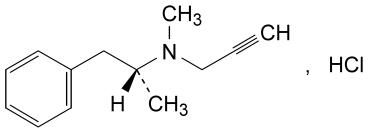
01/2008:1260

SELEGILINE HYDROCHLORIDE

Selegilini hydrochloridum



$C_{13}H_{18}ClN$ M_r 223.7
[14611-52-0]

DEFINITION

N-Methyl-*N*-[(1*R*)-1-methyl-2-phenylethyl]prop-2-yn-1-amine hydrochloride.

Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: freely soluble in water and in methanol, slightly soluble in acetone.

mp: about 143 °C.

IDENTIFICATION

A. Specific optical rotation (*2.2.7*): – 10.0 to – 12.0 (dried substance).

Dissolve 2.000g in *carbon dioxide-free water R* and dilute to 20.0 ml with the same solvent.

B. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs of *potassium chloride R*.

Comparison: *selegiline hydrochloride CRS*.

C. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

pH (*2.2.3*): 3.5 to 4.5.

Dissolve 0.20 g in *carbon dioxide-free water R* and dilute to 10 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 20 mg of the substance to be examined in the mobile phase and dilute to 10.0 ml with the mobile phase.

Reference solution (a). Dissolve 50.0 mg of *selegiline hydrochloride CRS* and 10.0 mg of *butyl parahydroxybenzoate R* in the mobile phase and dilute to 50.0 ml with the mobile phase. Dilute 1.0 ml of this solution to 20.0 ml with the mobile phase.

Reference solution (b). Dilute 1.0 ml of the test solution to 10.0 ml with the mobile phase. Dilute 1.0 ml of this solution to 50.0 ml with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;

– *stationary phase*: *octylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: dilute 500 ml of *acetonitrile R* to 1000.0 ml with a butylammonium acetate buffer solution pH 6.5 prepared as follows: dissolve 4 ml of *butylamine R* in 900 ml of *water R*, adjust to pH 6.5 with *acetic acid R* and dilute to 1000.0 ml with *water R*.

Flow rate: 1 ml/min.

Detection: spectrophotometer at 215 nm.

Injection: 20 µl.

Run time: 1.7 times the retention time of selegiline.

System suitability: reference solution (a):

– *resolution*: minimum 3 between the peaks due to selegiline and butyl parahydroxybenzoate.

Limits:

– *impurities A, B, C, D*: for each impurity, not more than the area of the peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

– *total*: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

– *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.02 per cent); disregard any peak due to chlorides.

Impurity E. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 20.0 mg of the substance to be examined in a mixture of 1 ml of *2-propanol R* and 10 µl of *butylamine R* and dilute to 10.0 ml with the mobile phase.

Reference solution (a). Dissolve 8.0 mg of *(RS)-selegiline hydrochloride CRS* in a mixture of 10 µl of *butylamine R* and 1 ml of *2-propanol R* and dilute to 10.0 ml with the mobile phase.

Reference solution (b). Dilute 0.5 ml of reference solution (a) to 20.0 ml with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;

– *stationary phase*: *silica gel OD for chiral separations R*.

Mobile phase: *2-propanol R, cyclohexane R* (0.2:99.8 *V/V*).

Flow rate: 1 ml/min.

Detection: spectrophotometer at 220 nm.

Injection: 20 µl.

Retention time: impurity E = about 10 min.

System suitability: reference solution (a):

– *resolution*: minimum 1.5 between the peaks due to impurity E and (*R*)-selegiline; if necessary, adjust the concentration of 2-propanol in the mobile phase.

Limit:

– *impurity E*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.5 per cent).

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying at 60 °C at a pressure not exceeding 0.5 kPa.

Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.180 g in 50 ml of *acetic anhydride R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

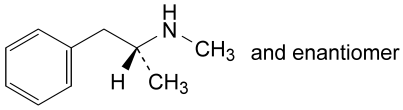
1 ml of *0.1 M perchloric acid* is equivalent to 22.37 mg of $C_{13}H_{18}ClN$.

STORAGE

Protected from light.

IMPURITIES

Specified impurities: A, B, C, D, E.

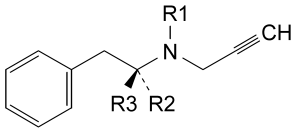


and enantiomer

A. (2*RS*)-*N*-methyl-1-phenylpropan-2-amine [(*RS*)-metamphetamine],

B. (2*R*)-1-phenylpropan-2-amine (amphetamine),

C. (1*RS*,2*SR*)-2-amino-1-phenylpropan-1-ol (phenylpropanolamine),



D. R1 = R3 = H, R2 = CH_3: *N*-[(1*R*)-1-methyl-2-phenylethyl]prop-2-yn-1-amine (demethylselegiline),

E. R1 = R3 = CH_3, R2 = H: *N*-methyl-*N*-[(1*S*)-1-methyl-2-phenylethyl]prop-2-yn-1-amine [(*S*)-selegiline].

01/2008:1147

SELENIUM DISULPHIDE

Selenii disulfidum

SeS_2 M_r 143.1
[7488-56-4]

DEFINITION

Content: 52.0 per cent to 55.5 per cent of Se.

CHARACTERS

Appearance: bright orange or reddish-brown powder.

Solubility: practically insoluble in water.

IDENTIFICATION

A. Gently boil about 50 mg with 5 ml of *nitric acid R* for 30 min. Dilute to 50 ml with *water R* and filter. To 5 ml of the filtrate add 10 ml of *water R* and 5 g of *urea R*. Heat to boiling, cool and add 1.5 ml of *potassium iodide solution R*. A yellow or orange colour is produced which darkens rapidly on standing. This solution is used in identification test B.

B. Allow the coloured solution obtained under identification A to stand for 10 min and filter through *kieselguhr for chromatography R*. 5 ml of the filtrate gives reaction (a) of sulphates (*2.3.1*).

TESTS

Soluble selenium compounds: maximum 5 ppm, calculated as Se.

To 10 g add 100 ml of *water R*, mix well, allow to stand for 1 h with frequent shaking and filter. To 10 ml of the filtrate add 2 ml of a 115 g/l solution of *anhydrous formic acid R*, dilute to 50 ml with *water R* and adjust to pH 2.0-3.0 with an 115 g/l solution of *anhydrous formic acid R*. Add 2 ml of a 5 g/l solution of *3,3′-diaminobenzidine tetrahydrochloride R*. Allow to stand for 45 min and then adjust to pH 6.0-7.0 with *dilute ammonia R1*. Shake the solution for 1 min with 10 ml of *toluene R* and allow the phases to separate. The absorbance (*2.2.25*) of the upper layer measured at 420 nm is not greater than that of a standard prepared at the same time and in the same manner beginning at the words “add 2 ml of an 115 g/l solution of *anhydrous formic acid R*” and using 5 ml of *selenium standard solution (1 ppm Se) R* instead of 10 ml of the filtrate.

ASSAY

To 0.100 g add 25 ml of *fuming nitric acid R* and heat on a water-bath for 1 h; a small insoluble residue may remain. Cool and dilute to 100.0 ml with *water R*. To 25.0 ml of this solution add 50 ml of *water R* and 5 g of *urea R* and heat to boiling. Cool, add 7 ml of *potassium iodide solution R* and 3 ml of *starch solution R*. Titrate immediately with *0.1 M sodium thiosulphate*. Carry out a blank titration.

1 ml of *0.1 M sodium thiosulphate* is equivalent to 1.974 mg of Se.

01/2008:0202

SENEGA ROOT

Polygalae radix

DEFINITION

Dried and usually fragmented root and root crown of *Polygala senega* L. or of certain other closely related species or of a mixture of these *Polygala* species.

CHARACTERS

Faint, sweet odour, slightly rancid or reminiscent of methyl salicylate.

Reduced to a powder, it is irritant and sternutatory. Shaken with water, the powder produces a copious froth.

IDENTIFICATION

A. The root crown is greyish-brown and wider than the root; it forms an irregular head consisting of numerous remains of stems and tightly packed purplish-brown buds. The taproot is brown or yellow, occasionally branched, sometimes flexuous, usually tortuous and without secondary roots, except in the Japanese varieties and species, which contain numerous fibrous rootlets. The diameter is usually 1-8 mm at the crown, gradually tapering to the tip; the surface is transversely and longitudinally striated and often shows a more or less distinct decurrent, elongated spiral keel. The fracture is short and shows a yellowish cortex of varying thickness surrounding a paler central woody area somewhat circular or irregular in shape depending on the species.

B. Examine under a microscope using *chloral hydrate solution R*. The transverse section of the root shows the following diagnostic characters: cork formed from several layers of thin-walled cells, phelloderm of slightly collenchymatous cells containing droplets of oil; the phloem and xylem arrangement is usually normal, especially near the crown but where a keel is present this is formed by increased development of phloem; other anomalous secondary development sometimes occurs, resulting in the formation of 1 or 2 large wedge-shaped rays in the phloem and xylem, the parenchymatous cells of which contain droplets of oil. The xylem is usually central and consists of vessels up to 60 µm in diameter associated with numerous thin-walled tracheids and a few small lignified parenchymatous cells.

C. Reduce to a powder (355) (*2.9.12*). The powder is light brown. Examine under a microscope using *chloral hydrate solution R*. The powder shows the following diagnostic characters: longitudinal fragments of lignified