Source: iron hollow-cathode lamp.

Wavelength: 248.3 nm.

Atomisation device: air-acetylene flame.

Carry out a basic correction using a deuterium lamp.

Magnesium and alkali metals: maximum 0.4 per cent.

To 0.50 g add a mixture of 1.0 ml of *dilute acetic acid R* and 10.0 ml of *water R* and rapidly boil, whilst shaking, until completely dissolved. To the boiling solution add 5.0 ml of *ammonium oxalate solution R* and allow to stand for at least 6 h. Filter through a sintered-glass filter (1.6) (*2.1.2*) into a porcelain crucible. Carefully evaporate the filtrate to dryness and ignite. The residue weighs not more than 2 mg.

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*.

Bacterial endotoxins (*2.6.14*): less than 167 IU/g.

Microbial contamination

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

ASSAY

Dissolve 0.350 g in 20 ml of hot *water R*, allow to cool and dilute to 300 ml with *water R*. Carry out the complexometric titration of calcium (*2.5.11*). Use 50 mg of *calconecarboxylic acid triturate R*.

1 ml of *0.1 M sodium edetate* is equivalent to 44.84 mg of $C_{12}H_{22}CaO_{14},H_2O$.

01/2009:0882

CALCIUM STEARATE

Calcii stearas

DEFINITION

Mixture of calcium salts of different fatty acids consisting mainly of stearic (octadecanoic) acid [$(C_{17}H_{35}COO)_2Ca$; M_r 607] and palmitic (hexadecanoic) acid [$(C_{15}H_{31}COO)_2Ca$; M_r 550.9] with minor proportions of other fatty acids.

Content:

– *calcium*: 6.4 per cent to 7.4 per cent (A_r 40.08) (dried substance);
– *stearic acid in the fatty acid fraction*: minimum 40.0 per cent;
– *sum of stearic acid and palmitic acid in the fatty acid fraction*: minimum 90.0 per cent.

CHARACTERS

Appearance: fine, white or almost white, crystalline powder.

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

IDENTIFICATION

First identification: C, D.

Second identification: A, B, D.

A. Freezing point (*2.2.18*): minimum 53 °C, for the residue obtained in the preparation of solution S (see Tests).

B. Acid value (*2.5.1*): 195 to 210.

Dissolve 0.200 g of the residue obtained in the preparation of solution S in 25 ml of the prescribed mixture of solvents.

C. Examine the chromatograms obtained in the test for fatty acid composition.

Results: the retention times of the principal peaks in the chromatogram obtained with the test solution are approximately the same as those of the principal peaks in the chromatogram obtained with the reference solution.

D. Neutralise 5 ml of solution S to *red litmus paper R* using *strong sodium hydroxide solution R*. The solution gives reaction (b) of calcium (*2.3.1*).

TESTS

Solution S. To 5.0 g add 50 ml of *peroxide-free ether R*, 20 ml of *dilute nitric acid R* and 20 ml of *distilled water R*. Boil under a reflux condenser until dissolution is complete. Allow to cool. In a separating funnel, separate the aqueous layer and shake the ether layer with 2 quantities, each of 5 ml, of *distilled water R*. Combine the aqueous layers, wash with 15 ml of *peroxide-free ether R* and dilute the aqueous layer to 50 ml with *distilled water R* (solution S). Evaporate the ether layer to dryness and dry the residue at 100-105 °C. Keep the residue for identification tests A and B.

Acidity or alkalinity. To 1.0 g add 20 ml of *carbon dioxide-free water R* and boil for 1 min with continuous shaking. Cool and filter. To 10 ml of the filtrate add 0.05 ml of *bromothymol blue solution R1*. Not more than 0.5 ml of *0.01 M hydrochloric acid* or *0.01 M sodium hydroxide* is required to change the colour of the indicator.

Chlorides (*2.4.4*): maximum 0.1 per cent.

Dilute 0.5 ml of solution S to 15 ml with *water R*.

Sulphates (*2.4.13*): maximum 0.3 per cent.

Dilute 0.5 ml of solution S to 15 ml with *distilled water R*.

Cadmium: maximum 3.0 ppm.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution. Place 50.0 mg in a polytetrafluoroethylene digestion bomb and add 0.5 ml of a mixture of 1 volume of *hydrochloric acid R* and 5 volumes of *cadmium- and lead-free nitric acid R*. Allow to digest at 170 °C for 5 h. Allow to cool. Dissolve the residue in *water R* and dilute to 5.0 ml with the same solvent.

Reference solutions. Prepare the reference solutions using *cadmium standard solution (10 ppm Cd) R*, diluted if necessary with a 1 per cent *V/V* solution of *hydrochloric acid R*.

Source: cadmium hollow-cathode lamp.

Wavelength: 228.8 nm.

Atomisation device: graphite furnace.

Lead: maximum 10.0 ppm.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution. Use the solution described in the test for cadmium.

Reference solutions. Prepare the reference solutions using *lead standard solution (10 ppm Pb) R*, diluted if necessary with *water R*.

Source: lead hollow-cathode lamp.

Wavelength: 283.3 nm; 217.0 nm may be used depending on the apparatus.

Atomisation device: graphite furnace.

Nickel: maximum 5.0 ppm.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution. Use the solution described in the test for cadmium.

Reference solutions. Prepare the reference solutions using *nickel standard solution (10 ppm Ni) R*, diluted if necessary with *water R*.

Source: nickel hollow-cathode lamp.
Wavelength: 232.0 nm.
Atomisation device: graphite furnace.

Loss on drying (*2.2.32*): maximum 6.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

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*).

ASSAY

Calcium. To 0.500 g in a 250 ml conical flask add 50 ml of a mixture of equal volumes of *anhydrous ethanol R* and *butanol R*, 5 ml of *concentrated ammonia R*, 3 ml of *ammonium chloride buffer solution pH 10.0 R*, 30.0 ml of *0.1 M sodium edetate* and 15 mg of *mordant black 11 triturate R*. Heat to 45-50 °C until the solution is clear. Cool and titrate with *0.1 M zinc sulphate* until the colour changes from blue to violet. Carry out a blank titration.
1 ml of *0.1 M sodium edetate* is equivalent to 4.008 mg of Ca.

Composition of fatty acids. Gas chromatography (*2.2.28*): use the normalisation procedure.
Test solution. In a conical flask fitted with a reflux condenser, dissolve 0.10 g of the substance to be examined in 5 ml of *boron trifluoride-methanol solution R*. Boil under a reflux condenser for 10 min. Add 4 ml of *heptane R* through the condenser. Boil under a reflux condenser for 10 min. Allow to cool. Add 20 ml of a *saturated sodium chloride solution R*. Shake and allow the layers to separate. Remove about 2 ml of the organic layer and dry over 0.2 g of *anhydrous sodium sulphate R*. Dilute 1.0 ml of the solution to 10.0 ml with *heptane R*.
Reference solution. Prepare the reference solution in the same manner as the test solution using 50.0 mg of *palmitic acid CRS* and 50.0 mg of *stearic acid CRS* instead of calcium stearate.
Column:
– *material*: fused silica;
– *size*: *l* = 30 m, Ø = 0.32 mm;
– *stationary phase*: *macrogol 20 000 R* (film thickness 0.5 µm).
Carrier gas: *helium for chromatography R*.
Flow rate: 2.4 ml/min.
Temperature:

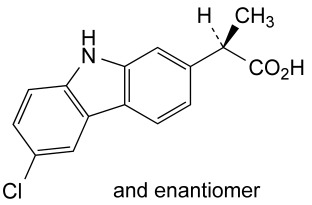
	Time (min)	Temperature (°C)
Column	0 - 2	70
	2 - 36	70 → 240
	36 - 41	240
Injection port		220
Detector		260

Detection: flame ionisation.
Injection: 1 µl.
Relative retention with reference to methyl stearate: methyl palmitate = about 0.88.
System suitability: reference solution:
– *resolution*: minimum 5.0 between the peaks due to methyl palmitate and methyl stearate.
Calculate the content of palmitic acid and stearic acid. Disregard the peak due to the solvent.

07/2008:2201
corrected 6.3

CARPROFEN FOR VETERINARY USE

Carprofenum ad usum veterinarium



$C_{15}H_{12}ClNO_2$ M_r 273.7
[53716-49-7]

DEFINITION
(2*RS*)-2-(6-Chloro-9*H*-carbazol-2-yl)propanoic acid.
Content: 98.5 per cent to 101.5 per cent (dried substance).

CHARACTERS
Appearance: white or almost white, crystalline powder.
Solubility: practically insoluble in water, freely soluble in acetone, soluble in methanol, slightly soluble in 2-propanol.
It shows polymorphism (*5.9*).

IDENTIFICATION
Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *carprofen CRS*.
If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in *acetone R*, evaporate to dryness and record new spectra using the residues.

TESTS

Appearance of solution. The solution is clear and not more intensely coloured than reference solution BY_3 (*2.2.2, Method II*).
Dissolve 1.0 g in *methanol R* and dilute to 25 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*). *Carry out the test protected from light.*
Test solution. Dissolve 50 mg of the substance to be examined in the mobile phase and dilute to 100.0 ml with the mobile phase.
Reference solution (a). Dissolve 2.5 mg of *carprofen for system suitability CRS* (containing impurity C) in the mobile phase and dilute to 10.0 ml with the mobile phase.
Reference solution (b). Dilute 1.0 ml of the test solution to 100.0 ml with the mobile phase. Dilute 1.0 ml of this solution to 10.0 ml with the mobile phase.
Column:
– *size*: *l* = 0.25 m, Ø = 4.6 mm;
– *stationary phase*: *end-capped polar-embedded octadecylsilyl amorphous organosilica polymer R* (5 µm).
Mobile phase: mix 30 volumes of a 1.36 g/l solution of *potassium dihydrogen phosphate R* adjusted to pH 3.0 with *phosphoric acid R* and 70 volumes of *methanol R2*.
Flow rate: 1.3 ml/min.
Detection: spectrophotometer at 235 nm.
Injection: 20 µl.
Run time: 4 times the retention time of carprofen.
Retention time: carprofen = about 10 min.