FINAL REPORT ON THE SAFETY ASSESSMENT OF SODIUM LAURAMINOPROPIONATE AND SODIUM LAURIMINODIPROPIONATE[1]

Sodium Lauraminopropionate and Sodium Lauriminodipropionate are used in a variety of cosmetic formulations as antistatic agents, hair conditioning agents, and surfactants. Current data on concentrations at which these ingredients appear in cosmetic formulations were unavailable. The oral LD_{50} for Sodium Lauraminopropionate in albino rats was reported to be 8 g/kg. Evidence from limited studies in rabbits suggests that Sodium Lauraminopropionate and Sodium Lauriminodipropionate are both dermal and ocular irritants. No evidence of sensitization was found in guinea pigs with either ingredient. No data were available on the teratogenic, mutagenic, or carcinogenic potential of these ingredients, nor was there any clinical test data available. Because of the lack of data, the safety of Sodium Lauraminopropionate and Sodium Lauriminodipropionate could not be substantiated. The data needed to make a safety assessment include the method of manufacture, chemical characterization (i.e., data on purity/impurities), chemical and physical properties of Sodium Lauraminopropionate, concentration of use in cosmetic formulations, 28-day dermal toxicity, dermal reproductive and developmental toxicity, any available *ocular irritation data (no new studies should be undertaken to provide this data), dermal irritation and sensitization at concentration of use, and two different genotoxicity studies (one using a mammalian system). If the latter data are positive, dermal carcinogenesis data using the methods of the National Toxicology Program will be needed. It cannot be concluded the these ingredients are safe for use in cosmetic products until these safety data have been obtained and evaluated.*

Sodium Lauraminopropionate and Sodium Lauriminodipropionate are the sodium salt and the partial sodium salt, respectively, of a substituted propionic acid. They are used as antistatic agents, hair conditioning agents, and surfactants. This report reviews the available safety data on these ingredients.

[1]Reviewed by the Cosmetic Ingredient Review Expert Panel.

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CHEMISTRY

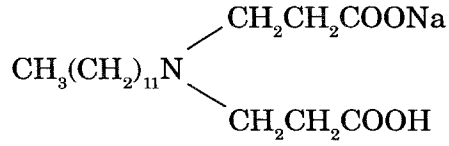
Definition and Structure

Sodium Lauraminopropionate (CAS No. 3546-96-1) is the sodium salt of a substituted propionic acid. It has the formula (Wenninger and McEwen, 1995a):

$$CH_3(CH_2)_{10}CH_2NH—CH_2CH_2COONa$$

Other technical names for this ingredient are β-Alanine; N-Dodecyl-, Monosodium Salt; and N-Dodecyl-β-Alanine, Monosodium Salt. Trade name mixtures containing Sodium Lauraminopropionate are Carsonol BDM and Mirataine XL (Wenninger and McEwen, 1995a).

Sodium Lauriminodipropionate (CAS No. 14960-06-6) is the partial sodium salt of a substituted β-aminopropionic acid. It conforms generally to the formula (Wenninger and McEwen, 1995a):



Other technical names for this ingredient include β-Alanine, N-(2-Carboxyethyl)-N-Dodecyl-, Monosodium Salt; N-(2-Carboxyethyl)-N-Dodecyl-β-Alanine, Monosodium Salt; and Sodium N-Lauryl-β-Iminodipropionate. Trade names for Sodium Lauriminodipropionate are Deriphat 160-C, Mirataine H2C-HA, Unitex 610-L (Wenninger and McEwen, 1995a), and Velvetex 610L (Salka, 1995).

Properties

The chemical and physical properties of Sodium Lauriminodipropionate are summarized in Table 1.

USE

Cosmetic

Sodium Lauraminopropionate and Sodium Lauriminodipropionate are used as antistatic agents, hair conditioning agents, surfactant-cleansing agents, and surfactant-foam boosters in cosmetic formulations (Wenninger and McEwen, 1995b). The product formulation data submitted to the Food and Drug Administration (FDA) in 1995 reported

Table 1. Chemical and physical properties of sodium lauriminodipropionate

Property	Description	Reference
Appearance	Thin, yellow liquid Clear, light amber liquid	Rhône-Poulenc, 1995a Nikitakis and McEwen, 1990
Odor	Mild fruity odor Faint metallic odor	Rhône-Poulenc, 1995b Nikitakis and McEwen, 1990
Boiling point	100°C	Rhône-Poulenc, 1994
% Solids	30% 29.0 (min)–31.0 (max)	Rhône-Poulenc, 1995a Rhône-Poulenc, 1994
pH	7.0 6.0 (min)–7.0 (max) (at 25°C) 7.0–8.0 (3.3% aq. soln.)	Rhône-Poulenc, 1995a Rhône-Poulenc, 1994 Nikitakis and McEwen, 1990
Acid number	42.0 (min)–55.0 (max) (mg KOH/g) 35–50	Rhône-Poulenc, 1994 Nikitakis and McEwen, 1990
Solubility	Soluble in water, clouds in ethanol	Nikitakis and McEwen, 1990
Moisture	69.0% (min)–71.0% (max)	Rhône-Poulenc, 1994
% Volatility	70%	Rhône-Poulenc, 1994
Refractive index	1.3800–1.3870 (at 25°C)	Nikitakis and McEwen, 1990
Specific gravity	1.03 at 25°C	Rhône-Poulenc, 1994

that Sodium Lauraminopropionate and Sodium Lauriminodipropionate were used in a total of 4 and 23 cosmetic product formulations, respectively (Table 2). Sodium Lauraminopropionate and Sodium Lauriminodipropionate were used in shampoos (noncoloring) and body and hand preparations (excluding shaving preparations). Sodium Lauriminodipropionate was also used in hair conditioners, hair coloring preparations, bath soaps and detergents, and cleansing and moisturizing preparations (FDA, 1995).

As stated earlier, concentration of use values are no longer reported to the FDA by the cosmetic industry (FDA, 1992); however, production formulation data submitted to the FDA in 1984 stated that Sodium Lauraminopropionate was used at concentrations of up to 5% in shampoos, but there was no listing for body and hand preparations. Sodium

Table 2. Cosmetic product formulation data

Ingredient	Product category	Total no. formulations in category	Total no. of formulations containing ingredient
Sodium Lauramino-propionate	Shampoos (noncoloring)	916	2
	Body and hand preparations (excluding shawing preparations)	987	2
	1995 Total		***4***
Sodium Laurimino-dipropionate	Hair conditioners	693	5
	Shampoos (noncoloring)	916	3
	Other hair coloring preparations	79	2
	Bath soaps and detergents	339	4
	Cleansing preparations (cold creams, cleaning lotions, liquids, and pads)	771	6
	Body and hand preparations (excluding shaving preparations)	987	1
	Moisturizing preparations	873	2
	1995 Total		***23***

Source. FDA, 1995.

Lauriminodipropionate was used at concentrations up to 1% in shampoos, 5% in moisturizers, and 10% in cleansing preparations. There was no listing for hair conditioners or hair coloring preparations in 1984 (FDA, 1984). Sodium Lauraminopropionate and Sodium Lauriminodipropionate are approved for use in cosmetics in Japan (Rempe and Santucci, 1997).

Noncosmetic

Sodium Lauriminodipropionate has applications in heavy-duty alkaline cleaners, corrosion inhibitors, leather cleaners, and acid cleaners (Rhône-Poulenc, 1995a).

ABSORPTION, DISTRIBUTION, AND METABOLISM

No published data on the absorption, distribution, or metabolism of Sodium Lauraminopropionate and Sodium Lauriminodipropionate were found.

ANIMAL TOXICOLOGY

Acute Toxicity

Oral

The oral LD_{50} for a mixture containing Sodium Lauraminopropionate (concentration and activity unknown) was 8.0 g/kg for six albino rats (Consumer Product Testing Company, Inc., 1976). Ten percent active solutions of Sodium Lauriminodipropionate and Lauraminopropionic Acid (solvent not stated) had LD_{50} values of 31.3 g/kg and 23.1 g/kg, respectively (General Mills).

No deaths or gross changes occurred when 10 Wistar albino rats were administered a single oral dose of 5.0 g/kg 23.8% Lauraminopropionic Acid (10% active) in water (Consumer Product Testing Company, Inc., 1976).

Three groups of 10 albino mice, 5 per sex per group, were dosed once by gavage with Sodium Lauriminodipropionate, 16% solids and pH 7.0. The oral LD_{50} was estimated to be 17.8 mL/kg (Product Safety Labs, 1982).

Dermal

In acute dermal studies using occlusive patches, no deaths or adverse reactions were observed when groups of six rabbits were treated topically with 6.8 g/kg or 10.2 g/kg Sodium Lauriminodipropionate (10% active) or Lauraminopropionic Acid (10% active) (General Mills).

Dermal Irritation

A mixture containing Sodium Lauraminopropionate (0.5 mL) (concentration and activity unknown) was applied under occlusive patches to abraded and nonabraded sites on the skin of three male and three female New Zealand rabbits. Each of the sites was graded at 24 h and 72 h. The primary irritation index (PII) was 6.58/8. The investigators concluded that this mixture was a primary dermal irritant and corrosive agent (Consumer Product Testing Company, Inc., 1976).

In a similar study, Sodium Lauriminodipropionate, 10% solids (Salka, 1995), was reported to have a mean PII of 3.04/8. Because eschar formation was observed at 72 h, this ingredient was considered corrosive to the skin of rabbits (Food and Drug Research Laboratories, 1982a). A 23.8% Lauraminopropionic Acid solution (10% active) was severely irritating, having a PII of 6.05/8 (Consumer Product Testing Company, Inc., 1976).

Sodium Lauriminodipropionate, 16% solids at pH 7.0, was applied under an occlusive patch to abraded and intact skin of three albino rabbits. The patches were removed 24 h after application, and observations were made at the time of patch removal and after 72 h. Sodium

Lauriminodipropionate was a moderate irritant to rabbit skin, with a PII of 2.17 (Product Safety Labs, 1982).

Ten percent active solutions of Sodium Lauriminodipropionate and Lauraminopropionic Acid had primary irritation scores of 0.15 and 0.35, respectively (General Mills).

Sensitization

Groups of 10 guinea pigs were injected intracutaneously with 0.1% solutions of Sodium Lauriminodipropionate and Lauraminopropionic Acid (solvent not stated) every other day for a total of 10 injections. The volume of the first injection was 0.05 mL, and the remaining injections were 0.10 mL. After a 2-week nontreatment period following the tenth injection, 0.05 mL of the test solution was injected at a site slightly below the original injection site. No evidence of sensitization was observed (General Mills).

Ocular Irritation

In a modified Draize test, a mixture containing Sodium Lauraminopropionate (pH not reported, concentration and activity unknown) was instilled into the conjunctival sacs of nine New Zealand rabbits. The eyes of three rabbits were rinsed 30 sec following instillation, while the eyes of the remaining six rabbits were left unrinsed. The eyes were scored on days 1, 2, 3, 4, and 7. The respective Draize scores (maximum possible score: 110) on each of these days were 17.3, 18.5, 14.0, 17.0, and 18.0 without rinsing, and 13.6, 15.3, 12.6, 10.6, and 4.0 with rinsing. The investigators observed fibrovascular overgrowth or scarring indicative of permanent damage in four of six rabbits in the nonrinsed group (Consumer Product Testing Company, Inc., 1976).

In a similar study, a solution of Sodium Lauriminodipropionate, 10% solids (Salka, 1995), caused mean irritation scores of 15.3 at 24 h and 3.7 at 48 h in unrinsed eyes. No irritation was observed after 72 h. With rinsed eyes, irritation (1.3) was observed only at 24 h. This solution was classified as mildly irritating to the eyes of rabbits without rinsing, and practically nonirritating with rinsing (Food and Drug Research Laboratories, 1982b).

One tenth of a milliliter of Sodium Lauriminodipropionate, 16% solids at pH 7.0, was placed in the conjunctival sac of one eye of each of three rabbits; the contralateral eye was used as a control. Observations were made after 24 h, 48 h, and 72 h and after 4 days and 7 days. Sodium Lauriminodipropionate was a moderate irritant, with maximum mean total scores of 20.7 after 24 h and 12.0 after 7 days (Product Safety Labs, 1982).

A 23.8% solution of Lauraminopropionic Acid (10% active) produced scores of 29.3 at 24 h, 20.2 at 48 h, 17.5 at 72 h, 10.3 on day 4, and 14.8 on day 7 in unrinsed eyes. Respective scores for rinsed eyes were 4.0, 2.7, 0.0, 0.0, and 0.0. The solution was considered a moderate ocular irritant (Consumer Product Testing Company, Inc., 1976).

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

No published data on the reproductive and developmental toxicity of Sodium Lauraminopropionate or Sodium Lauriminodipropionate were found.

MUTAGENICITY

No published data on the mutagenic potential of Sodium Lauraminopropionate or Sodium Lauriminodipropionate were found.

CARCINOGENICITY

No published carcinogenicity data on Sodium Lauraminopropionate or Sodium Lauriminodipropionate were found.

CLINICAL ASSESSMENT OF SAFETY

No published clinical studies of Sodium Lauraminopropionate were found.

Sodium Lauriminodipropionate was reported to be "practically nontoxic" to the skin and "minimally irritating" upon skin contact. It was also reported to be "minimally irritating" to the eye. Sodium Lauriminodipropionate was "practically nontoxic" upon ingestion (Rhône-Poulenc, 1995b).

SUMMARY

Sodium Lauraminopropionate and Sodium Lauriminodipropionate are used in cosmetics for their antistatic, hair conditioning, and surfactant properties. The limited safety data on Sodium Lauraminopropionate indicate that a chemical mixture containing Sodium Lauraminopropionate (concentration and activity unknown) had an LD_{50} of 8.0 g/kg for rats and caused both dermal and ocular irritation. In studies of 10% active solutions of Sodium Lauriminodipropionate, the oral LD_{50} for rats was 31.3 g/kg, and the dermal LD_{50} was greater than 10.2 g/kg; the oral LD_{50} for mice of a 16% solids solution was estimated as 17.8 mL/kg. A 10% active solution of Lauraminopropionic Acid had an oral LD_{50} of

23.1 g/kg. Both Sodium Lauriminodipropionate and Lauraminopropionic Acid, 10% active solutions, were severely irritating to the skin of rabbits, but there was no evidence of sensitization in studies with guinea pigs. Sodium Lauriminodipropionate at 16% solids was a moderate irritant to rabbit skin. Sodium Lauraminopropionate, Sodium Lauriminodipropionate, and Lauraminopropionic Acid were irritating to the eyes of rabbits.

DISCUSSION

Section 1, paragraph (p), of the CIR Procedures states that "A lack of information about an ingredient shall not be enough to justify a determination of safety." In accordance with Section 30(j)(2)(A) of the procedures, the Expert Panel informed the public of its decision that the data on Sodium Lauraminopropionate and Sodium Lauriminodipropionate are insufficient to determine whether these ingredients, under each relevant condition of use, is either safe or unsafe.

The Expert Panel released a "Notice of Insufficient Data Announcement" on December 13, 1994, outlining the data needed to assess the safety of these ingredients. Some data were supplied to the Panel and are included in this report; however, not all of the requested data were supplied. The types of data needed include:

1. Concentration of use
2. Chemical characterization (impurities/purity data)
3. Chemical and physical properties of Sodium Lauraminopropionate
4. Method of manufacture
5. 28 day dermal toxicity
6. Dermal teratogenicity*
7. Ocular irritation at concentration of use, if available
8. Dermal irritation and sensitization at concentration of use
9. Two different genotoxicity studies (one using a mammalian system); if positive, a dermal carcinogenesis assay by National Toxicology Program standards will be required

Depending on the results of these studies, additional data may be required.

In accordance with Section 45 of the CIR Procedures, the Expert Panel will issue a Final Report—Insufficient Data. When the requested new data are available, the Expert Panel will reconsider the Final Report in accordance with Section 46 of the CIR Procedures, Amendment of a Final Report.

*Teratogenicity is considered to include complete reproductive and developmental toxicity.

CONCLUSION

The CIR Expert Panel concludes that the available data are insufficient to support the safety of Sodium Lauraminopropionate and Sodium Lauriminodipropionate for use in cosmetics.

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