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Final Report on the Safety Assessment of Cocoamphoacetate, Cocoamphopropionate, Cocoamphodiacetate, and Cocoamphodipropionate

Cocoamphoacetate (CAA), Cocoamphopropionate (CAP), Cocoamphodiacetate (CADA), and Cocoamphodipropionate (CADP) are imidazoline-derived amphoteric organic compounds. These amphoteric compounds are used in cosmetics as surfactants, mild foaming and cleansing agents, detoxifying agents, and conditioners at concentrations ranging from ≤ 0.1 to 50 percent.

In acute oral toxicity studies, CADA and CAA were nontoxic in rats and mice, CADP was nontoxic in rats, and CAP was nontoxic in mice. An oral LD_{50} of 7.8 ml/kg was reported for mice dosed with 70% CADP.

The results of ocular irritation studies of these compounds, as commercially supplied, varied widely. CADA was moderately to severely irritating when eyes were not rinsed and practically nonirritating to mildly irritating when rinsed. CADP was practically nonirritating under unrinsed conditions. CAA was minimally to severely irritating and CAP was practically nonirritating to minimally irritating under unrinsed conditions. In a clinical ocular study, 1, 3, and 10% dilutions of a shampoo containing 28.1% CADA were nonirritating to the human eye.

CAP, CADA, and CADP were nonmutagenic in the Ames assay, both with and without metabolic activation.

CAA and CAP, at a concentration of 10%, were neither irritants nor sensitizers in a repeated insult patch test on 141 subjects.

Based upon the available data, it is concluded that CAA, CAP, CADA, and CADP are safe for use as cosmetic ingredients.

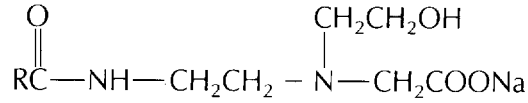
INTRODUCTION

The following report encompasses the four ingredients represented by the old nomenclature of Amphoterics-1 and -2: Cocoamphoacetate, Cocoamphopropion-

ate, Cocoamphodiacetate, and Cocoamphodipropionate.* Amphoteric-6, a complex of Amphoteric-2 and sodium lauryl sulfate, is currently regarded as a simple mixture and has been withdrawn from the third edition of the *CTFA Cosmetic Ingredient Dictionary*.[1]

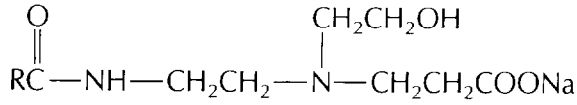
CHEMICAL AND PHYSICAL PROPERTIES

Cocoamphoacetate (CAA), Cocoamphopropionate (CAP), Cocoamphodiacetate (CADA), and Cocoamphodipropionate (CADP) are amphoteric organic compounds generally conforming to the following structural formulas:[2]



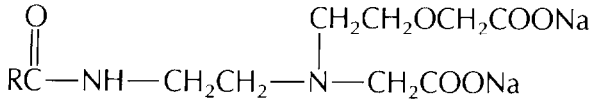
Cocoamphoacetate

I

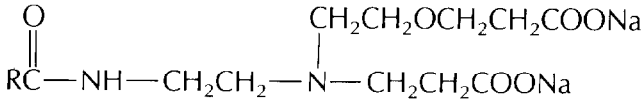


Cocoamphopropionate

II



Cocoamphodiacetate



Cocoamphodipropionate

where RCO– represents the mixed coconut acid moieties. The alkyl imidazolines were previously thought to be ring structured; however, they now are known to have a linear structure.[2–4] Cosmetic suppliers do not agree on the representation of the structures for CADA and CADP. In the opinion of some chemists, the second carboxylate group may be unattached to the amphoteric structure.[1]

These products are prepared by reacting coconut acid with aminoethylethanolamine and appear to form an imidazoline as an intermediate. The cocoimidazoline is

*New designations in supplement to the 3rd edition of the *CTFA Cosmetic Ingredient Dictionary*: Cocoamphoacetate formerly Cocoamphoglycinate (CAG), Cocoamphodiacetate formerly Cocoamphocarboxyglycinate (CACG); Cocoamphodiapropionate formerly Cocoamphocarboxypropionate (CACP). These substances are used as sodium salts in cosmetics.

then reacted with monochloracetic acid or monochloropropionic acid in the presence of sodium hydroxide to form the sodium salts either of a mono- (CAA and CAP) or dicarboxylated (CADA and CADP) product.[1,5,6]

These compounds are supplied as amber liquids, usually containing 40 to 50 percent solids, with a faintly fruity odor. Their viscosity can be controlled by the addition of sodium chloride (the more sodium chloride added, the more viscous the solution becomes). All of these products are soluble in water and insoluble in nonpolar organic solvents. CAP and CADP, containing only traces of sodium chloride ($\leq 0.02\%$), are also soluble in alcohol.[1,2] The pH range for solutions of these ingredients has been reported to be from 8.1 to 10.2 (Table 1).[2]

CAA, CAP, CADA, and CADP can be positively identified by close match to standard infrared spectra.[2] Another analytical method is based on the ionization curves formed by plotting pH changes upon addition of acids and alkalis to the amphoteric solution. Each ionization curve is unique and allows for immediate identification as well as giving information about the purity and degree of carboxylation of the compound.[7]

IMPURITIES

No information is available on impurities.

USE

Cosmetic

CAA, CAP, CADA, and CADP are used in cosmetics as surfactants, mild foaming and cleansing agents, detoxifying agents, and conditioners.[1,5,8–10]

Blends of cosmetic amphoterics and anionics act synergistically to reduce irritation potential, improve viscosity, and enhance foam volume and longevity.[11,12] Ampho-

TABLE 1. Physicochemical Properties

Property	*Cocoamphoacetate*	*Cocoamphopropionate*	*Cocoamphodiacetate*	*Cocoamphodipropionate*
Description (in aqueous solution)	Clear, viscous, light amber solution[1,2]	Clear, light amber solution[1,2]	Viscous, light tan solution[1,2]	Clear, light amber solution[1,2]
Odor	Faintly fruity[2]	Faintly fruity[2]	Faintly fruity[2]	Faintly fruity[2]
pH at 30°C	9.0–9.5[2]	9.8–10.2[2]	8.1–8.3[2] (of 20% aqueous soln)	9.4–9.8[2]
Solubility				
Water	S[1,2,5]	S[1,2,5]	S[2,5]	S[2,5]
Alcohol	I[2]	S[2]	I[2]	S[2]
Nonpolar organic solvents	I[2]	I[2]	I[2]	I[2]
Chloride (as NaCl)	7.0–7.7%[2]	0.02% maximum[2]	11.2–11.8%[2]	0.02% maximum[2]
Nitrogen	2.4–2.6%[2]	2.7–2.9%[2]	2.3–2.5%[2]	2.4% minimum[2]
Non-volatiles	43% minimum[2]	36–38%[2]	49% minimum[2]	38% minimum[2]

terics have less severe defatting effects compared with anionics and promote hair and skin substantivity at acid pH when they become cationic in character.[11] Goddard et al.[13] studied the effect of CAP on the adsorption of Polymer JR-400 on bleached and unbleached hair. CAP increased adsorption with each successive shampooing; CAP-Polymer JR-400 was one of the surfactant-polymer systems with the highest deposition on the hair.

The FDA product formulation data for CAA, CAP, CADA, and CADP are summarized in Table 2.[14] The cosmetic product formulation data, made available by the FDA, are compiled through voluntary filing in accordance with Title 21 part 720.4 (d)(1) of the Code of Federal Regulations.[15] Ingredients are listed in prescribed concentration ranges under specific product type categories. Since certain cosmetic ingredients are supplied by the manufacturer at less than 100 percent concentration, the value reported by the cosmetic formulator may not necessarily reflect the actual concentration found in the finished product; the actual concentration in such a case would be a fraction of that reported to the FDA. The fact that data are only submitted within the framework of preset concentration ranges also provides the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end, thus introducing the possibility of a two- to ten-fold error in the assumed ingredient concentration. CAA and CADA are used in cosmetic products at concentrations of $\geq$ 1.0 to 10.0% and $\leq$ 0.1 to 50.0%, respectively, and, CADP, at concentrations of $>$ 1.0 to 25.0%. There are no reported cosmetic uses of CAP.[14]

TABLE 2. Product Formulation Data

Product Category	*Total no. of formulations in category*	*Total no. containing ingredient*	*No. of product formulations within each concentration range (%)*						
			>25-50	*>10-25*	*>5-10*	*≥5*	*>1-5*	*>0.1-1*	*≤0.1*
Cocoamphoacetate									
Hair shampoos (noncoloring)	859	5	—	—	2	—	3	—	—
1989 Totals		5	—	—	2	—	3	—	—
Cocoamphopropionate									
1989 Totals	—	0	—	—	—	—	—	—	—
Cocoamphodiacetate									
Hair shampoo	878	13	1	7	4	—	1	—	—
Skin cleansing preparations	1298	10	—	1	—	—	7	1	1
Miscellaneous other cosmetics	2134	7	—	—	2	—	—	4	1
1989 Totals		30	1	8	6	—	8	5	2
Cocoamphodipropionate									
Hair shampoo	859	8	—	1	6	—	1	—	—
Other hair products	772	7	—	1	—	—	6	—	—
Skin cleansing preparations	751	2	—	—	1	—	1	—	—
1989 Totals		17	—	2	7	—	8	—	—

Source: From Ref. 14.

The formulation data presented in Table 2 indicate that cosmetic products containing these amphoterics may contact all external body surfaces and hair, conjunctivae, and other mucous membranes. These products may be used daily or occasionally over a period of up to several years. The frequency and duration of application could result in continuous exposure.

Noncosmetic

CAA, CAP, CADA, and CADP are widely used in heavy-duty liquid, steam, pressure, metal, and all-purpose cleaners.[5,16] They are used in the caustic lye peeling of fruit and potatoes and are commonly found in household products such as oven cleaners, wash and wax floor polishes, dishwashing machine compounds, copper and silver cleaners, and hard-surface cleaners.[5]

Other uses of these amphoterics include pharmaceutical formulations for the treatment of glaucoma (CADA, 0.2%) and hemorrhoids (CADP, 0.25%), contact lens disinfecting solution (CADP, 0.0035–0.04%), and in material for bandages (CADA).[17–20]

GENERAL BIOLOGY

Hirai et al.[21] studied the effects of surfactants on the nasal absorption of insulin in rats. The addition of 1% CADA to the solution administered nasally to rats significantly enhanced insulin absorption as measured by a 56.9% decrement in plasma glucose concentration from 0 to 4 h. The absolute bioavailability of insulin was increased from 5 to 30% by the addition of a surfactant such as CADA. The surfactants appeared to promote nasal absorption either by increasing the permeability of the nasal mucosa or by reducing the activities of proteolytic enzymes.

A blend containing CADA, sodium lauryl sulfate, and hexylene glycol was tested for antimicrobial activity and inhibition of the formation of *in vitro* plaque by oral bacteria. The blend had antimicrobial activity against *Actinomyces viscosus, A. naeslundii,* and *Streptococcus mutans.* However, it was significantly less effective than other detergents tested and had an ID_{50} (dose resulting in 50% inhibition of bacterial growth) of 2.0 to 5.0 $\times 10^{-5}$ M. The blend was not active against *A. viscosus* in the plaque assay and had very limited activity against *A. naeslundii* and *S. mutans* with ID_{50}s of 10^{-1}M or greater.[22]

ANIMAL TOXICOLOGY

Acute Toxicity

Oral

CADA, CADP, CAA, and CAP, as commercially supplied, have all been evaluated for acute oral toxicity using rats or mice. LD_{50} values ranged from >5.0 to 16.60 g/kg for CADA, >5.0 to 16.30 g/kg for CADP, 15.9 to 28.0 ml/kg for CAA, and a value of 20.0 ml/kg was reported for CAP in two studies. Results of these and other acute oral toxicity tests are reported in Table 3.

Additionally, CADA and CADP were each fed to albino rats (number unspecified) at concentrations of 0.25 and 0.50% in the diet for 10 days. Control groups were

TABLE 3. Acute Oral Toxicity

Ingredient	*Animal*	*LD_{50} Value*	*Comments*	*Reference*
CADA: As commercially supplied	Rats: 5 females	>5.0 g/kg	No toxic effects	23
CADA: As commercially supplied	Rats: 10	>5.0 ml/kg	—	26
CADA: As commercially supplied	Mice: 3 groups of 10	>15 ml/kg	—	27
CADA: As commercially supplied	Rats: groups of 10	16.60 g/kg	Nontoxic	24
CADA:				24
0.50% in the diet	Rats: unspecified no.	—	Rats fed daily for 10 days; nontoxic	
0.25% in the diet	Rats: unspecified no.	—	Rats fed daily for 10 days; nontoxic	24
CADP: As commercially supplied	Rats: groups of 10	16.30 g/kg	Nontoxic	25
CADP: As commercially supplied	Rats: 5 males 5 females	>5.0 ml/kg	—	28
CADP: 70% active (as commercially supplied)	Mice: 3 groups of 10	7.8 ml/kg	—	29
CADP:				25
0.50% in the diet	Rats: unspecified no.	—	Rats fed for 10 days; nontoxic	
0.25% in the diet	Rats: unspecified no.	—	Rats fed for 10 days; nontoxic	25
CAA: As commercially supplied	Mice: 3 groups of 5 males and 5 females each	28.0 ml/kg	—	30
CAA: As commercially supplied	Mice: 4 groups of 10	15.9 ml/kg	—	30
CAA: 25% (of supplied) in water	Rats: 10	>5.0 ml/kg	Nontoxic	31
CAP: As commercially supplied	Mice: 10	20.0 ml/kg	—	32
CAP: As commercially supplied	Mice: 4 groups of 10	20.0 ml/kg	—	33
CADA with sodium lauryl sulfate and hexylene glycol: 30%	Rats: groups of 10	10.25 g/kg	Nontoxic	34
CADA: 4% in a shampoo cream	Rats: 5 males 5 females	>5.0 ml/kg	No signs of systemic toxicity; no gross pathological effects	35
CADA: 4% in a shampoo cream	Rats: 5 males 5 females	>5.0 ml/kg	No signs of systemic toxicity; no gross pathological effects	35

maintained on a standard diet. At the end of the 10-day period, the rats were weighed and observed for changes in behavior, general appearance and activity. The rats on the test diets did not differ from the controls in any of the above parameters. CADA and CADP were considered nontoxic when fed to rats daily for ten days at concentrations of 0.25 and 0.50%.[24,25]

Dermal

Two shampoo creams, each containing 4.0% CADA, were evaluated for acute dermal toxicity in rabbits. Each test group consisted of two male and two female New Zealand albino rabbits. A single application of each undiluted shampoo was applied to the clipped, intact skin of the back of each rabbit at a dose of 10.0 ml/kg. Test sites were covered for 24 h with an impervious plastic binder and tape. Upon removal of the binders, excess test material was removed. Animals were observed for signs of systemic toxicity and dermal irritation for 14 days. No deaths occurred, although clinical signs of systemic toxicity included depression, labored respiration, phonation upon handling, tremors, and weight loss (in one animal only). At necropsy, six rabbits had no gross lesions and two had changes unrelated to treatment. Gross dermal lesions included moderate to marked erythema and edema accompanied by blanched areas (in two animals) and most of the lesions had cleared by day 8. Moderate to marked atonia and marked desquamation developed during the first week in all animals. Coriaceous areas and fissures were also observed. Sloughing of the damaged skin with eschar formation occurred in two rabbits. Slight to moderate desquamation was noted at termination in all animals and two animals had moderate atonia.[36]

Irritation

Ocular

CADA, CADP, CAA, and CAP, as commercially supplied, have been evaluated for ocular irritation primarily by Draize or modified Draize tests. In all tests, a 0.1 ml sample of the substance was instilled into the conjunctival sac of each rabbit; the other eye served as the untreated control. The eyes of those rabbits designated for testing with a rinse-out procedure were rinsed either 4 seconds after instillation with 20 or 60 ml of water or 10 seconds after instillation with 300 ml of water. Ocular irritation responses were scored according to Draize (max = 110) on days 1, 2, 3, 4, and 7. CADA, at concentrations of 10 to 12% active as well as solutions of unstated activity, was moderately to severely irritating when not rinsed from the eye and practically nonirritating to mildly irritating when tested using rinse-out procedures. CADP, at a concentration of 7.5% active, was practically nonirritating under unrinsed conditions. CAA, at concentrations of 16 to 50% active as well as solutions of unstated activity, was minimally to severely irritating under unrinsed conditions. CAP, at concentrations of 5 and 16% active, was practically nonirritating to minimally irritating under unrinsed conditions. Cosmetic products containing CADA (as supplied) at concentrations of 1.5 to 28.1% and CADP (as supplied) at concentrations of 25 to 36% also have been evaluated by the Draize test. All ocular irritation test results are given in Table 4.

North-Root et al.[37] also investigated the cellular toxicity of cationic, anionic, nonionic, and amphoteric surfactants *in vitro* using an established line of rabbit corneal cells and compared the results with those from an *in vivo* ocular irritation test in New Zealand albino rabbits. CADP had an LC_{50} of 35.5 ppm for the SIRC rabbit corneal cells (other surfactant LC_{50}s ranged from 2.2 to 36000 ppm); the CADP concentration predicted to cause a Draize score of 20 was approximately 90.0%. A 0.01 ml sample of CADP (at a concentration not exceeding 30%) was administered to the cornea of each of three male and three female rabbits. Corneal, iridial, and conjunctival responses were scored according to Draize 24, 48, and 72 hours after application. Individual

TABLE 4. Ocular Irritation

Ingredient	*Test method*	*No. of rabbits*	*Results*	*Reference*
CADA: As commercially supplied	Draize[a]	6: Unrinsed	HAIS[b] of 32 on day 1, 3 on day 7; moderately irritating	39
CADA: As commercially supplied	Draize	6: Unrinsed	HAIS of 30 on day 1, 3 on day 7; moderately irritating	40
CADA: As commercially supplied	Draize	6: Unrinsed	HAIS of 32 on day 1, 18 on day 7; moderately to severely irritating	41
CADA: As commercially supplied	Draize	3: Rinsed 4 s after instillation w/20 ml water	HAIS of 8 on day 1, eyes normal by day 4; minimally irritating	42
CADA: As commercially supplied	Draize	3: Rinsed 4 s after instillation w/20 ml water	HAIS of 1 on day 1, eyes normal by day 2; practically nonirritating	43
CADA: As commercially supplied	Draize	6: Unrinsed 3: Rinsed 4 s after instillation w/20 ml water	Unrinsed: HAIS of 37.17 on day 1, corneal and iridial irritation at day 7; severely irritating Rinsed: HAIS of 12.00 on day 1, some conjunctival irritation at day 7; mildly irritating	44
CADA: As commercially supplied	Draize (max = 104, discharge category omitted from scoring system)	3: Rinsed 10 s after instillation w/150 ml water/min for 2 min	HAIS of 5.33 for days 1–3, eyes normal by day 5; mildly irritating	45
CADA: 21% aqueous dilution of CADA (as supplied)	Draize	6: Unrinsed 3: Rinsed 4 s after instillation w/20 ml water	Unrinsed: HAIS of 3.67 at day 1, minimal conjunctival irritation at day 7; minimally irritating Rinsed: all scores of 0; nonirritating	46
CADA: 25% dilution of CADA (as supplied)	Draize	3: Unrinsed	HAIS of 5.33 on day 1, eyes normal by day 4; minimally irritating	47
CADA: 12% active (as commercially supplied)	Draize	3: Unrinsed	All scores: 0; nonirritating	48
CADA: 10% active (as commercially supplied)	Draize	3: Unrinsed	HAIS of 4.0 on day 1, eyes normal by day 3; minimally irritating	49
CADA: 5% (as commercially supplied) in water	—	6	Irritation cleared by 24 h	50
CADA: 5% (supplied w/1% $NaBH_4$) in water	—	6	Irritation cleared by 24 h	51
CADA: at 2, 10, and 20% in water	Draize	Groups of 5, unrinsed	Dose response observed; CADA was the second least irritating surfactant tested; 2%, score of 10 at 1 h, 0 at 24 h; 10%, score of 35 at 1 h, 5 at 7 days; 20%, score of 55 at 1 h, 5 at 7 days	52
CADP: 25% dilution of CACP (as commercially supplied) pH adjusted to 8	Draize	6: Unrinsed	HAIS of 1 on day 1, eyes normal by day 2; nonirritating	53

TABLE 4. *Continued*

Ingredient	*Test method*	*No. of rabbits*	*Results*	*Reference*
CADP: 7.5% active (as commercially supplied)	Draize	3: Unrinsed	HAIS of 1.33 on day 2, eyes normal by day 3; practically nonirritating	54
CADP	*In vitro* rabbit corneal cell toxicity test	—	LC_{50} = 35.5 ppm; least irritating amphoteric tested	37
CADP: concentration not > 30%	Draize	6: Unrinsed	CADP was the least irritating amphoteric; order of toxicity was cationic > anionic = amphoteric > nonionic; individual scores not given	37
CAA: As commercially supplied	Draize	6: Unrinsed	HAIS of 5.33 on day 1, eyes normal by day 7; minimally irritating	55
CAA: 50% active (as commercially supplied)	—	6	Draize scoring over 24 h, HAIS of 5.67 at 2 and 8 h, 1.0 at 24 h; minimally irritating	56
CAA: 50% active (as commercially supplied)	Modified Draize	6	HAIS of 29.4 on day 1, corneal and iridial irritation at day 7 in 2 rabbits; severely irritating	57
CAA: 16% active (as commercially supplied) pH adjusted to 7.0	Draize	3: Unrinsed	HAIS of 8.7 on day 1, minimal conjunctival irritation on day 7; minimally irritating	58
CAA: 25% aqueous dilution (of supplied)	Draize	6: Unrinsed	HAIS of 1.7 on day 1, eyes normal by day 2; nonirritating	31
CAA: 20% aqueous solution of 50% active CAG	Draize	6	HAIS of 5.67 on day 1, minimal conjunctival irritation on day 7; minimally irritating	59
CAA: 5% aqueous solution of 50% active CAG	Draize	6	HAIS of 1.0 on day 1, eyes normal by day 3; nonirritating	60
CAP: 16% active (as commercially supplied) pH adjusted to 7.0	Draize	3: Unrinsed	HAIS of 5.33 on day 1, eyes normal by day 4; minimally irritating	61
CAP: 5% active (as commercially supplied)	Draize	3: Unrinsed	HAIS of 1.33 on day 1, eyes normal by day 2; practically nonirritating	62
CADA: 28.1% in a shampoo (32% active)	Draize	6: Unrinsed	HAIS of 2.33 on day 1, eyes normal by day 3; practically nonirritating	63
CADA: 4% in a shampoo cream	Draize	5: Rinsed 4 s after instillation w/60 ml water	HAIS of 10.4 at 1 h, 4.8 by day 1, eyes normal by day 3; minimally irritating	64
CADA: 4% in a shampoo cream	Draize	5: Rinsed 4 s after instillation w/60 ml water	HAIS of 16.4 at 1 h, 5.2 by day 1, eyes normal by day 4; mildly irritating	64
CADA: 4% in an eye cream	Draize	5: Unrinsed	HAIS of 3 at 1 h, 1 by day 1, eyes normal by day 2; minimally irritating	65

TABLE 4. *Continued*

Ingredient	*Test method*	*No. of rabbits*	*Results*	*Reference*
CADA: 1.5% in a facial scrub	Draize	5: Unrinsed 5: Rinsed 4 s after instillation w/60 ml water	Unrinsed: HAIS of 27.4 on day 1, corneal and iridial irritation cleared by day 4, minimal conjunctival irritation at day 7; moderately irritating Rinsed: HAIS of 7.2 at 1 h, 0.4 by day 1, eyes normal by day 3; minimally irritating	66
CADA: at 0.14% with a formulation containing menthol	Draize	Unspecified	Totally eliminated the ocular irritation effects of menthol in the formulation— Draize score reduced to 0 (max = 110)	38
CADA: at 0.14% with a cologne	Draize	Unspecified	Reduced corneal irritation score of the cologne to 0; also reduced total score to 6 and 29 at 72 h and 7 days, respectively	38
CADA: 0.3% blend of CADA with sodium lauryl sulfate and a cologne	Draize	Unspecified	Equivocal reduction of ocular irritation; Draize scores of 7 and 27 for the cornea, 17 and 92 total scores, for 72 h and 7 days, respectively	38
CADP: 36.842% in a shampoo (38% active)	Draize	6: Unrinsed	HAIS of 8 at 1 h, 0 by day 1; not an ocular irritant	67
CADP: 25% in a shampoo (38% active) tested as 10 percent aqueous dilution	Draize	6: Unrinsed	HAIS of 1 on day 1, 0 thereafter; practically nonirritating	68

[a]Maximum score = 110.
[b]HAIS = Highest average irritation score (ocular).

results for CADP were not given. The order of ocular irritancy and cytotoxicity was cationic > anionic = amphoteric > nonionic. A significant correlation existed between relative toxicity in the rabbit corneal cells *in vitro* and relative ocular irritation when tested *in vivo*. CADP was the least irritating amphoteric surfactant; only the three nonionic surfactants were less irritating.

Additionally, Goldemberg[38] found that CADA had anti-irritant activity. CADA eliminated the ocular irritation effects of menthol in a Draize ocular irritation test using a pre-electric shave formulation consisting of 20% butyl stearate in ethanol as the "control." Groups of three rabbits received instillations of the control solution, the control solution with 0.7% menthol, and the control solution with 0.7% menthol and 0.14% CADA. The control formulation had baseline scores of 10, 6.2, and 5.0 at 24, 48, and 72 hours, respectively. The addition of menthol increased the scores to 14.7, 12.4, and 6.5 at 24, 48, and 72 hours, respectively. With addition of CADA, all scores were 0. The determination of the amount of CADA necessary to neutralize the effects of menthol was likened to titration by the investigator. At concentrations of CADA lower than 0.14% some ocular irritation was observed; higher concentrations were not more efficient. The efficiency ratio was 0.14/0.7 indicating that, in this case, 20% CADA neutralized the ocular irritation effects of menthol.

Goldemberg[38] conducted similar studies using a cologne formulation as the "control." Groups of three rabbits received instillations of the cologne alone, the

cologne with 0.14% CADA, and the cologne with 0.3% of a blend containing CADA and sodium lauryl sulfate. The addition of CADA alone was more effective in reducing ocular irritation than the blend. The cologne (96% SDA 39C ethanol) contained approximately 1% diethyl phthalate, which also may have had anti-irritant activity. The effective anti-irritant/irritant ratio for CADA/triethanolamine lauryl sulfate was 1:3.[38]

Dermal

CADA, CADP, CAA, and CAP, as commercially supplied, have been evaluated for dermal irritation primarily by single insult patch test (SIPT) procedures. In each test, an occlusive patch was applied for 24 hours to the clipped skin of the back of the rabbit. Intact or intact and abraded sites were used. In those tests using intact sites only, scores were taken 2 and 24 hours after patch removal on a maximum scale of 4. In those tests using the Draize procedure, with intact and abraded sites, scores were taken at 24 and 72 hours on a maximum scale of 8. CADA, at a concentration of 10 to 12% active, as well as solutions of unstated activity, was nonirritating to severely irritating to rabbit skin. CADP, at concentrations of 7.5 and 70% active, was nonirritating. CAA, at a concentration of 16% active as well as solutions of unstated activity, was nonirritating to severely irritating. CAP, at concentrations of 15 and 16% active, was slightly irritating. Cosmetic products containing CADA (as supplied) at concentrations of 1.5 to 4% and CADP (as supplied) at concentrations of 25 to 36.8% also have been evaluated for dermal irritation by the Draize procedure. Dermal irritation test results are given in Table 5.

These four ingredients also have been evaluated for dermal irritation in rabbits by use of a single intradermal injection. Each injection consisted of 0.5 ml of a 5% solution of CADA, CADP, or CAP (supplied as 20% active solutions—giving actual test concentrations of 1%); CAA was evaluated as a 0.1% solution. In each case, a second group of rabbits received injections of an olive oil castile shampoo as the control. The rabbits were observed for signs of irritation at the injection site 24 hours later and scored on a maximum scale of 4. CADA had a score of 0 and was considered nonirritating.[69] CADP, CAA, and CAP had scores of 1 and were considered less irritating than the control shampoos, which had scores of 2.[70–72]

Sensitization

The Magnusson-Kligman maximization test was used to evaluate the sensitization potential of CAA in 15 guinea pigs. CAA was tested at concentrations of 25, 50, and 100%. Negative (15 guinea pigs) and positive (15 guinea pigs) control groups were tested with distilled water and methylmethacrylate (25, 50, and 100%), respectively. CAA did not induce sensitization in any of the animals tested. Sensitization reactions were observed in the positive control group.[94]

MUTAGENICITY

The mutagenic potentials of CAP, CADA, and CADP were evaluated in the Ames *Salmonella*/microsome assay, using *Salmonella typhimurium* strains: TA-1535, TA-1537, TA-1538, TA-98, and TA-100.[95] CAP, CADA, and CADP (each diluted with deionized water) were tested at concentrations ranging from 0.005 to 1.00 μl per plate. Each test substance was incubated with each bacterial strain (three plates per dose, 37 ± 2°C) for 48 to 72 h in both the presence and absence of metabolic activation. The number of his+ revertant colonies was determined using an automated colony counter.

TABLE 5. Dermal Irritation

Ingredient	*Test method*	*No. of rabbits*	*Results*	*Reference*
CADA: As commercially supplied	SIPT[a]	9	AII[b] = 1.8; mildly irritating	73
CADA: As commercially supplied	SIPT	9	AII = 1.89; mildly irritating	74
CADA: As commercially supplied	SIPT	5	AII = 4.0; severely irritating	75
CADA: As commercially supplied	Draize[c]	6	PII[d] = 4.49; severely irritating	76
CADA: As commercially supplied	Draize	6	PII = 1.5; mildly irritating	48
CADA: 21% aqueous solution of CADA (as commercially supplied)	Draize	6	PII = 0.96; mildly irritating	77
CADA: 12% active (as commercially supplied)	Draize	3	PII = 0; nonirritating	78
CADA: 10% active (as commercially supplied)	Draize	3	PII = 0.85; slightly irritating	49
CADA: 10% in water	Draize	6	PII = 0; nonirritating	79
CADA: 10% in mineral oil	SIPT	9	AII = 0.11; minimally irritating	80
CADA: 2, 10, 20% aqueous solutions	Draize	6	PIIs = 2.25, 2.5, and 3.0 for the 2, 10, and 20% aqueous solutions; 2 and 10% solutions considered moderately irritating; 20% solution considered severely irritating	52
CADA: Actual concentration of 1% (5% of 20% active solution)	SIDI[e]	Unspecified	All scores = 0 (max = 4); nonirritating	69
CADP: 70% active (as commercially supplied)	Draize	3	PII = 0; nonirritating	81
CADP: 25% dilution of the CADP supplied	Draize	6	PII = 0; nonirritating	82
CADP: 7.5% active (as commercially supplied)	Draize	3	PII = 0; nonirritating	83
CADP: actual concentration of 1% (5% of 20% active solution)	SIDI	Unspecified	Score = 1 (max = 4); considered less irritating than control shampoo	72
CAA: As commercially supplied (pH adjusted to 7.0)	Draize	6	PII = 0; nonirritating	84
CAA: 25% (of supplied) in water	Draize	6	PII = 0.08; nonirritating	31
CAA: 16% active (as commercially supplied; pH adjusted to 7.0)	Draize	3	PII = 3.83; severely irritating	85
CAA: 0.1%	SIDI	Unspecified	Score = 1 (max = 4); considered less irritating than control shampoo	70
CAP: 16% active (as commercially supplied—pH adjusted to 7)	Draize	3	PII = 0.5; slightly irritating	86
CAP: 15% active (as commercially supplied)	Draize	6	PII = 0.5; slightly irritating	87
CAP: actual concentration of 1% (5% of 20% active solution)	SIDI	Unspecified	Score = 1 (max = 4); considered less irritating than control shampoo	71

TABLE 5. *Continued*

Ingredient	*Test method*	*No. of rabbits*	*Results*	*Reference*
CADA: 4% in an eye cream	Draize	4	PII = 3.13; severely irritating	88
CADA: 4% in a shampoo cream tested at 2.5% in water	Draize	4	PII = 1.56; mildly irritating	89
CADA: 4% in a shampoo cream tested at:	Draize			89
2.5% in water		4	PII = 2.94; moderately irritating	
1.25% in water		4	PII = 1.63; mildly irritating	
CADA: 1.5% in each of three facial scrubs; tested at	Draize	4	PII = 0.81; slightly irritating	90
1.25% in water		4	PII = 1.06; mildly irritating	
		4	PII = 2.00; moderately irritating	
CADA: with sodium lauryl sulfate and hexylene glycol; unspecified concentration	Draize	3	PII = 0.5; slightly irritating	91
CADP: 36.842% in a shampoo (38% active)	Draize	6	PII = 0.12; slightly irritating	92
CADP: 25% in a shampoo (38% active); tested as 10% aqueous dilution	Draize	6	PII = 0.21; slightly irritating	93

[a]SIPT = Single insult patch test = 24 h occlusive on intact site. Scores taken at 26 and 48 h.
[b]AII = Average irritation index (max = 4).
[c]Draize = Single 24 h occlusive patch on intact and abraded sites. Scores taken at 24 and 72 h.
[d]PII = Primary irritation index (max = 8).
[e]SIDI = Single intradermal injection.

Solvent controls were incubated with 50.0 μl of deionized water. Positive control cultures (all strains, metabolic activation) were incubated with 2-anthramine (2.5 μg/plate). Other positive control cultures (no metabolic activation) were incubated with: sodium azide in water (10.0 μg/plate, TA-1535 and TA-100), 2-nitrofluorene in dimethyl sulfoxide (DMSO) (10.0 μg/plate, TA-1538 and TA-98), and quinacrine mustard in DMSO (5.0 μg/plate, TA-1537). CAP, CADA, and CADP were not mutagenic to any of the strains tested in either the presence or absence of metabolic activation. The positive controls (with and without metabolic activation) induced large increases in the numbers of revertants in all of the strains tested.[96–98]

CLINICAL ASSESSMENT OF SAFETY

Ocular Irritation

A children's shampoo containing 28.1% CADA (32% active) was evaluated for ocular irritation using 30 adult subjects. Three dilutions of the shampoo were tested: 1, 3, and 10%. Each dilution was instilled into the conjunctival sac of one eye of each of 10 subjects; the other eye was treated with sterile distilled water. Positive reactions were noted only at the 30-s posttreatment evaluation. These consisted primarily of mild irritation scores for the bulbar and palpebral conjunctivae for all groups (including water treated); one subject each in the 3 and 10% groups as well as one treated with distilled water had a moderate score for irritation of the bulbar conjunctiva. Stinging

was noted in 1, 3, 4, and 2 subjects in the 1, 3, and 10% groups and water-treated eyes, respectively. When weighted for the number of eyes exposed, no significance was found in the positive responses. In all but seven of the positive reactions to the shampoo dilutions, distilled water elicited a positive reaction in the other eye. This was attributed to the eye sensitivity of individual subjects. None of the shampoo dilutions were considered more irritating than sterile distilled water.[99]

Dermal Irritation and Sensitization

The skin sensitization potential of CAA and CAP was evaluated using 32 male (18–65+ years) and 109 female (18–65 years) subjects. The chemicals were diluted to a concentration of 10% w/v in distilled water prior to testing. During induction, each chemical was applied to the back three times per week for three successive weeks. Sites were covered for 24 h with nonocclusive patches secured with surgical tape. Repeated applications of both chemicals were made to the same test sites. Reactions were scored 48 or 72 h after each induction application according to the Draize[100] scale: 0 (no erythema and eschar formation, no edema) to 4 (severe erythema to slight eschar formation, severe edema). The challenge phase was initiated 10 to 15 days after application of the final induction patch. Challenge patches (nonocclusive) were applied for 24 h to new sites on the back; reactions were scored 48 and 96 h later. CAA and CAP did not induce skin irritation or sensitization in any of the subjects tested.[101] Results of all irritation and sensitization tests are reported in Table 6.

A children's shampoo containing 28.1% CADA (32% active) was evaluated for irritation and sensitization by a Repeated Insult Patch Test (RIPT) using 105 subjects. Occlusive patches containing a 5.0% dilution of the shampoo were applied to the backs of the subjects on Mondays, Wednesdays, and Fridays for the first five inductions; however, due to the large number of irritant reactions, semiocclusive patches were used on a new site for the remaining four inductions. Sites were scored upon patch removal (and prior to next patch application) on a scale of 0–3+. After a two-week nontreatment period, a challenge patch was applied for 48 h to the same site and the site was scored after 48 and 72 h. Under semiocclusive conditions, the shampoo elicited, at most, two ? (barely perceptible erythema) reactions and one 1+ (definite erythema) reaction during induction. Three and one ? reactions were observed 48 and 72 h after the challenge, respectively. The shampoo was nonirritating and nonsensitizing under semiocclusive patch test conditions.[102]

A shampoo cream and a facial scrub containing 4 and 0.61% CADA, respectively, were evaluated for irritation and sensitization by RIPT at a concentration of 1% in water. In each test, a series of eight induction patches was applied to the upper portion of the arm of each subject on four consecutive days per week for two weeks. These patches were semiocclusive and contained 0.3 or 0.2 ml of the shampoo or scrub test solutions, respectively. Patches were removed after 24 h and sites scored on a scale of 0 to 5. After a 2-week nontreatment period, semiocclusive challenge patches were applied to adjacent sites for 24 h. Reactions were scored at 24, 48, and 72 h for both test solutions, and additionally at 96 h for the facial scrub. In both tests, slight erythema (score of 1) was noted during induction, whereas no reactions were observed at challenge. The shampoo and facial scrub were nonirritating and nonsensitizing in the 45 and 53 subjects, respectively, who completed the studies.[103,104]

TABLE 6. Clinical Irritation and Sensitization

Ingredient	*Test method*	*No. of subjects*	*Results*	*References*
CAA: 10% in distilled water	RIPT[a] (nonocclusive)	141	Nonirritating and nonsensitizing	101
CAP: 10% in distilled water	RIPT (nonocclusive)	141	Nonirritating and nonsensitizing	101
CADA: 28.1% in a shampoo (32% active); tested as 5% dilution in water	RIPT (occlusive switched to semiocclusive)	105	Large number of irritant reactions—to induction patches 1-5 under occlusive conditions; switched to semiocclusive patches; nonirritating and nonsensitizing	102
CADA: 4.0% in a shampoo cream and tested at 1% in water	RIPT (semiocclusive)	45	Nonirritating and nonsensitizing	103
CADA: 1.1% in an eye makeup remover (70% active)	RIPT (occlusive)	102	Nonirritating and nonsensitizing	105
CADA: 1.1% in an eye makeup remover (70% active)	RIPT (occlusive)	103	Produced some irritation; nonsensitizing	112
CADA: 0.61% in a facial scrub; tested at 1% in water	RIPT (semiocclusive)	53	Nonirritating and nonsensitizing	104
CADA: 25% in a facial cleanser (45.6% active)	Controlled use; twice daily for one month	54	No adverse reactions	106
CADP: 10% in a hair product (diluted to 1% in water)	Kligman maximization	25	No adverse reactions; nonsensitizing	107
CADP: 5% in a cleansing cream	RIPT (occlusive)	204	Nonirritating and nonsensitizing	108
CADP: 5% in a cleansing cream	21-Day cumulative irritation (occlusive)	12	Total score = 109 (max = 1008); very mildly irritating	109
CADP: 5% in a cleansing cream	Controlled use; daily for one month	53	Nonirritating	110
CADP: 5% in a cleansing cream	Controlled use; once or twice daily for two weeks	24	No adverse reactions	111

[a]RIPT = Repeated Insult Patch Test

An eye makeup remover containing 1.1% of 70% active CADA (actual concentration of 0.77%) was evaluated for irritation and sensitization by a modified Draize RIPT. Occlusive patches containing 0.3 ml of the test material were applied for 24 h to the upper portions of the arms of 102 volunteers on alternate days for a total of 10 applications. After a two to three week nontreatment period, an occlusive challenge patch was applied for 24 h to the same test site on each volunteer. Reactions were scored upon patch removal and at 24 h. All scores were 0 (max = 4); the eye makeup remover was considered neither a primary skin irritant, sensitizer, nor fatiguing agent.[105]

Another eye makeup remover also containing 1.1% of 70% active CADA (actual concentration of 0.77%) was evaluated for irritation and sensitization by an RIPT. Occlusive patches were applied for 48 h to the same site on the back of 113 panelists on

alternate days for a total of 10 applications. Patches applied on Friday remained in place until Monday. Sites were scored 15 minutes after patch removal. After a nontreatment period, an occlusive challenge patch was applied for 48 h to a fresh site on the back. Reactions were then scored at 15 min and 24 h after patch removal. Of the 103 panelists who completed the study, only one reaction (score of 2, max = 4) was noted at challenge. However, positive irritant reactions to the product were observed during the induction phase in 28 of 113 panelists. Except for one subject, none of the irritation scores exceeded 2, even with continued application of the product. This particular subject had a score of 4+ after six applications; however, no irritation was seen when the product was reapplied under nonocclusive conditions. The irritancy level of this product would not be considered significant when applied for a short duration to normal skin although the proximity of its use to the eye should be taken into consideration. The eye makeup remover produced no evidence of sensitization but did produce some irritation.[112]

A facial cleanser containing 25% CADA (45% active) was evaluated in a controlled use study with 54 subjects. The subjects were instructed to use the cleanser twice daily for one month; 29 of the subjects used the cleanser alone and 25 used the cleanser with an antiseptic lotion. The cleanser produced no adverse reactions.[106]

A Kligman maximization test was conducted to evaluate the skin sensitization potential of a hair product containing 10% CADP. Another formulation not containing CADP was simultaneously tested. Twenty-five subjects participated in the study. The study was conducted without sodium lauryl sulfate (SLS) pretreatment, as it was determined that both test materials were mildly irritating by pretest with test solutions and SLS. The hair product was diluted with distilled water to a concentration of 1% and applied (0.3 ml) to each patch. The occlusive induction patches remained in place for 48 h, after which there was a 24-h nontreatment period. These procedures were repeated for a total of five inductions. The induction sites were scored only in the event of exacerbation or a flare. Ten days after removal of the last induction patch, occlusive challenge patches were applied to previously untreated sites for 48 h. None of the subjects had reactions to induction or challenge patches that contained samples of the hair product with 10% CADP. The investigators concluded there was no evidence of contact sensitization elicited by this product.[107]

Cleansing creams containing 5% CADP were evaluated for irritation and sensitization by an RIPT, a 21-day cumulative irritation test, and two controlled use studies. In the modified Draize-Shelanski-Jordan RIPT, a series of 10 occlusive induction patches were applied on alternate days to 204 subjects (147 males, 57 females). These patches were left in place for 24 h and results were scored (max = 4) upon removal. After a 13-day nontreatment period, challenge patches were applied for 48 h to new sites on the back. Seven days later, a second challenge patch was applied for 48 h. Challenge site reactions were scored at 48 and 72 h. Mild erythema (score of 1) was noted in 16 subjects during induction and challenge; these reactions were considered isolated and clinically insignificant. Intense erythema (score of 2) was noted in a subject after the eighth induction patch. Open patches were used thereafter and no further reactions were observed. This was considered to be an example of nonspecific irritation typical of cleansing creams. The cleansing cream was nonirritating and nonsensitizing.[108]

In the 21-day cumulative irritation test using 12 subjects, occlusive patches containing the cream were applied daily for 21 consecutive days (patches applied on Saturday remained in place until Monday). Patches were applied to the back, removed

after 24 h, and reactions were scored immediately (max = 4). Solutions of 0.5 and 2% sodium lauryl sulfate were used as markers, and had total scores of 67 and 298 (max = 1008), respectively. The cream had a total score of 109 and was considered very mildly irritating.[109]

In the first controlled use study, the cream was used by 53 subjects on a daily basis for four weeks. One subject noted a feeling of "irritation" after a few days, although no specific erythema or dermatitis was evident. This subject discontinued use. No rash, itching, burning, or irritation was noted by the other subjects.[110]

In the second controlled use study, 24 subjects used the cream once or twice daily for two weeks. No adverse reactions were noted.[111]

Photoallergenicity

The photoallergenicity of CAA, CAP, and CADA was evaluated using 5 male and 25 female subjects (18–55 years). Distilled water served as the control. Each chemical was diluted to a concentration of 10% w/v in distilled water prior to testing. During induction, a total of nine duplicate applications of each chemical were made to the back three times per week for three weeks. Each site was covered for 24 h with a gauze pad secured with surgical tape. Within 10 min after each patch removal, sites were irradiated with UVA light (4.0 J/cm^2, 22–25 s). The application sites of 13 subjects were irradiated with twice the minimal erythemal dose of UVB light (2–5 min, 2–5 mJ/cm^2) immediately after UVA irradiation. UVA (320–400 nm) and UVB (290–320 nm) radiation was emitted from a 1000 W xenon arc solar simulator with appropriate filters. Reactions were scored 48 h after applications 1, 2, 4, 5, and 8, and 72 h after applications 3, 6, and 9 according to the scale: 0 (no evidence of any reaction) to 5 (vesicular/bullous eruption). The challenge phase was initiated two weeks after the conclusion of induction. Duplicate 24-h challenge applications of each test substance were made to new sites on the back. At the conclusion of exposure, half of the challenge patches applied (one per chemical) were removed and sites were irradiated with UVA light (4.0 J/cm^2, 22–23 s). Challenge patches were then removed from the remaining nonirradiated sites. Reactions were scored at approximately 24, 48, and 72 h after patch removal. Mild to moderate erythema, at either experimental or control induction sites, was observed in a total of 11 subjects. The 11 subjects were among the 13 exposed to UVA and UVB light. The authors stated that such reactions generally result from sunburn derived from UVB exposure. CAA, CAP, and CADA did not induce photoallergic reactions or delayed contact hypersensitivity in any of the subjects tested.[101]

SUMMARY

Cocoamphoacetate (CAA), Cocoamphopropionate (CAP), Cocoamphodiacetate (CADA), and Cocoamphodipropionate (CADP) are imidazoline-derived amphoteric organic compounds. These products are prepared by reacting coconut acid with aminoethylethanolamine to produce an imidazoline, which is then reacted with monochloracetic acid or monochloropropionic acid in the presence of sodium hydroxide to form the mono- (CAA and CAP) or dicarboxylated (CADA and CADP) products.

These amphoteric compounds are supplied as amber liquids containing 40 to 50% solids. The viscosity may be increased by the addition of sodium chloride. All are soluble in water and insoluble in nonpolar organic solvents; CAP and CADP are also soluble in alcohol. The pH range for commercially available solutions of CAA, CAP, CADA, and CADP has been reported to be from 8.1 to 10.2.

CAA, CAP, CADA, and CADP can be assayed by close match to standard infrared spectra and ionization curves.

The amphoteric compounds are used in cosmetics as surfactants, mild foaming and cleansing agents, detoxifying agents, and conditioners. These ingredients are present in cosmetics at concentrations ranging from ≤ 0.1 to 50%. Product use may lead to contact of all external body surfaces, hair, eyes, and mucous membranes; frequency and duration of application could result in continuous exposure.

The amphoteric compounds are used widely in industrial and household cleaning products.

In acute oral toxicity studies, CADA and CAA were nontoxic in rats and mice, CADP was nontoxic in rats, and CAP was nontoxic in mice. CADA and CADP were also nontoxic when fed to rats for 10 days at concentrations of 0.25 and 0.50% of the diet. An oral LD_{50} of 7.8 ml/kg was reported for mice dosed with 70% CADP (as commercially supplied).

In acute dermal toxicity studies, two shampoo creams containing 4.0% CADA had LD_{50}s >10.0 ml/kg. Primary signs of systemic toxicity included depression, labored respiration, and phonation upon handling. Moderate dermal irritation also was noted.

Results of Draize ocular irritation studies in rabbits were that these ingredients, as commercially supplied, varied widely in their ocular irritancy. CADA was moderately to severely irritating when eyes were not rinsed and practically nonirritating to mildly irritating when rinsed from the eye. CADP was practically nonirritating under unrinsed conditions. CAA was minimally to severely irritating and CAP was practically nonirritating to minimally irritating under unrinsed conditions. CADA also has distinct anti-irritant activity when used in formulations.

Single insult patch tests of these ingredients in rabbits with intact or intact and abraded skin have produced varying results. As commercially supplied, CADA and CAA were nonirritating to severely irritating, CADP was nonirritating, and CAP was slightly irritating. When intradermally injected into rabbits, CADA (1%) was nonirritating while CAA (0.1%), CADP (1%), and CAP (1%) were less irritating than the control shampoo.

CAA, at a concentration of 50% active, was nonsensitizing in guinea pigs when evaluated by the Magnusson-Kligman maximization test.

The mutagenic potential of CAP, CADA, and CADP was evaluated in the standard Ames assay with and without a metabolic activation system and with positive and negative controls. The three test compounds were not mutagenic.

In a clinical ocular study, 1, 3, and 10% dilutions of a shampoo containing 28.1% CADA (32% active) were no more irritating to the human eye than sterile distilled water. CAA and CAP (concentrations = 10% in distilled water) were nonirritating and nonsensitizing in a repeated insult patch test (RIPT) involving 141 subjects; nonocclusive patches were applied. In other RIPTs, products containing CADA at concentrations of 0.61 to 28.1% were essentially nonirritating and nonsensitizing under semiocclusive conditions. These products did produce some irritation under occlusive patch conditions. A facial cleanser containing 25% CADA (45.6% active) produced no adverse

reactions in 54 subjects using the product twice daily for one month. Cleansing creams containing 5% CADP were nonirritating and nonsensitizing in 204 subjects evaluated by RIPT (occlusive), very mildly irritating in 12 subjects evaluated by a 21-day cumulative irritation test (occlusive), and nonirritating in 53 and 24 subjects using the products daily for one month or once or twice daily for two weeks, respectively. In the maximization test, a hair product (diluted to 0.1% CADP) did not induce sensitization in any of the 25 subjects tested. CAA, CAP, and CADA (concentrations = 10% in distilled water) did not induce photoallergic reactions or delayed contact hypersensitivity in a study involving 30 subjects.

DISCUSSION

The Expert Panel recognizes that Cocoamphoacetate, Cocoamphopropionate, Cocoamphodiacetate, and Cocoamphodipropionte, as commercially supplied, induced mild to severe ocular irritation in the Draize test and, also, that cosmetic products containing these ingredients are buffered.

Mutagenicity data on Cocoamphoacetate were not available. However, the Expert Panel concluded that this ingredient was not mutagenic, based on negative Ames test results for Cocoamphodiacetate.

CONCLUSION

Based upon the available data included in this report, the Expert Panel concludes that CAA, CAP, CADA, and CADP are safe as cosmetic ingredients in the present practices of use.

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