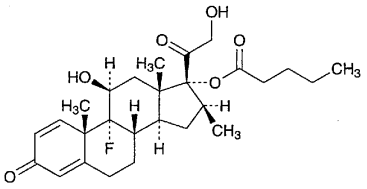
Amount (mg) of $C_{22}H_{28}FNa_2O_8P$
= amount (mg) of Betamethasone Sodium Phosphate Reference Standard, calculated on the anhydrous basis
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of butyl parahydroxybenzoate in methanol (1 in 5000).
Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 254 nm).
Column: A stainless steel column about 4 mm in inside diameter and about 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (7 μm in particle diameter).
Column temperature: A constant temperature of about 25°C.
Mobile phase: Dissolve 1.6 g of tetra-*n*-butylammonium bromide, 3.2 g of disodium hydrogenphosphate 12-water and 6.9 g of potassium dihydrogenphosphate in 1000 mL of water, and add 1500 mL of methanol.
Flow rate: Adjust the flow rate so that the retention time of betamethasone phosphate is about 5 minutes.
Selection of column: Proceed with 10 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of betamethasone phosphate and the internal standard in this order with the resolution between these peaks being not less than 10.

Containers and storage Containers—Tight containers.

Betamethasone Valerate

吉草酸ベタメタゾン



$C_{27}H_{37}FO_6$: 476.58
9-Fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17-valerate [*2152-44-5*]

Betamethasone Valerate, when dried, contains not less than 97.0% and not more than 103.0% of $C_{27}H_{37}FO_6$.

Description Betamethasone Valerate occurs as a white, crystalline powder. It is odorless.
It is freely soluble in chloroform, soluble in ethanol (95), sparingly soluble in methanol, slightly soluble in diethyl ether, and practically insoluble in water.
Melting point: about 190°C (with decomposition).

Identification **(1)** Proceed with 0.01 g of Betamethasone Valerate as directed under the Oxygen Flask Combustion Method, using a mixture of 0.5 mL of 0.01 mol/L sodium hydroxide TS and 20 mL of water as the absorbing liquid, and prepare the test solution: the test solution so obtained responds to the Qualitative Tests for fluoride.
(2) Determine the infrared absorption spectrum of Betamethasone Valerate, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of dried Betamethasone Valerate Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

Optical rotation $[\alpha]_D^{20}$: +77 – +83° (after drying, 0.10 g, methanol, 20 mL, 100 mm).

Purity Other steroids—Conduct this procedure without exposure to daylight. Dissolve 0.02 g of Betamethasone Valerate in 5 mL of a mixture of chloroform and methanol (9:1), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a mixture of chloroform and methanol (9:1) 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 5 μL 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 methanol (9:1) to a distance of about 12 cm, and air-dry the plate. Spray evenly alkaline blue tetrazolium TS 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% (1 g, 105°C, 3 hours).

Residue on ignition Not more than 0.2% (0.5 g, platinum crucible).

Assay Dissolve about 0.01 g each of Betamethasone Valerate and Betamethasone Valerate Reference Standard, previously dried and accurately weighed, in methanol to make exactly 100 mL. Pipet 10 mL each of these solutions, add 10 mL each of the internal standard solution, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following operating conditions, and calculate the ratios, Q_T and Q_S, of the peak area of betamethasone valerate to that of the internal standard, respectively.

Amount (mg) of $C_{27}H_{37}FO_6$
= amount (mg) of Betamethasone Valerate Reference Standard
$\times \frac{Q_T}{Q_S}$

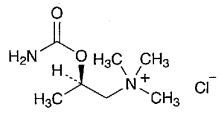
Internal standard solution—A solution of isoamyl benzoate in methanol (1 in 1000).
Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 254 nm).
Column: A stainless steel column about 4 mm in inside diameter and 20 to 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (7 μm in particle diameter).
Column temperature: A constant temperature of about 25°C.
Mobile phase: A mixture of methanol and water (7:3).
Flow rate: Adjust the flow rate so that the retention time of betamethasone valerate is about 10 minutes.

Selection of column: Proceed with 10 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of betamethasone valerate and the internal standard in this order with the resolution between these peaks being not less than 5.

Containers and storage Containers—Tight containers.

Bethanechol Chloride

塩化ベタネコール



and enantiomer

$C_7H_{17}ClN_2O_2$: 196.68
N-[(*RS*)-2-(Carbamoyloxy)propyl]-*N*,*N*,*N*-trimethylammonium chloride [*590-63-6*]

Bethanechol Chloride, when dried, contains not less than 98.0% of $C_7H_{17}ClN_2O_2$, and not less than 17.7% and not more than 18.3% of chlorine (Cl: 35.45).

Description Bethanechol Chloride occurs as colorless or white crystals or a white, crystalline powder. It has a slight amine-like odor, and has a slight, saline taste.

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

It is hygroscopic.

Melting point: about 211°C or about 219°C

Identification (1) To 2 mL of a solution of Bethanechol Chloride (1 in 40) add 0.1 mL of a solution of cobalt (II) chloride hexahydrate (1 in 100), then add 0.1 mL of potassium hexacyanoferrate (II) TS: A green color is produced, and almost entirely fades within 10 minutes.

(2) To 1 mL of a solution of Bethanechol Chloride (1 in 100) add 0.1 mL of iodine TS: a brown precipitate is produced, and the solution shows a greenish brown color.

(3) A solution of Bethanechol Chloride (1 in 100) responds to the Qualitative Tests for chloride.

Purity Heavy metals—Proceed with 1.0 g of Bethanechol Chloride according to Method 1, 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 1.0% (1 g, 105°C, 2 hours).

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

Assay (1) Bethanechol chloride—Weigh accurately about 0.4 g of Bethanechol Chloride, previously dried, dissolve in 2 mL of acetic acid (100), add 40 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through green to yellow-green (indicator: 2 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 19.668 mg of $C_7H_{17}ClN_2O_2$

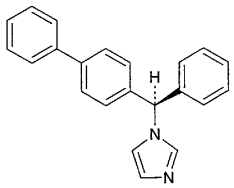
(2) Chlorine—Weigh accurately about 0.4 g of Bethanechol Chloride, previously dried, dissolve in 30 mL of water, and add exactly 40 mL of 0.1 mol/L silver nitrate VS. Then add 3 mL of nitric acid and 5 mL of nitrobenzene, shake vigorously for 2 to 3 minutes, and titrate the excess silver nitrate with 0.1 mol/L ammonium thiocyanate VS (indicator: 2 mL of ammonium iron (III) sulfate TS). Perform a blank determination.

Each mL of 0.1 mol/L silver nitrate VS = 3.5453 mg of Cl

Containers and storage Containers—Tight containers.

Bifonazole

ビホナゾール



and enantiomer

$C_{22}H_{18}N_2$: 310.39
1-[(*RS*)-(Biphenyl-4-yl)phenylmethyl]-1*H*-imidazole [*60628-96-8*]

Bifonazole, when dried, contains not less than 98.5% of $C_{22}H_{18}N_2$.

Description Bifonazole occurs as a white to pale yellow powder. It is odorless and tasteless.

It is freely soluble in dichloromethane, soluble in methanol, sparingly soluble in ethanol (95), slightly soluble in diethyl ether, and practically insoluble in water.

A solution of Bifonazole in methanol (1 in 100) does not show optical rotation.

Identification (1) Determine the absorption spectrum of a solution of Bifonazole in methanol (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 Bifonazole, 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.

Melting point 147 - 151°C

Purity (1) Chloride—To 2.0 g of Bifonazole add 40 mL of water, warm for 5 minutes, and after cooling, filter. To 10 mL of the filtrate add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.30 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.021%).

(2) Sulfate—To 10 mL of the filtrate obtained in (1) add