International Journal of Toxicology
2024, Vol. 43(Supplement 4) 108S–129S

DOI: 10.1177/10915818241259694
journals.sagepub.com/home/ijt
Sage

Safety Assessment of Alkanoyl Lactyl Lactate Salts as Used in Cosmetics

Wilbur Johnson Jr.*, Wilma F. Bergfeld, Donald V. Belsito**, Ronald A. Hill***, Curtis D. Klaassen**, Daniel C. Liebler***, James G. Marks Jr.***, Ronald C. Shank***, Thomas J. Slaga**, Paul W. Snyder**, Monice Fiume†, and Bart Heldreth††**

Abstract

The Expert Panel for Cosmetic Ingredient Safety (Panel) reviewed the safety of 10 alkanoyl lactyl lactate salts. These ingredients have the surfactant function in cosmetics in common. The Panel reviewed data relevant to the safety of these ingredients, and concluded that these 10 ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be nonirritating and nonsensitizing, which may be based on a quantitative risk assessment (QRA) or other accepted methodologies.

Keywords

Cosmetic Ingredient Review, Expert Panel for Cosmetic Ingredient Safety, Safety, Cosmetic Ingredient, Calcium Stearoyl Lactylate, Sodium Behenoyl Lactylate, Sodium Caproyl Lactylate, Sodium Caproyl/Lauroyl Lactylate, Sodium Cocoyl Lactylate, Sodium Cupheoyl Lactylate, Sodium Isostearoyl Lactylate, Sodium Lauroyl Lactylate, Sodium Oleoyl Lactylate, Sodium Stearoyl Lactylate

Introduction

The safety of the following 10 alkanoyl lactyl lactate salts as used in cosmetics is reviewed in this safety assessment.

Calcium Stearoyl Lactylate	Sodium Cupheoyl Lactylate
Sodium Behenoyl Lactylate	Sodium Isostearoyl Lactylate
Sodium Caproyl Lactylate	Sodium Lauroyl Lactylate
Sodium Caproyl/Lauroyl Lactylate	Sodium Oleoyl Lactylate
Sodium Cocoyl Lactylate	Sodium Stearoyl Lactylate

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), all of these ingredients are surfactants, while other functions are reported for some of the ingredients, as indicated in Table 1.[1] Functioning as an antifungal or antidandruff agent, as some of these ingredients are reported to do, is not considered a cosmetic function in the United States (US) and, therefore, the Expert Panel for Cosmetic Ingredient Safety (Panel) does not evaluate safety in relation to either of those uses.

This safety assessment includes relevant published and unpublished data for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A list of the typical search engines and websites used, sources explored, and endpoints that the Panel evaluates, is available 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.

Chemistry

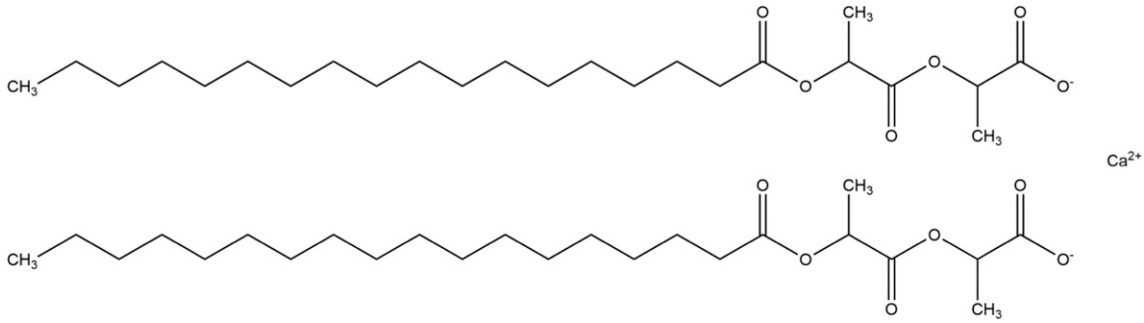
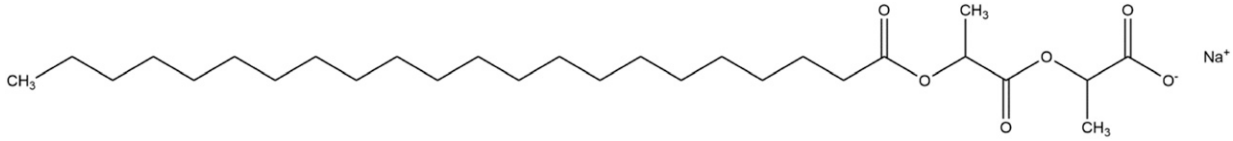
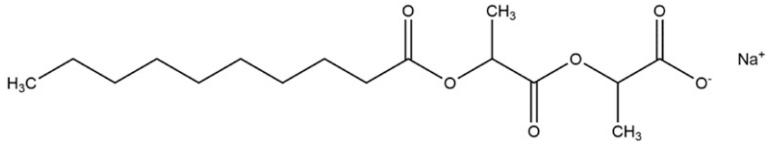
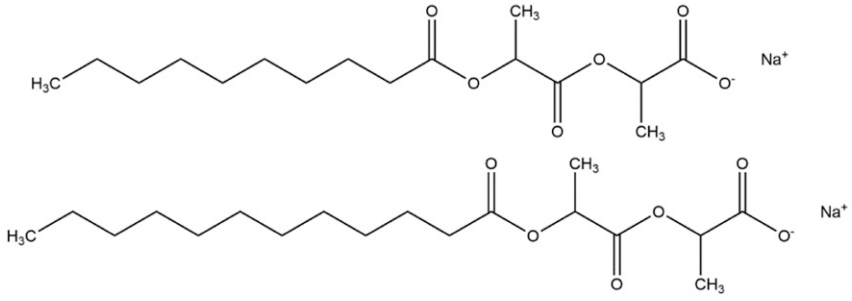
Definition and General Characterization

Alkanoyl lactyl lactates (i.e., alkanoyl lactylates) are the carboxylic acid salts of diesters that are formed between a fatty acid group and two equivalents of lactic acid.[2] The generic structure of alkanoyl lactyl lactates is presented below

*Cosmetic Ingredient Review Former Senior Scientific Analyst/Writer
**Expert Panel for Cosmetic Ingredient Safety Member
***Expert Panel for Cosmetic Ingredient Safety Former Member
†Cosmetic Ingredient Review Senior Director
††Cosmetic Ingredient Review Executive Director

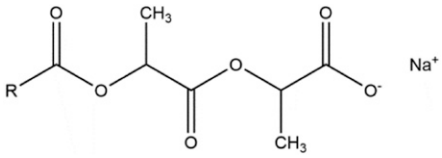
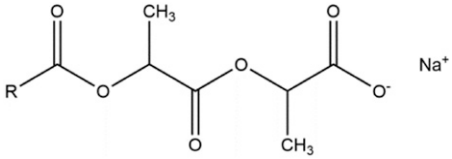
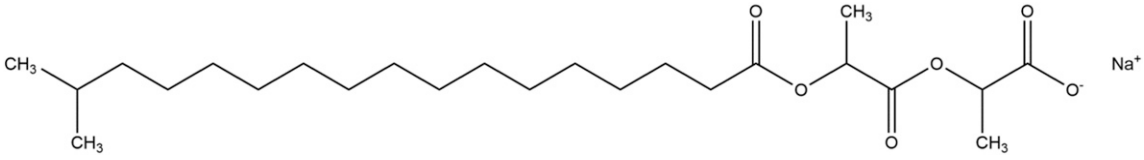
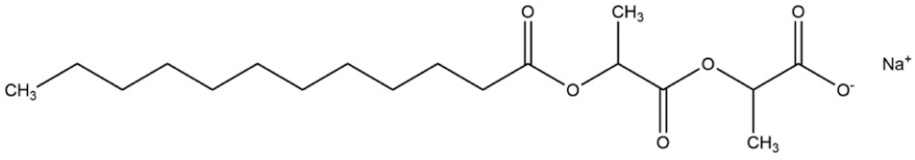
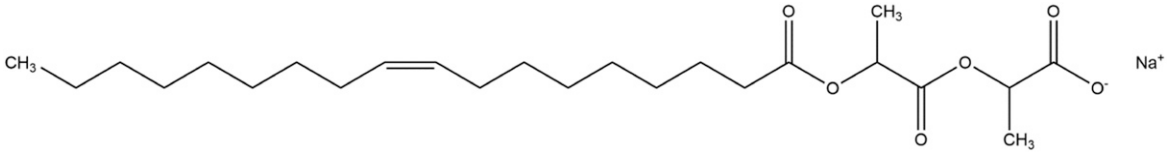
Corresponding Author:
Bart Heldreth, Executive Director, Cosmetic Ingredient Review, 555 13th St., NW, Suite 300W, Washington, DC 20004, USA.
Email: cirinfo@cir-safety.org

Table 1. Definitions, Idealized Structures, and Functions of the Ingredients in this Safety Assessment.[1,CIR Staff]

Ingredient CAS No.	Definition and Structures	Functions
Calcium Stearoyl Lactylate 5793-94-2	Calcium Stearoyl Lactylate is the calcium salt of the stearic acid ester of lactyl lactate. It conforms to the following formula: 	Surfactants–Emulsifying agents
Sodium Behenoyl Lactylate	Sodium Behenoyl Lactylate is the sodium salt of the behenic acid ester of lactyl lactate. It conforms to the following formula: 	Surfactants–Emulsifying Agents
Sodium Caproyl Lactylate 13557-74-9	Sodium Caproyl Lactylate is the sodium salt of the capryl ester of lactyl lactate. It conforms generally to the following formula:  [According to INCI naming conventions for these ingredients: a C10 ester is designated as Caproyl, a C8 ester could be designated as Capryoyl, and a C6 ester could be designated as Caprooyl].	Surfactants–Emulsifying Agents
Sodium Caproyl/Lauroyl Lactylate 1312021-45-6	Sodium Caproyl/Lauroyl Lactylate is the organic compound that conforms generally to the following formula, where RCO- represents a mixture of capric and lauric acid groups:  [According to INCI naming conventions for these ingredients: a C10 ester is designated as Caproyl, a C8 ester could be designated as Capryoyl, and a C6 ester could be designated as Caprooyl].	Antidandruff Agents; Antifungal Agents; Antimicrobial Agents; Surfactants–Cleansing Agents; and Surfactants–Emulsifying Agents

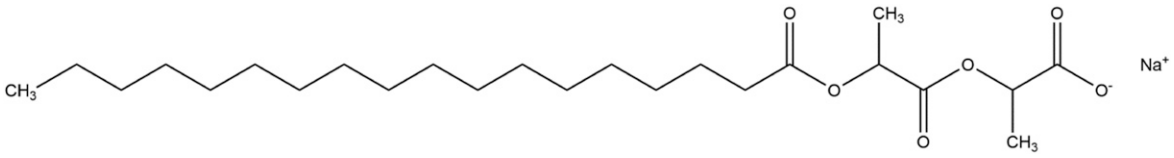
(continued)

Table 1. (continued)

Ingredient CAS No.	Definition and Structures	Functions
Sodium Cocoyl Lactylate	Sodium Cocoyl Lactylate is the sodium salt of the coconut acid ester of lactyl lactate. It conforms to the following formula:  where RC(O)- represents the fatty acids derived from coconut oil.	Surfactants–Emulsifying Agents
Sodium Cupheoyl Lactylate	Sodium Cupheoyl Lactylate is the organic compound that conforms to the following formula:  where RC(O)- represents the fatty acids derived from the seed oil of the hybrid, *Cuphea viscosissima x Cuphea lanceolata*. [The approximate fatty acid composition of this seed oil is: 70% capric acid , 9% oleic acid, 6% palmitic acid , 5% linoleic acid, 4% myristic acid, and 3% lauric acid[32]].	Surfactants–Cleansing Agents; Surfactants–Emulsifying Agents; and Surfactants–Foam Boosters
Sodium Isostearoyl Lactylate 66988-04-3	Sodium Isostearoyl Lactylate is the sodium salt of the isostearic acid ester of lactyl lactate. It conforms to the following formula: 	Surfactants–Emulsifying Agents
Sodium Lauroyl Lactylate 13557-75-01312021-45-6	Sodium Lauroyl Lactylate is the sodium salt of the lauric acid ester of lactyl lactate. It conforms to the following formula: 	Surfactants–Emulsifying Agents
Sodium Oleoyl Lactylate	Sodium Oleoyl Lactylate is the sodium salt of the oleic acid ester of lactyl lactate. It conforms to the following formula: 	Surfactants–Emulsifying Agents

(continued)

Table 1. (continued)

Ingredient CAS No.	Definition and Structures	Functions
Sodium Stearoyl Lactylate 18200-72-1 25383-99-7	Sodium Stearoyl Lactylate is the sodium salt of the stearic acid ester of lactyl lactate. It conforms to the following formula: 	Surfactants–Emulsifying Agents

(Figures 1 and 2). Like other anionic emulsifiers/surfactants, the properties of these ingredients result from the diametrically opposed lipophilic (fatty acid) tail and the hydrophilic (lactylate) head. The definitions and structures of the alkanoyl lactyl lactate salts are presented in Table 1.[1]

Chemical and Physical Properties

Alkanoyl lactyl lactates hydrate readily in water at ambient temperature.[3] Compositions comprising a greater proportion of free acids are more soluble in fatty products, and have a slower rate of hydration. Conversely, compositions comprising a greater proportion of fully deprotonated salt forms are less soluble in fatty products, and have a faster rate of hydration. Furthermore, the calcium salt, Calcium Stearoyl Lactylate, hydrates more slowly than the respective sodium salt, Sodium Stearoyl Lactylate. These ingredients vary in formula weights from as small as 338 Da for Sodium Caproyl Lactylate (315 Da without the sodium cation) to as large as 507 Da for Sodium Behenoyl Lactylate (484 Da without the sodium cation). Calcium Stearoyl Lactylate technically has the highest formula weight (895 Da; 855 Da without the calcium cation), but this is an artifact of the $^{2+}$ oxidation state of calcium and two equivalents of stearoyl lactylate needed to balance this salt formula (i.e., each stearoyl lactylate is only 428 Da). Properties of alkanoyl lactyl lactate salts are presented in Table 2.

Method of Manufacture

Calcium Stearoyl Lactylate. According to one food additive supplier, Calcium Stearoyl Lactylate (defined as a mixture of the calcium salts of stearoyl lactylic acids and its polymers and minor amounts of calcium salts of other related acids) is manufactured by base-catalyzed esterification of lactylic acid and commercial stearic acid.[4] However, the *Dictionary* describes Calcium Stearoyl Lactylate as the calcium salt of the stearic acid ester of lactyl lactate (i.e., no indication of polymers or other acids provided).

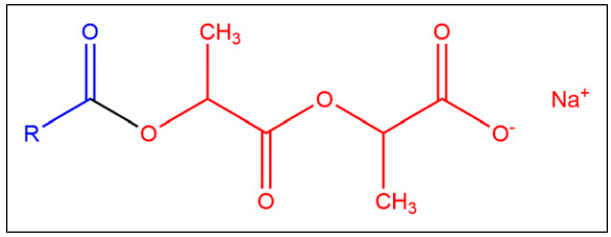


Figure 1. Generic structure of alkanoyl lactyl lactates.

Sodium Isostearoyl Lactylate. According to one method, Sodium Isostearoyl Lactylate is the reaction product of isostearic acid with lactic acid in the presence of sodium hydroxide.[5]

Sodium Stearoyl Lactylate. According to one food additive supplier, Sodium Stearoyl Lactylate (defined as a mixture of the sodium salts of stearoyl lactylic acids and its polymers and minor amounts of sodium salts of other related acids) is manufactured by base-catalyzed esterification of lactic acid and commercial stearic acid.[4] However, the *Dictionary* describes Sodium Stearoyl Lactylate as the sodium salt of the stearic acid ester of lactyl lactate (i.e., no indication of polymers or other acids).

Composition

Sodium Stearoyl Lactylate and Calcium Stearoyl Lactylate. As noted above, when used as food additives, Sodium Stearoyl Lactylate and Calcium Stearoyl Lactylate are manufactured using a base-catalyzed esterification process.[4] The distribution of the components in each is dependent upon the relative proportion of lactylic acid, fatty acid and the amount of sodium/calcium salt that is used in the neutralization process. The typical composition of the product of the neutralization process is approximately 50% stearoyl-mono-lactylate, 20% stearoyl-di-lactylate (equivalent to structure of Sodium Stearoyl Lactylate or Calcium Stearoyl Lactylate), 5% stearoyl-tri-lactylate, and trace amounts of stearoyl-tetra-lactylate. Other components may include sodium/calcium salts of fatty acids (depending on the

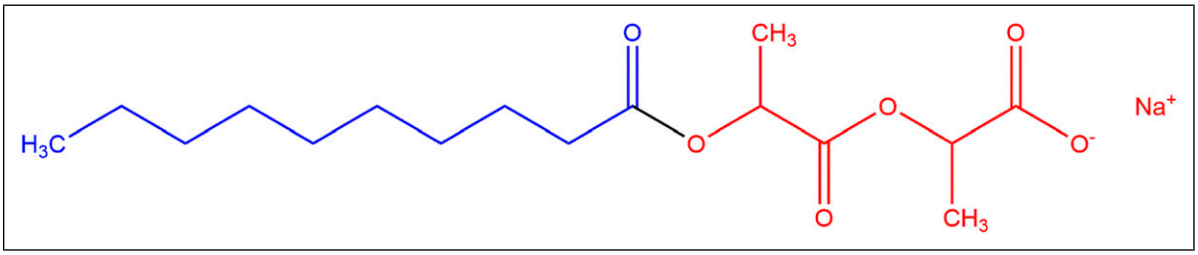


Figure 2. Example structure of an alkanoyl lactyl lactate, Sodium Caproyl Lactylate.

ingredient, i.e., if the ingredient is Sodium Stearoyl Lactylate or Calcium Stearoyl Lactylate) or free fatty acids (15–20%), non-neutralized stearoyl lactylic acid, sodium/calcium lactate, and free lactic acid or polymers of lactic acid. Additionally, the actual fatty acid profile of Sodium Stearoyl Lactylate and Calcium Stearoyl Lactylate will depend upon the source of the fatty acids. However, the *Dictionary* describes Sodium Stearoyl Lactylate and Calcium Stearoyl Lactylate as the salts of the stearic acid ester of lactyl lactate (i.e., no indication of stearoyl-mono-lactylate, stearoyl-tri-lactylate, or stearoyl-tetra-lactylate).

Impurities

Calcium Stearoyl Lactylate. The *Food Chemicals Codex* specifications for Calcium Stearoyl Lactylate are as follows: lead (not more than 2 mg/kg), acid value (between 50 and 86), ester value (between 125 and 164), calcium content (between 4.2% and 5.2%), and total lactic acid (between 32% and 38%).[6] According to European Commission regulations, specifications relating to the purity of Calcium Stearoyl Lactylate are as follows: calcium (not less than 1% and not more than 5.2%), ester value (not less than 125 and not more than 190), acid value (not less than 50 and not more than 130), total lactic acid (not less than 15% and not more than 40%), arsenic (not more than 3 mg/kg), lead (not more than 2 mg/kg), mercury (not more than 1 mg/kg), and cadmium (not more than 1 mg/kg).[7]

Sodium Stearoyl Lactylate. The *Food Chemicals Codex* specifications for Sodium Stearoyl Lactylate are as follows: lead (not more than 2 mg/kg), acid value (between 60 and 80), ester value (between 120 and 190), sodium content (between 3.5% and 5%), and total lactic acid (between 23% and 34%).[6] According to European Commission regulations, the following specifications relate to the purity of Sodium Stearoyl Lactylate: sodium (not less than 2.5% and not more than 5%), ester value (not less than 90 and not more than 190), acid value (not less than 60 and not more than 130), total lactic acid (not less than 15% and not more than 40%), arsenic (not more than 3 mg/kg), lead (not more than 2 mg/kg), mercury (not more than 1 mg/kg), and cadmium (not more than 1 mg/kg).[4]

Use

Cosmetic

The safety of the alkanoyl lactyl lactate salts 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 FDA's Voluntary Cosmetic Registration Program (VCRP) database.[8] Use concentration data are submitted by the cosmetics industry in response to surveys, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.[9]

According to 2019 VCRP data, Sodium Stearoyl Lactylate is reported to be used in 358 cosmetic products (334 leave-on and 24 rinse-off products).[8] Of the alkanoyl lactyl lactate salts that are being reviewed in this safety assessment, this is the greatest reported use frequency. The results of a concentration of use survey conducted by the Council in 2017 indicate that Sodium Lauroyl Lactylate is being used at maximum use concentrations up to 10% in skin cleansing products (rinse-off products).[9] Calcium Stearoyl Lactylate, Sodium Lauroyl Lactate, and Sodium Stearoyl Lactylate are being used at maximum use concentrations up to 7% in leave-on products (tonics, dressings, and other hair grooming aids); this is the highest maximum use concentration in leave-on products that is being reported for the alkanoyl lactyl lactate salts. The highest maximum use concentration in leave-on cosmetic products that are applied directly to the skin is 6.1% Sodium Lauroyl Lactylate in body and hand products that are not sprayed. Further use data are presented in Table 3.

According to VCRP and Council survey data, 3 of the 10 alkanoyl lactyl lactate salts reviewed in this safety assessment are not reported to be in use (Table 4).

Table 2. Chemical and Physical Properties of Alkanoyl Lactyl Lactate Salts.

Property	Value/Results	Reference
Calcium Stearoyl Lactylate		
Form	White to pale yellow, ivory-colored waxy material.	4
Formula weight (Da)	895.26	4
Solubility	Typically, dispersible in warm water and soluble in hot edible oils and fats. Slightly soluble in hot water	4
log $P_{o/w}$	9.41(estimated)	4
Vapor pressure (mm Hg)	9.06×10^{-13}	4
Melting point (°C)	45.7 to 48.7	4
Boiling point (°C)	532 to 534	4
Flash point (°C)	188.11; 166.2	4
Sodium Behenoyl Lactylate		
Formula weight (Da)	506.7	33
log K_{ow}	6.01 (estimated)	34
Sodium Caproyl Lactylate		
Formula weight (Da)	338.4	35
Sodium Caproyl/Lauroyl Lactylate		
Form	Yellowish to brownish/amber highly viscous liquid	13
vFormula weight (Da)	338.4–366.4	35
Density (g/cm^3 at 20°C)	1.13 (estimated)	13
Water solubility (g/l at 20°C)	0.12	13
Vapor pressure (mm Hg at ~ 25°C)	2.14×10^{-5}	13
(mm Hg at ~ 20°C	1.38×10^{-5}	13
Melting range (°C)	0.7 to 10.2	13
Boiling point (°C)	decomposition at ~ 240	13
Flash point (°C)	183.5	13
Sodium Cocoyl Lactylate		
Form	White or off-white waxy solid or paste	36
Solubility	Soluble in water	36
Sodium Stearoyl Lactylate		
Form	White to pale yellow, ivory-colored waxy material.	4
Formula weight (Da)	405.58	4
Solubility	Typically, dispersible in warm water and soluble in hot edible oils and fats. Soluble in ethanol, but insoluble in water. Very slightly soluble in cold water.	4
Specific gravity	1.063	4
log $P_{o/w}$	9.41(estimated); 2.58 (Sodium Stearoyl Lactylate trade name material, composition not stated)	4,29
Melting point (°C)	48.889	4
Boiling point (°C)	532 to 533	4
Flash point (°C)	166.20	4
Sodium Isostearyl Lactylate		
Form	Straw or honey-colored, clear viscous liquid	5
Formula weight (Da)	450.592	33
Solubility	Dispersible in distilled water. Soluble in propylene glycol, ethyl alcohol, mineral oil, and isopropyl myristate	5
log K_{ow}	3.98 (estimated)	34
Sodium Lauroyl Lactylate		
Formula weight (Da)	366.43	33
log K_{ow}	1.10 (estimated)	34
Sodium Oleoyl Lactylate		
Formula weight (Da)	448.6	35
log K_{ow}	3.83 (estimated)	34
Flash point (°C)	0	37

Cosmetic products containing alkanoyl lactyl lactate salts may be applied to the skin or, incidentally, may come in contact with the eyes (at maximum use concentrations up to 0.2%, for Sodium Stearoyl Lactylate in eye lotions). Similarly, products containing these ingredients may incidentally come in contact with mucous membranes (at maximum use concentrations up to 3.5%, for Sodium Isostearoyl Lactylate in bath soaps and detergents). The highest maximum use concentration of alkanoyl lactyl lactate salts in products that may be incidentally ingested is 0.00011% (for Sodium Stearoyl Lactylate in lipsticks). Products containing alkanoyl lactyl lactate salts may be applied as frequently as several times per day and may come in contact with the skin for variable periods following application. Daily or occasional use may extend over many years.

The alkanoyl lactyl lactate salts reviewed in this safety assessment are not included on the European Union's list of substances that are restricted or list of substances that are prohibited in cosmetic products.[10]

Non-Cosmetic

Calcium Stearoyl Lactylate and Sodium Stearoyl Lactylate. Both Calcium Stearoyl Lactylate and Sodium Stearoyl Lactylate have been known to have a dough strengthening effect in the process of bread making (high-protein breads).[11] Both salts can form a complex with gluten to stabilize the gluten-network in dough. It has been noted that the dough strengthening effect of these salts may be due to formation of this complex.

The US FDA has determined that Calcium Stearoyl Lactylate (defined as a mixture of calcium salts of stearoyl lactylic acid and minor proportions of other calcium salts of related acids) may be used safely as a direct food additive, provided that the specifications defined in the *Food Chemicals Codex* are met [21 CFR 172.844]. Furthermore, the FDA has established limits for this ingredient in food ranging from 0.05% to 0.5%, depending on the food product type. The FDA has also established a limit of 0.5 parts for each 100 parts by weight of flour for Calcium Stearoyl Lactylate in yeast-leavened bakery products and prepared mixes for yeast-leavened bakery products.

The FDA has also determined that Sodium Stearoyl Lactylate (defined as a mixture of sodium salts of stearoyl lactylic acids and minor proportions of sodium salts of related acids) may be used safely as a direct food additive, provided that it meets the specifications of the *Food Chemicals Codex* [21 CFR 172.846]. (The *Food Chemicals Codex* specifications for Sodium Stearoyl Lactylate are stated in the section on Impurities). Furthermore, the FDA has established limits for this ingredient in food ranging from 0.2% to 0.5%, depending on the food product type. The FDA has also established a limit of 0.5 parts for each 100 parts by weight of flour for Sodium Stearoyl Lactylate in baked products, pancakes, and waffles.

Following a request by the European Commission, the Panel of Food Additives and Nutrient Sources added to Food (ANS) was asked to issue a scientific opinion on the safety of Sodium Stearoyl Lactylate and Calcium Stearoyl Lactylate when used as food additives.[4] The Panel concluded that based on the no-observed-adverse-effect-level (NOAEL) of 2200 mg/kg body weight/day Sodium Stearoyl Lactylate that was derived from a 1-year oral toxicity study in rats and an uncertainty factor of 100, an acceptable daily intake (ADI) of 22 mg/kg body weight/day for Sodium Stearoyl Lactylate and Calcium Stearoyl Lactylate, either singly or in combination, can be established. The 1-year oral study is summarized in the section on Chronic Toxicity.

Toxicokinetic Studies

Dermal Penetration

Data on the dermal penetration of the alkanoyl lactyl lactate salts reviewed in this safety assessment were not found in the published literature, nor were these data submitted.

Absorption, Distribution, Metabolism, and Excretion

In Vitro

Calcium Stearoyl Lactylate. The hydrolysis of [^{14}C]-Calcium Stearoyl Lactylate, radiolabeled at the lactylate moiety, was demonstrated in vitro using liver homogenates from rats, mice, and guinea pigs.[12] [^{14}C]-Calcium Stearoyl Lactylate was rapidly hydrolyzed to lactic acid and stearic acid. Hydrolysis was also demonstrated using whole blood from rats and mice, but no significant hydrolysis of Calcium Stearoyl Lactylate was detected using human blood. Also, in a single sample of human duodenal mucosa, [^{14}C]-Calcium Stearoyl Lactylate was rapidly hydrolyzed to stearic acid and lactic acid.

Animal

Oral: Calcium Stearoyl Lactylate. The absorption, metabolism, tissue distribution, and excretion of Calcium Stearoyl Lactylate was studied using groups of 4 male Tuck TO mice and groups of 4 male Dunkin–Hartley guinea pigs.[12] A single oral dose of an aqueous suspension of [^{14}C]-Calcium Stearoyl Lactylate (90 or 900 mg/kg body weight) was administered by gavage. Radioactivity was determined in exhaled air, urine, feces, liver, kidneys, heart, lungs, spleen, testes, and in the gastrointestinal tract. Following oral administration, rapid absorption of radioactivity from the gastrointestinal tract was observed in mice as well as in guinea pigs. More than 50% of the applied radioactivity was exhaled as $^{14}CO_2$ within 7 h. In both species, ~80% of the applied dose was exhaled as $^{14}CO_2$

Table 3. Frequency (2019) and Concentration of Use (2017) According to Duration and Type of Exposure.[8,9]

	Calcium Stearoyl Lactylate		Sodium Behenoyl Lactylate		Sodium Caproyl/Lauroyl Lactylate	
	# of Uses	Conc. (%)	# of Uses	Conc. (%)	# of Uses	Conc. (%)
Totals*/Conc. Range**	**NR**	**7**	**7**	**1.9–2**	**2**	**NR**
Duration of Use						
Leave-On	*NR*	*7*	*7*	*1.9*	*2*	*NR*
Rinse off	*NR*	*NR*	*NR*	*2*	*NR*	*NR*
Diluted for (bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation – Sprays	NR	7[a]	5[a];1[c]	NR	2[a]	NR
Incidental Inhalation – Powders	NR	NR	1[c]	NR	NR	NR
Dermal Contact	NR	NR	7	1.9–2	2	NR
Deodorant (underarm)	NR	NR	NR	NR	1[a]	NR
Hair – Non-Coloring	NR	7	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	2	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

	Sodium Cocoyl Lactylate		Sodium Isostearoyl Lactylate		Sodium Lauroyl Lactylate	
	# of Uses	Conc. (%)	# of Uses	Conc. (%)	# of Uses	Conc. (%)
Totals/Conc. Range	**4**	**NR**	**27**	**0.04-3.5**	**226**	**0.001-10**
Duration of Use						
Leave-On	*1*	*NR*	*9*	*0.04-1*	*108*	*0.001-7*
Rinse off	*3*	*NR*	*18*	*0.08-3.5*	*113*	*0.53-10*
Diluted for (bath) Use	*NR*	*NR*	*NR*	*0.5*	*5*	*NR*
Exposure Type						
Eye Area	NR	NR	NR	NR	8	NR
Incidental Ingestion	NR	NR	1	NR	NR	NR
Incidental Inhalation – Sprays	1[c]	NR	1[a];2[c]	0.04[a]	47[a];35[c]	7[a]
Incidental Inhalation – Powders	1[c]	NR	2[c]	0.5–1[b]	35[c]	0.001-6.1[b]
Dermal Contact	1	NR	20	0.5–3.5	211	0.001-10
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair – Non-Coloring	3	NR	6	0.5–2	14	0.078-7
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	3	0.5–3.5	80	1.9
Baby Products	NR	NR	NR	NR	1	NR

	Sodium Stearoyl Lactylate	
	# of Uses	Conc. (%)
Totals/Conc. Range	**358**	**0.00011-7**
Duration of Use		
Leave-On	*334*	*0.00011-7*
Rinse off	*24*	*0.00011-0.02*
Diluted for (bath) Use	*NR*	*NR*
Exposure Type		
Eye Area	20	0.18-0.2

(continued)

Table 3. (continued)

	Sodium Stearoyl Lactylate	
	# of Uses	Conc. (%)
Incidental Ingestion	5	0.00011
Incidental Inhalation – Sprays	208[a];73[c]	0.1-7[a]
Incidental Inhalation – Powders	1;5[b];73[c]	0.001-0.63[b]
Dermal Contact	354	0.00011-1.1
Deodorant (underarm)	NR	NR
Hair – Non-Coloring	3	7
Hair-Coloring	NR	NR
Nail	NR	NR
Mucous Membrane	7	0.00011
Baby Products	5	0.45

NR = Not Reported; Totals = Rinse-off + Leave-on + Diluted for Use Product Uses.
[a]It is possible that these products may be sprays, but it is not specified whether the reported uses are sprays.
[b]It is possible that these products may be powders, but it is not specified whether the reported uses are powders.
[c]Not specified whether a powder or spray, so this information is captured for both categories of incidental inhalation
Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum of total uses.

Table 4. Alkanoyl Lactyl Lactate Salts Not Reported to Be in Use in Cosmetic Products.[8,9]

Ingredients
Sodium Caproyl Lactylate
Sodium Cupheoyl Lactylate
Sodium Oleoyl Lactylate

within 48 h. Most of the remaining radioactivity was excreted in the urine within 24 h after dosing. Only minor amounts were detected in the feces of both species. No relevant differences were detected between the 90 and 900 mg/kg doses of [^{14}C]-Calcium Stearoyl Lactylate. Approximately 2 % (in mice) or 6 % (in guinea pigs) of the administered dose remained in the tissues, mainly in the liver and gastrointestinal tract. Only traces of radioactivity were found in other organs (kidneys, lungs, testes, spleen, and heart). Thin layer chromatography of the urine of mice and guinea pigs indicated that lactic acid is a metabolite of Calcium Stearoyl Lactylate. Furthermore, the authors suggested that the additional radioactivity in the urine of treated animals is lactylate (i.e., without the stearic acid residue).

Toxicological Studies

Acute Toxicity Studies

Oral

Calcium Stearoyl Lactylate. In an acute oral toxicity study involving male rats (strain not stated), an oral LD_{50} of 25 g/kg body weight was reported for Calcium Stearoyl Lactylate.[2] Details relating to the test protocol were not included.

Sodium Isostearoyl Lactylate. The acute oral toxicity of Sodium Isostearoyl Lactylate was evaluated using white rats (number not stated).[5] Administration of a single oral dose was followed by a 14-day observation period. An LD_{50} of > 6.1 g/kg was reported.

Sodium Lauroyl Lactylate. In an acute oral toxicity study in which male rats (number not stated) were dosed orally with Sodium Lauroyl Lactylate, the LD_{50} was 6.81 g/kg.[2] The test protocol was not stated.

The acute oral toxicity of Sodium Lauroyl Lactylate was also evaluated using male and female rats (numbers and strains not stated).[13] The doses administered orally (dosing method not stated) ranged from 2.4 g/kg to 6 g/kg. Additional details were not included. The oral LD_{50} was estimated to be 4.88 g/kg.

Sodium Stearoyl Lactylate. In an acute oral toxicity study involving male rats (strain not stated), an oral LD_{50} of 25 g/kg body weight was reported for Sodium Stearoyl Lactylate.[2] Details relating to the test protocol were not included.

Short-Term, Subchronic, and Chronic Toxicity Studies

The short-term, subchronic, and chronic toxicity studies on alkanoyl lactyl lactate salts that are summarized below are presented in more detail in Table 5.

Sodium Caproyl/Lauroyl Lactylate (25 µl, in acetone-olive oil (AOO) vehicle) was applied to the ears of 4 mice of the CRL:NMRI BR strain at a concentration of 25% or 50% on 3 consecutive days.[13] There was no evidence of systemic toxicity. (Appropriately, results from this local lymph node assay (LLNA) are presented in the section on Sensitization). Calcium Stearoyl Lactylate was evaluated in short-term oral toxicity studies at dietary concentrations ranging from 0.5% to 12.5%.[14] Groups of up to 32 rats were tested. Increased liver weight was observed at concentrations of 2% and 12.5%, but not at 0.5% (43-day feeding study), 5% and 7.5% in the diet (1-month feeding study), and at 5% in the diet (4-week feeding study). However, in other feeding studies at 5% in the diet (27 days, 32 days, and duration unspecified), liver weight/histology was normal. Kidney histology was normal in a feeding study on 0.5% Calcium Stearoyl Lactylate in which the duration was not specified. In short-term feeding studies on Sodium Stearoyl Lactylate, a transient increase in liver weight was observed in 20 rats fed 5% in the diet for 28 days, and organ weights were normal in a dog fed up to 15% in the diet for 1 month.

The subchronic oral toxicity of Calcium Stearoyl Lactylate was evaluated in a study in which groups of 10 male and 10 female rats were fed dietary concentrations of 0.5%, 5%, and 12.5% for 98 days.[14] There was no evidence of histological abnormalities in internal organs, but lipogranulomata in adipose tissue were detected at the 12.5% concentration. Relative weights of the liver, spleen, and brain were also increased after feeding with 12.5% Calcium Stearoyl Lactylate. The Joint FAO/WHO Expert Committee on Food Additives noted that the appearance of lipogranulomata and increased liver weight are related to excessive intake of abnormal proportions of long-chain fatty acids. Groups of 10 male and 10 female rats (strain not stated) were fed Sodium Stearoyl Lactylate in the diet at concentrations of 0.5%, 5%, and 12.5% for 102 days. The results of gross and histopathological evaluations were normal.

In a chronic study, groups of 5 rats were maintained on diets containing 8 to 22% Calcium Stearoyl Lactylate for periods of up to 6 months.[14] Mortality was high (number of deaths not reported) at concentrations of ≥ 20%. Relative liver weights were normal at a saturated to unsaturated (S:U) fatty acid ratio of 0.6, but increased with higher ratios in the absence of histopathological abnormalities. When the experiment was repeated using 40 male and 40 female rats fed 25% Calcium Stearoyl Lactylate in the diet, all of the animals developed severe lipogranulomata. In a 1-year chronic oral toxicity study performed in accordance with Organization for Economic Co-operation and Development (OECD) Test Guideline (TG) 452, groups of 60 Wistar rats were fed a diet that yielded doses of Sodium Stearoyl Lactylate up to 2214 mg/kg/day (males) and 2641 mg/kg/day (females).[15] No treatment-related toxic effects were observed, and NOAELs of 2214 mg/kg/day and 2641 mg/kg/day were reported for males and females, respectively. Results relating to tumorigenicity in this study are included in the section on Carcinogenicity.

There were no test substance-related gross or microscopic changes in 4 Beagle dogs fed a diet containing 7.5% Calcium Stearoyl Lactylate for 2 years.[14]

Developmental and Reproductive Toxicity

Data on the developmental and reproductive toxicity of the alkanoyl lactyl lactate salts reviewed in this safety assessment were not found in the published literature, and unpublished data were not submitted.

Genotoxicity Studies

In Vitro

Calcium Stearoyl Lactylate. The genotoxicity of Calcium Stearoyl Lactylate (in benzene), with and without metabolic activation, was evaluated in the Ames test using the following *Salmonella typhimurium* strains: TA92, TA94, TA98, TA100, TA1535, and TA1537.[16] Doses of the test substance at up to 300 µg/plate were tested. Cytotoxicity data on the test substance were not included. Calcium Stearoyl Lactylate was non-genotoxic with and without metabolic activation.

In a chromosome aberration test involving a Chinese hamster fibroblast cell line, the genotoxicity of Calcium Stearoyl Lactylate (in ethanol) was evaluated at concentrations up to 63 µg/ml (highest non-cytotoxic dose) without metabolic activation.[16] One hundred metaphases per concentration were analyzed for polyploid cells and structural chromosomal aberrations. Chromosome and chromatid gaps were included in the evaluation. Calcium Stearoyl Lactylate did not cause polyploidy or clastogenic effects.

Sodium Caproyl/Lauroyl Lactylate. The genotoxicity of Sodium Caproyl/Lauroyl Lactylate (in dimethyl sulfoxide (DMSO)) was evaluated in the Ames test using the following *S. typhimurium* strains, with and without metabolic activation: TA97a, TA98, TA100, TA102, and TA1535.[13] The test substance was tested at doses up to 502 µg/plate, considering that doses of 1500 and 5000 µg/plate were cytotoxic. Water and DMSO served as the negative and solvent controls, respectively. The positive controls were sodium azide, benzo[a]pyrene, 4-nitro-*O*-phenylenediamine, and 2-aminoanthracene. Sodium Caproyl/

Table 5. Short-Term, Subchronic, and Chronic Toxicity Studies.

Ingredient	Animals	Protocol	Results
Short-Term Dermal Toxicity Study			
Sodium Caproyl/Lauroyl Lactylate (25% or 50% in AOO vehicle))	4 mice (CRL:NMRI BR strain); 2 tested per concentration	Range-finding test that was performed prior to local lymph node assay (LLNA). Because test substance was highly viscous, application in undiluted form was not possible. Based on solubility, maximum available concentration was 50%. Test substance (25 μl) applied to ears on 3 consecutive days	None of the animals died. No evidence of systemic toxicity or significant effects on body weight.[13]
Short-Term Oral Studies			
Calcium Stearoyl Lactylate (0.5%, 2%, and 12.5% in the diet)	Groups of 5 male rats (strain not stated)	Feeding for 43 days	No deaths. Increased weight of liver, heart, brain, stomach, and testes (at 12.5% concentration). Increased relative liver weight (at 2% concentration). Reduced growth (at 2% and 12.5% concentrations).[14]
Calcium Stearoyl Lactylate (0.1%, 1%, 2%, 3%, 4%, 5%, and 7.5% in diet)	Groups of 25 rats (strain not stated)	Feeding for 1 month	Growth retardation and increased relative liver weight at concentrations of 5% and 7.5%.[14]
Calcium Stearoyl Lactylate (5% in diet)	Groups of 10 rats (strain not stated)	Paired feeding for 27 days	Decreased food efficiency. Increased liver weight, but no effects on liver histopathology, except slight increase in glycogen.[14]
Calcium Stearoyl Lactylate (5% in diet)	Groups of 12 rats (strain not stated)	Feeding for 4 weeks	Liver weights of test group greater than those of controls fed diet without Calcium Stearoyl Lactylate. No other pathological changes observed.[14]
Calcium Stearoyl Lactylate (5% in diet)	30 male rats (strain not stated)	Feeding for 32 days. Groups of 5 killed at days 32, 60, 90, and 140.	Relative liver weights were normal.[14]
Calcium Stearoyl Lactylate (5% in diet)	Groups of 5 male rats (strain not stated)	Short-term (duration not stated) feeding study	Slightly reduced body weight. Mortality was not affected by treatment. Liver histology revealed no abnormalities.[14]
Calcium Stearoyl Lactylate (5% in diet)	Groups of 32 male rats (strain not stated)	Short-term (duration not stated) feeding study	Relative liver weights less than that of control rats fed diet without Calcium Stearoyl Stearate.[14]
CalciumStearoyl Lactylate (0.5% in diet)	Groups of 10 male and 10 female rats (strain not stated)	Short-term feeding study (paired feeding, duration not stated)	Histology of livers and kidneys normal. X-rays of femurs comparable.[14]
Sodium Stearoyl Lactylate (5% in diet)	20 male rats (strain not stated)	Feeding for 28 days. Groups of 5 killed at days 32, 60, 90, and 140.	Relative liver weights slightly elevated. Liver weights normal after 90 days.[14]
Sodium Stearoyl Lactylate (7.5%, 12.5%, and 15% in diet)	1 dog	Sodium Stearoyl Lactylate at 7.5% in the diet for 1 month, followed by 12.5% in the diet for 2 weeks, and followed by 15% in the diet for an additional month	No evidence of hematological changes. Organ weights and microscopic appearance of the tissues were normal.[14]

(continued)

Table 5. (continued)

Ingredient	Animals	Protocol	Results
Subchronic Oral Studies			
Calcium Stearoyl Lactylate (0.5%, 5%, and 12.5% in the diet)	Groups of 10 male and 10 female rats (strain not stated)	Feeding in the diet for 98 days	Slight growth retardation at 5% in diet and significant growth retardation at 12.5% in diet. Increased relative liver, stomach, heart, spleen, and brain weights at 12.5% in diet. No evidence of histological abnormalities in kidneys, brain, lungs, spleen, or liver at 12.5% in diet, but lipogranulomata detected in adipose tissue. No increase in stainable liver fat. Urinalyses, blood morphology, and radiological studies of femurs were normal. Joint FAO/WHO Expert Committee on food Additives noted that the appearance of lipogranulomata and increased liver weight are related to excessive intake of abnormal proportions of long-chain fatty acids.[14]
Sodium Stearoyl Lactylate (0.5%, 5%, and 12.5% in the diet)	Groups of 10 male and 10 female rats (strain not stated)	Feeding in the diet for 102 days	When compared to controls fed diet without Sodium Lauroyl Lactylate, there were no abnormalities regarding urinalyses, hematology, or fecal excretion. Liver, brain, stomach, and spleen weights increased at 12.5% in diet. Results of gross and histopathological evaluations were normal.[14]
Chronic Oral Studies			
Calcium Stearoyl Lactylate (8% to 22% in the diet)	Groups of 5 rats (strain not stated)	Feeding in diet for 6 months.	Growth depression at ≥ 16% in diet. High mortality (deaths not reported) at ≥ 20% in diet. Relative liver weights normal at saturated to unsaturated (S: U) fatty acid ratio of 0.6 (17% fat plus 3% Calcium Stearoyl Lactylate), but increased with higher ratios. Lipogranulomata appeared at ratios of > 1.4. Disappearance of lipogranulomata in 4 to 6 months, after restoration to diet containing 20% fat. Histopathological abnormalities not observed.[14]
Calcium Stearoyl Lactylate (25% in the diet)	40 male and 40 female rats (strain not stated)	Feeding in diet for up to 6 months.	All animals developed severe lipogranulomata, with high mortality (deaths not reported). Growth rate was depressed. When animals were placed on diet containing 20% fat (half corn oil and half lard), recovery of growth rate was noted.[14]
Calcium Stearoyl Lactylate (7.5% in the diet)	2 groups of 4 Beagle dogs (1 male, 3 females per group; one group was control)	Feeding in diet for 2 years	No noteworthy differences when 2 groups were compared. Urinalysis and hematological findings and liver weights were normal. No gross or microscopic changes observed.[14]
Sodium Stearoyl Lactylate (1.25%, 2.5%, and 5% in diet)	3 groups of 60 Wistar WU rats (Crl:WI(Wu), outbred; 30 males and 30 females per group)	Feeding in diet for 1 year	Hematological, clinical chemistry, and urinalysis findings were normal. NOAEL = 2214 mg/kg/day (males) and 2641 mg/kg/day (females).[15]

Lauroyl Lactylate was non-genotoxic in all of the bacterial strains that were tested. The positive controls were genotoxic.

In Vivo

In vivo genotoxicity data on the alkanoyl lactyl lactate salts reviewed in this safety assessment were not found in the published literature, and unpublished data were not submitted.

Carcinogenicity Studies

Sodium Stearoyl Lactylate

As described earlier, a 1-year chronic oral toxicity study was performed in accordance with OECD TG 452.[15] Three groups of 60 Wistar rats (30 males and 30 females per group) were fed a diet that yielded mean daily Sodium Stearoyl Lactylate intakes of 558, 1115, and 2214 mg/kg/day (males) and 670, 1339, and 2641 mg/kg/day (females); the corresponding diet concentrations were 1.25%, 2.5%, and 5%, respectively. The negative control group was fed diet only. At histopathological examination, the incidence of endometrial stromal polyps in the uterus was reported as follows: 1 control female rat, 2 female rats fed 1.25% Sodium Stearoyl Lactylate in the diet, 6 female rats fed 2.5% in the diet, and 6 female rats fed 5% in the diet. However, these data lack statistical significance, and there is an absence of biological evidence to suggest a mechanism for the slightly higher incidence in the groups fed 2.5% and 5%. Furthermore, a comparison of these data with historical incidences of this tumor type (up to 10% in control rats of 1-year studies in the laboratory conducting this study) demonstrated that endometrial stromal polyps are common in rats of this strain and age. It was concluded that the endometrial polyps observed in females fed Sodium Stearoyl Lactylate in the diet were not treatment-related.

Other Relevant Studies

Protein Binding

Sodium Stearoyl Lactylate. Sodium Stearoyl Lactylate was mixed with gluten (protein in wheat, barley, and rye) in the presence of water.[17] Approximately 49% of the Sodium Stearoyl Lactylate remained bound until it was released by protease digestion of the protein. Details relating to the protocol for this experiment were not included. However, using a Tissue Metabolism Simulator Skin Sensitization model (TIMES-SS), it was determined that Sodium Lauroyl Lactylate is a non-binder to skin proteins, despite being a weak sensitizer in the LLNA (see Sensitization section).[18] TIMES-SS is defined as an expert system describing structure-toxicity and structure–metabolism relationships through a number of transformations simulating skin metabolism and interaction of the generated reactive metabolites with skin proteins.

Dermal Irritation and Sensitization Studies

The skin irritation and sensitization studies summarized below are presented in detail in Table 6

Irritation

Sodium Caproyl/Lauroyl Lactylate was considered non-corrosive when the irritation/corrosive potential of this ingredient was evaluated using a tissue model that consisted of human-derived epidermal keratinocytes (EpiDerm® tissue model).[13] The skin irritation potential of alkanoyl lactyl lactate salts has been evaluated in the following experiments involving albino rabbits:[2] undiluted Calcium Stearoyl Stearate (nonirritating), 10% Sodium Lauroyl Lactylate (nonirritating), and undiluted Sodium Stearoyl Lactylate (nonirritating; primary irritation index (PII) = 0.5 in 2 studies).[2,19] Sodium Caproyl/Lauroyl Lactylate (in AOO vehicle) caused erythema and an increase in ear thickness in 4 mice (CRL:NMRI BR strain) when tested at concentrations of 25% and 50%.[13] In a skin irritation test on Sodium Isostearyl Lactylate involving 6 albino rabbits, the PII was 7.17 (severe irritation) for the undiluted ingredient and 1.13 (slight irritation) for 15% Sodium Isostearyl Lactylate.[5]

The skin irritation potential of Sodium Stearoyl Lactylate was evaluated using 51 subjects.[20] Twenty-five and 26 subjects were patch tested with 2% and 5% Sodium Stearoyl Lactylate in petrolatum, respectively. Details relating to the test protocol were not included. Sodium Stearoyl Lactylate was classified as having skin irritation potential. A diluted hair styling product (Calcium Stearoyl Lactylate effective concentration = 2.5%) was classified as a skin irritant in a study involving 54 subjects.[21] In 4 separate skin irritation studies, each involving 50 subjects, a hair molding cream containing 7% Calcium Stearoyl Lactylate was classified as nonirritating to the skin.[22-25]

Sensitization

The skin toxicity of Sodium Stearoyl Lactylate was investigated using reconstructed human epidermis (RHE) and detection of the inflammation markers interleukin (IL)-1α and IL-8.[26] Sodium Stearoyl Lactylate was predicted to be an allergen based on the results of this assay. The LLNA was used to evaluate the sensitization potential of Sodium Caproyl/Lauroyl Lactylate and Sodium Lauroyl Lactylate using the following test concentrations (in AOO vehicle): 2.5%, 5%, 10%, 25%, or 50%.[13] Sodium Caproyl/Lauroyl Lactylate was classified as a weak-moderate sensitizer (EC3 = 12.4%; EC3 = 9.3%),[13] and Sodium Lauroyl Lactylate was classified as a

Table 6. Skin Irritation and Sensitization Studies on Alkanoyl Lactyl Lactate Salts.

Test Substance	Animals/Subjects/Cells	Test Protocol	Results
Irritation (In Vitro)			
Sodium Caproyl/Lauroyl Lactylate	EpiDerm® tissue model: normal human-derived epidermal keratinocytes cultured to form multi-layered highly differentiated model of human epidermis	Test substance (~ 25 mg) applied, with 25 µl of deionized water, topically to the model for 3 min to 1 h. Cell viability measured by dehydrogenase conversion of 3-(4,5-dimethylthiazole 2-yl)-2,5-diphenyltetrazoli-umbromide (MTT) into blue formazan salt. Optical density of extracted formazan determined via spectrophotometry. Mean formazan production (irritation parameter) calculated from decrease in absorbance values when compared to negative control (deionized water)	Test substance considered non-corrosive because following criteria for non-corrosive substance were fulfilled: formazan production after 3 min of incubation was > 50% of negative control, and formazan production after 1 h of incubation was > 15% of negative control. Positive control (potassium hydroxide) caused clear corrosive effects after both treatment intervals.[13]
Irritation (Animal)			
Calcium Stearoyl Lactylate (undiluted)	Albino rabbits (number not stated)	Test protocol not stated	Nonirritant.[2]
Sodium Caproyl/Lauroyl Lactylate (25% or 50% in AOO vehicle). [Because test substance was highly viscous, maximum available concentration was 50%].	2 mice/group (CRL:NMRI BR strain)	Range-finding test performed prior to LLNA. Test substance (25 µl) applied on 3 consecutive days. Measurement of ear thickness on day 1 prior to application and on days 3 (~ 48 h after first dose) and 6.	Erythema observed at both concentrations on days 1 to 6 (maximum score of 2), but reaction not considered significant. Increased ear thickness also observed at both concentrations. Maximum value for ear thickness (18.2%) observed at 50% concentration. Test substance did not cause significant skin irritation at either test concentration.[13]
Sodium Isostearoyl Lactylate (undiluted and 15% concentration)	6 albino rabbits	Test substance (0.5 ml) applied for 24 h under 1″ × 1″ occlusive patch secured with adhesive tape. Application to abraded and intact skin. Reactions scored at 24 h and at 48 h later. PII calculated (scale not stated)	Primary irritation index (PII) = 7.17 (undiluted ingredient) and 1.13 (15% concentration). Individual irritation scores not reported.[5]
Sodium Lauroyl Lactylate (10%)	Albino rabbits (number not stated)	Test protocol not stated	Nonirritant.[2]
Sodium Stearoyl Lactylate (undiluted)	Albino rabbits (number not stated)	Test protocol not stated. PII calculated (scale not stated)	PII = 0.5.[2]
Sodium Stearoyl Lactylate (undiluted)	6 albino rabbits	Undiluted Sodium Stearoyl Lactylate (0.5 g moistened with physiological saline) applied for 24 h under 1 in2 surgical gauze patch to the saddle area (abraded and intact skin). Each patch secured with adhesive tape, rubber dental damming, and an outer layer of gauze. Reactions scored at 24 h and 72 h.	At 24 h, slight erythema at 5 intact and 5 abraded sites. At 72 h, very slight erythema only at 1 intact site and 1 abraded site. PII of 0.50 reported, and Sodium Stearoyl Lactylate was neither classified as a primary skin irritant nor a corrosive material.[19]

(continued)

Table 6. (continued)

Test Substance	Animals/Subjects/Cells	Test Protocol	Results
Irritation (Human)			
Hair styling product containing 5% Calcium Stearoyl Lactylate (50% in distilled water; effective concentration = 2.5%)	54 subjects (17 males, 37 females)	Semi-occlusive patch containing 0.2 ml of the test substance applied for 48 h along paraspinal region of back. Dose per cm^2 not stated. Sodium lauryl sulfate and distilled water served as positive and negative controls, respectively.	Test substance produced slight to mild erythema (scores of + to 1) in 18 of the subjects tested. Results also indicated that negative control caused slight to moderate skin irritation in 7 subjects. The positive control caused skin irritation in 49 subjects. The diluted hair styling product was classified as having skin irritation potential that is consistent with the product type (styling products).[21]
Hair molding cream containing 7% Calcium Stearoyl Lactylate	50 subjects (18 males, 32 females)	Product (20 µl) applied for 24 h to the ventral forearm using Finn chambers (8 mm). Reactions scored at 24 h, 48 h, and 72 h post-application. Sodium dodecyl sulfate (2%) and demineralized water served as positive and negative controls, respectively.	The mean 24-h irritation score for the product was not statistically significantly different ($p = 1$) from the negative control, and the product was classified as a nonirritant.[22]
Hair molding cream containing 7% Calcium Stearoyl Lactylate	50 subjects (14 males, 36 females)	Same protocol (immediately above)	The mean 24-h irritation score for the product was not statistically significantly different ($p = 1$) from the negative control, and the product was classified as a nonirritant.[23]
Hair molding cream containing 7% Calcium Stearoyl Lactylate	50 subjects (18 males, 32 females)	Same protocol	The mean 24-h irritation score for the product was not statistically significantly different ($p = 1$) from the negative control, and the product was classified as a nonirritant.[24]
Hair molding cream containing 7% Calcium Stearoyl Lactylate	50 subjects (19 males, 31 females)	Same protocol	The mean 24-h irritation score for the product was not statistically significantly different ($p = 0.13$) from the negative control, and the product was classified as a nonirritant.[25]
Sodium Lauroyl Lactylate (2% and 5% in petrolatum)	25 tested with 2%; 26 tested with 5%	Protocol details not state	Fifteen negative reactions and 10 doubtful reactions (probably irritant) to 2% Sodium Lauroyl Lactylate. Eleven negative reactions and 14 doubtful reactions to 5% Sodium Lauroyl Lactylate (also, + reaction in 1 subject). Study results indicated that Sodium Lauroyl Lactylate has skin irritation potential.[20]

(continued)

Table 6. (continued)

Test Substance	Animals/Subjects/Cells	Test Protocol	Results
Sensitization (In Vitro)			
Sodium Stearoyl Lactylate reconstructed human epidermis (RHE)		In vitro assay used to assess skin toxicity was detection of the inflammation markers interleukin (IL)-1α and IL-8. It was noted that inflammation markers have been released in the growth medium of RHE as a consequence of the immune response to the presence of surfactants. Value for IL release of >1 corresponds to production of IL-1α or IL-8 induced by presence of surfactant. Il-α is expressed as an intracellular protein; it accumulates in keratinocytes and is released by injured cells or after membrane alteration. IL-8 is a secondary inflammatory cytokine, secreted in response to IL-1α release during inflammation. Relative inflammation potency was evaluated by measuring release of interleukins by flow cytometry. Threshold for IL-1α and IL-8 release was defined as 3 times that of the control (untreated RHE)	IL-8/IL-1α ratio was 5.85 (i.e., > 1). Value for release of IL-8 (3.407) was above the threshold of 3, whereas the value for the release of IL-1α (0.582) was not. Chemicals applied to the skin can be considered allergens when the extracellular IL-8 > 1L-1α, and as irritants when extracellular IL-8 < IL-1α. Sodium Stearoyl Lactylate was predicted to be an allergen.[26]
Sensitization (Animal)			
Sodium Caproyl/Lauroyl Lactylate (2.5%, 5%, 10%, 25%, and 50% in AOO vehicle)	Groups of 4 CRL:NMRI BR mice	LLNA (OECD TG 429). Mice were treated topically on dorsum of both ears with 25 μl of test substance or equal volume of vehicle alone. At day 6 after initiation of exposure, all mice injected (tail vein) with phosphate buffered saline containing tritiated thymidine. Mice killed 5 h later, and draining lymph nodes excised and pooled for each experiment. Test substance concentration required to produce stimulation of proliferation of at least three-fold greater when compared to controls (i.e., EC3 value) calculated to provide measure of relative skin sensitizing potential.	EC3 (calculated by linear interpolation) = 12.4%, classifying test substance as a weak sensitizer. EC3 (calculated based on equation of regression curve) = 9.3%, classifying test substance as moderate sensitizer. Study results indicated that, at the concentrations tested in AOO, Sodium Caproyl/Lauroyl Lactylate has sensitization potential (sensitizer). Collectively, the EC3 values calculated using the 2 methods (dose response and regression curve) classify Sodium Caproyl/Lauroyl Lactylate as a weak-moderate sensitizer in the LLNA.[13]
Sodium Lauroyl Lactylate (2.5%, 5%, 10%, 25%, and 50% in AOO vehicle)	Groups of 4 CBA/Ca female mice	LLNA (OECD TG 429). Protocol similar to that stated immediately above, except for the mouse strain used and intravenous injection on day 5.	EC3 = 15%, classifying Sodium Lauroyl Lactylate as a weak sensitizer.[27,28]
Sodium Lauroyl Lactylate trade name material	Groups of CBA female mice	LLNA (OECD TG 429)	EC3 = 15%, classifying Sodium Lauroyl Lactylate as a weak sensitizer.[29]

(continued)

Table 6. (continued)

Test Substance	Animals/Subjects/Cells	Test Protocol	Results
Sodium Lauroyl Lactylate (0.5%)	15 Dunkin–Hartley guinea pigs (10 treated, 5 controls)	Guinea pig maximization test (OECD TG 406). Injection and dermal doses not stated. Challenge concentration of 0.5%.	Weak sensitizer.[27]
A silicone antifoam emulsion containing 2% Sodium Stearoyl Lactylate (75% dilution; effective test concentration = 1.5% Sodium Stearoyl Lactylate)	20 adult female guinea pigs (Dunkin–Hartley strain). Ten guinea pigs (treated with sterile water, solvent) served as controls.	Guinea pig model using methods of Buehler. During induction, test substance (0.5 ml) applied to left flank for 6 h, under a 20 × 20 mm gauze patch secured with adhesive strapping. At 24 h after patch removal, reactions scored. Procedure repeated at weekly intervals (days 8 to 9 and 16 to 15 of study). Challenge phase initiated on day 29. A 20 × 20 mm absorbent patch containing test substance (0.5 ml) applied (secured with adhesive strapping) for 6 h to right flank. A patch containing sterile water (control) also applied to right flank. At 24 h and 48 h after patch removal, reactions scored.	No reactions at test or control sites during induction or following challenge patch application. Test substance was a nonsensitizer in guinea pigs.[30]

weak sensitizer (EC3 = 15%).[27,28] An EC3 of 15% was also reported for a Sodium Lauroyl Lactylate trade name material in the LLNA.[29] Sodium Lauroyl Lactylate (challenge concentration = 0.5%; injection and dermal induction doses not stated) was classified as a weak sensitizer in the guinea pig maximization test (10 guinea pigs).[27] A silicone antifoam emulsion containing Sodium Stearoyl Lactylate (75% dilution; effective test concentration = 1.5 %) Sodium Stearoyl Lactylate) was a nonsensitizer in guinea pigs.[30]

Computational Analyses/Predictions

The modeling of skin sensitization data on a number of diverse compounds, including data on Sodium Stearoyl Lactylate, and calculated descriptors was performed to develop multiple predictive classification models.[31] The following 2 automated procedures were used to select significant and independent descriptors in order to build the models: (1) D-optimal design to select optimal members of the training and test sets and (2) k-Nearest Neighbor classification (kNN) method along with Genetic Algorithms (GA-kNN Classification). The EC3 values (from LLNAs) of the compounds were ranked quantitatively according to their potencies. Class 1 signified extreme/strong/moderate sensitizers (EC3 < 10%) and Class 2 signified weak/nonsensitizers (EC3 ≥ 10%). Sodium Stearoyl Lactylate was identified as a Class 2 sensitizer, and the LLNA data on this chemical are included in the preceding section. Of the 5 models developed, 4 placed Sodium Stearoyl Lactylate in Class 2, and 1 placed the chemical in Class 1. Thus, the consensus prediction based on the models 1–5 was Class 2.

Ocular Irritation Studies

In Vitro

Sodium Caproyl/Lauroyl Lactylate. The ocular irritation potential of Sodium Caproyl/Lauroyl Lactylate was evaluated using the bovine corneal opacity and permeability test method for identifying ocular corrosives and severe irritants (OECD TG 437).[13] Corneas were exposed to the test substance (750 µl; 10% solution diluted in 0.9% sodium chloride solution) for 10 min, and exposure was followed by rinsing with and without phenol red. Exposure was followed by a 2-h observation period. A mean in vitro irritation score (for cornea) of 46.308 for the 10% solution was reported, classifying the solution as non-corrosive.

Animal

Calcium Stearoyl Lactylate, Sodium Lauroyl Lactylate, Sodium Stearoyl Lactylate, and Sodium Isostearoyl Lactylate. In an ocular irritation study involving 6 albino rabbits, Sodium Isostearoyl Lactylate (undiluted or 15% concentration, 0.1 ml) was instilled into one eye.[5] Ocular reactions were scored at 24 h, 48 h, and 72 h post-instillation. The undiluted ingredient was irritating to the eyes, whereas 15% Sodium Isostearoyl Lactylate was not. When other alkanoyl lactyl lactate salts were

tested according to the same procedure using groups of 6 albino rabbits, the results were as follows: undiluted Calcium Stearoyl Lactylate (nonirritating), 10% Sodium Lauroyl Lactylate (nonirritating), and undiluted Sodium Stearoyl Lactylate (nonirritating, 2 tests).[2] In another study, undiluted Sodium Lauroyl Lactylate (0.1 g) was applied to the right eye of each of 6 albino rabbits according to the same procedure.[19] Mild conjunctivitis was observed in 3 of 6 rabbits, and Sodium Lauroyl Lactylate was classified as a nonirritant in rabbit eyes.

Clinical Studies

Case Reports

Sodium Stearoyl Lactylate. A female patient with a 20-year history of palmoplantar pustulosis and chronic hand and foot dermatitis had a positive patch test reaction (score not stated) to 5% Sodium Stearoyl Lactylate in petrolatum.[20] The patient was patch tested with ingredients of the cosmetic products that she had been using, and Sodium Stearoyl Lactylate was the only ingredient that caused a positive reaction. When the patient was re-tested with a 2% Sodium Stearoyl Lactylate (in petrolatum) preparation, a + reaction was observed. A use test that involved 2 daily applications of 5% Sodium Stearoyl Lactylate in petrolatum to the lower arm was also performed. Small papules and itching resulted after a few days, and the reaction was clearly positive on day 18. The control groups consisted of 51 subjects patch tested with 2% or 5% Sodium Stearoyl Lactylate in petrolatum, and Sodium Stearoyl Lactylate was classified as having skin irritation potential in this skin irritation test. (This study was described in the Irritation and Sensitization section). The authors noted that the reproducible patch test and use test reactions are considered to be of an allergic nature, because of the clinical picture, patient history, and patch test results for the 51 controls. Furthermore, the authors noted that this patient seemingly belongs to a group of patients with sensitive, labile skin that easily contracts new allergies.

Summary

The safety of 10 alkanoyl lactyl lactate salts as used in cosmetics is reviewed in this safety assessment. According to the *Dictionary*, all of these ingredients are surfactants, while some have additional possible functions reported.

According to 2019 VCRP data, Sodium Stearoyl Lactylate is reported to be used in 358 cosmetic products (334 leave-on and 24 rinse-off products). Of the alkanoyl lactyl lactate salts that are reviewed in this safety assessment, this is the greatest reported use frequency. The results of a concentration of use survey conducted by the Council in 2017 indicate that Sodium Lauroyl Lactylate is being used at maximum use concentrations up to 10% in skin cleansing products (rinse-off products).[9] Calcium Stearoyl Lactylate, Sodium Lauroyl Lactate, and Sodium Stearoyl Lactylate are being used at maximum use concentrations up to 7% in leave-on products (tonics, dressings, and other hair grooming aids); this is the highest maximum use concentration in leave-on products that is being reported for the alkanoyl lactyl lactate salts. The highest maximum use concentration in leave-on cosmetic products that are applied directly to the skin is 6.1% for Sodium Lauroyl Lactylate in body and hand products that are not sprayed.

Sodium Stearoyl Lactylate, the most frequently used alkanoyl lactyl lactate salt in cosmetic products, can be manufactured by base-catalyzed esterification of lactic acid and stearic acid. *Food Chemicals Codex* and European Commission specifications on the composition of this ingredient as a food additive are available, and the same is true for Calcium Stearoyl Lactylate.

In a single sample of human duodenal mucosa in vitro, [^{14}C]-Calcium Stearoyl Lactylate was rapidly hydrolyzed to stearic acid and lactic acid. In an oral dosing study on [^{14}C]-Calcium Stearoyl Lactylate involving mice and guinea pigs, ~80% of the administered dose was exhaled as $^{14}CO_2$ within 48 h and most of the remaining radioactivity was excreted in the urine within 24 h post-dosing. Approximately 2% (in mice) and 6% (in guinea pigs) of the administered dose remained in the tissues, mainly in the liver and gastrointestinal tract.

In acute oral toxicity studies involving male rats, an oral LD_{50} of 25 g/kg body weight was reported for Sodium Stearoyl Lactylate and for Calcium Stearoyl Lactylate. The following other acute oral LD_{50} values have been reported: > 6.1 g/kg (Sodium Isostearoyl Lactylate, in rats), 6.81 g/kg (Sodium Lauroyl Lactylate, in male rats), and 4.88 g/kg (Sodium Lauroyl Lactylate, in male and female rats).

When Sodium Caproyl/Lauroyl Lactylate was applied to the ears of mice at concentrations of 25% and 50% (2 mice/group) on 3 consecutive days, none of the animals died, and there was no evidence of systemic toxicity.

Some of the findings reported in short-term feeding studies on Calcium Stearoyl Lactylate (rats) at various concentrations were: no deaths (at 12.5% in diet – 43 days), increased relative liver weight (at 5% and 7.5% in the diet – 1 month), no significant liver pathology (at 5% in diet – 27 days), increased liver weight (at 5% in diet – 4 weeks), relative liver weights normal (at 5% in diet – 32 days), liver histology normal (at 5% in diet – duration unknown), relative liver weights normal (at 5% in diet – duration unknown), and kidney histology normal (0.5% in diet – duration unknown). A transient increase in liver weights was observed in rats fed 5% Sodium Stearoyl Lactylate in the diet for 28 days, and organ weights were normal in a dog fed up to 15% Sodium Stearoyl Lactylate in the diet for 1 month.

In a subchronic oral toxicity study, groups of 20 male and female rats were fed Calcium Stearoyl Lactylate at dietary concentrations up to 12.5% for 98 days. Increased relative

weights of major organs were observed after feeding with 12.5% Calcium Stearoyl Lactylate. There was no evidence of histological abnormalities in major organs, but lipogranulomata was observed in the adipose tissue of animals fed a dietary concentration of 12.5%. It has been noted that the appearance of lipogranulomata and the increased relative liver weight reported were related to the excessive intake of abnormal portions of long-chain fatty acids. The results of gross and histopathological evaluations of groups of 20 rats fed up to 12.5% Sodium Stearoyl Lactylate in the diet for 102 days were normal.

In a chronic oral toxicity study in which groups of 5 rats were fed diets containing 8% to 22% Calcium Stearoyl Lactylate for periods of up to 6 months, mortality was high (number of deaths not reported) at concentrations of ≥ 20%. Histopathological abnormalities were not observed in this study. Neither gross nor microscopic changes were observed in a 2-year study in which 4 Beagle dogs were fed 7.5% Calcium Stearoyl Lactylate in the diet. Liver weights were in the normal range. A 1-year chronic oral toxicity study involved groups of 60 male and female rats fed a diet containing Sodium Stearoyl Lactylate at concentrations up to 5%. The NOAELs for Sodium Stearoyl Lactylate were 2214 mg/kg/day for males and 2641 mg/kg/day for females, which were the highest doses tested).

Sodium Caproyl/Lauroyl Lactylate and Calcium Stearoyl Lactylate were not genotoxic to any of the *S. typhimurium* strains evaluated in the Ames test, with or without metabolic activation. Calcium Stearoyl Lactylate also was not genotoxic, with or without metabolic activation, in the chromosome aberrations test involving a Chinese hamster fibroblast cell line.

In a 1-year oral study, the occurrence of endometrial stromal polyps in the uterus of female animals was reported after groups of 30 male and 30 female Wistar rats were fed Sodium Stearoyl Lactylate in the diet at concentrations of 1.25%, 2.5%, and 5%. The incidence in treated rats was higher than that in concurrent controls, but was not statistically significant. Additionally, data on the historical incidences of this this tumor type at the laboratory where the study was performed demonstrated that endometrial stromal polyps are common in the rat strain that was tested. Therefore, this finding was not considered treatment-related.

The following results are from skin irritation studies involving albino rabbits (number of animals not stated): undiluted Calcium Stearoyl Stearate (nonirritating), 10% Sodium Lauroyl Lactylate (nonirritating), and undiluted Sodium Stearoyl Lactylate (PII = 0.5, 2 tests). Sodium Caproyl/Lauroyl Lactylate (in AOO vehicle) caused erythema and an increase in ear thickness in 4 mice (CRL:NMRI BR strain; 2/group) when tested at concentrations of 25% and 50%. In a skin irritation test on Sodium Isostearyl Lactylate involving 6 albino rabbits, the PII was 7.17 for the undiluted ingredient and 1.13 for 15% Sodium Isostearyl Lactylate. In a human skin irritation study, 25 and 26 subjects were patch tested with 2% and 5% Sodium Stearoyl Lactylate in petrolatum, respectively. The 2% concentration produced 10 reactions that were classified as doubtful (i.e., probably irritating), and the 5% concentration produced 14 reactions with the same classification. It was concluded that Sodium Stearoyl Lactylate has skin irritation potential. A diluted hair styling product (Calcium Stearoyl Lactylate effective concentration = 2.5%) was classified as a skin irritant in a study involving 54 subjects. In 4 separate skin irritation studies, each involving 50 subjects, a hair molding cream containing 7% Calcium Stearoyl Lactylate was classified as nonirritating to the skin.

In LLNAs of Sodium Caproyl/Lauroyl Lactylate and Sodium Lauroyl Lactylate at test concentrations up to 50%, Sodium Caproyl/Lauroyl Lactylate was classified as a weak-moderate skin sensitizer and Sodium Lauroyl Lactylate was classified as a weak skin sensitizer. A Sodium Lauroyl Lactylate trade name material was also classified as a weak sensitizer in the LLNA. Sodium Lauroyl Lactylate was also classified as a weak skin sensitizer in a guinea pig maximization test in which 10 animals were challenged with a test concentration of 0.5%. A silicone antifoam emulsion containing Sodium Stearoyl Lactylate (75% dilution; effective test concentration = 1.13% Sodium Stearoyl Lactylate) was a nonsensitizer in 20 guinea pigs.

An in vitro assay involving the RHE and detection of inflammation markers (IL-1α [released by injured cells] and IL-8 [secondary inflammatory cytokine]) was used to evaluate the skin toxicity of Sodium Stearoyl Lactylate. Sodium Stearoyl Lactylate was predicted to be an allergen based on the results of this assay. In a study on the modeling of skin sensitization data on a number of diverse compounds, EC3 values (from LLNAs) were ranked for these compounds quantitatively based on sensitization potency. Sodium Stearoyl Lactylate was classified as a Class 2 (weak/non-sensitizers) sensitizer in the ranking.

Caproyl/Lauroyl Lactylate (10% in saline solution) was classified as a non-corrosive substance in the in vitro bovine corneal opacity and permeability test. The results of ocular irritation tests on alkanoyl lactyl lactate salts involving groups of 6 albino rabbits were as follows: undiluted Calcium Stearoyl Lactylate (nonirritating), undiluted Sodium Isostearoyl Lactylate (irritating), 15% Sodium Isostearoyl Lactylate (nonirritating), 10% Sodium Lauroyl Lactylate (nonirritating), and undiluted Sodium Stearoyl Lactylate (nonirritating, 2 tests). In another study, undiluted Sodium Lauroyl Lactylate (0.1 g) was applied to the right eye of each of 6 albino rabbits.[19] Mild conjunctivitis was observed in 3 of 6 rabbits, and Sodium Lauroyl Lactylate was classified as a nonirritant.

A female patient with a 20-year history of hand and foot dermatitis had positive patch test reactions to Sodium Stearoyl Lactylate (2% and 5% in petrolatum) that were considered allergic in nature. A use test that involved 2 daily applications of 5% Sodium Stearoyl Lactylate in petrolatum to the lower arm of this patient was also performed. Small papules and

itching resulted after a few days, and the reaction was clearly positive on day 18.

Discussion

The Panel noted that based on the preponderance of data included in this report, alkanoyl lactyl lactate salts may have the potential to induce skin sensitization. Although a silicone antifoam emulsion containing Sodium Stearoyl Lactylate (75% dilution; effective test concentration = 1.5% Sodium Stearoyl Lactylate) was a nonsensitizer in guinea pigs, LLNA results indicated weak or moderate sensitization potential. Specifically, in LLNAs of Sodium Caproyl/Lauroyl Lactylate and Sodium Lauroyl Lactylate at test concentrations up to 50%, Sodium Caproyl/Lauroyl Lactylate was classified as a weak or moderate skin sensitizer (EC3 = 12.4%; EC3 = 9.3%, respectively), and Sodium Lauroyl Lactylate was classified as a weak skin sensitizer (EC3 = 15%). A Sodium Lauroyl Lactylate trade name material was also classified as a weak sensitizer in the LLNA (EC3 = 15%). Additionally, Sodium Lauroyl Lactylate was classified as a weak skin sensitizer in a guinea pig maximization test in which animals were challenged with a test concentration of 0.5%. In a case report, a patient with a history of hand and foot dermatitis had positive patch test reactions to Sodium Stearoyl Lactylate (2% and 5% in petrolatum) that were considered allergic in nature. Furthermore, following daily applications of 5% Sodium Stearoyl Lactylate in petrolatum to this patient, a positive reaction was observed. After reviewing these sensitization data on alkanoyl lactyl lactate salts, the Panel noted that the potential for induction of skin sensitization varies depending on a number of factors, including the area of product application; thus, formulators should assess the potential for final formulations to induce sensitization using a QRA or other accepted methodologies.

DART data were lacking for these ingredients. However, the concern over any potential developmental or reproductive toxicities was mitigated by the consistently negative short-term, subchronic, and chronic toxicity data, and the lack of clinical reports associated with the long-term historical use of these ingredients as food additives.

The Panel was also concerned that the potential exists for dermal irritation with the use of products formulated using alkanoyl lactyl lactate salts. The Panel also specified that products containing these ingredients must be formulated to be nonirritating.

Food Chemicals Codex specifications and European Commission regulations relating to the following components/ impurities of Calcium Stearoyl Lactylate/Sodium Stearoyl Lactylate are available: arsenic, calcium, cadmium, lactic acid, lead, mercury, and sodium. The Panel stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities.

Conclusion

The Expert Panel for Cosmetic Ingredient Safety concluded that the following alkanoyl lactyl lactate salts are safe in cosmetics in the present practices of use and concentration described in the safety assessment, when formulated to be nonirritating and nonsensitizing, which may be based on a QRA or other accepted methodologies:

Calcium Stearoyl Lactylate	Sodium Cocoyl Lactylate	Sodium Oleoyl Lactylate*
Sodium Behenoyl Lactylate	Sodium Cupheoyl Lactylate*	Sodium Stearoyl Lactylate
Sodium Caproyl Lactylate*	Sodium Isostearoyl Lactylate	
Sodium Caproyl/ Lauroyl Lactylate	Sodium Lauroyl Lactylate	

**Not reported to be in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.*

Author's Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, 555 13th St., NW, Suite 300W, Washington, DC 20004, USA.

Author Contributions

The articles in this supplement were sponsored by the Cosmetic Ingredient Review.

Declaration of Conflicting Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The articles in this supplement were sponsored by the Cosmetic Ingredient Review. The Cosmetic Ingredient Review is financially supported by the Personal Care Products Council.

References

1. Nikitakis J, Kowcz A. International cosmetic ingredient dictionary and handbook online version (wINCI). https://webdictionary.personalcarecouncil.org/jsp/Home.jsp. Washington, DC. Last Updated 2018. Date Accessed 4-27-2018.
2. Murphy LJ, Baiocchi F. Acyl lactylates in cosmetics. *Drug Cosmet Ind*. 1978;122:35-45.
3. Boutte T, Skogerson L. Stearoyl-2-lactylates and oleoyl lactylates. Chapter: 9. In: *Emulsifiers in Food Technology*. Oxford, UK: Blackwell Publishing Ltd; 2004:206-225.

4. European Food Safety Authority. Scientific opinion on the re-evaluation of sodium stearoyl-2-lactylate (E 481) and calcium stearoyl-2-lactylate (E 482) as food additives. 2013:1-35. https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2013.3144. Date Accessed 1-3-2019.
5. Baiocchi F, Jennings D, Del Vecchio AJ. Use of acyl lactylates in cosmetics and toiletries. *Cosmet Perfum*. 1975;90:31-34.
6. United States Pharmacopeial Convention. *Food Chemicals Codex*. 10th ed. Rockville, MD: The United States Pharmacopeial Convention; 2016.
7. European Commission. Commission regulation (EU) No. 231/2012 of March 9, 2012. Laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No. 1333/2008 of the European Parliament and of the Council. https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2012R0231:20121129:EN:PDF. Last Updated 2012. Date Accessed 12-2-2018.
8. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. College Park, MD. Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 3 2019; received February 13 2019): 2019.
9. Personal Care Products Council. Concentration of use by FDA product category: alkyl lactyl lactate salts. Unpublished data submitted by the Personal Care Products Council on 12-14-2017. 2017.
10. European Commission. CosIng database; following Cosmetic Regulation No. 1223/2009. https://ec.europa.eu/growth/tools-databases/cosing/. Last Updated 2009. Date Accessed 6-30-2018.
11. Tsen CC, Hoover W, Phillips D. High-protein breads. Use of sodium stearoyl-2 lactylate and calcium stearoyl-2 lactylate in their producton. *Baker's Digest*. 1971;45(2):10-74.
12. Phillips JC, Topp C, Gangolli SD. Studies on the metabolism of calcium stearoyl-2-lactylate in the rat, mouse, guinea-pig and man. *Food Cosmet Toxicol*. 1981;19(1):7-11.
13. European Chemicals Agency (ECHA). Registration, Evaluation, Authorization, and Restriction of Chemical Substances (REACH) Dossier. Fatty acids, C10-12, esters with polylactic acid, sodium salts (Sodium Lauroyl Lactylate). https://echa.europa.eu/registration-dossier/-/registered-dossier/5333/7/3/2. Last Updated 2018. Date Accessed 12-2-2018.
14. World Health Organization. Seventeenth report of the Joint FAO/WHO Expert Committee on Food Additives. Stearoyl lactylic acid, calcium and sodium salts. https://www.inchem.org/documents/jecfa/jecmono/v05je92.htm. Last Updated 1974. Date Accessed 7-11-2018.
15. Lamb J, Hentz K, Schmitt D, et al. A one-year oral toxicity study of sodium stearoyl lactylate (SSL) in rats. *Food Chem Toxicol*. 2010;48(10):2663-2669.
16. Ishidate M Jr., Sofuni T, Yoshikawa K, et al. Primary mutagenicity screening of food additives currently used in Japan. *Food Chem Toxicol*. 1984;22(8):623-636.
17. Murphy LJ. Sorption of acyl lactylates by hair and skin as documented by radio tracer studies. *Cosmet Toiletries*. 1979;94:43-45.
18. Patlewicz G, Roberts DW, Uriarte E. A comparison of reactivity schemes for the prediction of skin sensitization potential. *Chem Res Toxicol*. 2008;21(2):521-541.
19. International Bio-Research Inc. 1974. Primary skin and acute eye irritation studies of SSL (Sodium Stearoyl Lactylate). Unpublished data submitted by Personal Care Products Council on 9-19-2018.
20. Jensen CD, Andersen KE. Allergic contact dermatitis from sodium stearoyl lactylate, an emulsifier commonly used in food products. *Contact Dermatitis*. 2005;53(2):116.
21. Hill-Top Research Inc. 2004. Evaluation of primary irritation potential in humans (single 48-hour application) - hair styling product containing 5% Calcium Stearoyl Lactylate. Unpublished data submitted by Personal Care Products Council on 9/21/18.
22. Anonymous. 2005. Epicutaneous patch test of a moulding cream containing 7% Calcium Stearoyl Lactylate. Unpublished data submitted by Personal Care Products Council on 9/21/18.
23. Anonymous. 2005. Epicutaneous patch test of a moulding cream containing 7% Calcium Stearoyl Lactylate. Unpublished data submitted by Personal Care Products Council on 9/21/18.
24. Anonymous. 2005. Epicutaneous patch test of a moulding cream containing 7% Calcium Stearoyl Lactylate. Unpublished data submitted by Personal Care Products Council on 9/21/18.
25. Anonymous. 2006. Epicutaneous patch test of a moulding cream containing 7% Calcium Stearoyl Lactylate. Unpublished data submitted by Personal Care Products Council on 9/21/18.
26. Lemery E, Briancon S, Chevalier Y, et al. Skin toxicity of surfactants: Structure/toxicity relationships. *Colloids Surf A: Physicochem Eng Asp*. 2015;469:166-179.
27. Basketter DA, Kan-King-Yu D, Dierkes P, et al. Does irritation potency contribute to the skin sensitization potency of contact allergens? *Cutaneous and Ocular Toxicology*. 2007;26(4):279-286.
28. Roberts DW, Patlewicz G, Kern PS, et al. Mechanistic applicability domain classification of a local lymph node assay dataset for skin sensitization. *Chem Res Toxicol*. 2007;20(7):1019-1030.
29. Gerberick G, Ryan C, Kern P, et al. Compilation of historical local lymph node data for evaluation of skin sensitization alternative methods. *Dermatitis*. 2005;16(4):157-202.
30. Research Toxicology Centre S.p.A. 1995. Delayed dermal sensitization study in the guinea pig (test material is a silicone antifoam emulsion with 2% Sodium Stearoyl Lactylate). Unpublished data submitted by Personal Care Products Council on 9-19-2018.
31. Gunturi SB, Theerthala SS, Patel NK, et al. Prediction of skin sensitization potential using D-optimal design and GA-kNN

classification methods. *SAR and QSAR in Environ Res*. 2010; 21(3-4):305-335.
32. Evangelista R, Cermak S. Full-press oil extraction of Cuphea (PSR23) seeds. *J Am Oil Chem Soc*. 2007;84: 1169-1175.
33. National Center for Biotechnology Information. PubChem Open Chemistry Database: Sodium behenoyl lactylate. Chemical and physical properties. https://pubchem.ncbi.nlm.nih.gov/compound/71587094#section=Top. Last Updated 2018. Date Accessed 7-20-2018.
34. United States Environmental Protection Agency (EPA). EPISuite™ - Estimation Program Interface v4.11 - EPA. 2017.
35. PerkinElmer Informatics. ChemDraw® 17. 2017.
36. Jinan Changji Co., Ltd. Surface Active Agent e-Library (SAAPedia): Sodium Cocoyl Lactylate. Properties. https://www.saapedia.org/en/saa/?type=detail&id=1306. Last Updated 2018. Date Accessed 7-20-2018.
37. The Good Scents Company. Sodium oleoyl lactylate. Physical properties. https://www.thegoodscentscompany.com/data/rw1355561.html. Last Updated 2018. Date Accessed 7-20-2018.