

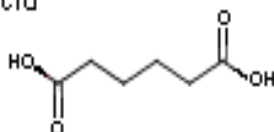
Polyamidoamine epichlorohydrin resin

SYNONYMS

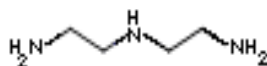
Adipic acid/epoxypropyl diethylenetriamine copolymer
 Adipic acid, diethylenetriamine, epichlorohydrin polymer
 Adipic acid, diethylenetriamine, epichlorohydrin resin
 Diethylenetriamine, epichlorohydrin, adipic acid polymer
 Epichlorohydrin, adipic acid, diethylenetriamine polymer
 PAAE Resin
 PAE Resin

CHEMICAL STRUCTURE

Adipic acid



Epichlorohydrin



Diethylenetriamine

CHEMICAL FORMULA OF POLYMER

$(C_6H_{10}O_4 \cdot C_4H_{13}N_3 \cdot C_3H_5ClO)_x$

IDENTIFIER DETAILS

CAS Number : 25212-19-5 [polymer] (containing 124-04-9 [Adipic acid], 106-89-8 [Epichlorohydrin] and 111-40-0 [Diethylenetriamine])
 CoE Number : -
 FEMA : -
 EINECS Number : -
 E Number : -

SPECIFICATIONS

Melting Point: Not known

Boiling point: Not known

PURPOSE

Paper additive to enhance wet-strength.

STATUS IN FOOD AND DRUG LAWS

CoE limits:

Beverages	Food (mg/kg)	Exceptions (mg/kg)
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(mg/kg)		
-	-	-

Acceptable Daily Intake:

ADI (mg/kg)	ADI Set by	Date Set	Comments
-	-	-	-

FDA Status:

Section Number	Comments
-	-

HUMAN EXPOSURE

Natural Occurrence: Does not occur in nature

Reported Uses: No data identified

TOXICITY DATA

No data was identified for the complete resin. Toxicity data for the individual monomers is presented. Polyamidoamine epichlorohydrin resin is composed of the following components: Adipic acid, Epichlorohydrin and Diethylenetriamine.

In Vivo Toxicity Status

Adipic acid

Species	Test Type	Route	Reported Dosage
Rat	LD ₅₀	Gavage	5560mg/kg/BW
Mice	LD ₅₀	Oral	1900mg/kg/BW [SIDs, 2004]

The acceptable daily intake of adipic acid was deemed to be 0-5mg/kg/day [JECFA, 1978].

Epichlorohydrin

Species	Test Type	Route	Reported Dosage
Rat	LD ₅₀	oral	260mg/kg
Rat	6hr LC ₅₀	inhalation	1360mg/m ³
Rabbit	24hr LC ₅₀	dermal	754mg/kg [IPCS INCHEM, 1984]

The toxic effects of epichlorohydrin administered by gavage for 10 or 90 days were examined by Daniel *et al.* (1996). Both male and female Sprague-Dawley rats received doses of 3, 7, 19 or 46 mg/kg/day (for the 10 day period group) or 1, 5 or 25 mg/kg/day (for a 90 day period group). There was no increase in mortality compared to controls. Notably, animals receiving the highest doses had reduced body and organ weights; reduced food and water intake; and haematological abnormalities (decreased haemoglobin, haemocrit

and erythrocyte levels). The haematological abnormalities were only observed in male rats after 10 and 90 day exposures. Both sexes receiving 25 mg/kg/day in the 90 day study had increased liver and kidney weights. Histological assessment revealed that a dose related increase in mucosal hyperplasia and hyperkeratosis occurred. The NOAEL for a 90 day oral exposure for both male and female rats was deemed to be 1 mg/kg/day [Daniel *et al.*, 1996].

Diethylenetriamine

Species	Test Type	Route	Reported Dosage
Rat	LD ₅₀	Oral	1080mg/kg
Rat	LC _{Lo}	Inhalation	70mg/m ³
Rabbit	LD ₅₀	Skin	1090mg/kg

[ChemIDplus Lite, viewed 21/09/09]

Leung *et al.* (1997) studied the effects of feeding Fischer 344 rats a dihydrochloride salt of diethylenetriamine for 90 days at concentrations of 1000 ppm, 7500 ppm or 15,000 ppm. These concentrations equated to (when food consumption and bodyweight were taken in to consideration) 70, 530 and 1060 mg/kg for male rats and 80, 620 and 1210 mg/kg for female rats. Ingestion of the highest concentration of diethylenetriamine caused sporadic decreases in food consumption in both males and females. Male and female rats exposed to concentrations of 7,500 or 15,000 ppm caused a reduction in weight gain and body weight. Also males exposed to 7,500 and 15,000 ppm had an increased mean corpuscular volume and mean corpuscular haemoglobin; whilst females at these concentrations had increased mean corpuscular volume, total leukocytes and urine pH. In male rats exposed to 15,000 ppm of dihydrochloride salt of diethylenetriamine the weights of the kidneys, brain and testes was increased. In females the weights of the brain, kidneys and liver were increased in animals exposed to 7,500 and 15,000 ppm; the heart and adrenal weight was increased in females exposed to 15,000 ppm. No histopathological effects were noted. The NOAEL for this study was deemed to be 1000 ppm [Leung *et al.*, 1997].

Carcinogenicity / Mutagenicity

Adipic acid

A two year oral study was performed in male and female rats to assess the carcinogenicity of adipic acid [SIDs, 2004]. Males were exposed to 0, 0.1, 1, 3, and 5%; (ca. 75, 750, 2250, 3750 mg/kg bw/day) adipic acid, whilst females were only exposed to 0 or 1% (ca. 750 mg/kg bw/day) adipic acid. Autopsy and histopathological examination was performed on the animals at the end of the study period. The incidence of tumours was the same in the tested and control animals [SIDs, 2004].

The mutagenicity of adipic acid was assessed *in vivo* via a dominant lethal assay [SIDs, 2004]. Male rats were exposed via gavage either acutely to 3.75, 37.5, 375 or 5000 mg/kg/BW or subacutely to 3.75, 37.5, 375 or 2500

mg/kg/day for 5 days [SIDs, 2004]. It was concluded that no dose or time response occurred therefore adipic acid does not cause dominant lethal mutations [SIDs, 2004].

Epichlorohydrin

The IARC (1987) states that there is inadequate evidence for epichlorohydrin being a human carcinogen; but there is sufficient evidence for it being an animal carcinogen. Overall, the IARC deems epichlorohydrin to be a probable human carcinogen (Group 2A).

Dermal toxicity / Irritation studies

Adipic acid

Dermal application of 7940 mg/kg/BW of adipic acid to 2 rabbits for 24 hours only resulted in decreased activity and appetite [SIDs, 2004]. Rabbits dermally exposed to 50% adipic acid had slight irritation to intact skin and moderate irritation to broken skin [SIDs, 2004].

Diethylenetriamine

Kydd (1960) examined the dermal toxicity and sensitisation effect of Diethylenetriamine by applying the compound direct to the arms of 50 human volunteers. The area of skin tested was assessed 24 and 48 hours post exposure to screen for any effect. At 14 days post exposure the compound was re-applied to detect any sensitisation. At 24 hours post exposure 9/50 volunteers had developed reactions, 6/9 of which were deemed to be mild and the other 3/9 were moderate reactions. There was no increase in numbers with skin reactions at 48 hours post exposure. The sensitisation test performed at 14 days post exposure was negative [Kydd, 1960].

Inhalation toxicity

Adipic acid

Rats exposed to adipic acid via inhalation displayed no morbidity or mortality when exposed to concentrations of 7700 mg/m³ for 4 hours [SIDs, 2004].

Industrial workers occupationally exposed to 0.47-0.79 mg/m³ adipic acid for an average of 9 years experienced respiratory irritation. These symptoms are explained by the acidic nature of the compound causing irritation [SIDs, 2004].

Epichlorohydrin

The inhalation carcinogenicity potential of epichlorohydrin was tested by Laskin et al., (1980). Sprague-Dawley rats were exposed to 100 ppm epichlorohydrin for 6 hour periods 5 days a week for 30 days. Of the 140 rats exposed for this period 15/140 developed malignant squamous cell carcinomas of the nasal cavity and 3/140 rats developed papillomas of the

respiratory tract. Lifetime exposure of 100 rats to 30 ppm epichlorohydrin resulted in 1/100 rat developing malignant squamous carcinoma of the nasal cavity and another 1/100 developing nasal papillomas. Another lifetime exposure of 100 rats inhaling 10 ppm epichlorohydrin produced no tumours. From these results it was concluded that a dose-rate effect occurs for epichlorohydrin [Laskin *et al.*, 1980].

A 90 day study evaluating the effects of exposing rats to epichlorohydrin vapours for 6 hours/day for 5 days/week was located by IPCS INCHEM (1984). This study was performed by Quast *et al.*, (1979) in house for Dow Chemicals Ltd. Concentrations of 19, 94 or 189 mg/m³ epichlorohydrin were tested. Surviving rats were euthanized at either day 30 or 90 of the study. The biochemistry, haematology and urinalysis of all the rats were unaffected. At the 94 and 189 mg/m³ doses the epithelium of the nasal turbinates displayed dose related changes and kidney weights were seen to increase. Specifically at the 189 mg/m³ epichlorohydrin dose there was a reduction in body weight gain and focal tubular nephrosis [Quast *et al.*, 1979].

Laskin *et al.*, (1980) exposed Sprague-Dawley rats to a single 6 hour exposure to epichlorohydrin vapour with follow-up for 14 days afterward. Results showed that the inhalation median lethal concentration was 360 ppm.

Reproductive / Developmental toxicity

Adipic acid

Female Wistar rats were exposed to 0, 2.9, 13, 62, 288 mg/kg bw/day adipic acid during the 6-15th days of gestation [SIDs, 2004]. The rats were observed for any changes in behaviour, weight, food consumption and appearance. At day 20 the foetuses were removed and with their parents had complete macroscopic examination. There was no increased incidence of soft tissue or skeletal deformities. The NOAEL for both foetuses and mothers was 288 mg/kg [SIDs, 2004].

Epichlorohydrin

John *et al.*, (1983) assessed the effects of exposing pregnant Sprague-Dawley rats and New Zealand white rabbits to epichlorohydrin through an inhalation route. Both test species were exposed to concentrations of 0, 2.5 or 25 ppm epichlorohydrin for 7 hours/day for the period between the 6th-15th (rats) or 6th -18th days of gestation. Mothers exposed to 25 ppm epichlorohydrin showed decreases in body weight and feeding. No embryotoxic or teratogenic effects were found in either rats or rabbits exposed to epichlorohydrin even at concentrations that induced effects in mothers.

In Vitro Toxicity Status

Carcinogenicity/Mutagenicity

Adipic acid

The mutagenicity of adipic acid was studied via the Ames test, using *S. typhimurium* (Strains TA 1535, TA 1537, TA 1538, TA 98, TA 100) and *Escherichia coli* (Strain WP2). The following doses of adipic acid were added per plates; 0.033, 0.10, 0.33, 1.0, 3.3 and 10 mg with or without metabolic activation. No mutagenicity resulted in any of the bacterial strains [SIDs, 2004].

Epichlorohydrin

A summary of positive mutagenicity tests for epichlorohydrin

Species (Test System)	End Point	Result
<i>Escherichia coli</i> WP ₂ uvrA	Reverse Mutation	+
<i>Salmonella typhimurium</i> TA1535, TA100, GA46	Base pair substitution, frame shifts	+
Mouse Lymphoma Cells	Forward mutations	+
Chinese hamster ovary	Chromosome breaks	+
Human Lymphocytes	Chromatid and chromosome breaks	+
Human Lymphocytes	Sister chromatid exchanges	+

[IPCS INCHEM, 1984]

However, a negative mutagenicity result was recorded when epichlorohydrin was tested on primary rat hepatocytes for the unscheduled DNA synthesis assay [IPCS INCHEM, 1984].

Diethylenetriamine

The mutagenicity of Diethylenetriamine was evaluated via the Ames test using *S. typhimurium* (Strains TA 98, 100, 1535, 1537, 1538) with or without metabolic activation. All of these strains did not detect any mutagenicity. Diethylenetriamine was also not deemed to be mutagenic in the Chinese hamster ovary gene mutation and unscheduled DNA synthesis assays [Leung, 1994].

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