BASIC ACRYLIC MONOMER MANUFACTURERS, INC.

ACRYLATES AND HUMAN HEALTH: Category Review

(Last Updated 5/7/12)

Disclaimer

This category of substances has been well studied to determine their physical-chemical properties.

Substance	Acronym	CAS Number
Acrylic acid	AA	79-10-7
Methyl acrylate	MA	96-33-3
Ethyl acrylate	EA	140-88-5
n-Butyl acrylate	n-BA	141-32-2
i-Butyl acrylate	i-BA	106-63-8
t-Butyl acrylate	t-BA	1663-39-4
2-Ethylhexyl acrylate	2-EHA	103-11-7

Physicochemical Properties

Acrylic acid (AA) is a strong acid. AA and the acrylate esters are clear, colorless liquids which have a characteristic unpleasant odor and high chemical reactivity. AA has high water solubility (1000 g/l) and low vapor pressure (5.29 hPa) at room temperature (25°C).

The vapor pressure, water solubility, and density of the esters decrease with increasing chain length and molecular weight. They are less soluble in water than AA with values ranging from 60 g/l (MA) to 9.6 mg/L (2-EHA). The vapor pressure values at room temperature range from 90 hPa (MA) to 0.24 hPa (2-EHA).

Environmental Fate

AA and its esters are unlikely to persist in the environment. Acrylates have medium to high mobility for adsorption and desorption to soils. They are not expected to bind to soil or sediment. If released to air, they will undergo photo-degradation within days. AA and all of the esters are readily biodegradable except t-BA, which is inherently biodegradable. In contact with water, abiotic hydrolysis occurs very slowly. In water, sewage treatment plants, and soil, degradation is expected due to the action of bacteria in these media. Based on their physicochemical properties and biodegradability, there is no indication that they have the potential to bioaccumulate.

Ecotoxicity

The acrylate esters have a moderate to low acute toxicity in fish, algae, and daphnia. AA is highly toxic to algae and moderately toxic to fish and daphnia. The moderate to low acute toxicity values (EC50 or LC50) for AA and the acrylate esters range between 1 and 100 mg/L. In algae, AA EC50 values range between 0.1 and 1 mg/L.

Chronic toxicity has been assessed using invertebrate studies conducted with AA, EA, and BA. The 21-day chronic life-cycle studies with *Daphnia magna* for acrylic acid show NOECs in the range of 1 - 10 mg/l, while NOECs for ethyl and butyl acrylate are in the range of 0.1 - 1 mg/L. In addition, several algal studies are available with NOECs in the same range. These values in combination with the ready biodegradability indicate moderate to low chronic toxicity.

Human Health Effects

AA and the acrylate esters are generally of low to moderate toxicity, but are moderate to strong irritants. AA is corrosive and the irritancy of the esters tends to decrease with increasing molecular weight. The esters can cause skin allergies. Most of the effects seen in animal studies are associated with the irritancy of the chemical. Animal studies do not indicate long-term target organ effects.

Acute Toxicity

AA and its esters are harmful if swallowed. The dermal and inhalation lethality values (LD50 or LC50) indicate a moderate to low order of toxicity. Concentration dependent irritation at the site of contact can occur for all routes of exposure. The acute toxicity of the esters decreases with increasing ester carbon chain length.

Irritation/Sensitization

Acrylic acid is corrosive to the skin and eye, while the esters are strong to moderate irritants. Esters exhibit a low but definable potential for dermal sensitization, while acrylic acid is not considered a sensitizer. If inhaled, the vapor of acrylic acid or the esters can also cause irritation to the mucous membranes of the respiratory tract.

Repeated Dose Toxicity

Acrylic acid and the acrylate esters demonstrate similar toxicity profiles in rats and mice via inhalation, dietary and/or dermal routes of administration in tests ranging from 28 days to 2 years. No evidence of systemic toxicity was observed; effects seen in these studies are consistent with direct irritation effects.

Genetic Toxicity

Extensive genetic toxicity testing of acrylic acid and the acrylate esters indicates a lack of potential for genetic toxicity. In vitro tests conducted include one or more of the following: the Ames test for mutagenicity both with and without metabolic activation, the mouse lymphoma assay and the chromosomal aberration tests in mammalian cell lines, the in vitro micronucleus test and the in vitro Unscheduled DNA Synthesis (UDS) test. Similarly, the in vivo tests conducted include one or more of the following: the mouse micronucleus assay, the rat unscheduled DNA synthesis assay, the rat and mouse chromosomal aberration assay and the rat dominant lethal assay.

Developmental/Reproductive Toxicity

AA and its esters have been tested for developmental toxicity in at least one species via oral administration or inhalation. Neither evidence of fetotoxicity nor birth defects were seen at dose levels which did not cause maternal toxicity.

Subchronic and chronic testing indicates no effects on reproductive organs. Acrylic acid has been tested in a guideline two-generation reproduction study. The NOAEL for reproductive effects was an order of magnitude higher than that for parental toxicity in the F1 generation. There was no indication of an adverse reproductive effect at any dose level tested. A guideline two-generation reproduction study has also been conducted for methyl acrylate as representative for the other esters. In this study, the no-observed-effect concentration (NOEC) for parental systemic toxicity was based on microscopic changes in the nasal tissues seen at higher concentrations. Secondary to this parental toxicity, pup body weights were decreased, but no further developmental effects were observed. The NOEC for reproductive toxicity was 75 ppm, the highest concentration tested.

Carcinogenicity

AA and the acrylate esters have been assessed for carcinogenicity in a number of studies by various routes of exposure and found in most studies to be not carcinogenic. AA did not cause an increase in tumors in a rat 2-year drinking water study or in chronic mouse skin painting studies. MA, EA, and BA did not cause increases in tumors in rats in 2-year inhalation studies. EA was also negative for carcinogenicity in chronic dermal and drinking water studies. It did cause tumors in the forestomachs of rats and mice given by gavage in doses that caused marked local irritation, a situation that is not considered relevant to humans. 2-EHA caused an increase in skin tumors in some, but not all, chronic dermal studies in mice. 2-EHA induced skin tumors at concentrations that were highly irritating, and this damage was presumed to be the mode of action for tumor formation. These studies illustrate that none of the members tested produced evidence of carcinogenicity of known relevance to humans in chronic/oncogenicity studies.

Toxicokinetics

AA and its esters are rapidly metabolized and do not accumulate in the mammalian body. Acrylate esters were found to disappear rapidly in rat whole blood *in vitro*; the $t_{½}$ was 3.6, 4.6, and 7.1 minutes for disappearance of methyl, ethyl, and butyl acrylate, respectively.

Studies demonstrated that acrylic acid was quite stable in rat blood as well as in rat liver, kidney and lung homogenates *in vitro*. In rats and mice a high percentage (> 75%) of orally administered AA was absorbed and eliminated as carbon dioxide within 24 hours. Ethyl acrylate disappeared in tissue homogenates *in vitro*; the rate of hydrolysis was ~20 times greater in liver homogenates than in kidney or lung homogenates. Similar results were obtained for methyl acrylate. The rate of hydrolysis in rat liver homogenates increased in the order butyl < ethyl < methyl. Disappearance of the acrylate esters *in vitro* in tissue homogenates, but not in blood, was quantitatively associated with the appearance of acrylic acid, indicating that the esters hydrolyze to the acid and the associated alcohol.

Disclaimer

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