Cyanocobalamini (57Co) solution

**DEFINITION**

Cyanocobalamin (57Co) solution is a solution of [57Co]-α-(5,6-dimethylbenzimidazol-1-yl)cobamide cyanide and may contain a stabiliser and an antimicrobial preservative. Cobalt-57 is a radioactive isotope of cobalt and may be produced by the irradiation of nickel with protons of suitable energy. Cyanocobalamin (57Co) may be prepared by the growth of suitable micro-organisms on a medium containing (57Co) cobaltous ion. The solution contains not less than 90.0 per cent and not more than 110.0 per cent of the declared cobalt-57 radioactivity at the date stated on the label. Not less than 90 per cent of the cobalt-57 is in the form of cyanocobalamin.

**CHARACTERS**

A clear, colourless or slightly pink solution. Cobalt-57 has a half-life of 271 days and emits gamma radiation.

**IDENTIFICATION**

A. Record the gamma-ray spectrum using a suitable instrument. The spectrum does not differ significantly from that of a standardised cobalt-57 solution. Standardised cobalt-57 and cobalt-58 solutions are available from laboratories recognised by the competent authority. The most prominent gamma photon of cobalt-57 has an energy of 0.122 MeV.

B. Examine the chromatograms obtained in the test for radiochemical purity. The principal peak in the radiochromatogram obtained with the solution to be examined has a retention time similar to that of the peak in the chromatogram obtained with the reference solution.

**TESTS**

**pH** (2.2.3). The pH of the solution is 4.0 to 6.0.

**RADIONUCLIDIC PURITY**

Record the gamma-ray spectrum using a suitable instrument calibrated with the aid of standardised cobalt-57 and cobalt-58 solutions. The spectrum does not differ significantly from that of the standardised cobalt-57 solution. Determine the relative amounts of cobalt-57, cobalt-56 and cobalt-58 present. Cobalt-56 has a half-life of 78 days and its presence is shown by gamma photons of energy 0.847 MeV. Cobalt-58 has a half-life of 70.8 days and its presence is shown by gamma photons of energy 0.811 MeV. Not more than 0.1 per cent of the total radioactivity is due to cobalt-56, cobalt-58 and other radionuclidic impurities.

**RADIOCHEMICAL PURITY**

Examine by liquid chromatography (2.2.29).

**Reference solution**. Dissolve 10 mg of cyanocobalamin CRS in the mobile phase and dilute to 100 ml with the mobile phase. Dilute 2 ml of the solution to 100 ml with the mobile phase. Use within 1 h.

**Test solution**. Dissolve 10 mg of cyanocobalamin CRS in 1.0 ml of water R and allow to stand for 10 min. Centrifuge at 2000 r/min for 10 min. Use the supernatant.

The chromatographic procedure may be carried out using:

- a stainless steel column 0.25 m long and 4 mm in internal diameter packed with octylsilyl silica gel for chromatography R (5 µm),
- as mobile phase at a flow rate of 1.0 ml/min a mixture prepared as follows: mix 26.5 volumes of methanol R and 73.5 volumes of a 10 g/l solution of disodium hydrogen phosphate R adjusted to pH 3.5 using phosphoric acid R and use within 2 days,
- a radioactivity detector adjusted for cobalt-57,
- as detector a spectrophotometer set at 361 nm,
- a loop injector.

Inject 100 µl of the test solution and record the chromatogram for three times the retention time of cyanocobalamin. Determine the peak areas and calculate the percentage of cobalt-57 present as cyanocobalamin. Inject 100 µl of the reference solution and record the chromatogram for 30 min.

**RADIOACTIVITY**

The average radioactivity determined in the test for uniformity of content is not less than 90.0 per cent and not more than 110.0 per cent of the declared cobalt-57 radioactivity, at the date stated on the label.

**STORAGE**

Store in an airtight container, protected from light, at a temperature of 2 °C to 8 °C.
Cobalt-58 has a half-life of 70.9 days and emits beta (β-) radiation and gamma radiation.

**CHARACTERS**

Hard gelatin capsules.

Cobalt-58 has a half-life of 70.9 days and emits beta (β-), as well as gamma radiation.

**IDENTIFICATION**

A. Record the gamma-ray spectrum using a suitable instrument. The spectrum does not differ significantly from that of a standardised cobalt-58 solution.

B. Examine the chromatograms obtained in the test for radiochemical purity. The principal peak in the radiochromatogram obtained with the test solution has a retention time similar to that of the peak in the chromatogram obtained with the reference solution.

**RADIOACTIVITY**

Measure the radioactivity using suitable counting equipment by comparison with a standardised cobalt-58 solution.

**STORAGE**

Store protected from light at a temperature of 2 °C to 8 °C.

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**CYANOCOBALAMIN (58Co) CAPSULES**

**Cyanocobalamin (58Co) capsules**

**DEFINITION**

Cyanocobalamin (58Co) capsules contain [58Co]-α-(5,6-dimethylbenzimidazol-1-yl)cobamide cyanide and may contain suitable auxiliary substances. Cobalt-58 is a radioactive isotope of cobalt and may be produced by neutron irradiation of nickel. Cyanocobalamin (58Co) may be prepared by the growth of suitable micro-organisms on a medium containing (58Co) cobaltous ion. Not less than 84 per cent of the cobalt-58 is in the form of cyanocobalamin. The capsules comply with the requirements for hard capsules in the monograph on Capsules (0016), unless otherwise justified and authorised. The average radioactivity is not less than 90.0 per cent and not more than 110.0 per cent of the declared cobalt-58 radioactivity at the date stated on the label.

**CHARACTERS**

Hard gelatin capsules.

Cobalt-58 has a half-life of 70.9 days and emits beta (β-) radiation and gamma radiation.

**TESTS**

**Disintegration.** The capsules comply with the test for disintegration of tablets and capsules (2.9.1) except that one capsule is used in the test instead of six.

**Uniformity of content.** Determine by measurement in a suitable counting assembly and under identical geometrical conditions the radioactivity of each of not less than ten capsules. Calculate the average radioactivity per capsule. The radioactivity of no capsule differs by more than 10 per cent from the average. The relative standard deviation is less than 3.5 per cent.

**RADIONUCLIDIC PURITY**

Record the gamma-ray spectrum using a suitable instrument calibrated with the aid of standardised cobalt-58, cobalt-57 and cobalt-60 solutions. The spectrum does not differ significantly from that of the standardised cobalt-58 solution.

Standardised cobalt-58, cobalt-57 and cobalt-60 solutions are available from laboratories recognised by the competent authority. Determine the relative amounts of cobalt-58, cobalt-57 and cobalt-60 present. Cobalt-58 has a half-life of 272 days and its presence is shown by gamma photons of energy 0.122 MeV. Cobalt-60 has a half-life of 5.27 years and its presence is shown by gamma photons of energies 1.173 MeV and 1.333 MeV. Not more than 1 per cent of the total radioactivity is due to cobalt-60 and not more than 2 per cent of the total radioactivity is due to cobalt-57, cobalt-60 and other radionuclidic impurities.

**RADIOCHEMICAL PURITY**

Examine by liquid chromatography (2.2.29). Test solution. Dissolve the contents of a capsule in 1.0 ml of water R and allow to stand for 10 min. Centrifuge at 2000 r/min for 10 min. Use the supernatant.

Reference solution. Dissolve 10 mg of cyanocobalamin CRS in the mobile phase and dilute to 100 ml with the mobile phase. Dilute 2 ml of the solution to 100 ml with the mobile phase. Use within 1 h of preparation.

The chromatographic procedure may be carried out using:

- a stainless steel column 0.25 m long and 4 mm in internal diameter packed with octylsilyl silica gel for chromatography R (5 µm),
- as mobile phase at a flow rate of 1.0 ml/min a mixture prepared as follows: mix 26.5 volumes of methanol R and 73.5 volumes of a 10 g/l solution of disodium hydrogen phosphate R adjusted to pH 3.5 with phosphoric acid R and use within 2 days,

a radioactivity detector adjusted for cobalt-58,
a detector a spectrophotometer set at 361 nm,
a loop injector.

Inject 100 µl of the test solution and record the chromatogram for three times the retention time of cyanocobalamin. Determine the peak areas and calculate the percentage of cobalt-58 present as cyanocobalamin. Inject 100 µl of the reference solution and record the chromatogram for 30 min.

**STORAGE**

Store in an airtight container, protected from light, at a temperature of 2 °C to 8 °C.