B. Dissolve about 15 mg in 2 ml of *dilute nitric acid R* and neutralise with *dilute sodium hydroxide solution R*. The solution gives the reaction of magnesium (*2.3.1*).

C. Loss on ignition (see Tests).

TESTS

Solution S. Dissolve 5.0 g in a mixture of 30 ml of *distilled water R* and 70 ml of *acetic acid R*, boil for 2 min, allow to cool and dilute to 100 ml with *dilute acetic acid R*. Filter, if necessary, through a previously ignited and tared porcelain or silica filter crucible of a suitable porosity to give a clear filtrate.

Appearance of solution. Solution S is not more intensely coloured than reference solution B_2 (*2.2.2, Method II*).

Soluble substances: maximum 2.0 per cent.

To 2.00 g add 100 ml of *water R* and boil for 5 min. Filter whilst hot through a sintered-glass filter (40) (*2.1.2*), allow to cool and dilute to 100 ml with *water R*. Evaporate 50 ml of the filtrate to dryness and dry at 100-105 °C. The residue weighs a maximum of 20 mg.

Substances insoluble in acetic acid: maximum 0.1 per cent.

Any residue obtained during the preparation of solution S, washed, dried, and ignited at 600 ± 50 °C, weighs a maximum of 5 mg.

Chlorides (*2.4.4*): maximum 0.15 per cent.

Dilute 0.7 ml of solution S to 15 ml with *water R*.

Sulphates (*2.4.13*): maximum 1.0 per cent.

Dilute 0.3 ml of solution S to 15 ml with *distilled water R*.

Arsenic (*2.4.2, Method A*): maximum 4 ppm, determined on 5 ml of solution S.

Calcium (*2.4.3*): maximum 1.5 per cent.

Dilute 1.3 ml of solution S to 150 ml with *distilled water R*. 15 ml of this solution complies with the test.

Iron (*2.4.9*): maximum 0.1 per cent.

Dissolve 50 mg in 5 ml of *dilute hydrochloric acid R* and dilute to 10 ml with *water R*. Dilute 2 ml of this solution to 10 ml with *water R*.

Heavy metals (*2.4.8*): maximum 30 ppm.

To 20 ml of solution S add 15 ml of *hydrochloric acid R1* and shake with 25 ml of *methyl isobutyl ketone R* for 2 min. Allow to stand, then separate and evaporate the aqueous layer to dryness. Dissolve the residue in 1.5 ml of *acetic acid R* and dilute to 30 ml with *water R*. 12 ml of the solution complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Loss on ignition: maximum 8.0 per cent, determined on 1.00 g at 900 ± 25 °C.

ASSAY

Dissolve 0.320 g in 20 ml of *dilute hydrochloric acid R* and dilute to 100.0 ml with *water R*. Using 20.0 ml of this solution, carry out the complexometric titration of magnesium (*2.5.11*).

1 ml of *0.1 M sodium edetate* is equivalent to 4.030 mg of MgO.

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MAGNESIUM STEARATE

Magnesii stearas

DEFINITION

Magnesium stearate is a mixture of magnesium salts of different fatty acids consisting mainly of stearic (octadecanoic) acid [$(C_{17}H_{35}COO)_2Mg$; M_r 591.3] and palmitic (hexadecanoic) acid [$(C_{15}H_{31}COO)_2$ Mg; M_r 535.1] with minor proportions of other fatty acids. It contains not less than 4.0 per cent and not more than 5.0 per cent of Mg (A_r 24.30), calculated with reference to the dried substance. The fatty acid fraction contains not less than 40.0 per cent of stearic acid and the sum of stearic acid and palmitic acid is not less than 90.0 per cent.

CHARACTERS

A white or almost white, very fine, light powder, greasy to the touch, practically insoluble in water and in ethanol.

IDENTIFICATION

First identification: C, D.

Second identification: A, B, D.

A. The residue obtained in the preparation of solution S (see Tests) has a freezing point (*2.2.18*) not lower than 53 °C.

B. The acid value of the fatty acids (*2.5.1*) is 195 to 210, determined on 0.200 g of the residue obtained in the preparation of solution S dissolved in 25 ml of the prescribed mixture of solvents.

C. Examine the chromatograms obtained in the test for fatty acid composition. 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. 1 ml of solution S gives the reaction of magnesium (*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* and heat 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 4 ml, of *distilled water R*. Combine the aqueous layers, wash with 15 ml of *peroxide-free ether R* and dilute to 50 ml with *distilled water R* (solution S). Evaporate the organic 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 stirring. 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*). 0.5 ml of solution S diluted to 15 ml with *water R* complies with the limit test for chlorides (0.1 per cent).

Sulphates (*2.4.13*). 0.3 ml of solution S diluted to 15 ml with *distilled water R* complies with the limit test for sulphates (0.5 per cent).

Cadmium. Not more than 3.0 ppm of Cd, determined by atomic absorption spectrometry (*2.2.23, Method II*).

Test solution. Place 50.0 mg of the substance to be examined 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 as necessary with a 1 per cent *V/V* solution of *hydrochloric acid R*.

Measure the absorbance at 228.8 nm, using a cadmium hollow-cathode lamp as a source of radiation and a graphite furnace as atomic generator.

Lead. Not more than 10.0 ppm of Pb, determined by 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 as necessary with *water R*.

Measure the absorbance at 283.3 nm, using a lead hollow-cathode lamp as a source of radiation and a graphite furnace as atomic generator, depending on the apparatus the line at 217.0 nm may be used.

Nickel. Not more than 5.0 ppm of Ni, determined by 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 as necessary with *water R*.

Measure the absorbance at 232.0 nm, using a nickel hollow-cathode lamp as a source of radiation and a graphite furnace as atomic generator.

Loss on drying (*2.2.32*). Not more than 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

Magnesium. To 0.500 g in a 250 ml conical flask add 50 ml of a mixture of equal volumes of *butanol R* and *ethanol 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 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 2.431 mg of Mg.

Fatty acid composition. Examine by gas chromatography (*2.2.28*).

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 and boil again 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 magnesium stearate.

The chromatographic procedure may be carried out using:

– a fused-silica column 30 m long and 0.32 mm in internal diameter coated with *macrogol 20 000 R* (film thickness 0.5 µm),

– *helium for chromatography R* as the carrier gas at a flow rate of 2.4 ml/min,

– a flame-ionisation detector,

with the following temperature programme:

	Time (min)	Temperature (°C)	Rate (°C/min)	Comment
Column	0 - 2	70	–	isothermal
	2 - 36	70 → 240	5	linear gradient
	36 - 41	240	–	isothermal
Injection port		220		
Detector		260		

Inject 1 µl of the reference solution. When the chromatogram is recorded in the prescribed conditions, the relative retention of methyl palmitate to that of methyl stearate is about 0.88. The test is not valid unless, in the chromatogram obtained with the reference solution, the resolution between the peaks corresponding to methyl stearate and methyl palmitate is at least 5.0.

Inject 1 µl of the test solution. Calculate the percentage content of stearic acid and palmitic acid from the areas of the peaks in the chromatogram obtained with the test solution by the normalisation procedure, disregarding the peak due to the solvent.

FUNCTIONALITY-RELATED CHARACTERISTICS

This section provides information on characteristics that are recognised as being relevant control parameters for one or more functions of the substance when used as an excipient (see chapter 5.15). This section is a non-mandatory part of the monograph and it is not necessary to verify the characteristics to demonstrate compliance. Control of these characteristics can however contribute to the quality of a medicinal product by improving the consistency of the manufacturing process and the performance of the medicinal product during use. Where control methods are cited, they are recognised as being suitable for the purpose, but other methods can also be used. Wherever results for a particular characteristic are reported, the control method must be indicated.

The following characteristic may be relevant for magnesium stearate used as a lubricant in solid dosage forms (compressed and powder).

Specific surface area (*2.9.26, Method I*). Determine the specific surface area in the P/P_o range of 0.05 to 0.15.

Sample outgassing: 2 h at 40 °C.