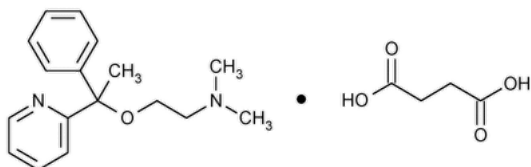


Status: Currently Official on 14-Feb-2025  
 Official Date: Official as of 01-May-2020  
 Document Type: USP Monographs  
 DocId: GUID-CCB7BE4D-1C9C-48BE-B90C-8FAB34403D7D\_3\_en-US  
 DOI: [https://doi.org/10.31003/USPNF\\_M28400\\_03\\_01](https://doi.org/10.31003/USPNF_M28400_03_01)  
 DOI Ref: akd7r

© 2025 USPC  
 Do not distribute

## Doxylamine Succinate



$C_{17}H_{22}N_2O \cdot C_4H_6O_4$  388.46

Ethanamine, *N,N*-dimethyl-2-[1-phenyl-1-(2-pyridinyl)ethoxy]-, butanedioate (1:1);

2-[ $\alpha$ -[2-(Dimethylamino)ethoxy]- $\alpha$ -methylbenzyl]pyridine succinate (1:1);

*N,N*-Dimethyl-2-[1-phenyl-1-(pyridin-2-yl)ethoxy]ethan-1-amine succinate CAS RN®: 562-10-7.

### DEFINITION

#### Change to read:

Doxylamine Succinate contains NLT 98.0% and ▲NMT 102.0%▲ (USP 1-May-2019) of doxylamine succinate ( $C_{17}H_{22}N_2O \cdot C_4H_6O_4$ ), calculated on the dried basis.

### IDENTIFICATION

#### Change to read:

- A. ▲[SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Ultraviolet-Visible Spectroscopy: 197U](#)▲ (CN 1-MAY-2020)

**Analytical wavelength:** 262 nm

**Sample solution:** 20 µg/mL of Doxylamine Succinate in [0.1 N hydrochloric acid](#)

**Acceptance criteria:** Absorptivities, calculated on the dried basis, do not differ by more than 3.0%

#### Delete the following:

- ▲ B. [IDENTIFICATION—ORGANIC NITROGENOUS BASES \(181\)](#): It meets the requirements.▲ (USP 1-May-2019)

#### Add the following:

- ▲ B. The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.▲ (USP 1-May-2019)

- C.

**Sample solution:** Dissolve 500 mg of Doxylamine Succinate in 5 mL of [water](#), and add a slight excess of [6 N ammonium hydroxide](#). Extract the liberated doxylamine with several portions of ether, discard the ether extracts, and evaporate the aqueous solution on a steam bath to dryness. Add 2 mL of 3 N [hydrochloric acid](#), and again evaporate on the steam bath to dryness. Cool, add about 10 mL of ether, allow to stand for a few minutes, and decant the clear supernatant. Evaporate the ether solution to dryness, and dry the residue at 105° for 30 min.

**Acceptance criteria:** The succinic acid melts between 184° and 188°, as indicated for Class I under [Melting Range or Temperature \(741\)](#).  
[Procedures](#).

### ASSAY

#### Change to read:

##### • PROCEDURE

▲**Solution A:** 50 mM [ammonium acetate](#) in [water](#); adjusted with [glacial acetic acid](#) to a pH of 4.0

**Solution B:** [Acetonitrile](#)

**Mobile phase:** See [Table 1](#).

Table 1

| Time (min) | Solution A (%) | Solution B (%) |
|------------|----------------|----------------|
| 0          | 90             | 10             |

| Time<br>(min) | Solution A<br>(%) | Solution B<br>(%) |
|---------------|-------------------|-------------------|
| 2             | 90                | 10                |
| 15            | 40                | 60                |
| 20            | 40                | 60                |
| 21            | 90                | 10                |
| 25            | 90                | 10                |

**Diluent:** *Solution A and Solution B (90:10)*

**Standard solution:** 0.1 mg/mL of [USP Doxylamine Succinate RS](#) in *Diluent*

**Sample solution:** 0.1 mg/mL of Doxylamine Succinate in *Diluent*

#### Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

**Mode:** LC

**Detector:** UV 262 nm

**Column:** 4.6-mm × 15-cm; 5-μm packing [L7](#)

**Column temperature:** 30°

**Flow rate:** 1 mL/min

**Injection volume:** 20 μL

#### System suitability

**Sample:** *Standard solution*

#### Suitability requirements

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 0.73%

#### Analysis

**Samples:** *Standard solution and Sample solution*

Calculate the percentage of doxylamine succinate ( $C_{17}H_{22}N_2O \cdot C_4H_6O_4$ ) in the portion of Doxylamine Succinate taken:

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

$r_U$  = peak response of doxylamine from the *Sample solution*

$r_S$  = peak response of doxylamine from the *Standard solution*

$C_S$  = concentration of [USP Doxylamine Succinate RS](#) in the *Standard solution* (mg/mL)

$C_U$  = concentration of Doxylamine Succinate in the *Sample solution* (mg/mL)

**Acceptance criteria:** 98.0%–102.0% on the dried basis ▲ (USP 1-May-2019)

#### IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

**Delete the following:**

#### ▲ • VOLATILE RELATED COMPOUNDS

**Sample solution:** Dissolve 650 mg in 20 mL of [0.1 N hydrochloric acid](#) in a separator. Render the solution alkaline with 2.5 N [sodium hydroxide](#), and immediately extract with four 25-mL portions of ether, filtering each extract through an ether-saturated pledget of cotton. Evaporate the combined ether extracts on a water bath with the aid of a current of air to dryness at a temperature not exceeding 50°, and dissolve the residue in 5 mL of alcohol.

#### Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

**Mode:** GC

**Detector:** Flame ionization

**Column:** 4-mm × 2-m glass column containing 5% packing [G16](#) and 5% packing [G12](#) on 60- to 80-mesh [S1A](#)

#### Temperatures

**Column:** 212°

**Injection port:** 250°

**Detector block:** 250°

**Carrier gas:** Dry helium