

Limit:

- *sum of the peaks with retention times less than that of the principal peak*: maximum 6.0 per cent.

Charged variants. Capillary electrophoresis (2.2.47).

Test solution (a). Prepare a solution of the substance to be examined containing 1 mg/ml of somatropin.

Test solution (b). Mix equal volumes of test solution (a) and the reference solution.

Reference solution. Dissolve the contents of a vial of *somatropin CRS* in *water R* and dilute with the same solvent to obtain a concentration of 1 mg/ml.

Capillary:

- *material*: uncoated fused silica;
- *size*: effective length = at least 70 cm, $\varnothing = 50\ \mu\text{m}$.

Temperature: 30 °C.

CZE buffer: 13.2 g/l solution of *ammonium phosphate R* adjusted to pH 6.0 with *phosphoric acid R* and filtered.

Detection: spectrophotometer at 200 nm.

Set the autosampler to store the samples at 4 °C during analysis.

Preconditioning of the capillary: rinse with 1 M *sodium hydroxide R* for 20 min, with *water R* for 10 min and with the CZE buffer for 20 min.

Between-run rinsing: rinse with 0.1 M *sodium hydroxide R* for 2 min and with the CZE buffer for 6 min.

Note: rinsing times may be adapted according to the length of the capillary and the equipment used.

Injection: test solution (a) and the reference solution; under pressure or vacuum, using the following sequence: sample injection for at least 3 s then CZE buffer injection for 1 s.

The injection time and pressure may be adapted in order to meet the system suitability criteria.

Migration: apply a field strength of 217 V/cm (20 kV for capillaries of 92 cm total length) for 80 min, using CZE buffer as the electrolyte in both buffer reservoirs.

Relative migration with reference to somatropin: deamidated forms = 1.02 to 1.11.

System suitability: reference solution:

- the electropherogram obtained is similar to the electropherogram of somatropin supplied with *somatropin CRS*; 2 peaks (I_1 , I_2) eluting prior to the principal peak and at least 2 peaks (I_3 , I_4) eluting after the principal peak are clearly visible.

Note: peak I_2 corresponds to the cleaved form and peak I_4 corresponds to the deamidated forms, eluting as a doublet.

Limits:

- *deamidated forms*: maximum 6.5 per cent;
- *any other impurity*: for each impurity, maximum 2.0 per cent;
- *total*: maximum 11.5 per cent.

Water (2.5.32): maximum 3.0 per cent, unless otherwise justified and authorised.

Bacterial endotoxins (2.6.14): less than 5 IU/mg.

ASSAY

Size-exclusion chromatography (2.2.30) as described in the test for dimer and related substances of higher molecular mass.

Calculate the content of somatropin ($\text{C}_{990}\text{H}_{1528}\text{N}_{262}\text{O}_{300}\text{S}_7$) from the declared content of $\text{C}_{990}\text{H}_{1528}\text{N}_{262}\text{O}_{300}\text{S}_7$ in *somatropin CRS*.

STORAGE

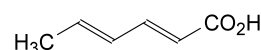
In a sterile, airtight, tamper-proof container, at a temperature of 2 °C to 8 °C.

LABELLING

The label states:

- the content of somatropin in the container, in milligrams;
- the composition and volume of the liquid to be added for reconstitution;
- the time within which the reconstituted solution shall be used and the storage conditions during this period;
- the name and quantity of any added substance;
- the storage temperature;
- that the preparation shall not be shaken during reconstitution.

01/2008:0592

SORBIC ACID**Acidum sorbicum**

$\text{C}_6\text{H}_8\text{O}_2$
[110-44-1]

M_r 112.1

DEFINITION

(*E,E*)-Hexa-2,4-dienoic acid.

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

CHARACTERS

Appearance: white or almost white, crystalline powder.

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

IDENTIFICATION

First identification: A, C.

Second identification: A, B, D.

A. Melting point (2.2.14): 132 °C to 136 °C.

B. Ultraviolet and visible absorption spectrophotometry (2.2.25).

Test solution. Dissolve 50.0 mg in *water R* and dilute to 250.0 ml with the same solvent. Dilute 2.0 ml of this solution to 200.0 ml with 0.1 M *hydrochloric acid*.

Spectral range: 230-350 nm.

Absorption maximum: at 264 nm.

Specific absorbance at the absorption maximum: 2150 to 2550.

C. Infrared absorption spectrophotometry (2.2.24).

Comparison: *sorbic acid CRS*.

D. Dissolve 0.2 g in 2 ml of *ethanol (96 per cent) R* and add 0.2 ml of *bromine water R*. The solution is decolorised.

TESTS

Solution S. Dissolve 1.25 g in *ethanol (96 per cent) R* and dilute to 25 ml with the same solvent.

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

Aldehydes: maximum 0.15 per cent, calculated as C_2H_4O . Dissolve 1.0 g in a mixture of 30 ml of *water R* and 50 ml of *2-propanol R*, adjust to pH 4 with 0.1 M *hydrochloric acid* or 0.1 M *sodium hydroxide* and dilute to 100 ml with *water R*. To 10 ml of this solution add 1 ml of *decolorised fuchsin solution R* and allow to stand for 30 min. Any colour in the solution is not more intense than that in a standard prepared at the same time by adding 1 ml of *decolorised fuchsin solution R* to a mixture of 1.5 ml of *acetaldehyde standard solution (100 ppm C_2H_4O) R*, 4 ml of *2-propanol R* and 4.5 ml of *water R*.

Heavy metals (2.4.8): maximum 10 ppm.

12 ml of solution S complies with test B. Prepare the reference solution using 5 ml of *lead standard solution (1 ppm Pb) R* and 5 ml of *ethanol (96 per cent) R*.

Water (2.5.12): maximum 1.0 per cent, determined on 2.000 g.

Sulphated ash (2.4.14): maximum 0.2 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.1000 g in 20 ml of *ethanol (96 per cent) R*. Using 0.2 ml of *phenolphthalein solution R* as indicator, titrate with 0.1 M *sodium hydroxide* until a pink colour is obtained.

1 ml of 0.1 M *sodium hydroxide* is equivalent to 11.21 mg of $C_{18}H_{34}O_2$.

STORAGE

Protected from light.

Composition of fatty acids. Gas chromatography (2.4.22, Method C).

Prepare reference solution (a) as indicated in tables 2.4.22-1 and 2.4.22-2.

Composition of the fatty acid fraction of the substance:

- *caproic acid*: maximum 1.0 per cent,
- *caprylic acid*: maximum 10.0 per cent,
- *capric acid*: maximum 10.0 per cent,
- *lauric acid*: 40.0 per cent to 60.0 per cent,
- *myristic acid*: 14.0 per cent to 25.0 per cent,
- *palmitic acid*: 7.0 per cent to 15.0 per cent,
- *stearic acid*: maximum 7.0 per cent,
- *oleic acid*: maximum 11.0 per cent,
- *linoleic acid*: maximum 3.0 per cent.

Heavy metals (2.4.8): maximum 10 ppm.

2.0 g complies with limit test D. Prepare the standard using 2 ml of *lead standard solution (10 ppm Pb) R*.

Water (2.5.12): maximum 1.5 per cent, determined on 1.00 g.

Total ash (2.4.16): maximum 0.5 per cent.

STORAGE

Protected from light.

01/2008:1041

SORBITAN OLEATE

Sorbitani oleas

01/2008:1040

SORBITAN LAURATE

Sorbitani lauras

DEFINITION

Mixture usually obtained by partial esterification of sorbitol and its mono- and di-anhydrides with lauric (dodecanoic) acid.

CHARACTERS

Appearance: brownish-yellow, viscous liquid.

Solubility: practically insoluble, but dispersible in water, miscible with alcohol.

Relative density: about 0.98.

IDENTIFICATION

- A. It complies with the test for hydroxyl value (see Tests).
- B. It complies with the test for iodine value (see Tests).
- C. It complies with the test for composition of fatty acids (see Tests).

TESTS

Acid value (2.5.1): maximum 7.0, determined on 5.0 g.

Hydroxyl value (2.5.3, Method A): 330 to 358.

Iodine value (2.5.4): maximum 10.

Peroxide value (2.5.5): maximum 5.0.

Saponification value (2.5.6): 158 to 170.

Carry out the saponification for 1 h.

DEFINITION

Mixture usually obtained by esterification of 1 mole of sorbitol and its mono- and di-anhydrides per mole of oleic (*cis*-9-octadecenoic) acid. A suitable antioxidant may be added.

CHARACTERS

Appearance: brownish-yellow, viscous liquid.

Solubility: practically insoluble but dispersible in water, soluble in fatty oils producing a hazy solution, miscible with alcohol.

Relative density: about 0.99.

IDENTIFICATION

- A. It complies with the test for hydroxyl value (see Tests).
- B. It complies with the test for iodine value (see Tests).
- C. It complies with the test for composition of fatty acids (see Tests).

Margaric acid: maximum 0.2 per cent for oleic acid of vegetable origin and maximum 4.0 per cent for oleic acid of animal origin.

TESTS

Acid value (2.5.1): maximum 8.0, determined on 5.0 g.

Hydroxyl value (2.5.3, Method A): 190 to 210.

Iodine value (2.5.4): 62 to 76.

Peroxide value (2.5.5): maximum 10.0.

Saponification value (2.5.6): 145 to 160.

Carry out the saponification for 1 h.