

any difference appears between the spectra, dissolve Metildigoxin and Metildigoxin Reference Standard in acetone, respectively, then evaporate the acetone to dryness, and repeat the test on the residues.

Optical rotation $[\alpha]_{546.1}^{20}$: +22.0 – +25.5° (1 g, calculated on the anhydrous basis, pyridine, 10 mL, 100 mm).

Purity (1) Arsenic—Prepare the test solution with 0.5 g of Metildigoxin according to Method 3, and perform the test using Apparatus B (not more than 4 ppm).

(2) Related substances—Dissolve 0.010 g of Metildigoxin in 10 mL of chloroform, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add chloroform to make exactly 50 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 20 μ 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 2-butanone and chloroform (3:1) to a distance of about 15 cm, and air-dry the plate. Spray evenly dilute sulfuric acid on the plate, and heat at 110°C for 10 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Acetone Weigh accurately about 0.1 g of Metildigoxin, dissolve in exactly 2 mL of the internal standard solution, add *N,N*-dimethylformamide to make 10 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.4 g of acetone in a 50-mL volumetric flask containing about 10 mL of *N,N*-dimethylformamide, and add *N,N*-dimethylformamide to make 50 mL. Pipet 5 mL of this solution, add exactly 20 mL of the internal standard solution, then add *N,N*-dimethylformamide to make 100 mL, and use this solution as the standard solution. Perform the test with 1 μ L each of the sample solution and the standard solution as directed under the Gas Chromatography, and calculate the ratios, Q_T and Q_S , of the peak area of acetone to that of the internal standard: the amount of acetone is between 2.0% and 5.0%.

$$\begin{aligned} &\text{Amount (\% of acetone)} \\ &= \frac{Q_T}{Q_S} \times \frac{\text{amount (g) of acetone taken}}{\text{amount (g) of the sample taken}} \end{aligned}$$

Internal standard solution—A solution of *t*-butanol in *N,N*-dimethylformamide (1 in 2000).

Operating conditions—

Detector: A hydrogen flame-ionization detector.

Column: A glass column about 2 mm in inside diameter and 1 to 2 m in length, packed with porous ethylvinylbenzene-divinylbenzene copolymer for gas chromatography (150 to 180 μ m in particle diameter).

Column temperature: A constant temperature between 170°C and 230°C.

Carrier gas: Nitrogen

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

Selection of column: Proceed with 1 μ L of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of acetone and *t*-butanol in this order with the resolution between these peaks being not less than 2.0.

Water Not more than 3.0% (0.3 g, direct titration).

Residue on ignition Not more than 0.1% (0.5 g).

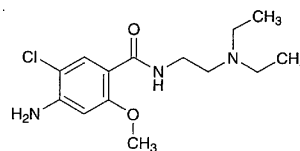
Assay Weigh accurately 0.1 g each of Metildigoxin and Metildigoxin Reference Standard, and dissolve each in methanol to make exactly 50 mL. Pipet 5 mL each of the solutions, add methanol to each to make exactly 100 mL, and use these solutions as the sample solution and the standard solution, respectively. Pipet 5 mL each of the sample solution and the standard solution, add 15 mL of 2,4,6-trinitrophenol-ethanol TS and 2 mL of sodium hydroxide TS to each, shake well, add methanol to make exactly 25 mL, and allow to stand at 20 \pm 0.5°C for 20 minutes. Perform the test with these solutions as directed under the Ultraviolet-visible Spectrophotometry using a solution prepared by mixing 15 mL of 2,4,6-trinitrophenol-ethanol TS and 2 mL of sodium hydroxide TS and adding methanol to make exactly 25 mL as the blank. Determine the maximum absorbances, A_T and A_S , of the subsequent solutions obtained from the sample solution and the standard solution, respectively, by measuring every 5 minutes, at 495 nm.

$$\begin{aligned} &\text{Amount (mg) of } C_{42}H_{66}O_{14} \cdot \frac{1}{2}C_3H_6O \\ &= \text{amount (mg) of Metildigoxin Reference Standard,} \\ &\quad \text{calculated on the anhydrous basis} \\ &\quad \times \frac{A_T}{A_S} \end{aligned}$$

Containers and storage Containers—Tight containers.

Metoclopramide

メトクロプラミド



$C_{14}H_{22}ClN_3O_2$: 299.80

4-Amino-5-chloro-*N*-(2-diethylaminoethyl)-2-methoxybenzamide [364-62-5]

Metoclopramide, when dried, contains not less than 99.0% of $C_{14}H_{22}ClN_3O_2$.

Description Metoclopramide occurs as white crystals or a crystalline powder, and is odorless.

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

It dissolves in dilute hydrochloric acid.

Identification (1) Dissolve 0.01 g of Metoclopramide in 1 mL of dilute hydrochloric acid and 4 mL of water: the solution responds to the Qualitative Tests for Primary Aromatic Amines.

(2) Dissolve 0.01 g of Metoclopramide in 5 mL of dilute hydrochloric acid and 20 mL of water, and to 5 mL of this solution add 1 mL of Dragendorff's TS: a reddish orange precipitate is produced.

(3) Dissolve 0.1 g of Metoclopramide in 1 mL of 1

mol/L hydrochloric acid TS, and dilute with water to make 100 mL. To 1 mL of the solution add water to make 100 mL, determine the absorption spectrum of the solution 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.

Melting point 146 – 149°C

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Metoclopramide in 10 mL of 1 mol/L hydrochloric acid TS: the solution is clear and colorless.

(2) Heavy metals—Proceed with 1.0 g of Metoclopramide as directed under 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—Dissolve 1.0 g of Metoclopramide in 5 mL of 1 mol/L hydrochloric acid TS, and use this solution as the sample solution. Perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.10 g of Metoclopramide in 10 mL of methanol, and use this solution as the sample solution. Dilute 1 mL of this solution, exactly measured, with methanol to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μ L each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of 1-butanol and ammonia solution (28) (19:1) to a distance of about 10 cm. Dry the plate, first in air and then at 80°C for 30 minutes. Examine under ultraviolet light (main wavelength: 254 nm): 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% (1 g, 105°C, 3 hours).

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

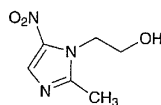
Assay Dissolve about 0.4 g of Metoclopramide, previously dried and accurately weighed, in 50 mL of acetic acid (100), add 5 mL of acetic anhydride, and warm for 5 minutes. Allow to cool, and titrate with 0.1 mol/L perchloric acid VS (indicator: 2 drops of crystal violet TS). Perform the blank determination, and make any necessary correction.

$$\begin{aligned} \text{Each mL of 0.1 mol/L perchloric acid VS} \\ = 29.980 \text{ mg of } C_{14}H_{22}ClN_3O_2 \end{aligned}$$

Containers and storage Containers—Well-closed containers.

Metronidazole

メトロニダゾール



$C_6H_9N_3O_3$: 171.15

2-(2-Methyl-5-nitro-1H-imidazol-1-yl)ethanol [443-48-1]

Metronidazole, when dried, contains not less than 99.0% of $C_6H_9N_3O_3$.

Description Metronidazole occurs as white to pale yellowish white crystals or crystalline powder. It is odorless, and has a slightly bitter taste.

It is freely soluble in acetic acid (100), sparingly soluble in ethanol (95) and in acetone, slightly soluble in water, and very slightly soluble in diethyl ether.

It dissolves in dilute hydrochloric acid.

It is affected by light.

Identification (1) Determine the absorption spectrum of a solution of Metronidazole in 0.1 mol/L hydrochloric acid TS (1 in 100,000) 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 Metronidazole 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.

Melting point 159 – 163°C

Purity (1) Heavy metals—Proceed with 1.0 g of Metronidazole 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).

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

(3) 2-Methyl-5-nitroimidazol—Dissolve 0.10 g of Metronidazole in acetone to make exactly 10 mL, and use this solution as the sample solution. Separately, dissolve 0.020 g of 2-methyl-5-nitroimidazole for thin-layer chromatography in acetone to make exactly 20 mL, then 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 20 μ L each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Immediately develop the plate with a mixture of acetone, water and ethyl acetate (8:1:1) to a distance of about 15 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spot from the sample solution corresponding to the spot from the standard solution is not more intense than the spot from the standard solution.

Loss on drying Not more than 0.5% (1 g, in vacuum, silica gel, 24 hours).

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

Assay Weigh accurately about 0.2 g of Metronidazole, previously dried, and dissolve in 30 mL of acetic acid (100). Titrate with 0.1 mol/L perchloric acid VS (indicator: 0.5 mL of *p*-naphtholbenzein TS) until the color of the solution changes from orange-yellow to green. Perform a blank determination, and make any necessary correction.

$$\begin{aligned} \text{Each mL of 0.1 mol/L perchloric acid VS} \\ = 17.116 \text{ mg of } C_6H_9N_3O_3 \end{aligned}$$

Containers and storage Containers—Tight containers. Storage—Light-resistant.