Safety Assessment of Sigesbeckia Orientalis Extract as Used in Cosmetics

Status:	Draft Report for Panel Review
Release Date:	September 11, 2026
Panel Meeting Date:	October 5 - 6, 2026

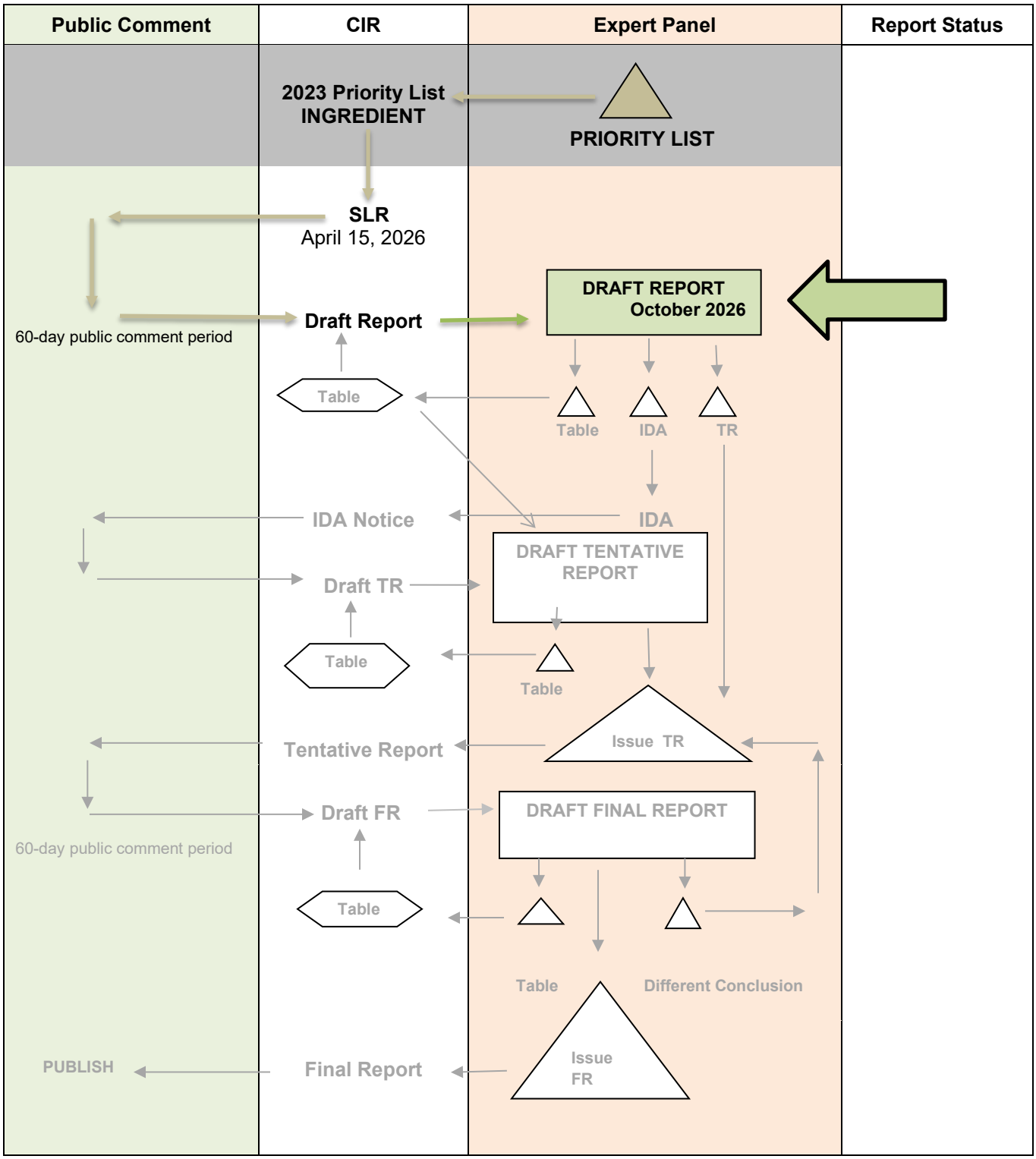
The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Bruce A. Brod, M.D., M.H.C.I., F.A.A.D.; Samuel M. Cohen, M.D., Ph.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D., and the Senior Director is Monice Fiume, M.B.A. This safety assessment was prepared by Litta Paulson, M.P.H., Scientific Analyst/Writer, CIR.

© Cosmetic Ingredient Review
555 13th Street, NW, Suite 300W, Washington, DC 20004
cirinfo@cir-safety.org

Distributed for Comment Only -- Do Not Cite or Quote

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Sigesbeckia Orientalis Extract
MEETING October 2026



Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Litta Paulson, M.P.H., Scientific Analyst/Writer, CIR
Date: September 11, 2026
Subject: Safety Assessment of Sigesbeckia Orientalis Extract as Used in Cosmetics

Enclosed is the Draft Report on the Safety Assessment of Sigesbeckia Orientalis Extract as Used in Cosmetics. It is identified as *report_SigesbeckiaOrientalis_102026* in the pdf document. The Scientific Literature Review (SLR) was issued on April 15, 2026. This is the first time the Panel is reviewing this report.

Results of a concentration of use survey using FDA cosmetic product categories under MoCRA were received and incorporated (*data_SigesbeckiaOrientalis_102026*). No additional data have been received since the issuing of the SLR.

Other information included in this packet includes:

- comments on the Scientific Literature Review (SLR) from Council (*PCPCcomments_SigesbeckiaOrientalis_102026*)
- responses to comments on SLR (*response-PCPCcomments_SigesbeckiaOrientalis_102026*)
- flow chart (*flow_SigesbeckiaOrientalis_102026*)
- report history (*history_SigesbeckiaOrientalis_102026*)
- search strategy (*search_SigesbeckiaOrientalis_102026)*
- data profile (*dataprofile_SigesbeckiaOrientalis_102026)*

If no further data are needed to reach a conclusion of safety, the Panel should formulate a Discussion and issue a Tentative Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an Insufficient Data Announcement.

Sigesbeckia Orientalis Extract History

April 2026

- SLR posted
- Comments on SLR from Council received

October 2026

- Panel reviews Draft Report

Sigesbeckia Orientalis Extract Data Profile* – October 2026 – Litta Paulson																														
					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
Sigesbeckia Orientalis Extract	**X**			X				X			X																		

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

Sigesbeckia Orientalis Extract

Ingredient	CAS #	PubMed	FDA	CompTox	ChemPort	NIOSH	NTIS	NTP	FEMA	EU	ECHA	SIDS	SCCS	AICIS	FAO	WHO	Web
Sigesbeckia Orientalis Extract	90106-87-9	X		X	X		X			X	X					X	X

"X" indicates data was found

Botanical and/or Fragrance Websites (if applicable)

Ingredient	CAS #	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	AHPA	AGRICOLA	IFRA	RIFM
Sigesbeckia Orientalis Extract	90106-87-9	X	X	X					

"X" indicates data was found

Search Strategy

The following search string was used in PubMed:

(((siegesbeckia orientalis) OR (siegesbeckia orientalis extract)) OR (sigesbeckia orientalis)) OR (sigesbeckia orientalis extract)
[*59 hits / 8 useful*]

The following search terms were used in all links other than PubMed:

Sigesbeckia orientalis extract
Sigesbeckia orientalis
90106-87-9

LINKS

Search Engines

- Pubmed - http://www.ncbi.nlm.nih.gov/pubmed
  - appropriate qualifiers are used as necessary
  - search results are reviewed to identify relevant documents
- CompTox: https://comptox.epa.gov/dashboard/chemical/pubmed-abstract-sifter/DTXSID3039242; https://www.epa.gov/comptox-tools/downloadable-computational-toxicology-data#LM
- eChemPortal: https://www.echemportal.org/echemportal/
- DeepDyve: https://www.deepdyve.com/
- Connected Papers - https://www.connectedpapers.com/

Pertinent Websites

- wINCI - https://incipedia.personalcarecouncil.org/winci/ingredient-custom-search/
- FDA Cosmetics page - https://www.fda.gov/cosmetics
- eCFR (Code of Federal Regulations) - https://www.ecfr.gov/
- FDA search databases: https://www.fda.gov/industry/fda-basics-industry/search-databases
- Substances Added to Food (formerly, EAFUS): https://www.fda.gov/food/food-additives-petitions/substances-added-food-formerly-eafus
- GRAS listing: https://www.fda.gov/food/food-ingredients-packaging/generally-recognized-safe-gras
- SCOGS database: https://www.fda.gov/food/generally-recognized-safe-gras/gras-substances-scogs-database
- Inventory of Food Contact Substances Listed in 21 CFR: https://www.cfsanappsexternal.fda.gov/scripts/fdcc/index.cfm?set=IndirectAdditives
- Drug Approvals and Database: https://www.fda.gov/drugs/development-approval-process-drugs/drug-approvals-and-databases
- FDA Orange Book: https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book
- OTC Monographs - https://dps.fda.gov/omuf
- Inactive Ingredients Approved For Drugs: https://www.accessdata.fda.gov/scripts/cder/iig/
- FEMA (Flavor & Extract Manufacturers Association) GRAS: https://www.femaflavor.org/fema-gras
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
  - technical reports search page: https://ntrl.ntis.gov/NTRL/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- EUR-Lex - https://eur-lex.europa.eu/homepage.html
- Scientific Committees (SCCS, etc) opinions: https://health.ec.europa.eu/scientific-committees_en https://health.ec.europa.eu/scientific-committees/scientific-committee-consumer-safety-sccs_en
- ECHA (European Chemicals Agency – REACH dossiers) – https://echa.europa.eu/
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- EFSA (European Food Safety Authority) - https://www.efsa.europa.eu/en
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- AICIS (Australian Industrial Chemicals Introduction Scheme)- https://www.industrialchemicals.gov.au/
- International Programme on Chemical Safety http://www.inchem.org/
- Office of Dietary Supplements https://ods.od.nih.gov/
- 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) IRIS library - https://apps.who.int/iris/
- a general Google and Google Scholar search should be performed for additional background information, to identify references that are available, and for other general information - www.google.com https://scholar.google.com/

Botanical Websites

- Dr. Duke's - https://phytochem.nal.usda.gov/
- 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 (2nd Edition; 2013) - http://abc.herbalgram.org/site/DocServer/AHPABotanicalSafety_FMexcerpt.pdf?docID=4601
- 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

Personal Care Products Council

Memorandum

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

FROM: Jaap Venema, Ph.D.
EVP and Chief Scientist – Personal Care Products Council
Industry Liaison to the CIR Expert Panel

DATE: April 24, 2026

SUBJECT: Scientific Literature Review: Safety Assessment of Sigesbeckia Orientalis Extract as Used in Cosmetics (release date: April 15, 2026)

The Personal Care Products Council respectfully submits the following comments on the scientific literature review, Safety Assessment of Sigesbeckia Orientalis Extract as Used in Cosmetics.

Cytotoxicity – In the description of reference 7, rather than indicating the range of doses as 0-150 µg/ml, it would be helpful to state the lowest concentration (is it at a similar order of magnitude as the high concentration, or much lower), and indicate that untreated (or maybe ethanol treated) cells were used as the control. Were the results at the lowest test concentration significantly different from the control?

Summary – The description of the study that measured inflammatory markers, e.g., interleukins, in the section on Effect on Inflammatory Mediators says they were measured in livers from treated rats. In contrast, the Summary says: "An assay of rat liver tissues treated with an aqueous extract of *Sigesbeckia orientalis*" which suggests an in vitro exposure study. Please revise the Summary to make it clear the livers of rats treated with *Sigesbeckia orientalis* were studied.

Sigesbeckia Orientalis Extract – October 2026 – Litta Paulson	
Comment Submitter: Personal Care Products Council **Date of Submission: April 24, 2026**	
Comment	**Response/Action**
Cytotoxicity – In the description of reference 7, rather than indicating the range of doses as 0-150 µg/ml, it would be helpful to state the lowest concentration (is it at a similar order of magnitude as the high concentration, or much lower), and indicate that untreated (or maybe ethanol treated) cells were used as the control. Were the results at the lowest test concentration significantly different from the control?	addressed Statistical significance values were only provided for the cell viability assay
Summary – The description of the study that measured inflammatory markers, e.g., interleukins, in the section on Effect on Inflammatory Mediators says they were measured in livers from treated rats. In contrast, the Summary says: "An assay of rat liver tissues treated with an aqueous extract of *Sigesbeckia orientalis*" which suggests an in vitro exposure study. Please revise the Summary to make it clear the livers of rats treated with *Sigesbeckia orientalis* were studied.	addressed

Safety Assessment of Sigesbeckia Orientalis Extract as Used in Cosmetics

Status: Draft Report for Panel Review
Release Date: September 11, 2026
Panel Meeting Date: October 5 - 6, 2026

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Bruce A. Brod, M.D., M.H.C.I., F.A.A.D.; Samuel M. Cohen, M.D., Ph.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D., and the Senior Director is Monice Fiume, M.B.A. This safety assessment was prepared by Litta Paulson, M.P.H., Scientific Analyst/Writer, CIR.

© Cosmetic Ingredient Review
555 13th Street, NW, Suite 300W, Washington, DC 20004
cirinfo@cir-safety.org

ABBREVIATIONS

A549	human lung carcinoma
ACE	angiotensin converting enzyme
AGEs	advanced glycated end products
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
CIR	Cosmetic Ingredient Review
CK	creatine kinase
Council	Personal Care Products Council
COX-2	cyclooxygenase-2
Dictionary	*International Cosmetic Ingredient Dictionary*
DMSO	dimethyl sulfoxide
ELISA	enzyme-linked immunosorbent assay
FaDu	human pharynx squamous cell carcinoma
FDA	US Food and Drug Administration
GC-MS	gas chromatography–mass spectrometry
HaCaT	human keratinocytes
HEC-1A	human endometrial adenocarcinoma
Hepa1-6	murine hepatoma cell
HepG2	human hepatoblastoma
HPLC	high-performance liquid chromatography
IL	interleukin
iNOS	nitric oxide synthase
LDH	lactate dehydrogenase
LNCaP	human prostate carcinoma
l.o.	leave-on
LPS	lipopolysaccharide
MCP-1	monocyte chemoattractant protein-1
MDA-MB-231	human breast adenocarcinoma
MIP-1α	macrophage inflammatory protein-1α
MoCRA	Modernization of Cosmetics Regulation Act of 2022
mPGES-1	microsomal Prostaglandin E synthase-1
mRNA	messenger ribonucleic acid
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NR	not reported
OECD	Organisation for Economic Co-operation and Development
Panel	Expert Panel for Cosmetic Ingredient Safety
PGE_2	prostaglandin E_2
RANTES	regulated on activation, normal T-cell expressed and secreted
RAW264.7	mouse macrophage cell
RLD	Registration and Listing Data
RL95-2	human endometrial carcinoma
r.o.	rinse-off
RT-PCR	real-time polymerase chain reaction
TG	test guideline
TGFβ1	transforming growth factor beta 1
TNF-α	tumor necrosis factor-α
US	United States
WoE	weight-of-evidence

INTRODUCTION

This assessment reviews the safety of Sigesbeckia Orientalis Extract as used in cosmetic formulations. According to the *International Cosmetic Ingredient Dictionary* (*Dictionary*), this ingredient is reported to function in cosmetics as a skin conditioning agent.[1]

Botanicals, such as Sigesbeckia Orientalis Extract, may contain hundreds of constituents. In this assessment, the Expert Panel for Cosmetic Ingredient Safety (Panel) is evaluating the potential toxicity of Sigesbeckia Orientalis Extract as a whole, complex substance; toxicity from single components may not predict the potential toxicity of botanical ingredients.

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 extensive search of the world's literature; a search was last conducted in August 2026. 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 Cosmetic Ingredient Review (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 name, according to the *Dictionary*, is written as listed above, without italics and without abbreviations. When referring to the plant from which this ingredient is derived, the standard scientific practice of using italics will be followed (i.e., *Sigesbeckia orientalis*). If it is not known whether the substance being discussed is equivalent to the cosmetic ingredient, the test substance will be identified by the name used in the publication that is cited (i.e., *Sigesbeckia orientalis* extract). However, if it is known that the substance is a cosmetic ingredient, the *Dictionary* nomenclature (i.e., Sigesbeckia Orientalis Extract) will be used.

CHEMISTRY

Definition and Plant Identification

The *Dictionary* defines Sigesbeckia Orientalis Extract as the extract of *Sigesbeckia orientalis*.[1] It has the CAS No. 90106-87-9.[2] *Sigesbeckia orientalis*, commonly known as St. Paul's Wort, is an herb from the family Asteraceae that is generally found in Asia, Africa, and other tropical or temperate regions.[3,4] The plant can grow between 0.6 - 1.2 m high, with stiff stems and dichotomous branches that are purple-tinged and pubescent. The leaves are triangular-ovate, irregularly toothed, pubescent on both sides, and range from 2.5 - 11 cm in length and 1.5 - 7 cm in width. *Sigesbeckia orientalis* flowers are yellow in color with two distinct rows of bracts; the outer bract is long, spreading, and covered in glandular hairs on top, and the inner bract is short, boat-shaped, and enclosing ray flowers. The plant produces black, slightly rough, glabrous achenes, that are enclosed in a boat-shaped bract. *Sigesbeckia orientalis* is also considered to have an unpleasant smell and taste.

Chemical Properties

Chemical properties of Sigesbeckia Orientalis Extract were not found in the published literature, and unpublished data were not submitted.

Method of Manufacture

Methods used to manufacture Sigesbeckia Orientalis Extract were not found in the published literature, and unpublished data were not submitted.

Composition and Impurities

Sigesbeckia orientalis comprises phytochemicals such as flavonoids, diterpenoids (including pimarenoids, kaurenoids, and chain diterpenes) and sesquiterpenoids.[4] *Sigesbeckia orientalis* leaves consist of high levels of saponins, alkaloids, and flavonoids, and moderate levels of oxalates, tannins, phytates and phenols.[3,5] The leaves also contain significant amounts of vitamin A and vitamin C. Due to its metal accumulation tendencies, the *Sigesbeckia orientalis* plant is known to be a hyperaccumulator of cadmium, especially collected in its roots and shoots.[6]

The major compounds of an ethanolic extract of *Sigesbeckia orientalis* (prepared using the dried aerial parts), determined through gas chromatography–mass spectrometry (GC-MS), were caryophyllene oxide, [−]-spathulenol, hexadecanoic acid ethyl ester, and caryophyllene.[7] Complete composition information may be found in Table 1. The total polyphenol and flavonoid content of 4 different extracts of the dried aerial parts of *Sigesbeckia orientalis* (ethanol, *n*-hexane, ethyl acetate, and methanol) were measured using Folin–Ciocalteu and aluminum chloride colorimetric methods, with the ethanol extract possessing the highest content of both polyphenols and flavonoids (Table 2).[8] Additionally, high-performance liquid chromatography (HPLC) was used to determine the identity and values of various phenolic constituents present in these extracts (Table 2).[8,9]

USE

Cosmetic

The safety of the cosmetic ingredient 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 Sigesbeckia Orientalis Extract in cosmetics. Registration and Listing Data (RLD) obtained from the FDA report frequency of use, and responses to a survey conducted by the Personal Care Products Council (Council) indicate maximum reported concentrations of use; it is these values that define the present practices of use and concentration that are assessed by the Panel. Since 2024, as a result of the Modernization of Cosmetics Regulation Act of 2022 (MoCRA), manufacturers and processors are required to register facilities and list their products (and ingredients therein) with the FDA (i.e., RLD). An exception is made for small businesses (average gross annual sales in the US of cosmetic products for the previous 3-yr period is less than $1,000,000, adjusted for inflation), which are exempt from MoCRA reporting for most cosmetic product categories. Eye area products, injected products, internal use products, or products that alter appearance for more than 24 h, and the facilities that manufacture these products, are not included in this exemption.[10] Another change resulting from MoCRA is the addition of tattoo preparations (permanent tattoo inks, temporary tattoo inks, and other tattoo products) to the product categories for which companies need to list their products with FDA. However, evaluating the safety of ingredients as used in tattoo preparations is not within the purview of the Panel; accordingly, such use is not included as part of the present practices of use that are assessed by the Panel.

According to RLD obtained from the FDA in 2025, Sigesbeckia Orientalis Extract is reported to be used in 252 formulations (Table 3).[11,12] Concentration of use data submitted in 2024 in response to the Council survey indicates that the highest maximum concentration of use of Sigesbeckia Orientalis Extract is 0.046% in a facial a toner that is used before applying a facial peel.[13] The highest known maximum leave-on concentration of use of Sigesbeckia Orientalis Extract is in eye lotions at 0.0015%.

Following the passage of MoCRA, the FDA created a number of new product categories including, "(17) Other preparations (i.e., those preparations that do not fit another category)" (Category 17). CIR and the Panel utilize these product categories to inform, in part, the weight-of-evidence (WoE) in exposure and risk analyses. However, citation of Category 17, alone, as the product use category is uninformative. When a product is co-categorized with both Category 17 and one or more common product use categories (e.g., eye makeup preparations), or other information in the RLD such as the product name are indicative of use type (e.g., "lip balm" is part of the product name), then those uses are accounted for and may be considered to be part of the "the present practices of use" for those products; as such, the Panel's safety conclusion may be inclusive thereon. Conversely, for instances wherein the use of an ingredient in a cosmetic product is only categorized as Category 17 and other information in the RLD is not indicative of use type, the present practices of use for these products remain unknown and the Panel's safety assessment conclusion, therefore, does not apply thereon.

It is possible that some products containing Sigesbeckia Orientalis Extract may be marketed for use with airbrush delivery systems. With the advent of MoCRA and the current product categories outlined therein, it is now mandatory that cosmetic products used in airbrush delivery systems be reported as such for some, but not all, product categories in the RLD. In other words, a reliable source of frequency of use data regarding the use of cosmetic ingredients in conjunction with airbrush delivery systems is now available, in some instances. None of the reported product categories for this ingredient as listed in the RLD include a designation using airbrush application, so it is possible that this ingredient is used with airbrush delivery systems, but not reported as such. Additionally, the concentration of use surveys are conducted based on product categories as stated in the RLD, but airbrush use was not reported in response to the survey. No consumer habits and practices data or particle size data are publicly available to evaluate the exposure associated with airbrush technology, thereby preempting the ability to evaluate risk or safety. Without information regarding the consumer habits and practices data or product particle size data (or other relevant particle data, e.g., diameter) related to this use technology, the data profile is incomplete, and the Panel is not able to determine safety for use in airbrush formulations. If this ingredient was to be used in airbrush formulations, the data are insufficient to evaluate the exposure resulting from cosmetics applied in such a manner.

Sigesbeckia Orientalis Extract is not restricted from use in any way under the rules governing cosmetic products in the European Union.[14]

Non-Cosmetic

Sigesbeckia orientalis is valued as a medicinal plant in various cultures for its anti-inflammatory effects.[3] Particularly in traditional Chinese medicine, it is a remedy for rheumatic arthritis, hypertension, malaria, and snakebites. The plant is reported to stimulate blood circulation and has also been utilized in inducing menstruation and easing indigestion. Tinctures made from *Sigesbeckia orientalis* have traditional use topically for parasitic infections, as a cover over wounds, and as an anti-fungal treatment.[5] The Medicines and Healthcare Regulatory Agency in the United Kingdom approved a tablet containing a water extract of *Sigesbeckia orientalis* (also containing *Sigesbeckia pubescens* extract), for use as a traditional medicine to treat aches, pains, and minor injuries.[4]

TOXICOKINETIC STUDIES

No toxicokinetics studies on Sigesbeckia Orientalis Extract were 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

An acute oral toxicity assay was conducted with albino rats (strain not stated; 3/group) treated with an aqueous extract of *Sigesbeckia orientalis* (prepared using the whole plant; 5, 50, 300, and 2000 mg/kg), in accordance with the Organisation for Economic Co-operation and Development (OECD) test guideline (TG) 423.[15] After the 14-d observation period, no mortality or signs of toxicity were observed at the maximum dose of 2000 mg/kg.

Sprague-Dawley rats (5/sex/group) were intragastrically administered an aqueous extract of *Sigesbeckia orientalis* (prepared using the dried aerial parts; 0 or 5000 mg/kg) and observed for 14 d in an acute oral toxicity study.[16] No signs of toxicity or mortality were observed.

Chronic Toxicity Studies

Oral

A 24-wk oral toxicity assay was conducted in Sprague-Dawley rats (10/sex/group) that were intragastrically administered an aqueous extract of *Sigesbeckia orientalis* (0, 560, 1670, or 5000 mg/kg; given 6 d/wk).[16] All test groups showed significant decrease in body weight gain in the later weeks of the study, when compared to the control. Relative liver and lung weights were significantly elevated in the highest dose group (5000 mg/kg), and all test groups showed histopathological alterations in tissues of the liver (bile duct hyperplasia and enlarged portal vein) and lung (abnormal enlargement of the alveolar spaces and thickened alveolar walls). Additionally, all test groups showed significant serum level elevation of alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH), when compared to the control.

A 6-mo oral toxicity study was performed in male Sprague-Dawley rats (8/group) that were intragastrically administered 2 different aqueous extracts (raw and processed (prepared with the addition of rice wine)) of the dried aerial parts of *Sigesbeckia orientalis* (0 or 5000 mg/kg/d).[17] After the treatment period, LDH serum levels were found to be significantly higher in the raw extract group than in the control, and significantly lower in the processed extract group than in the raw extract group. Serum levels of ALT, AST, urea, and creatine kinase (CK) did not show any significant changes. Pulmonary tissues of the raw extract group exhibited inflammatory cell infiltration and cellular edema; however, the observed damage in the processed extract group was mild. No significant changes were seen in liver or heart tissues.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

No developmental and reproductive studies on Sigesbeckia Orientalis Extract were found in the published literature, and unpublished data were not submitted.

GENOTOXICITY STUDIES

No genotoxicity studies on Sigesbeckia Orientalis Extract were found in the published literature, and unpublished data were not submitted.

CARCINOGENICITY STUDIES

No carcinogenicity studies on Sigesbeckia Orientalis Extract were found in the published literature, and unpublished data were not submitted.

OTHER RELEVANT STUDIES

Cytotoxicity

A 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was conducted on human endometrial cancer cells (RL95-2 and HEC-1A) treated for 24 - 72 h with an ethanolic extract of the dried aerial parts of *Sigesbeckia orientalis* (25 – 150 µg/ml; in dimethyl sulfoxide (DMSO)), with and without transforming growth factor beta 1 (TGFβ1) stimulation.[18] Cell viability was inhibited for both cell lines in a dose- and time-dependent manner, with and without TGFβ1 stimulation.

Various cytotoxicity assays were performed on RL95-2 cells that were treated with an ethanolic extract of *Sigesbeckia orientalis* (prepared using dried aerial parts; test substance concentration of 20 - 150 µg/ml; medium used as untreated control, DMSO used as vehicle control).[7] Results showed that the test substance significantly inhibited cell-viability in a

dose- and time-dependent manner (at all test concentrations; when compared to the vehicle control). The test substance also induced apoptosis through morphological changes and up/downregulation of protein expression (statistical significance not stated for these assays). An MTT assay was performed to further test the cytotoxicity of an ethanolic extract of *Sigesbeckia orientalis* (prepared using dried aerial parts; concentrations not stated) against various human cancer cell lines: RL95-2, lung carcinoma (A549), hepatoblastoma (HepG2), pharynx squamous cell carcinoma (FaDu), breast adenocarcinoma (MDA-MB-231), and prostate carcinoma (LNCaP). The resulting IC_{50} values were 163.5, 179.1, 135.4, 105, 124.3, and 87.2 µg/ml, respectively.

In a cell viability assay, murine hepatoma (Hepa1-6), HepG2, and human keratinocyte (HaCaT) cell lines were treated with an ethanolic extract of the dried aerial parts of *Sigesbeckia orientalis* (62.5 - 1000 µg/ml).[19] After treatment with the test substance, cell proliferation was inhibited in a dose dependent manner. The resulting IC_{50} values for Hepa1-6, HepG2, and HaCaT cells were 282.4, 344.3, and 892.4 µg/ml, respectively, indicating increased cytotoxicity against the cancer cells. Several MTT assays performed with mouse macrophages (RAW264.7), with and without lipopolysaccharide (LPS) stimulation, to test the cytotoxic effects of an aqueous extract of *Sigesbeckia orientalis* (100 - 600 µg/ml), a 50% ethanol extract of *Sigesbeckia orientalis* (25 - 125 µg/ml), a 50% ethanol extract of the dried aerial parts of *Sigesbeckia orientalis* (20 -160 µg/ml), and a 95% ethanol extract of *Sigesbeckia orientalis* (10 -50 µg/ml), gave non-cytotoxic results.[20,21]

Effects on Inflammatory Mediators

An enzyme-linked immunosorbent assay (ELISA) was used to quantify the levels of interleukin (IL)-6, IL-1β, and tumor necrosis factor (TNF-α) in liver tissues from SD rats that were treated with an aqueous extract of *Sigesbeckia orientalis* (0, 560, 1670, or 5000 mg/kg; see study details under "Chronic Toxicity Studies").[16] Results showed dose dependent up-regulation in all pro-inflammatory cytokine levels.

ELISA and real-time polymerase chain reaction (RT-PCR) were used to determine the secretion levels of several inflammatory mediators in LPS-stimulated RAW264.7 cells treated with a 50% ethanolic extract of *Sigesbeckia orientalis* (prepared using dried aerial parts; 20 - 80 µg/ml).[21] The test substance dose-dependently inhibited the secretion of prostaglandin E_2 (PGE_2), monocyte chemoattractant protein-1 (MCP-1), macrophage inflammatory protein-1α (MIP-1α) and regulated on activation, normal T-cell expressed and secreted (RANTES). The test substance also decreased the messenger ribonucleic acid (mRNA) levels of nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2), IL-1β, IL-6, TNF-α, microsomal prostaglandin E synthase-1 (mPGES-1), MCP-1, MIP-1α, and RANTES.

Anti-Tumor Effects

A 2-wk tumorigenesis mouse model study (tumor induced with Hepa1-6) was conducted in male C57BL/6JNarl mice (6/group).[9] The tested groups were as follows: control (no cancer cells transplanted; normal diet), tumor-control (transplanted cancer cells; normal diet), tumor-vehicle (transplanted cancer cells; 5% ethanol (vehicle) in diet), tumor-test substance (transplanted cancer cells; 95% ethanol extract of the dried aerial parts of *Sigesbeckia orientalis* (25 mg/kg bw/d) in diet). When compared with the tumor-control group, the weight of the hepatoma was significantly reduced by 59.7% in the group treated with the test substance. Treatment with the test substance promoted apoptosis and suppressed angiogenesis. No mortality or significant changes in liver or kidney weights were reported under the conditions of this study.

Metabolic Effects

Several assays (inhibition of advanced glycation end products (AGEs), antiglycemic, lipase activity, and angiotensin converting enzyme (ACE) activity) were conducted with 4 different extracts (ethanol, *n*-hexane, ethyl acetate, and methanol) of the dried aerial parts of *Sigesbeckia orientalis*.[8] The ethyl acetate extract exhibited the strongest inhibitory effects against the formation of AGEs and the activity of key enzymes related to metabolic syndrome (pancreatic α-amylase, intestinal α-glucosidase, pancreatic lipase, and ACE).

DERMAL IRRITATION AND SENSITIZATION STUDIES

No dermal irritation and sensitization studies on Sigesbeckia Orientalis Extract were found in the published literature, and unpublished data were not submitted.

OCULAR IRRITATION STUDIES

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

SUMMARY

The safety of Sigesbeckia Orientalis Extract is reviewed in this safety assessment. According to the *Dictionary*, this ingredient is reported to function as a skin-conditioning agent in cosmetics.

According to RLD obtained from the US FDA in 2025, Sigesbeckia Orientalis Extract was reported to be used in 252 formulations. Concentration of use data submitted in 2024 indicates that Sigesbeckia Orientalis Extract has the highest

concentration of use at 0.046% in a facial toner that is used before applying a facial peel; the highest known maximum leave-on concentration of use is 0.0015% in eye lotions.

An acute oral toxicity assay performed in rats treated with an aqueous extract of *Sigesbeckia orientalis* (5 - 2000 mg/kg) showed no mortality or observable signs of toxicity at the maximum dose. Another acute oral toxicity study conducted in rats administered an aqueous extract of *Sigesbeckia orientalis* (5000 mg/kg) found no signs of toxicity or mortality.

A 24-wk oral toxicity assay conducted in rats treated with an aqueous extract of *Sigesbeckia orientalis* (560 - 5000 mg/kg) resulted in reduced body weight gain and several signs of toxicity (liver and lung histopathological changes, elevated serum levels of ALP, AST, ALT, and LDH). A 6-mo oral toxicity assay performed in rats given 2 different aqueous *Sigesbeckia orientalis* extracts (raw and rice-wine processed; 5000 mg/kg/d) resulted in elevated serum levels of LDH and alterations in lung tissues in the group treated with the raw extract.

Several studies found that ethanolic extracts of *Sigesbeckia orientalis* were cytotoxic to endometrial cancer cells (RL95-2 and HEC-1A), reducing cell viability in a dose- and time-dependent manner. Various human cancer cell lines were treated with an ethanolic extract of *Sigesbeckia orientalis*, resulting in IC_{50} values ranging from 87.2 - 179.1 µg/ml. An ethanolic extract of *Sigesbeckia orientalis* inhibited proliferation of Hepa1-6, HepG2, and HaCaT cell lines (IC_{50} = 282.4, 344.3, and 892.4 µg/ml, respectively) with greater cytotoxicity toward the cancer cells. Multiple MTT assays conducted with RAW264.7 cells found that aqueous, 50% ethanolic, and 95% ethanolic extracts of *Sigesbeckia orientalis* were non-cytotoxic.

An assay of liver tissues from rats that were treated with an aqueous extract of *Sigesbeckia orientalis* showed a dose-dependent increase in the pro-inflammatory cytokines IL-6, IL-1β, and TNF-α. An assay conducted in LPS-stimulated RAW264.7 cells treated with an ethanolic extract of *Sigesbeckia orientalis* resulted in dose-dependent suppression of the secretion levels of PGE_2, MCP-1, MIP-1α, and RANTES, and decreased mRNA levels of iNOS, COX-2, IL-1β, IL-6, TNF-α, mPGES-1, MCP-1, MIP-1α, and RANTES.

In a 2-wk hepatoma mouse model, dietary administration of an ethanolic extract of *Sigesbeckia orientalis* (25 mg/kg bw) reduced tumor weight by 59.7% without any observable signs of toxicity. Treatment with the extract also promoted apoptosis and suppressed angiogenesis in the transplanted tumors.

Several extracts of *Sigesbeckia orientalis* (ethanol, n-hexane, ethyl acetate, and methanol) were tested for inhibitory effects against AGE formation and enzyme activity related to metabolic syndrome. The ethyl acetate extract showed the strongest effects of inhibition in all the conducted tests.

DISCUSSION

To be developed.

CONCLUSION

To be determined.

TABLES

Table 1. Chemical composition of an ethanolic extract of *Sigesbeckia orientalis* determined using GC-MS[7]

Component	% of the total composition
2-oxabicyclo[2,2,2]octane-6-ol	1.8
2-*tert*-butyl-1,4-dimethoxy-benzene	3.8
caryophyllene	3.1
cis-α-bisabolene	4.1
spathulenol	25.7
caryophyllene oxide	46.9
cis-lanceol	1.7
[*Z,Z,Z*]-9,12,15-Octadecatrienoic acid ethyl ester	1.2
6,10,14-trimethyl-2-pentadecanone	2.1
hexadecanoic acid ethyl ester	9.6

Table 2. Total polyphenol, flavonoid, and phenolic constituent content (mg/g extract) of different extracts of *Sigesbeckia orientalis*[8,9]

Extract Type	total polyphenol[a]	total flavonoid[b]	chlorogenic acid[c]	syringic acid[c]	*p*- coumaric acid[c]	syringaldehyde[c]	kirenol[c]
ethanol	31.7	4.1	0.98 - 2.04	0.26 - 10.76	0.70 – 0.71	0.39	7.88
n-hexane	13.7	0.4	NR	NR	NR	0.34	NR
ethyl acetate	76.9	5.3	0.72	2.21	1.76	0.57	NR
methanol	15.7	1.9	0.95	NR	NR	NR	NR

NR – not reported

[a] total polyphenol content determined by Folin-Ciocalteu method

[b] total flavonoid content determined by aluminum chloride colorimetric method

[c] phenolic constituent content determined by HPLC

Table 3. Frequency and concentration of use of according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use
	RLD (2025)[11,12]	% (2024)[13]
Totals*	**252**	**0.0015 – 0.046**
summarized by likely duration and exposure**		
Duration of Use		
Leave-On	*273*	*0.0015*
Rinse-Off	*14*	*NR*
Diluted for (Bath) Use	*NR*	*NR*
Unknown	*2*	*0.046*
Exposure Type		
Baby Products	NR	NR
Children's Makeup	NR	NR
Eye Area	43	0.0015
Incidental Ingestion	NR	NR
Mucous Membrane	NR	NR
Incidental Inhalation-Spray	43[a]; 183[b]	0.0015[b]
Incidental Inhalation-Airbrush	NR	NR
Incidental Inhalation-Powder	183[b]	0.0015[b]
Dermal Contact	287	0.0015 - 0.046
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	NR	NR
Hair-Coloring	NR	NR
Nail	NR	NR
Other Preparations (Unknown Exposure Type)	2	0.046[c]
as reported by product category		
Eye Makeup Preparations (other than children's eye makeup preparations)		
Eye Shadow	5	NR
Eye Lotion	34	0.0015
Eye Makeup Remover	2	NR
Eyelash and Eyebrow Preparations (primers, conditioners, serums, fortifiers)	1	NR
Eyelash Cleansers	1	NR
Makeup Preparations (not eye; not children's)		
Foundations	10 (traditional application)	NR
Skin Care Preparations (creams, lotions, powder, and sprays)		
Cleansing (cold creams, cleansing lotions, liquids, and pads)	8	NR
Face and Neck (excluding shaving preparations)	151 (l.o.); 3 (r.o.)	NR
Body and Hand (excluding shaving preparations)	16 (l.o.)	NR
Moisturizing	26	NR
Night	12	NR
Skin Fresheners	2	NR
Other Skin Care Preparations	16 (l.o.)	0.0015[d]
Other Preparations (i.e., those preparations that do not fit another category)	2	0.046[c]

NR – not reported
l.o. – leave-on; r.o. – rinse-off
*The sum of the counts given for duration of use and by exposure type, and the sum of the frequency reported by product category, may not equal the sum of total uses because each ingredient may be used in cosmetic formulations that are reported under more than one product category.
**Likely duration and exposure are derived from survey data based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether 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
[c] facial toner used before applying facial peel
[d] not specified whether leave-on or rinse-off exposure

REFERENCES

1. Personal Care Products Council. 2026. *International Cosmetic Ingredient Dictionary*. https://incipedia.personalcarecouncil.org/winci/. Date Accessed: February 27, 2026.
2. Chemical Book. 2025. Siegesbeckia orientalis, ext. | 90106-87-9. https://www.chemicalbook.com/ChemicalProductProperty_EN_CB9879296.htm. Date Accessed: Apr 8, 2026.
3. Sukanya M, Babu A, Azamthulla M. A detailed review on *Siegesbeckia orientalis*. *Zeichen Journal*. 2022;8(2):23.
4. Tao HX, Zhao GD, Linghu KG, et al. Botany, traditional use, phytochemistry, pharmacology and toxicology of Sigesbeckiae Herba (Xixiancao): a review. *Phytochem Rev*. 2021;20(3):569–587.
5. Nwaogu L, Igwe C, Ujowundu C, Obasi U, Okeke U. Chemical composition of *Siegesbeckia orientalis*: a valuable, but less known ethnomedicinal plant. *Biokemistri*. 2017;29(2):54–60.
6. Zhang S, Lin H, Deng L, et al. Cadmium tolerance and accumulation characteristics of *Siegesbeckia orientalis* L. *Ecological Engineering*. 2013;51:133–139.
7. Chang C, Hsu H, Huang K, et al. Anti-proliferative effects of *Siegesbeckia orientalis* ethanol extract on human endometrial RL-95 cancer cells. *Molecules*. 2014;19(12):19980–19994.
8. Hung W, Ling X, Chang C, et al. Inhibitory effects of *Siegesbeckia orientalis* extracts on advanced glycation end product formation and key enzymes related to metabolic syndrome. *Molecules*. 2017;22(10):1785.
9. Chen TH, Houng JY, Chang TH, Chen YL, Chang CC, Chang LS. *Siegesbeckia orientalis* suppresses growth and migration through apoptosis and inhibition of matrix metalloproteinases expression on hepatoma in mice. *Preprints*. 2024.
10. United States Food and Drug Administration. Federal Food, Drug, and Cosmetic Act Section 612 Title 21.
11. US Food and Drug Administration (FDA) Office of Colors & Cosmetics (OCAC). 2025. Data from: Registration and Listing of Cosmetic Product Facilities and Products. College Park, MD [Obtained under the Freedom of Information Act].
12. Hicks J., Eisenmann C., Nikitakis J., Kim D., Flores W. 2025. Personal Care Products Council (PCPC) RLD Mapping Project Report. Washington, DC. [Analysis results provided as a courtesy to CIR].
13. Personal Care Products Council. 2024. Concentration of use by FDA product categories - Sigesbeckia Orientalis Extract. [Unpublished data submitted by Personal Care Products Council on December 10, 2024].
14. EUR-Lex. 2025. Commission implementing decision (EU) 2025/1175 of 16 June 2025 laying down rules for the application of regulation (EC) no 1223/2009 of the European Parliament and of the Council as regards the glossary of common ingredient names for use in the labelling of cosmetic products and repealing commission implementing decision (EU) 2022/677. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32025D1175&qid=1767818754806. Date Accessed: Feb 13, 2026.
15. Asif M, Saleem M, Yousaf S, et al. Antidiabetic activity of aqueous extract of *Sigesbeckia orientalis* (St. Paul's Wort) in alloxan-induced diabetes model. *Braz J Pharm Sci*. 2019;55:e18408.
16. Wu J, Chan Y, Guo H, et al. Twenty-four-week oral dosing toxicities of Herba Siegesbeckiae in rats. *BMC Complement Med Ther*. 2020;20(1):341.
17. Jiang T, Liu L, Zhang M, et al. Metabolomics reveals the mechanisms for the pulmonary toxicity of *Siegesbeckia orientalis* L. and the toxicity-reducing effect of processing. *Front Pharmacol*. 2021;12:630319.
18. Chang C, Ling X, Hsu H, et al. *Siegesbeckia orientalis e*xtract inhibits TGFβ1-induced migration and invasion of endometrial cancer cells. *Molecules*. 2016;21(8):1021.
19. Chen T, Chang C, Houng J, et al. Suppressive effects of *Siegesbeckia orientalis* ethanolic extract on proliferation and migration of hepatocellular carcinoma cells through promoting oxidative stress, apoptosis and inflammatory responses. *Pharmaceuticals*. 2022;15(7):826.
20. Guo H, Zhang Y, Cheng BC, et al. Comparison of the chemical profiles and inflammatory mediator-inhibitory effects of three *Siegesbeckia* herbs used as Herba Siegesbeckiae (Xixiancao). *BMC Complement Altern Med*. 2018;18(1):141.
21. Guo H, Zhang Y, Cheng BC, et al. An ethanolic extract of the aerial part of *Siegesbeckia orientalis* L. inhibits the production of inflammatory mediators regulated by AP-1, NF-κB and IRF3 in LPS-stimulated RAW 264.7 cells. *BioScience Trends*. 2018;12(3):330–337.

Concentration of Use by FDA Product Categories[1] – Sigesbeckia Orientalis Extract

Product Category	Maximum Concentration of Use
Eye lotions	0.0015%
Other skin care preparations	0.0015%
Other preparations (i.e., those preparations that do not fit another category)	0.046% (facial toner used before applying facial peel)

Information collected in 2024

Table prepared: December 10, 2024

[1] The new FDA cosmetic product categories under MoCRA were used for this survey.