

**PHARMACOPOEIAL DISCUSSION GROUP**

**CORRECTION**

CODE: E50

NAME: BUTYL PARAHYDROXYBENZOATE

(Correction 1 to revision 1 of the sign-off document signed 9 June 2010)

**Item to be corrected:**

- Addition of CAS numbers: [94-13-3]
- Appearance of solution/color: addition of comparison with alcohol

Attribute	EP	JP	USP
Definition	+	+	+
Identification A (melting point)*	+	+	+
Identification B	+	+	+
Appearance of solution/color	+	+	+
Acidity	+	+	+
Related substances**	+	+	+
Sulphated ash	+	+	+
Assay	+	+	+

\* Melting point: listed in JP as a test and not as part of identification

\*\* Related substances: JP uses the term "relative response factor" instead of "correction factor"

**Legend**

- + will adopt and implement
- will not stipulate

**Non-harmonised attributes**

Characters, Storage

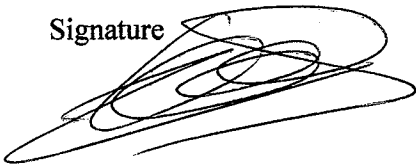
**Local requirements**

Ph. Eur.	JP	USP
Second identification (melting point, TLC)	Related substances: test for required detectability, system repeatability Heavy metals (20 ppm)	none

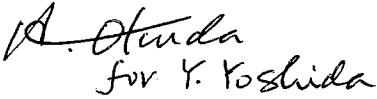
**Reagents and reference materials**

Each pharmacopoeia will adapt the text to take account of local reference materials and reagent specifications.

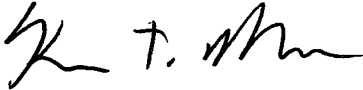
**European Pharmacopoeia**

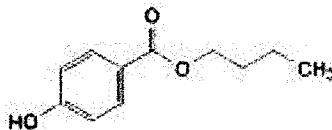
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**Japanese Pharmacopoeia**

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**United States Pharmacopoeia**

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**E50 - BUTYL PARAHYDROXYBENZOATE**C<sub>11</sub>H<sub>14</sub>O<sub>3</sub>

Mr 194.2

[94-26-8]

**DEFINITION**

Butyl 4-hydroxybenzoate.

*Content:* 98.0 per cent to 102.0 per cent.**IDENTIFICATION**A. *Melting point:* 68 °C to 71 °C.B. *Infrared absorption spectrophotometry.*

Record the infrared absorption spectrum of butyl parahydroxybenzoate and compare with the Reference Spectrum or the spectrum obtained with the Reference Standard: the transmission minima correspond in position and relative size.

**TESTS****Solution S.** Dissolve 1.0 g in *alcohol* and dilute to 10 ml with the same solvent.**Appearance of solution.** Solution S is clear and not more intensely coloured than *alcohol* or the reference solution.*Primary solutions:*

- *Ferric chloride primary solution:* a 45.0 g/l solution of ferric chloride (FeCl<sub>3</sub>, 6H<sub>2</sub>O).
- *Cobalt chloride primary solution:* a 59.5 g/l solution of cobalt chloride (CoCl<sub>2</sub>, 6H<sub>2</sub>O).
- *Copper sulphate primary solution:* a 62.4 g/l solution of copper sulphate (CuSO<sub>4</sub>, 5H<sub>2</sub>O).

*Reference solution:*

To 5.0 ml of cobalt chloride primary solution, 12.0 ml of ferric chloride primary solution and 2.0 ml of copper sulphate primary solution, add hydrochloric acid (10 g/l HCl) to make 1000.0 ml.

**Acidity.** To 2 ml of solution S add 3 ml of *alcohol*, 5 ml of *carbon dioxide-free water* and 0.1 ml of *bromocresol green solution*. 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.

**Test solution.** Dissolve 50.0 mg of the sample to be examined in 2.5 ml of *methanol* 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 each of *propyl parahydroxybenzoate R*, *4-hydroxybenzoic acid R* and the substance to be examined in mobile phase and dilute to 100.0 ml with the same solvent. Dilute 1 ml of this solution to 10.0 ml with the mobile phase.

**Reference solution (b).** Dissolve 50.0 mg of *butyl parahydroxybenzoate CRS* in 2.5 ml of *methanol* 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.

**Reference solution (d).** Dissolve 5 mg of *iso-butyl parahydroxybenzoate R* in mobile phase and dilute to 100.0 ml with the same solvent.

**Reference solution (e).** Dilute 0.5 ml of reference solution (d) to 50.0 ml with reference solution (b).

**Column:**

— *size:*  $l = 0.15$  m,  $\varnothing = 4.6$  mm;

— *stationary phase:* *octadecylsilyl silica gel for chromatography* (5  $\mu$ m);

— *temperature:* 35 °C.

**Mobile phase:** 6.8 g/l solution of *potassium dihydrogen phosphate*, *methanol* (50:50 V/V).

**Flow rate:** 1.3 ml/min.

**Detection:** 272 nm.

**Injection:** 10  $\mu$ l of the test solution and reference solutions (a), (c) and (e).

**Run time:** 1.5 times the retention time of *butyl parahydroxybenzoate*.

**Relative retention** with reference to *butyl parahydroxybenzoate* (retention time = about 22 min): *4-hydroxybenzoic acid* = about 0.1; *propyl parahydroxybenzoate* = about 0.5; *iso-butyl parahydroxybenzoate* = about 0.9.

**System suitability:**

- **resolution:** minimum of 5.0 between the peaks due to *propyl parahydroxybenzoate* and to *butyl parahydroxybenzoate* in the chromatogram obtained with reference solution (a), minimum of 1.5 between the peaks due to *iso-butyl parahydroxybenzoate* and to *butyl parahydroxybenzoate* in the chromatogram obtained with reference solution (e).

**Limits:**

- *correction factor*: for the calculation of content, multiply the peak area of 4-hydroxybenzoic acid by 1.4;
- *4-hydroxybenzoic acid*: 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).

**Sulphated ash**: maximum 0.1 per cent, determined on 1.0 g.

**ASSAY**

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

*Injection*: test solution and reference solution (b).

*System suitability*:

- *repeatability*: maximum relative standard deviation of 0.85 per cent after 6 injections of the reference solution (b).

Calculate the percentage content of  $C_{11}H_{14}O_3$  in the sample to be examined from the peak areas in the chromatograms obtained with test solution and reference solution (b) and the declared content of *butyl parahydroxybenzoate CRS*.

**REAGENTS****Bromocresol green solution.**

Dissolve 50 mg of *bromocresol green* in 0.72 ml of 0.1 M *sodium hydroxide* and 20 ml of *alcohol* and dilute to 100 ml with *water*.

*Test for sensitivity*. To 0.2 ml of the bromocresol green solution add 100 ml of *carbon dioxide-free water*. The solution is blue. Not more than 0.2 ml of 0.02 M *hydrochloric acid* is required to change the colour to yellow.

*Colour change*: pH 3.6 (yellow) to pH 5.2 (blue).

Iso-butyl parahydroxybenzoate.  $C_{11}H_{14}O_3$ . ( $M_r$  194.23). [4247-02-3].

A white or almost white powder.

$m_p$ : 74 - 78° C

CU H<sub>2</sub>O  
K<sub>2</sub>M