

mixtures of dichlorodifluoromethane and trichlorofluoromethane with 9 to 12% w/w of ethylene oxide have been employed, but restrictions on the release of fluorocarbons or CFCs limit their use.

Effective sterilisation by ethylene oxide depends on exposure time, temperature, humidity, the amount and type of microbial contamination, and the partial pressure of the ethylene oxide in the exposure chamber. Concentrations of between 400 and 1000 mg/litre are usually used for sterilisation and the process time may vary from 30 minutes to 10 hours. The material being sterilised must be permeable to ethylene oxide if occluded micro-organisms are present. The bactericidal action is accelerated by increase of temperature; the average temperature used is between 40° and 50°.

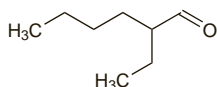
Moisture is essential for sterilisation by ethylene oxide. In practice, dry micro-organisms need to be rehydrated before ethylene oxide can be effective; humidification is normally carried out under vacuum prior to introduction of ethylene oxide. Relative humidities of 40 to 60% are used.

Control of physical factors does not assure sterility, and the process should be monitored usually by using standardised suspensions of aerobic spores such as those of *Bacillus subtilis* var. *niger*.

Ethylhexanal

2-Ethylcaproaldehyde; 2-Ethylhexylaldehyde; Octylaldehyde. 2-Ethylhexanal.

$C_8H_{16}O = 128.2$.
CAS — 123-05-7.



Profile

Ethylhexanal is an aldehyde disinfectant used for instrument disinfection.

Preparations

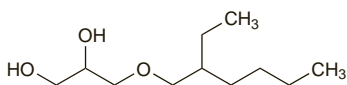
Proprietary Preparations (details are given in Part 3)

Multi-ingredient: Ger.: Buraton 10 F; Heliplus H plus N; Lysetol FF; Sekucid konz.

Ethylhexylglycerin

Octoxyglycerin. 3-[(2-Ethylhexyl)oxy]-1,2-propanediol.

Этилгексилглицерин
 $C_{11}H_{24}O_3 = 204.3$.
CAS — 70445-33-9.



Profile

Ethylhexylglycerin is a disinfectant used in a concentration of 0.3% in topical deodorant preparations. It is also used in products for disinfection of the hands.

References

1. Stausbøl-Grøn B, Andersen KE. Allergic contact dermatitis to ethylhexylglycerin in a cream. *Contact Dermatitis* 2007; **57**: 193-4.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: Braz.: Effidrate†; Chile: Uriage Desodorante Tri-Actif.

Formaldehyde

Formaldehid; Formaldehído; Formaldehyd.

Формальдегид
 $CH_2O = 30.03$.
CAS — 50-00-0.
ATC Vet — QP53AX19.



Formaldehyde Solution

Formaldehído, solución de; Formaldehído tirpalas; Formaldehid-öldat; Formaldehyd roztok; Formaldehyde, solution de; Formaldehydi solutio; Formaldehydliuos; Formaldehydlösning; Formaldehydu roztwór.

NOTE. The names formalin and formol have been used for formaldehyde solution but in some countries they are trade marks.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, *US*, and *Viet*. **Ph. Eur. 6.2** (Formaldehyde Solution (35 per cent); Formaldehyde Solution BP 2008). It contains 34.5 to 38.0% w/w of formaldehyde with methyl alcohol as a stabiliser. It is a clear, colourless, liquid. Miscible with water and with alcohol. It may be cloudy after storage. Store at a temperature between 15° and 25°. Protect from light.

USP 31 (Formaldehyde Solution). It contains not less than 34.5% w/w of formaldehyde with 9 to 15% methyl alcohol added to prevent polymerisation. It is a clear, colourless, or practically colourless liquid with a pungent, irritating odour. Miscible with water and with alcohol. Store at a temperature above 15° in airtight containers. It may become cloudy on standing due to the separation of paraformaldehyde, especially if the solution is kept in a cold place; the cloudiness disappears on warming.

Strength of solutions. Formaldehyde solution is sometimes known simply as formaldehyde and this has led to confusion in interpreting the strength and the form in which formaldehyde is being used. In practice formaldehyde is available as formaldehyde solution which is diluted before use, the percentage strength being expressed in terms of formaldehyde solution rather than formaldehyde. For example, in the UK, formaldehyde solution 3% consists of 3 volumes of Formaldehyde Solution (35 Per Cent) (Ph. Eur. 6.2) diluted to 100 volumes with water and thus contains 1.04 to 1.14% w/w of formaldehyde; it is **not** prepared by diluting Formaldehyde Solution (35 Per Cent) (Ph. Eur. 6.2) to arrive at a solution containing 3% w/w of formaldehyde.

Incompatibility. Formaldehyde reacts with protein and this may diminish its antimicrobial activity.

Adverse Effects and Precautions

Concentrated formaldehyde solutions applied to the skin cause whitening and hardening. Contact dermatitis and sensitivity reactions have occurred after the use of conventional concentrations and after contact with residual formaldehyde in resins.

Ingestion of formaldehyde solution causes intense burning pain in the mouth, throat, chest, and stomach, with inflammation, ulceration, and necrosis of mucous membranes. There may be nausea, vomiting, haematemesis, blood-stained diarrhoea, haematuria, and anuria; metabolic acidosis, vertigo, convulsions, loss of consciousness, and circulatory and respiratory failure may occur. Death has occurred after the ingestion of the equivalent of about 30 mL of formaldehyde solution. If the patient survives 48 hours, recovery is probable. Formaldehyde vapour is irritant to the eyes, nose, and upper respiratory tract, and may cause coughing, dysphagia, spasm and oedema of the larynx, bronchitis, pneumonia, and rarely, pulmonary oedema. Asthma-like symptoms have been reported after repeated exposure.

General references.

1. Health and Safety Executive. Formaldehyde. *Toxicity Review* 2. London: HMSO, 1981.
2. WHO. Formaldehyde. *Environmental Health Criteria* 89. Geneva: WHO, 1989. Available at: <http://www.inchem.org/documents/ehc/ehc/ehc89.htm> (accessed 15/03/06)
3. WHO. Formaldehyde health and safety guide. *IPCS Health and Safety Guide* 57. Geneva: WHO, 1991. Available at: <http://www.inchem.org/documents/hsg/hsg/hsg057.htm> (accessed 15/03/06)
4. WHO. Formaldehyde. *Concise International Chemical Assessment Document* 40. Geneva: WHO, 2002. Available at: <http://whqlibdoc.who.int/hq/2002/a73769.pdf> (accessed 15/03/06)

Abuse. References to the abuse of embalming fluid (the primary ingredient of which is formaldehyde), usually in the form of marijuana treated with embalming fluid and in some cases phencyclidine, a mixture known as 'fry'.¹⁻⁴

1. Holland JA, et al. Embalming fluid-soaked marijuana: new high or new guise for PCP? *J Psychoactive Drugs* 1998; **30**: 215-9.
2. Peters RJ, et al. Beliefs and social norms about cigarettes or marijuana sticks laced with embalming fluid and phencyclidine (PCP): why youth use 'fry'. *Subst Use Misuse* 2005; **40**: 563-71.

3. Singer M, et al. Dust in the wind: the growing use of embalming fluid among youth in Hartford, CT. *Subst Use Misuse* 2005; **40**: 1035-50.
4. Singer M, et al. When the drug of choice is a drug of confusion: embalming fluid use in inner city Hartford, CT. *J Ethn Subst Abuse* 2005; **4**: 73-96.

Carcinogenicity. There is controversy as to the risk formaldehyde presents as a carcinogen. Studies on the occupational exposure of medical personnel and industrial workers¹⁻³ to formaldehyde have generally concluded that although the risk is small or non-existent, the possibility that formaldehyde is a human carcinogen cannot be excluded. Reanalyses of some studies have led to different interpretations of the results, with some workers concluding that the risk of cancer from formaldehyde is greater than originally thought.⁴ Analysis of mortality data⁵ for a cohort of 25619 workers exposed to formaldehyde in the USA found some evidence of an association with nasopharyngeal cancer and possibly cancers at other upper respiratory-tract sites. Based on the results of this large cohort study and supported by evidence from other epidemiological and animal studies, the International Agency for Research on Cancer (IARC) concluded,⁶ in 2004, that occupational exposure to formaldehyde does cause nasopharyngeal cancer. Furthermore, they found strong, but not sufficient, evidence to establish a causal link with leukaemia and limited evidence to suggest it causes sinonasal cancer. IARC has concluded that formaldehyde is a definite human carcinogen.⁶

1. Gérin M, et al. Cancer risks due to occupational exposure to formaldehyde: results of a multi-site case-control study in Montreal. *Int J Cancer* 1989; **44**: 53-8.
2. Blair A, et al. Mortality from lung cancer among workers employed in formaldehyde industries. *Am J Ind Med* 1990; **17**: 683-99.
3. Coggon D, et al. Extended follow-up of a cohort of British chemical workers exposed to formaldehyde. *J Natl Cancer Inst* 2003; **95**: 1608-15.
4. Sterling TD, Weinkam JJ. Mortality from respiratory cancers (including lung cancer) among workers employed in formaldehyde industries. *Am J Ind Med* 1994; **25**: 593-602.
5. Hauptmann M, et al. Mortality from solid cancers among workers in formaldehyde industries. *Am J Epidemiol* 2004; **159**: 1117-30.
6. IARC/WHO. Formaldehyde, 2-butoxyethanol and 1-tert-butyl-2-propanol. *IARC monographs on the evaluation of carcinogenic risks to humans volume 88* 2004. Available at: <http://monographs.iarc.fr/ENG/Monographs/vol88/volume88.pdf> (accessed 23/05/06)

Effects on the blood. Haemolysis during chronic haemodialysis was due to formaldehyde eluted from filters.¹

1. Orringer EP, Mattern WD. Formaldehyde-induced hemolysis during chronic hemodialysis. *N Engl J Med* 1976; **294**: 1416-20.

Effects on the urinary tract. Adverse effects have resulted from intravesical instillation of formaldehyde solutions, ranging in strength from 1 to 10%, in the treatment of haemorrhagic cystitis. They include dysuria, suprapubic pain, ureteric and bladder fibrosis, hydronephrosis, vesicoureteral reflux, bilateral ureteral obstruction, papillary necrosis, bladder rupture, and acute tubular necrosis. Intrapertoneal spillage through a fistula, leading to adverse systemic effects, has also occurred.¹ Fatalities have resulted from cardiac arrest and acute renal failure.¹⁻³ See also Haemorrhagic Cystitis under Uses, below.

There has also been a report⁴ of 4 patients exposed to high levels of atmospheric formaldehyde who developed membranous nephropathy, suggesting that there may be genetic susceptibility for this effect.

1. Capen CV, et al. Intrapertoneal spillage of formalin after intravesical instillation. *Urology* 1982; **19**: 599-601.
2. Melekos M, Lalos J. Intravesical instillation of formalin and its complications. *Urology* 1983; **21**: 331-2.
3. Sarnak MJ, et al. Intravesicular formaldehyde instillation and renal complications. *Clin Nephrol* 1999; **51**: 122-5.
4. Breyse P, et al. Membranous nephropathy and formaldehyde exposure. *Ann Intern Med* 1994; **120**: 396-7.

Hypersensitivity. Hypersensitivity to formaldehyde has had several manifestations. Effects on the skin have included acute exacerbation of eczema after injection of hepatitis B vaccine containing formaldehyde up to 20 micrograms/mL.¹ In another case, formaldehyde sensitivity was characterised by pruritus, burning, and redness within minutes of exposure to sunlight.² Painful, enlarged, and haemorrhagic gingival margins have occurred after the use of a toothpaste containing a solution of formaldehyde.³ There is conflicting evidence of the respiratory effects of formaldehyde: although a low concentration has been reported not to trigger an asthma attack in patients with severe bronchial hyperresponsiveness,⁴ occupational asthma has been documented.⁵ More severe manifestations of hypersensitivity include 7 cases of shock of possible toxic or anaphylactic aetiology that occurred after the use of formaldehyde solutions during surgical removal of hydatid cysts.⁶

For mention of an allergic response to root canal paste containing paraformaldehyde, see p.1655.

1. Ring J. Exacerbation of eczema by formalin-containing hepatitis B vaccine in formaldehyde-allergic patients. *Lancet* 1986; **ii**: 522-3.
2. Shelley WB. Immediate sunburn-like reaction in a patient with formaldehyde photosensitivity. *Arch Dermatol* 1982; **118**: 117-18.
3. Laws IM. Toothpaste formulations. *Br Dent J* 1984; **156**: 240.
4. Harving H, et al. Low concentrations of formaldehyde in bronchial asthma: a study of exposure under controlled conditions. *BMJ* 1986; **293**: 310.