ASSAY

Dissolve 0.150 g in 20 ml of *anhydrous acetic acid R*, heating to about 50 °C. Allow to cool. Titrate with *0.1 M perchloric acid* using 0.25 ml of *naphtholbenzein solution R* as indicator until a green colour is obtained.

1 ml of *0.1 M perchloric acid* is equivalent to 10.21 mg of $C_6H_5K_3O_7$.

STORAGE

In an airtight container.

01/2008:0920
corrected 6.3

POTASSIUM DIHYDROGEN PHOSPHATE

Kalii dihydrogenophosphas

KH_2PO_4 M_r 136.1
[7778-77-0]

DEFINITION

Content: 98.0 per cent to 100.5 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder or colourless crystals.

Solubility: freely soluble in water, practically insoluble in ethanol (96 per cent).

IDENTIFICATION

A. Solution S (see Tests) is faintly acid (*2.2.4*).

B. Solution S gives reaction (b) of phosphates (*2.3.1*).

C. 0.5 ml of solution S gives reaction (b) of potassium (*2.3.1*).

TESTS

Solution S. Dissolve 10.0 g in *carbon dioxide-free water R* prepared from *distilled water R* and dilute to 100 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

pH (*2.2.3*): 4.2 to 4.5.

To 5 ml of solution S add 5 ml of *carbon dioxide-free water R*.

Reducing substances. To 5 ml of solution S add 5 ml of *dilute sulphuric acid R* and 0.25 ml of *0.02 M potassium permanganate*. Heat on a water-bath for 5 min. The colour of the permanganate is not completely discharged.

Chlorides (*2.4.4*): maximum 200 ppm.

Dilute 2.5 ml of solution S to 15 ml with *water R*.

Sulphates (*2.4.13*): maximum 300 ppm.

To 5 ml of solution S add 0.5 ml of *hydrochloric acid R* and dilute to 15 ml with *distilled water R*.

Arsenic (*2.4.2, Method A*): maximum 2 ppm, determined on 0.5 g.

Iron (*2.4.9*): maximum 10 ppm, determined on solution S.

Sodium: maximum 0.10 per cent, if intended for use in the manufacture of parenteral dosage forms.

Atomic emission spectrometry (*2.2.22, Method I*).

Test solution. Dissolve 1.00 g of the substance to be examined in *water R* and dilute to 100.0 ml with the same solvent.

Reference solutions. Prepare the reference solutions using the following solution, diluted as necessary with *water R*: dissolve 0.5084 g of *sodium chloride R*, previously dried at 100-105 °C for 3 h, in *water R* and dilute to 1000.0 ml with the same solvent (200 µg of Na per millilitre).

Wavelength: 589 nm.

Heavy metals (*2.4.8*): maximum 10 ppm.

12 ml of solution S complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 2.0 per cent, determined on 1.000 g by drying in an oven at 125-130 °C.

ASSAY

Dissolve 1.000 g in 50 ml of *carbon dioxide-free water R*. Titrate with carbonate-free *1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*).

1 ml of *1 M sodium hydroxide* is equivalent to 0.1361 g of KH_2PO_4.

LABELLING

The label states, where applicable, that the substance is suitable for use in the manufacture of parenteral dosage forms.

01/2009:0355

POTATO STARCH

Solani amylum

DEFINITION

Potato starch is obtained from the tuber of *Solanum tuberosum* L.

CHARACTERS

Appearance: very fine, white or almost white powder which creaks when pressed between the fingers.

Solubility: practically insoluble in cold water and in ethanol (96 per cent).

Potato starch does not contain starch grains of any other origin. It may contain a minute quantity, if any, of tissue fragments of the original plant.

IDENTIFICATION

A. Examined under a microscope using a mixture of equal volumes of *glycerol R* and *water R*, it presents granules, either irregularly shaped, ovoid or pear-shaped, usually 30-100 µm in size but occasionally exceeding 100 µm, or rounded, 10-35 µm in size. There are occasional compound granules having 2-4 components. The ovoid and pear-shaped granules have an eccentric hilum and the rounded granules acentric or slightly eccentric hilum. All granules show clearly visible concentric striations. Between orthogonally orientated polarising plates or prisms, the granules show a distinct black cross intersecting at the hilum.

B. Suspend 1 g in 50 ml of *water R*, boil for 1 min and cool. A thick, opalescent mucilage is formed.

C. To 1 ml of the mucilage obtained in identification test B, add 0.05 ml of *iodine solution R1*. An orange-red to dark blue colour is produced which disappears on heating.

TESTS

pH (*2.2.3*): 5.0 to 8.0.

Shake 5.0 g with 25.0 ml of *carbon dioxide-free water R* for 60 s. Allow to stand for 15 min.

Foreign matter. Examined under a microscope using a mixture of equal volumes of *glycerol R* and *water R*, not more than traces of matter other than starch granules are present. No starch grains of any other origin are present.

Oxidising substances (*2.5.30*): maximum 20 ppm, calculated as H_2O_2.

Sulphur dioxide (*2.5.29*): maximum 50 ppm.

Iron (*2.4.9*): maximum 10 ppm.

Shake 1.5 g with 15 ml of *dilute hydrochloric acid R*. Filter. The filtrate complies with the limit test for iron.

Loss on drying (*2.2.32*): maximum 20.0 per cent, determined on 1.000 g by drying in an oven at 130 °C for 90 min.

Sulphated ash (*2.4.14*): maximum 0.6 per cent, determined on 1.0 g.

Microbial contamination

TAMC: acceptance criterion 10^3 CFU/g (*2.6.12*).

TYMC: acceptance criterion 10^2 CFU/g (*2.6.12*).

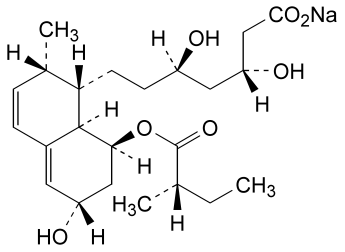
Absence of *Escherichia coli* (*2.6.13*).

Absence of *Salmonella* (*2.6.13*).

01/2009:2059

PRAVASTATIN SODIUM

Pravastatinum natricum



$C_{23}H_{35}NaO_7$ M_r 446.5
[81131-70-6]

DEFINITION

Sodium (3*R*,5*R*)-3,5-dihydroxy-7-[(1*S*,2*S*,6*S*,8*S*,8a*R*)-6-hydroxy-2-methyl-8-[[(2*S*)-2-methylbutanoyl]oxy]-1,2,6,7,8,8a-hexahydronaphthalen-1-yl]heptanoate.

Content: 97.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or yellowish-white powder or crystalline powder, hygroscopic.

Solubility: freely soluble in water and in methanol, soluble in anhydrous ethanol.

IDENTIFICATION

A. Specific optical rotation (see Tests).

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *Ph. Eur. reference spectrum of pravastatin sodium*.

C. 1 ml of solution S (see Tests) gives reaction (a) of sodium (*2.3.1*).

TESTS

Solution S. Dissolve 1.00 g in *carbon dioxide-free water R* and dilute to 20.0 ml with the same solvent.

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution BY_6 (*2.2.2, Method II*).

Dilute 2.0 ml of solution S to 10.0 ml with *water R*.

pH (*2.2.3*): 7.2 to 9.0 for solution S.

Specific optical rotation (*2.2.7*): + 153 to + 159 (anhydrous substance).

Dilute 2.0 ml of solution S to 20.0 ml with *water R*.

Related substances. Liquid chromatography (*2.2.29*).

Solvent mixture: *methanol R, water R* (9:11 *V/V*).

Test solution (a). Dissolve 0.1000 g of the substance to be examined in the solvent mixture and dilute to 100.0 ml with the solvent mixture.

Test solution (b). Dilute 10.0 ml of test solution (a) to 100.0 ml with the solvent mixture.

Reference solution (a). Dissolve the contents of a vial of *pravastatin impurity A CRS* in 1.0 ml of test solution (b).

Reference solution (b). Dilute 2.0 ml of test solution (a) to 100.0 ml with the solvent mixture. Dilute 1.0 ml of this solution to 10.0 ml with the solvent mixture.

Reference solution (c). Dissolve 12.4 mg of *pravastatin 1,1,3,3-tetramethylbutylamine CRS* in the solvent mixture and dilute to 100.0 ml with the solvent mixture.

Column:

– *size*: *l* = 0.15 m, Ø = 4.6 mm;
– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm);
– *temperature*: 25 °C.

Mobile phase: *glacial acetic acid R, triethylamine R, methanol R, water R* (1:1:450:550 *V/V/V/V*).

Flow rate: 1.3 ml/min.

Detection: spectrophotometer at 238 nm.

Injection: 10 µl of test solution (a) and reference solutions (a) and (b).

Run time: 2.5 times the retention time of pravastatin.

Relative retention with reference to pravastatin (retention time = about 21 min): impurity F = about 0.1; impurity B = about 0.2; impurity E = about 0.3; impurity A = about 0.6; impurity D = about 1.9; impurity C = about 2.1.

System suitability: reference solution (a):

– *resolution*: minimum 7.0 between the peaks due to impurity A and pravastatin.

Limits:

– *impurity A*: not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);
– *impurities B, C, D, E*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);