COCONUT OIL DIETHANOLAMINE CONDENSATE

1. Exposure Data

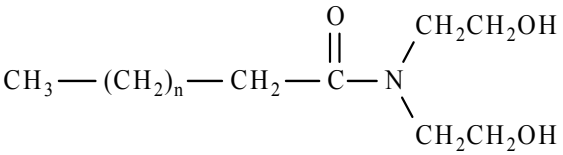
1.1 Chemical and physical data

Coconut oil diethanolamine condensate is a mixture of diethanolamides of the fatty acids that constitute coconut oil, which is composed of approximately 48.2% lauric acid (12:0), 18% myristic acid (14:0), 8.5% palmitic acid (16:0), 8% caprylic acid (8:0), 7% capric acid (10:0), 6% oleic acid (18:1, n-9), 2.3% stearic acid (18:0) and 2% linoleic acid (18:2, n-6) (NTP, 2001).

1.1.1 Nomenclature

Chem. Abstr. Serv. Reg. No.: 68603-42-9
Deleted Chem. Abstr. Serv. Reg. Nos: 8036-48-4; 8040-31-1; 8040-33-3; 12751-06-3; 53028-62-9; 56448-72-7; 56832-66-7; 63091-31-6; 66984-58-5; 67785-10-8; 67785-14-2; 71343-51-6; 71343-71-0; 83652-14-6; 87714-18-9; 90651-47-1; 118104-13-5; 153189-69-6; 186615-78-1 (ChemID plus)
Chem. Abstr. Name: Amides, coco, *N*,*N*-bis(hydroxyethyl)
Synonyms: *N*,*N*-Bis(hydroxyethyl)coco amides; *N*,*N*-bis(hydroxyethyl)coco fatty acid amides; cocamide DEA; cocamide diethanolamine; coco diethanolamides; coco diethanolamine; coco fatty acid diethanolamides; coconut DEA; coconut diethanolamides; coconut oil diethanolamides; coconut oil diethanolamine

1.1.2 Structural and molecular formulae and relative molecular mass



n = 5, 7, 9, 11, 13, 15

$C_{(7+n)}H_{(15+2n)}NO_3$
Relative molecular mass: range, 231–371

1.1.3 Chemical and physical properties of the pure substance

Description: Clear, amber-coloured liquid with a faint coconut odour (CTFA, 1986)
Boiling-point: 169–275 °C
Melting-point: 23–35 °C (CTFA, 1986)
Density: 0.99 g/cm^3 at 20 °C (IUCLID, 2000)
Solubility: Miscible with water at 20 °C; produces an alkali in aqueous solution (CTFA, 1986)
Octanol/water partition coefficient (P): log P, 3.52 (IUCLID, 2000)

1.1.4 Technical products and impurities

Coconut oil diethanolamine condensate is available in several grades, which differ on the basis of the molar ratio of coconut oil

methyl esters and diethanolamine used during their manufacture; the purest product is obtained with a molar ratio of 1:1. Free diethanolamine is present in the final product at concentrations ranging from 4 to 8.5% (CTFA, 1986).

In one lot of commercial coconut oil diethanolamine condensate to be used in animal toxicology studies, impurities identified by high-performance liquid chromatography analysis with ultraviolet detection included diethanolamine (18.2%), alkanolamides of unsaturated acids, amine salts of the acids and *N*-nitrosodiethanolamine (219 ppb) (NTP, 2001).

Trade names: Trade names for coconut oil diethanolamine condensate include: Agent 565–14RC; Alkamide 2104; Alkamide CDE; Alkamide CDO; Alkamide DC 212S; Amicol CDE 1; Amicol CDE 2; Amicol CDE-G; Amidet B 112; Amidet SB 13; Aminol HCA; Aminol KDE; Amisol CD; Amisol CD-E; Arcalon 12; CDE 100; Calamide C; Calimide C; Carsamide CA; Cedemide CX; Cedemide DX; Clindrol 200CGN; Clindrol 206CGN; Clindrol Superamide 100CG; COA; Cocamide DEA; Cocamide diethanolamine; Coco diethanolamides; Coco diethanolamine; Coco fatty acid diethanolamides; Coconut DEA; Coconut diethanolamides; Coconut oil diethanolamides; Colamid C; Comperlan COD; Comperlan KD; Comperlan LS; Comperlan PD; Conco Emulsifier K; Crillon CDY; Cyclomide CD; Diterol 87; Elromid KD 80; Empilan 2502; EMP 6501; Empilan CDE; Empilan CDE/FF; Ethylan A 15; Ethylan LD; Eur-Amid; Foamid C; Foamole 2AC; Homelead CD; Incromide CA; Lauridit KDG; Marlamid D 1218; Marpon MM; Mazamide 80; Monamid 150AD; Monamid 150DR; Monamid 705; Monamid ADD; Monolube 29–78; *N*,*N*-Bis(hydroxyethyl) coco amides; *N*,*N*-Bis(hydroxyethyl) coco amides; Naxonol CO; Naxonol PN 66; Ninol 11CM; Ninol 1281; Ninol 2012 Extra; Ninol 2012E; Ninol 40CET; Ninol 40CO; Ninol 49CE; Ninol P 621; Nissan Stafoam DF; Oramix DL 200; P and G Amide 72; Profan 128 Extra; Profan EX 24; Profan Extra 24; Purton CFD; Rewomid DC 212S; Rewomid DL 240240; Rolamid CD; Schercomid CDA; Schercomid SCO; Stafoam DF; Stafoam DF 4; Stafoam DFC; Standamid KD; Standamid KDO; Standamid SD; Standamid SD-K; Steinamid DC 212S; Steinamid DC 212SE; Tohol N 220XM; Varamide A 10; Varamide A 2; Varamide MA 1; Vicamid 528; Witcamide 5133; Witcamide 82.

1.1.5 Analysis

Analytical methods to determine the diethanolamide composition of coconut oil diethanolamine condensate have been reported using gas chromatography (O'Connell, 1977) and high-performance liquid chromatography (Nakae & Kunihiro, 1978).

1.2 Production and use

1.2.1 Production

Coconut oil diethanolamine condensate is produced by a condensation reaction at a 1:1 or 1:2 molar ratio of the appropriate fatty acids (methyl cocoate, coconut oil, whole coconut acids or stripped coconut fatty acids) to diethanolamine at temperatures of up to 170 °C and in the presence of an alkaline catalyst. The 1:2 mixture of fatty acid (or methyl fatty acid) to diethanolamine results in a lower-quality diethanolamide with residues of ethylene glycol and free diethanolamine. The 1:1 mixture produces a higher-quality diethanolamide with much less free amine, which is consequently used at lower concentrations than the 1:2 diethanolamide (CTFA, 1986).

It has been estimated that 10 300 and 8650 tonnes of coconut oil diethanolamine condensate were produced in the United States of America in 1977 and 1985, respectively (HSDB, 2010).

Information available in 2010 indicated that coconut oil diethanolamine condensate

was produced by 10 companies in Mexico, three companies in the USA, two companies each in France and China, Hong Kong Special Administrative Region, and one company each in India and Pakistan (Chemical Sources International, 2010). Other sources indicated that it was produced by 15 companies in the USA (HSDB, 2010), four companies in the United Kingdom, three companies each in Germany and Spain, two companies each in Italy and Sweden, and one company each in Belgium, France, and the Netherlands (IUCLID, 2000).

1.2.2 Use

Fatty acid diethanolamides, including coconut oil diethanolamine condensate, are widely used in cosmetics. In 1985, coconut oil diethanolamine condensate was reported to be present in nearly 600 cosmetic formulations of bath oil, shampoo, conditioner, lipstick and hair dye. The concentration of diethanolamide in these preparations ranged from 1 to 25%. Non-cosmetic applications include use as a surfactant in soap bars, light-duty detergents and dishwashing detergents and as a delinting agent for cottonseed (CTFA, 1986).

Coconut oil diethanolamine condensate is used as a corrosion inhibitor in water-based soluble, semi-synthetic and synthetic metal-working fluids and in polishing agents (Byers, 2006). It is also used widely as an antistatic agent in plastics, e.g. in polyethylene film for food packaging and rigid poly(vinyl) chloride. It has been employed in combination with metallic salts as an antistatic for polystyrene and in impact-resistant rubber polystyrene blends (HSDB, 2010).

1.3 Occurrence

1.3.1 Natural occurrence

Coconut oil diethanolamide is not known to occur in nature.

1.3.2 Occupational exposure

Occupational exposure to coconut oil diethanolamide in various materials has been inferred from reports of dermatitis, verified by a patch test, among workers; materials identified were barrier creams, hand-washing liquids and metalworking fluids that contained coconut oil diethanolamine (Grattan *et al.*, 1989; Pinola *et al.*, 1993), hydraulic mining oil (Hindson & Lawlor, 1983), and materials used in a printing facility (Nurse, 1980).

1.3.3 Personal care and cleaning products

Exposure to coconut oil acid diethanolamine condensate may occur by skin contact with cosmetic formulations of bath oil, shampoo, conditioner, lipstick, hair dye, soap bars, light-duty detergents and dishwashing detergents (NTP, 2001).

The composition of 2354 registered washing and cleaning agents in the Danish Product Register Data Base in 1992 was reviewed. Of these, 12/70 automotive cleaners, 3/250 detergents for washing textiles, 36/118 dishwashing fluids, 11/94 floor polishes, 83/507 general cleaners, 127/200 shampoos, 9/115 high-pressure cleaning agents and 75/224 skin cleaners contained coconut diethanolamide (Flyvholm, 1993).

1.3.4 Environmental occurrence

A total of 35 samples of coastal water and 39 samples of harbour sediment collected from several hot spots on the Spanish coast in 1999–2000 were analysed. Coconut diethanolamide was detected in seawater collected from Spanish harbours at Barcelona (< 0.05–4.2 µg/L), Tarragona (< 0.05–24 µg/L) and Almeria (< 0.05 µg/L), and in sediment collected from several locations on the southern and eastern coasts. It was detected in bottom sediment taken from harbours in Barcelona (90–830 µg/kg), Tarragona (30–150 µg/kg), Almeria (275–720 µg/kg),

Almerimar (250–750 µg/kg), Aguadulce (85–820 µg/kg), Cadiz (230 µg/kg), Sancti Petri (380 µg/kg), Sotogrande (120 µg/kg), Duquesa (310 µg/kg), Estepona (220–440 µg/kg), Banus (120–140 µg/kg) and Marbella (110–190 µg/kg). Coastal sediment collected in San Fernando adjacent to an untreated urban wastewater discharge point contained 2710 µg/kg coconut diethanolamide (Petrović *et al.*, 2002).

Sludge from five sewage-treatment plants in Spain, Portugal and Germany was found to contain C9 coconut diethanolamide (not detected–0.2 mg/kg dry weight), C11 coconut diethanolamide (0.3–6.2 mg/kg dry weight), C13 coconut diethanolamide (0.2–10.5 mg/kg dry weight), C15 coconut diethanolamide (not detected–7 mg/kg dry weight) and C17 coconut diethanolamide (not detected–5.5 mg/kg dry weight) (Petrović & Barceló, 2000).

1.4 Regulations and guidelines

No occupational exposure limits or recommended guidelines for maximum safe levels in drinking-water have been established for coconut oil diethanolamine condensate.

2. Cancer in Humans

No data were available to the Working Group.

3. Cancer in Experimental Animals

3.1 Skin application

3.1.1 Mouse

Groups of 50 male and 50 female B6C3F$_1$ mice, 6 weeks of age, received dermal applications of 0, 100 or 200 mg/kg body weight (bw) coconut oil diethanolamine condensate (purity, > 99%) in 95% ethanol (0, 50 or 100 mg/mL ethanol) on 5 days a week for 2 years. Survival of treated males and females was similar to that of the vehicle-control group. The mean body weights of treated males were similar to those of the controls throughout the study; those of the 100- and 200-mg/kg females were lower than those of the controls from weeks 93 and 77, respectively. In male mice, the incidence of hepatocellular adenoma was significantly greater in both treated groups than in vehicle controls (22/50 (44%), 35/50 (70%) and 45/50 (90%); $P = 0.002$ and $P < 0.001$, respectively, poly-3 trend test, for control, low-dose and high-dose groups, respectively), and that of hepatocellular carcinoma was significantly greater in the high-dose group than in vehicle controls (12/50 (24%), 12/50 (24%) and 20/50 (40%); $P = 0.041$ poly-3 trend test). In addition, the incidence of hepatocellular adenoma, hepatocellular carcinoma or hepatoblastoma combined in the low- and high-dose groups was significantly increased compared with that in the vehicle-control group (29/50 (56%), 39/50 (78%, $P = 0.011$ poly-3 trend test), and 49/50 (98%, $P < 0.001$ poly-3 trend test) in the control, low- and high-dose groups, respectively). The incidence of hepatoblastomas in high-dose males was significantly increased compared with controls ($P = 0.03$). In females, the incidence of hepatocellular neoplasms was significantly higher in treated groups than in vehicle controls (hepatocellular adenoma: 32/50 (64%), 44/50 (88%, $P = 0.006$ poly-3 trend test), and 43/50 (86%, $P = 0.005$ poly-3 trend test); hepatocellular carcinoma: 3/50 (6%), 21/50 (42%) and 32/50 (64%, $P < 0.001$ poly-3 trend test) in the control, low- and high-dose groups, respectively). In addition, the incidence of hepatocellular adenoma and hepatocellular carcinoma combined in the low- and high-dose groups was significantly increased in comparison with the vehicle-control group (33/50 (66%), 46/50 (92%) and 48/50 (96%, $P < 0.001$ poly-3 trend test)). The incidence of renal tubular adenoma (1/50 (2%),

1/50 (2%), 7/50 14%)) and renal tubular adenoma or carcinoma combined (1/50 (2%), 1/50 (2%), 9/50 (18%)) was significantly increased in high-dose males ($P < 0.05$ poly-3 trend test). One high-dose female had a renal tubular adenoma (NTP, 2001).

[The Working Group noted that tumours of the kidney and hepatoblastoma are rare spontaneous neoplasms in experimental animals.]

3.1.2 Rat

Groups of 50 male and 50 female F344/N rats, 6 weeks of age, received dermal applications of 0, 50 or 100 mg/kg bw coconut oil acid diethanolamine condensate (purity, > 99%) in 95% ethanol on 5 days a week for 2 years. Survival rates for treated males and females were similar to those of corresponding vehicle controls, as were mean body weights. No increase in the incidence of tumours was observed in treated groups compared with the vehicle controls (NTP, 2001).

4. Other Relevant Data

In 2-year studies of dermal application of coconut oil diethanolamine condensate in B6C3F$_1$ mice (0, 100 or 200 mg/kg bw) and F344/N rats (0, 50 or 100 mg/kg bw), neoplasms were induced in male (liver and kidney) and female (liver) mice, while there was no evidence of neoplastic effects in either sex of rats (NTP, 2001). This pattern of tumour response is the same as that of diethanolamine applied to the skin of mice and rats (NTP, 1999). The content of unreacted diethanolamine in the coconut oil diethanolamine condensate was estimated to be approximately 18.2%, and the increased incidence of neoplasms in mice was associated with the level of free diethanolamine that was present in the solutions of diethanolamine condensate tested (NTP, 1999, 2001). Sufficient free diethanolamine was present in the coconut oil diethanolamine condensate to account for the tumour responses observed in mice. If the tumour responses were due to diethanolamine, then the results of the dermal carcinogenicity study of coconut oil diethanolamine condensate confirm the findings of the study on diethanolamine, and Section 4 of the *Monograph* on diethanolamine (in this volume) would pertain to this *Monograph*.

4.1 Absorption, distribution, metabolism, excretion

4.1.1 Humans

No data were available to the Working Group.

4.1.2 Experimental systems

Although no studies have been conducted specifically on coconut oil diethanolamine condensate, a mixture of diethanolamides and the fatty acids found in coconut oil, a study on the disposition of lauric acid (the major fatty acid present in coconut oil) diethanolamine condensate (1:1) in rats after intravenous, oral and dermal administration and in mice after intravenous and dermal administration has been reported (Mathews *et al.*, 1996). Lauramide diethanolamine was absorbed by rats and mice after oral or dermal administration, and was rapidly cleared from all tissues except adipose. Unlike diethanolamine, lauramide diethanolamine did not accumulate in the tissues of rats after repeated dermal applications. The major route of excretion of the administered dose was as polar metabolites in the urine (80–90%) of both species. No unchanged diethanolamine, diethanolamine-derived metabolites or parent compound were detected in the urine. Lauramide diethanolamine was readily metabolized *in vivo* and *in vitro*; metabolites identified in the plasma and urine of treated rats, and in media from human and rat liver slices incubated with this

compound reflected ω- and ω-1 to 4 hydroxylation followed by β-oxidation to chain-shortened carboxylic acids. Thus, fatty acid diethanolamine condensates are readily metabolized by hydroxylation of the fatty acid moiety, but are resistant to hydrolysis of the amide linkage. Therefore, metabolism of lauramide diethanolamine does not release free diethanolamine in rats or mice.

4.2 Genetic and related effects

4.2.1 Humans

No data were available to the Working Group.

4.2.2 Experimental systems

Coconut oil diethanolamine condensate was not mutagenic in *Salmonella typhimurium* strains TA97, TA98, TA100 or TA1535, or in L5178Y mouse lymphoma cells incubated in the presence or absence of metabolic activation systems (see Tables E1 and E2 in NTP, 2001). It did not induce sister chromatid exchange or chromosomal aberrations in cultured Chinese hamster ovary cells in the presence or absence of metabolic activation systems (see Tables E3 and E4 in NTP, 2001). Coconut oil diethanolamine condensate increased the frequencies of micronucleated erythrocytes in the peripheral blood of male and female B6C3F$_1$ mice that received dermal applications for 14 weeks (see Table E5 in NTP, 2001).

4.3 Mechanisms of carcinogenesis

The tumour response in mice exposed to coconut oil diethanolamine condensate appears to be due to the presence of free diethanolamine in the solution tested. This suggestion is based on the association of the mouse liver tumour responses with exposures to diethanolamine in studies of diethanolamine condensates with varying levels of diethanolamine contamination. Because the frequency of micronucleated erythrocytes was not increased in mice exposed to diethanolamine (NTP, 1999), free diethanolamine in the solution tested does not account for the observed increase in frequency of micronucleated erythrocytes in mice exposed to coconut oil diethanolamine condensate (NTP, 2001), which may act via a genotoxic mechanism.

5. Summary of Data Reported

5.1 Exposure data

Coconut oil diethanolamine condensate is a mixture of amides produced by the condensation of coconut oil fatty acids with diethanolamine. Exposure of the general population occurs through dermal contact due to its wide use as a surfactant in cosmetics, soaps and detergents. Occupational exposure may occur by inhalation and skin absorption from some metalworking fluids. Coconut oil diethanolamine condensate may contain diethanolamine as a contaminant.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

In a study of dermal application in mice, coconut oil diethanolamine condensate increased the incidence of hepatocellular carcinoma and hepatocellular adenoma in males and females, and of hepatoblastoma in males. The incidence of renal tubule adenoma and carcinoma combined was also increased in males. In a study of dermal application in rats, no increase in tumour incidence was observed.

Tumours of the kidney and hepatoblastoma are rare spontaneous neoplasms in experimental animals.

5.4 Other relevant data

No data on the absorption, distribution, metabolism or excretion of coconut oil diethanolamine condensate were available to the Working Group.

The amide linkage between diethanolamine and the fatty acid moiety is resistant to metabolic hydrolysis.

The carcinogenic effects of the coconut oil diethanolamine condensate used in the cancer bioassay may be due to the levels of diethanolamine (18.2%) in the solutions tested. Mechanistic data are very weak to evaluate the carcinogenic potential of coconut oil diethanolamine condensate *per se*.

6. Evaluation

6.1 Cancer in humans

No data were available to the Working Group.

6.2 Cancer in experimental animals

There is *sufficient evidence* in experimental animals for the carcinogenicity of coconut oil diethanolamine condensate.

6.3 Overall evaluation

Coconut oil diethanolamine condensate is *possibly carcinogenic to humans (Group 2B).*

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