

Sodium: maximum 0.5 per cent.

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

Test solution. Dissolve 1.0 g in *water R* and dilute to 100 mL with the same solvent.

Reference solutions. Prepare the reference solutions using *sodium standard solution (200 ppm Na) R*, diluted as necessary with *water R*.

Wavelength: 589.0 nm.

Heavy metals (2.4.8): maximum 40 ppm.

Dissolve 1.0 g in *water R* and dilute to 20 mL with the same solvent. 12 mL of the solution complies with limit test A. Prepare the standard using *lead standard solution (2 ppm Pb) R*.

Readily oxidisable substances. Dissolve 2.0 g in 100 mL of boiling *water R*, add 6 mL of a 150 g/L solution of *sulfuric acid R* and 0.3 mL of 0.02 M *potassium permanganate*. Mix and boil gently for 5 min. The pink colour is not completely discharged.

Water (2.5.12): 33.0 per cent to 35.0 per cent, determined on 0.100 g.

ASSAY

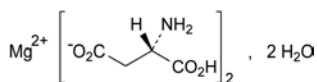
Dissolve 0.150 g in 300 mL of *water R*. Carry out the complexometric titration of magnesium (2.5.11).

1 mL of 0.1 M *sodium edetate* is equivalent to 14.24 mg of $C_4H_6MgO_4$.

01/2008:1445
corrected 6.0

MAGNESIUM ASPARTATE DIHYDRATE

Magnesii aspartas dihydricus



$C_8H_{12}MgN_2O_8 \cdot 2H_2O$

M_r 324.5

DEFINITION

Magnesium aspartate dihydrate contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of magnesium di[(S)-2-aminohydrogenobutane-1,4-dioate], calculated with reference to the anhydrous substance.

CHARACTERS

A white or almost white, crystalline powder or colourless crystals, freely soluble in water.

IDENTIFICATION

- Specific optical rotation (see Tests).
- Examine the chromatograms obtained in the test for ninhydrin-positive substances. The principal spot in the chromatogram obtained with test solution (b) is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (a).
- Ignite about 15 mg until a white residue is obtained. Dissolve the residue in 1 mL of *dilute hydrochloric acid R*, neutralise to *red litmus paper R* by the addition of *dilute sodium hydroxide solution R* and filter if necessary. The solution gives the reaction of magnesium (2.3.1).

TESTS

Solution S. Dissolve 2.5 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). The pH of solution S is 6.0 to 8.0.

Specific optical rotation (2.2.7). Dissolve 0.50 g in a 515 g/L solution of *hydrochloric acid R* and dilute to 25.0 mL with the same acid. The specific optical rotation is + 20.5 to + 23.0, calculated with reference to the anhydrous substance.

Ninhydrin-positive substances. Examine by thin-layer chromatography (2.2.27), using a *TLC silica gel plate R*.

Test solution (a). Dissolve 0.10 g of the substance to be examined in *water R* and dilute to 10 mL with the same solvent.

Test solution (b). Dilute 1 mL of test solution (a) to 50 mL with *water R*.

Reference solution (a). Dissolve 10 mg of *magnesium aspartate dihydrate CRS* in *water R* and dilute to 50 mL with the same solvent.

Reference solution (b). Dilute 5 mL of test solution (b) to 20 mL with *water R*.

Reference solution (c). Dissolve 10 mg of *magnesium aspartate dihydrate CRS* and 10 mg of *glutamic acid CRS* in 2 mL of *water R* and dilute to 25 mL with the same solvent.

Apply to the plate 5 µL of each solution. Allow the plate to dry in air. Develop over a path of 15 cm using a mixture of 20 volumes of *glacial acetic acid R*, 20 volumes of *water R* and 60 volumes of *butanol R*. Allow the plate to dry in air and spray with *ninhydrin solution R*. Heat at 100 °C to 105 °C for 15 min. Any spot in the chromatogram obtained with test solution (a), apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.5 per cent). The test is not valid unless the chromatogram obtained with reference solution (c) shows two clearly separated principal spots.

Chlorides (2.4.4). Dilute 10 mL of solution S to 15 mL with *water R*. The solution complies with the limit test for chlorides (200 ppm).

Sulfates (2.4.13). Dilute 12 mL of solution S to 15 mL with *distilled water R*. The solution complies with the limit test for sulfates (500 ppm). Carry out the evaluation of the test after 30 min.

Ammonium (2.4.1). 50 mg complies with limit test B for ammonium (200 ppm). Prepare the standard using 0.1 mL of *ammonium standard solution (100 ppm NH₄) R*.

Iron (2.4.9). In a separating funnel, dissolve 0.20 g in 10 mL of *dilute hydrochloric acid R*. Shake with three quantities, each of 10 mL, of *methyl isobutyl ketone R1*, shaking for 3 min each time. To the combined organic layers add 10 mL of *water R* and shake for 3 min. The aqueous layer complies with the limit test for iron (50 ppm).

Heavy metals (2.4.8). Dissolve 2.0 g with gentle heating in 20 mL of *water R*. 12 mL of the solution complies with limit test A for heavy metals (10 ppm). Prepare the standard using *lead standard solution (1 ppm Pb) R*.

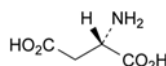
Water (2.5.12). 10.0 per cent to 14.0 per cent, determined on 0.100 g by the semi-micro determination of water. Dissolve the substance in 10 mL of *formamide R1* at 50 °C protected from moisture, add 10 mL of *anhydrous methanol R* and allow to cool. Carry out a blank determination.

ASSAY

Dissolve 0.260 g in 10 mL of *water R* and carry out the complexometric titration of magnesium (2.5.11).

1 mL of 0.1 M *sodium edetate* is equivalent to 28.85 mg of $C_8H_{12}MgN_2O_8$.

IMPURITIES



A. (2S)-2-aminobutanedioic acid (aspartic acid).

07/2008:0043
corrected 6.5**MAGNESIUM CARBONATE, HEAVY****Magnesii subcarbonas ponderosus****DEFINITION**

Hydrated basic magnesium carbonate.

Content: 40.0 per cent to 45.0 per cent, calculated as MgO (M_r 40.30).

CHARACTERS

Appearance: white or almost white powder.

Solubility: practically insoluble in water. It dissolves in dilute acids with effervescence.

IDENTIFICATION

- Bulk density (2.9.34): minimum 0.25 g/mL.
- It gives the reaction of carbonates (2.3.1).
- 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).

TESTS

Solution S. Dissolve 5.0 g in 100 mL of *dilute acetic acid R*. When the effervescence has ceased, 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 suitable porosity to give a clear filtrate.

Appearance of solution. Solution S is not more intensely coloured than reference solution B₄ (2.2.2, *Method II*).

Soluble substances: maximum 1.0 per cent.

Mix 2.00 g with 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 not more than 10 mg.

Substances insoluble in acetic acid: maximum 0.05 per cent.

Any residue obtained during the preparation of solution S, washed, dried, and ignited at 600 ± 50 °C, weighs not more than 2.5 mg.

Chlorides (2.4.4): maximum 700 ppm.

Dilute 1.5 mL of solution S to 15 mL with *water R*.

Sulfates (2.4.13): maximum 0.6 per cent.

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

Arsenic (2.4.2, *Method A*): maximum 2 ppm, determined on 10 mL of solution S.

Calcium (2.4.3): maximum 0.75 per cent.

Dilute 2.6 mL of solution S to 150 mL with *distilled water R*. 15 mL of the solution complies with the test.

Iron (2.4.9): maximum 400 ppm.

Dissolve 0.1 g in 3 mL of *dilute hydrochloric acid R* and dilute to 10 mL with *water R*. Dilute 2.5 mL of the solution to 10 mL with *water R*.

Heavy metals (2.4.8): maximum 20 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, separate the aqueous lower layer and evaporate to dryness. Dissolve the residue in 1 mL of *acetic acid R* and dilute to 20 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*.

ASSAY

Dissolve 0.150 g in a mixture of 2 mL of *dilute hydrochloric acid R* and 20 mL of *water R*. 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.

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 characteristics may be relevant for heavy magnesium carbonate used as filler in tablets.

Particle-size distribution (2.9.31 or 2.9.38).

Bulk and tapped density (2.9.34).

04/2009:0042

MAGNESIUM CARBONATE, LIGHT**Magnesii subcarbonas levis**

[546-93-0]

DEFINITION

Hydrated basic magnesium carbonate.

Content: 40.0 per cent to 45.0 per cent, calculated as MgO (M_r 40.30).

CHARACTERS

Appearance: white or almost white powder.

Solubility: practically insoluble in water. It dissolves in dilute acids with effervescence.

IDENTIFICATION

- Bulk density (2.9.34): maximum 0.15 g/mL.
- It gives the reaction of carbonates (2.3.1).
- 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).

TESTS

Solution S. Dissolve 5.0 g in 100 mL of *dilute acetic acid R*. When the effervescence has ceased, 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 suitable porosity to give a clear filtrate.

Appearance of solution. Solution S is not more intensely coloured than reference solution B₄ (2.2.2, *Method II*).

Soluble substances: maximum 1.0 per cent.

Mix 2.00 g with 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 10 mg.

Substances insoluble in acetic acid: maximum 0.05 per cent.

Any residue obtained during the preparation of solution S, washed, dried and ignited at 600 ± 50 °C, weighs a maximum of 2.5 mg.

Chlorides (2.4.4): maximum 700 ppm.

Dilute 1.5 mL of solution S to 15 mL with *water R*.

Sulfates (2.4.13): maximum 0.3 per cent.

Dilute 1 mL of solution S to 15 mL with *distilled water R*.