

Phenytoin Powder

Diphenylhydantoin Powder

フェニトイン散

Phenytoin Powder contains not less than 95% and not more than 105% of the labeled amount of phenytoin ($C_{15}H_{12}N_2O_2$; 252.27).

Method of preparation Prepare as directed under Powders, with Phenytoin.

Identification Weigh a portion of Phenytoin Powder, equivalent to 0.3 g of Phenytoin according to the labeled amount, stir well with two 100-mL portions of diethyl ether, and extract. Combine the diethyl ether extracts, and filter. Evaporate the filtrate on a water bath to dryness, and proceed with the residue as directed in the Identification under Phenytoin.

Assay Weigh accurately Phenytoin Powder, equivalent to about 0.5 g of phenytoin ($C_{15}H_{12}N_2O_2$), add exactly 100 mL of ethanol (95), stir for 30 minutes, and centrifuge. Pipet 50 mL of the supernatant liquid, add 0.5 mL of thymolphthalein TS, titrate with 0.1 mol/L sodium hydroxide VS until a light blue color develops, then add 1 mL of pyridine, 5 drops of phenolphthalein TS and 12.5 mL of silver nitrate TS, and titrate with 0.1 mol/L sodium hydroxide VS until a light red color persists for 1 minute.

$$\begin{aligned} \text{Each mL of 0.1 mol/L sodium hydroxide VS} \\ = 25.227 \text{ mg of } C_{15}H_{12}N_2O_2 \end{aligned}$$

Containers and storage Containers—Well-closed containers.

Phenytoin Tablets

Diphenylhydantoin Tablets

フェニトイン錠

Phenytoin Tablets contain not less than 95% and not more than 105% of the labeled amount of phenytoin ($C_{15}H_{12}N_2O_2$; 252.27).

Method of preparation Prepare as directed under Tablets, with Phenytoin.

Identification Proceed with the residue obtained in the Assay as directed in the Identification under Phenytoin.

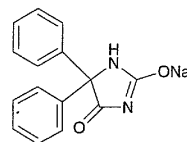
Assay Weigh accurately and powder not less than 20 Phenytoin Tablets. Weigh accurately a portion of the powder, equivalent to about 0.3 g of phenytoin ($C_{15}H_{12}N_2O_2$), transfer to a separator, and add 1 mL of dilute hydrochloric acid and 10 mL of water. Extract with 100 mL of diethyl ether, then with four 25-mL portions of diethyl ether. Combine the extracts, and evaporate the diethyl ether. Dry the residue at 105°C for 2 hours, and weigh it as the mass of phenytoin ($C_{15}H_{12}N_2O_2$).

Containers and storage Containers—Well-closed containers.

Phenytoin Sodium for Injection

Diphenylhydantoin Sodium for Injection

注射用フェニトインナトリウム



$C_{15}H_{11}N_2NaO_2$: 274.25
Monosodium 5,5-diphenyl-4-oxoimidazolidin-2-olate
[630-93-3]

Phenytoin Sodium for Injection is a preparation for injection which is dissolved before use. When dried, it contains not less than 98.5% of phenytoin sodium ($C_{15}H_{11}N_2NaO_2$), and contains not less than 92.5% and not more than 107.5% of the labeled amount of phenytoin sodium ($C_{15}H_{11}N_2NaO_2$).

Method of preparation Prepare as directed under Injections.

Description Phenytoin Sodium for Injection occurs as white crystals or crystalline powder. It is odorless.

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

The pH of a solution of Phenytoin Sodium for Injection (1 in 20) is about 12.

It is hygroscopic.

A solution of Phenytoin Sodium for Injection absorbs carbon dioxide gradually when exposed to air, and a crystalline precipitate of phenytoin is produced.

Identification (1) With the residue obtained in the Assay, proceed as directed in the Identification under Phenytoin.

(2) Ignite 0.5 g of Phenytoin Sodium for Injection, cool, and dissolve the residue in 10 mL of water: the solution changes red litmus paper to blue, and responds to the Qualitative Tests (1) for sodium salt.

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Phenytoin Sodium for Injection in 20 mL of freshly boiled and cooled water in a glass-stoppered test tube: the solution is clear and colorless. If any turbidity is produced, add 4.0 mL of 0.1 mol/L sodium hydroxide VS: the solution becomes clear and colorless.

(2) Heavy metals—Proceed with 1.0 g of Phenytoin Sodium for Injection 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).

Loss on drying Not more than 2.5% (1 g, 105°C, 4 hours).

Assay Weigh accurately the content of not less than 10 preparations of Phenytoin Sodium for Injection, transfer about 0.3 g of the content, previously dried and accurately weighed, to a separator, dissolve in 50 mL of water, add 10 mL of dilute hydrochloric acid, and extract with 100 mL of diethyl ether, then with four 25-mL portions of diethyl ether. Combine the diethyl ether extracts, and evaporate on a water bath. Dry the residue at 105°C for 2 hours, and

weigh it as the mass of phenytoin ($C_{15}H_{12}N_2O_2$: 252.27).

Amount (mg) of phenytoin sodium ($C_{15}H_{11}N_2NaO_2$)
= amount (mg) of phenytoin ($C_{15}H_{12}N_2O_2$) \times 1.0871

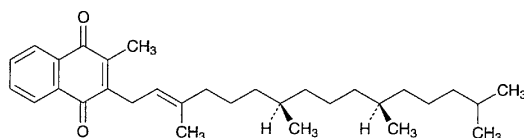
Containers and storage Containers—Hermetic containers.

Phytonadione

Phytomenadione

Vitamin K₁

フィトナジオン



$C_{31}H_{46}O_2$: 450.70

2-Methyl-3-[(2*E*,7*R*,11*R*)-3,7,11,15-tetramethylhexadec-2-en-1-yl]-1,4-naphthoquinone [84-80-0]

Phytonadione contains not less than 97.0% and not more than 102.0% of $C_{31}H_{46}O_2$.

Description Phytonadione is a clear yellow to orange-yellow, viscous liquid. It is odorless.

It is miscible with diethyl ether and with isooctane.

It is sparingly soluble in methanol and in ethanol (95), and practically insoluble in water.

It decomposes gradually and darkens by light.

Specific gravity d_{20}^{20} : about 0.967

Identification (1) Dissolve 0.05 g of Phytonadione in 10 mL of ethanol (95), and add 1 mL of a solution of potassium hydroxide in ethanol (95) (1 in 10): a blue color develops and changes to purple, then to brown upon standing.

(2) Dissolve 0.05 g of Phytonadione in 10 mL of a mixture of methanol and diethyl ether (1:1), add a freshly prepared solution of 0.75 g of sodium hydrosulfite in 2 mL of warm water, and shake vigorously: a yellow color disappears immediately.

(3) Determine the absorption spectrum of a solution of Phytonadione in isooctane (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 1: both spectra exhibit similar intensities of absorption at the same wavelengths. Separately, determine the absorption spectrum of a solution of Phytonadione in isooctane (1 in 10,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 2: both spectra exhibit similar intensities of absorption at the same wavelengths.

Refractive index n_D^{20} : 1.525 – 1.529

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Phytonadione in 10 mL of isooctane: the solution is clear, and shows a yellow color.

(2) Ratio of absorbances—Determine the absorbances, A_1 , A_2 and A_3 , of a solution of Phytonadione in isooctane (1 in 100,000) at 248.5 nm, 253.5 nm and 269.5 nm, respec-

tively: the ratio A_2/A_1 is between 0.69 and 0.73, and the ratio A_2/A_3 is between 0.74 and 0.78. Determine the absorbances, A_4 and A_5 , of a solution of Phytonadione in isooctane (1 in 10,000) at 284.5 nm and 326.0 nm, respectively: the ratio A_4/A_5 is between 0.28 and 0.34.

(3) Heavy metals—Carbonize 1.0 g of Phytonadione by gentle heating. Cool, add 10 mL of a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 10), and ignite the ethanol to burn. Cool, add 1 mL of sulfuric acid, proceed according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(4) Menadione—Dissolve 0.020 g of Phytonadione in 0.5 mL of a mixture of water and ethanol (95) (1:1), add 1 drop of a solution of 3-methyl-1-phenyl-5-pyrazolone in ethanol (95) (1 in 20) and 1 drop of ammonia solution (28), and allow to stand for 2 hours: no blue-purple color develops.

Assay Perform the test quickly under the protection from sunlight. Weigh accurately about 0.1 g of Phytonadione, dissolve in isooctane to make exactly 100 mL. Measure exactly 10 mL of this solution, and add isooctane to make exactly 100 mL. Pipet 10 mL of this solution, and add isooctane to make exactly 100 mL. Determine the absorbance A of this solution at the wavelength of maximum absorption at about 248.5 nm, as directed under the Ultraviolet-visible Spectrophotometry, adjusting the slit of the spectrophotometer to a band width of 0.5 nm.

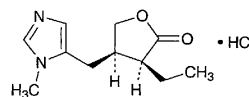
$$\text{Amount (mg) of } C_{31}H_{46}O_2 = \frac{A}{422} \times 100,000$$

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Pilocarpine Hydrochloride

塩酸ピロカルピン



$C_{11}H_{16}N_2O_2 \cdot HCl$: 244.72

(3*S*,4*R*)-3-Ethyldihydro-4-(1-methyl-1*H*-imidazol-5-ylmethyl)furan-2(3*H*)-one monohydrochloride [54-71-7]

Pilocarpine Hydrochloride, when dried, contains not less than 99.0% of $C_{11}H_{16}N_2O_2 \cdot HCl$.

Description Pilocarpine Hydrochloride occurs as colorless crystals or white powder. It is odorless, and has a slightly bitter taste.

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

The pH of a solution of Pilocarpine Hydrochloride (1 in 10) is between 3.5 and 4.5.

It is hygroscopic.

It is affected by light.

Identification (1) Dissolve 0.1 g of Pilocarpine