Diethanolamine

1 Nonproprietary Names

USPNF: Diethanolamine

2 Synonyms

Bis(hydroxyethyl)amine; DEA; diethylolamine; 2,2′-dihydroxydiethylamine; diolamine; 2,2′-iminodiethanol.

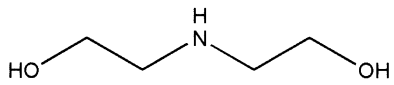
3 Chemical Name and CAS Registry Number

2,2′-Iminobisethanol [111-42-2]

4 Empirical Formula and Molecular Weight

$C_4H_{11}NO_2$ 105.14

5 Structural Formula



6 Functional Category

Alkalizing agent; emulsifying agent.

7 Applications in Pharmaceutical Formulation or Technology

Diethanolamine is primarily used in pharmaceutical formulations as a buffering agent, such as in the preparation of emulsions with fatty acids. In cosmetics and pharmaceutics it is used as a pH adjuster and dispersant.

Diethanolamine has also been used to form the soluble salts of active compounds, such as iodinated organic acids that are used as contrast media. As a stabilizing agent, diethanolamine prevents the discoloration of aqueous formulations containing hexamethylenetetramine-1,3-dichloropropene salts.

Diethanolamine is also used in cosmetics.

8 Description

The USPNF 20 describes diethanolamine as a mixture of ethanolamines consisting largely of diethanolamine. At about room temperature it is a white, deliquescent solid. Above room temperature diethanolamine is a clear, viscous liquid with a mildly ammoniacal odor.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for diethanolamine.

Test	USPNF 20
Identification	+
Limit of triethanolamine	≤1.0%
Organic volatile impurities	+
Refractive index at 30°C	1.473–1.476
Water	≤0.15%
Assay (anhydrous basis)	98.5–101.0%

10 Typical Properties

Acidity/alkalinity: pH = 11.0 for a 0.1 N aqueous solution.
Autoignition temperature: 662°C
Boiling point: 268.8°C
Density:
1.0881 g/cm^3 at 30°C
1.0693 g/cm^3 at 60°C
Dissociation constant: pK_a = 8.88
Flash point (open cup): 138°C
Hygroscopicity: very hygroscopic.
Melting point: 28°C
Refractive index: n_D^{30} = 1.4753
Solubility: *see* Table II.

Table II: Solubility of diethanolamine.

Solvent	Solubility at 20°C
Acetone	Miscible
Benzene	1 in 24
Chloroform	Miscible
Ether	1 in 125
Glycerin	Miscible
Methanol	Miscible
Water	1 in 1

Surface tension: 49.0 mN/m (49.0 dynes/cm) at 20°C.
Vapor density (relative): 3.65 (air = 1)
Vapor pressure : >1 Pa at 20°C.
Viscosity (dynamic):
351.9 mPa s (351.9 cP) at 30°C
53.85 mPa s (53.85 cP) at 60°C

11 Stability and Storage Conditions

Diethanolamine is hygroscopic and light- and oxygen-sensitive; it should be stored in an airtight container, protected from light, in a cool, dry place.

See Monoethanolamine for further information.

12 Incompatibilities

Diethanolamine is a secondary amine that contains two hydroxy groups. It is capable of undergoing reactions typical of secondary amines and alcohols. The amine group usually exhibits the greater activity whenever it is possible for a reaction to take place at either the amine or a hydroxy group.

Diethanolamine will react with acids, acid anhydrides, acid chlorides, and esters to form amide derivatives, and with propylene carbonate or other cyclic carbonates to give the corresponding carbonates. As a secondary amine, diethanolamine reacts with aldehydes and ketones to yield aldimines and ketimines. Diethanolamine also reacts with copper to form complex salts. Discoloration and precipitation will take place in the presence of salts of heavy metals.

13 Method of Manufacture

Diethanolamine is prepared commercially by the ammonolysis of ethylene oxide. The reaction yields a mixture of monoethanolamine, diethanolamine, and triethanolamine which is separated to obtain the pure products.

14 Safety

Diethanolamine is used in topical and parenteral pharmaceutical formulations, with up to 0.3% w/v being used in intravenous infusions. Experimental studies in dogs have shown that intravenous administration of larger doses of diethanolamine results in sedation, coma, and death.

Animal toxicity studies suggest that diethanolamine is less toxic than monoethanolamine, although in rats the oral acute and subacute toxicity is greater.[1] Diethanolamine is said to be heptacarcinogenic in mice and has also been reported to induce hepatic choline deficiency in mice.[2]

Diethanolamine is an irritant to the skin, eyes, and mucous membranes when used undiluted or in high concentration. However, in rabbits, aqueous solutions containing 10% w/v diethanolamine produce minor irritation. The lethal human oral dose of diethanolamine is estimated to be 5–15 g/kg bodyweight.

The US Cosmetic Ingredient Review Expert Panel evaluated diethanolamine and concluded that it is safe for use in cosmetic formulations designed for discontinuous, brief use followed by thorough rinsing from the surface of the skin. In products intended for prolonged contact with the skin, the concentration of ethanolamines should not exceed 5%. Diethanolamine should not be used in products containing *N*-nitrosating agents.[1] *See also* Section 18.

LD_{50} (guinea pig, oral): 2.0 g/kg[3]
LD_{50} (mouse, IP): 2.3 g/kg
LD_{50} (mouse, oral): 3.3 g/kg
LD_{50} (rabbit, skin): 12.2 g/kg
LD_{50} (rat, IM): 1.5 g/kg
LD_{50} (rat, IP): 0.12 g/kg
LD_{50} (rat, IV): 0.78 g/kg
LD_{50} (rat, oral): 0.71 g/kg
LD_{50} (rat, SC): 2.2 g/kg

15 Handling Precautions

Diethanolamine is irritating to the skin, eyes, and mucous membranes. Protective clothing, gloves, eye protection, and a respirator are recommended. Ideally, diethanolamine should be handled in a fume cupboard. In the UK, the long-term (8-hour TWA) exposure limit for diethanolamine is 13 mg/m^3 (3 ppm).[4] Diethanolamine poses a slight fire hazard when exposed to heat or flame.

16 Regulatory Status

Included in the FDA Inactive Ingredients Guide (IV infusions). Included in medicines licensed in the UK.

17 Related Substances

Monoethanolamine; triethanolamine.

18 Comments

Through a standard battery of rodent studies, diethanolamine has been identified by the US National Toxicology Program as a potential carcinogen following topical administration. Several possible confounding issues have been noted during the review of these studies, which may affect the ultimate conclusion made regarding the carcinogenicity of diethanolamine and the relevance of these findings to humans.

19 Specific References

1 Neudahl GA. Diethanolamine (DEA) and diethanolamides toxicology. *Drug Cosmet Ind* 1998; **162**(4): 26–29.
2 Lehman-McKeeman LD, Gamsky EA, Hicks SM, *et al.* Diethanolamine induces hepatic choline deficiency in mice. *Toxicol Sci* 2002; **67**(1): 38–45.
3 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 10th edn. New York: Wiley, 2000: 1242.
4 Health and Safety Executive. *EH40/2002: Occupational Exposure Limits 2002*. Sudbury: Health and Safety Executive, 2002.

20 General References

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21 Author

K Fowler.

22 Date of Revision

15 August 2002.