Phenylethyl Alcohol

1 Nonproprietary Names

USP: Phenylethyl alcohol

2 Synonyms

Benzeneethanol; benzyl carbinol; benzylmethanol; β-hydroxyethyl benzene; PEA; phenethanol; β-phenylethyl alcohol; 2-phenylethyl alcohol; phenylethanol.

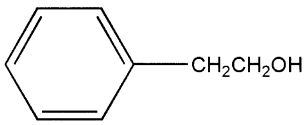
3 Chemical Name and CAS Registry Number

2-Phenylethanol [60-12-8]

4 Empirical Formula | Molecular Weight

$C_8H_{10}O$ | 122.17

5 Structural Formula



6 Functional Category

Antimicrobial preservative.

7 Applications in Pharmaceutical Formulation or Technology

Phenylethyl alcohol is used as an antimicrobial preservative in nasal, ophthalmic, and otic formulations at 0.25–0.5% v/v concentration; it is generally used in combination with other preservatives.[1–3] Phenylethyl alcohol has also been used on its own as an antimicrobial preservative at concentrations up to 1% v/v in topical preparations. At this concentration, mycoplasmas are inactivated within 20 minutes, although enveloped viruses are resistant.[4] Phenylethyl alcohol is also used in flavors and as a perfumery component, especially in rose perfumes.

8 Description

Phenylethyl alcohol is a clear, colorless liquid with an odor of rose oil. It has a burning taste that irritates and then anesthetizes mucous membranes.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for phenylethyl alcohol.

Test	USP 25
Identification	+
Specific gravity	1.017–1.020
Refractive index	1.531–1.534
Residue on ignition	⩽0.005%
Chlorinated compounds	+
Aldehyde	+
Organic volatile impurities	+

10 Typical Properties

Antimicrobial activity: phenylethyl alcohol has moderate antimicrobial activity although it is relatively slow acting; it is not sufficiently active to be used alone.[5] Greatest activity occurs at less than pH 5; it is inactive above pH 8. Synergistic effects have been reported when combined with benzalkonium chloride, chlorhexidine gluconate or diacetate, polymyxin B sulfate, and phenylmercuric nitrate.[6–10] With either benzalkonium chloride or chlorhexidine, synergistic effects were observed against *Pseudomonas aeruginosa* and apparently additive effects against Gram-positive organisms. With phenylmercuric nitrate, the effect was additive against *Pseudomonas aeruginosa*. Additive effects against *Pseudomonas cepacia* in combination with either benzalkonium chloride or chlorhexidine have also been reported.[11] *See also* Section 12.

Bacteria: fair activity against Gram-positive bacteria; for *Staphylococcus aureus*, the minimum inhibitory concentration (MIC) may be more than 5 mg/mL. Greater activity is shown against Gram-negative organisms.[12] Typical MIC values are: *Salmonella typhi* 1.25 mg/mL; *Pseudomonas aeruginosa* 2.5 mg/mL; *Escherichia coli* 5.0 mg/mL.

Fungi: poor activity against molds and fungi.

Spores: inactive, e.g., at 0.6% v/v concentration, reported to be ineffective against spores of *Bacillus stearothermophilus* at 100 °C for 30 minutes.

Boiling point: 219–221 °C

Flash point: 102 °C (open cup)

Melting point: −27 °C

Partition coefficients:

Chloroform : water = 15.2

Heptane : water = 0.58

Octanol : water = 21.5

Solubility: *see* Table II.

11 Stability and Storage Conditions

Phenylethyl alcohol is stable in bulk, but is volatile and sensitive to light and oxidizing agents. It is reasonably stable in both acidic and alkaline solutions. Aqueous solutions may be sterilized by autoclaving. If stored in low-density polyethylene containers, phenylethyl alcohol may be absorbed by the containers. Losses to polypropylene containers have been reported to be insignificant over 12 weeks at 30 °C. Sorption to rubber closures is generally small.

Table II: Solubilty of phenylethyl alcohol.

Solvent	Solubility at 20 °C
Benzyl benzoate	Very soluble
Chloroform	Very soluble
Diethyl phthalate	Very soluble
Ethanol (95%)	Very soluble
Ether	Very soluble
Fixed oils	Very soluble
Glycerin	Very soluble
Mineral oil	Slightly soluble
Propylene glycol	Very soluble
Water	1 in 60

The bulk material should be stored in a well-closed container, protected from light, in a cool, dry place.

12 Incompatibilities

Incompatible with oxidizing agents and protein, e.g., serum. Phenylethyl alcohol is partially inactivated by polysorbates, although this is not as great as the reduction in antimicrobial activity that occurs with parabens and polysorbates.[13]

13 Method of Manufacture

Phenylethyl alcohol is prepared by reduction of ethyl phenylacetate with sodium in absolute alcohol; by hydrogenation of phenylacetaldehyde in the presence of a nickel catalyst; or by addition of ethylene oxide or ethylene chlorohydrin to phenylmagnesium bromide, followed by hydrolysis. Phenylethyl alcohol also occurs naturally in a number of essential oils, especially rose oil.

14 Safety

Phenylethyl alcohol is generally regarded as a nontoxic and nonirritant material. However, at the concentration used to preserve eye-drops (about 0.5% v/v) or above, eye irritation may occur.[14]

LD_{50} (rabbit, skin): 0.79 g/kg[15]
LD_{50} (rat, oral): 1.79 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Phenylethyl alcohol is combustible when exposed to heat or flame, and emits acrid smoke when heated to decomposition. Eye protection and gloves are recommended.

16 Regulatory Status

Included in the FDA Inactive Ingredients Guide (nasal, ophthalmic, and otic preparations). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

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18 Comments

The EINECS number for phenylethyl alcohol is 200-456-2.

19 Specific References

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20 General References

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21 Author

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22 Date of Revision

1 May 2002.