Safety Assessment of *Portulaca oleracea*- 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 Preethi S. Raj, M.Sc., Senior 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: Preethi S. Raj, M.Sc.
Senior Scientific Analyst, CIR

Date: November 13, 2020

Subject: Safety Assessment of *Portulaca oleracea*-Derived Ingredients as Used in Cosmetics

Enclosed is the draft report of the Safety Assessment of *Portulaca oleracea*-Derived Ingredients as Used in Cosmetics (identified as *porole122020rep* in the pdf). This is the first time the Panel is seeing a safety assessment of these 4 cosmetic ingredients. A Scientific Literature Review (SLR) was announced on July 15, 2020.

Concentration of use data were received from the Council, in 2018, prior to issue of the SLR (*porole122020data1*). The following data were received in response to the SLR, and have been incorporated in the report:

porole122020data2

- Anonymous. (2020) Certificate of origin and method of manufacture water/butylene glycol extract of *Portulaca oleracea*
- Anonymous. (2020) Certificate of ingredient source and method of manufacture water extract of *Portulaca oleracea*

porole122020data3

- Anonymous. (2006) Human patch test (product containing 0.1% Portulaca Oleracea Extract).
- Anonymous. (2017) Summary: Clinical use test of a product containing 0.1% Portulaca Oleracea Extract
- KGL, Inc. (2007). An evaluation of the contact sensitization potential of a topical coded product in human skin by means of the maximization assay (product containing 0.1% Portulaca Oleracea Extract)

Comments on the SLR (*porole122020pcpc*) that were received from the Council have been addressed. Also included in this package, for your review, are a flow chart (*porole122020flow*), literature search strategy (*porole122020strat*), ingredient data profile (*porole122020prof*), ingredient history (*porole122020hist*), and 2020 FDA VCRP data (*porole122020FDA*).

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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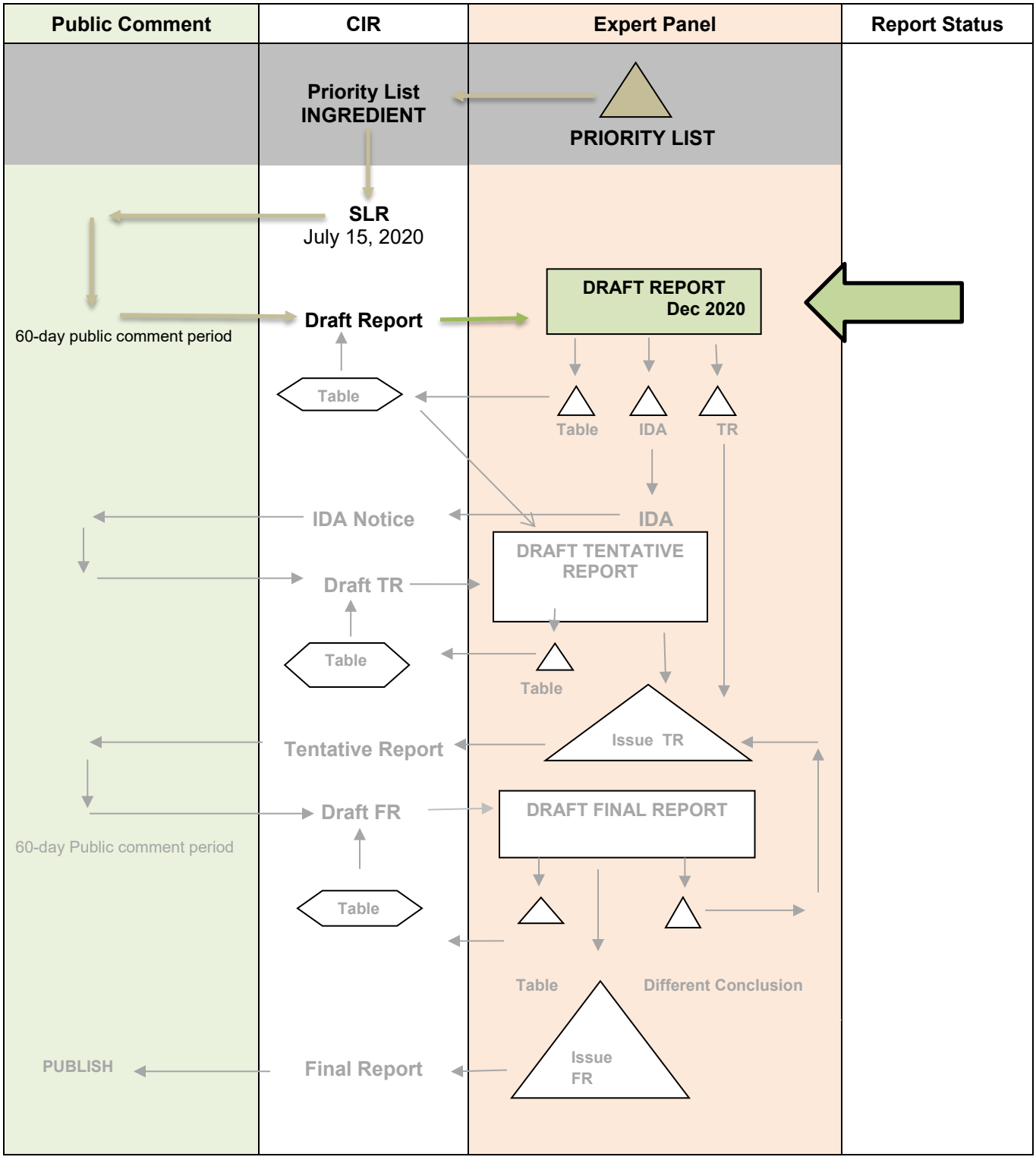
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY *Portulaca oleracea*-derived ingredients

MEETING December 2020



CIR History of:

Portulaca oleracea-derived Ingredients

January 2019

-Concentration of use data submitted by Council

January 2020

-FDA frequency of use data obtained

July 2020

- SLR posted on the CIR website

Data received (for Portulaca Oleracea Extract):

- July 29, 2020: Certificates of origin, method of manufacture, and ingredient source information for water and water/butylene glycol extracts of *Portulaca oleracea*

- August 12, 2020: Human patch test, clinical test summary, contact sensitization study results, all testing products containing 0.1% Portulaca Oleracea Extract

December 2020

-A Draft Report is being presented to the Panel.

***Portulaca oleracea*-derived Ingredients Data Profile* – December 7-8th, 2020 – Writer, Preethi Raj**																															
				Toxicokinetics			**Acute Tox**			**Repeated Dose Tox**			**DART**		**Genotox**		**Carci**		**Dermal Irritation**			**Dermal Sensitization**				**Ocular Irritation**		**Clinical Studies**	
	Reported Use	**Method of Mfg**	**Impurities**	**log P/log K_{ow}**	**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**
Portulaca Oleracea Extract	X	X	X					X			X										X			X						
Portulaca Oleracea Flower/Leaf/Stem Extract		X	X					X			X			X																
Portulaca Oleracea Juice		X									X																			
Portulaca Oleracea Water		X																													

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

Portulaca oleracea – derived ingredients (4 ingredients- December 2020 Panel Mtg)

Ingredient	CAS #	InfoB	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Portulaca Oleracea Extract	90083-07-1	✓	✓	✓	NR	✓*	✓*	NR	NR	NR	NR	NR	✓*	NR	✓	NR	NR	NR	✓
Portulaca Oleracea Flower/Leaf/Stem Extract	90083-07-1	✓	✓	✓	NR	NR	NR	NR	NR	NR	NR	NR	✓*	NR	NR	NR	NR	NR	✓
Portulaca Oleracea Juice	NR	✓	NR	NR	NR	✓*	NR	NR	NR	NR	NR	NR	✓*	NR	NR	NR	NR	NR	✓
Portulaca Oleracea Water	90083-07-1	✓	NR	NR	NR	✓*	NR	NR	NR	NR	NR	NR	✓*	NR	NR	NR	NR	NR	✓

Botanical and/or Fragrance Websites (if applicable)

Ingredient	CAS #	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	IFRA	RIFM
Portulaca Oleracea Extract	90083-07-1	✓	NR	#29453	NR	NR	NR
Portulaca Oleracea Flower/Leaf/Stem Extract	90083-07-1	NR	NR	NR	NR	NR	NR
Portulaca Oleracea Juice	NR	NR	NR	NR	NR	NR	NR
Portulaca Oleracea Water	90083-07-1	NR	NR	NR	NR	NR	NR

✓- found in database, or, data was available
✓*- found in database, but data was either irrelevant or not accessible
NR – not reported

Search Strategy

[*document search strategy used for PubMed and/or Toxnet]:* - [*total # of hits/#hits that were useful*]
((((physical chemical properties) AND portulaca oleracea extract) OR portulaca oleracea whole extract) OR portulaca oleracea juice) OR portulaca oleracea water – 97/3

Whole extract
Portulaca oleracea Persian medicine – 4/2
Chinese traditional medicine ma chi xian – 4/2
Alkaloids from Portulaca oleracea – 44/10
Portulaca oleracea pharmacokinetics – 18/2
portulaca oleracea toxicokinetics humans – 4/0
Portulaca oleracea dermal toxicity – 0/0
Portulaca oleracea extract dermatology – 2/0
Portulaca oleracea skin irritation -0/0
Portulaca oleracea dermal sensitization – 0/0
Portulaca oleracea skin sensitization -0/0
Portulaca oleracea genotoxicity -1/0
Portulaca oleracea reproductive toxicity OR pregnancy OR fetal development -0/0
Portulaca oleracea inhalation toxicity
Purslane cosmetics – 3/0
Purslane topical – 5/1
Portulaca oleracea clinical study – 13/6

Stem/Flower/Leaf
Portulaca oleracea flower cosmetic toxicity – 182,000/0
Juice
Portulaca oleracea juice – 3/0
Portulaca oleracea juice toxicity -0/0
((((Portulaca Oleracea Juice) AND toxicokinetics) OR acute dermal toxicity) OR acute oral toxicity) OR acute inhalation toxicity – 9798/0
Water
Portulaca oleracea water toxicity – 0/0
Portulaca oleracea steam distillate toxicity – 0/0

General Web Search
portulaca oleracea dermal toxicity - 717,000/2
portulaca oleracea dermal sensitization – 16/1
portulaca oleracea folk medicine dosage – 111,000/6
portulaca oleracea animal toxicity – 112,000/4

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://iaspub.epa.gov/oppthpv/public_search.html_page
- 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 *Portulaca oleracea*-derived ingredients, as used in cosmetic formulations:

Portulaca Oleracea Extract	Portulaca Oleracea Juice
Portulaca Oleracea Flower/Leaf/Stem Extract	Portulaca Oleracea Water

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), all of these ingredients are reported to function as skin-conditioning agents in cosmetics (Table 1).[1] Additionally, Portulaca Oleracea Flower/Leaf/Stem Extract is reported to function as an antioxidant.

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 Expert Panel for Cosmetic Ingredient Safety (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.

Botanicals, such as *Portulaca oleracea*-derived ingredients, may contain hundreds of constituents, some of which may have the potential to cause toxic effects. In this assessment, the Panel is reviewing the potential toxicity of each of these botanical ingredients as a whole, complex mixture. The Panel is not reviewing the potential toxicity of the individual constituents.

The cosmetic ingredient names, according to the *Dictionary*, are written as listed above, without italics. In many of the published studies, it is not known how the substance being tested compares to the cosmetic ingredient. Therefore, if it is not known whether the test substance is the same as the cosmetic ingredient, the test substances will be identified by the standard scientific practice of using italics to identify genus and species (i.e., a *Portulaca oleracea* extract). However, if it is known that the substance is a cosmetic ingredient, the International Nomenclature Committee (INC) terminology "Portulaca Oleracea…" (e.g. Portulaca Oleracea Extract) will be used.

CHEMISTRY

Definition and Plant Identification

The definitions and functions for the 4 *Portulaca oleracea*-derived ingredients reviewed in this safety assessment are provided in Table 1.[1] The flower is the reproductive shoot in flowering plants, usually with sepals, petals, stamens, and pistil(s). The stem is defined as a slender or elongated structure which supports the plant, plant part, or plant organ, while the leaves are defined as the flattened photosynthetic organs, attached to the stems.

Portulaca oleracea is an annual herbaceous weed of the Portulacaceae family.[2] The genus *Portulaca* is thought to be derived from Latin 'porto,' to carry, and 'lac,' meaning milk, owing to the milky juice obtained upon expressing the plant.[3] It is commonly referred to as purslane, pigweed, Ma-Chi-Xian, and many other regionally specific names.[4] Although it is thought to originate from tropical and subtropical countries in Eastern Asia, it currently grows throughout the world, in unshaded areas. In spite of growing optimally in temperate climates, *Portulaca oleracea* also thrives under diverse geographic and climactic conditions due to its relatively low water and soil nutrient requirements, and tolerance to salt and drought.[5,6] As a dicotyledonous, C4 photosynthesis plant, displaying Kranz anatomy structure, *Portulaca oleracea* has high water efficiencies in conditions that promote carbon loss through photorespiration, such as high temperatures, high light intensities, and decreased water availability.[7,8]

The plant is a succulent, which usually grows close to the ground, and is up to 30 cm in height, with a cylindrical stem of 2 - 3 mm in diameter.[9] The leaves are oblong and grow in an alternate arrangement, broad at the apex and tapered at the base. The leaf apex is obtuse and smooth, with no teeth or lobes. The flowers are terminal in cluster, with 2 - 6 foliar involucres, and five bright yellow petals enclosed by two subequal lanceolate sepals. The fruit is a shell and the seed is kidney-shaped and flaky.[10] The stem is smooth, red, and circular, and consists of a distinct ~ 60 µm epidermis, 800 µm broad cortex, and a pith consisting of cells similar to cortical parenchyma. The xylem elements are thick-walled and angular, and possess dense calcium oxalate crystals.

Chemical Properties

In an ultraviolet (UV) spectral analysis of crude, and methanol-soluble fractions of whole *Portulaca oleracea* extract, optical spectra maxima were recorded between 200 and 400 nm, in which phenolic compounds showed maximum absorbence.[11] The Fourier transform infrared spectroscopy (FTIR) spectrum of a chloroform extract of whole *Portulaca oleracea* showed peaks at 1019.52 and 1396.21/cm, corresponding to the wavenumber ranges for alcohols and phenols, amines, organic, and, possibly, nitrogen or oxygen-containing compounds.[12]

Method of Manufacture

An overview of 2 supplier-provided methods of manufacture for Portulaca Oleracea Extract, one using the whole plant[13] and the other using the leaf and stem,[14] is outlined in Figure 1.

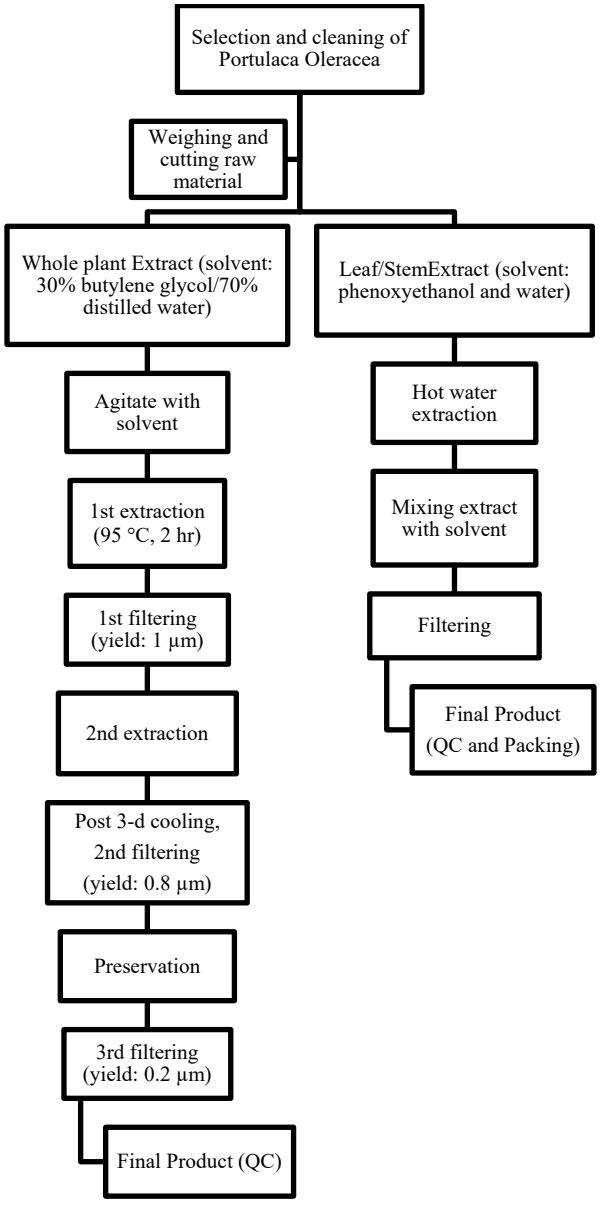

Figure 1. Overview of methods of manufacture for Portulaca Oleracea Extracts.[13,14]

Most of the methods below are general to the processing of *Portulaca oleracea*, and it is unknown if they apply to cosmetic ingredient manufacturing.

Portulaca Oleracea Extract

Extracts of *Portulaca oleracea* may be obtained through maceration of the fresh or dried plant in an alcoholic or aqueous solvent.[15] Most *Portulaca oleracea* extracts are obtained using ethanol or methanol solvents.[16] Methanol is preferred as a polar solvent which elutes the highest level of constituents from *Portulaca oleracea*, in turn affecting phenolic compound content and potential antioxidant activity.[17-20] Levels of individual compounds detected in crude *Portulaca oleracea* extracts may be low, and enhanced via techniques, such as reversed-phase separation, to isolate phenol-enriched fractions.[11]

A method of preparing the aqueous extract of *Portulaca oleracea* (whole plant) is described as follows: distilled water (1500 ml) was added to 300 g of dried plant powder in a sealed glass container, set aside for 72 h, and then the filtrated extract was concentrated in a rotary evaporator under reduced pressure at 55 °C.[15] The resulting extract was dried in a warm water bath.

An alcoholic extract of *Portulaca oleracea* seeds was obtained by refluxing 500 g of powdered seeds with 2 l of rectified spirit for 10 h on a 100 °C water bath.[21] The initial filtrate was collected while hot, and the residual seeds were refluxed thrice more with 2 l of rectified spirit. Filtrates from the successive extractions were mixed and the rectified spirit was distilled off under reduced pressure, resulting in 50 g of an oily brown syrup. This syrup extract was suspended in 250 ml of sterile olive oil.

Portulaca Oleracea Flower/Leaf/Stem Extract

The aerial parts of *Portulaca oleracea* were used to prepare several extracts.[19] Four solvents (300 ml, each) of increasing polarity, namely, hexane, ethyl acetate, methanol, and water, were placed in the cartridge of separate Soxhlet extractors with 30 mg powdered aerial parts of *Portulaca oleracea*. The extractions took place over 24 h, after which the recovered extracts were conserved at 4 °C.

Aerial parts of the plant were washed with water, and the leaves along with the stems were stripped from the plant and divided into three equal batches.[22] The first batch was cut into small pieces and air dried at 45 °C. The second batch was boiled in water at 100 °C for 15 min in the ratio of 1:10 (w/v). The third batch was blanched in boiling water (at 100 °C) for 10 min in the ratio of 1:10 (w/v). After boiling and blanching, the remaining water was discarded and the three processed samples were cut into small pieces and dried at 45 °C. After drying, the samples were ground to a fine powder and extracted in aqueous acetone.

Portulaca Oleracea Juice

In another study, the aerial parts of *Portulaca oleracea* were washed with water, cut into small pieces, and blended.[23] The juice was obtained from the resultant puree by centrifugation (10,000 x g, 20 min, 4 °C) and was sterilized by filtration on 0.22 μm membrane filters.

Portulaca Oleracea Water

Portulaca Oleracea Water is the steam distillate obtained from the whole plant.[1]

Composition and Impurities

Water content is high in *Portulaca oleracea* (up to 92.32%).[10,11,24] Moisture migrates from the leaves to the stems as the plant matures.

Portulaca oleracea contains nutrients which are also found in major cultivated vegetables, and it contains a high amount of α-linolenic acid, an essential omega -3 fatty acid, compared to other leafy vegetables.[11,25] In a study comparing nutrients found in chamber and wild-grown *Portulaca oleracea* and spinach, although β-carotene levels were lower, ascorbic acid and glutathione levels were higher, and α-linolenic acid content and α-tocopherol levels were 7 times higher in both chamber and wild-grown *Portulaca oleracea*, than those found in spinach.[26] One serving of fresh chamber-grown *Portulaca oleracea* (100 g) was reported to contain 300 - 400 mg α-linolenic acid, 26.6 mg ascorbic acid, 12.2 mg α-tocopherol, 14.8 mg glutathione, and 1.9 mg β-carotene.

As a weed plant, the roots of *Portulaca oleracea* draw minerals from deeper layers of the soil, by degrading and absorbing residual solid parts of other plants.[10] The dry weight (mmol/kg DW) concentrations of calcium, magnesium, sodium, potassium, iron, and zinc monitored on day 15, 30, 45, and 60 of growth, were highest in the leaves of 60-d old *Portulaca oleracea* plants.[17] Varying climate and soil conditions among *Portulaca oleracea* plants grown in different locations also affected mineral composition, flavonoid, and carotenoid content.[27,28] Additionally, the composition and determination of individual constituents found in *Portulaca oleracea*-derived ingredients varies considerably depending on extraction solvent and method,[10,16] part of the plant,[24,29] and growth stage or time of harvest.[17,24] A list of constituents, isolated across different studies, by plant part, is presented in Table 2.

Oxalic acid, or oxalate, is found in a variety of plants, and is generally present in *Portulaca oleracea* at 1.3%.[30] Oxalate is also found in soluble (bound to potassium, sodium, and magnesium) and insoluble forms (bound to calcium and iron) in *Portulaca oleracea* plants, with mean soluble oxalate values of 33% in the leaves, and 67% in the stems.[31] In a chemical analysis of oxalate content in *Portulaca oleracea*, the highest total concentration of soluble and insoluble oxalate was found in the leaves (23.45 g/kg fresh weight (fw)), and in lesser amounts in the buds (9.09 g/kg fw) and stems (5.58 g/kg fw).[31] In the same study, cooking the whole plant resulted in a 49% reduction of soluble oxalate content in plant buds, 33.5% reduction in the leaves, and 18% reduction in the stems, while pickling the plant in white vinegar resulted in a 67% overall oxalate reduction. *Portulaca oleracea* is mentioned in the US FDA Poisonous Plant Database.[32] Toxic effects of the oxalate content, upon consumption of *Portulaca oleracea*, has been observed in dogs, cats, horses, and ruminant species.[33,34]

Portulaca Oleracea Extract

Portulaca oleracea extract is composed of a wide range of constituents, of which flavonoids, alkaloids, terpenes, phenolic acids, and coumarins are preeminent.[2,35] Other notable constituents are omega-3-fatty acids, polysaccharides, vitamins, and amino acids.[29]

The phenolic and flavonoid content of hydrothermally processed *Portulaca oleracea* was evaluated.[22] The gallic acid equivalents of boiled, blanched, and raw *Portulaca oleracea* were determined to be 19.25, and 10.02 , and 22.94 g/extract, respectively. Boiling and blanching significantly increased the rutin equivalent to 85.14 and 81.57, compared to 64.99 mg/g extract in raw *Portulaca oleracea*.

Portulaca Oleracea Flower/Leaf/Stem Extract

The chemical composition and nutritional value of *Portulaca oleracea* plants was assessed, by plant part (leaves and stems) and stage of harvest, for up to 52 d after sowing.[24] The moisture content of leaves was the highest at day 29, while stems contained the most water on day 43. Higher macronutrient content and protein values were observed in the leaves at the last harvest, while the carbohydrate and α-linolenic acid content of leaves was highest at day 29. In a study of total flavonoid and total phenolic content in *Portulaca oleracea* flowers, leaves, and stems, total phenolic content was significantly higher in stems compared to leaves and flowers (1008.6 vs. 441.8 - 455.6 gallic acid equivalents), in spite of total flavonoid content not differing significantly.[36]

The impact of the dehydration method (100 W microwave, tray, vacuum, or low temperature, low humidity infrared) upon the retention of bioactive compounds in extracts made from dried *Portulaca oleracea* leaves and stems was evaluated.[20] Flavonoid content and fatty acid composition was highest in the extract of vacuum-dried leaves.

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.

Portulaca Oleracea Extract is the only ingredient included in this report that is reported to be used in cosmetic formulations. According to 2020 VCRP survey data, Portulaca Oleracea Extract is reported to be used in 579 formulations (Table 3), of which 189 uses are in face and neck products, and 133 uses are in moisturizing products.[37] The results of the concentration of use survey conducted by the Council in 2018 indicate that the reported maximum concentration of use for Portulaca Oleracea Extract is 0.008%, in leave-on, moisturizing, formulations.[38] According to VCRP and Council survey data, Portulaca Oleracea Flower/Leaf/Stem Extract, Portulaca Oleracea Juice, and Portulaca Oleracea Water were not reported to be in use in cosmetic products.

Portulaca Oleracea Extract is reported to be used in products which may allow exposure near the eye or mucous membranes. Concentration of use data were not reported for these categories of use.

According to VCRP data, Portulaca Oleracea Extract is reportedly used in 2 face powder formulations,[37] and could possibly be inhaled; concentration of use data were not reported for this use.[38] Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[39-41]

All of the ingredients named in the report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[42]

Non-Cosmetic

Portulaca oleracea is consumed raw in salads, or is used as a potherb in cooked sauces, soups, and pickled dishes across many cultures.[4,43] Uses as an apotropaic agent and a source of violet and gray dye for wool are also noted.[43]

Historically, *Portulaca oleracea* is reported to be widely used in traditional folk medicine. In Chinese traditional medicine, the plant is used for the treatment of dysentery with bloody stools, as a topical emollient, collyrium, and as an external muscle relaxant.[3,4] Native Americans use the plant to treat gout and headaches, and as a febrifuge.[4] In Africa, the *Portulaca oleracea* plant is considered to exhibit anti-inflammatory, analgesic, and antifungal activity; fresh juice is used in the treatment of dysuria, coughs, and as an anti-diabetic agent.[4,44] Additionally, it is used in religious ceremonies for purification, as an antiphlogistic substance, and for the treatment of skin diseases, erysipelas, insect and snake bites, abscesses, and eczema.[4,16] The World Health Organization (WHO) describes *Portulaca oleracea* as a medicinal plant, with antibacterial, anti-inflammatory and antihelminth properties; poultices of fresh leaves are used to treat mastitis, boils, and impetigo.[45]

TOXICOKINETIC STUDIES

No relevant toxicokinetic studies on *Portulaca oleracea*-derived ingredients were found in the public literature, and unpublished data were not submitted. In general, toxicokinetic 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

The acute toxicity studies summarized below are described in Table 4.

The oral LD_{50} of an extract of whole *Portulaca oleracea* (water: ethanol; 1:1), in Swiss albino mice, was determined to be ≤ 500 mg/kg bw.[46,47] The oral LD_{50} of a petroleum ether *Portulaca oleracea* leaf extract, in Sprague-Dawley rats, was determined to be > 2000 mg/kg bw. [48] Maximum oral doses of 5000 mg/kg chloroform and methanolic *Portulaca oleracea* leaf extracts were well tolerated in rats.[49,50]

Short-Term Toxicity Studies

The short-term toxicity studies summarized below are described in Table 5.

Groups of 6 Swiss albino mice were administered an oral dose of 0, 200, or 400 mg/kg bw/d, ethanolic extract of whole *Portulaca oleracea* (water: ethanol; 1:1), via gavage, for 14 d.[46,47] No mortality occurred during observation; a statistically significant increase in hypoglycemic activity was observed in both treated groups, and to a greater extent in the 400 mg/kg bw group. Groups of 5 albino rats dosed at up to 75 mg/kg bw/d of aqueous or methanolic extract of whole *Portulaca oleracea* for 30 d showed a statistically significant decrease in white blood cell and neutrophil counts, and increased lymphocyte counts in the 25 and 50 mg/kg bw/d aqueous extract groups.[51] Rats in the 25 mg/kg bw/d methanolic extract group showed a significant increase in mean corpuscular volume and mean corpuscular hemoglobin, while rats in the 75 mg/kg bw/d methanolic extract group had a significant decrease in total plasma protein and albumin levels. In a 14-d study, groups of 6 Sprague-Dawley rats were orally dosed with 0, 500, 1000, or 2000 mg/kg/d petroleum ether extract of *Portulaca oleracea* leaves.[48] No mortality occurred during observation; a non-significant increase in body weights, and a significant, dose-dependent increase in hematological parameters and cholesterol levels was observed in all treated rats. Groups of 16 male albino Wistar rats were administered 0, 125, 250, or 500 mg/kg bw/d methanolic or chloroform extract of *Portulaca oleracea* leaves, via gavage, for 60 d.[49,50] The 500 mg/kg group showed a significant decrease in the mean hematocrit on day 28, which was considered incidental, and a significant increase in white blood cell count on day 42. Platelet count was increased in all treatment groups, and was significantly higher in the 125 and 500 mg/kg treated rats on day 60. Groups of 6 male albino Wistar rats were dosed with either distilled water or 1.5 ml/kg/d *Portulaca oleracea* juice extract, via gavage, for 12 d.[52] Blood samples in rats treated with *Portulaca oleracea* juice exhibited significant variability in enzymes and hematological parameters pertinent to kidney and liver function, such as a decrease in urea, creatine, and bilirubin, and an increase in glutathione and related enzymes.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Details of the developmental and reproductive studies summarized below are described in Table 6.

Male albino rats treated with 75 mg/kg bw aqueous or methanolic *Portulaca oleracea* leaf and stem extract for 50 d, were cohabited with 3 female rats each for 4 wk.[53] No pregnancy (or sterile mating) occurred between males from either extract group and the untreated female rats. Groups of 5 male albino rats orally dosed with 0, 25, 50, or 75 mg/kg/d aqueous, or methanolic *Portulaca oleracea* leaf and stem extracts for 50 d, had blood samples from day 51 analyzed for testosterone levels, and the animals were sacrificed for semen and histological analyses of the testes.[54] A statistically significant decrease in testosterone levels was observed in rats in the aqueous 75 mg/kg group, and in all methanolic extract groups. Animals in all dose groups had significantly reduced sperm motility, sperm count, and increased sperm abnormalities. Groups of 5 - 6 female Wistar albino rats dosed with 0, 250, or 500 mg/kg bw/d, flavonoid-rich, *Portulaca oleracea* stem and leaf extract, were examined for potential effects on reproductive organ weight, estrous cycles, uterine characteristics, abortifacient activity, and implantation; significant uterine changes included larger diameter and endometrial thickness.[55] In two similarly completed, but separate studies, ovary and uterine weights were significantly lower in immature, bilaterally ovariectomized rats dosed with 250 or 500 mg/kg bw/d *Portulaca oleracea* stem and leaf extract for 7 d, and, significantly higher in the mature rats dosed with 250 and 500 mg/kg bw/d of the same extract for 10 d; both effects were associated with significantly reduced protein and cholesterol uterine content, and suppression of follicular stimulating hormone, respectively.[55] In a 21-d study, female albino rats were first dosed with 75 mg/kg/d aqueous or methanolic *Portulaca oleracea* leaf and stem extracts, and then served as their own controls after an additional 21 d of no dosing to observe changes in estrous cycles.[56] Treatment for 21 d with either extract did not produce any significant changes in duration of estrous cycle phases. However, during the 21-day withdrawal of treatment, a significant decrease in the proestrus phase of both treated groups, increase in the estrous phase of the aqueous extract-treated rats, and increase in the metestrus phase of the methanolic extract group was observed. Groups of 5 female albino rats were dosed with either 0.5 ml distilled water, or 75 mg/kg/d of aqueous or methanolic *Portulaca oleracea* leaf and stem extract for 25 d, to examine ovarian and uterine histopathology.[56] No significant pathological effects or changes in ovarian or uterine weights were observed. In another study, dams dosed with up to 500 mg/kg bw/d *Portulaca* oleracea leaf and stem extract showed a statistically significant 30 % abortion rate and 50% inhibition in implantation in the 250 mg/kg bw/d group, while animals in the 500 mg/kg bw/d group had a statistically significant 50% abortion rate and 70% inhibition in implantation, compared to controls.[55] In a teratology study of albino rats, animals were dosed with 0.5 ml distilled water or 75 mg/kg/d aqueous or methanolic *Portulaca oleracea* leaf and stem extract at three

different time frames during 21 d of gestation.[53] No significant differences related to pregnancy stage, fetal development, or delivery were observed.

GENOTOXICITY STUDIES

Genotoxicity data on *Portulaca oleracea*-derived ingredients were not found in the published literature, and unpublished data were not submitted.

ANTI- GENOTOXICITY STUDIES

Three aqueous extracts of *Portulaca oleracea* flowers, leaves, and stems were prepared using distilled water.[36] *Escherichia coli* DNA interjected with pBR322 plasmid, exposed to hydrogen peroxide in a DNA nicking assay, was incubated with 5 µl (80 µg/ml) of each extract for 10 min and measured for plasmid DNA damage. Aqueous extracts from each plant part showed a protective effect against DNA damage, through the inhibition of Fenton reaction free radicals; the highest effect was observed with the stem extract, and the lowest effect was observed in the flower extract.

CARCINOGENICITY STUDIES

Carcinogenicity data on *Portulaca oleracea*-derived ingredients were not found in the published literature, and unpublished data were not submitted.

ANTI-CARCINOGENICITY STUDIES

In Vitro

Portulaca Oleracea Extract

A 70% ethanolic crude extract of whole *Portulaca oleracea* (70%; 30% water) was tested at doses of 0.2, 0.4, 0.8, 1.6, 3.2, or 6.4 mg/ml on human peripheral lymphocytes for the effect on mitotic index (MI) and blast index (BI).[57] Increased MI and BI values were observed, but were not significantly different when compared with those in the positive control group (not specified).

The cytotoxic potential of the chloroform extract of whole *Portulaca oleracea* against human colon adenocarcinoma (HCT-15) and normal (Vero) cell lines was examined in a (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay, with doxorubicin as a reference.[12] The 50% cell growth inhibition dose (IC_{50}) for the chloroform extract was 1132.02 µg/ml in HCT-15 cells and 767.60 µg/ml in Vero cells, while the IC_{50} for doxorubicin was 460.13 µg/ml in HCT-15 cells and 2392.71 µg/ml in Vero cells. The chloroform extract was not considered cytotoxic to HCT-15 cells, but was considered possibly toxic to Vero cells. Cell viability was recorded to be 67%, 31%, 21%, and 17% in human hepatocellular carcinoma cells (HepG2) exposed to 50, 100, 250, and 500 µg/ml *Portulaca oleracea* seed extracts, respectively.[58]

Portulaca Oleracea Flower/Leaf/Stem Extract

The antiproliferative potential of aqueous and methanolic extracts of *Portulaca oleracea* leaves was examined in murine mammary adenocarcinoma (AMN3) cells, human Rhabdomyosarcoma (RD) cells, and normal kidney epithelium cells of the African green monkey, at concentrations up to 10,000 µg/ml, over 72 h.[59] Both extracts exhibited time-dependent antiproliferative effects against both cancer cell lines, with more sensitivity in the AMN3 cells. The normal cells showed resistance towards all concentrations of both extracts, except the 10,000 µg/ml dose. Similarly, significantly reduced cell viability was seen in HeLa cervical cancer cells exposed to 0, 300, 500, 700, 1000, 1200, or 1500 µg/ml of *Portulaca oleracea* stems and leaf extracts for up to 48 h.[60]

OTHER RELEVANT STUDIES

Anti-Inflammatory Studies

Portulaca oleracea extracts were shown to significantly reduce lipopolysaccharide (LPS)-induced synthesis of nitric oxide, the production of tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and the expression levels of various transcription factors, in murine macrophage cells.[61] Luteolin, kaempferol, and quercitrin components identified in the extracts were postulated to account for these anti-inflammatory effects.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

Portulaca Oleracea Extract

A single-insult occlusive patch test (SIOPT) was performed with a body lotion containing 0.1% Portulaca Oleracea Extract.[62] The test material was applied, undiluted, for 24 h to 22 subjects. Twenty-two subjects were patched with a reference control lotion. No significant differences were observed in the irritation response of subjects exposed to the test material and the reference control, and the primary irritation index (PII) was 0.0 for both materials.

Sensitization

Portulaca Oleracea Extract

The skin sensitization potential of a body moisturizer containing 0.1% Portulaca Oleracea Extract was evaluated in a maximization study completed in 26 subjects; the test article was tested as supplied.[63] Prior to each induction, irritation was induced with a dermal application of 0.05 ml 0.25% aqueous sodium lauryl sulfate (SLS), under an occlusive patch, for 24 h. After patch removal, a 48-h (72 h over the weekend) occlusive application of 0.05 ml of the body moisturizer was applied to the pre-treated sites. A total of 5 induction applications were made. After a 10-d non-treatment period, irritation was again induced on a virgin site using a 1-h occlusive application of 0.05 ml 5.0% aqueous SLS, for 1 hr. Following patch removal, 0.05 ml, an occlusive application of the body moisturizer was applied for 48 h. The challenge site was graded 15 - 30 min and 24 h after patch removal. Scores for all 26 subjects who completed the study were 0 at both readings (on a 0 - 3 scoring scale). The test substance was considered non-sensitizing.

OCULAR IRRITATION STUDIES

Data on the ocular irritation potential of *Portulaca oleracea*- derived ingredients reviewed in this safety assessment were neither found in the published literature, nor were they submitted.

CLINICAL STUDIES

Clinical Use

A 3-wk use study of a formulation containing 0.1% Portulaca Oleracea Extract was performed in 46 subjects.[64] Dermatologist-assessed facial exams were conducted at the test center during the initial and final visit. Thirty-three (72%) of subjects were assessed as having sensitive skin, based on test center results for various skin conditions, as well as self-reported sensitivity to sun, allergies, and eczema at the end of the 3-wk use period. Subjects were instructed to apply the test product over their entire face (including the eye area, but avoiding contact with the eyes), at least twice a day. Subjects were also allowed to apply their own moisturizer following use of the test material, if desired. No product-related irritation was observed. Changes in scaling/flaking and conditions of acne, including papules and pustules which occurred, were determined to be within expected fluctuation in the general population. No irritation was observed.

SUMMARY

The safety of the following 4 *Portulaca oleracea*-derived ingredients, as used in cosmetics, is reviewed in this safety assessment: Portulaca Oleracea Extract, Portulaca Oleracea Flower/Leaf/Stem Extract, Portulaca Oleracea Juice, and Portulaca Oleracea Water. These ingredients are all reported to function as skin-conditioning agents in cosmetics.

Portulaca Oleracea Extract is the only ingredient included in this report that is reported to be used in cosmetic formulations. According to 2020 VCRP survey data, Portulaca Oleracea Extract is reported to be used in 579 formulations, of which 189 uses are in face and neck products and 133 are in moisturizing products. The results of the concentration of use survey conducted by the Council indicate Portulaca Oleracea Extract is used at a maximum concentration of 0.008% (in moisturizing products).

Portulaca oleracea is consumed raw in salads, or is used as a potherb in cooked sauces, soups, and pickled dishes across many cultures. It is a medicinal plant widely used in traditional and folk medicine, to which the WHO ascribes antibacterial, anti-inflammatory, and antihelminth properties. Fresh leaf poultices are used to treat mastitis, boils, and impetigo.

The oral LD_{50} of an ethanolic extract of whole *Portulaca oleracea* was determined to be ≤ 500 mg/kg bw in Swiss albino mice, while the oral LD_{50} of a petroleum ether *Portulaca oleracea* leaf extract was determined to be > 2000 mg/kg bw in Sprague-Dawley rats. Maximum oral doses of 5000 mg/kg methanolic and chloroform *Portulaca oleracea* leaf extracts were well tolerated in rats.

No mortality occurred, and a significant increase in hypoglycemic activity was observed, in groups of 6 Swiss albino mice dosed at up to 400 mg/kg bw/d of a whole ethanolic *Portulaca oleracea* extract for 14 d. Albino rats dosed at up to 75 mg/kg bw/d of aqueous or methanolic extract of whole ethanolic *Portulaca oleracea* extract for 30 d showed a significant decrease in white blood cell and neutrophil count in the 25 and 50 mg/kg bw/d aqueous extract groups, as well as a significant increase in mean corpuscular volume and mean corpuscular hemoglobin in the 25 and 75 mg/kg bw/d methanolic extract groups. No mortality occurred and a significant, dose-dependent increase in hematological parameters and cholesterol levels was observed in all Sprague-Dawley rats orally dosed with 500, 1000, or 2000 mg/kg bw/d petroleum ether extract of *Portulaca oleracea* leaves for 14 d. Groups of 16 male albino Wistar rats were administered 125, 250, or 500 mg/kg bw/d of methanolic or chloroform extract of *Portulaca oleracea* leaves, for 60 d; a significant decrease in the mean hematocrit on day 28 and a significant increase in white blood cell count on day 42 was observed in the 500 mg/kg group. Platelet count was increased in all treatment groups, and was significantly higher in the 125 and 500 mg/kg treated rats on day 60. Blood samples of male albino Wistar rats dosed with 1.5 ml/kg/d *Portulaca oleracea* juice extract for 12 d exhibited significant variability in enzyme and hematological parameters such as urea, creatine, glutathione, and bilirubin.

No pregnancies resulted from mating between male albino rats treated with 75 mg/kg bw aqueous or methanolic *Portulaca oleracea* leaf extract for 50 d, and untreated female rats. Groups of 5 male albino rats orally dosed with 0, 25, 50, or 75 mg/kg/d aqueous or methanolic *Portulaca oleracea* leaf and stem extracts for 50 d exhibited significantly decreased testosterone levels at the maximum aqueous extract dose, and in all methanolic extract dose groups. Animals in all dose groups had significantly reduced sperm motility, sperm count, and increased sperm abnormalities. In two separate studies of groups of 5 - 6 female Wistar albino rats, ovary and uterine weights were significantly higher in mature rats, and significantly lower in immature bilaterally ovariectomized rats dosed with 0, 250, or 500 mg/kg bw/d *Portulaca oleracea* stem and leaf extract. In a 21-d study of female albino rats dosed with either 75 mg/kg/d aqueous or methanolic *Portulaca oleracea* leaf and stem extracts, no significant changes in duration of estrous cycle phases were observed, however, upon withdrawal of both treatments in a 21-d follow-up period, a significant decrease in the proestrus phase was observed in both treated groups, as well as a significant increase in the estrous phase of the aqueous-treated rats, and increase in the metestrus phase of the methanolic extract group. No significant pathological effects or changes in ovarian and uterine weights were observed in rats dosed with 75 mg/kg/d of aqueous or methanolic *Portulaca oleracea* leaf and stem extract for 25 d. In another study, dams dosed with up to 500 mg/kg bw/d of multiple *Portulaca oleracea* extracts had a statistically significant 30% abortion rate and 50% inhibition in implantation in the 250 mg/kg bw/d group, while animals in the 500 mg/kg bw/d group had a statistically significant 50% abortion rate and 70% inhibition in implantation, compared to controls. No significant differences in pregnancy stage, fetal development, or delivery were observed in albino rats dosed with 75 mg/kg/d aqueous or methanolic *Portulaca oleracea* leaf and stem extract during 3 different timeframes during 21 d of gestation.

An aqueous extract (80 µg/ml) of *Portulaca oleracea* stems had the most protective effect against *E. coli* plasmid DNA damage in a DNA nicking assay, compared to leaf and flower extracts.

A 70% ethanolic crude extract of whole *Portulaca oleracea*, tested at doses of up to 6.4 mg/ml on human peripheral lymphocytes, produced a non-significant increase in MI and BI values compared to the positive control group. In an MTT assay, the chloroform extract of whole *Portulaca oleracea* exhibited an IC_{50} of 1132.02 µg/ml in HCT-15 cells and 767.60 µg/ml in Vero cells, compared to 460.13 µg/ml and 2392.71 µg/ml, for doxorubicin, respectively. The chloroform extract was not considered cytotoxic to HCT-15 cells, but was considered possibly toxic to Vero cells. Cell viability was recorded to be 67%, 31%, 21%, and 17% in HepG2 cells exposed to increasing doses of up to 500 µg/ml *Portulaca oleracea* seed extracts. The antiproliferative potential of aqueous and methanolic extracts of *Portulaca oleracea* leaves was examined in AMN3 cells, RD cells, and normal kidney epithelium cells of the African green monkey, at concentrations up to 10,000 µg/ml, over 72 h. Both extracts exhibited time-dependent antiproliferative effects against both cancer cell lines, with more sensitivity in the AMN3 cells. Similarly, significantly reduced cell viability was seen in HeLa cervical cancer cells exposed to up to 1500 µg/ml *Portulaca oleracea* stems and leaf extracts for up to 48 h.

Portulaca oleracea extracts were shown to significantly reduce LPS-induced synthesis of nitric oxide, the production of TNF-α, IL-6, and the expression levels of various transcription factors, in murine macrophage cells.

No dermal irritation responses were seen in an SIOPT of a body lotion containing 0.1% Portulaca Oleracea Extract, in 22 subjects. The skin sensitization potential of a body moisturizer containing 0.1% Portulaca Oleracea Extract was tested in a maximization study involving 26 subjects. The test substance was deemed non-sensitizing.

In a 3-wk use study, 46 subjects were instructed to apply a formulation containing 0.1% Portulaca Oleracea Extract at least two times a day to the entire face. Dermatological changes in skin texture and acne were determined to be within expected ranges; no irritation was observed.

DISCUSSION

To be developed.

CONCLUSION

To be determined.

TABLES

Table 1: Definitions and functions of *Portulaca oleracea*-derived ingredients in this safety assesment[1]

Ingredient/CAS No.	Definition & Chemical Class	Function
Portulaca Oleracea Extract 90083-07-1	Portulaca Oleracea Extract is the extract of the whole plant, *Portulaca oleracea.*	Skin- Conditioning Agent - Humectant
Portulaca Oleracea Flower/Leaf/Stem Extract	Portulaca Oleracea Flower/Leaf/Stem Extract is the extract of the flowers, leaves and stems of *Portulaca oleracea.*	Antioxidants; Skin-Conditioning Agent – Misc.
Portulaca Oleracea Juice	Portulaca Oleracea Juice is the liquid expressed from the whole plant, *Portulaca oleracea.*	Skin-Conditioning Agent – Misc.
Portulaca Oleracea Water	Portulaca Oleracea Water is the steam distillate obtained from the whole plant, *Portulaca oleracea.*	Skin-Conditioning Agent – Misc.

Table 2. Constituents found in *Portulaca oleracea*, by plant part*[29]

Classification	Whole plant	Flower, Leaf, and Stem**	Leaf and Stem***	Leaf	Stem
Flavonoids	genistein genistin luteolin myricetin quercetin	portulacanones a portulacanones b portulacanones c portulacanones d 2,2'-dihydroxy-4',6'-dimethoxychalcone	apigenin kaempferol		
Alkaloids	adenosine oleraceins A oleraceins B oleraceins C oleraceins D oleraceins E	aurantiamide aurantiamide acetate cyclo(L-tyrosinyl-L-tyrosinyl *N-trans*-feruloyltyramine (7*R*)-*N*-feruloylnormetanephrine *N-cis*-feruloyltryramine *N-trans*-feruloyloctopamine *N-cis*-feruloyloctopamine Thymine trollisine uracil 1,5- dimethyl-6-phenyl-1,2-dihydro-1,2,4-triazin-3(2H)-one 1,5-dimethyl-6-phenyl-1,6,3,4-tetrahydro-1,2,4-2(1H)-triazin (3*R*)-3,5-bis(3-methoxy-4-hydroxyphenyl)-2,3-dihydro-2(1H)-pyridinone	dopamine noradrenalin		oleraceins I oleraceins II
Terpenoids		friedelane lupeol portuloside A portuloside B portulene (2α, 3α)-3-((4-*O*-(β-D-glucopyranosyl)-β-D-xylopyranosyl)oxy)-2,23-dihyroxy-30-methoxy-30-oxoolean-12-en-28-oic acid (2α, 3α)-2,23,30-trihydroxy-3-((β-D-xylopyranosyl)oxy)olean-12-en-28-oic acid (3*S*)-3-*O*-(β-D-glucopyranosyl)-3,7-dimethylocta-1,6-dien-3-ol (3*S*)-3-*O*-(β-D-glucopyranosyl)-3,7-dimethylocta-1,5-dien-3,7-diol			
Organic Acids	*p*-Coumaric acid Ferulic acid	caffeic acid indole-3-carboxylic acid 3-quinolinecarboxylic acid		α- linoleic acid linoleic acid oleic acid oxalic acid palmitic acid stearic acid	docosapentaenoic acid
Vitamins				α-tocopherol folates hesperidin niacin pantothenic acid pyridoxine riboflavin thiamin vitamin A vitamin C	
Minerals			calcium copper iron phosphorus manganese	magnesium selenium zinc	

Table 2. Constituents found in *Portulaca oleracea*, by plant part*[29]

Classification	Whole plant	Flower, Leaf, and Stem**	Leaf and Stem***	Leaf	Stem
Other compounds		β-sitosterol daucosterol portulacerebroside A		β-carotene chlorophyll glutathione melatonin proline tannin 1,4-di-*O*-acetyl-2,3,5-tri-*O*- methyl-L-arabinitol 1,4,5-tri-*O*-acetyl-2,3-di-*O*- methyl-L-arabinitol 1,5-di-*O*-acetyl-2,3,4,6-tetra-*O*-methyl-D-galactitol 1,4,5-tri-*O*-acetyl-2,3,6-tri-*O*-methyl-D-galactitol 1,3,4,5-tetra-*O*-acetyl-2,6-di-*O*-methyl-D-galactitol	

*the solvent used for extraction determines total constituent content
**defined as aerial part(s) in primary reference
***sometimes includes root or seed

Table 3. Frequency (2020)[37] and concentration of use (2019)[38] data for Portulaca Oleracea Extract

	# of Uses[37]	Max Conc of Use (%)[38]
Totals*	579	0.001-0.008
Duration of Use		
Leave-On	493	0.001 – 0.008
Rinse-Off	85	0.002
Diluted for (Bath) Use	1	NR
Exposure Type		
Eye Area	33	NR
Incidental Ingestion	NR	NR
Incidental Inhalation-Spray	160[a];199[b]	NR
Incidental Inhalation-Powder	2; 199[b]; 8[c]	0.002[c]
Dermal Contact	568	0.001 – 0.008
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	10	NR
Hair-Coloring	NR	NR
Nail	NR	NR
Mucous Membrane	10	NR
Baby Products	15	NR

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

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

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

NR – not reported

Table 4. Acute toxicity studies

Ingredient/ Extraction Method	Animals	No./Group	Vehicle/Control	Concentration/Dose/Protocol	LD_{50}/Results	Reference
ORAL						
Portulaca oleracea extract (water:ethanol; 1:1)	Swiss albino mice (sex not specified)	2/group	2 % gum acacia	0, 500, 1000, 1500, or 2000 mg/kg bw, via gavage; Performed in accordance with OECD TG 423. The animals were observed 72 h for behavioral changes and mortality.	$LD_{50} \leq 500$ mg/kg bw. After 48 h, half of the animals in the 500 mg/kg group, and all the animals in the 1000, 1500, and 2000 mg/kg bw groups showed sedation, respiratory arrest, convulsions, decreased motor activity, and mortality.	46,47
Portulaca oleracea leaf extract, Petroleum ether	Sprague-Dawley Rats (sex not specified)	6/group	10 ml/kg saline	0, 500, 1000, or 2000 mg/kg bw; The rats were observed up to 24 h for general changes in behavior, physiological function, and mortality.	LD > 2000 mg/kg bw. No mortality occurred, and no signs of toxicity were observed in the control and 500 mg /kg bw dose groups. The animals in the 1000 and 2000 mg /kg bw dose groups exhibited heightened asthenia, defecation, salivation, and urination compared to the control group.	48
Portulaca oleracea leaf extract, Chloroform/Methanolic extract	Rats (sex not specified)	strain and # not specified	80% aqueous methanol	NR	Well tolerated at the maximum dose of 5000 mg/kg. Not toxic.	49,50

NR- not reported

Table 5. Short-Term Toxicity Studies

Ingredient Extraction method	Animals/Group	Study Duration	Vehicle/Control	Dose/Concentration	Results	Reference
			ORAL			
Portulaca oleracea extract (water: ethanol; 1:1)	Swiss albino mice; 6/group	14 d	2% gum acacia	0, 200, or 400 mg/kg bw/d, via gavage	No mortality occurred during observation. Biochemical evaluations were performed on day 15. A statistically significant increase in hypoglycemic activity was observed in both treated groups, and to a greater extent in the 400 mg/kg bw group. The hepatotoxic potential of *Portulaca oleracea* extract was assessed by fixing and examining liver tissue. Histopathology results in treated mice showed no abnormalities and were comparable to control mice.	[46,47]
Portulaca oleracea extract Aqueous extract or 70% Methanolic extract	Albino rats; 5/group/sex	30 d	0.5 ml distilled water	25, 50, or 75 mg/kg bw; aqueous and methanolic extracts	Red blood cell production was not affected by oral administration of aqueous and methanolic extracts. Rats treated with 25 and 50 mg/kg bw of an aqueous extract for 15 d showed a statistically significant decrease in white blood cell and neutrophil counts, and significant increase in lymphocyte counts, relative to controls. Rats dosed with 25 mg/kg bw of a methanolic extract showed a significant increase in mean corpuscular volume and mean corpuscular hemoglobin relative to their respective controls. Thirty-day treatment with 25 mg/kg bw aqueous extract and 75 mg/kg bw methanolic extract produced a significant decrease in total plasma protein and albumin levels.	[51]
Portulaca oleracea leaf extract Petroleum ether extract	Sprague-Dawley rats; 6/group	14 d	10 ml/kg normal saline	500, 1000, or 2000 mg/kg/d	Rats dosed with 2000 mg/kg *Portulaca* oleracea leaf extract exhibited decreased motor activity. Body weights were increased in the treatment groups, but the increase was not statistically significant. No mortality occurred during observation. Animals were sacrificed on the 15th day, during which blood samples were collected for hematological assay, and liver, kidney, spleen, and stomach tissue were fixed and stained for examination. A significant, dose-dependent increase in hematological parameters was observed, and cholesterol levels were slightly increased, in all treated rats. Although renal weights had increased, and epithelial inflammation, oxalate stones, and hemorrhagic spots were observed in the 1000 and 2000 mg/kg groups, statistically relevant weight difference in the organ weights were not observed, compared to controls.	[48]
Portulaca oleracea leaf extract Chloroform/methanolic extract	Male albino Wistar rats; 16/group	60 d	0.5 ml/kg bw, 20% Tween 80	0, 125, 250, or 500 mg/kg bw/d, via gavage	Blood samples were collected on day 14, 28, 42, and 60 of treatment. The 500 mg/kg group showed a significant decrease in the mean hematocrit level on day 28, which was considered incidental, while a significant increase in white blood cell count was observed on day 42. Platelet count was increased in all treatment groups, and was significantly higher in the 125 and 500 mg/kg treated rats on day 60. No significant differences were observed in leukocyte (white blood cell) or erythrocyte (red blood cell) counts.	[49,50]
Portulaca oleracea juice Aqueous extract, 1.5 w/v	Male albino Wistar rats; 6/group	12 d	Distilled water	0.2 ml saline water (control) or 1.5 ml/kg/d extract/d, via gavage	Blood samples were obtained, prior to animal sacrifice, and analyzed to assess the effect of the extract upon liver and kidney function. Samples from rats treated with *Portulaca oleracea* juice showed a statistically significant increase in uric acid (28%), decrease in urea and creatine (33.2 and 28%), reduction in malondialdehyde of liver and kidney (30.9 and 8.7%), and an increase in glutathione, glutathione reductase, glutathione peroxidase, and glutathione-S-transferase in the liver, kidney, and testes (up to 94.1%). A significant reduction in AST, γ-GT, ALP, and bilirubin was observed (-7.4, -10.1, -31, and -13.3%), while the change in ALT was not significant.	[52]

Abbreviations: γ- GT- γ-glutamyl transpeptidase; AST – aspartate aminotransferase; ALP- alkaline phosphatase; ALT- alanine aminotransferase

Table 6. Reproductive and Developmental Toxicity Studies

Test Article/ Extraction Solvent	Animals/Group	Vehicle	Dose/Concentration	Type of Study/Procedure	Results	Reference
ORAL						
Portulaca oleracea leaf and stem extract AEPO and MEPO	albino rats; 4/group, with 1 male: 3 females	distilled water	0, 75 mg/kg bw AEPO or MEPO	Fertility study in male albino rats (mating experiment). Three male albino rats were orally administered either 100 ml distilled water, 75 mg/kg bw AEPO, or 75 mg/kg bw MEPO for 50 d. Three untreated, fertile female rats were cohabitated with each of the treated male rats for 4 wk. Vaginal lavages were obtained from these females daily to identify the presence of sperm.	No pregnancy (or sterile mating) occurred between males from either extract group and the untreated female rats. Cohabitation of the control male rat with the untreated female rats resulted in pregnancy.	[53]
Portulaca oleracea leaf and stem extract AEPO and MEPO	Male albino rats; 5/group	100 ml distilled water	0, 25, 50, 75 mg/kg AEPO or MEPO	Reproductive parameters in male albino rats. Animals were orally dosed for 50 d. Body weight was monitored on a weekly basis. One day after the last dose (day 51), blood samples were collected to measure testosterone levels using ELISA and animals were sacrificed to collect semen and prepare testes for histological analysis.	Exposure to either *Portulaca oleracea* extract did not produce any significant changes in body weight, relative to controls. A statistically significant decrease in testosterone levels was observed in rats in the 75 mg/kg AEPO group, and in all MEPO groups. Testosterone decline may explain the concurrently observed acellular seminiferous tubules and Leydig cell hyperplasia in all-treated animals, which was most pronounced in the highest dosage group (75mg/kg). All animals dosed with the extracts had significantly reduced sperm motility, sperm count, and increased % of sperm abnormalities. These differences were mostly dose-dependent. A non-significant reduction in % of viable sperm was observed.	[54]
Portulaca oleracea leaf and stem extract "Total flavonoid extract"*	Female Wistar albino rats; 6/group	1% Tween 80	0, 250, or 500 mg/kg bw/d, via gavage	Estrogenic/anti-estrogenic activity. Bilaterally ovariectomized, immature female rats received "total flavonoid extract" of *Portulaca oleracea* leaves and stems for 7 d. On day 8, all animals were sacrificed, uteri were fixed in Bouin's fluid and dissected. Biochemical analysis of the adrenal glands and uteri of treated rats was also performed.	Administration of the "total flavonoids extract" at both doses caused a significant decrease in the uterine weight of the immature rats, and produced estrous cycles characterized by significantly longer diestrus phases. Protein and cholesterol (a precursor for steroidal hormone) content of the uterus was also significantly reduced in both doses, by 50% and 30%, respectively. Significant uterine changes included larger diameter and endometrial thickness.	[55]
Portulaca oleracea leaf and stem extract Multiple*	Female Wistar albino rats; 5/group	1% Tween 80	0, 250, or 500 mg/kg bw/d, via gavage	Flavonoid (estrogenic) effect on reproductive organ and body weight. All three groups were dosed for 10 d. On day 11, all animals were weighed and sacrificed. The ovaries and uteri were freed from surrounding tissue, weighed, and dissected.	The ovary and uterine weights were significantly higher in both extract-treated groups. The increase in the wet weight of the ovary was postulated to indicate inhibition of ovulation through suppression of follicular stimulating hormone.	[55]

Table 6. Reproductive and Developmental Toxicity Studies

Test Article/ Extraction Solvent	Animals/Group	Vehicle	Dose/Concentration	Type of Study/Procedure	Results	Reference
Portulaca oleracea leaf and stem extract AEPO and MEPO	Female albino rats; 5/group	100 ml distilled water	75 mg/kg/d AEPO or MEPO	Estrous cycle effects. Vaginal smears were microscopically examined daily for 21 d to classify rats into estrous cycle phase and determine cycle length. Vaginal smears were evaluated both during 21 d of dosing and for 21 d after cessation of dosing with the extracts; the experimental animals served as their own controls.	Rats were examined for changes in the estrous cycle, both during the 21 d of dosing with either extract, and for 21 d after termination of dosing. No significant changes in duration of estrous cycle phases were observed during dosing, relative to pre-treatment. However, during the 21-d withdrawal of treatment with both extracts, a statistically significant decrease occurred in the proestrus phase. A significant increase in the estrous phase was seen when the AEPO group ceased treatment, and a significant increase in the metestrus phase was seen when the MEPO group ceased treatment, relative to the pre-treatment period.	[56]
Portulaca oleracea leaf and stem extract AEPO and MEPO	Female albino rats; 5/group	100 ml distilled water	0.5 ml distilled water, 75 mg/kg/d of AEPO or MEPO	Ovarian and uterine histology. Rats showing at least 3 regular 4 - 5-d estrous cycles received either the control, AEPO, or MEPO extract for 25 d. On day 26, all rats were sacrificed and ovaries and uteri were weighed, fixed with Bouin's fluid, and dissected.	Changes in ovarian and uterine weights were not considered significant. No significant pathologic effects on the ovaries or uterus were observed. Both AEPO and MEPO were considered non-toxic to female rat reproductive function.	[56]
Portulaca oleracea leaf and stem extract Multiple*	Female Wistar albino rats; 6/group	1% Tween 80	0, 250, or 500 mg/kg bw/d, via gavage	Abortifacient activity. Same mating strategy and female selection as above study. These rats received *Portulaca oleracea* extract, via gavage, from day 7 to day 14 of pregnancy. On day 15, all animals were sacrificed and uterine horns were examined for aborted embryos.	Dams in the 250 mg/kg bw/d group had a 30% abortion rate, while animals in the 500 mg/kg bw/d group had a statistically significant 50% abortion rate.	[55]
Portulaca oleracea leaf and stem extract Multiple*	Female Wistar albino rats; 6/group	1% Tween 80	0, 250, or 500 mg/kg bw/d, via gavage	Implantation study. Female rats of estrus phase were kept with male rats of proven fertility in a ratio of 2:1. Rats found with thick clumps of spermatozoa in vaginal smears were separated from the male partner and divided into groups of 6. These rats were dosed, via gavage, from day 1 to day 7 of gestation. On day 10, all animals were sacrificed and uterine horns were examined for number of implants.	A 50% inhibition in implantation was seen at the 250 mg/kg dose, while a statistically significant, 70% inhibition in implantation was seen in the 500 mg/kg dose group (3.22 ± 0.02 vs. 8.12 ± 0.44, in controls). The anti-implantation of the extract was observed after 24 h of the last administered dose.	[55]
Portulaca oleracea leaf and stem extract AEPO and MEPO	Female albino rats; 5/group	100 ml distilled water	0.5 distilled water, or 75 mg/kg/d AEPO or MEPO	Adult female rats exhibiting 4 - 5-d estrous cycles, found in the estrous phase, were caged, with virile males, in a 2:1 ratio. Pregnant rats were exposed to control or AEPO/MEPO from: - day 1 to day 5 (implantation/early pregnancy study); - day 6 to day 15 (mid-pregnancy/organogenesis study); or - day 16 to day 21 (late pregnancy study)	A non-significant increase in implantations occurred in rats treated from day 1 to day 5 of gestation with AEPO and MEPO. Treatment of rats from day 6 to 15 with AEPO and MEPO caused a decrease in fetal size for the pups of AEPO-treated dams, and an increase in fetal size for the pups of MEPO-treated dams, relative to controls. Changes in fetal size were not statistically significant. No premature births or abortions occurred, and pups were delivered normally. Treatment of rats from day 16 to 20 caused no significant increase in delivery litter size, and litter weights relative to controls. No resorption or gross malformations were observed in treated and control rats in mid or late pregnancy.	[53]

Abbreviations: AEPO- aqueous extract *Portulaca* oleracea; ELISA- enzyme-linked immunosorbent assay; MEPO – methanolic extract *Portulaca oleracea*; NMRI- nuclear magnetic resonance imaging
*Methanol, ethanol, ethyl acetate, petroleum ether, diethyl ether, sulfuric acid, chloroform, HCL, potassium hydroxide, hexane, silica Gel 60-120 mesh, Tween 80 phosphate buffer saline, Folin- Ciocalteu reagent, are named as used chemicals, but are not specified as extract solvents.

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2020 VCRP Frequency of Use Data – *Portulaca oleracea*- Derived Ingredients

INGREDIENT_NAME Total Uses: 579	CATEGORY CODE	CATEGORY_DESCRIPTION	CPIS COUNT
Portulaca oleracea (purslane) extract	01A	Baby Shampoos	3
Portulaca oleracea (purslane) extract	01B	Baby Lotions, Oils, Powders, and Creams	8
Portulaca oleracea (purslane) extract	01C	Other Baby Products	4
Portulaca oleracea (purslane) extract	02D	Other Bath Preparations	1
Portulaca oleracea (purslane) extract	03B	Eyeliner	1
Portulaca oleracea (purslane) extract	03D	Eye Lotion	20
Portulaca oleracea (purslane) extract	03E	Eye Makeup Remover	3
Portulaca oleracea (purslane) extract	03G	Other Eye Makeup Preparations	9
Portulaca oleracea (purslane) extract	05A	Hair Conditioner	1
Portulaca oleracea (purslane) extract	05F	Shampoos (non-coloring)	6
Portulaca oleracea (purslane) extract	07B	Face Powders	2
Portulaca oleracea (purslane) extract	07C	Foundations	13
Portulaca oleracea (purslane) extract	07F	Makeup Bases	2
Portulaca oleracea (purslane) extract	07I	Other Makeup Preparations	3
Portulaca oleracea (purslane) extract	10A	Bath Soaps and Detergents	3
Portulaca oleracea (purslane) extract	10C	Douches	1
Portulaca oleracea (purslane) extract	10E	Other Personal Cleanliness Products	5
Portulaca oleracea (purslane) extract	11A	Aftershave Lotion	1
Portulaca oleracea (purslane) extract	11G	Other Shaving Preparation Products	1
Portulaca oleracea (purslane) extract	12A	Cleansing	34
Portulaca oleracea (purslane) extract	12C	Face and Neck (exc shave)	189
Portulaca oleracea (purslane) extract	12D	Body and Hand (exc shave)	10
Portulaca oleracea (purslane) extract	12F	Moisturizing	133
Portulaca oleracea (purslane) extract	12G	Night	9
Portulaca oleracea (purslane) extract	12H	Paste Masks (mud packs)	28
Portulaca oleracea (purslane) extract	12I	Skin Fresheners	16
Portulaca oleracea (purslane) extract	12J	Other Skin Care Preps	71
Portulaca oleracea (purslane) extract	13A	Suntan Gels, Creams, and Liquids	2

Concentration of Use by FDA Product Category – *Portulaca oleracea*-Derived Ingredients*

Portulaca Oleracea Extract
Portulaca Oleracea Flower/Leaf/Stem Extract
Portulaca Oleracea Juice
Portulaca Oleracea Water

Ingredient	Product Category	Maximum Concentration of Use
Portulaca Oleracea Extract	Face and neck products Not spray	0.002%
Portulaca Oleracea Extract	Foot products Not spray or powder	0.001%
Portulaca Oleracea Extract	Moisturizing products Not spray	0.008%
Portulaca Oleracea Extract	Paste masks and mud packs	0.002%
Portulaca Oleracea Extract	Other skin care preparations	0.001%

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

Information collected in 2018
Table prepared: January 31, 2019

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 29, 2020

SUBJECT: Portulaca Oleracea Extract

Anonymous. 2020. Certificate of origin and method of manufacture water/butylene glycol extract of *Portulaca oleracea*.

Anonymous. 2020. Certificate of ingredient source and method of manufacture water extract of *Portulaca oleracea*.

July 2020

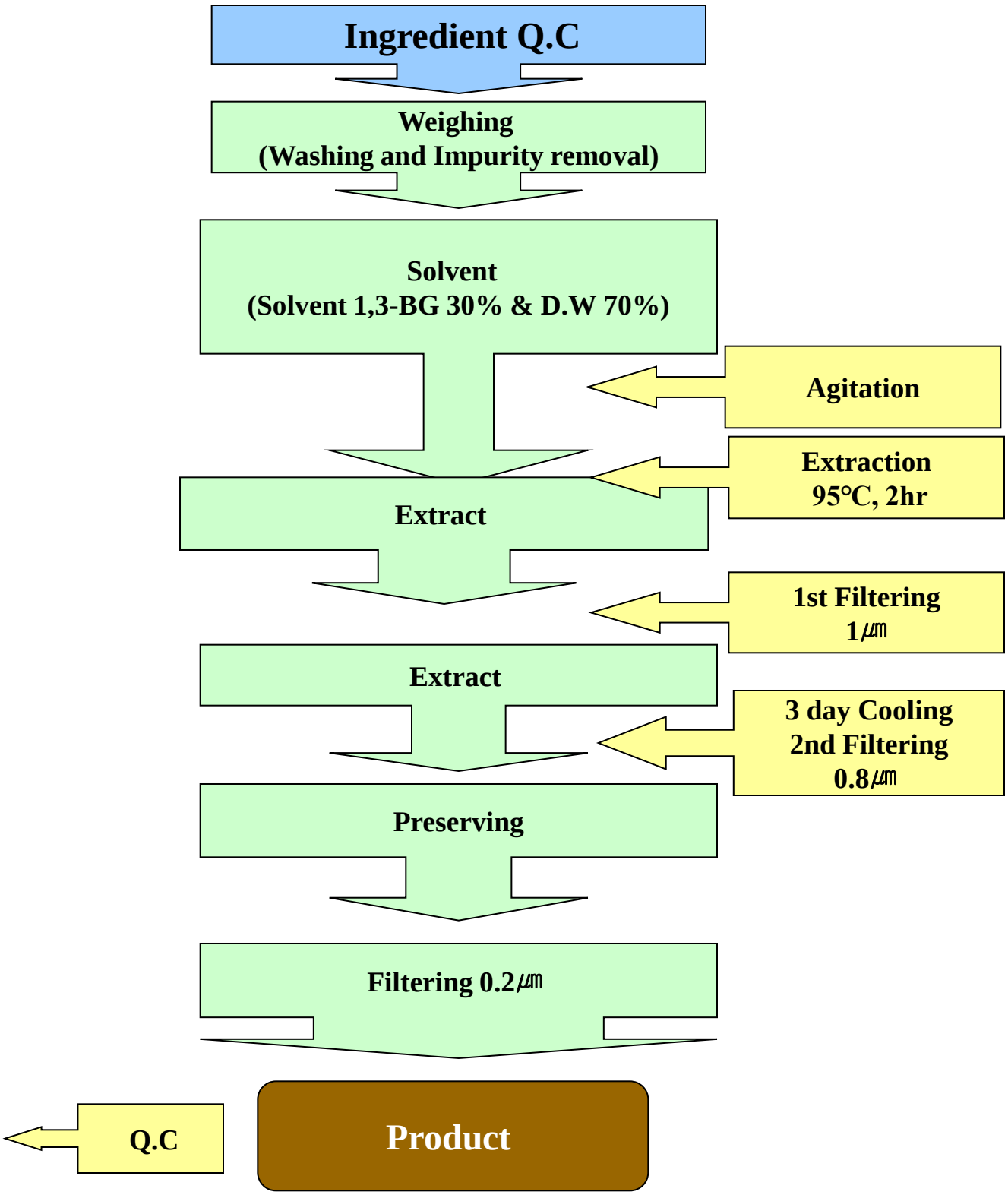
Certificate of Origin

Product Name: [redacted] **Extract**

Product Name	INCI Name	Origin	Part of used
[redacted] **Extract**	Water	Natural	-
	Butylene Glycol	Synthesis	-
	Portulaca Oleracea Extract	Plant	Whole
	Phenoxyethanol	Synthesis	-
	Ethylhexylglycerin	Synthesis	-

Portulaca oleracea Extract

Portulaca Oleracea is the aquens solution of extracted in Water and Butylene Glycol.



Certificate of ingredient source

Product Name : W Portulaca Oleracea Extract

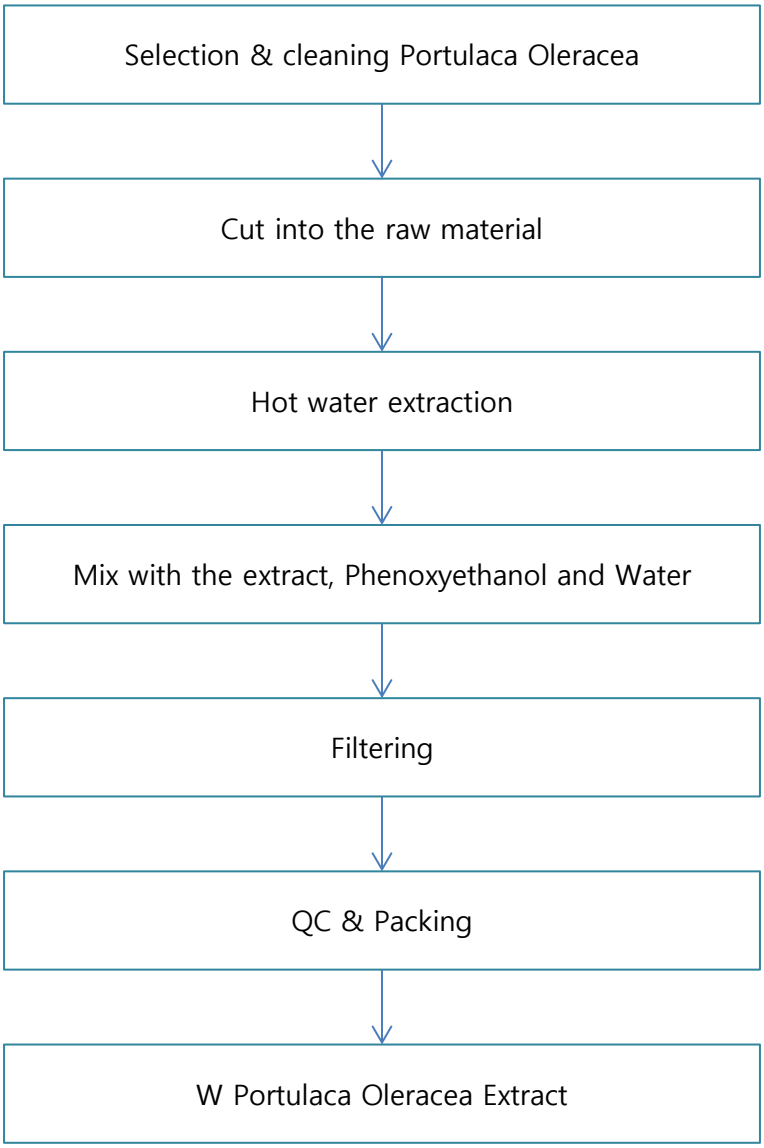
We, [redacted] d hereby confirm that the source and used part of each ingredient which is originated from plants in the above mentioned product is as follows;

No	INCI Name	Source	Used plant part
1	Portulaca Oleracea Extract	Plant(*Portulaca Oleracea*)	Leaf, Stem
2	Phenoxyethanol	Synthetic	-
3	Water	Natural	-

We confirm that the above information is all true and correct.

2020. 07. 28

Manufacturing Process
W Portulaca Oleracea Extract



Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: August 12, 2020

SUBJECT: Portulaca Oleracea Extract

Anonymous. 2006. Human patch test (product containing 0.1% Portulaca Oleracea Extract).

Anonymous. 2017. Summary: Clinical use test of a product containing 0.1% Portulaca Oleracea Extract.

KGL, Inc. 2007. An evaluation of the contact sensitization potential of a topical coded product in human skin by means of the maximization assay (product contains 0.1% Portulaca Oleracea Extract).

Study Ref. No.: C06-1166
Patch Date: December 12, 2006

HUMAN PATCH TEST

1. TEST MATERIAL: Body Lotion [redacted] contains 0.1% Portulaca Oleracea Extract
   CPTC NO.: C06-1166.07
2. CONTROL MATERIAL: Body Lotion [redacted]
   CPTC NO.: C06-1166.08
3. TEST PROCEDURE:

   Single-Insults (24 hr.) X Occlusive Patch X Semi-Occlusive Patch _____

4. CONCENTRATION:

   Full-Strength X Aqueous _____ Solution _____ Dispersion _____ Aqueous Paste _____
   Other: _____

   Volatiles were allowed to evaporate on the patch for thirty minutes. _____ Patch was hydrated just prior to application to skin _____

5. TEST RESULTS:

TEST MATERIAL	*SUBJECTS*	*IRRITATION SCORE**									
		0	±	1	1+	2	2+	3	3+	4	P.I.I.
Body Lotion [redacted]	22	22	0	0	0	0	0	0	0	0	0.00
Body Lotion [redacted]	22	22	0	0	0	0	0	0	0	0	0.00

6. CONCLUSIONS:

   A There were no significant differences in irritancy observed between the Test Material (s) and the Reference Control (s). X
   B _____

Consulting Dermatologist

* SCORE
0 = No evidence of any effect.
+ = (Barely Perceptible) = minimal faint uniform or spotty erythema
1 (Mild) = Pink uniform erythema covering most of the contact site.
2 (Moderate) = Pink-red erythema visibly uniform in entire contact area.
3 (Marked) = Bright red erythema with accompanying edema petechiae or papules.
4 (Severe) = Deep red erythema with vesiculation or weeping with or without edema.

+, 1+, 2+ and 3+ = Intermediate scores contributing 0.5, 1.5, 2.5 and 3.5 respectively, to the P.I.I.
P.I.I. - Primary Irritation Index - a value depicting the average skin response of the test panel as a whole. It is calculated by adding the Peak Irritation Score and dividing by the total number of test subjects.

STUDY REF.# TC298417

SUMMARY

product contains 0.1% Portulaca Oleracea Extract

[redacted]Solar SPF70 [redacted] was tested via a three-week Dermatologist-supervised Clinical Use study. The study was a single-blind, baseline controlled monadic design with Dr. [redacted], a Board-Certified Dermatologist, as the principal investigator. The Dermatologist conducted the evaluations at the initial and final study visits. Thirty-three (72%) of the subjects who completed the study had assessed sensitive skin. Subjects were instructed to use the product over the entire face, including the eye area, twice a day, morning and evening, for three weeks. Subjects were allowed to use their own regular facial moisturizer following use of the Sunscreen, if desired.

The Dermatologist did not observe any **visible clinical irritation** that was specifically related to use of [redacted] Solar SPF70.

None of the subjects reported any subjective discomfort and/or irritation while using the Sunscreen.

[redacted] Solar SPF70 is considered to be acceptable for consumer use. Claims of "Suitable for sensitive skin" and "Gentle enough to use around the eye area" are supported by the results of this study.

Reported By:

Approved By:

Approved By:

[redacted]

STUDY REF. # TC298417

TO: [redacted] [redacted]-2984-17

FROM: [redacted]

DATE: December 1, 2017

SUBJECT: Clinical Use Test Results of [redacted] Solar SPF70 [redacted]

SUMMARY

[redacted] Solar SPF70 [redacted] was tested via a three-week Dermatologist-supervised Clinical Use study. The study was a single-blind, baseline controlled monadic design with Dr. [redacted] a Board-Certified Dermatologist, as the principal investigator. The Dermatologist conducted the evaluations at the initial and final study visits. Thirty-three (72%) of the subjects who completed the study had assessed sensitive skin. Subjects were instructed to use the product over the entire face, including the eye area, twice a day, morning and evening, for three weeks. Subjects were allowed to use their own regular facial moisturizer following use of the Sunscreen, if desired.

The Dermatologist did not observe any **visible clinical irritation** that was specifically related to use of [redacted] Solar SPF70.

None of the subjects reported any subjective discomfort and/or irritation while using the Sunscreen.

[redacted] Solar SPF70 is considered to be acceptable for consumer use. Claims of "Suitable for sensitive skin" and "Gentle enough to use around the eye area" are supported by the results of this study.

STUDY OBJECTIVES

* To determine the potential of [redacted] Solar SPF70 [redacted] to evoke clinical irritation and/or subject-perceived discomfort/irritation when used under consumer use conditions.

* To provide support for claims of "Suitable for sensitive skin" and "Gentle enough to use around the eye area" for [redacted] Solar SPF70.

TEST DESIGN

A total of forty-six (46) individuals completed this three-week, Dermatologist-supervised Clinical Use Test. Thirty-three (72%) of the subjects had Testing Center-assessed sensitive skin. Facial exams by the Dermatologist were conducted at the baseline and final visits. Test design and Criteria for Testing Center Assessed Skin Sensitivity are presented in Appendix I. Product identification and product use instructions are presented in Appendix II. Subject demographics are listed in the study file.

STUDY SITE

[redacted]

STUDY DATES

October 26, 2017 - November 16, 2017

RESULTS: DERMATOLOGIST-ASSESSED VISIBLE IRRITATION

The Dermatologist did not observe any product related irritation. A tabulation of clinical changes may be found in Appendix III.

The Dermatologist observed clinical changes in skin conditions such as scaling/flaking and conditions of acne, including papules and pustules. Visible observations in scaling/flaking were equally divided between positive and negative changes. The level of negative changes observed in conditions of acne was slightly higher than that of positive changes. However, all observed changes were determined to be within the parameters for normally and/or seasonally occurring fluctuations in skin conditions in the general population.

PERCEIVED IRRITATION

None of the subjects reported any subjective discomfort and/or irritation while using [redacted] Solar SPF70.

CONCLUSION

[redacted] Solar SPF70 [redacted] exhibited acceptable results. Claims of "Suitable for sensitive skin" and "Gentle enough to use around the eyes" are supported by the results of this study.

Prepared By:

Approved By:

[redacted]

APPENDIX I

TEST DESIGN

Forty-six (46) subjects completed a three-week, Dermatologist-supervised clinical use test. The panel was conducted as single-blind, baseline controlled monadic design evaluation.
The test product was supplied to all of the subjects for the 3-week evaluation period.
Test products were packaged in appropriate containers and labeled with product type, i.e. SPF70 SUNSCREEN FOR FACE. Products were supplied to subjects with use instructions. Dermatologist-assessed facial exams were conducted initially and upon completion of the study. Questionnaires seeking subject perceived problems were completed by the subjects at the end of the three-week use period.

CRITERIA FOR DETERMINING TESTING CENTER-ASSESSED SENSITIVITY

A SENSITIVES: Must have at least **3** characteristics from List #1
B SENSITIVES: Must have **2** characteristics from List #1 and at least **2** characteristics from List #2.
C SENSITIVES: Must have **2** characteristics from List #1 and at least **1** characteristic from List #2.

(NOTE: All data for parameters designated as self-assessed or self-acknowledged is obtained from questionnaires completed by panelists. Testing Center Assessed data was obtained via facial screening exams conducted by Testing Center personnel.)

LIST #1

Self-Assessed Very Sensitive / Sensitive Skin
Self-Assessed Sun Sensitivity - (i.e. Fitzpatrick Types I, II)
Allergies - (self-acknowledged - including but not limited to pollen, dust, drugs, foods – ranging from one to multiple)
Flusher/Blusher - (self-acknowledged)
Eczema History - (self-acknowledged)
Testing Center-Assessed Rosacea - (based upon evaluation screening by Testing Center personnel)
Testing Center-Assessed Seborrheic Dermatitis - (based upon evaluation screening by Testing Center personnel)

LIST #2

Self-Assessed Skin Type of Normal to Dry or Dry
Blonde/Red Hair Color - (self-acknowledged)
Non-Soap User - (self-acknowledged user of facial cleanser)
Testing Center-Assessed Telangiectasia - (based upon evaluation screening by Testing Center Personnel)
Testing Center-Assessed Very Fair/Fair Complexion - (based upon evaluation screening by Testing Center Personnel)
Testing Center-Assessed Freckling - (based upon evaluation screening by Testing Center Personnel)

APPENDIX II

INSTRUCTIONS [redacted]-2984-17
SPF70 SUNSCREEN FOR FACE

USE THIS PRODUCT AT LEAST TWICE A DAY !!
YOU MAY APPLY MORE OFTEN, IF DESIRED
USE IN PLACE OF YOUR REGULAR FACE AND BODY SUNSCREEN

TO USE:

1. Apply this product at least twice a day.
2. For continued sun protection, the product should be reapplied as needed or after towel drying, swimming or sweating.
3. Dispense product into palms of hands.
4. Dab small amounts of the product over the forehead, upper and lower cheeks and chin.
5. With fingertips, smooth over face using **gentle** upward and outward strokes. Use the product around the eyes, however you should AVOID CONTACT WITH EYES.

PLEASE NOTE:

- For external use only.
- Avoid contact with eyes. If contact occurs, rinse thoroughly with water.
- Keep out of reach of children.

PLEASE:

- DO NOT WEAR ANY PRODUCT ON THE FACE ON STUDY DATES.

REMEMBER:

1. Bring your remaining product with you on the exam date (Thursday, November 16th).
2. This product is for your use only. Do not let other members of your family use it
3. Should any problems arise while using the product, please call the [redacted] and ask for [redacted].

APPENDIX III

Total Tabulation of Clinical Changes
Dermatologist-Supervised
N=47*

	#	%
# of subjects that exhibited a change**	13	18
# of subjects that exhibited no change	33	72

Scaling/Flaking	Test
increased	1
decreased	1
Acne	
increased	5
decreased	7
Papules	
increased	4
decreased	6
Pustules	
increased	2
decreased	0
Macules	
increased	0
decreased	1
Seborrheic Dermatitis	
increased	1
decreased	0

* - One subject dropped from the study due to non-product related reasons.
** - Subjects may have exhibited more than one visible clinical change.

FINAL REPORT dated February 15, 2007
KGL Protocol: #6186
Sample: Body Moisturizer coded [redacted]

www.kgl-inc.com or www.ivylabs.com

505 Parkway
Broomall, PA 19008-4204 (USA)

Telephone: [215] 387-8400
FAX: [215] 387-1046

E-mail address: ivystudies@verizon.net

[redacted]

Title: An Evaluation of the Contact-Sensitization Potential of a Topical Coded Product in Human Skin by means of the Maximization Assay

Sponsor: [redacted] Product contains 0.1% Portulaca Oleracea Extract

Principal Investigator: Kays Kaidbey, M.D. (Board Certified Dermatologist)

Testing Facility: Ivy Laboratories (KGL, INC.)
505 Parkway
Broomall, PA 19008-4204 (USA)
(Phone: 215-387-8400)

Protocol: KGL Protocol #**6186** – Authorization letter dated January 4, 2007

Final Report Date: **February 15, 2007**

Kays Kaidbey, M.D.
Principal Investigator

February 15, 2007
Date

F I N A L R E P O R T

KGL PROTOCOL:

Ivy Laboratories - KGL Protocol #**6186**

SPONSOR:

[redacted]

[redacted]

SPONSOR STUDY:

Authorization Letter Dated: January 4, 2007

STUDY TITLE:

Evaluation of the contact-sensitizing potential of a coded topically-applied test agent.

STUDY OBJECTIVE:

The objective of this study is to assess the skin sensitizing potential of any preparation designed for topical use by means of the Maximization Test (see references #1 and #2).

TEST MATERIAL:

The test sample, supplied by the sponsor, was a product labeled Body Moisturizer and coded [redacted] The coded product was tested as supplied viz. neat.

TEST PRODUCT ACCOUNTABILITY:

All test samples and materials were received in good condition by our Quality Assurance Department. The test materials and quantities were checked for (1) amount (2) product number or code (3) material container etc. The materials were individually listed on a special sheet (drug/test product log form) signed by the receiver, the laboratory supervisor and the investigator (physician). All test materials were stored under ambient conditions in an inaccessible location under the supervision of the investigator.

PRINCIPAL INVESTIGATOR:

Kays Kaidbey, M.D. (Board Certified Dermatologist)

Medical Director, KGL, INC.

Telephone: (215) 387-8400 - FAX: (215) 387-1046

KGL ADMINISTRATIVE STRUCTURE:

Jane Chitwood (Screening, Patch Applications/Removals, Recognize AE's)

John B. Chicchi (Expert Grader)

Bernadette Lonergan (Panel Recruitment/Receptionist)

Mary Jean Massing (Quality Assurance)

TESTING FACILITY:

Ivy Laboratories (KGL, INC.)

505 Parkway

Broomall, PA 19008-4204

CONDUCTION DATES:

This study was conducted from January 8, 2007 through February 9, 2007

PANEL COMPOSITION:

Healthy, adult volunteers over the age of 18 years were recruited for this study. None of the subjects had a medical or dermatological illness and none were sensitive to sunlight or to topical preparations and/or cosmetics. The criteria for exclusion were:

1 - History of sun hypersensitivity and photosensitive dermatoses

2 - History of drug hypersensitivity or recurrent dermatological diseases

3 - Pregnancy or mothers who are breastfeeding

4 – History of recurrent urticaria or hives

5 - Scars, moles or other blemishes over the test site which can interfere with the study

6 - Subjects receiving systemic or topical drugs or medications, including potential sensitizers within the previous 4 weeks

7 - Other medical conditions considered by the investigator as sound reasons for disqualification from enrollment into the study.

INFORMED CONSENT:

After the protocol, reasons for the study, possible associated risks and potential benefits or risks of the treatment had been completely explained, signed, informed subject consent was obtained from each volunteer prior to the start of the study. Copies of all consent forms are on file at Ivy Laboratories (KGL, INC.).

METHOD:

Patches were applied to the upper outer arm, volar forearm or the back of each subject. The entire test was composed of two distinct phases: (1) an Induction phase and (2) a Challenge phase.

(1) **Induction Phase**:

Approximately 0.05ml of aqueous SLS (0.25%) was applied to a designated site under a 15mm disc of Webril cotton cloth and the patch was fastened to the skin with occlusive tape for a period of 24 hours. After 24 hours, the SLS patch was removed and 0.05ml of the test material coded [redacted] (Body Moisturizer) was applied to the same site before the site was again covered with occlusive tape (induction patch). The induction patch was left in place for 48 hours (or for 72 hours when placed over a weekend) following which it was removed and the site again examined for irritation. If no irritation was present, a 0.25% aqueous SLS patch was again reapplied to the same site for 24 hours, followed by reapplication of a fresh induction patch with the test material to the same site. This sequence viz. 24 hour SLS pre-treatment followed by 48 hours of test material application was continued for a total of 5 induction exposures.

If irritation developed at any time-point during the induction phase as previously outlined, the 24-hour SLS pre-treatment patch was eliminated and only the test material was reapplied to the same site after a 24-hour rest period during which no patch was applied.

The aim during this phase of the study was to maintain at least a minimal degree of irritation in order to enhance penetration through the corneum barrier.

(2) **Challenge Phase**:

After a ten day rest period which follows the last induction patch application, the subjects were challenged with a single application of the test material to a new skin site on the opposite arm, forearm or side of back in order to determine if sensitization had developed.

Pre-treatment with SLS was performed prior to challenge. Approximately 0.05ml of a 5.0% aqueous solution was applied to a fresh skin site under a 15mm disc of Webril cotton and covered with occlusive tape. The SLS patch was left in place for one hour. It was then removed and the test material was applied to the same site, as outlined above. The challenge patch was then covered by occlusive tape and left in place for 48 hours. After that period, the patch was removed and the site graded 15-30 minutes later and again 24 hours later for any reaction.

SCORING SCALE:

0 = not sensitized

1 = mild sensitization (viz. erythema and a little edema)

2 = moderate sensitization (erythema with infiltration, raised, spreading beyond the borders of the patch, with or without vesiculation)

3 = strong sensitization (large vesiculo-bullous reaction).

Based on these findings the number of subjects with positive responses were tabulated for the test material. The test system shown below was used to classify the allergenic potential of the test substance.

SENSITIZATION RATES:	**GRADES:**	**CLASSIFICATION:**
0 - 2/25	1	Weak
3 - 7/25	2	Mild
8 - 13/25	3	Moderate
14 - 20/25	4	Strong
21 - 25/25	5	Extreme

RESULTS:

A total of twenty-eight (28) healthy, adult volunteers of both sexes who satisfied the inclusion criteria were enrolled into this study. There were 23 females and 5 males. Their ages ranged from 24 to 64 years. Subject #16 failed to maintain the scheduled study visits and was dropped from the study. Subject #20 could not complete the challenge phase for personal reasons and voluntarily withdrew from the study. The remaining 26 subjects completed this investigation as outlined in the standard protocol. The demographic data are shown in Table 1. No adverse or unexpected reactions were seen in any of the panelists during the induction phase.

The results of the challenge are shown in the enclosed table (Table 2). No instances of contact allergy were recorded at either 48 or 72 hours after the application of the challenge patches.

CONCLUSION:

Under the conditions of this test, the test sample labeled Body Moisturizer and coded [redacted] does not possess a detectable contact-sensitizing potential and hence is not likely to cause contact sensitivity reactions under normal use conditions.

References:

(1) Kligman, A.M.: The Maximization Test. J.I.D., Vol. 47, No. 5, pp. 393-409, 1966.

(2) Kligman, A.M. and Epstein W.: Updating the Maximization Test for Identifying Contact Allergens. Contact Dermatitis. Vol. 1, 231-239, 1975.

TABLE 1

DEMOGRAPHIC DATA

Subject Number:	Subject Initials:	Age:	Sex:	Race:
01	M-F	44	F	C
02	P-M	44	F	B
03	G-R	46	F	C
04	NJU	49	F	C
05	R-B	46	F	B
06	S-B	50	F	C
07	F-C	42	F	C
08	T-U	50	M	C
09	T-C	38	F	B
10	K-R	39	F	C
11	B-M	60	M	C
12	R-M	56	F	C
13	N-H	50	F	B
14	LMC	61	M	C
15	S-M	64	F	C
16	J-C	28	F	C
17	G-P	52	F	B
18	CLG	45	F	C
19	T-B	48	M	C
20	MPP	54	F	C
21	J-S	31	F	C
22	E-H	24	F	C
23	N-S	31	F	C
24	LAS	36	F	C
25	A-C	26	F	C
26	D-C	31	M	C
27	S-M	38	F	C
28	M-N	25	F	C

C = Caucasian
B = Black

TABLE 2

MAXIMIZATION TESTING RESULTS

Sample: Body Moisturizer coded [redacted]

Subject Number:	48-Hour Grading	72-Hour Grading
01	0	0
02	0	0
03	0	0
04	0	0
05	0	0
06	0	0
07	0	0
08	0	0
09	0	0
10	0	0
11	0	0
12	0	0
13	0	0
14	0	0
15	0	0
16	Dropped from the study	
17	0	0
18	0	0
19	0	0
20	Voluntarily withdrew from the study	
21	0	0
22	0	0
23	0	0
24	0	0
25	0	0
26	0	0
27	0	0
28	0	0

Challenge Readings:

48-Hour Reading – February 8, 2007
72-Hour Reading – February 9, 2007

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 23, 2020

SUBJECT: Scientific Literature Review: Safety Assessment of *Portulaca oleracea*-Derived Ingredients as Used in Cosmetics (release date: July 15, 2020)

The Personal Care Products Council has no suppliers listed for Portulaca Oleracea Flower/Leaf/Stem Extract.

The Personal Care Products Council respectfully submits the following comments on the scientific literature review, Safety Assessment of *Portulaca oleracea*-Derived Ingredients as Used in Cosmetics.

Composition and Impurities - It is not clear why information on oxalate is found in the first paragraph of this section as well as the fourth paragraph of this section. It would be helpful if all the information on oxalate was presented in the same paragraph.

Please revise the following sentence as it is the composition of the ingredients rather than the "natural content" of the plant that varies depending on the extraction solvent. "Additionally, the determination of individual constituents and natural content in *Portulaca oleracea* varies considerably depending on extraction solvent and method, part of the plant and growth stage or time of harvest."

Cosmetic Use - Please state the specific FDA product category in which the highest concentration of Portulaca Oleracea Extract was reported.

Non-Cosmetic Use - Please provide some indication of the doses of *Portulaca oleracea* used in folk medicine.

The information about the potential of *Portulaca oleracea* to be poisonous does not appear appropriate for the use section. Perhaps it belongs in the composition section or in the general information about the plant. Reference 42 appears to be about incidents in Brazil. Are there other reports of nitrite/nitrate poisoning from *Portulaca oleracea* from

other countries? Why did the FDA Poisonous Plant Database consider *Portulaca oleracea* to be poisonous? The ASPCA database (https://www.aspca.org/pet-care/animal-poison-control/toxic-and-non-toxic-plants/purslane) indicates that *Portulaca oleracea* is poisonous to dogs, cats and horses because of the oxalate content.

Acute; Short-term - It should be made clear that the studies in Swiss mice (references 43 and 44) were completed with a 50% ethanolic extract (as indicated in Tables 4 and 5). The 50% water also present will affect the composition of the extract.

DART - In the male rat exposure study (reference 50), did the investigators observe mating behavior?

DART; Table 6The following sentence (also in the Summary) is not clear. "Embryos of 250 mg/kg bw/d rats had a statistically significant 30% abortion rate and 50% inhibition in implantation...." As the dams were treated, the rates should be the percentage of dams that were affected. The structure of the sentence suggested that it is a percentage of the embryos. The last phrase of the sentence: "while animals in the 500 mg/kg bw/day group had a statistically significant 50% absorption rate and 70% inhibition in implantation, compared to controls" appears to refer to the dams.

DART; Table 6 - The text and Table 6 indicate that the route of exposure was not stated for the studies described in reference 53. For the histopathological study, this reference states: "The different groups received the following doses of the extracts and vehicle (control) orally per day for 25 days as follows..." The studies from this reference should be considered oral exposure studies.

Anti-Carcinogenicity, In Vitro; Summary - The meaning of "A 70% whole *Portulacca oleracea* ethanolic extract...." is not clear. The reference (54) says: "70% ethanolic crude extract" - meaning that the extract was made with 70% ethanol (30% water).

Table 4 - In the last study in rats the No./Group column says "Species not specified" - the study was in rats, perhaps the strain of rats was not specified.

Table 5 - If there was no post-treatment observation period in the 60 day study in rats, in the results column, it would be clearer to state that blood samples were collected on "day 14, 28, 42, and 60 of treatment" (rather than observation).

Table 6 - Were the changes in fetal size observed in reference 50 increases or decreases?

Reference 54 - The journal name still needs to be added to this reference.