

Preservative Comparison Chart

Preservative	Concentrations Generally Used ^{1,2}	Solubility Profile	pH efficacy range	Thermal Stability	Spectrum of Activity	Special Considerations
Alcohol	Topical: ≥10%	Miscible with water	Specific pH ranges for efficacy are not available, but wide pH compatibility, though ethanol solutions may react with oxidizing materials at very acidic pH	Aqueous alcohol mixtures may be sterilized via autoclave	Effective against viruses as well as gram positive and gram-negative bacteria ³ Not effective against bacterial spores	Alcohol is primarily used as a solvent or as a disinfectant at concentrations between 60-90% Not commonly used as a sole antimicrobial preservative, but concentrations greater than or equal to 10% may confer preservative properties The preservative activity of ethanol is inactivated in the presence of non-ionic surfactants ²
Benzalkonium chloride	Otic: 0.01-0.02% Ophthalmic: 0.01-0.02% Inhalation: 0.01-0.02% Nasal 0.01-0.1% Topical: 0.01-0.2%	Soluble in ethanol, propanol, and water ²	Inhibitory activity increases with pH, active range is 4-10 ²	Solutions may be autoclaved without loss of efficacy ²	Wide range of activity, particularly efficacious against gram-positive bacteria Poor activity against spores and molds, but does have some activity against viruses ²	Used as an antimicrobial preservative, cationic surfactant, and solubilizing agent Frequently used in ophthalmic preparations at 0.01-0.02% in combination with 0.1% EDTA to enhance activity against pseudomonas ² May be incompatible with high concentrations of nonionic surfactants and can be adsorbed by some filtering membranes (hydrophobic or anionic filters) ²
Benzethonium chloride	Otic: 0.01-0.02% Intramuscular: 0.01% Intravenous: 0.01% Ophthalmic: 0.01-0.02%	Soluble in acetone, ethanol, and water ²	Inhibitory activity between pH 4-10, preservative efficacy is enhanced with ethanol, but decreased by anionic surfactants ²	Solutions may be stabilized by autoclaving without loss of efficacy ²	Activity against e-coli and gram positives such as staphylococcus and streptococcus, some activity against fungi such as candida or aspergillus ²	Toxic for oral use, doses of 50-500mg/kg could be lethal in humans ² Oral use can cause vomiting, collapse, convulsions, or coma ² One of the few preservatives with good activity at elevated pH
Benzoic acid	Intramuscular: 0.2 Intravenous: 0.2% Irrigation: 0.02% Oral: 0.1%	Soluble in ethanol and fixed oils, some solubility in water ²	Antimicrobial activity is predicated on undissociated acid, so activity with pH <4.5, but above pH 5 little to no activity ²	Solutions may be stabilized by autoclaving without loss of efficacy ²	Active against gram-positive activity, not as active against gram-negative bacteria. Moderate mold and yeast	Mostly considered to be tasteless and odorless ² WHO sets acceptable daily intake of benzoates for humans at up to 20mg/kg ¹⁸

	Rectal: 0.1% Topical: 0.1-0.25%				activity, not active against spores. ²	Repeated doses or single large doses in cats can result in hyperaesthesia, behavior changes, and possibly death. Similar reports have not been documented in dogs. It is commonly in oral liquids in too small a concentration to be harmful, between 0.01 and 0.15%. One study found that doses of benzoic acid greater than 0.2g/kg daily or single doses exceeding 0.45g/kg resulted in hyperaesthesia, apprehension, and depression 48 to 72 hours post uptake eventually resulting in death in some cats. Some sources urge caution when working with cats and especially those with decreased liver function. ^{4,5,6} A related preservative, benzyl alcohol, has been associated with neonatal deaths upon infusion or when used as a line flush. Do not use in neonates <8 weeks of age ⁷
Benzyl alcohol	Otic: 0.9% Epidural: 1% Intra-articular: 1% Intravenous: 0.9-2% Nasal: 0.5-0.9% Topical 1-3%	Miscible in ethanol and fixed and volatile oils. Poorly miscible with pure water ²	Primary activity at pH <5, and little to no activity at pH > 8 ²	May be sterilized by autoclaving, though, this process may generate benzaldehyde, a decomposition product ²	Primary activity against gram-positive bacteria, molds, fungi, and yeast, poor activity against spore unless heated ²	*See above note about benzoic acid in neonates, the same applies to benzyl alcohol ⁷ *see above note about benzoic acid in cats, the same applies to benzyl alcohol ^{4,5,6} Antimicrobial activity is decreased in the presence of nonionic surfactants such as polysorbate 80 ² Store preparations containing benzyl alcohol in a glass or metal container or PP plastic containers. Adsorption may occur with polyethylene plastics ²
Boric acid	Otic: 0.05-0.6% Intravenous: 0.3-0.5% Ophthalmic: 0.1-1% Topical: 0.3-2% Vaginal: 1%	Soluble in ethanol, glycerin, and water (esp. in presence of citric acid), and in fixed and volatile oils ²	5% aqueous solution adjusts pH to ~3.5-4.1, efficacy related to its acidity ²	Boric acid can break down to metaboric acid or other metabolites at high temperatures ²	Not commonly used as a solo agent as it has weak bacteriostatic and anti-fungal properties ²	Can form a complex with glycerin, that is a stronger acid than boric acid is originally ² Boric acid is poorly absorbed topically, but can be toxic orally and death has been reported at doses as low as 5-20g in adults ²

Butylated hydroxyanisole	Nasal: 0.1-1%	Insoluble in water, soluble in ethanol, propylene glycol, and many oils ²	Often used in anhydrous compounds where pH is not a concern, though stability has been demonstrated between pH 2-9 ¹⁰	Breakdown can occur at temperatures of 150°C and higher, BHA has demonstrated stability in food oils during frying ^{8,9}	Good activity against mold and gram-positive bacteria, some activity against gram-negative bacteria ²	Acts as an antioxidant as well as an antimicrobial² Often used in foods to delay rancidity in oils or fats and to prevent loss of activity in oil miscible vitamins² Generally non-irritating and well tolerated² Exposure to light can result in reduced activity²
	Oral: 0.01%					
	Topical: 0.01-0.02%					
	Intramuscular: 0.03%					
Butylparaben	Vaginal: 0.02-0.03%					
	Ophthalmic: 0.01-0.02%	Soluble in acetone, ethanol and good solubility in propylene glycol. Poor solubility in water and glycerin ²	Antimicrobial activity between pH 4-8, but preservative efficacy decreases with increasing pH ²	Solutions with pH between 3-6 can be sterilized by autoclaving without decomposition. At pH 8 hydrolysis can occur under heat ²	Active against yeasts and molds, better activity against gram-positive bacteria than gram-negative ²	A long chain paraben More active than methylparaben² Reduced activity in the presence of non-ionic surfactants (such as polysorbate 80)²
	Oral: 0.005-0.1%					
	Rectal: 0.01%					
	Topical: 0.02-0.15%					
Chlorhexidine (available as gluconate, acetate, or HCl salt forms)	Ophthalmic: 0.01%	Soluble in ethanol, some solubility in water, propylene glycol, glycerin, and PEGs ²	Optimum antimicrobial activity between pH 5-7, precipitation may occur if pH increases above 8 ²	Solutions can degrade when heated, at pH 5.6 (the pH for optimal stability) it may be reasonable to autoclave, at other pH's degradation products may form ²	Active against gram-positive and gram-negative microorganisms. Some activity against viruses and fungi, though activity against fungi is less significant than antibacterial activity ²	Incompatible with soaps and most surfactants Acacia, sodium alginate, sodium carboxymethylcellulose, starch, and tragacanth are incompatible with chlorhexidine When used in dental preparations, staining of the teeth may occur²
Chlorobutanol		Soluble in acetone, ethanol, glycerin, and volatile oils. Slightly soluble in water (increased solubility with increased temp) ²	Antimicrobial activity is decreased above pH 5.5 (pH 3-5 ideal) ²	Significant potency lost during autoclaving, this effect increases the higher the pH ²	Active against gram-positive, gram-negative bacteria and some fungi ²	Incompatible with plastic vials, also antimicrobial activity can be reduced in the presence of polysorbate 80 and carboxymethylcellulose² Increased efficacy in combination with phenyl ethanol 0.5%
	Intramuscular: 0.5%					
	Intravenous: 0.5%					
	Nasal: 0.5%					
	Ophthalmic: 0.5-1%					
	Inhalation: 0.5%					
	Topical: 0.3-0.5%					

m-Cresol (Methylphenol)	Intramuscular: 0.15-0.3% Intradermal: 0.15-0.3% Subcutaneous: 0.15-0.3% Topical: 0.1%	Soluble in alcohol, some solubility in water ²	Antimicrobial activity is greatest at acidic pH, but activity is present at <pH 9 ²	Some studies have noted that no appreciable loss occurs during autoclaving ¹⁹	Moderate activity against gram-positive bacteria, less active against gram negatives. No activity against bacterial spores ²	Similar to phenol, but has slightly more antimicrobial activity Antimicrobial activity is reduced in the presence of nonionic surfactants ²
Ethylparaben	Oral: 0.01-0.05% Topical: 0.01-0.05%	Freely soluble in acetone, good solubility in ethanol and propylene glycol, poor solubility in glycerin and water ²	Antimicrobial activity primarily between 4-8, decreases with increasing pH ²	Solutions with pH of 3-6 can be sterilized by autoclaving without decomposition ²	Most active against yeasts and molds, better activity against gram-positive than gram-negative bacteria ²	Historically of the most frequently used preservatives in cosmetics ² Parabens are often used in combinations due to synergistic effects ² Preservative efficacy decreased in the presence of nonionic surfactant ² WHO set the approximate max daily dose of ethyl-, methyl-, and propylparabens at 10mg/kg ²
Methylparaben	Otic: 0.01% Ophthalmic: 0.01-0.05% Epidural: 0.1% Intra-articular: 0.2% Intramuscular: 0.1-0.25% Intravenous: 0.1-0.25% Iontophoresis: 0.1% Irrigation: 0.033-0.1% Oral: 0.015-0.2% Topical: 0.1-0.3%	Soluble in ethanol and propylene glycol, poor solubility in water and glycerin, practically insoluble in mineral oil ²	Antimicrobial activity primarily between 4-8, decreases with increasing pH ²	Solutions with pH of 3-6 can be sterilized by autoclaving without decomposition ²	Most active against yeasts and molds, better activity against gram-positive than gram-negative bacteria ²	Preservation is improved by the presence of propylene glycol (2-5%) or by synergistic activity with other parabens ² Antimicrobial activity is reduced in the presence of nonionic surfactants such as polysorbate 80 ² Propylene glycol ~10% can potentiate the antimicrobial activity of parabens and can prevent the interaction between polysorbate and methylparaben ² Used less often in ophthalmic and injected preparations due to potential for irritation ² WHO set the approximate max daily dose of ethyl-, methyl-, and propylparabens at 10mg/kg ²

Phenol	Intramuscular: 0.5% Intravenous: 0.45-0.5% Subcutaneous: 0.55% Ophthalmic: 0.01%	Soluble in ethanol, fixed oils, and glycerin, some solubility in water ²	Most active in acidic solution, increased temperature increases efficacy ²	Oily solutions of phenol may be sterilized in hermetically sealed containers via dry heat ²	Activity against a variety of organisms including many gram-positive, gram-negative bacteria in addition to fungi, viruses, mycobacteria and a little activity against spores ²	Activity reduced in the presence of nonionic surfactants ¹⁷ Primarily used in parenteral pharmaceutical products, occasionally used topically ² Also used as a disinfectant at 5% and a local anesthetic at 0.5-1% ²
Phenoxyethanol	Topical: 0.5-1%	Soluble in acetone, ethanol, propylene glycol, and glycerin, some solubility in water or olive oil ²	Activity across a wide pH range ² (3-10)	Aqueous solutions may be sterilized by autoclaving ²	Rather narrow spectrum of activity, so it is often combined with other preservatives such as parabens ² Activity against pseudomonas aeruginosa and some other gram-negative bacteria ²	Activity may be reduced in the presence of nonionic surfactants or cellulose based derivatives ²
Potassium Sorbate	Ophthalmic: 0.1-0.2% Oral: 0.1% - 0.2% Topical: 0.2%	Soluble in water and propylene glycol, poorly soluble in ethanol, insoluble in oil ²	Antibacterial activity is at acidic pH, practically no preservative activity above pH 6 ²	Aqueous solutions may be sterilized by autoclaving ²	Primary use as an antifungal preservative, though does have some antibacterial properties ²	Fairly non-toxic, WHO sets acceptable daily intake at 25mg/kg ² Unlike some other preservatives, it is compatible with nonionic surfactants Potassium sorbate has less antimicrobial efficacy than sorbic acid, but is more water soluble ² Synergistic effects can occur with other preservatives or propylene glycol ²
Propylene Glycol	Ophthalmic: 15% Oral: 20-50% Topical: 1.5-30% Otic: 10% Intramuscular: 30-40%	Miscible with acetone, ethanol, glycerin, and water ²	Specific pH ranges for efficacy are not available	Propylene glycol is subject to oxidation when exposed to oxygen at high temperatures, though aqueous solutions may be	Efficacy against gram-negative bacteria such as e-coli has been demonstrated, but concentrations of 25% or even 50% have been needed	Widely used as solvent and preservative in parenteral and nonsterile preparations ² Has a sweet, slightly acrid taste with similarities to glycerin in flavor ² Propylene glycol can have some intoxicant effects, approximately 1/3 as intoxicating as ethanol ²

	Intravenous: 5-50% Nasal: 12% Inhalation: 10-25% Vaginal: 3-20%			sterilized by autoclaving ²	to achieve this effect ¹²	WHO sets maximum propylene glycol daily intake at 25mg/kg ²
Propylparaben	Intramuscular: 0.2% Intra-articular: 0.03% Intravenous: 0.02-0.2% Ophthalmic 0.01-0.02% Oral: 0.02- 0.14% (can have a slight numbing effect at high enough concentrations) Inhalation: 0.01% Topical: 0.03-0.1%	Freely soluble in acetone, soluble in ethanol and propylene glycol, some solubility in glycerin and water (especially at elevated temperature) ²	Antimicrobial activity primarily between 4-8, decreases with increasing pH ²	Solutions with pH of 3-6 can be sterilized by autoclaving without decomposition ²	Most active against yeasts and molds, better activity against gram-positive than gram-negative bacteria ²	Note that California plans to ban this paraben from food products for human consumption starting January 2027 ¹¹ Activity is improved by using combinations of parabens, additive effects occur ² Antimicrobial efficacy is decreased in the presence of nonionic surfactants ² WHO set the approximate max daily dose of ethyl-, methyl-, and propylparabens at 10mg/kg ²
Sodium acetate	Otic: 0.02-0.5% Ophthalmic: 0.05-0.5% Oral: 0.01 – 0.4%	Soluble in water, slightly soluble in alcohol ¹²	Best around slightly acidic to neutral pH, though explicit data not available	Information not available on stability under heat greater than 60C ¹⁴	Effective against bacteria including pseudomonas and mainly gram-negative species ¹⁵	Can also function as a buffering agent when combined with acetic acid. Also reduces bitterness of some oral drugs ² Enhances antimicrobial properties of a formulation and is often used in food industry ²
Sodium benzoate	Intramuscular: 0.1-0.5% Intravenous: 0.1-0.5% Oral: 0.02-0.5% Rectal: 0.1-1%	Soluble in water, some solubility in ethanol ²	Antimicrobial activity due to undissociated benzoic acid, so best activity seen between pH 2-5 ²	Aqueous solutions may be sterilized by autoclaving ²	Effective against a wide range of bacteria and some fungi ¹³	**See warnings under benzoic acid section, the same applies here as benzoic acid is a component**

	Topical: 0.1-0.2%					
Sodium borate	Otic: 0.3% Ophthalmic: 0.1-1% Topical: 0.5%	Slightly soluble in glycerin and water, practically insoluble in ethanol ²	Does have some antimicrobial/bacteriostatic activity, but generally considered pretty weak ²	Heat stable, product has intentionally been heated up to 880C to make borax beads ²	Some broad spectrum bacteriostatic activity ²	Functions as an alkalizing agent, buffering agent, and emulsifying agent in addition to having antimicrobial activity ² Boric acid is easily absorbed via mucus membranes and non-intact skin, toxicities have resulted in children and babies as a result ²
Sodium metabisulfite	Epidural: 0.05% Intramuscular: 0.6% Intravenous: 0.03-0.6% Iontophoresis: 0.05% Ophthalmic: 0.1-0.2% Oral: 0.01-0.2% Inhalation: 0.3% Topical: 0.2-0.3%	Soluble in glycerin and water, slightly soluble in ethanol ²	Best activity at acidic pH (for more basic preparations, sodium sulfite is usually preferred) ²	Subject to degradation if autoclaved in the presence of oxygen, it is recommended that if a solution containing sodium metabisulfite is to be autoclaved, it be stored under nitrogen ²	Some activity against fungi and aerobic bacteria, primarily an antioxidant rather than a preservative	Used as a preservative and an antioxidant in foods and wines ² Higher concentrations can confer what is described as an "acidic, saline taste" ² Dextrose in aqueous solution can reduce stability of the metabisulfite ²
Sodium propionate	Oral: 0.1-0.2%	Soluble in water and some solubility in ethanol ²	Best activity at acidic pH, pH <5 is best (antimicrobial effect is mainly derived from free acid form) ²	Information on thermal stability not available	Primary activity is antifungal (good activity against mold, poor to no activity against yeast), but some activity against gram-positive cocci ²	Fairly harmless, in humans 6g per day have been administered without evident harm ²
Sorbic acid	Ophthalmic: 0.1-0.2% Oral: 0.1-0.2% Topical: 0.1-0.2%	Fairly soluble in ethanol, and propylene glycol. Poor solubility in water at room temp ²	Optimum activity at ~pH 4.5, no activity above pH 6.	Information on thermal stability in aqueous solutions not available, degradation could occur if autoclaving ²	Primary activity is antifungal, so often combined with another agent when used for antibacterial purposes ²	The solubility of sorbic acid decreases with increasing sugar content ² Sensitive to oxidation in the presence of light, especially in aqueous solution form ² Sorbic acid powder is combustible when exposed to heat ²

Thimerosal	Intramuscular: 0.01%	Soluble in water, some solubility in ethanol ²	Bactericidal at low pH, and bacterio- and fungistatic at neutral or high pH	Aqueous solutions may be sterilized by autoclaving ²	Antibacterial and antifungal across a broad range of pH with fairly low MICs, not effective against spore forming organisms ²	Thimerosal contains 39% mercury by weight ² Sensitive to photodegradation ² EDTA sometimes used to stabilize solutions, but may have an effect on antimicrobial efficacy ² Hypersensitivity can occur with vaccines preserved with thimerosal, and given the controversy around mercury containing compounds use is generally not recommended ²
	Intravenous: 0.01%					
	Ophthalmic: 0.001-0.15%					
	Topical: 0.01%					

Sources:

1. United States Food and Drug Administration. Inactive Ingredient Search for Approved Drug Products. <https://www.accessdata.fda.gov/scripts/cder/iig/index.cfm> Updated July 5th 2019. Updated July 24th 2019, Accessed August 19th, 2019.
2. Rowe R, Sheskey P, Cook W, Fenton M. Handbook of Pharmaceutical Excipients. Philadelphia, PA: Pharmaceutical Press.
3. Kampf G, Hollingsworth A. Comprehensive bactericidal activity of an ethanol-based hand gel in 15 seconds. Ann Clin Microbiol Antimicrob. 2008;7:2. Published 2008 Jan 22. doi:10.1186/1476-0711-7-2
4. Rowe R, Sheskey P, Quinn M. Handbook of Pharmaceutical Excipients. 6th ed. Pharmaceutical Press. Italy. 2009
5. Bedford P, Clarke E. Experimental benzoic acid poisoning in the cat. Veterinary Record. 1972; 90(3): 55-58
6. Davidson G. To benzoate or not to benzoate: cats are the question. International Journal of Pharmaceutical Compounding. 2001; 5(2): 89-90
7. Centers for Disease Control. Neonatal Deaths Associated With Use of Benzyl Alcohol – United States. MMWR/ 1982; 31(22);290-1. <https://www.cdc.gov/mmwr/preview/mmwrhtml/00001109.htm>. Accessed 8/19/2019
8. Butylated Hydroxyanisole. Report on Carcinogens. 14th ed. National Toxicology Program, Department of Health and Human Services. Pg 1-2. Accessed 8/23/2019
9. Cruz J, Conde E, Dominguea H, Parajo J. Thermal stability of antioxidants obtained from wood and industrial wastes. Food Chemistry. 2007; 100(3): 1059-1064.
10. Racine P. Influence of pH and light on the stability of some antioxidants. Int J Cosmet Sci. 1981; 3(3):125-37.
11. The California Food Safety Act, Cal. Assembly Bill No § 418 Chapter 328 et seq.
12. Nalawade T, Bhat K, Sogi S. Bactericidal activity of propylene glycol, glycerine, polyethylene glycol 400, and polyethylene glycol 1000 against selected microorganisms. J Int Soc Prev Community Dent. 2015; 5(2):114-119.
13. Lide D. (1993) *CRC Handbook of Chemistry and Physics*. 73rd ed. Boca Raton, GL. CRC Press Inc.
14. Sallam K. Antimicrobial and antioxidant effects of sodium acetate, sodium lactate, and sodium citrate in refrigerated sliced salmon. Food Control. 2007; 18(5): 566-575.
15. Stanojevic D, Comic L, Stefanovic O, Solujic-Sukdolac S. Antimicrobial effects of sodium benzoate, sodium nitrite, and potassium sorbate, and their synergistic action in vitro. Bulgarian Journal of Agricultural Science. 2009; 15(4): 307-311.
16. Allen L. Excipients Used in Nonsterile Compounding, Part 3: Preservatives. International Journal of Pharmaceutical Compounding. 2019; 23(6). 472-477.
17. Stroppel L, Schultz-Fademrecht T, Cebulla M, Blech M, Marhöfer RJ, Selzer PM, Garidel P. Antimicrobial Preservatives for Protein and Peptide Formulations: An Overview. *Pharmaceutics*. 2023; 15(2):563. <https://doi.org/10.3390/pharmaceutics15020563>
18. Joint FA/WHO Expert Committee on Food Additives. 92nd meeting (Safety evaluation of certain food additives) Virtual meeting, 7-18 June 2021. World Health Organization. [jeffa92-7to18june2021-summary-and-conclusions.pdf \(who.int\)](https://www.who.int/publications-detail/92nd-joint-fa-who-expert-committee-on-food-additives-virtual-meeting).

19. Suflita, K. Anaerobic degradation of m-cresol in anoxic aquifer slurries: carboxylation reactions in a sulfate-reducing bacterial enrichment. Microbiology. 1991.
DOI: <https://doi.org/10.1128/aem.57.6.1689-1695.1991>