

Long Acting Barbiturates- BY LIPSA SAMAL

Phenobarbitone

Identification

Test A may be omitted if tests B, C, D and E are carried out. Tests C, D and E may be omitted if tests A and B are carried out.

A. Determine by infrared absorption spectrophotometry. Compare the spectrum with that obtained with phenobarbitone RS or with the reference spectrum of phenobarbitone.

B. Determine the melting point of the substance under examination and of a mixture of equal quantities of the substance under examination and phenobarbitone RS. The difference between the melting points, which are about 175° , is not greater than 2° .

C. Complies with the test for identification of barbiturates

D. Dissolve about 20 mg in 5 ml of ethanol, add a drop of cobalt chloride solution and a drop of dilute ammonia solution; a violet colour is produced.

E. Gives the reaction of non-nitrogen substituted barbiturates.

Assay.

Weigh accurately about 0.1 g, dissolve in 5 ml of pyridine, add 0.25 ml of thymolphthalein solution and 10 ml of silver nitrate-pyridine reagent and titrate with 0.1 M ethanolic sodium hydroxide until a pure blue colour is obtained. Repeat the operation without the substance under examination. The difference between the titrations represents the amount of sodium hydroxide required. 1 ml of 0.1 M ethanolic sodium hydroxide is equivalent to 0.01161 g of $C_{12}H_{12}N_2O_3$.

Phenobarbitone Sodium

A. Dissolve 0.2 g in 20 ml of ethanol (50 per cent), acidify with dilute hydrochloric acid and extract with 50 ml of ether. Wash the ether layer with 10 ml of water, dry over anhydrous

sodium sulphate and filter. Evaporate the filtrate to dryness and dry the residue at 105° .

On the residue, determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with phenobarbitone RS or with the reference spectrum of phenobarbitone.

B. Determine the melting point (2.4.21), of the residue obtained in test A and of a mixture of equal quantities of the residue and phenobarbitone RS. The difference between the melting points, which are about 175° , is not greater than 2° .

C. Complies with the test for identification of barbiturates but using the following solutions.

Test solution. A 0.1 per cent w/v solution of the substance under examination in ethanol (50 per cent). Reference solution. A 0.09 per cent w/v solution of phenobarbitone RS in ethanol (50 per cent).

D. 1 g dissolves completely in 20 ml of ethanol (90 per cent) (distinction from barbitone sodium).

E. Gives the reaction of non-nitrogen substituted barbiturates.

F. Ignite about 0.1 g; the residue gives the reactions of sodium.

Assay.

Weigh accurately about 0.15 g, dissolve in 2 ml of water and add 8 ml of 0.05 M sulphuric acid. Heat to boiling and cool. Add 30 ml of methanol and shake until dissolution is complete. Titrate with 0.1 M sodium hydroxide, determining the end-point potentiometrically. After the first inflection, stop the addition of the sodium hydroxide, add 10 ml of pyridine, mix and continue the titration until the second inflection is reached. The difference between the volumes represents the amount of sodium hydroxide required. 1 ml of 0.1 M sodium hydroxide is equivalent to 0.02542 g of $C_{12}H_{11}N_2NaO_3$.

Short Acting Barbiturate

Pentobarbitone

Identification

A. To 10 ml of a 10 per cent w/v solution add 5 ml of 2 M acetic acid; a white, crystalline precipitate is produced. Filter, wash the precipitate with water and dry at 105°. Determine the melting point of the dried precipitate (2.4.21). Mix equal parts of the dried precipitate and phenobarbitone RS and determine the melting point. The difference between the melting points (which are about 131°) is not greater than 2°.

B. Complies with the test for identification of barbiturates using the dried precipitate obtained in test A for preparing the test solution.

C. To 10 mg add 10 mg of vanillin and 2 ml of sulphuric acid, mix and heat on a water-bath for 2 minutes; a reddish-brown colour is produced. Cool and add 5 ml of ethanol; the colour changes to violet and then blue.

D. Ignite 1 g; the residue gives reaction A of sodium salts

Assay.

Weigh accurately about 0.4 g, dissolve in 25 ml of a 12.75 per cent w/v solution of silver nitrate in pyridine and titrate with 0.1 M ethanolic sodium hydroxide using 0.5 ml of thymolphthalein

solution as indicator, until a pure blue colour is obtained. Carry out a blank titration. 1 ml of 0.1 M ethanolic sodium hydroxide is equivalent to 0.02483 g of $C_{11}H_{17}N_2NaO_3$.

Pentobarbitone Tablet

Identification

A. Shake a quantity of the powdered tablets containing 0.1 g of Pentobarbitone Sodium with 10 ml of a 10 per cent w/v solution of pyridine and filter. Add to the filtrate 1 ml of cupric sulphate with pyridine solution and set aside for 10 minutes; a reddish violet precipitate is produced.

B. Shake a quantity of the powdered tablets containing 0.1 g of Pentobarbitone Sodium with 10 ml of water and filter. To the filtrate add 2 ml of hydrochloric acid; a white precipitate is produced (distinction from pentobarbitone).

C. The residue obtained in the Assay melts at 127° to 130° .

D. The powdered tablets, when moistened with hydrochloric acid and introduced on platinum wire into a flame, impart a yellow colour to the flame.

Assay.

Weigh and powder 20 tablets. Weigh accurately a quantity of the powder containing about 0.3 g of Pentobarbitone Sodium, dissolve as completely as possible in 10 ml of a 2 per cent w/v solution of sodium hydroxide saturate with sodium chloride, acidify with hydrochloric acid and extract with successive quantities, each of 15 ml, of ether until complete extraction is effected. Wash the combined extracts with two quantities, each of 2 ml, of water and extract the combined washings with 10 ml of ether. Add the ether to the main ether layer, filter and wash the filter with ether. Evaporate the solvent and dry the residue to constant weight at 105° . 1 g of residue is equivalent to 1.097 g of $C_{11}H_{17}N_2NaO_3$.

Ultra Short Acting Barbiturate

Thiopentone Sodium

Principle for IR

IRS involves absorption. The absorption of radiation depends on increasing the energy of vibration or rotation associated with a covalent bond in a molecule provided that such an increase in energy causes a change in the dipole moment of the molecule. To absorb IR

radiation a molecule must suffer a net change in its dipole moment due to vibration or rotation.

Identification

A. Acidify 10 ml of a 10 per cent w/v solution in carbon dioxide free water with 2 M hydrochloric acid; the solution effervesces. Shake the solution with 20 ml of ether, separate the ether layer, wash with 10 ml of water and dry over anhydrous sodium sulphate. Filter, evaporate the filtrate to dryness and dry the residue at 105°. On the residue, determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with thiopentone RS or with the reference spectrum of thiopentone.

B. Complies with the test for identification of barbiturates but using the following solutions. Test solution. A 0.1 per cent w/v solution of the substance under examination in water.

Reference solution. Dissolve 85 mg of thiopentone RS in 10 ml of 2 M sodium hydroxide and dilute to 100 ml with water.

C. Acidify 5 ml of a 5 per cent w/v solution with dilute acetic acid and filter. Wash the precipitate with water, recrystallise from water and dry at 70°; the crystals melt at about 160°.

D. Dissolve 1 mg of the crystals obtained in test A in 1 ml of 0.1 M sodium hydroxide. Add about 1 mg of sodium nitroprusside and, after 15 minutes, 1 ml of dilute hydrochloric acid; a reddish violet colour is produced.

E. Gives the reactions of sodium salts.

Assay.

For thiopentone — Weigh accurately about 0.15 g, dissolve in 5 ml of water, add 2 ml of 1 M sulphuric acid and extract with four quantities, each of 10 ml, of chloroform. Filter the combined chloroform extracts, evaporate the filtrate to dryness on a water-bath and dissolve the residue in 30 ml of dimethylformamide, previously neutralised with 0.1 M lithium methoxide. Titrate immediately with 0.1 M lithium methoxide, using 1 drop of a 0.2 per cent w/v solution of thymol blue in methanol as indicator, until a blue colour is obtained. Protect the solution from absorption of carbon dioxide during the titration. 1 ml of 0.1 M lithium methoxide is equivalent to 0.02423 g of C₁₁H₁₈N₂O₂S.

For sodium—Weigh accurately about 0.4 g, dissolve in 30 ml of water, add 1 drop of methyl red solution and titrate with 0.05 M sulphuric acid until the yellow colour changes to red. Boil gently for 2 minutes, cool and, if necessary, continue the titration with 0.05 M sulphuric acid until the red colour is restored. 1 ml of 0.05 M sulphuric acid is equivalent to 0.002299 g of Na.

Non Barbiturate

Alprazolam

Identification

A. Determine by infrared absorption spectrophotometry. Compare the spectrum with that obtained with alprazolam RS or with the reference spectrum of alprazolam.

B. Dissolve 10.0 mg in water and dilute to 500.0 ml with the same solvent. Dilute 20.0 ml of this solution to 100.0 ml with water. When examined in the range 210 nm to 360 nm the solution shows an absorption maximum at about 220 nm.

Assay. Determine by liquid chromatography. Test solution. Weigh accurately about 25 mg and dissolve in sufficient acetonitrile to produce 100.0 ml. Dilute 10.0 ml of this solution to 100.0 ml with acetonitrile. Reference solution. A solution containing 0.0025 per cent w/v of alprazolam RS in acetonitrile. Chromatographic system— a stainless steel column 25 cm x 4.6 mm, packed with porous silica particles 3 to 10 μm ,— mobile phase: a mixture of 850 volumes of acetonitrile, 80 volumes of chloroform, 50 volumes of 1-butanol, 20 volumes of water and 0.5 volume of glacial acetic acid, — flow rate. 2 ml per minute,

— spectrophotometer set at 254 nm, — a 10 μl or 20 μl loop injector. Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 2.0 per cent. Inject alternately the test solution and the reference solution.

Calculate the percentage content of $\text{C}_{17}\text{H}_{13}\text{ClN}_4$.