Diphtheria Toxoid for Adult Use in the Minimum Requirements of Biological Products.

Description Adsorbed Diphtheria Toxoid for Adult Use becomes a homogeneous, whitish turbid liquid on shaking.

Diphtheria-Tetanus Combined Toxoid

ジフテリア破傷風混合トキソイド

Diphtheria-Tetanus Combined Toxoid is a liquid for injection containing diphtheria toxoid and tetanus toxoid which are prepared by treating diphtheria toxin and tetanus toxin, respectively, with formaldehyde by a method involving no appreciable loss of the immunogenicity.

It conforms to the requirements of Diphtheria-Tetanus Combined Toxoid in the Minimum Requirements of Biological Products.

Description Diphtheria-Tetanus Combined Toxoid is a colorless or light yellow-brown, clear liquid.

Adsorbed Diphtheria-Tetanus Combined Toxoid

沈降ジフテリア破傷風混合トキソイド

Adsorbed Diphtheria-Tetanus Combined Toxoid is a liquid for injection containing diphtheria toxoid and tetanus toxoid which are prepared by treating diphtheria toxin and tetanus toxin, respectively, with formaldehyde by a method involving no appreciable loss of the immunogenicity and rendered insoluble by adding aluminum salt.

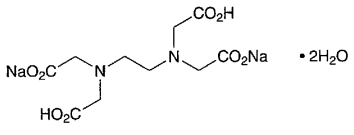
It conforms to the requirements of Adsorbed Diphtheria-Tetanus Combined Toxoid in the Minimum Requirements for Biological Products.

Description Adsorbed Diphtheria-Tetanus Combined Toxoid becomes a homogeneous, whitish turbid liquid on shaking.

Disodium Edetate

Disodium Ethylenediaminetetraacetate
EDTA Sodium

エデト酸ナトリウム



$C_{10}H_{14}N_2Na_2O_8.2H_2O$: 372.24
Disodium dihydrogen ethylenediaminetetraacetate dihydrate [*6381-92-6*]

Disodium Edetate contains not less than 99.0% of $C_{10}H_{14}N_2Na_2O_8.2H_2O$.

Description Disodium Edetate occurs as white crystals or crystalline powder. It is odorless and has a slight, acid taste.

It is soluble in water, and practically insoluble in ethanol (95) and in diethyl ether.

Identification **(1)** Dissolve 0.01 g of Disodium Edetate in 5 mL of water, add 2 mL of a solution of potassium chromate (1 in 200) and 2 mL of arsenic (III) trioxide TS, and heat in a water bath for 2 minutes: a purple color develops.

(2) Dissolve 0.5 g of Disodium Edetate in 20 mL of water, and add 1 mL of dilute hydrochloric acid: a white precipitate is produced. Collect the precipitate, wash with 50 mL of water, and dry at 105°C for 1 hour: the precipitate melts between 240°C and 244°C (with decomposition).

(3) A solution of Disodium Edetate (1 in 20) responds to the Qualitative Tests (1) for sodium salt.

pH Dissolve 1 g of Disodium Edetate in 100 mL of water: the pH of this solution is between 4.3 and 4.7.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Disodium Edetate in 50 mL of water: the solution is clear and colorless.

(2) Cyanide—Transfer 1.0 g of Disodium Edetate to a round-bottomed flask, dissolve in 100 mL of water, add 10 mL of phosphoric acid, and distil. Place 15 mL of 0.5 mol/L sodium hydroxide VS in a 100-mL measuring cylinder, which is used as a receiver, and immerse the bottom end of the condenser into the solution. Distil the mixture until the distillate measures 100 mL, and use this solution as the sample solution. Transfer 20 mL of the sample solution to a glass-stoppered test tube, add 1 drop of phenolphthalein TS, neutralize with dilute acetic acid, and add 5 mL of phosphate buffer solution, pH 6.8, and 1.0 mL of diluted sodium toluensulfonchloramide TS (1 in 5). Immediately stopper the tube, mix gently, and allow to stand for a few minutes. Mix well with 5 mL of pyridine-pyrazolone TS, and allow to stand between 20°C and 30°C for 50 minutes: the solution has no more color than the following control solution.

Control solution: Pipet 1.0 mL of Standard Cyanide Solution, add 15 mL of 0.5 mol/L sodium hydroxide VS and water to make exactly 1000 mL, transfer 20 mL of this solution to a glass-stoppered test tube, and proceed as directed for the sample solution.

(3) Heavy metals—Proceed with 2.0 g of Disodium Edetate 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).

(4) Arsenic—Prepare the test solution with 1.0 g of Disodium Edetate according to Method 1, and perform the test using Apparatus B (not more than 2 ppm).

Residue on ignition 37.0 - 39.0% (1 g).

Assay Weigh accurately about 1 g of Disodium Edetate, dissolve in 50 mL of water, add 2 mL of ammonia-ammonium chloride buffer solution, pH 10.7, and 0.04 g of eriochrome black T-sodium chloride indicator, and titrate with 0.1 mol/L zinc VS until the color of the solution changes from blue to red.

Each mL of 0.1 mol/L zinc VS
= 37.224 mg of $C_{10}H_{14}N_2Na_2O_8.2H_2O$

Containers and storage Containers—Well-closed containers.

Ephedra Herb

Ephdrae Herba

マオウ

Ephedra Herb is the terrestrial stem of *Ephedra sinica* Stapf, *Ephedra intermedia* Schrenk et C.A. Meyer or *Ephedra equisetina* Bunge (*Ephedraceae*).

Ephedra Herb, when dried, contains not less than 0.7% of total alkaloids [as ephedrine ($C_{10}H_{15}NO$: 165.23) and pseudoephedrine ($C_{10}H_{15}NO$: 165.23)].

Description Thin cylindrical or ellipsoidal cylinder, 0.1 - 0.2 cm in diameter; 3 - 5 cm in length of internode; light green to yellow-green; numerous parallel vertical furrows on the surface; scaly leaves at the node portion; leaves, 0.2 - 0.4 cm in length, light brown to brown in color, usually being opposite at every node, adhering at the base to form a tubular sheath around the stem. Under a magnifying glass, the transverse section of the stem appears as circle and ellipse, the outer portion grayish green to yellow-green in color, and the center filled with a red-purple substance or hollow. When fractured at internode, the outer part is fibrous and easily split vertically. Odor, slight; taste, astringent and slightly bitter, giving a slight sensation of numbness on the tongue.

Identification To about 0.5 g of pulverized Ephedra Herb add 10 mL of methanol, shake for 2 minutes, filter, and use the filter, and use the filtrate as the sample solution. Perform the test with this solution as directed under the Thin-layer Chromatography. Spot 10 μL of the sample solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of 1-butanol, water and acetic acid (100) (7:2:1) to a distance of abour 10 cm, and air- day the plate. Spray evenly 2% ninhydrin-ethanol TS, and heat the plate at 105°C for 5 minutes: a rep-purple spot appears near *Rf* 0.35.

Purity **(1)** Woody stem—The amount of the woody stems contained in Ephedra Herb does not exceed 5.0%.

(2) Foreign matter—Ephedra Herb does not contain stems of *Equisetaceae* or *Gramineae* plants, or any other foreign matter.

Total ash Not more than 11.0%.

Acid-insoluble ash Not more than 2.0%.

Assay Weigh accurately about 0.5 g of medium powder of Ephedra Herb, previously dried in a desiccator (silica gel) for 24 hours, in a glass-stoppered centrifuge tube, add 20 mL of diluted methanol (1 in 2), shake for 30 minutes, centrifuge, and separate the supernatant liquid. Repeat this procedure twice with the residue using 20-mL portion of diluted methanol (1 in 2). Combine all the extracts, add diluted methanol (1 in 2) to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of ephedrine hydrochloride for assay, previously dried at 105°C for 3 hours, and dissolve in diluted methanol (1 in 2) to make exactly 20 mL. Pipet 2 mL of the solution, add diluted methanol (1 in 2) to make exactly 100 mL, and use this solution as the standard solution. Pipet 10 μL each of the sample solution and the standard solution, and perform the test as directed under the Liquid Chromatography according to the following conditions. Determine the peak areas, A_{TE} and A_{TP}, of ephedrine and pseudoephedrine (the relative retention time to ephedrine is about 0.9) in the sample solution, and the peak area, A_S, of ephedrine in the standard solution.

Amount (mg) of total alkaloids (ephedrine and pseudoephedrine)
= amount (mg) of ephedrine hydrochloride for assay
$\times \frac{A_{TE} + A_{TP}}{A_S} \times \frac{1}{10} \times 0.819$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 210 nm).

Column: A stainless steel column 4 to 6 mm in inside diameter and 15 to 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 to 10 μm in particle diameter).

Column temperature: A constant temperature of about 45°C.

Mobile phase: A mixture of a solution of sodium lauryl sulfate (1 in 128), acetonitrile and phosphoric acid (640: 360:1).

Flow rate: Adjust the flow rate so that the retention time of ephedrine is about 14 minutes.

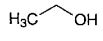
Selection of column: Dissolve 1 mg of ephedrine hydrochloride for assay and 4 mg of Atropine Sulfate in diluted methanol (1 in 2) to make 100 mL. Perform the test with 10 μL of this solution under the above operating conditions. Use a column giving elution of ephedrine and atropine in this order, clearly dividing each peak.

System repeatability: Repeat the test 6 times with the standard solution under the above operating conditions: the relative standard deviation of the peak area of ephedrine is not more than 1.5%.

Ethanol

Alcohol

エタノール



C_2H_6O: 46.07
Ethanol [*64-17-5*]

Ethanol contains not less than 95.1 vol% and not more than 95.6 vol% (by specific gravity) of C_2H_6O at 15°C.

Description Ethanol is a clear, colorless liquid. It has a characteristic odor and a burning taste.

It is miscible with water and with diethyl ether.

It is flammable and burns with a light blue flame on igni-