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

Status:	Draft Tentative Report for Panel Review
Release Date:	November 10, 2021
Panel Meeting Date:	December 6-7, 2021

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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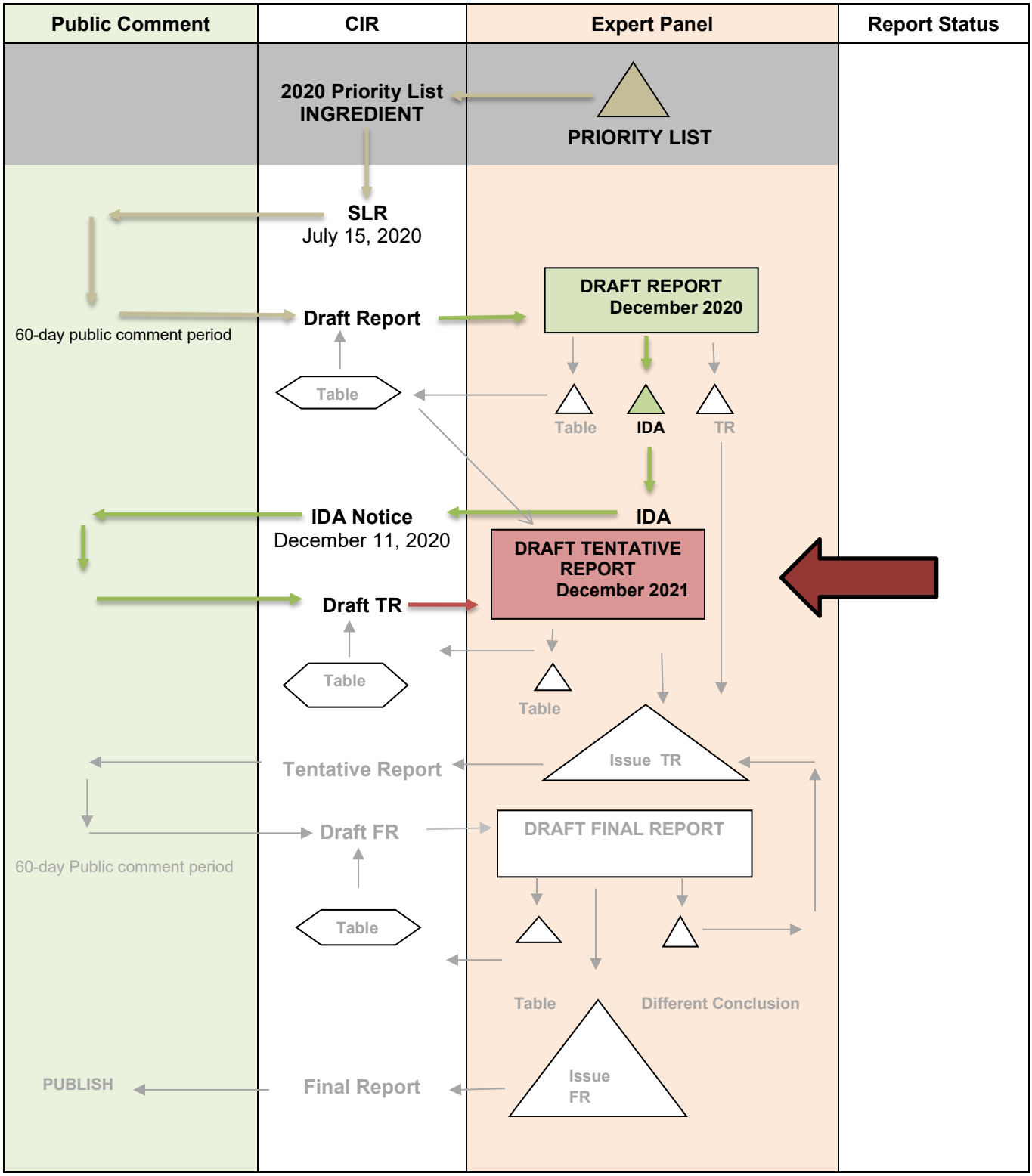
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY *Portulaca oleracea*-derived ingredients

MEETING December 2021



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 10, 2021

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

Enclosed is the Draft Tentative Report of the Safety Assessment of *Portulaca oleracea*-Derived Ingredients as Used in Cosmetics (identified as *report_PortulucaOleracea_122021* in the pdf). This is the second time the Panel is seeing a safety assessment of these 4 cosmetic ingredients. At the December 2020 meeting, a draft report was presented to the Panel. Upon review, the Panel issued an Insufficient Data Announcement for clarification on the current maximum concentrations of use for these ingredients, as well as a 28-d dermal toxicity study at the maximum concentration of use and an Ames test, both preferably with the ingredient in an hydroalcoholic solvent.

As a reminder, shortly after Panel documents were mailed for the December meeting, a memo clarifying that a method of manufacture description for Portulaca Oleracea Extract was using the whole plant was received. The original memo and clarification have been included for Panel review (*data1_PortulacaOleracea_122021*; *data2_PortulacaOleracea_122021*). Revisions to concentration of use data and updated VCRP data were received from Council and the FDA, respectively, in 2021, and have been incorporated (*data3_PortulacaOleracea_122021; VCRP_PortulacaOleracea_122021*). The maximum concentration of use for Portulaca Oleracea Extract was verified as 0.5% in non-spray face and neck products. Newly added data are highlighted in yellow in the report.

The following data were also received and have been incorporated in the report:

data4_PortulacaOleracea_122021

- Anonymous. (2004) Contact-sensitizing potential of a topical coded product in human skin in a maximization assay (facial lotion containing 0.5% Portulaca Oleracea Extract).
- Anonymous. (2007) Summary: Contact-sensitizing potential of a topical coded product in human skin in a maximization assay (face treatment product containing 0.5% Portulaca Oleracea Extract)

Included in this package, for your review, are a flow chart (*flow_PortulacaOleracea_122021*), literature search strategy (*search_PortulacaOleracea_122021*), ingredient data profile (*dataprofile_PortulacaOleracea_122021*), ingredient history (*history_PortulacaOleracea_122021*), and transcripts from the previous meeting (*transcripts_PortulacaOleracea_122021*).

The Panel should carefully consider and discuss the data (or lack thereof), and the draft Abstract and draft Discussion presented in this report. A Tentative Report with a safe as used, safe with qualifications, insufficient, or unsafe conclusion should then be issued.

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 (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
- November 16, 2020: Correction for previously received method of manufacture of a phenoxyethanol and water extract of Portulaca Oleracea Extract (made with the whole plant)

December 2020

-A Draft Report was presented to the Panel. The Panel issued an IDA with the following data needs:

- Clarification on the current maximum concentration of use
- A 28-d dermal toxicity study at the maximum concentration of use (preferably with the ingredient in an hydroalcoholic solvent)
    - o If these data are positive, further systemic toxicity data may be needed
- An Ames test (preferably with the ingredient in an hydroalcoholic solvent)

January 2021

- New VCRP data were received

Data received (Portulaca Oleracea Extract):

- January 4, 2021: Two maximization studies in a facial lotion and face treatment product, both containing 0.5% Portulaca Oleracea Extract
- January 4, 2021: Revisions/clarifications to concentration of use data for *Portulaca oleracea*-derived ingredients

December 2021

A Draft Tentative Report is being presented for Panel review.

***Portulaca oleracea*-derived Ingredients Data Profile* – December 6-7th, 2021 – 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 2021 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

Updated search on 10/20/2021:
(((((((portulaca oleracea extract) OR (90083-07-1)) OR (portuluca oleracea flower extract)) OR (portulaca oleracea leaf extract)) OR (portulaca oleracea stem extract)) OR (portulaca oleracea juice)) OR (portulaca oleracea water)) OR (portulaca extract) – 373/3

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)

DECEMBER 2020 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT

Belsito Team – December 7, 2020

DR. BELSITO: Okay. Okey-doke. So, we're moving on to *Portulaca oleracea*. This is the first time that we're seeing this, four ingredients. And I guess a prior data submission it was just pointed out that the extract was said to be derived from the leaf and stem only, but that now we've been told the extract is from the whole plant.

Let me save this last one. Okay. Yes. Okay. So comments. For developmental and reproductive toxicity, I had a note that there were lots of effects and no NOAEL. How do we handle that? The doses were high. Use concentration is 0.08 percent, but still we have these effects. Paul, what did you think of that?

DR. SNYDER: I'm sorry, Don. I was printing a paper that Preethi just sent me. Can you repeat that, please?

DR. BELSITO: So if you look at PDF page 14 on the DART studies, there were lots of different, little effects for which we don't have an NOAEL. And the highest concentration of use is 0.008 percent, but we still don't have an NOAEL for DART. I just was wondering what you thought, or maybe you thought these effects were not --?

DR. SNYDER: I did not ping them to be honest. And I'll have another look here, but I did not ping them at all.

DR. KLAASSEN: My thoughts were that there definitely are effects, but those were mainly at pretty high doses at 250 and 500 milligrams per kilogram. And I noted that there were no effects at 75 milligram per kilogram, and this compound is used at 0.008 percent. So I considered this not to be a problem.

DR. BELSITO: Well, but Curt, if you look, it says a statistically significant decrease in testosterone levels were observed in rats in the aqueous 75 milligram per kilogram dose, and in all methanolic extracts. That's the one, two, three, four, five, fifth and sixth line down in the first paragraph.

DR. KLAASSEN: Okay. I'm going to see if I can find that.

DR. BELSITO: It's PDF page 14. It's the first paragraph under where it says refer to table six, the fifth and sixth line down.

MS. RAJ: Yeah. I'm looking at these papers, and I don't think they provided that information, the NOEL or the NOAEL.

DR. BELSITO: Yeah. I mean, what they do say is that 75 -- 50 would appear to be a NOAEL on this study for aqueous. But in the methanolic, 25 percent also had that effect. So it looks like it's vehicle dependent.

DR. LIEBLER: If you read through the rest of that whole paragraph, there are other endpoints that compare aqueous and methanolic extracts and show no effects. So it's not as if there is a systematic problem with the methanolic extract versus an aqueous extract.

DR. BELSITO: Right. I agree except for this specific endpoint.

DR. LIEBLER: Yeah. Yeah.

DR. BELSITO: The other issue that I have about the 0.008 percent, as we look at it, is if it's used at 0.008 percent, why did we get a sensitization and irritation study with its use at 0.1? This is PDF page 15.

DR. EISENMANN: It could have been a study on a -- I have to look at the date of the -- it could have been an older product. They go back in their files sometimes and give me studies that they have done previously on older products. I don't know if that's for sure, because I haven't checked on the data on that study.

DR. BELSITO: It's reference 62.

MS. FIUME: It's 2006.

DR. BELSITO: 2006?

MS. FIUME: Yes.

MS. RAJ: There also seems to be a 2017, right?

DR. BELSITO: It's reference 63 and 62. Sixty-two is irritation, sixty-three is sensitization.

MS. FIUME: Sixty-three is 2007. A clinical use test was done in 2017. It was 0.1 percent.

DR. BELSITO: Yeah. Anonymous. And yeah, it's odd to me that we're looking at data that would at least suggest that this could be used in leave-on products to 0.1 percent not 0.008 percent.

MS. RAJ: If anything, does receiving data at a higher concentration than what's reported, I guess, confirm more surety of safeness or safety?

DR. BELSITO: Well, yeah. Unless you had other endpoint concerns. In this case, looking at the doses that caused effects in the DART study that's still significantly higher than 0.1 percent, I agree. The major issue is I don't see that we have an NOAEL for the DART studies on this. So I'm just curious as to what other people think about that.

DR. LIEBLER: I mean it's the one endpoint. It's the testosterone levels in the methanolic extract groups. It says in all methanolic extract groups. Presumably, that does not include the vehicle control, but that would be worth taking a look at, because we got 0, 25, 50, and 75. For the aqueous, only the 75 had an effect, so we have an NOAEL for the aqueous. But for the methanolic, it's ambiguous. It looks like we don't.

DR. BELSITO: And are we comfortable with the composition and impurities that we have on this material? They're very vague.

DR. LIEBLER: So method of manufacture I thought was quite good.

DR. BELSITO: Yes.

DR. LIEBLER: And composition and impurities, let's see, I didn't flag anything.

DR. BELSITO: No. Nothing pops out, but it's not, you know, they're just sort of vague chemical categories.

DR. SNYDER: It appears, from the title of the references for the DART studies, that they were concerned about the flavonoids, in the fertility effects of the impurities in the botanical.

DR. LIEBLER: I think that the data profile for the organic components of these is not that different from what we get from a lot of other botanicals. (Audio skip) summarizes these. I think that this is adequate, so I don't have any concern. And the one interesting thing was the oxalate bubbles; and oxalate, of course, can be a toxicant, but only at high concentrations. I think we could deal with that in the discussion.

DR. KLAASSEN: Right.

DR. BELSITO: Okay. We don't have a absorption distribution metabolism. Do we need a 28-day dermal in light of the DART studies or not?

DR. LIEBLER: Some of the constituents of these are going to be absorbed because they're small organics.

DR. BELSITO: And we have no genotoxicity data.

DR. LIEBLER: Yeah. I'd like to see an Ames on this. There's no genotox, no carcinogenicity. A negative Ames would put this away for me. But we don't -- yeah.

DR. KLAASSEN: Yeah.

DR. BELSITO: Okay. So we need a 28-day dermal and a Ames test, or just an Ames test?

DR. LIEBLER: Yes.

DR. BELSITO: Okay. So we need the 28-day dermal and we need an Ames test. And in the discussion the --assuming we get those and they're clear -- the discussion will go along with the DART studies at very high doses. Hopefully, relevant --

DR. EISENMANN: You do recognize that this material, that this plant is eaten in many places of the world?

DR. BELSITO: But it's not GRAS.

DR. EISENMANN: No. But for other plant materials you have accepted use for systemic toxicity. And so far we haven't heard that a methanol extract is being used in cosmetics.

DR. BELSITO: Well, I think, Carol, this is the first time we're looking at it. If it doesn't (audio skip).

DR. EISENMANN: Correct. And I'm not arguing with you on toxicity. I'm only arguing the 28-day dermal.

DR. BELSITO: Again, I think it's the first time we're looking at it. It doesn't hurt to ask for it and see if we get it or get additional data. I mean I don't know. What do you guys think?

DR. LIEBLER: Well, the method of manufacture describes a hydroalcoholic extract. And we got this one flag for methanolic extracts and the effect on testosterone. So I think that the -- it's not as if the method of manufacture says only aqueous extracts are used, and therefore the alcoholic extract is not relevant. I don't think we can say that. So I'm still in the camp of requiring the 28-day dermal.

DR. BELSITO: Okay. So we're going to go insufficient for 28-day dermal at concentration of use and genotox data. And you're not asking for mammalian, Dan, you're just asking for Ames?

DR. LIEBLER: I think that's fine unless my colleagues disagree?

DR. KLAASSEN: I agree with you.

DR. SNYDER: I'm fine.

DR. LIEBLER: And, Don, you're okay with this sensitization?

DR. BELSITO: Yeah. The sensitization and irritation is fine. It just raised the sort of a flag for me that they were doing it at a concentration ten times higher than what we're told it was used at, which makes me think that there's a manufacturer out there who submitted data, who's using it at 0.1 percent, who didn't report to Carol the concentration of use. I think it's still fine at 0.1. I mean, I'm not concerned about that level of use.

I just, again, there were just -- I guess there were several -- the methicones are an example of several reports where it just seems that there may be information that we're not getting for various reasons. And that bothers me. But I think 0.1 percent would be fine. I don't have an issue with that.

DR. LIEBLER: Okay.

DR. BELSITO: Okay. So insufficient, 28-day dermal, and an Ames genotox assay. Okay?

MS. FIUME: Don, I was just --

DR. BELSITO: Yeah.

MS. FIUME: -- can I ask? So for the IDA, because the vehicle may or may not be a concern, would you like us to specify in the IDA that the solvent is needed with the data submission? Would that make a difference?

DR. BELSITO: Yeah. I think it should be hydroalcoholic.

MS. FIUME: Thank you.

MS. RAJ: Thank you.

Cohen Team – December 7, 2020

DR. COHEN: This is a draft report. Preethi has this. This is the first time we're reviewing it. The safety assessment is for four derived ingredients: the extract, the juice, the water, and the flower, leaf, and stem extract.

This is apparently used as a food well. It has a max use of 0.008 on leave-on products, and 0.002 in rinse-off products. Frequency of use is reported in 2020, for products of the face, neck, and moisturizers. We have method of manufacturing for the extract, which is the whole plant. (Audio skip) is to include the whole plant, and can we read across on that? So I'll open it up to the Panel.

MS. RAJ: I do --

DR. COHEN: Lisa, you want to start on the chemistry?

MS. RAJ: Sorry, I do want to bring up that you'll notice that the method of manufacture that was originally received, the second one, you'll see in the diagram they had called it a leaf and stem extract, but later, when we asked them to clarify, it was actually from the whole plant.

DR. COHEN: Ah, okay. That's very helpful.

MS. RAJ: Yeah.

DR. COHEN: So then we could use that data for the flower/leaf/stem. It's the whole plant.

MS. RAJ: Yeah.

DR. COHEN: The extract. So flower/leaf/stem -- so what's missing between the extract and the flower/leaf/stem extract? What am I missing?

MS. RAJ: Well, I guess, it needs -- the ingredient that we use needs to fit the dictionary definition, which would need to be either the whole plant or the other ingredient is the flower, leaf, and stem extract.

DR. COHEN: Okay.

DR. PETERSON: So you're saying we don't have the method of manufacturing for the flower/leaf/stem extract unless you extrapolate?

MS. RAJ: No. Yeah, I guess, what I was clarifying, Dr. Peterson, is what they had sent us first. Like, I think, it's in this binder on, let's see, PDF Page -- what is this -- PDF Page 34. You'll see that they put the used plant part as leaf and stem only.

And when we got back to Council and asked them to clarify, is it just the leaf and stem, or is the whole plant. They got back to us and said they used the whole plant. So we have that file which says now that the used plant part was the whole plant.

DR. COHEN: Okay. So, Lisa, what are your thoughts?

DR. PETERSON: Well, I thought that, you know, it's -- I guess, now then it will be insufficient for method of manufacturing of the leaf/stem/flower and then impurities on the juice and the water. But, for the extract, which is the reported use, I mean, we have everything for the chemistry part of it.

DR. COHEN: Tom, thoughts, comments?

DR. SLAGA : Yeah. Well, the whole plant has some data. It doesn't have irritation or sensitization like the extract, but what's the difference of the extract from the whole plant or the one up above? Are they the same?

MS. RAJ: I'm sorry if I confused you all. Yes, the extract is using the whole plant.

DR. SLAGA : The extract -- the first one, is that the whole plant too?

DR. PETERSON: Yeah.

MS. RAJ: Yes.

DR. SLAGA : Does the extract in the second one, when it says flower, leaf, and stem, that's the whole plant. So are the first two very -- are similar, right? We can use the data.

MS. RAJ: Yeah. The flower, leaf, and stem meaning everything above the ground. I guess the whole plant could possibly include roots.

DR. COHEN: The aerial.

MS. RAJ: Yeah.

DR. SLAGA : Yeah. But isn't that true? In the first one listed where it has the -- it just says extract. It doesn't give you flower and stem in that, but I interpret that it would be the whole plant too.

DR. BERGFELD: Hmm. Yeah, I mean --

DR. COHEN: Well, the second one is at least the aerial components, and the whole plant may include the fruit.

DR. SLAGA : Huh?

DR. COHEN: The whole plant may include the root.

DR. SLAGA : What's the difference between the first -- but it doesn't say the root.

DR. BERGFELD: Well, let's see.

DR. COHEN: Tom.

DR. BERGFELD: No roots.

DR. SLAGA : No root. They're the same then. So I -- you know, there is sufficient sensitivity and irritation data. Also, it's an anti-inflammatory or anti-irritant. It's anti-genotoxic, anti-cancer. So, even though we don't have certain others, the fact that it has anti activity-related genotoxicity, and carcinogenicity, and it's an anti-inflammatory, I think it's safe.

DR. COHEN: Ron?

DR. SHANK: I'm trying to find the genotox. I thought we needed genotox?

DR. SLAGA : There's no genotox. It's called anti-genotox. There's some data.

DR. SHANK: We don't have genotox data.

DR. PETERSON: There is no genotox.

DR. SHANK: We don't have genotox data.

DR. SLAGA : I know there isn't, just the anti-genotox. So, if it's anti-genotox, to me, it's not genotoxic. And it's anti-carcinogenic. So in a way, then, you don't need genotoxicity. Hello.

DR. COHEN: Yeah. No, I was just giving Ron some time to digest the comments.

DR. SHANK: Right. Okay. Yeah, if the extract and the flower and leaf/stem extract are the same, we have enough data there.

DR. SLAGA : Right.

DR. SHANK: The leave-on concentration is very, very low, 0.008 percent. So that takes care of the data needs.

DR. PETERSON: That's right.

DR. SLAGA : Right.

DR. COHEN: Yeah, this -- I don't have, again, the PDF, but on Table 2, it says, "constituents found by plant part," and for flower, leaf, and stem, it says, "defined as the aerial parts." And for leaf and stem, it says, "sometimes includes root or seed." So Preethi, do you have any concern with us assuming one and two are very similar to each other, and if there is, is it the root?

MS. RAJ: Yeah, Dr. Cohen. And actually this particular table you mentioned, I used a publication that kind of arranged it this way. And that was, I guess, the closest I could get it to match our purposes for this report.

But you're right. I mean, looking at the INCI dictionary definition, it does seem like the flower, leaf, and stem extract is referring to the aerial parts, whereas the whole extract would, you know, be the whole plant, possibly including roots. And I'm obviously not an expert in this, but, from what I understand, the roots could possibly have a very different constituent profile and possible -- I don't know -- effects.

DR. SLAGA : But we don't know though.

DR. COHEN: Yeah, so --

DR. PETERSON: Yeah.

DR. COHEN: -- we need impurities on the leaf, stem, the water. We still need more information on that.

MS. RAJ: Okay.

DR. COHEN: Is that right, Lisa?

DR. PETERSON: Um --

DR. SLAGA : We don't. We have impurities for (audio skip).

DR. SHANK: We have a lot of impurity.

DR. PETERSON: But I don't know what the impurities are.

DR. COHEN: Do we have enough?

DR. PETERSON: But, you know what? I think we have a lot of information about the composition, but I was having trouble identifying, in the text, what the impurities were. Because everything -- it's more composition than impurities. So I would say that it's actually -- there's no information about impurities, like, heavy metals or anything else.

The whole -- on PDF Pages 12 and 13, even though the subject line is composition and impurities, there's really no -- it's all discussion of composition. And there's no impurities, so I would say that they're all insufficient for impurities.

DR. BERGFELD: Lisa, we can put into the discussion --

DR. COHEN: What was that, Wilma?

DR. BERGFELD: Lisa, we can put into the discussion the boiler- -- we can put into the discussion the boilerplate of the acceptable impurities for heavy metals and control it that way.

DR. PETERSON: Okay.

DR. SHANK : Good.

DR. PETERSON: All right. I mean, I just think there's no information --

DR. BERGFELD: We need something other than that.

DR. PETERSON: Yeah. I mean, this --

DR. BERGFELD: Is that what you're concerned with mainly, the heavy metals?

DR. PETERSON: Well, you know, it's the heavy metals and the pesticides and --

DR. BERGFELD: Yeah, we can put that -- we have boilerplates for those.

DR. PETERSON: Okay.

DR. BERGFELD: Bart, are you on? Bart?

DR. PETERSON: But, I think, otherwise you have a pretty good description of the composition of the -- at least of the plant extracts and the plant leaf extract. There's not much information about the water and the juice. So I would say that the water and the juice are insufficient but, you know, they're not used.

DR. SHANK: You mean the water and juice? Wouldn't the water and juice be covered by the plant extract?

DR. SLAGA : Yeah, it's a food.

DR. BERGFELD: Mainly water. It's a succulent.

DR. SLAGA : Yeah.

DR. PETERSON: But I think you have lots and lots on the compositions, so the question is then what would the impurities be? And, you know, the impurities would be, you know, heavy metals and pesticides, which if you've got the boilerplate on that, it would suffice.

DR. COHEN: We have that covered.

DR. PETERSON: And that would be acceptable? Then I say it's fine.

DR. COHEN: As long as the plant -- as long as the composition -- the properties between the plant, the whole plant, and the flowers, leaf, and stem were similar to each other, and it sounds like we're agreeing on that, then we could read across on what we have here.

We have some irritation and sensitization data that looks pretty good. There's a comment about the spectral absorption at 200 to 400 nanometers. Do we need phototox on that?

DR. SHANK: It's used at a pretty low concentration.

DR. COHEN: It is. Would that sway your concerns then on that (audio skip) concentration?

DR. SHANK: No, I think -- yeah, it's used as an herbal -- a folk medicine with a topical application. So I don't think --

DR. COHEN: Okay. So?

DR. SHANK: I don't see a need to ask for the phototox.

MS. RAJ: And this is --

DR. SLAGA : I agree. I don't think it's needed either.

MS. RAJ: Sorry to interrupt. This is colloquially known as Purslane, even though it doesn't have GRAS, and it's consumed.

DR. COHEN: Okay.

DR. SHANK: Yeah, it's a food.

DR. SLAGA : It's a food, yeah.

DR. COHEN: So I don't want to be redundant, I just want to make sure we have the insufficient data. It is impurities. Do we need the impurities, or are we covering everything with the boilerplates?

DR. BERGFELD: Boilerplates.

DR. SLAGA : Boiler -- yeah.

DR. COHEN: Okay. So we need method of manufacturing for the leaf, stem, and flower?

DR. SLAGA : We have that, don't we?

DR. COHEN: Sorry. I'm just -- let's see.

DR. PETERSON: Well, technically we don't have that because it was retracted, right? But is there coverage somewhere else, like in that Reference 20- -- the reference used in Table 2?

MS. RAJ: Yeah, I don't know if it was --

DR. PETERSON: What reference --

MS. RAJ: Yeah, let me just check.

DR. PETERSON: Well, I mean, they did the analysis. Somebody must have reported how they got the different parts. It might be buried.

MS. RAJ: Are you referring to Reference 22, Dr Peterson?

DR. PETERSON: No, Reference 29 is the reference that's used for the Table 2.

MS. RAJ: Yes.

DR. HELDRETH: Yeah, that's a very general -- it's a review of phytochemistry and --

DR. PETERSON: Oh, it's a review (audio skip). But there's --

MS. RAJ: Yeah.

DR. HELDRETH: So it may not be relevant to cosmetic ingredient methods.

MS. RAJ: Yeah.

DR. COHEN: So we do need -- so the method of manufacturing we have is for the whole plant, correct?

MS. RAJ: Yes.

DR. SHANK: Correct.

DR. COHEN: Right. So we need the flower/leaf/stem. Let me just see here.

MS. FIUME: Hi. This is Monice. I'm coming in a little late to the discussion, so, in case this is already deemed as not sufficient, but on PDF Page 12, is that method of manufacture acceptable for the flower, leaf, and stem extract?

DR. COHEN: Yeah, I'm just looking at that right now. I think it is.

DR. PETERSON: Yeah, it's fine with me.

DR. COHEN: Do we have any insufficiencies after -- because we sort of created a list, and then we walked back many of the issues here. Are there any remaining insufficiencies right now?

DR. SLAGA : I don't have any.

DR. PETERSON: No. I don't have any.

DR. COHEN: Ron?

DR. SHANK: It looks okay.

DR. COHEN: Lisa?

DR. PETERSON: It looks okay.

DR. COHEN: All right. So we move on as safe as used?

DR. SLAGA : Yes.

DR. PETERSON: Uh-huh.

DR. BERGFELD: The only thing I see is that, in your discussion, you need to speak about the photoactivation, why it's not a problem.

DR. COHEN: Preethi, do you have enough from our discussion just now to do that?

MS. RAJ: Um, I'm just trying to see what would I be referencing in the report for the phototox concerns? Was there something in there that signaled phototox?

DR. COHEN: The absorption.

DR. BERGFELD: The (inaudible) of 200.

DR. COHEN: I thought it was absorption.

DR. BERGFELD: Two hundred.

DR. COHEN: A comment of it being absorbed between -- the phenolics being absorbed between 200 and 400 nanometers.

MS. RAJ: Okay. This is in the ADME section?

DR. COHEN: It's in Chemical Properties. It said, "In an UV spectral analysis of crude, and methanol-soluble fractions of whole Portulaca oleracea extract, optical spectra maxima were recorded between 200 and 400 nanometers, in which phenolic compounds showed maximum absorbance."

MS. RAJ: Okay.

DR. COHEN: Am I overreading into that?

DR. PETERSON: I think you might be.

MS. RAJ: Yeah.

DR. COHEN: Okay.

MS. RAJ: I remember taking that from a paper, but I'm not sure if it was -- yeah. I'll leave it to you all to decide on whether it (overtalking) --

DR. PETERSON: So the way I --

DR. COHEN: No, we're not going to ask for phototox.

DR. PETERSON: The way I read that part was that they used the UV --

DR. COHEN: Just one second. So, Lisa, do you think that was a method of analysis for the product using that --

DR. PETERSON: So it's a method of chemical characterization because the wavelength of absorbance would tell you something about the chemical structures. I mean, I thought it was sort of not useful because it's going to be this complicated mixture. So, you know, I think what they came away with it is that there were some alcohols and some carbonyls and blah, blah, blah.

DR. COHEN: Got it.

DR. PETERSON: I mean, I'm not a photo toxicity expert person, but to me that reference was more for a chemical characterization attempts.

DR. COHEN: Understood.

DR. PETERSON: But two crudes, they really amount to anything?

DR. COHEN: I completely get it. It was an analytical chemistry analysis, not anything more than that. So I'm fine withdrawing the discussion on phototox based on that.

DR. PETERSON: Okay.

DR. COHEN: Wilma, the absorption material in 200 to 400 nanometers was more an analytical chemistry thing then a phototox issue. So we got through the whole deck.

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DR. BELSITO: Okay, so, Portulaca oleracea. This is the first time looking at these four ingredients. And, we're now told that previously the extract was derived from leaf and stem only. But now we're told that it is derived from the whole plant. So, we looked at all of this information and felt that we had no absorption distribution metabolism. And we need a 28-day dermal at concentration of use in a hydroalcoholic solvent.

And, the other interesting thing is we were told that the maximum concentration of use is .008 percent. But it was curious, at least to me, that in the sensitization and irritation studies it was done at 0.1 percent, including a study that was done in 2017. So we would like some clarification as to really what the maximum concentration of use is.

And then we also felt that the results in the DART section needed to be explain; they were very (audio skip). (Inaudible) particularly absorption through the skin (audio skip). And, finally, there was no genotox data. We felt we needed that. Dan felt we needed -- we only had Ames test, we did not need mammalian. But I'm sure that Dr. Shank will want mammalian as well.

So we found this insufficient, 28-day dermal at concentration of use, specifying the vehicle was hydroalcoholic. That may help us explain the DART data. Further clarification of maximum concentration of use as to why someone studied it at 0.1 percent if the maximum is .008, and genotox data.

DR. BERGFELD: So that's a motion to go out as an IDA with all those needs?

DR. BELSITO: Correct.

DR. BERGFELD: Is there a second? Is there a comment?

DR. COHEN: Yeah, Don, we considered the very low concentrations and those signals for irritation and sensitization. Same issue, the lotion used in the sensitization study was .1 percent. So, we had a safer consideration for it, but I think in light of your issues we would concur.

DR. BERGFELD: So you're seconding it? You're seconding the motion?

DR. COHEN: Yes.

DR. BERGFELD: Any other discussion?

DR. BELSITO: David, I have no problem with the sensitization and irritation. I'm just wondering why someone would do it at .1 if in fact the maximum concentration is .008. So, what I'm asking is maybe a referral could go out to whoever did that study, if she's aware of it, and find out whether they are in fact marketing products at .1 percent. I don't think it'll change our conclusion.

DR. COHEN: It's the same as the Acetyl Hexapeptide discussion.

DR. BELSITO: Right.

DR. BERGFELD: Okay, any other comments before we move this question of an IDA on this ingredient?

MS. RAJ: Dr. Bergfeld?

DR. BERGFELD: Yes.

MS. RAJ: I quickly wanted to ask this -- I'm glad this is going as an IDA, but I know -- I think the Belsito team had discussed dealing with the oxalates in the -- personally in the discussion section. So I was just curious, I guess, how the Panel would like to see that. And also, discussion regarding the effects seen in the DART study for testosterone effects?

DR. BELSITO: Yeah, so, we actually -- that's, Preethi, why we wanted the ADME. That may get rid of all of the issues with the DART effects that we're seeing.

MS. RAJ: Okay.

DR. BELSITO: And, in terms of the oxalates we really weren't -- I mean, the concern with oxalates is irritation.

MS. RAJ: Okay.

DR. BELSITO: We weren't really seeing irritation. So, you know, we could mention it that oxalates can be irritating, but at the concentrations that these are being used there's no evidence of irritation in cosmetic products.

MS. RAJ: Okay, thank you.

DR. BERGFELD: All right. So, I'm going to call the question now. And those that are opposed to moving forward with an IDA please indicate by stating your name. Hearing and seeing none, I will say unanimously this is approved to go out as an IDA.

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

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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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DRAFT ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 4 *Portulaca oleracea*-derived ingredients as used in cosmetic formulations. These ingredients are mostly reported to function as skin-conditioning agents. Industry should use current good manufacturing practices to minimize impurities that could be present in botanical ingredients. The Panel reviewed data relevant to the safety of these ingredients in cosmetic formulations, and concluded [TBD].

INTRODUCTION

This is a safety assessment of the following 4 *Portulaca oleracea*-derived ingredients, as used in cosmetic formulations:

Portulaca Oleracea Extract
Portulaca Oleracea Flower/Leaf/Stem Extract
Portulaca Oleracea Juice
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. Thus, in this assessment, the Panel will assess the safety of each of the *Portulaca oleracea*-derived ingredients as a whole, complex mixture; toxicity from single components may not predict the potential toxicity of botanical ingredients.

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, both using the whole plant,[13-15] is outlined in Figure 1.

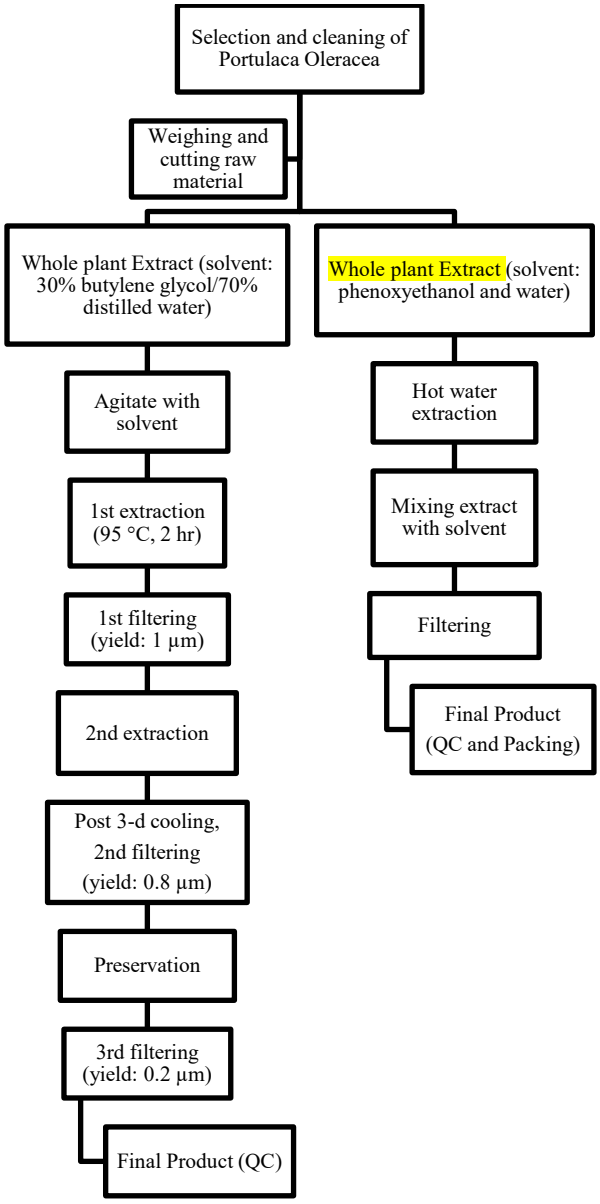

Figure 1. Overview of methods of manufacture for Portulaca Oleracea Extracts.[13-15]

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.[16] Most *Portulaca oleracea* extracts are obtained using ethanol or methanol solvents.[17] 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.[18-21] 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.[16] 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.[22] 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.[20] 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.[23] 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.[24] 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%).[10,11,25] 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.[11,26] 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.[27] 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.[18] Varying climate and soil conditions among *Portulaca oleracea* plants grown in different locations also affected mineral composition, flavonoid, and carotenoid content.[28,29] Additionally, the composition and determination of individual constituents found in *Portulaca oleracea*-derived ingredients varies considerably depending on extraction solvent and method,[10,17] part of the plant,[25,30] and growth stage or time of harvest.[18,25] 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%.[31] 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.[32] 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).[32] 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.[33] Toxic effects of the oxalate content, upon consumption of *Portulaca oleracea*, has been observed in dogs, cats, horses, and ruminant species.[34,35]

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.[2,19] Other notable constituents are omega-3-fatty acids, polysaccharides, vitamins, and amino acids.[30]

The phenolic and flavonoid content of hydrothermally processed *Portulaca oleracea* was evaluated.[23] 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.[25] 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.[21] 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 2021 VCRP survey data, Portulaca Oleracea Extract is reported to be used in 490 formulations (Table 3), of which 190 uses are in face and neck products, and 124 uses are in moisturizing products.[37] The results of the concentration of use survey, conducted by the Council in 2018, and updated in 2021, indicate that the reported maximum concentration of use for Portulaca Oleracea Extract is 0.5%, in non-spray face and neck formulations.[38,39] 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.[40-42]

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.[43]

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.[4,44] Uses as an apotropaic agent and a source of violet and gray dye for wool are also noted.[44]

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.[4,45] 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.[4,17] 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.[46]

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.

A 10% ethanolic extract of *Portulaca oleracea* was tested for skin sensitivity, in rabbits, via intradermal injection. No sensitivity was observed, and the LD_{50} was determined to be 1865 mg/kg bw.[47] 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.[48,49] The oral LD_{50} of a petroleum ether *Portulaca oleracea* leaf extract, in Sprague-Dawley rats, was determined to be > 2000 mg/kg bw.[50] Maximum oral doses of 5000 mg/kg chloroform and methanolic *Portulaca oleracea* leaf extracts were well tolerated in rats.[51,52]

Short-Term Toxicity Studies

The short-term oral 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.[48,49] 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 orally 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 increase in lymphocyte counts in the 25 and 50 mg/kg bw/d aqueous extract groups.[53] 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.[50] 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.[51,52] 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.[54] 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, that were orally administered either 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.[55] No pregnancy (or sterile mating) occurred between males from either extract group and the untreated female rats. Body weight changes, blood samples, sperm, testes, and epididymis were analyzed in groups of 5 male Wistar rats orally dosed with 0, 400, or 800 mg/kg bw methanolic *Portulaca* oleracea leaf and stem extracts for 14 d.[56] Although no significant differences in luteinizing hormone and testosterone levels were seen in the animals treated with the methanolic extracts, significant increases in follicle-stimulating hormone and reduction in sperm count occurred in the 800 mg/kg group and a significant reduction in sperm motility was seen in both treatment groups, compared to controls. Groups of 5 male albino rats were orally dosed with 0, 25, 50, or 75 mg/kg/d aqueous, or methanolic, *Portulaca oleracea* leaf and stem extracts for 50 d, and had blood samples from day 51 analyzed for testosterone levels; the animals were sacrificed for semen and histological analyses of the testes.[57] 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. In another study, groups of 16 male albino rats were orally dosed with 0, 125, 250, or 500 mg/kg chloroform, or 80% aqueous methanolic extract, for 60 d; blood samples, testes, and epididymis were harvested from 4 animals in each treatment group on days 14, 28, 42, and 60.[58] A significant increase in sperm count was observed in the animals treated with both extracts in the 250 mg/kg groups on day 28 and a significant decrease in testosterone levels was observed in the animals treated with 125 and 500 mg/kg methanolic extract on days 28 and 60. Groups of 5 - 6 female Wistar albino rats were orally 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.[59] In two similarly completed, but separate studies, ovary and uterine weights were significantly lower in immature, bilaterally ovariectomized rats orally 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 orally 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.[59] In a 21-d study, female albino rats were first orally 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.[60] 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. The effects of 0, 125, 250, or 500 mg/kg chloroform, or 80% aqueous methanolic, *Portulaca oleracea* leaf extracts upon estrous cycle, ovarian and uterine histology, and luteinizing hormone (LH), follicle-stimulating hormone (FSH), progesterone, and estrogen serum levels were examined in groups of 5 female albino rats for 21 d.[61] Significant decreases in luteinizing hormone levels in the 250 mg/kg chloroform extract group, and in follicle-stimulating hormone levels in the 250 and 500 mg/kg chloroform extract groups were observed. Hypertrophied ovarian follicles were observed in the 125 mg/kg methanolic extract group; no other significant effects were exhibited in estrous phase, hormone levels, or histology. Groups of 5 female albino rats were orally 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.[60] 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, via gavage, 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.[59] 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.[55] 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.

CARCINOGENICITY STUDIES

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

OTHER RELEVANT STUDIES

Anti-Inflammatory and Antioxidant 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.[62] Luteolin, kaempferol, and quercitrin components identified in the extracts were postulated to account for these anti-inflammatory effects.

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.

Cytotoxicity

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).[63] 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.[64]

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.[65] 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.[66]

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.[67] 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.[68] 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. Two additional maximization studies, performed in an identical fashion, tested the sensitization potential of a face lotion and face treatment product, both containing 0.5% Portulaca Oleracea Extract, and were completed in 27 and 26 subjects, respectively.[69,70] No signs of sensitization were observed for either product during the induction or challenge phase; both test articles were 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.[71] 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 490 formulations, of which 190 uses are in face and neck products and 124 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 0.5% (in non – spray face and neck products).

The intradermal LD_{50} of a 10% ethanolic *Portulaca oleracea* extract was determined to be 1865 mg/kg in rabbits. 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 orally dosed with up to 400 mg/kg bw/d of a whole ethanolic *Portulaca oleracea* extract for 14 d. Albino rats dosed, orally, 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 orally 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 orally 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 dosed, via gavage, with 75 mg/kg bw aqueous or methanolic *Portulaca oleracea* leaf extract for 50 d, and untreated female rats. Groups of 5 male Wistar rats were orally dosed with 0, 400, or 800 mg/kg bw methanolic *Portulaca oleracea* leaf and stem extract for 14 d. Significant increases in follicle-stimulating hormone and reduction in sperm counts were seen in the 800 mg/kg group, and sperm motility was significantly reduced in both 400 and 800 mg/kg groups, compared to controls; differences in luteinizing hormone and testosterone levels were not significant. 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. Groups of 16 male albino rats were orally dosed with 0, 125, 250, or 500 mg/kg/d chloroform or methanolic extract for 60 d; significant increases in sperm count were seen in the 250 mg/kg groups for both extracts on day 28, and testosterone levels were significantly decreased in the 125 and 500 mg/kg methanolic extracts groups on days 28 and 60. 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 orally 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, via gavage 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. Groups of 5 female albino rats orally dosed with 0, 125, 250, or 500 chloroform, or 80% aqueous methanolic extract for 21 d exhibited significant decreases in LH, from the 250 mg/kg chloroform extract group, and FSH from the 250 and 500 mg/kg chloroform extract groups. No other significant effects upon estrous cycle, ovarian and uterine histology, or LH, FSH, estrogen, or progesterone levels were observed. No significant pathological effects or changes in ovarian and uterine weights were observed in rats orally dosed with 75 mg/kg/d of aqueous or methanolic *Portulaca oleracea* leaf and stem extract for 25 d. In another study, dams orally 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, via gavage, during 3 different timeframes during 21 d of gestation.

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. 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.

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. A face lotion containing 0.5% Portulaca Oleracea Extract and a face treatment product containing 0.5% Portulaca Oleracea Extract were not considered sensitizing when tested in a maximization study involving 27 and 26 subjects, respectively.

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.

DRAFT DISCUSSION

[Note: This Discussion is in draft form, and changes may be made following the Panel meeting.]

This assessment reviews the safety of 4 *Portulaca oleracea*-derived ingredients as used in cosmetic formulations. The Panel concluded [TBD].

Adverse effects that were reported in developmental and reproductive toxicity studies, including anomalies in testosterone levels and sperm quality for male rats and abortifacient activity for dams, were noted by the Panel. Due to contradictory results across studies, using aqueous, ethanolic, or methanolic *Portulaca oleracea* extracts, the Panel sought to clarify if these effects were solvent-driven by requesting a 28-d dermal toxicity study of Portulaca Oleracea Extract, at the maximum use concentration, in an hydroalcoholic solvent. […]

The Panel also expressed concern about pesticide residues, heavy metals, and other plant species that may be present in botanical ingredients. For these *Portulaca oleracea*-derived ingredients, the Panel acknowledged the presence of oxalate, which is a possible irritant, but only at high concentrations; thus, at the present concentrations of use, the Panel did not find any evidence of irritation. They stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities.

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*[30]

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*[30]

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 (2021)[37] and concentration of use (2019)[38,39] data for Portulaca Oleracea Extract

	# of Uses	Max Conc of Use (%)
Totals*	490	0.001-0.5
Duration of Use		
Leave-On	432	0.001 – 0.5
Rinse-Off	58	0.002
Diluted for (Bath) Use	NR	NR
Exposure Type		
Eye Area	21	NR
Incidental Ingestion	1	NR
Incidental Inhalation-Spray	148[a];198[b]	NR
Incidental Inhalation-Powder	2; 198[b]; 5[c]	0.002 – 0.5[c]
Dermal Contact	480	0.001 – 0.008
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	9	NR
Hair-Coloring	NR	NR
Nail	NR	NR
Mucous Membrane	7	NR
Baby Products	9	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
INTRADERMAL						
Portulaca oleracea extract 10% in ethanol	Rabbits (strain and sex not specified)	NR	NR	0.05 ml, via intradermal injection; The test article was administered to the shaved backs of rabbits and observed for skin sensitivity.	LD_{50} was determined to be 1865 mg/kg bw. No sensitivity was observed and no further details were provided.	47
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.	48,49
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.	50
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.	51,52,58,61

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.	[48,49]
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.	[53]
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, via gavage	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.	[50]
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.	[51,52]
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.	[54]

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, via gavage	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.	[55]
Portulaca oleracea leaf and stem extract MEPO	Male Wistar rats; 5/group	20 ml distilled water	0, 400, or 800 mg/kg bw MEPO, via gavage	Reproductive parameters in male Wistar rats. Animals were orally dosed for 14 d, fasted overnight after the last dosing, and then killed. Body weight was measured before and after administration of the test substance. After sacrifice, blood samples, sperm, testes, and epididymis were collected for serum hormones, sperm, and histological analyses.	Body weight significantly increased in both the control and 800 mg/kg MEPO group. No significant changes in serum LH and testosterone levels were observed in either MEPO group, compared to the controls. However, the 800 mg/kg bw group had a significant increase in FSH levels and reduction in sperm count, when compared to controls. Significant reduction in sperm motility was seen in both MEPO-treated groups compared to the controls. While the testis showed no abnormalities in its histology across groups, the epididymis showed some blood congestion in MEPO-treated groups.	[56]
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, via gavage	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.	[57]
Portulaca oleracea leaf extract Chloroform and 80% aqueous methanol	Male albino rats; 16/group	0.5 ml 20% Tween 80	0, 125, 250, or 500 mg/kg chloroform or methanolic extract, via gavage	Reproductive parameters in male albino rats. Animals were orally dosed for 60 d. Blood samples, testes, and epididymis were harvested from 4 animals from each of the experimental groups on days 14, 28, 42, and 60.	Neither extract had a significant effect on the testicular weights, or sperm motility, viability, and morphology of treated rats, relative to the controls. A significant increase in sperm count was observed in the animals treated with the 250 mg/kg chloroform extract on days 14 and 28 and in the 250 mg/kg methanolic extract group on day 28, compared to controls. No effects on testosterone levels were observed in animals treated with the chloroform extract; a significant decrease in testosterone levels was observed in the animals treated with 125 and 500 mg/kg methanolic extract on days 28 and 60. No significant changes in testes histology were observed in animals from either treatment groups.	[58]

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 "Total flavonoid extract"*	Female Wistar albino rats; 5-6/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.	[59]
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.	[59]
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, via gavage	Estrous cycle effects. Animals were dosed for 21 d and vaginal smears were microscopically examined daily to classify rats into estrous cycle phase and determine cycle length. Vaginal smears were also evaluated 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.	[60]
Portulaca oleracea leaf extract Chloroform and 80% aqueous methanol	Female albino rats; 5/group	0.5 ml 20% Tween 80	0, 125, 250, or 500 mg/kg chloroform or methanolic extract, via gavage	Estrous cycle and ovarian/uterine histology effects. Animals were dosed for 21 d, which began at the start of the estrous cycle. Vaginal smears were examined daily to assess the phase of the estrous cycle and blood samples were collected on day 21 for hormonal analysis of LH, FSH, progesterone, and estrogen serum levels. After the last dose, animals were killed and the uterine horns and ovaries were harvested for histological analyses (the estrous cycle phase at which the samples were collected was not stated).	No obvious or significant effects were observed on the estrous cycle and ovarian and uterine histology for animals treated with either extract, compared to controls. However, the ovarian sections from 125 mg/kg methanolic extract group showed hypertrophied ovarian follicles. Treatment with both extracts resulted in a decline in the mean serum levels of LH in the proestrus phase, which was not entirely significant. A significant decrease in LH was observed in the 250 mg/kg chloroform extract group; significant decreases in mean serum levels of FSH were also observed in the 250 and 500 mg/kg chloroform extract groups. No other significant effects were seen in LH, FSH, progesterone or estrogen serum levels in the estrus, mestrus, or diestrus phases.	[61]
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, via gavage	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.	[60]

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 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, 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.	[59]
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 estrous 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 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.	[59]
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, via gavage	Teratology study. 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.	[55]

Abbreviations: AEPO- aqueous extract *Portulaca* oleracea; ELISA- enzyme-linked immunosorbent assay; FSH-follicle-stimulating hormone; LH- luteinizing hormone; 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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71. Anonymous. 2017. Summary: Clinical use test of a product containing 0.1% Portulaca Oleracea Extract. (Unpublished data submitted by the Personal Care Products Council on August 12, 2020.)

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

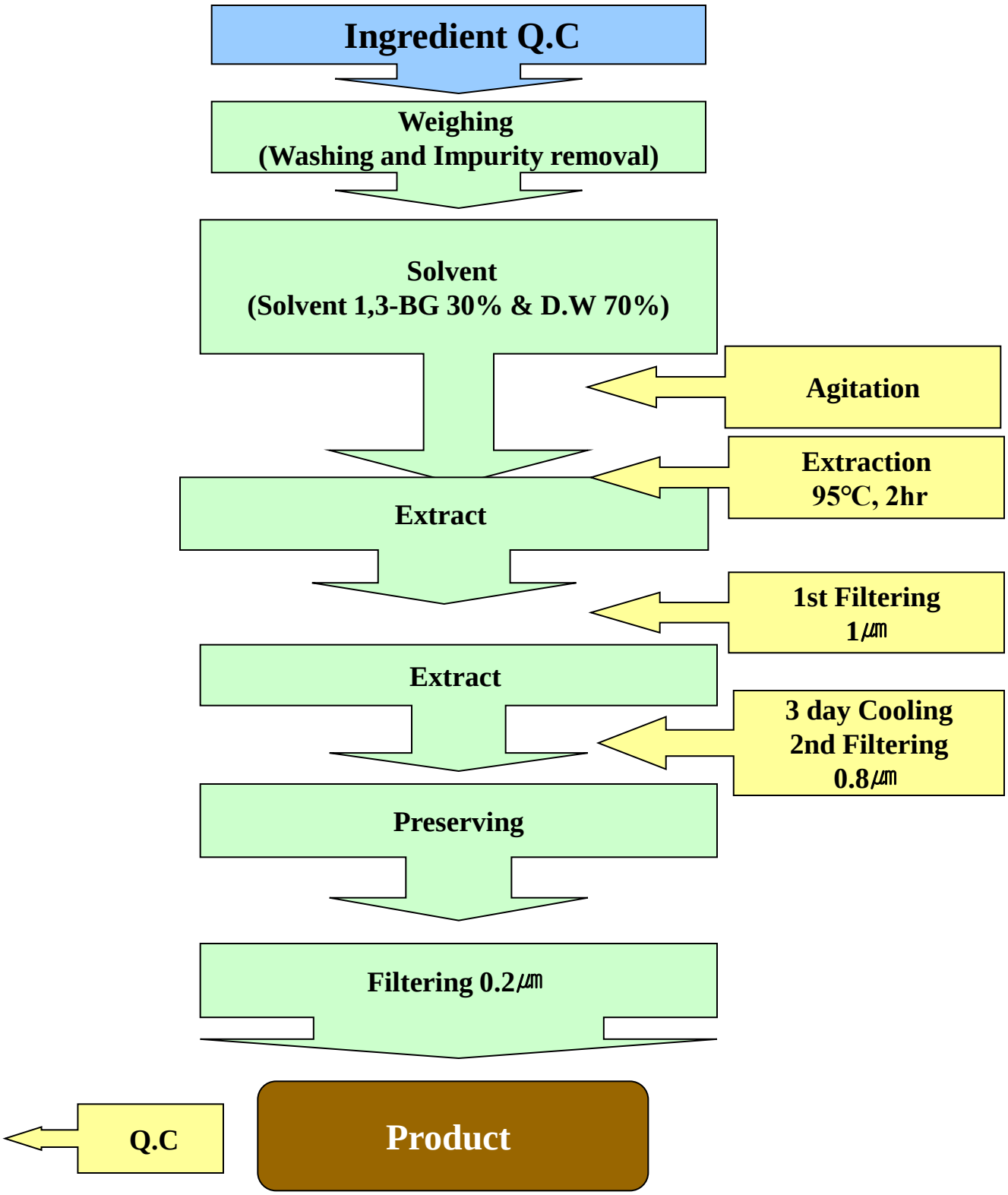
Certificate of Origin

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

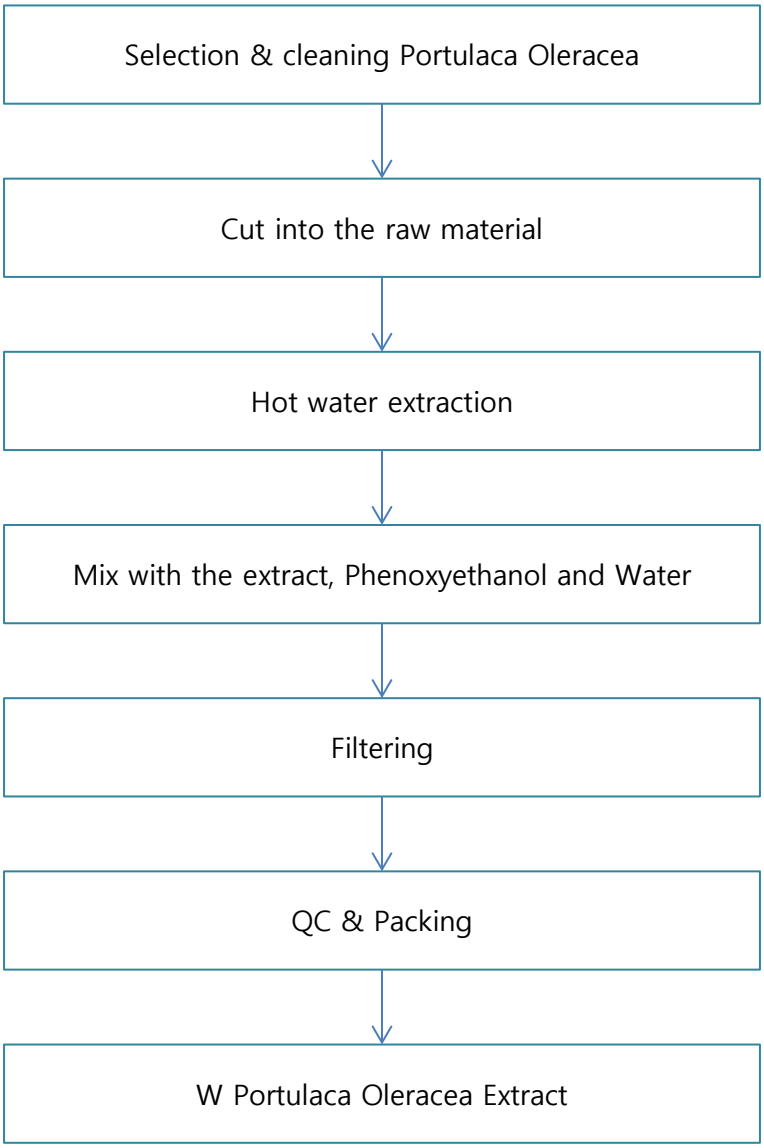
We, [redacted] d hereby confirm that the source and used part of each ingredient which is originated from plants in the above mentioned product is as follows;

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: November 16, 2020

SUBJECT: Portulaca Oleracea Extract

Anonymous. 2020. Correction of source to whole plant (information associated with PCPC memo 3).

Certificate of ingredient source

Product Name :	W Portulaca Oleracea Extract
Manufacturer :	[redacted]

We, [redacted] 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*)	Whole plant
2	Phenoxyethanol	Synthetic	-
3	Water	Natural	-

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

2020. 11. 16.

[redacted]

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	0.002-0.5%
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
Additional response (face and neck product not spray 0.5%) added January 4, 2021

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: January 4, 2021

SUBJECT: Portulaca Oleracea Extract

Anonymous. 2004. An Evaluation of the Contact-Sensitizing Potential of a Topical Coded Product in Human Skin by Means of the Maximization Assay (Product contains 0.5% Portulaca Oleracea Extract).

Anonymous. 2007. An Evaluation of the Contact-Sensitizing Potential of a Topical Coded Product in Human Skin by Means of the Maximization Assay (Product contains 0.5% Portulaca Oleracea Extract).

[redacted] .. [redacted] ..

FINAL REPORT January 23, 2004

[redacted] Protocol: #5486

Sample: Facial Lotion coded [redacted]

[redacted]

Telephone: [redacted]
FAX: [redacted]

E-mail address: [redacted]

[redacted]

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

Product contains 0.5% Portulaca Oleracea Extract

Sponsor: [redacted]

Principal Investigator: [redacted]. (Board Certified Dermatologist)

Testing Facility: [redacted]

Protocol: [redacted] Protocol #**5486**

Final Report Date: **January 23, 2004**

[redacted]
Principal Investigator

1/23/04
Date

FINAL REPORT

[redacted] PROTOCOL:

[redacted] Protocol **#5486**

SPONSOR:

[redacted]

[redacted]

SPONSOR STUDY:

Authorization Letter Dated: November 24, 2003

STUDY TITLE:

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

STUDY OBJECTIVE:

[redacted]

FINAL REPORT

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 Facial Lotion coded [redacted] and tested as supplied.

[redacted]

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:

[redacted]. (Board Certified Dermatologist)

Medical Director, [redacted].

[redacted]

FAX: [redacted]

[redacted] ADMINISTRATIVE STRUCTURE:

[redacted] (Screening, Patch Applications/Removals, Recognize AE's)

[redacted] (Expert Grader)

[redacted] (Recruitment, Initial Screening and Medical Records Database)

TESTING FACILITY:

[redacted]

CONDUCTION DATES:

This study was conducted from December 1, 2003 through January 9, 2004

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

5 - Recent sunburn

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 [redacted] ([redacted]).

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] (Facial Lotion) 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 one hour 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 10 females and 18 males. Their ages ranged from 19 to 55 years. One subject was dropped from the study. Subject #06 (initials LCP, a female) failed to return for the challenge phase and was lost to follow-up. The remaining 27 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 Facial Lotion 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	RAT	44	M	B
02	D-M	42	M	B
03	VCC	44	M	B
04	SEF	44	M	B
05	JJM	51	M	B
06	LCP	20	F	C
07	MAC	36	F	C
08	RDM	54	M	B
09	MDG	22	M	C
10	BSB	44	M	B
11	CEM	55	M	B
12	VBW	46	F	B
13	CAB	19	F	C
14	SRM	52	F	C
15	V-S	21	F	C
16	AMK	53	M	B
17	MPN	20	M	C
18	ACB	25	M	B
19	TAA	55	F	B
20	DKO	51	F	C
21	ALK	19	F	C
22	AAA	29	M	B

23	MJS	35	M	C
24	MLF	48	F	B
25	D-M	45	M	B
26	DLJ	48	M	B
27	C-H	27	M	B
28	JPS	42	M	B

B = Black
C = Caucasian

TABLE 2

MAXIMIZATION TESTING RESULTS

Sample: Facial Lotion 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	Dropped from study	
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	0	0
17	0	0
18	0	0
19	0	0
20	0	0
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 – January 8, 2004
72-Hour Reading – January 9, 2004

[redacted]

FINAL REPORT dated November 26, 2007

[redacted] Protocol: #6409

Sample: Face Treatment coded [redacted]

[redacted] or [redacted]

[redacted]

Telephone: [redacted]
FAX: [redacted]

E-mail address: [redacted]

[redacted]

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

Product contains 0.5% Portulaca Oleracea Extract

Sponsor: [redacted]

Principal Investigator: [redacted]. (Board Certified Dermatologist)

Testing Facility: [redacted]

Phone: [redacted]
FAX: [redacted]

Final Report Date: November 26, 2007

[redacted] M.D.
Principal Investigator

November 26, 2007
Date

FINAL REPORT

[redacted] PROTOCOL:

[redacted] Protocol **#6409**

SPONSOR:

[redacted]

SPONSOR STUDY:

Authorization Letter Dated: October 2, 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 Face Treatment and coded [redacted] The 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:

[redacted] (Board Certified Dermatologist)

Medical Director, [redacted].

Telephone: [redacted]

FAX: [redacted]

E-mail: [redacted]

[redacted] **ADMINISTRATIVE STRUCTURE:**

[redacted] (Screening, Patch Applications/Removals, Recognize AE's)

[redacted] (Expert Grader)

[redacted] (Panel Recruitment/Receptionist)

TESTING FACILITY:

[redacted]

Telephone: [redacted]

CONDUCTION DATES:

This study was conducted from October 8, 2007 through November 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 [redacted] ([redacted]).

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 0.05gm of the test material 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-seven (27) healthy, adult male and female volunteers who satisfied the inclusion criteria were enrolled into this study. There were 19 females and 8 males ranging in age from 18 to 61 years. The demographic data are shown in Table 1.

Subject #26 (initials L-D., a female) failed to return to the laboratory following the initial SLS patch. No test products were applied to this subject. She was lost to follow-up and subsequently dropped from the study. The remaining 26 subjects completed this investigation as outlined in the standard protocol. 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 Face Treatment 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	C-G	21	F	C
02	M-D	34	F	C
03	T-K JR.	21	M	C
04	J-M	19	F	C
05	P-D	52	F	C
06	L-M	50	F	C
07	J-M	49	F	C
08	KMG	53	F	C
09	C-S	35	F	C
10	B-Y	41	F	C
11	G-P	53	F	B
12	K-B	61	F	C
13	P-K	61	M	C
14	T-K SR.	51	M	C
15	M-S	32	F	C
16	R-D	59	M	C
17	N-R	39	F	C
18	B-C	58	F	C
19	J-S	18	F	C
20	N-C	41	M	C
21	M-D	52	F	C
22	S-N	19	M	C
23	M-K	29	F	C

24	S-F	22	M	C
25	D-S	60	M	C
26	L-D	20	F	C
27	J-C	51	F	C

C = Caucasian
B = Black

TABLE 2

MAXIMIZATION TESTING RESULTS

Sample: Face Treatment 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	0	0
17	0	0
18	0	0
19	0	0
20	0	0
21	0	0
22	0	0
23	0	0
24	0	0
25	0	0
26	Dropped from the study	
27	0	0

Challenge Readings:

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

2021 VCRP Frequency of Use Data – *Portulaca oleracea*- Derived Ingredients

Ingredient Name	Category Code	Description	CPIS count
Portulaca Oleracea (Purslane) Extract Total Uses: 490			
Portulaca oleracea (purslane) extract	01A	Baby Shampoos	2
Portulaca oleracea (purslane) extract	01B	Baby Lotions, Oils, Powders, and Creams	5
Portulaca oleracea (purslane) extract	01C	Other Baby Products	2
Portulaca oleracea (purslane) extract	03B	Eyeliner	1
Portulaca oleracea (purslane) extract	03D	Eye Lotion	12
Portulaca oleracea (purslane) extract	03G	Other Eye Makeup Preparations	8
Portulaca oleracea (purslane) extract	05A	Hair Conditioner	1
Portulaca oleracea (purslane) extract	05F	Shampoos (non-coloring)	5
Portulaca oleracea (purslane) extract	05I	Other Hair Preparations	1
Portulaca oleracea (purslane) extract	07B	Face Powders	2
Portulaca oleracea (purslane) extract	07C	Foundations	8
Portulaca oleracea (purslane) extract	07E	Lipstick	1
Portulaca oleracea (purslane) extract	10A	Bath Soaps and Detergents	2
Portulaca oleracea (purslane) extract	10E	Other Personal Cleanliness Products	4
Portulaca oleracea (purslane) extract	11A	Aftershave Lotion	1
Portulaca oleracea (purslane) extract	12A	Cleansing	27
Portulaca oleracea (purslane) extract	12C	Face and Neck (exc shave)	190
Portulaca oleracea (purslane) extract	12D	Body and Hand (exc shave)	8
Portulaca oleracea (purslane) extract	12F	Moisturizing	124
Portulaca oleracea (purslane) extract	12G	Night	9
Portulaca oleracea (purslane) extract	12H	Paste Masks (mud packs)	17
Portulaca oleracea (purslane) extract	12I	Skin Fresheners	14
Portulaca oleracea (purslane) extract	12J	Other Skin Care Preps	45
Portulaca oleracea (purslane) extract	13A	Suntan Gels, Creams, and Liquids	1