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

AV H.O.
KM

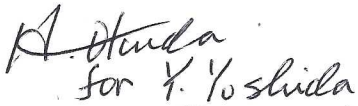
Reagents and reference materials

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

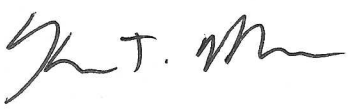
European Pharmacopoeia

Signature	Name	Date
	Vierce Calhoun	22-Dec-2020

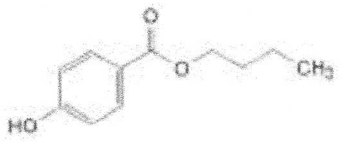
Japanese Pharmacopoeia

Signature	Name	Date
	Haruhiro Okuda	16 Dec/2020

United States Pharmacopeia

Signature	Name	Date
	Kevin Moore	19-NOV-2020

E50 - BUTYL PARAHYDROXYBENZOATE



$C_{11}H_{14}O_3$ 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 ($FeCl_3$, $6H_2O$).
- *Cobalt chloride primary solution:* a 59.5 g/l solution of cobalt chloride ($CoCl_2$, $6H_2O$).
- *Copper sulphate primary solution:* a 62.4 g/l solution of copper sulphate ($CuSO_4$, $5H_2O$).

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, Ø = 4.6 mm;

— *stationary phase: octadecylsilyl silica gel for chromatography* (5 µm);

— *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 µl 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).

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KTM

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