONCLUSION

To be determined.

TABLES

Table 1. INCI names, definitions, and functions of the *Saccharum officinarum* (sugarcane)-derived ingredients in this safety assessment[1]

Ingredient (CAS No.)	Definition	Function
Saccharum Officinarum (Sugarcane) Bagasse Powder	Saccharum Officinarum (Sugarcane) Bagasse Powder is the powder obtained from the dried, ground residue, or bagasse, from the stalks of *Saccharum officinarum* after the juice has been removed.	skin-conditioning agents – humectant; surfactants – cleansing agents
Saccharum Officinarum (Sugarcane) Extract (91722-22-4 [generic])	Saccharum Officinarum (Sugarcane) Extract is the extract of the sugarcane, *Saccharum officinarum*	exfoliants; skin-conditioning agents – miscellaneous; solvents
Saccharum Officinarum (Sugarcane) Juice Extract (91722-22-4 [generic])	Saccharum Officinarum (Sugarcane) Juice Extract is the extract of the juice of the sugarcane, *Saccharum officinarum*	deodorant agents; skin-conditioning agents – miscellaneous
Saccharum Officinarum (Sugarcane) Wax (142583-61-7; 91722-22-4 [generic])	Saccharum Officinarum (Sugarcane) Wax is the wax obtained from *Saccharum officinarum*	binders; emulsion stabilizers; skin protectants

Table 2. Frequency and concentration of use of *Saccharum officinarum* (sugarcane)-derived ingredients[16-18]

	# of Uses[16]	Conc of Use (%)[17]	# of Uses[16]	Conc of Use (%)[18]	# of Uses[16]	Conc of Use (%)[17]
	Saccharum Officinarum (Sugarcane) Extract		Saccharum Officinarum (Sugarcane) Juice Extract		Saccharum Officinarum (Sugarcane) Wax	
Totals*	**466**	**0.00024 – 2.4**	**NR**	**0.0009 – 0.26**	**NR**	**0.0012**
Duration of Use						
Leave-On	*245*	*0.00024 – 2.4*	*NR*	*0.0009 – 0.001*	*NR*	*NR*
Rinse-Off	*219*	*0.00024 – 0.5*	*NR*	*0.001 – 0.26*	*NR*	*0.0012*
Diluted for (Bath) Use	*2*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	5	0.0075	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1; 90[a]; 73[b]	0.0019 – 0.12; 2.4[a]; 0.0024 – 0.25[b]	NR	NR	NR	NR
Incidental Inhalation-Powder	90[a]	2.4[a]; 0.036[c]	NR	NR	NR	NR
Dermal Contact	359	0.00024 – 2.4	NR	0.0009 – 0.26	NR	0.0012
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	104	0.00024 – 0.25	NR	0.001	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	3	NR	NR	NR	NR	NR
Mucous Membrane	84	0.00093	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

	# of Uses[16]	Conc of Use (%)
	Saccharum Officinarum (Sugarcane)[d]	
Totals*	**3**	**NS**
Duration of Use		
Leave-On	*3*	*NS*
Rinse-Off	*NR*	*NS*
Diluted for (Bath) Use	*NR*	*NS*
Exposure Type		
Eye Area	NR	NS
Incidental Ingestion	NR	NS
Incidental Inhalation-Spray	1[a]; 1[b]	NS
Incidental Inhalation-Powder	1[a]	NS
Dermal Contact	3	NS
Deodorant (underarm)	NR	NS
Hair - Non-Coloring	NR	NS
Hair-Coloring	NR	NS
Nail	NR	NS
Mucous Membrane	NR	NS
Baby Products	NR	NS

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

[a] Not specified that these products or a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories

[b] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

[c] It is possible these products are powders, but it is not specified whether the reported uses are powders

[d] Reported in the VCRP under a non-INCI name and presented here for informational purposes

NR – no reported use

NS – not surveyed

Table 3. Repeated dose oral toxicity studies

Test Substance	Animals/Group	Study Duration	Vehicle/Method	Dose/Concentration	Results	Reference
a mixture of higher aliphatic primary acids purified from sugarcane wax	Sprague-Dawley rats (3 rats/sex/group)	90 d	Acacia gum and distilled water; gavage	50, 100, 1250 mg/kg/d	One death was observed, corresponding to a female rat treated with a mixture of higher aliphatic primary acids purified from sugarcane wax at 500 mg/kg, who died 9 d after treatment. The death was considered to be related to gastric gavage manipulation. No signs of clinical toxicity attributable to the test substance were observed throughout the study. No signs of toxicity were observed based on hematological or necropsy results.	31
a mixture of higher aliphatic primary acids purified from sugarcane wax	Sprague-Dawley rats (20 rats/sex/group)	6 mo	Acacia gum and distilled water; gavage	250, 500, or 1000 mg/kg/d	Bodyweight gain, food consumption, clinical observations, blood biochemistry, hematology, organ weight ratios and histopathological findings were similar between control and treated groups.	32
a mixture of higher aliphatic primary acids purified from sugarcane wax	Sprague-Dawley rats (60 rats/sex/group)	24 mo	Acacia gum and water; gavage; administration 5 d/wk	50, 500, or 1500 mg/kg/d	Toxicity results relating to mortality, clinical symptoms, weight gain, food consumption, and organ weight were similar among control and treated groups. However, serum cholesterol levels in groups treated with 500 and 1500 mg/kg a mixture of higher aliphatic primary acids purified from sugarcane wax were lower than controls. No other differences in blood indicators were found.	33
a mixture of long-chain primary alcohols purified from sugarcane wax	Beagle Dogs (4 dogs/sex/group)	12 mo	Acacia gum and water; gavage	30 or 180 mg/kg/d	No signs of toxicity were observed throughout the study. Lipid profile determinations showed that a mixture of long-chain primary alcohols purified from sugarcane wax decreased total cholesterol by 20% from wk 8 to 52 of treatment. No hematological or histopathological disturbances attributable to treatment were observed.	15
a mixture of long-chain primary alcohols purified from sugarcane wax	Male *Macaca artoides* monkeys (6 monkeys/group)	54 wk	Test substance was fed wrapped in a piece of banana	0.25, 2.5, or 25 mg/kg/d	No signs of toxicity were observed when behavior, physical condition, hematological, or blood biochemistry was evaluated. In addition, no negative effects were observed when ophthalmological and pathological anatomy were performed at the end of the administration period. After 8 wk, a significant reduction of serum total cholesterol and low-density lipoprotein cholesterol was observed in a mixture of long-chain primary alcohols purified from sugarcane wax-treated animals when compared with controls. This effect persisted throughout the study.	34

Table 4. Oral developmental and reproductive toxicity studies

Test Article	Animals/Group	Vehicle	Dose/Concentration	Procedure	Results	Reference
a mixture of higher aliphatic primary acids purified from sugarcane wax	CEN/NMRI mice (8 males/group)	Acacia gum and water	5, 50, and 500 mg/kg/d	Mice were treated via gavage for 90 d and killed 24 h after the last administration. Control animals were left untreated.	The test substance did not change the sperm count or frequency of all types of abnormal head shapes, compared with controls.	[35]
a mixture of higher aliphatic primary acids purified from sugarcane wax	Pregnant Sprague-Dawley Rats (25 females/group)	Acacia gum and water	5, 100, and 1000 mg/kg/d	Rats were given the test substance by gavage on days 6 through 15 of gestation. Cyclophosphamide (50 mg/kg/d) was given as a positive control. Negative control animals were given the vehicle only.	The positive control caused embryotoxic and teratogenic effects. No adverse effects on reproductive performance, or on embryonic or fetal development were seen in any of the groups treated with a mixture of higher aliphatic primary acids purified from sugarcane wax. No signs of developmental toxicity were observed in a mixture of higher aliphatic primary acids purified from sugarcane wax treated groups. No signs of maternal toxicity were observed, and body weight gain during treatment period was comparable among treated and control rats.	[36]
a mixture of higher aliphatic primary acids purified from sugarcane wax	Sprague-Dawley rats (25 females/group)	Acacia gum and water	500 or 1000 mg/kg/d	Pregnant females received the test substance via gavage on day 15 of pregnancy, through gestation, until day 21 post-partum. A control group was given the vehicle only. Dams and F1 pups were evaluated for signs of toxicity.	No spontaneous or dose-related maternal deaths were reported during the study. The general health and condition of offspring was good in treated and control groups. No significant differences between treated and control groups were reported regarding litter size, survival through weaning period, sex ratio, and pup weight.	[37]
a mixture of higher aliphatic primary acids purified from sugarcane wax	Sprague-Dawley rats (30 females and 15 males/group)	Acacia gum and water	500 or 1000 mg/kg/day	The test substance was given via gavage to female rats for 15 d prior to mating, through mating and gestation, to day 21 of lactation. Male rats were treated for 4 wk prior and during mating. A control group of 15 males and 30 females were given the vehicle only. Effects on growth, development, reproductive performance, and fertility of the F1 generation were assessed.	There were no significant reductions in the number of animals that conceived, in the number of pups born to those that did conceive, in the number of pups that survived until weaning, and body weights of pups at weaning. Control and treated group's offspring were comparable in growth, physical and behavioral development, and reproductive performance. The NOAEL was considered to be 1000 mg/kg/day.	[38]
a mixture of higher aliphatic primary acids purified from sugarcane wax	New Zealand White rabbits (27 females/group)	Acacia gum and water	500 or 1000 mg/kg/d	Mated females were given the test substance via gavage on gestation days 6-18. An additional control group of 27 mated females were given the vehicle only. All animals were euthanized on gestation day 29, the corpora lutea were counted, the location and number of implantation sites were recorded, and all fetuses were weighed, sexes, and examined.	No evidence of embryotoxicity or teratogenicity was observed. The NOAEL was considered to be 1000 mg/kg/day.	[38]

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FDA – VCRP Data on *Saccharum officinarum* (Sugarcane)-Derived Ingredients

Saccharum Officinarum (Sugarcane) Extract

Bubble Baths	2
Eye Lotion	3
Other Eye Makeup Preparations	2
Perfumes	1
Other Fragrance Preparation	6
Hair Conditioner	35
Hair Spray (aerosol fixatives)	1
Shampoos (non-coloring)	40
Tonics, Dressings, and Other Hair Grooming Aids	11
Wave Sets	1
Other Hair Preparations	16
Other Makeup Preparations	1
Cuticle Softeners	2
Other Manicuring Preparations	1
Bath Soaps and Detergents	48
Other Personal Cleanliness Products	34
Aftershave Lotion	1
Preshave Lotions (all types)	1
Cleansing	41
Depilatories	3
Face and Neck (exc shave)	67
Body and Hand (exc shave)	21
Foot Powders and Sprays	2
Moisturizing	45
Night	4
Paste Masks (mud packs)	16
Skin Fresheners	4
Other Skin Care Preps	48
Indoor Tanning Preparations	9

Saccharum Officinarum (not included in the wINCI Dictionary)

Body and Hand (exc shave)	1
Moisturizing	1
Other Skin Care Preps	1

No VCRP data for Saccharum Officinarum (Sugarcane) Juice Extract, Saccharum Officinarum (Sugarcane) Bagasse Powder, or Saccharum Officinarum (Sugarcane) Wax

Concentration of Use by FDA Product Category – Sugarcane*

Saccharum Officinarum (Sugarcane) Extract
Saccharum Officinarum (Sugarcane) Wax

Ingredient	Product Category	Maximum Concentration of Use
Saccharum Officinarum (Sugarcane) Extract	Eyebrow pencils	0.0075%
Saccharum Officinarum (Sugarcane) Extract	Hair conditioners	0.00024-0.0011%
Saccharum Officinarum (Sugarcane) Extract	Hair sprays Aerosol Pump spray	 0.0019-0.023% 0.001%
Saccharum Officinarum (Sugarcane) Extract	Shampoos (noncoloring)	0.0019%
Saccharum Officinarum (Sugarcane) Extract	Tonics, dressings and other hair grooming aids	0.25%
Saccharum Officinarum (Sugarcane) Extract	Bath soaps and detergents	0.00093%
Saccharum Officinarum (Sugarcane) Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.13-0.5%
Saccharum Officinarum (Sugarcane) Extract	Face and neck products Not spray	 0.036%
Saccharum Officinarum (Sugarcane) Extract	Body and hand products Spray	 0.12%
Saccharum Officinarum (Sugarcane) Extract	Foot powders and sprays	2.4%
Saccharum Officinarum (Sugarcane) Extract	Paste masks and mud packs	0.4%
Saccharum Officinarum (Sugarcane) Extract	Other skin care preparations	0.96%
Saccharum Officinarum (Sugarcane) Extract	Indoor tanning preparations	0.00024%
Saccharum Officinarum (Sugarcane) Wax	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0012%

*Ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but no uses were reported.

Information collected in 2019
Table prepared July 23, 2019

Concentration of Use by FDA Product Category – Sugarcane Additions*

Saccharum Officinarum (Sugarcane) Bagasse Powder
Saccharum Officinarum (Sugarcane) Juice Extract

Ingredient	FDA Product Category	Maximum Concentration of Use
Saccharum Officinarum (Sugarcane) Juice Extract	Hair conditioners	0.001%
Saccharum Officinarum (Sugarcane) Juice Extract	Other hair preparations (noncoloring)	0.001%
Saccharum Officinarum (Sugarcane) Juice Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.26%
Saccharum Officinarum (Sugarcane) Juice Extract	Paste masks and mud packs	0.03%
Saccharum Officinarum (Sugarcane) Juice Extract	Other skincare preparations	0.0009%

*Ingredients found only in the title of the table were included in the concentration of use survey, but no uses were reported

Information collected in 2020
Table prepared: October 5, 2020

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review (CIR)

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: October 1, 2020

SUBJECT: Saccharum Officinarum (Sugarcane) Extract

Anonymous. 2020. Saccharum Officinarum (Sugarcane) Extract.

- **Saccharum Officinarum (Sugarcane) Extract**

Manufacturing Process:

The sugarcane is extracted with specified **eluent(s) under appropriate temperature conditions,** to yield a **concentrate**. The concentrate containing the phytochemical constituents is then blended with the desired diluent(s) and preservation system to produce the final ingredient. The ingredient is evaluated for physiochemical properties according to the specification requirements for the batch to be released. In addition, the concentrate is also evaluated for contaminants and physiochemical properties as needed.

Typical eluents include Water, Butylene Glycol, Glycerin, and Propylene Glycol.

Additional information:

- A typical product with the **Saccharum Officinarum (Sugarcane) Extract** prepared in glycerin and water has the following specifications:

Analysis:

Specification	Range	Actual
APPEARANCE	Clear Liquid	PASS
COLOR	Colorless to yellow	PASS
MICROBIAL PLATE COUNT	Less than 100 organisms per gram	PASS
ODOR	Characteristic	PASS
PH	1.5 - 5.0	2.0
REFRACTIVE INDEX	1.3920 - 1.5000 at 25° C	1.4016
SOLUBILITY	Soluble in any proportion in water	PASS
SPECIFIC GRAVITY	1.20 - 1.50	1.14

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: September 28, 2020

SUBJECT: Scientific Literature Review: Safety Assessment of *Saccharum officinarum* (Sugarcane)-Derived Ingredients as Used in Cosmetics (release date September 17, 2020)

The Personal Care Products Council respectfully submits the following comments on the scientific literature review, Safety Assessment of *Saccharum officinarum* (Sugarcane)-Derived Ingredients as Used in Cosmetics.

Introduction; Summary – As there is only one more function listed in the Dictionary (emulsion stabilizer), it would be better to state this additional function than to state: "functions of these ingredients include, but are not limited to".

Cosmetic Use – Only one concentration of use was reported for Saccharum Officinarum (Sugarcane) Wax. It would be clearer to state the product category and the concentration reported than to state: "Use concentration data were reported for Saccharum Officinarum (Sugarcane) Wax". As "data" is plural, this suggests that more than one concentration was reported.

Non-Cosmetic Use, Medicine – Please correct: "medicines used to ulcers of the skin"

Subchronic and Chronic – Table 3 indicates that necropsies were also completed in the rat 90-day oral study of the sugarcane wax component. This should also be stated in the text.

Table 2 – For Saccharum Officinarum (Sugarcane) Extract, the frequency of use information from FDA's VCRP is also shown in the concentration of use column.

Tables 3 and 4 – As the test substance is stated in the first column, it is not necessary to repeat it in the Results column (rows 1, 3, 4, 5 of Table 3 and twice in row 2 of Table 4).