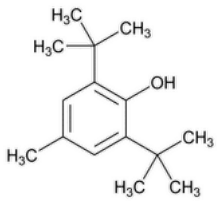
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2021
Document Type: NF Monographs
DocId: GUID-0CFFA0B2-4883-4F4D-8F0F-53D7DC4E0A20_5_en-US
DOI: https://doi.org/10.31003/USPNF_M11070_05_01
DOI Ref: 66231

Butylated Hydroxytoluene



$C_{15}H_{24}O$ 220.35

Phenol, 2,6-bis(1,1-dimethylethyl)-4-methyl-;

2,6-Di-*tert*-butyl-*p*-cresol CAS RN®: 128-37-0.

DEFINITION

Butylated Hydroxytoluene contains NLT 99.0% and NMT 101.5% of butylated hydroxytoluene ($C_{15}H_{24}O$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests (197), *Infrared Spectroscopy*:** 197K

Sample: Undried sample

Acceptance criteria: Meets the requirements

• **B.** The retention time of the butylated hydroxytoluene peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*. The chromatographic profile of the *Sample solution* should exhibit only one major peak corresponding to the main compound.

ASSAY

• **Procedure**

Solution A: 5% acetic acid, prepared by diluting 50 mL of glacial acetic acid in a 1-L flask with water to volume

Mobile phase: Acetonitrile and *Solution A* (65:35)

Standard solution: 0.5 mg/mL of USP Butylated Hydroxytoluene RS in *Mobile phase*

Sample solution: 0.5 mg/mL of Butylated Hydroxytoluene in *Mobile phase*

Chromatographic system

(See *Chromatography (621), System Suitability*.)

Mode: LC

Detector: UV 275 nm

Column: 3.0-mm × 15-cm; 3-µm packing L1

Column temperature: 40°

Flow rate: 0.75 mL/min

Injection volume: 10 µL

Run time: 15 min

System suitability

Sample: *Standard solution*

[Note—The retention time of butylated hydroxytoluene is about 10.8 min.]

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 0.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of butylated hydroxytoluene ($C_{15}H_{24}O$) in the portion of Butylated Hydroxytoluene taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak area of butylated hydroxytoluene from the *Sample solution*

r_S = peak area of butylated hydroxytoluene from the *Standard solution*

C_S = concentration of USP Butylated Hydroxytoluene RS in the *Standard solution* (mg/mL)

C_U = concentration of Butylated Hydroxytoluene in the *Sample solution* (mg/mL)

Acceptance criteria: 99.0%–101.5%

IMPURITIES

Change to read:

• **Residue on Ignition** ⟨281⟩

Sample: 50 g

Analysis: Transfer the *Sample* to a tared crucible, ▲heat gently at a temperature as low as practicable until the *Sample* is thoroughly charred,▲ (NF 1-May-2021) and cool. Moisten the ash with 1 mL of sulfuric acid, and complete the ignition by heating at 800 ± 25° for 15-min periods to constant weight.

Acceptance criteria: NMT 0.002%

• **Organic Impurities**

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*, except extend the *Run time* to 20 min.

Standard solution: 2 µg/mL of USP Butylated Hydroxytoluene RS in *Mobile phase*

Sample solution: 2.0 mg/mL of Butylated Hydroxytoluene in *Mobile phase*

System suitability

Sample: *Standard solution*

[Note—The retention time of butylated hydroxytoluene is about 10.8 min.]

Suitability requirements

Signal-to-noise ratio: NLT 40

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the corrected peak area of each individual impurity in the *Sample solution*:

$$\text{Result} = r_U / F$$

r_U = peak area of the individual impurity from the *Sample solution*

F = relative response factor (see *Table 1*)

Acceptance criteria

Individual impurity: NMT 0.1%; the corrected peak area of each impurity in the *Sample solution* is NMT the area of the principal peak in the *Standard solution*.

Total impurities: NMT 0.7%; the sum of all the corrected peak areas due to impurities in the *Sample solution*, excluding the butylated hydroxytoluene peak area, is NMT 7 times the butylated hydroxytoluene peak area in the *Standard solution*.

Table 1

Name	Relative Retention Time	Relative Response Factor
p-Cresol or *m*-cresol[a]	0.12	1.9
3-*tert*-Butyl-4-hydroxyanisole (BHA)	0.19	1.1
3,5-Di-*tert*-butyl-4-hydroxybenzoic acid	0.20	3.6
2-*tert*-Butyl-4-methylphenol or 2-*tert*-butyl-5-methylphenol[b]	0.27	1.7
3,5-Di-*tert*-butyl-4-hydroxy benzaldehyde	0.37	6.6
4,6-Di-*tert*-butyl-*m*-cresol	0.66	1.1
2,6-Di-*tert*-butyl-phenol	0.77	0.9
Any unspecified impurity	—	1.0

[a] The *p*-cresol and *m*-cresol peaks are not separated under the method conditions.

[b] The 2-*tert*-butyl-4-methylphenol and 2-*tert*-butyl-5-methylphenol peaks are not separated under the method conditions.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨11⟩
  USP Butylated Hydroxytoluene RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
BUTYLATED HYDROXYTOLUENE	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(6)

Current DocID: GUID-0CFFA0B2-4883-4F4D-8F0F-53D7DC4E0A20_5_en-US
DOI: https://doi.org/10.31003/USPNF_M11070_05_01
DOI ref: 66231