

## Methyltestosterone Tablets

メチルテストステロン錠

Methyltestosterone Tablets contain not less than 90% and not more than 110% of the labeled amount of methyltestosterone ( $C_{20}H_{30}O_2$ ; 302.45).

**Method of preparation** Prepare as directed under Tablets, with Methyltestosterone.

**Identification (1)** To a portion of powdered Methyltestosterone Tablets, equivalent to 0.01 g of Methyltestosterone according to the labeled amount, add 50 mL of chloroform, shake for 30 minutes, and filter. Evaporate the filtrate to dryness, dissolve the residue in 10 mL of acetone, and use this solution as the sample solution. Separately, dissolve 0.01 g of methyltestosterone in 10 mL of acetone, 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 chloroform and ethanol (95) (9:1) to a distance of about 12 cm, and air-dry the plate. Spray evenly dilute sulfuric acid on the plate, and heat at 110°C for 10 minutes: the spots from the sample solution and the standard solution show the same *R<sub>f</sub>* value.

(2) Evaporate 1 mL of the sample solution obtained in (1) to dryness, and proceed with the residue as directed in the Identification (1) under Methyltestosterone.

**Content uniformity** To 1 tablet of Methyltestosterone Tablets add 5 mL of water to disintegrate, add 50 mL of methanol, and shake for 30 minutes. Add methanol to make exactly 100 mL, and centrifuge. Measure exactly *x* mL of the supernatant liquid, add methanol to make exactly *V* mL of a solution containing about 10  $\mu$ g of methyltestosterone ( $C_{20}H_{30}O_2$ ) per mL, and use this solution as the sample solution. Separately, weigh accurately about 0.01 g of Methyltestosterone Reference Standard, previously dried in a desiccator (in vacuum, phosphorus (V) oxide) for 10 hours, and dissolve in 5 mL of water and 50 mL of methanol, then add methanol to make exactly 100 mL. Pipet 5 mL of this solution, add methanol to make exactly 50 mL, and use this solution as the standard solution. Determine the absorbances, *A<sub>T</sub>* and *A<sub>S</sub>*, of the sample solution and the standard solution at the wavelength of maximum absorption at about 241 nm, respectively, as directed under the Ultraviolet-visible Spectrophotometry.

$$\begin{aligned} &\text{Amount (mg) of methyltestosterone (C}_{20}\text{H}_{30}\text{O}_2\text{)} \\ &= \text{amount (mg) of Methyltestosterone} \\ &\quad \text{Reference Standard} \\ &\quad \times \frac{A_T}{A_S} \times \frac{V}{10} \times \frac{1}{x} \end{aligned}$$

**Assay** Weigh accurately and powder not less than 20 Methyltestosterone Tablets. Weigh accurately a portion of the powder, equivalent to about 0.01 g of methyltestosterone ( $C_{20}H_{30}O_2$ ), transfer to a 100-mL separator with 5 mL of water, and extract with four 25-mL portions of chloroform. Filter the combined chloroform extracts through dry filter paper, evaporate the filtrate to dryness by heating

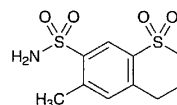
on a water bath with the aid of a current of air. Dissolve the residue in ethanol (95) to make exactly 50 mL, measure exactly 5 mL of this solution, add ethanol (95) to make exactly 100 mL, and determine the absorbance *A* of this solution at the wavelength of maximum absorption at about 241 nm as directed under the Ultraviolet-visible Spectrophotometry.

$$\begin{aligned} &\text{Amount (mg) of methyltestosterone (C}_{20}\text{H}_{30}\text{O}_2\text{)} \\ &= \frac{A}{536} \times 10,000 \end{aligned}$$

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

## Meticrane

メチ克蘭



$C_{10}H_{13}NO_4S_2$ ; 275.35  
6-Methylthiochroman-7-sulfonamide 1,1-dioxide  
[1084-65-7]

Meticrane, when dried, contains not less than 98.0% of  $C_{10}H_{13}NO_4S_2$ .

**Description** Meticrane occurs as white, crystals or crystalline powder. It is odorless and has a slight bitter taste.

It is freely soluble in dimethylformamide, slightly soluble in acetonitrile and in methanol, very slightly soluble in ethanol (95), and practically insoluble in water.

Melting point: about 234°C (with decomposition).

**Identification (1)** Determine the absorption spectrum of a solution of Meticrane in methanol (3 in 10,000) 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 Meticrane, 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.

**Purity (1) Ammonium**—Perform the test with 0.10 g of Meticrane. Prepare the control solution with 3.0 mL of Standard Ammonium Solution (not more than 0.03%).

(2) **Heavy metals**—Proceed with 1.0 g of Meticrane according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(3) **Arsenic**—Prepare the test solution with 1.0 g of Meticrane according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(4) **Related substances**—Dissolve 0.05 g of Meticrane in 50 mL of acetonitrile, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add acetonitrile to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 2  $\mu$ L each of the sample

solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and determine each peak area of both solutions by the automatic integration method: the total area of the peaks other than meticrane from the sample solution is not larger than the peak area of meticrane from the standard solution.

**Operating conditions 1—**

**Detector:** An ultraviolet absorption photometer (wavelength: 230 nm).

**Column:** A stainless steel column 4.6 in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5  $\mu$ m in particle diameter).

**Column temperature:** A constant temperature of about 40°C.

**Mobile phase:** A mixture of water and acetonitrile (17:3).

**Flow rate:** Adjust the flow rate so that the retention time of meticrane is about 7 minutes.

**Selection of column:** Dissolve 0.01 g each of Meticrane and caffeine in acetonitrile to make 100 mL. Proceed with 2  $\mu$ L of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of caffeine and meticrane in this order with the resolution between these peaks being not less than 10.

**Detection sensitivity:** Adjust the detection sensitivity so that the peak height of meticrane obtained from 2  $\mu$ L of the standard solution is 20 – 50% of the full scale.

**Time span of measurement:** About 4 times as long as the retention time of meticrane, after the solvent peak.

**Operating conditions 2—**

**Detector, column, and column temperature:** Proceed as directed in the operating conditions 1.

**Mobile phase:** A mixture of water and acetonitrile (1:1).

**Flow rate:** Adjust the flow rate so that the retention time of meticrane is about 2 minutes.

**Selection of column:** Dissolve 0.02 g each of Meticrane and methyl parahydroxybenzoate in acetonitrile to make 100 mL. Proceed with 2  $\mu$ L of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of meticrane and methyl parahydroxybenzoate in this order with the resolution between these peaks being not less than 4.

**Detection sensitivity:** Adjust the detection sensitivity so that the peak height of meticrane from 2  $\mu$ L of the standard solution is 20 – 50% of the full scale.

**Time span of measurement:** About 10 times as long as the retention time of meticrane, after the solvent peak.

**Loss on drying** Not more than 0.5% (1 g, 105°C, 4 hours).

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

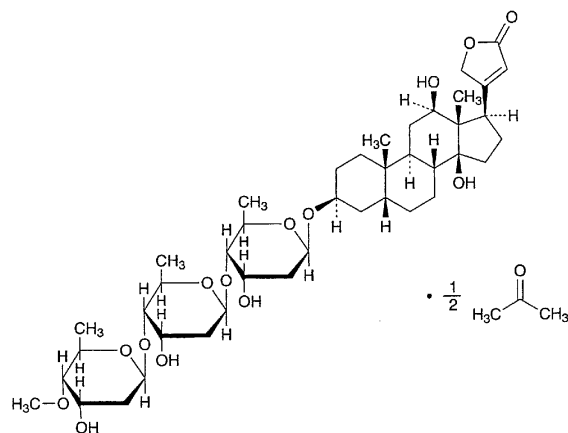
**Assay** Weigh accurately about 0.5 g of Meticrane, previously dried, dissolve in 50 mL of dimethylformamide, add 5 mL of water, and titrate with 0.1 mol/L potassium hydroxide-ethanol VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L potassium hydroxide-ethanol VS = 27.535 mg of C<sub>10</sub>H<sub>13</sub>NO<sub>4</sub>S<sub>2</sub>

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

## Metildigoxin

メチルジゴキシン



C<sub>42</sub>H<sub>66</sub>O<sub>14</sub> · 1/2 C<sub>3</sub>H<sub>6</sub>O: 824.00

3 $\beta$ -[O-2,6-Dideoxy-4-O-methyl- $\beta$ -D-ribo-hexopyranosyl-(1 $\rightarrow$ 4)-O-2,6-dideoxy- $\beta$ -D-ribo-hexopyranosyl-(1 $\rightarrow$ 4)-2,6-dideoxy- $\beta$ -D-ribo-hexopyranosyloxy]-12 $\beta$ ,14-dihydroxy-5 $\beta$ -card-20(22)-enolide—acetone (2/1) [30685-43-9, acetone free]

Metildigoxin contains not less than 96.0% and not more than 103.0% of C<sub>42</sub>H<sub>66</sub>O<sub>14</sub> · 1/2 C<sub>3</sub>H<sub>6</sub>O, calculated on the anhydrous basis.

**Description** Metildigoxin occurs as a white to light yellowish white, crystalline powder.

It is freely soluble in *N,N*-dimethylformamide, in pyridine and in acetic acid (100), soluble in chloroform, sparingly soluble in methanol, slightly soluble in ethanol (95) and in acetone, very slightly soluble in water, and practically insoluble in diethyl ether.

**Identification (1)** Dissolve 2 mg of Metildigoxin in 2 mL of acetic acid (100), shake well with 1 drop of iron (III) chloride TS, and add gently 2 mL of sulfuric acid to divide into two layers: a brown color develops at the interface, and a deep blue color gradually develops in the acetic acid layer.

**(2)** Dissolve 2 mg of Metildigoxin in 2 mL of 1,3-dinitrobenzene TS, add 2 mL of a solution of tetramethylammonium hydroxide in ethanol (95) (1 in 200), and shake: a purple color gradually develops, and changes to blue-purple.

**(3)** Determine the absorption spectrum of a solution of Metildigoxin in methanol (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Metildigoxin Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

**(4)** Determine the infrared absorption spectrum of Metildigoxin as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Metildigoxin Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers. If