

Please rewrite in English:

The Efficacy and Safety of Phenoxyethanol and Ethylhexylglycerin in Skin Care Products

Phenoxyethanol

Phenoxyethanol is an aromatic ether alcohol [glycol ether] also known as 2-phenoxyethanol, phenoxetol, or ethylene glycol monophenyl ether. [1-2] Phenoxyethanol is an oily, slightly viscous liquid, colorless, to off-white in appearance. It has a faint aromatic or rose-like odor. It is practically insoluble in mineral oil, slightly soluble in water, and soluble in alcohol and ether, and in alkaline solutions. [2-4] It is also stable in acid solutions. [4]

Introduced in the 1950s, it has had a long history of safe use as a cosmetic preservative. [5] In [cosmetics and personal care products](#), phenoxyethanol is used in the formulation of skin care products and can also be found in eye makeup, fragrances, blushers, foundations and makeup bases, lipstick, cuticle softeners, bath soaps and detergents, baby products, suntan and sunscreen products, and face, body and foot powders. Cosmetic grades are of high purity and do not impart free phenol, odor or color to the final formulation. [6] Although the phenoxyethanol used in personal care is typically synthetic, it does occur naturally in green tea. The natural form has been employed to preserve "natural" personal care products. In addition to its function as a preservative, phenoxyethanol is used as a solvent for low water-soluble cosmetic ingredients such as fragrances and other preservative actives. [7] It is also listed as an ingredient for many United States vaccines by the Center for Disease Control. In Japan and the EU, its usage level in cosmetic products is restricted to concentrations of up to 1%. [8-9] In recent years, the use of phenoxyethanol has expanded due to its low sensitization potential and global approval. [5]

Phenoxyethanol is compatible with most cosmetic raw materials used in rinse-off and leave-on products. Its thermal stability [up to 85°C] facilitates viability through numerous manufacturing processes and use in a broad range of products types. It has functional activity and efficacy at a pH range of 3 to 10, and is typically well-dispersed throughout a formulation, although changes in viscosity have been observed in some formulations, depending on the thickening mechanism and use level. [10]

Phenoxyethanol acts as a bactericide, by inhibiting synthesis of nucleic acids in bacteria, as well as acting on bacterial cell walls by causing them to become more permeable to potassium ions.

[11] Phenoxyethanol has a broad range of antimicrobial activity, but the greatest activity is against gram-negative organisms. It is particularly effective against *Pseudomonas aeruginosa* [minimum inhibitory concentration MIC, 0.32%]. At higher concentrations, it is effective against gram-positive organisms [MIC, *Staphylococcus aureus*, 0.85%] and yeasts [MIC, *Candida albicans*, 0.54%]. [12-13] Phenoxyethanol is also effective as a broad-spectrum preservative

when used in combination with other preservatives such as neomycin and streptomycin

[antibiotics], isothiazolinones, organic acids and parahydroxybenzoic acids [in order to protect against fungi], hexachlorophane, tribromosalicylanilide or aminacrine hydrochloride, and with the parabens. [14-15,10].

The safety profile of 2-phenoxyethanol has been extensively investigated in pre-clinical studies assessing the endpoints of acute and repeated dose toxicity, genotoxicity, reproductive toxicity, developmental toxicity, dermal irritation and sensitization, skin penetration and toxicokinetics. Clinical studies have evaluated its potential for irritation, sensitization and phototoxicity. In 1990, phenoxyethanol was reviewed by the Cosmetic Ingredient Review [CIR] Expert Panel in the United States. Undiluted phenoxyethanol was a strong eye irritant, but was nonirritating when tested at 2.2%. Phenoxyethanol at 2.0% was a slight irritant to rabbit skin, but was neither an irritant nor sensitizer to guinea pig skin. In dermal treatment studies, phenoxyethanol was neither teratogenic, embryotoxic, or fetotoxic at doses which were maternally toxic. Phenoxyethanol was nonmutagenic in the Ames test, with and without metabolic activation, and in the mouse micronucleus test. In clinical studies phenoxyethanol was shown to be neither a primary nor a cumulative skin irritant and demonstrated to not be a sensitizer and or phototoxic. Phenoxyethanol was therefore concluded to be safe as a cosmetic ingredient in the present practices of use and concentration, generally < 1%. [16]

There are some researches that show a possible risk of phenoxyethanol usage, but this researches do not have strong evidence. German research in 1999., concluded that phenoxyethanol has neurotoxic potential, but in a concentration-dependent manner. The EPA [Environmental Protection Agency] data sheets show chromosomal changes and genetic mutation effects in testing as well as testicular atrophy and interference with reproductivity in mice for other glycol ethers, although phenoxyethanol is not mentioned in the abstract. [23-24]

Although, The Food and Drug Administration has warned that the chemical is toxic to infants via ingestion, and can depress the central nervous system and may cause vomiting and diarrhea. Combined with chlorphenesin, these two chemicals can cause respiratory depression in infants. Chlorphenesin relaxes skeletal muscle and can depress the central nervous system and cause slow or shallow breathing in infants. Since these chemicals are often present in cosmetics, caution should be exercised. [25]

In 2007, the CIR Expert Panel reviewed studies that had become available since its initial review, along with updated information on use. The panel reconfirmed that phenoxyethanol is safe in the present practices of use and concentration [$< 1\%$], and did not reopen the safety assessment. Among the new data presented were clinical patch-test results from a study conducted by the North American Contact Dermatitis Group on patients with skin disorders showing a very low frequency, 0.2%, of positive allergic responses to phenoxyethanol at 1%. [17-18]

Phenoxyethanol is also approved by the European Commission for use in cosmetics at concentrations up to 1%. [19] A review of phenoxyethanol was conducted in 2011. by the Agence Nationale de Sécurité du Médicament et des Produits de Santé in France. [20] This report concluded that phenoxyethanol should be limited to 0.4% in products intended for children under three and prohibited in products intended for the diaper area. However, the risk assessment was not conducted according to the Notes of Guidance issued by the European Union's Scientific Committee on Consumer Safety [SCCS]. [21] In October 2013, the European Commission issued a public call for relevant scientific information on phenoxyethanol safety, and a mandate for SCCS review is expected in the near future. A comprehensive dossier was submitted to the SCCS in December 2013. to support the use of phenoxyethanol in all categories of personal care products, including products for children under three, at levels up to 1%. [22]

Phenoxyethanol is safe and effective at the designated levels in personal care products and cosmetics. It has a long history of effective preservation of these products, and its safety has been extensively documented on human health.