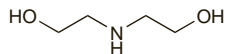


Diolamine (pINN)

Diaethanolamin; Diethanolamina; Diethanolamine; Diolamina; Diolaminum. Bis(2-hydroxyethyl)amine; 2,2'-Iminobisethanol.

Диоламин
 $C_4H_{11}NO_2 = 105.1$.
 CAS — 111-42-2.

**Pharmacopoeias.** In *USNF*.

USNF 26 (Diethanolamine). It is a mixture of olamines, consisting largely of diolamine. White or clear, colourless crystals, deliquescent in moist air, or a colourless liquid. Miscible with water, with alcohol, with acetone, with chloroform, and with glycerol; slightly soluble to insoluble in ether, in petroleum spirit, and in benzene. Store in airtight containers. Protect from light.

Profile

Diolamine is an organic base that is used as an emulsifier and dispersant.

It is used to solubilise fusidic acid and sulfafurazole by the formation of the diolamine salt. It has been used for the preparation of salts of iodinated organic acids used as contrast media. It may be irritating to the skin and mucous membranes.

Dioxins

Dioxinas.

NOTE. The name Dioxin has also been applied to dimethoxane.

Profile

The term 'dioxins' encompasses a large group of closely related chemicals known as polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs). The most toxic is 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD).

Dioxins are byproducts in the manufacture of commercial chemical products such as chlorinated phenols and polychlorinated biphenyls (PCBs), and can also be produced in smaller quantities by combustion processes and industrial waste. They first came to public attention during the Vietnam war, when they were found to be present in the herbicide Agent Orange used as a defoliant. They are incriminated as causing chloracne (a severe and persistent acne caused by chlorinated compounds). They are potent teratogens and carcinogens in animals. An increased incidence of cancer at different organs due to dioxins has been claimed but this has not been substantiated by clinical and follow-up studies. An effect on cell-mediated immunity has been observed. Exposure should be limited to the lowest feasible concentration.

Adverse effects. The impact of dioxins in food and the environment has been reviewed.^{1,4}

An excess of soft tissue sarcomas was found in workers exposed to chlorophenoxy herbicides including those contaminated with TCDD,⁵ but cautious interpretation of these results was advised.⁶ In Vietnam veterans the risk of non-Hodgkin's lymphoma was about 50% higher than control subjects, but was not related to exposure to Agent Orange, nor was there evidence for an increase in other cancers.⁷ Exposure to TCDD was implicated in an increase in cancer mortality in chemical workers,^{8,9} but confounding factors such as smoking may have been present.^{9,10} Other studies^{11,12} have not shown an association between dioxin exposure and an increase in the incidence of human cancer, and epidemiological studies after occupational or accidental exposures have found no clear persistent systemic effects, except for chloracne, and no clear association with carcinogenesis or reproductive disorders.¹² Decreased plasma immunoglobulin G concentrations were measured in people after exposure to TCDD 20 years earlier as a result of accidental environmental contamination in Seveso, Italy.¹³ A statistically significant increase in the incidence of breast cancer related to serum levels of TCDD was observed in a cohort of 981 women who ranged in age from infancy to 40 years in 1976 at the time of the Seveso accident.¹⁴ The authors pointed out that this cohort is relatively young and continued follow-up would clarify any possible pathogenic role of TCDD.

In the USA, the National Academy of Sciences' Institute of Medicine is reported to have carried out an evaluation of publications on herbicide exposure, largely in industrial and agricultural workers.¹⁵ They concluded that exposure to herbicides or dioxin was associated with soft-tissue sarcomas, Hodgkin's disease, non-Hodgkin lymphoma, chloracne, and porphyria cutanea tarda, and that there was limited evidence of an association with respiratory and prostate cancers and multiple myeloma. An update to the report has also suggested a link between Agent Orange exposure and spina bifida in veterans' offspring.¹⁶ There is some evidence that exposure of men to TCDD is associated with a decreased male to female sex ratio in their offspring.¹⁷ Results from studies¹⁸⁻²⁰ suggest that prenatal exposure to PCBs has an effect on mental and motor development in early childhood, although this may be counteracted by an advantageous home envi-

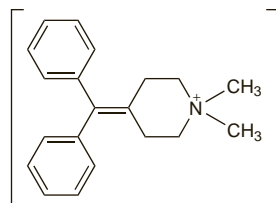
ronment. However, virtually no adverse effects in relation to postnatal exposure to PCBs present in breast milk were demonstrated.²⁰

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7. Suskind R. The association of selected cancers with service in the US military in Vietnam. *Arch Intern Med* 1990; **150**: 2449-50.
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11. Coggon O, et al. Mortality and incidence of cancer at four factories making phenoxy herbicides. *Br J Ind Med* 1991; **48**: 173-8.
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19. Vreugdenhil HJ, et al. Effects of prenatal PCB and dioxin background exposure on cognitive and motor abilities in Dutch children at school age. *J Pediatr* 2002; **140**: 48-56.
20. Jacobson JL, Jacobson SW. Association of prenatal exposure to an environmental contaminant with intellectual function in childhood. *J Toxicol Clin Toxicol* 2002; **40**: 467-75.

Diphepanil Metilsulfate (BAN, rINN)

Diphepanil Methylsulfate; Diphepanil Methylsulphate; Diphémanil, Métilsulfate de; Diphepanil Metilsulfas; Diphenmethanil Methylsulphate; Metilsulfato de difemanilo; Vagophemanil Methylsulphate. 4-Benzhydrylidene-1,1-dimethylpiperidinium methylsulphate.

Дифеманила Метилсульфат
 $C_{20}H_{24}N_2CH_3SO_4 = 389.5$.
 CAS — 62-97-5.
 ATC — A03AB15.
 ATC Vet — QA03AB15.

**Profile**

Diphepanil metilsulfate is a quaternary ammonium antimuscarinic with peripheral effects similar to those of atropine (p.1219). It is used topically as a 2% cream or powder to treat hyperhidrosis (p.1580).

Diphepanil metilsulfate, given orally, has been used for the treatment of symptomatic bradycardia in infants.

◇ References.

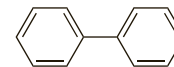
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Preparations

Proprietary Preparations (details are given in Part 3)
Austral: Prantal; **Chile:** Nivelon†; **Ital:** Prantal†; **NZ:** Prantal.

Diphenyl

Difenil; E230; Phenylbenzene. Biphenyl.
 $C_{12}H_{10} = 154.2$.
 CAS — 92-52-4.

**Profile**

Diphenyl is fungistatic against a limited number of moulds and has been employed for impregnating the material used for wrapping citrus fruits.

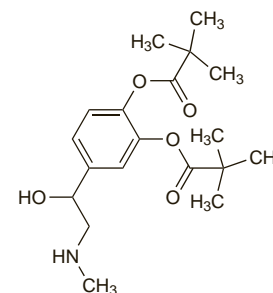
Adverse effects. Workers exposed to high concentrations of diphenyl (up to 128 mg/m³) developed toxic symptoms that included irritation of the throat and eyes, headache, nausea, diffuse abdominal pain, numbness, aching of limbs, and general fatigue.¹ One of the workers, who also had somnolence, icterus, ascites, and oedema of the legs, died; at autopsy, the liver showed necrosis. Chronic hepatitis was reported in a woman exposed over a 25-year period to diphenyl in the paper used to pack citrus fruit.²

1. Häkkinen I, et al. Diphenyl poisoning in fruit paper production. *Arch Environ Health* 1973; **26**: 70-4.
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Dipivefrine (BAN, rINN) ⊗

Dipivalyl Epinephrine; Dipivefrini; Dipivefrin (USAN); Dipivefrina; Dipivefrine; Dipivefrinum; DPE.

Дипивефрин
 $C_{19}H_{29}NO_5 = 351.4$.
 CAS — 52365-63-6.
 ATC — S01EA02.
 ATC Vet — QS01EA02.

**Dipivefrine Hydrochloride** (BANM, rINN) ⊗

Dipivalyl Adrenaline Hydrochloride; Dipivalyl Epinephrine Hydrochloride; Dipivefrinihydrokloridi; Dipivefrin Hydrochloride; Dipivefrine, chlorhydrate de; Dipivefrin-hydrochlorid; Dipivefrinhydroklorid; Dipivefrini hydrochloridum; Dipivefrino hydrochloridas; Dipivefriny chlorowodorek; Hidrocloruro de dipivefrina. (R)-4-[1-Hydroxy-2-(methylamino)ethyl]-o-phenylene dipivalate hydrochloride.

Дипивефрина Гидрохлорид
 $C_{19}H_{29}NO_5 \cdot HCl = 387.9$.
 CAS — 64019-93-8.
 ATC — S01EA02.
 ATC Vet — QS01EA02.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.

Ph. Eur. 6.2 (Dipivefrine Hydrochloride). A white or almost white crystalline powder. Freely soluble in water, in alcohol, and in dichloromethane; very soluble in methyl alcohol.

USP 31 (Dipivefrin Hydrochloride). White, crystalline powder or small crystals, having a faint odour. Very soluble in water. Store in airtight containers.

Profile

Dipivefrine is an ester and prodrug of adrenaline (p.1203). A 0.1% solution of the hydrochloride is used topically as eye drops to reduce intra-ocular pressure in patients with open-angle glaucoma or ocular hypertension (p.1873).

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