

**Description** Noscapine occurs as white crystals or crystalline powder. It is odorless and tasteless.

It is very soluble in acetic acid (100), slightly soluble in ethanol (95) and in diethyl ether, and practically insoluble in water.

**Identification (1)** Determine the absorption spectrum of a solution of Noscapine in methanol (1 in 20,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Noscapine, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

**Optical rotation**  $[\alpha]_D^{20}$ : +42 – +48° (after drying, 0.5 g, 0.1 mol/L hydrochloric acid TS, 25 mL, 100 nm).

**Melting point** 174 – 177°C

**Purity (1) Chloride**—Dissolve 0.7 g of Noscapine in 20 mL of acetone, add 6 mL of dilute nitric acid and water to make 50 mL, and perform the test with this solution. Prepare the control solution as follows: To 0.4 mL of 0.01 mol/L hydrochloric acid add 20 mL of acetone, 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.02%).

(2) **Heavy metals**—Proceed with 2.0 g of Noscapine according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(3) **Morphine**—Dissolve 0.010 g of Noscapine in 1 mL of water and 5 mL of 1-nitroso-2-naphthol TS with shaking, add 2 mL of a solution of potassium nitrate (1 in 10), and warm at 40°C for 2 minutes. Add 1 mL of a solution of sodium nitrite (1 in 5000), and warm at 40°C for 5 minutes. After cooling, shake the solution with 10 mL of chloroform, centrifuge, and collect the aqueous layer: the solution so obtained has no more color than a pale red.

(4) **Related substances**—Dissolve 0.7 g of Noscapine in 50 mL of acetone, and use this solution as the sample solution. Pipet 5 mL of the sample solution, add acetone to make exactly 50 mL. Pipet 5 mL of this solution, add acetone to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10  $\mu$ L each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of acetone, toluene, ethanol (99.5) and ammonia solution (28) (60:60:9:2) to a distance of about 10 cm, and air-dry the plate. Spray evenly dilute bismuth subnitrate-potassium iodide TS for spray on the plate: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

**Loss on drying** Not more than 0.5% (2 g, 105°C, 4 hours).

**Residue on ignition** Not more than 0.10% (1 g).

**Assay** Weigh accurately about 0.8 g of Noscapine, previously dried, dissolve in 30 mL of acetic acid (100) and titrate with 0.1 mol/L perchloric acid VS (indicator: 3 drops of

crystal violet TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS  
= 41.34 mg of  $C_{22}H_{23}NO_7$

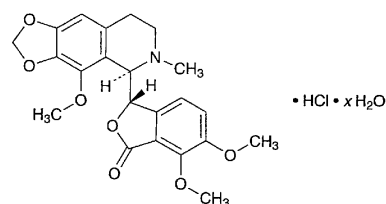
**Containers and storage** Containers—Well-closed containers.

Storage—Light-resistant.

## Noscapine Hydrochloride

### Narcotine Hydrochloride

塩酸ノスカピン



$C_{22}H_{23}NO_7 \cdot HCl \cdot xH_2O$

(3*S*)-6,7-Dimethoxy-3-[(5*R*)-5,6,7,8-tetrahydro-4-methoxy-6-methyl-1,3-dioxolo[4,5-*g*]isoquinolin-5-yl]isobenzofuran-1(3*H*)-one monohydrochloride hydrate  
[912-60-7, anhydride]

Noscapine Hydrochloride, when dried, contains not less than 98.0% of  $C_{22}H_{23}NO_7 \cdot HCl$ : 449.88.

**Description** Noscapine Hydrochloride occurs as colorless or white crystals or crystalline powder. It is odorless, and has a bitter taste.

It is freely soluble in water, in acetic acid (100), and in acetic anhydride, soluble in ethanol (95), and practically insoluble in diethyl ether.

**Identification (1)** To 1 mg of Noscapine Hydrochloride add 1 drop of formaldehyde-sulfuric acid TS: a purple color, changing to yellow-brown, is produced.

(2) To 1 mg of Noscapine Hydrochloride add 1 drop of a solution of ammonium vanadate (V) in sulfuric acid (1 in 200): an orange color is produced.

(3) Dissolve 0.02 g of Noscapine Hydrochloride in 1 mL of water, and add 3 drops of sodium acetate TS: a white, flocculent precipitate is produced.

(4) Dissolve 1 mg of Noscapine Hydrochloride in 1 mL of diluted sulfuric acid (1 in 35), shake with 5 drops of a solution of disodium chlomotropate dihydrate (1 in 50), and add 2 mL of sulfuric acid dropwise: a purple color is produced.

(5) Dissolve 0.1 g of Noscapine Hydrochloride in 10 mL of water, make the solution alkaline with ammonia TS, and shake with 10 mL of chloroform. Separate the chloroform layer, wash with 5 mL of water, and filter. Distil most of the filtrate on a water bath, add 1 mL of ethanol (99.5), and evaporate to dryness. Dry the residue at 105°C for 4 hours: the residue so obtained melts between 174°C and 177°C.

(6) Make a solution of Noscapine Hydrochloride (1 in 50) alkaline with ammonia TS, and filter the precipitate.

Acidify the filtrate with dilute nitric acid: the solution responds to the Qualitative Tests (2) for chloride.

**Purity** Morphine—Dissolve 0.010 g of Noscapine Hydrochloride in 1 mL of water, add 5 mL of 1-nitroso-2-naphthol TS and 2 mL of a solution of potassium nitrate (1 in 10), and warm at 40°C for 2 minutes. Add 1 mL of a solution of sodium nitrite (1 in 5000), and warm at 40°C for 5 minutes. After cooling, shake the mixture with 10 mL of chloroform, centrifuge, and separate the aqueous layer: the solution so obtained has no more color than a pale red color.

**Loss on drying** Not more than 9.0% (0.5 g, 120°C, 4 hours).

**Residue on ignition** Not more than 0.5% (1 g).

**Assay** Weigh accurately about 0.5 g of Noscapine Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS  
= 44.99 mg of  $C_{22}H_{23}NO_7 \cdot HCl$

**Containers and storage** Containers—Well-closed containers.

Storage—Light-resistant.

## Nystatin

ナイスタチン

Nystatin contains not less than 4600 units (potency) per mg, calculated on the dried basis. The potency of Nystatin is expressed as the unit of nystatin ( $C_{47}H_{75}NO_{17}$ : 926.09), and 1 unit corresponds to 0.27  $\mu$ g of nystatin ( $C_{47}H_{75}NO_{17}$ ).

**Description** Nystatin occurs as a white to light yellow-brown powder.

It is soluble in formamide, sparingly soluble in methanol, slightly soluble in ethanol (95), and very slightly soluble in water.

It dissolves in sodium hydroxide TS.

**Identification** (1) Dissolve 1 mg of Nystatin in 5 mL of water and 1 mL of sodium hydroxide TS, heat for 2 minutes, and cool. To this solution add 3 mL of a solution of 4-aminoacetophenone in methanol (1 in 200) and 1 mL of hydrochloric acid: a red-purple color develops.

(2) To 0.010 g of Nystatin add a mixture of diluted methanol (4 in 5) and sodium hydroxide TS (200:1), heat at not exceeding 50°C to dissolve, then add diluted methanol (4 in 5) to make 500 mL. Determine the absorption spectrum of this solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Nystatin Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelength.

**Purity** Heavy metals—Proceed with 1.0 g of Nystatin ac-

ording to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

**Loss on drying** Not more than 5.0% (0.3 g, in vacuum, 60°C, 3 hours).

**Assay** Perform the test according to the Cylinder-plate method as directed under the Microbial Assay for Antibiotics according to the following conditions.

(1) Test organism—*Saccharomyces cerevisiae* ATCC 9763

(2) Culture medium—Use the medium 2) Medium for test organism [12] under (1) Agar media for seed and base layer.

(3) Standard solution—Use a light-resistant container. Weigh accurately an amount of Nystatin Reference Standard equivalent to about 60,000 units, previously dried at 40°C for 2 hours in vacuum (not more than 0.67 kPa), dissolve in formamide to make a solution of 3000 units per mL, and use this solution as the standard stock solution. Keep the standard stock solution at 5°C or below and use within 3 days. Take exactly a suitable amount of the standard stock solution before use, add phosphate buffer solution, pH 6.0 to make solutions so that each mL contains 300 units and 150 units, and use these solutions as the high concentration standard solution and the low concentration standard solution, respectively.

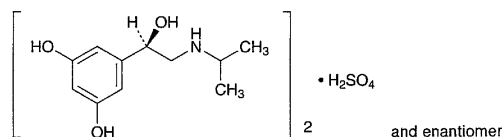
(4) Sample solution—Use a light-resistant container. Weigh accurately an amount of Nystatin equivalent to about 60,000 units, dissolve in formamide to make a solution of 3000 units per mL, and use this solution as the sample stock solution. Take exactly a suitable amount of the sample stock solution, add phosphate buffer solution, pH 6.0 to make solutions so that each mL contains 300 units and 150 units, and use these solutions as the high concentration sample solution and the low concentration sample solution, respectively.

**Containers and storage** Containers—Tight containers.

Storage—Light-resistant, and in a cold place.

## Orciprenaline Sulfate

硫酸オルシプレナリン



$(C_{11}H_{17}NO_3)_2 \cdot H_2SO_4$ : 520.59

(*RS*)-1-(3,5-Dihydroxyphenyl)-2-isopropylaminoethanol hemisulfate [5874-97-5]

Orciprenaline Sulfate contains not less than 98.5% of  $(C_{11}H_{17}NO_3)_2 \cdot H_2SO_4$ , calculated on the dried basis.

**Description** Orciprenaline Sulfate occurs as white crystals or crystalline powder.

It is freely soluble in water, slightly soluble in ethanol (95) and in acetic acid (100), and practically insoluble in diethyl