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# Handbook of Pharmaceutical Excipients

Sixth edition

Edited by  
Raymond C Rowe, Paul J Sheskey and Marian E Quinn

**(DD)**



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# Handbook of Pharmaceutical Excipients

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SIXTH EDITION

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## 21 Authors

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## 22 Date of Revision

3 February 2009.

# Methylparaben

## 1 Nonproprietary Names

BP: Methyl Hydroxybenzoate  
 JP: Methyl Parahydroxybenzoate  
 PhEur: Methyl Parahydroxybenzoate  
 USP-NF: Methylparaben

## 2 Synonyms

*Aseptoform M*; *CoSept M*; E218; 4-hydroxybenzoic acid methyl ester; metagin; *Methyl Chemosept*; methylis parahydroxybenzoas; methyl *p*-hydroxybenzoate; *Methyl Parasept*; *Nipagin M*; *Solbrol M*; *Tegosept M*; *Uniphen P-23*.

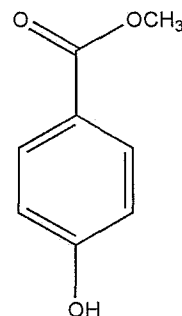
## 3 Chemical Name and CAS Registry Number

Methyl-4-hydroxybenzoate [99-76-3]

## 4 Empirical Formula and Molecular Weight

C<sub>9</sub>H<sub>8</sub>O<sub>3</sub> 152.15

## 5 Structural Formula



## 6 Functional Category

Antimicrobial preservative.

## 7 Applications in Pharmaceutical Formulation or Technology

Methylparaben is widely used as an antimicrobial preservative in cosmetics, food products, and pharmaceutical formulations; see Table I for methylparaben uses in combination with other

parabens or with other antimicrobial agents. In cosmetics, methylparaben is the most frequently used antimicrobial preservative.<sup>(1)</sup>

The parabens are effective over a wide pH range and have a broad spectrum of antimicrobial activity, although they are most effective against yeasts and molds. Antimicrobial activity increases as the chain length of the alkyl moiety is increased, but aqueous solubility decreases; therefore a mixture of parabens is frequently used to provide effective preservation. Preservative efficacy is also improved by the addition of propylene glycol (2–5%), or by using parabens in combination with other antimicrobial agents such as imidurea; see Section 10.

Owing to the poor solubility of the parabens, paraben salts (particularly the sodium salt) are more frequently used in formulations. However, this raises the pH of poorly buffered formulations.

Methylparaben (0.18%) together with propylparaben (0.02%) has been used for the preservation of various parenteral pharmaceutical formulations; see Section 14.

**Table I:** Uses of methylparaben.

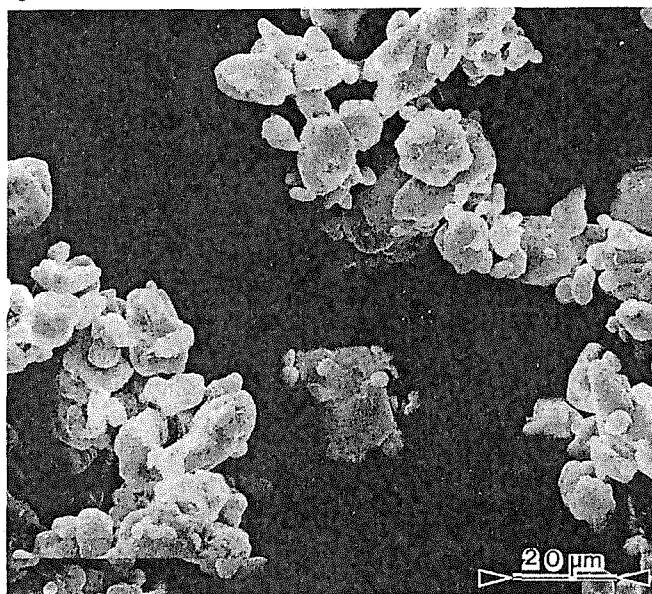
Use	Concentration (%)
IM, IV, SC injections <sup>(a)</sup>	0.065–0.25
Inhalation solutions	0.025–0.07
Intradermal injections	0.10
Nasal solutions	0.033
Ophthalmic preparations <sup>(a)</sup>	0.015–0.2
Oral solutions and suspensions	0.015–0.2
Rectal preparations	0.1–0.18
Topical preparations	0.02–0.3
Vaginal preparations	0.1–0.18

(a) See Section 14.

## 8 Description

Methylparaben occurs as colorless crystals or a white crystalline powder. It is odorless or almost odorless and has a slight burning taste.

**SEM 1:** Excipient: methylparaben; supplier: Bate Chemical Co. Ltd; magnification: 600×.



## 9 Pharmacopeial Specifications

See Table II. See also Section 18.

**Table II:** Pharmacopeial specifications for methylparaben.

Test	JP XV	PhEur 6.0	USP32-NF27
Identification	+	+	+
Characters	—	+	—
Appearance of solution	+	+	+
Acidity	+	+	+
Heavy metals	≤20 ppm	—	—
Impurities	—	+	—
Melting range	—	—	125–128°C
Related substances	+	+	+
Sulfated ash	—	≤0.1%	—
Residue on ignition	≤0.1%	—	≤0.1%
Assay (dried basis)	98.0–102.0%	98.0–102.0%	98.0–102.0%

## 10 Typical Properties

**Antimicrobial activity** see Table III. Methylparaben exhibits antimicrobial activity of pH 4–8. Preservative efficacy decreases with increasing pH owing to the formation of the phenolate anion. Parabens are more active against yeasts and molds than against bacteria. They are also more active against Gram-positive bacteria than against Gram-negative bacteria.

Methylparaben is the least active of the parabens; antimicrobial activity increases with increasing chain length of the alkyl moiety. Activity may be improved by using combinations of parabens as synergistic effects occur. Therefore, combinations of methyl-, ethyl-, propyl-, and butylparaben are often used together. Activity has also been reported to be enhanced by the addition of other excipients such as: propylene glycol (2–5%);<sup>(2)</sup> phenylethyl alcohol;<sup>(3)</sup> and edetic acid.<sup>(4)</sup> Activity may also be enhanced owing to synergistic effects by using combinations of parabens with other antimicrobial preservatives such as imidurea.<sup>(5)</sup>

The hydrolysis product *p*-hydroxybenzoic acid has practically no antimicrobial activity.

See also Section 12.

**Table III:** Minimum inhibitory concentrations (MICs) of methylparaben in aqueous solution.<sup>(4)</sup>

Microorganism	MIC (μg/mL)
<i>Aerobacter aerogenes</i> ATCC 8308	2000
<i>Aspergillus oryzae</i>	600
<i>Aspergillus niger</i> ATCC 9642	1000
<i>Aspergillus niger</i> ATCC 10254	1000
<i>Bacillus cereus</i> var. <i>mycooides</i> ATCC 6462	2000
<i>Bacillus subtilis</i> ATCC 6633	2000
<i>Candida albicans</i> ATCC 10231	2000
<i>Enterobacter cloacae</i> ATCC 23355	1000
<i>Escherichia coli</i> ATCC 8739	1000
<i>Escherichia coli</i> ATCC 9637	1000
<i>Klebsiella pneumoniae</i> ATCC 8308	1000
<i>Penicillium chrysogenum</i> ATCC 9480	500
<i>Penicillium digitatum</i> ATCC 10030	500
<i>Proteus vulgaris</i> ATCC 8427	2000
<i>Proteus vulgaris</i> ATCC 13315	1000
<i>Pseudomonas aeruginosa</i> ATCC 9027	4000
<i>Pseudomonas aeruginosa</i> ATCC 15442	4000
<i>Pseudomonas stutzeri</i>	2000
<i>Rhizopus nigricans</i> ATCC 6227A	500
<i>Saccharomyces cerevisiae</i> ATCC 9763	1000
<i>Salmonella typhosa</i> ATCC 6539	1000
<i>Sarcina lutea</i>	4000
<i>Serratia marcescens</i> ATCC 8100	1000
<i>Staphylococcus aureus</i> ATCC 6538P	2000
<i>Staphylococcus epidermidis</i> ATCC 12228	2000
<i>Trichoderma lignorum</i> ATCC 8678	250
<i>Trichoderma mentagrophytes</i>	250

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