



Edition: BP 2025 (Ph. Eur. 11.6 update)

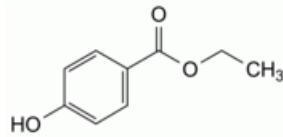
## Ethyl Hydroxybenzoate<sup>1</sup>



### General Notices

Ethylparaben

(*Ethyl Parahydroxybenzoate, Ph. Eur. monograph 0900*)



C<sub>9</sub>H<sub>10</sub>O<sub>3</sub> 166.2 120-47-8

Ph Eur

### DEFINITION

Ethyl 4-hydroxybenzoate.

### Content

98.0 per cent to 102.0 per cent.

### ◆ CHARACTERS

#### Appearance

White or almost white, crystalline powder or colourless crystals.

#### Solubility

Very slightly soluble in water, freely soluble in ethanol (96 per cent) and in methanol.◆

### IDENTIFICATION

*First identification: A, B.*

◆ *Second identification: A, C. ◆*

- A. Melting point ([2.2.14](#)): 115 °C to 118 °C.
- B. Infrared absorption spectrophotometry ([2.2.24](#)).

*Comparison ethyl parahydroxybenzoate CRS.*

*Test solution (a)* Dissolve 0.10 g of the substance to be examined in *acetone R* and dilute to 10 mL with the same solvent.

*Test solution (b)* Dilute 1 mL of test solution (a) to 10 mL with *acetone R*.

*Reference solution (a)* Dissolve 10 mg of *ethyl parahydroxybenzoate CRS* in *acetone R* and dilute to 10 mL with the same solvent.

*Reference solution (b)* Dissolve 10 mg of *methyl parahydroxybenzoate R* in 1 mL of test solution (a) and dilute to 10 mL with *acetone R*.

*Plate* *TLC octadecylsilyl silica gel F<sub>254</sub> plate R*.

*Mobile phase* *glacial acetic acid R, water R, methanol R* (1:30:70 V/V/V).

*Application* 2 µL of test solution (b) and reference solutions (a) and (b).

*Development* Over 2/3 of the plate.

*Drying* In air.

*Detection* Examine in ultraviolet light at 254 nm.

*System suitability* Reference solution (b):

— the chromatogram shows 2 clearly separated principal spots.

*Results* The principal spot in the chromatogram obtained with test solution (b) is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a).◊

## TESTS

### Solution S

Dissolve 1.0 g in *ethanol (96 per cent) R* and dilute to 10 mL with the same solvent.

### Appearance of solution

Solution S is clear (2.2.1) and not more intensely coloured than reference solution BY<sub>6</sub> (2.2.2, *Method II*).

### Acidity

To 2 mL of solution S add 3 mL of *ethanol (96 per cent) R*, 5 mL of *carbon dioxide-free water R* and 0.1 mL of *bromocresol green solution R*. Not more than 0.1 mL of *0.1 M sodium hydroxide* is required to change the colour of the indicator to blue.

### Related substances

Liquid chromatography (2.2.29).

*Test solution* Dissolve 50.0 mg of the substance to be examined in 2.5 mL of *methanol R* and dilute to 50.0 mL with the mobile phase. Dilute 10.0 mL of this solution to 100.0 mL with the mobile phase.

*Reference solution (a)* Dissolve 5 mg of *4-hydroxybenzoic acid R* (impurity A), 5 mg of *methyl parahydroxybenzoate R* (impurity B) and 5 mg of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

*Reference solution (b)* Dissolve 50.0 mg of *ethyl parahydroxybenzoate CRS* in 2.5 mL of *methanol R* and dilute to 50.0 mL with the mobile phase. Dilute 10.0 mL of this solution to 100.0 mL with the mobile phase.

*Reference solution (c)* Dilute 1.0 mL of the test solution to 20.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Column:

- size:  $l = 0.15$  m,  $\varnothing = 4.6$  mm;
- stationary phase: end-capped octadecylsilyl silica gel for chromatography R (5  $\mu\text{m}$ ).

Mobile phase 6.8 g/L solution of potassium dihydrogen phosphate R, methanol R (35:65 V/V).

Flow rate 1.3 mL/min.

Detection Spectrophotometer at 272 nm.

Injection 10  $\mu\text{L}$  of the test solution and reference solutions (a) and (c).

Run time 4 times the retention time of ethyl parahydroxybenzoate.

Relative retention With reference to ethyl parahydroxybenzoate (retention time = about 3.0 min): impurity A = about 0.5; impurity B = about 0.8.

System suitability Reference solution (a):

- resolution: minimum 2.0 between the peaks due to impurity B and ethyl parahydroxybenzoate.

Limits:

- correction factor: for the calculation of content, multiply the peak area of impurity A by 1.4;
- impurity A: not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.5 per cent);
- unspecified impurities: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.5 per cent);
- total: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (c) (1.0 per cent);
- disregard limit: 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1 per cent).

### **Sulfated ash (2.4.14)**

Maximum 0.1 per cent, determined on 1.0 g.

## **ASSAY**

Liquid chromatography (2.2.29) as described in the test for related substances with the following modification.

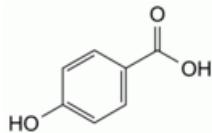
Injection Test solution and reference solution (b).

Calculate the percentage content of  $\text{C}_9\text{H}_{10}\text{O}_3$  from the declared content of ethyl parahydroxybenzoate CRS.

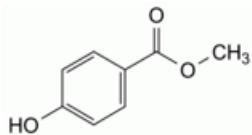
## **IMPURITIES**

Specified impurities A.

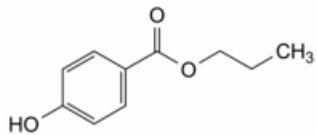
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) B, C, D.



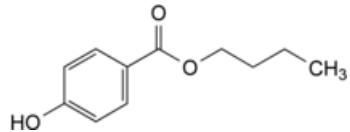
A. 4-hydroxybenzoic acid,



B. methyl 4-hydroxybenzoate (methyl parahydroxybenzoate),



C. propyl 4-hydroxybenzoate (propyl parahydroxybenzoate),



D. butyl 4-hydroxybenzoate (butyl parahydroxybenzoate).

---

Ph Eur

<sup>1</sup> This monograph has undergone pharmacopoeial harmonisation. See chapter 5.8. *Pharmacopoeial harmonisation*.