भारतीय भेषज संहिता आयोग
स्वास्थ्य एवं परिवार कल्याण मंत्रालय, भारत सरकार
सैक्टर २३, राज नगर
गाज़ियाबाद २०१००२ (उ. प्र.), भारत

INDIAN PHARMACOPOEIA COMMISSION
Ministry of Health & Family Welfare, Government of India
Sector 23, Raj Nagar
Ghaziabad 201002 (U.P.), INDIA

डा. राजीव सिंह रघुवंशी
सचिव-सह-वैज्ञानिक निदेशक

Dr. Rajeev Singh Raghuvanshi
Secretary-cum-Scientific Director

F. No. T.11015/01/2020-AR&D

Date: May 9, 2025

NOTICE

Subject: Publication of Monographs on 'Prussian Blue Insoluble' and 'Prussian Blue Insoluble and Magnesium Hydroxide Capsules' in the IP 2022-reg.

The 9th Edition of Indian Pharmacopoeia (IP) 2022 has become effective from 1st December, 2022. In continuation, following monographs are being published for their inclusion in the IP 2022 (copy enclosed) so as to take effect immediately:

1. Prussian Blue Insoluble
2. Prussian Blue Insoluble and Magnesium Hydroxide Capsules

All concerned are requested to bring it to the notice of all authorities under their control for its compliance.

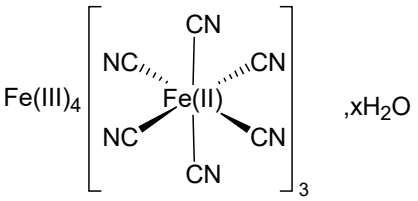
(Dr. Rajeev Singh Raghuvanshi)

Encl. Monographs of 'Prussian Blue Insoluble' and 'Prussian Blue Insoluble and Magnesium Hydroxide Capsules'

To,

1. The Drugs Controller General (India)
2. All State Drug Controllers
3. CDSCO Zonal Offices
4. Members of the Scientific Body of the IPC
5. Directors of the Drugs Testing Laboratories
6. IDMA/OPPI/BDMA/FOPE/FSSAI/Small Scale Industry Associations

Prussian Blue Insoluble



$C_{18}Fe_7N_{18},xH_2O$ Mol. Wt. 859.2 (anhydrous)

Prussian Blue Insoluble is insoluble ferric hexacyanoferrate(II).

Prussian Blue Insoluble contains not less than 30.0 per cent of Fe, calculated on the dried basis.

Category. Antidote for radioactive and nonradioactive cesium and thallium.

Description. A dark blue granular powder.

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *prussian blue insoluble IPRS* or with the reference spectrum of prussian blue insoluble.

B. Moisten 0.1 g of the substances with 1 ml of *water* and add gradually while shaking 1 ml of *1 M sodium hydroxide*; A reddish-brown precipitate is formed within 10 minutes of incubation.

Tests

Solution A. Dissolve 100.0 g of the substance under examination in 40 ml of *hydrochloric acid*, heat to boiling, cool and add 80 ml of *water*, filter, wash the filtrate and residue with *water* and dilute the filtrate and washing to 200.0 ml with *water*.

Chlorides (2.3.12). 25 ml of solution A complies with the limit test for chlorides (20 ppm).

Potassium (2.3.16). 20 ml of solution A complies with the limit test for potassium (20 ppm).

Sulphates (2.3.17). 30 ml of solution A complies with the limit test for sulphates (10 ppm).

Ferricyanide. Not more than 200 ppm.

Transfer 8.0 ml of solution A to three separate 50-ml volumetric flasks, marked as test, reference and blank solution, add 1.0 ml of *ferricyanide standard solution (50 ppm $Fe(CN)_6$)* to the volumetric flask marked as reference solution. Add 1.0 ml of a 0.5 per cent w/v solution of *ferrous ammonium sulphate* to each volumetric flask and dilute to volume with *water*. Allow to stand for 30 minutes. Measure the absorbance of the resulting solutions at the maximum at about 720 nm (2.4.7) using blank solution as compensation liquid. The absorbance obtained with the test solution is not more than the absorbance obtained with the reference solution.

Ferrocyanide. Not more than 200 ppm.

Transfer 20.0 ml of solution A to three separate 50-ml volumetric flasks, marked as test, reference and blank solution, add 2.0 ml of *ferrocyanide standard solution (100 ppm $Fe(CN)_6$)* to the volumetric flasks marked as reference solution. Add 1.0 ml of *ferric chloride solution* to the volumetric flasks marked as test solution and reference solution and dilute to volume with *water*. Allow to stand for 30 minutes. Measure the absorbances of the resulting solutions at the maximum at about 695 nm (2.4.7) using blank solution as compensation liquid. The absorbance obtained with the test solution is not more than the absorbance obtained with the reference solution.

Maximum binding capacity. Not less than 300 mg per g for Cs. Determine by atomic absorption spectrophotometry (2.4.2), measuring at 852.12 nm using caesium lamp.

Buffer solution. Dissolve 12.8 g of *dipotassium hydrogen orthophosphate* and 3.6 g of *potassium dihydrogen orthophosphate* in 1000 ml with *water*, adjusted to pH 7.5 with *dilute orthophosphoric acid* or *dilute sodium hydroxide solution*.

Reference solution (a) (Caesium (Cs) 1500 ppm). Dissolve 1.9005 g of *caesium chloride* in 1000.0 ml of the buffer solution.

Reference solution (b) (Caesium (Cs) 600 ppm). Dilute 20.0 ml of reference solution (a) to 50.0 ml with the buffer solution.

Reference solution (c) (Caseium (Cs) 750 ppm). Dilute 25.0 ml of reference solution (a) to 50.0 ml with the buffer solution.

Reference solution (d) (Caesium (Cs) 900 ppm). Dilute 30.0 ml of reference solution (a) to 50.0 ml with the buffer solution.

Reference solution (e) (Caesium (Cs) 1200 ppm). Dilute 40.0 ml of reference solution (a) to 50.0 ml with the buffer solution.

Procedure. Transfer 50.0 ml, each of, reference solution (a), reference solution (b), reference solution (c), reference solution (d) and reference solution (e) to five separate 250-ml volumetric flasks. Add 100 mg of substance under examination to each of the volumetric flask. Incubate the mixture for 24 hours with constant shaking at 25°. After 24 hours, filter the solutions and aspirate to AAS.

Measure caesium (Cs) concentrations in all the solutions using caesium lamp at 852.12 nm (2.4.2).

Calculate maximum binding capacity by Langmuir adsorption isotherm model. Ce and qe is calculated and a graph is plotted.

$$\frac{Ce}{qe} = \frac{Ce}{qm} + \left(\frac{1}{qm} \times \frac{1}{KL} \right)$$

where,

Ce (mg per litre) = Concentration of caesium (Cs) at equilibrium,

qe (mg per liter) = Amount of caesium (Cs) adsorbed at equilibrium,

qm (mg per g) = Maximum binding capacity of adsorbent,

KL (L per mg) = Constant related to energy of adsorption.

Plot the line between Ce/qe vs Ce and from which the constants qm and KL are calculated.

Cyanide. Not more than 400 µg per g at pH 1 with 24 hours of dwelling time.

Buffer solution. Dissolve 12.8 g of *dipotassium hydrogen orthophosphate* and 3.6 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 7.5 with *dilute orthophosphoric acid* or *dilute sodium hydroxide solution*.

Pyridine barbituric acid reagent. Dissolve 6 g of *barbituric acid* in minimum volume of *water* and add 30 ml of *pyridine* and mix. Add 6 ml of *hydrochloric acid*, mix and cool to room temperature, dilute to 100 ml with *water*.

Solution A. Dissolve 410 g of *sodium acetate* in 500 ml of *water*, adjusted to pH 4.5 with *glacial acetic acid* and dilute to 1000 ml with *water*.

Test solution. Weigh and transfer 1 g of the substance under examination to a 100-ml volumetric flask, add 50 ml of the buffer solution and incubate in a shaking water-bath at 37° with 75 shakes per minute for 24 hours, filter. Transfer 10.0 ml of the filtrate to 50-ml volumetric flask.

Reference solution. Dissolve 0.251 g of *potassium cyanide* in *water* and dilute to 100.0 ml with *water*. This solution contains 1 µg cyanide (CN) per ml.

Transfer 1.0 ml, 2.0 ml, 3.0 ml, 4.0 ml, 5.0 ml, 6.0 ml, 7.0 ml, 8.0 ml, 9.0 ml and 10.0 ml of the solution to separate 50-ml volumetric flasks (containing cyanide (CN) from 0.02 to 0.2 µg per ml).

Blank solution. Pipette 10 ml of *water* into a 50-ml volumetric flask.

Procedure. To each volumetric flask of the reference solutions, test solution and blank solution, add 1.0 ml of solution A and 1.0 ml *chloramine T solution*, mix. Add 5.0 ml of pyridine barbituric acid reagent and dilute to volume with *water*. Stand for 10 minutes. Measure the absorbances of reference solutions and test solution at 578 nm (2.4.7) using blank solution as compensation liquid.

Plot the reference solution curve on the abscissa and concentration of the cyanide on the ordinate.

Calculate the cyanide concentration as follows from slope and intercept of reference solution drawn.

$$\text{CN (mg per litre)} = (\text{Slope} \times A_1 + \text{intercept}) \times \frac{50}{W} \times \frac{250}{Y}$$

where, A_1 = Absorbance of test solution,

W = Weight of the substance under examination,

Y = Volume of test solution taken for colourimetric.

Loss on drying (2.4.19). Not more than 10.0 per cent, determined on 1.0 g by drying in an oven at 105° for 3 hours.

Assay. Determine by atomic absorption spectrophotometry (2.4.2), measuring at 248 nm using iron lamp.

Test solution. Weigh and transfer 10 mg of the substance under examination to a 25-ml volumetric flask, add 10 ml of *1 M sodium hydroxide* and mix with constant stirring followed by 10 minutes of incubation at room temperature, a reddish-brown precipitate is formed, allow for sedimentation. Collect the clear supernatant liquid into a measuring cylinder (solution A).

To the sedimented precipitate, add 10 ml of *hydrochloric acid* and heat until solution turns clear (solution B).

Both solution A and solution B are analyzed for Iron content after appropriate dilution using atomic absorption spectrophotometry (2.4.2).

The sum of the Iron content in solution A and solution B gives the total iron content.

Storage. Store at a temperature not exceeding 30°.

Prussian Blue Insoluble and Magnesium Hydroxide Capsules

Prussian Blue Insoluble and Magnesium Hydroxide Capsules contain not less than 30.0 per cent of Fe, calculated on the dried basis and not less than 90.0 per cent and not more than 110.0 per cent of magnesium hydroxide, $Mg(OH)_2$.

Usual strength. Prussian Blue Insoluble 340 mg and Magnesium Hydroxide 500 mg.

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *prussian blue insoluble IPRS* or with the reference spectrum of prussian blue insoluble.

B. Moisten 0.1 g of the mixed contents of capsules with 1 ml of *water* and add gradually while shaking 1 ml of *1 M sodium hydroxide*. A reddish-brown precipitate is formed within 10

minutes of incubation.

Tests

Disintegration (2.5.1). Not more than 30 minutes.

Cyanide. Not more than 400 µg per g at pH 1 with 27 hours of dwelling time.

Buffer solution. Dissolve 12.8 g of *dipotassium hydrogen orthophosphate* and 3.6 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 7.5 with *dilute orthophosphoric acid* or *dilute sodium hydroxide solution*.

Pyridine barbituric acid reagent. Dissolve 6 g of *barbituric acid* in minimum volume of *water*, add 30 ml of *pyridine* and mix. Add 6 ml of *hydrochloric acid*, mix and cool to room temperature, dilute to 100 ml with *water*.

Solution A. Dissolve 410 g of *sodium acetate* in 500 ml of *water*, adjusted to pH 4.5 with *glacial acetic acid* and dilute to 1000 ml with *water*.

Test solution. Weigh and transfer 1 g of mixed contents of 20 capsules to a 100-ml volumetric flask, add 50 ml of the buffer solution and incubate in a shaking water-bath at 37° with 75 shakes per minute for 24 hours, filter. Transfer 10.0 ml of the filtrate to 50-ml volumetric flask.

Reference solution. Dissolve 0.251 g of *potassium cyanide* in *water* and dilute to 100.0 ml with *water*. This solution contains 1 µg cyanide (CN) per ml.

Transfer 1.0 ml, 2.0 ml, 3.0 ml, 4.0 ml, 5.0 ml, 6.0 ml, 7.0 ml, 8.0 ml, 9.0 ml and 10.0 ml of the solution to separate 50-ml volumetric flask (containing cyanide (CN) from 0.02 to 0.2 µg per ml).

Blank solution. Pipette 10 ml of *water* into a 50-ml volumetric flask.

Procedure. To each volumetric flask of the reference solutions, test solution and blank solution, add 1.0 ml of solution A and 1.0 ml *chloramine T solution*, mix. Add 5.0 ml of pyridine barbituric acid reagent and dilute to volume with *water*. Stand for 10 minutes. Measure the absorbances of reference solution and test solution at 578 nm (2.4.7) using blank solution as compensation liquid.

Plot the reference solution curve on the abscissa and concentration of the cyanide on the ordinate.

Calculate the cyanide concentration as follows from slope and intercept of reference solution drawn.

$$\text{CN (mg per liter)} = (\text{Slope} \times A_1 + \text{intercept}) \times \times \frac{50}{W} \times \frac{250}{Y}$$

where, A_1 = Absorbance of test solution,
W = Weight of the substance under examination,
Y = Volume of test solution taken for colourimetric.

Maximum binding capacity. Not less than 300 mg per g for Cs. Determine by atomic absorption spectrophotometry (2.4.2), measuring at 852.12 nm using caesium lamp.

Buffer solution. Dissolve 12.8 g of *dipotassium hydrogen orthophosphate* and 3.6 g of *potassium dihydrogen orthophosphate* in 1000 ml with *water*, adjusted to pH 7.5 with *dilute orthophosphoric acid* or *dilute sodium hydroxide solution*.

Reference solution (a) (Caesium (Cs) 1500 ppm). Dissolve 1.9005 g of *caesium chloride* in 1000.0 ml of the buffer solution.

Reference solution (b) (Caesium (Cs) 600 ppm). Dilute 20.0 ml of reference solution (a) to 50.0 ml with the buffer solution.

Reference solution (c) (Caseium (Cs) 750 ppm). Dilute 25.0 ml of reference solution (a) to 50.0 ml with the buffer solution.

Reference solution (d) (Caesium (Cs) 900 ppm). Dilute 30.0 ml of reference solution (a) to 50.0 ml with the buffer solution.

Reference solution (e) (Caesium (Cs) 1200 ppm). Dilute 40.0 ml of reference solution (a) to 50.0 ml with the buffer solution.

Procedure. Transfer 50.0 ml, each of, reference solution (a), reference solution (b), reference solution (c), reference solution (d) and reference solution (e) to five separate 250-ml volumetric flasks. Add one capsule to each of the volumetric flask. Incubate the mixture for 24 hours with constant shaking at 25°. After 24 hours, filter the solution and aspirate to AAS.

Measure caesium (Cs) concentrations in all the solutions using caesium lamp at 852.12 nm (2.4.2).

Calculate maximum binding capacity by Langmuir adsorption isotherm model. Ce and qe is calculated and a graph is plotted.

$$\frac{Ce}{qe} = \frac{Ce}{qm} + \left(\frac{1}{qm} \times \frac{1}{KL} \right)$$

where,

Ce (mg per litre) = Concentration of caesium (Cs) at equilibrium,
qe (mg per liter) = Amount of caesium (Cs) adsorbed at equilibrium,
qm (mg per g) = Maximum binding capacity of adsorbent,
KL (L per mg) = Constant related to energy of adsorption.

Plot the line between Ce/qe Vs Ce and from which the constants qm and KL are calculated.

Loss on drying (2.4.19). Not more than 10.0 per cent, determined on 1.0 g by drying in an oven at 105° for 60 minutes.

Assay.

For Iron — Determine by atomic absorption spectrophotometry (2.4.2), measuring at 248 nm using iron lamp.

Test solution. Weigh and transfer the mixed contents of 20 capsules containing 10 mg of Prussian Blue Insoluble into a 25-ml volumetric flask, add 10 ml of *1 M sodium hydroxide* and mix it with constant stirring followed by 10 minutes of incubation at room temperature, a reddish-brown precipitate is formed and allow for sedimentation. After sedimentation of precipitates, the supernatant is collected in a measuring cylinder (solution A). Add 10 ml of *hydrochloric acid* to the sedimented precipitate and heat until a clear solution is obtained (solution B).

Reference solution (a). Dissolve 7.022 g of *ferrous ammonium sulphate* in 25 ml of *sulphuric acid* and dilute to 1000.0 ml with *water*.

Reference solution (b). Dilute 0.2 ml of reference solution (a) to 100.0 ml with 2.5 per cent v/v solution of *nitric acid*.

Reference solution (c). Dilute 0.4 ml of reference solution (a) to 100.0 ml with 2.5 per cent v/v solution of *nitric acid*.

Reference solution (d). Dilute 0.6 ml of reference solution (a) to 100.0 ml with 2.5 per cent v/v solution of *nitric acid*.

Reference solution (e). Dilute 0.8 ml of reference solution (a) to 100.0 ml with 2.5 per cent v/v solution of *nitric acid*.

Reference solution (f). Dilute 1.0 ml of reference solution (a) to 100.0 ml with 2.5 per cent v/v solution of *nitric acid*.

Measure the absorbance of reference solution A and solution B at 248 nm using atomic absorption spectrophotometry (2.4.2).

Calculate the total iron content in the capsules by adding iron content in solution A and solution B.

For Magnesium Hydroxide — Weigh and transfer the mixed contents of 20 capsules containing about 0.5 g of Magnesium Hydroxide to a 250-ml conical flask, add 50 ml of *0.5 M sulphuric acid*. Titrate with *1 M sodium hydroxide*, using *methyl orange solution* as an indicator. Carry out a blank titration.

1 ml of *0.5 M sulphuric acid* is equivalent to 0.02916 g of $Mg(OH)_2$.