Cocamide MEA is a mixture of ethanolamines of fatty acids derived from coconut oil. This cosmetic ingredient functions as a surfactant—foam booster and an aqueous viscosity-increasing agent. To supplement the available data on Cocamide MEA, data from previous safety assessments of Coconut Oil and its derivatives, Monoethanolamine (MEA), and Cocamide DEA (Diethanolamine) were included in this safety assessment. These data suggest little acute, short-term, or chronic toxicity associated with dermal application. MEA vapor, however, is highly toxic. Although DEA is readily nitrosated to form N-nitrosodiethanolamine, a known animal carcinogen, MEA has not been found to form a stable nitrosoamine. Dermal application of Cocamide MEA at concentrations of 50% was nonirritating to mildly irritating in animal tests. For comparison, Cocamide DEA at a concentration of 30% was a moderate irritant; Coconut Oil was nonsensitizing; and MEA was irritating and corrosive. Cocamide MEA was negative in the Ames Test. Cocamide DEA was positive in some mutagenesis assays, but negative in others. In clinical tests, Cocamide MEA at a concentration of 50% was not irritating in a single-insult patch test. Cocamide DEA at 2% in formulation caused irritation, but not sensitization. Predictive patch tests with a surfactant containing Cocamide DEA at 10% produced no adverse effects. Inhalation of MEA by humans is toxic. Based on the limited data available data on Cocamide MEA, and on the data on those ingredients previously reviewed, particularly Cocamide DEA, it was concluded that Cocamide MEA is safe as used in rinse-off products and safe at concentrations up to 10% in leave-on products. It was further concluded, however, that Cocamide MEA should not be used as an ingredient in cosmetic products in which N-nitroso compounds are formed or in formulations that will be aerosolized.

Cocamide Monoethanolamine (MEA) functions as a surfactant—foam booster and aqueous viscosity-increasing agent—in cosmetic formulations. Safety assessments on Cocamide Diethanolamine (DEA), Stearamide DEA, Isostearamide MEA, Myristamide MEA, Coconut Oil and its derivatives, and MEA have been previously evaluated by the Cosmetic Ingredient Review (CIR) Expert Panel. Information from those safety assessments has been included in this report (in italics). The following conclusions were made:

Cocamide DEA is safe as used in rinse-off products and safe at concentrations up to 10% in leave-on cosmetic products. Cocamide DEA should not be used as an ingredient in cosmetic products in which N-nitroso compounds are formed (Andersen 1996).

Cocamide DEA and MEA, Myristamide DEA and MEA are safe for use in rinse-off products; safe for use in leave-on products at concentrations that will limit the release of free ethanolamines to 5%, but with a maximum use concentration of 17% for the MEA forms and 40% for the DEA forms; and none should be used in cosmetic products in which N-nitroso compounds may be formed (Cosmetic Ingredient Review [CIR] 1995).

CHEMISTRY

Definition and Structure

Cocamide MEA (CAS No. 68140-00-1) is a mixture of ethanolamides of coconut acid (q.v.) that conforms generally to the structure shown in Figure 1, where the radical, RCO-, represents the fatty acids derived from coconut oil (Wenninger and McEwen 1997). According to Nikitakis and McEwen (1990), Cocamide MEA contains 82–88% amide.

Other names for Cocamide MEA include Amides, Coco, N-(2-Hydroxyethyl); Coco Monoethanolamide; Coconut Fatty Acid Monoethanolamide; Cocoyl Monoethanolamine; Eqex AEM; N-(2-Hydroxyethyl) Coco Fatty Acid Amide; Monoethanolamine Coconut Acid Amide (Wenninger and McEwen 1997); Coconut Oil, Monoethanolamide; Coconut Oil Fatty Acids, Monoethanolamide; and Coconut Oil Fatty Acid Ethanolamide (Chemline 1995).

Cocamide MEA is a tan, granular solid that is water-soluble. The pH of a 10% aqueous solution of Cocamide MEA is 9.5–10.5. The compound has acid and alkali values of 1 (maximum) and 10–20, respectively. Cocamide MEA melts at 60–64°C (Nikitakis and McEwen 1990).

Chemical and Physical Properties

Cocamide DEA is very stable in neutral, moderately alkaline, or acid systems, but is subject to hydrolysis at high concentrations of mineral acids and alkali (Andersen 1996).
The primary constituents of Coconut Oil are trimyristin, trilaurin, tripalmitin, tristearin, and various other triglycerides. About 90% of the oil is saturated. Coconut Acid is a mixture of fatty acids derived from Coconut Oil by hydrolysis; the fatty acid composition is the same as that for Coconut Oil. Due to the high degree of saturation, Coconut Oil undergoes little change in melting point and consistency following hydrogenation, and is resistant to atmospheric oxidation (Elder 1986a).

MEA is the amino alcohol formed by aminating ethylene oxide with ammonia and replacing one of the ammonia hydrogens with an ethanol group. MEA reacts at room temperature with fatty acids to form ethanalamine soaps, and will react at temperatures between 140 and 160°C with fatty acids to form ethanalamides. The ethanalamines can act as antioxidants in the autoxidation of fats of both animal and vegetable origin. MEA has not, as yet, been found to form a stable nitrosamine; however, MEA can react with an aldehyde to form DEA, which can then be nitrosated to form N-nitrosodiethanolamine (Elder 1983).

Method of Manufacture

Cocamide DEA is produced by the condensation of DEA with coconut fatty acids or their esters. It has also been produced by the reaction of refined coconut oil with DEA in the presence of a sodium methoxide catalyst, yielding Cocamide DEA, 10% glycerine, and 5% coconut fatty acid ester amide (Andersen 1996).

Coconut Oil is obtained from copra, where it is present in quantities of 60–70%, and from the kernels of the seeds of Cocos nucifera. The expressed material has a water content of 4–10%. Coconut Acid is derived from Coconut Oil by hydrolysis and isolation of the fatty material, which is then distilled (Elder 1986a).

Impurities

Coconut Oil is usually quite low in color bodies, pigments, phosphatides, gums, and other nonglyceride substances commonly found in much larger quantities in other vegetable oils. It may contain free fatty acids and low concentrations of sterols, tocopherol, and squalene. The presence of approximately 150 ppm lactones (a series of 8-lactones with 6, 8, 10, 12, and 14 carbon atoms) provides the characteristic coconut flavor. Crude sam-

![Chemical structure of Cocamide MEA](image)

**FIGURE 1**

Chemical formula for Cocamide MEA, where the radical, $RCO_-$, represents the fatty acids derived from coconut oil (Nikitakis and McEwen 1990; Wenninger and McEwen 1997).

**USE**

**Cosmetic**

Cocamide MEA serves as a surfactant—foam booster and aqueous viscosity-increasing agent—in cosmetic formulations (Wenninger and McEwen 1997). Data submitted to the Food and Drug Administration (FDA) in 1996 stated that Cocamide MEA was used in 285 cosmetic product formulations, listed in Table 1 (FDA 1996). The cosmetic industry is no longer required to submit concentration of use data to the FDA (FDA 1992). Data submitted in 1984 stated that 0–0.1% to 10–25% Cocamide MEA was used in cosmetic formulations, with the majority of products containing 1–5% Cocamide MEA (FDA 1984).

**TABLE 1**

Cosmetic formulation data on Cocamide MEA (FDA 1996)

<table>
<thead>
<tr>
<th>Product category</th>
<th>Total no. formulations in category</th>
<th>Total no. of formulations containing ingredient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baby shampoos</td>
<td>23</td>
<td>1</td>
</tr>
<tr>
<td>Bath oils, tablets, and salts</td>
<td>147</td>
<td>4</td>
</tr>
<tr>
<td>Bubble baths</td>
<td>211</td>
<td>12</td>
</tr>
<tr>
<td>Other bath preparations</td>
<td>166</td>
<td>11</td>
</tr>
<tr>
<td>Shampoos (noncoloring)</td>
<td>972</td>
<td>131</td>
</tr>
<tr>
<td>Tonics, dressings, and other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hair grooming aids</td>
<td>604</td>
<td>1</td>
</tr>
<tr>
<td>Other hair preparations</td>
<td>395</td>
<td>2</td>
</tr>
<tr>
<td>Hair dyes and tints</td>
<td>1612</td>
<td>77</td>
</tr>
<tr>
<td>Hair shampoos (coloring)</td>
<td>29</td>
<td>5</td>
</tr>
<tr>
<td>Other hair coloring preparations</td>
<td>71</td>
<td>2</td>
</tr>
<tr>
<td>Blushers (all types)</td>
<td>277</td>
<td>1</td>
</tr>
<tr>
<td>Bath soaps and detergents</td>
<td>372</td>
<td>16</td>
</tr>
<tr>
<td>Deodorants (underarm)</td>
<td>303</td>
<td>3</td>
</tr>
<tr>
<td>Douches</td>
<td>19</td>
<td>2</td>
</tr>
<tr>
<td>Other personal cleanliness products</td>
<td>339</td>
<td>3</td>
</tr>
<tr>
<td>Shaving cream</td>
<td>158</td>
<td>5</td>
</tr>
<tr>
<td>Shaving soap</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Cleansing</td>
<td>820</td>
<td>14</td>
</tr>
<tr>
<td>Body and hand (excluding shaving)</td>
<td>1012</td>
<td>1</td>
</tr>
<tr>
<td>Other skin care preparations</td>
<td>810</td>
<td>2</td>
</tr>
<tr>
<td><strong>1996 total</strong></td>
<td><strong>294</strong></td>
<td></td>
</tr>
</tbody>
</table>
Noncosmetic
Cocamide MEA has been used to separate mammalian sperm acrosomes for use in cattle artificial insemination programs, either by itself (1%), or in a commercially mixed liquid detergent comprised of sodium tetrapropylene benzene sulfonate, sodium lauryl ether sulfate, and Cocamide MEA (4:1:1) (Gombe, Norman, and Mbogo 1975).

International
Cocamide MEA is listed in the Comprehensive Licensing Standards of Cosmetics by Category (CLS) and must conform to the standards of the Japanese Cosmetic Ingredient Codex (JCIC). It can be used without restriction in all CLS categories except eyeliners, lipsticks and lip creams, and dentifrices (Yakuji Nippo, Ltd. 1994).

GENERAL BIOLOGY
Absorption, Distribution, Metabolism, and Excretion
Intubation studies using rats demonstrated that 60% of a 6 g/kg Coconut Oil dose was absorbed within 6 hours. In clinical studies in which subjects received 50–140 g Coconut Oil over 3 days, digestibility was 98% (Elder 1986a).

MEA is the only naturally occurring ethanamine in mammals and 11% is excreted in the urine (half-life = 19 days). It is converted to phosphatidylethanolamine in all tissues and is methylated to phosphatidylcholine, even in human arteries. In radioactive studies, it was observed that a coenzyme B12-dependent ethanamine deaminase–mediated conversion of MEA to acetaldehyde and ammonia can also occur. Feed studies have demonstrated that ATP can phosphorylate MEA, and researchers have hypothesized that the removal of phosphorylated MEA by its conversion to acetate from acetaldehyde may exert a regulatory effect on phosphatidylethanolamine biosynthesis (Elder 1983).

Antimicrobial Effects
MEA inhibits the growth of a wide variety of microorganisms. The concentration required to inhibit growth varies with genus and species. MEA also has some antimycotic activity when applied to the skin of guinea pigs (Elder 1983).

Pharmacodynamic Effects
Administration of 60 mg/kg/day MEA to albino rats with experimentally induced coarctation of the aorta for 30 days resulted in elevated levels of phosphatidylethanolamine, phosphatidylcholine (lecithin), and phosphatidylserine in the myocardium. These results may have been produced by inhibition of the development of cardiac insufficiency due to MEA-induced metabolic changes. MEA inhibited the action of purified acetylcholinesterase obtained from bovine erythrocytes. MEA stimulated the activity of purified aspartate transaminase from porcine heart and decreased the enzyme’s action in rabbit kidney and heart following oral or intravenous administration. Additionally, intravenous administration of MEA increased the levels of aspartate and glutamate in the kidneys and decreased the levels in the brain of rabbits. Alanine transaminase activity in the kidneys and heart of rabbits was inhibited by MEA. Oral administration of MEA to rats inhibited the activity of alcohol dehydrogenase. MEA can also inactivate and partially dissociate β-galactosidase from Escherichia coli. MEA can affect the metabolism of catecholamines by increasing norepinephrine and decreasing epinephrine concentrations in the hearts of rats after intraperitoneal injection of 10 mg/kg. An injection of 25 mg/kg had the opposite effect. Also, MEA strongly inhibited the in vitro conversion of paraparathyroid hormone to parathyroid hormone. Other effects of MEA administration include the increase of serum albumin and total protein concentrations when given to castrated rams in subchronic oral studies; the increase of RNA in the kidneys, heart, and brain of rabbits; the decrease of DNA in the heart and brain of rabbits; increased myocardial contractility in rats; increased atrial rats and force of contraction in rabbit atria; and increased glycogen, ATP, and ascorbic acid concentrations in the liver, kidneys, brain, and heart of rats (Elder 1983).

ANIMAL TOXICOLOGY
Acute Toxicity
Undiluted Coconut Oil was judged nontoxic by ingestion when 10 rats were administered 5 g/kg by gavage. No deaths occurred during the 7-day observation period as a result of treatment (Elder 1986a).

The acute oral LD₅₀ of undiluted Cocamide DEA in male and female Sprague-Dawley rats was 12.2 g/kg (12.4 ml/kg). The 95% confidence limit was 10.7–14.4 ml/kg. Tests on formulations containing 10% Cocamide DEA and 12% Cocamide DEA had LD₅₀ of >5 g/kg and >5 ml/kg, respectively (Elder 1986b).

MEA has an acute oral LD₅₀ in rats of 1.72–2.74 g/kg and was deemed slightly toxic. In an oral corrosivity study using four rabbits, 0.229 g/kg (0.210 ml) of a hair preparation containing 1.6% DEA, 5.9% MEA, and 3.2% sodium borate was placed, undiluted, on the posterior tongue surface. The rabbits were then allowed to swallow. Two each were killed at 24 and 96 hours. No observable abnormalities were observed at gross and microscopic examination, and the preparations were found to be neither irritating nor corrosive under the conditions of this test (Elder 1983). The mouse acute intraperitoneal LD₅₀ of MEA was 1.05 g/kg (Elder 1983).

Short-Term Dermal Toxicity
In a 4-week dermal toxicity study, five products, including a shaving cream containing 1.92% Cocamide DEA, were evaluated. Forty-eight New Zealand White rabbits were allotted into six groups of eight animals (four male and four female).
Each rabbit received daily applications (500 mg/kg) of the test material 5 days/week to a shaved area of the back. The site was abraded in four rabbits and intact in the remaining four. Four rabbits per sex served as controls. Moderate erythema, wrinkling, cracking, and dry skin were noted during the first week and continued throughout the study. Skin irritation was observed at both intact and abraded sites. Blood glucose concentrations and serum alkaline phosphatase activities were significantly greater and blood urea nitrogen values were significantly smaller than control values. All other observed parameters were comparable to controls and no systemic effects were attributed to treatment with the shaving cream (Elder 1986b).

Subchronic Toxicity

The subchronic dermal toxicity of Cocamide DEA was evaluated using male and female Fischer 344 rats and B6C3F1 mice. Cocamide DEA was applied to the skin for up to 13 consecutive weeks at doses of 25–400 mg/kg/day (rat) and 50–800 mg/kg/day (mice). Test concentrations were 30–485 mg/ml (rat) and 20–320 mg/ml (mice) in 95% ethanol. Dermal application of Cocamide DEA was associated with microscopic lesions in the skin of male and female F344 rats and in the kidneys of female rats. Treatment-related microscopic lesions were observed in the skin of B6C3F1 mice. In both species, the skin lesions tended to have a dose response with regard to the incidence and severity of the changes present. Renal tubule regeneration was increased in female rats given 200–400 mg/kg/day of Cocamide DEA (Andersen 1996).

A diet containing 25% Coconut Oil was fed to 12 male and 13 female Wistar rats. Eight rats were fed stock feed and served as controls. Three rats of each sex were killed at 15, 30, 60, and 90 days; tissues were microscopically examined and the hepatic lipid content was determined. The treatment group had a progressive increase in fat content of the liver, 20–30% higher than controls by the end of the study. Fatty change of the liver was slight and no other pathological changes were observed (Elder 1986a).

A subchronic percutaneous application study using rats resulted in nonspecific microscopic changes in the heart and lung after administration of 4 mg/kg/day MEA. Effects noted were fatty degeneration of the liver and focal necrosis (Elder 1983). Inhalation studies (90 days) in which dogs and rodents were exposed to 12–26 ppm MEA did not result in any deaths. Skin irritation and lethargy were seen in dogs, guinea pigs, and rats continuously exposed to 5–6 ppm MEA. Some deaths occurred as a result of the inhalation of 102 ppm MEA vapor in dogs at 25 days and rodents exposed to 66–75 ppm after 24–28 days. Exposure to 66–102 ppm MEA caused behavioral changes, pulmonary and hepatic inflammation, hepatic and renal lesions, and hematologic changes in dogs and rodents (Elder 1983).

Dermal Irritation

Kastner (1977) compared the topical irritancy potential of fatty or fat-derived cosmetic ingredients, including 50% Cocamide MEA in vaseline on skin of various animals (four animals per species) in 24-hour skin patch tests. Patches were applied to the shaven backs of adult male New Zealand White rabbits, male Pietrain white guinea pigs (average weight 300 g), and male and female adult mutant hairless mice. Porous cellulose fixed the patches to the guinea pigs and hairless mice. All testing sites were observed at 24 hours (when the patches were removed) and 48 hours. Any reactions were then scored and placed into reaction classes 1–5, with 5 indicating the highest skin irritation potential. Rabbids had the greatest sensitivity to Cocamide MEA, with a class 3 reaction (slight, with the resulting rash fading). Guinea pigs and hairless mice failed to react to Cocamide MEA, and were classified in the lowest reaction group.

The dorsal area of each of six rabbits was shaved and 0.3 ml 30% Cocamide DEA in propylene glycol was applied via a patch to either an intact or abraded site. The entire trunk of each animal was wrapped in cellophane, and patches remained in place for 23 hours. Test sites were scored for irritation 1 and 49 hours after patch removal. 30% Cocamide DEA was a moderate skin irritant; the primary irritation index (PII) was 3.1 (maximum 8). No control data were available (Elder 1986b).

No skin irritation was observed when undiluted Coconut Oil was applied to the skin of nine rabbits in a 24-hour single-insult occlusive patch test. In a second study using either undiluted or 10% (in corn oil) Coconut Acid, PII scores were 0.13/4.0 and 0.12/4.0, respectively, indicating minimal irritation (Elder 1986c).

Bar soaps containing 13% Coconut Oil were evaluated for skin irritation in 14 separate primary irritation studies. Two sites on New Zealand White rabbits of both sexes were clipped of hair and abraded by four perpendicular epidermal abrasions. A 0.5-M dose of a 5% aqueous solution of the soap was applied under occlusive gauze to the abraded sites for 24 hours. The application sites were scored at 24 and 72 hours. PII scores ranged from 1.6 to 4.0 out of 8.0 (Elder 1986a).

Primary skin irritation tests have suggested that MEA is irritating to rabbit skin. 85 and 100% MEA administered by semiocclusive patch applications to intact and abraded shaved skin (evaluated at 4 hours) resulted in visible destructive alteration of the tissue at the test site (corrosive). 30% MEA applied in the same manner and evaluated at 4 and 24 hours had the same result, as well as necrosis at 24 hours (corrosive). When 10 0.1-mL open applications of 1–100% MEA to the ear over 14 days and 10 24-hour semioccluded patch applications were made to the shaved abdomen, it was observed that 10% or higher was corrosive to the skin, >1% was extremely irritating, and 1% was irritating. MEA was thereby classified as “extremely corrosive to the skin” (Elder 1983).

Ocular Irritation

A single 0.1-mL aliquot of 30% Cocamide DEA in propylene glycol was instilled into the conjunctival sac of one eye of each of three female rabbits. The eyes were examined 1 hour after instillation and daily for 7 days thereafter and were scored by
the Draize scoring system. Maximum scores for the 1-hour and
day-3 readings were the only ones reported. Irritation scores for
the iris and cornea were 0, and the maximum conjunctival score
was 6 at 1 hour and 4 at day 3. All effects subsided by day 4.
The cumulative ocular irritation rating was not reported, but
30% Cocamide DEA was at least a mild ocular irritant (Elder
1986b).

A modified Draize test was used to test a mixture of Cocamide
DEA and DEA at effective concentrations of >0.6% and >0.3%,
respectively. The highest mean score was reported on day 3
(57.67). On day 7, a mean score of 37 was reported. The test
material was deemed a severe ocular irritant due to continued
corneal damage in all three New Zealand white rabbits treated
(Andersen 1996).

Undiluted Coconut Oil instilled into the conjunctival sac of
each of 12 rabbits (6 per group). Without subsequent rinsing
of the eyes, maximum irritation scores of 2 and 1 were reported
for the two groups (maximum 110). Cocamit was considered a
minimal eye irritant (Elder 1986a).

Undiluted Coconut Acid caused mild irritation (8/100 and
9/110) in two tests using three groups of six rabbits each. The
eyes were considered normal by the 4th day. In one test, minimal
irritation was observed (1/110), and the eyes returned to normal
by the 3rd day (Elder 1986a).

A 0.2-ml dose of MEA (50% in water) instilled into the
conjunctival sac of each of six rabbits (rinsed after 15 sec-
onds) caused slight discomfort, slight conjunctival irritation,
and slight corneal clouding (healed by 48 hours). 1, 5, and 100%
MEA applied to the corneal center of rabbits (0.005 ml while
lids retracted; lids released after 1 minute) produced scores of
<5.0, >5, and >5, respectively, out of 20 points, when scored
at 18 and 24 hours. 5.0 is the score representative of severe injury;
necrosis was visible after staining and covered ~75% of the
corneal surface. In a third test, a hair preparation containing
1.6% DEA, 5.9% MEA, and 3.2% sodium borate was instilled
(0.1 ml) into the conjunctival sac of each of nine rabbits. Three
eyes were rinsed after 30 seconds, and all eyes were examined
at 24, 48, and 72 hours, and 4 and 7 days. The maximum average
irritation score for both rinsed and unrisned eyes was 0.7 on the
Draize scale (Elder 1983).

Skin Sensitization

A Magnusson-Kligman Maximization test using 10 female
Dunkin Hartley DLA guinea pigs was used to determine the skin
sensitization potential of 5% Coconut Oil. Two injections each
of 50% aqueous Freund’s complete adjuvant, 5% Coconut Oil in
propylene glycol, and 5% Coconut Oil in 50% Freund’s adjuvant
were made to separate sites on the back in the induction phase.
Control animals received injections of the vehicles only. One
week after induction, 5% sodium lauryl sulfate in petrolatum
was applied to each induction site. A booster of 100% Coconut
Oil was applied to the same sites 24 hours later. Control animals
received 5% sodium lauryl sulfate in petrolatum and, as the
booster, full strength petrolatum. All guinea pigs were wrapped
occlusively for 48 hours. Two weeks after the topical booster,
the guinea pigs were challenged with topical applications of
50% and 100% Coconut Oil and wrapped with an occlusive
patch, which was removed after 24 hours. Challenge sites were
evaluated 48 and 72 hours after the beginning of the challenge.
Coconut Oil was nonirritating and failed to produce an allergic
response (Elder 1986a).

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

A composite hair dye and base containing 22% MEA was
given to 60 female rats at concentrations between 0–7800 ppm
in the diet from days 6–15 of gestation. The rats were killed on
day 19. No evidence of adverse effects were observed in the rats
or their pups. No differences were noted in the average number
of implantation sites, live pups, early or late resorptions per litter,
or females with one or more resorption sites. Thirty male rats
were fed the same amounts of MEA for 8 weeks prior to mating
and during mating to 60 female rats fed a basal diet. Sixty female
rats were fed the treated diet 8 weeks prior to mating (to 30 males
fed basal diet) through day 21 of lactation. No treatment-related
differences in male and female fertility were detected compared
to controls (Elder 1983).

No evidence of teratologic effects were observed in the fetuses of
artificially inseminated rabbits that were exposed by gavage
to 0–19.5 mg/kg/day MEA in a hair base and dye. Fetal survival
was not adversely affected and no gross abnormalities were seen
in the fetuses after the doses were killed on day 30 of gestation
(Elder 1983). The incubation of chicken eggs with 0.03% MEA
increased the number of eggs with visible blastodisks, the syn-
thesis of proteins, fats, and carbohydrates, and the number of
hatching chicks. Peroxidase activity and the number of organic
peroxide molecules in the blood, liver, and homogenates of chick
embryos were decreased (Elder 1983).

MUTAGENICITY

Blevins and Taylor (1982) screened 25 cosmetic ingredients,
including Cocamide MEA (50 mg/ml diluted to the test concen-
tration) in distilled water, with the Salmonella typhimurium/ microsome test using S. typhimurium strains TA93, TA100,
TA1535, TA1537, and TA1538. Negative controls were water,
ethanol, dimethyl sulfoxide (DMSO), and no treatment. Posi-
tive controls were 2-aminonitroantracene, 4-nitro-o-phenylene di-
amine in DMSO, sodium azide in water, and 9-aminocacidine in
ethanol. In a screening spot test, Cocamide MEA (50 µg/plate)
was mutagenic only in strain TA100 with Aroclor 1254-induced
S9 liver homogenates from male Sprague-Dawley rats. In the
other strains, and without S9 activation (including TA100), Co-
camide MEA was not mutagenic.

In a plate incorporation assay within the same study, Co-
camide MEA was tested at 5, 0.5, 0.05, and 0.005 mg/ml with
and without metabolic activation. Cocamide MEA gave approxi-
ately a twofold increase in the number of revertants over the
ethanol counts in TA1535; however, a dose-related increase was
not demonstrated. Cocamide MEA falsely appeared to be mutagenic at the high dose concentrations (0.5 and 0.05 mg/plate). Plate counts were several-fold greater than those of the solvent controls, but there was no background lawn of unreverted bacteria. When several of the "revertant" colonies were transferred to minimal glucose agar, they failed to grow, demonstrating that they were not revertants. The investigators attributed this to the toxicity of the dose concentrations used: most of the bacteria were killed, and as a result, more histidine was available for utilization by the surviving unreverted mutants. Also, at 5 mg/plate Cocamide MEA, a precipitate formed in all plates tested, such that they could not be counted (Blevins and Taylor 1982).

Cocamide DEA was not mutagenic in the Ames Test, with or without metabolic activation. Cocamide DEA induced sister chromatid exchanges in Chinese hamster ovary cells with metabolic activation, but did not induce chromosomal aberrations with or without metabolic activation. In a more recent study, Cocamide DEA did not induce either sister chromatid exchanges or chromosomal aberrations, with or without activation. When tested in L5178Y mouse lymphoma forward mutation assays, both negative and inconclusive results were noted (Andersen 1996).

MEA was not mutagenic in the Ames test using S. typhimurium strains TA100 and TA1535, with or without metabolic activation (Elder 1983).

CARCINOGENICITY

High concentrations of dietary fat promoted the development of mammary tumors induced in rats by 7,12-dimethylbenz(a)-anthracene. Coconut Oil, a saturated fat, was less effective than polyunsaturated fats (Elder 1986a).

CLINICAL ASSESSMENT OF SAFETY

MEA inhalation by humans has been reported to cause immediate allergic responses of dyspnea and asthma, as well as clinical signs of acute liver damage and chronic hepatitis (Elder 1983).

Skin Irritation

Kastner (1977) evaluated the topical irritancy of 50% Cocamide MEA (in vaseline) for human skin. Four volunteers each received a patch containing the test substance to the upper arm. All sites were observed at 24 hours, when the patches were removed, and at 48 hours. Reactions were rated between classes 1–5, with class 5 having the greatest irritation. No positive responses were observed.

One hundred and four women participated in an in-use study to determine the safety and efficacy of a shampoo containing 2% Cocamide DEA. Each subject was patch tested on the upper arm with the aqueous shampoo, 15 ppm (in water) of the shampoo's preservative system, and 5% shampoo fragrance in mineral oil. Irritation was scored 48 hours after application, when the patches were removed. The subjects then used the shampoo daily for 87 days. Ten days after the final use, challenge patches were applied using the same procedure as the initial patches, except the preservative concentration was increased to 50 ppm and an additional scoring for reactions was made 24 hours after patch removal. No reactions were observed to the preservative or fragrance patches. Eleven subjects reacted to the 2% shampoo initial patch; eight had mild erythema (1+ scores on a 0–4 scale), one had intense erythema (2+), and two subjects had erythema and edema (3+). 24 panelists had irritation scores of 1+ (18/24), 2+ (3/24), and 3+ (3/24) 48 hours after challenge patch application of the shampoo. Thirty subjects had 1+ (25/30) or 2+ (5/30) irritation scores at the second challenge reading. The shampoo was considered an irritant but not a sensitizer (Elder 1986b).

A bar soap containing 13% Coconut Oil was evaluated for skin irritation using standard Draize procedures. A 1% aqueous solution of the soap was applied using occlusive patches to the forearms of 106 subjects over a 3-week period. Very minimal skin reactions were recorded and the researchers concluded that the soap was not hazardous under conditions of normal use. In a similar test (bar soap with 13% Coconut Oil) using 72 panelists over 2 weeks, investigators reported no unusual irritation responses under normal conditions of use. Soap chamber tests employing Duhring chambers applied to the forearm were conducted using 8% aqueous suspensions of bar soaps containing 13% Coconut Oil. One 24-hour patch and four 6-hour patches were applied over 5 days. In one test using 10 panelists, the soap was moderately irritating, and researchers concluded that the soap was not hazardous under normal use conditions. In a second soap chamber test, minimal irritation was noted among members of the 10-subject panel (Elder 1986a).

Skin Sensitization

Cocamide DEA has been classified as a definite occupational allergen in the hairdressing, medical, fitter, food handling, printing, and cleaning groups. Cocamide DEA exposure produced allergic contact dermatitis in a number of occupational studies. Various concentrations of Cocamide DEA were tested in predictive patch tests; concentrations up to 10% did not produce adverse effects (Andersen 1996).

No erythematos reactions were observed in 103 panelists during a repeat-insult predictive patch test in which a tanning butter containing 2.5% Coconut Oil was applied (Elder 1986a).

A repeated-insult patch test was performed using 0.3 ml of a hair preparation (1.6% DEA, 5.9% MEA, and 3.2% sodium borate) in which an occlusive patch was placed on the forearm for 48 hours during a pretest. In the induction phase of the test, five 48-hour occlusive patches were used. After a 10-day non-treatment period, then a 48-hour challenge patch was applied. Reactions were scored on a scale from 0–3 at patch removal and after 24 hours. The test material was irritating during the pretest. No reactions were observed during the induction and challenge phases; no evidence of contact sensitization was observed in any
a plate incorporation assay, Cocamide MEA at 0.005–5 mg/plate was toxic to the bacterial test strains. In one Chinese hamster ovary cell assay, Cocamide DEA induced sister chromatid exchanges with metabolic activation. In another assay, the results were negative, both with and without activation. In the former set of assays, Cocamide DEA did not induce chromosomal aberrations either with or without metabolic activation. Both negative and inconclusive results were noted for Cocamide DEA in the L5178Y mouse lymphoma forward mutation assay.

In clinical studies, Cocamide MEA at a concentration of 50% was not a human skin irritant in a single-insult patch test. Cocamide DEA at a concentration of 2% in shampoo caused irritation, but was not a sensitizer. No adverse effects were observed during predictive patch tests of a surfactant containing 10% Cocamide DEA. Soap containing 13% Coconut Oil caused minimal irritation when applied to the skin as a 1% aqueous solution. Coconut Oil was not a human skin sensitizer. A cosmetic formulation containing approximately 0.03% MEA was irritating to the skin, but was nonsensitizing, in repeated-insult patch tests. Bar soaps containing 13% Coconut Oil were not phototoxic or photosensitizing.

Cocamide DEA is classified as a known occupational allergen that causes allergic contact dermatitis. However, no adverse effects were reported in patch tests using up to 10% of the test compound. Inhalation of MEA by humans has resulted in dyspnea and asthma, as well as clinical signs of acute liver damage and chronic hepatitis.

CONCLUSION

On the basis of the animal and clinical data presented in this report, the CIR Expert Panel concludes that Cocamide MEA is safe as used in rinse-off cosmetic products and safe at concentrations up to 10% in leave-on products. Cocamide MEA should not be used as an ingredient in cosmetic products containing N-nitrosating agents, or in product formulations intended to be aerosolized.

REFERENCES


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2 Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, N.W., Suite 310, Washington, DC 20036, USA.
of the 25 subjects. The same hair preparation was tested using 0.2 ml of the material applied to patches on the back for 23 hours daily for 21 days. Reactions were scored daily on a scale of 0 to 7. In the panel of 12 females, the subjects had 4, 3, and 225 scores of barely perceptible erythema, definite erythema, and erythema and papules, respectively. The test compound was deemed an experimental cumulative irritant (Elder 1983).

A dyeless noncommercial base formulation (11.47% MEA) was diluted to 25% in alcohol and 0.3 ml was applied to the upper arms of 165 volunteers 3 days/week for three weeks using 24-hour semiocclusive patches. Sites were evaluated 24 and 48 hour after patch removal. Challenge applications were made on the same site and a virgin site after 15–17 days. Scores (out of 5) were made 24 and 72 hours later. There were 19 instances of mild erythema and one each of definite papular response, definite edema, and definite edema and papules, respectively, during induction. No adverse reactions were observed at challenge; the test substance was therefore an irritant, but not a contact sensitizer (Elder 1983).

Phototoxicity

Aqueous solutions (3%) prepared from bar soaps containing 13% Coconut Oil were applied using occlusive patches to the tape-stripped backs of 10 volunteers over a 6-week period. After each application, the treatment sites were exposed to an inspectrolamp for 45 minutes. After UVA exposure, the area was exposed to about two thirds of the Minimal Erythematic Dose from an air-cooled Kromayer lamp. No evidence of phototoxicity was observed (Elder 1986a).

Photosensitization

Bar soaps (13% Coconut Oil) were tested as 3% aqueous solutions in a photosensitization test using 10 panelists. Patches containing 0.2 ml were applied to stripped skin three times per week for 24 hours over a 3-week period. Sites were exposed to a Wood's lamp for 40 minutes and a sun lamp for 15 minutes after each application. Following a 2-week nontreatment period, duplicate challenge patches were applied. No evidence of photosensitization was observed. A similar soap containing 13% Coconut Oil (1% and 5% aqueous solutions) was tested using 52 subjects. Occlusive patches containing 0.4 ml of the test solutions were applied to the arms three times per week for 3 weeks. Sites were exposed to sunlight for 30 minutes 24 hours after application. After a 2-week nontreatment period, duplicate challenge patches were applied. Sun exposures were made 24 hours later. No photosensitization reactions were noted (Elder 1986a).

SUMMARY

Cocamide MEA is a mixture of ethanolamines of fatty acids derived from coconut oil. It functions as a surfactant—foam booster and aqueous viscosity-increasing agent—in cosmetic formulations. In 1996, Cocamide MEA was reported to be used in 285 cosmetic formulations of various product categories.

Data on the chemical and physical properties, method of manufacture, impurities, absorption, distribution, metabolism, and excretion of Cocamide MEA were not available. Data have been included from previous CIR safety assessments on Coconut Oil and its derivatives, MEA, and Cocamide DEA.

MEA is the only naturally occurring ethanolamine in mammals. MEA can be converted to ammonia and acetaldehyde, and can be reacted with an aldehyde to form DEA. DEA is readily nitrosated to form N-nitrosodiethanolamine, a carcinogen in laboratory animals. MEA has not yet been found to form a stable nitrosamine.

The acute oral LD₅₀s of Cocamide DEA in rats ranged from >5 g/kg to 12.2 g/kg at concentrations of 10–12% and 100%, respectively. Undiluted Coconut Oil did not cause mortality in acute toxicity studies using rats. The acute oral LD₅₀ of MEA was 1.72–2.74 g/kg in rats; MEA was deemed slightly toxic. MEA was noncorrosive in an oral study using rabbits. The acute intraperitoneal LD₅₀ of MEA in mice was 1.05 g/kg.

A formulation containing 1.92% Cocamide DEA caused irritation but no systemic effects in a 4-week dermal toxicity study using rabbits. Coconut Oil (25% in feed) administered to rats for up to 90 days produced no signs of toxicity. Subchronic percutaneous application of 4 mg/kg/day MEA to rats caused nonspecific histologic changes of the heart and lung tissue, fatty degeneration and focal necrosis of the liver. MEA vapor was highly toxic when concentrations of 66–102 ppm were continuously inhaled by dogs and rodents during 90-day studies. Signs of toxicity included behavioral changes, pulmonary and hepatic inflammation, renal and hepatic damage, and increased mortality.

Cocamide MEA at a concentration of 50% was nonirritating to the skin of guinea pigs and mice and was slightly irritating in rabbits during a single-insult patch test. Cocamide DEA at a concentration of 30% was moderately irritating to the skin of rabbits. Undiluted Coconut Oil was a minimal irritant. Soap containing 13% Coconut Oil produced slight irritation. Coconut Oil was nonsensitizing in the Magnusson-Kligman Maximization Test using female guinea pigs. MEA was irritating and corrosive to the skin of rabbits.

Cocamide DEA was at least a mild ocular irritant in rabbits when administered at a concentration of 30%. Undiluted Coconut Oil caused minimal irritation. Undiluted Coconut Acid produced mild ocular irritation. MEA at a concentration of 30% caused slight discomfort, conjunctival irritation, and corneal clouding in rabbits, but these reactions were slight. Severe ocular injury, including necrosis, occurred when 5–100% MEA was applied to the corneal center of rabbits.

Rats given up to 19.5 mg/kg/day by gavage of a hair balse and dye containing 22% MEA had no signs of reproductive and developmental toxicity.

Cocamide MEA, Cocamide DEA, and MEA were not mutagenic in the Ames Test, with or without metabolic activation. In