

From the line equation and the clot-lysis time for the test solution, calculate the logarithm of the activity  $U_A$  from the following equation:

$$\log U_A = \frac{[(\log t) - a]}{b}$$

Calculate the alteplase activity in International Units per millilitre from the following expression:

$$D \times U_A$$

in which  $D$  is the dilution factor for the test solution. Calculate the specific activity in the portion of the substance to be examined from the following expression:

$$\frac{U_A}{P}$$

in which  $P$  is the concentration of protein obtained in the test for protein content.

The estimated potency is not less than 90 per cent and not more than 110 per cent of the stated potency.

#### STORAGE

Store in a colourless, glass container, under vacuum or under an inert gas, protected from light, at a temperature of 2 °C to 30 °C.

#### LABELLING

The label states:

- the number of International Units per container;
- the amount of protein per container.

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## ALUM

### Alumen

$\text{AlK}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$   
[7784-24-9]

$M_r$  474.4

#### DEFINITION

*Content:* 99.0 per cent to 100.5 per cent of  $\text{AlK}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$ .

#### CHARACTERS

*Appearance:* granular powder or colourless, transparent, crystalline masses.

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

#### IDENTIFICATION

- A. Solution S (see Tests) gives the reactions of sulphates (2.3.1).
- B. Solution S gives the reaction of aluminium (2.3.1).
- C. Shake 10 ml of solution S with 0.5 g of *sodium bicarbonate R* and filter. The filtrate gives reaction (a) of potassium (2.3.1).

#### TESTS

**Solution S.** Dissolve 2.5 g in *water R* and dilute to 50 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):** 3.0 to 3.5.

Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 10 ml with the same solvent.

**Ammonium (2.4.1):** maximum 0.2 per cent.

To 1 ml of solution S add 4 ml of *water R*. Dilute 0.5 ml of this solution to 14 ml with *water R*.

**Iron (2.4.9):** maximum 100 ppm.

Dilute 2 ml of solution S to 10 ml with *water R*. Use in this test 0.3 ml of *thioglycollic acid R*.

**Heavy metals (2.4.8):** maximum 20 ppm.

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

#### ASSAY

Dissolve 0.900 g in 20 ml of *water R* and carry out the complexometric titration of aluminium (2.5.11).

1 ml of 0.1 M *sodium edetate* is equivalent to 47.44 mg of  $\text{AlK}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$ .

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## ALUMINIUM CHLORIDE HEXAHYDRATE

### Aluminii chloridum hexahydricum

$\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$   
[7784-13-6]

$M_r$  241.4

#### DEFINITION

*Content:* 95.0 per cent to 101.0 per cent.

#### CHARACTERS

*Appearance:* white or slightly yellow, crystalline powder or colourless crystals, deliquescent.

*Solubility:* very soluble in water, freely soluble in ethanol (96 per cent), soluble in glycerol.

#### IDENTIFICATION

- A. Dilute 0.1 ml of solution S2 (see Tests) to 2 ml with *water R*. The solution gives reaction (a) of chlorides (2.3.1).
- B. Dilute 0.3 ml of solution S2 to 2 ml with *water R*. The solution gives the reaction of aluminium (2.3.1).

#### TESTS

**Solution S1.** Dissolve 10.0 g in *distilled water R* and dilute to 100 ml with the same solvent.

**Solution S2.** Dilute 50 ml of solution S1 to 100 ml with *water R*.

**Appearance of solution.** Solution S2 is clear (2.2.1) and not more intensely coloured than reference solution B<sub>7</sub> (2.2.2, *Method II*).

**Sulphates (2.4.13):** maximum 100 ppm, determined on solution S1.

**Iron (2.4.9):** maximum 10 ppm, determined on solution S1.

**Alkali and alkaline-earth metals:** maximum 0.5 per cent. To 20 ml of solution S2 add 100 ml of *water R* and heat to boiling. To the hot solution add 0.2 ml of *methyl red solution R*. Add *dilute ammonia R1* until the colour of the indicator changes to yellow and dilute to 150 ml with *water R*. Heat to boiling and filter. Evaporate 75 ml of the filtrate to dryness on a water-bath and ignite to constant mass. The residue weighs a maximum of 2.5 mg.

**Heavy metals (2.4.8):** maximum 20 ppm.

12 ml of solution S1 complies with test A. Prepare the reference solution using *lead standard solution (2 ppm Pb) R*.

**Water (2.5.12):** 42.0 per cent to 48.0 per cent, determined on 50.0 mg.

#### ASSAY

Dissolve 0.500 g in 25.0 ml of *water R*. Carry out the complexometric titration of aluminium (2.5.11). Titrate with 0.1 M zinc sulphate until the colour of the indicator changes from greyish-green to pink. Carry out a blank titration.

1 ml of 0.1 M sodium edetate is equivalent to 24.14 mg of  $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$ .

#### STORAGE

In an airtight container.

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## ALUMINIUM HYDROXIDE, HYDRATED, FOR ADSORPTION

### Aluminii hydroxidum hydricum ad adsorptionem

$[\text{AlO}(\text{OH})]_n\text{H}_2\text{O}$

#### DEFINITION

**Content:** 90.0 per cent to 110.0 per cent of the content of aluminium stated on the label.

**NOTE:** shake the gel vigorously for at least 30 s immediately before examining.

#### CHARACTERS

**Appearance:** white or almost white, translucent, viscous, colloidal gel. A supernatant may be formed upon standing.

**Solubility:** a clear or almost clear solution is obtained with alkali hydroxide solutions and mineral acids.

#### IDENTIFICATION

Solution S (see Tests) gives the reaction of aluminium.

To 10 ml of solution S add about 0.5 ml of *dilute hydrochloric acid R* and about 0.5 ml of *thioacetamide reagent R*. No precipitate is formed. Add dropwise 5 ml of *dilute sodium hydroxide solution R*. Allow to stand for 1 h. A gelatinous white precipitate is formed which dissolves upon addition of 5 ml of *dilute sodium hydroxide solution R*. Gradually add 5 ml of *ammonium chloride solution R* and allow to stand for 30 min. The gelatinous white precipitate is re-formed.

#### TESTS

**Solution S.** Add 1 g to 4 ml of *hydrochloric acid R*. Heat at 60 °C for 1 h, cool, dilute to 50 ml with *distilled water R* and filter if necessary.

**pH (2.2.3):** 5.5 to 8.5.

**Adsorption power.** Dilute the substance to be examined with *distilled water R* to obtain an aluminium concentration of 5 mg/ml. Prepare *bovine albumin R* solutions with the following concentrations of bovine albumin: 0.5 mg/ml, 1 mg/ml, 2 mg/ml, 3 mg/ml, 5 mg/ml and 10 mg/ml. If necessary, adjust the gel and the *bovine albumin R* solutions to pH 6.0 with *dilute hydrochloric acid R* or *dilute sodium hydroxide solution R*.

For adsorption, mix 1 part of the diluted gel with 4 parts of each of the solutions of *bovine albumin R* and allow to stand at room temperature for 1 h. During this time shake the mixture vigorously at least 5 times. Centrifuge or filter through a non-protein-retaining filter. Immediately determine the protein content (2.5.33, *Method 2*) of either the supernatant or the filtrate.

It complies with the test if no bovine albumin is detectable in the supernatant or filtrate of the 2 mg/ml *bovine albumin R* solution (maximum level of adsorption) and in the supernatant or filtrate of *bovine albumin R* solutions of lower concentrations. Those containing 3 mg/ml, 5 mg/ml and 10 mg/ml *bovine albumin R* solutions may show bovine albumin in the supernatant or filtrate, proportional to the amount of bovine albumin in the solutions.

**Sedimentation.** If necessary, adjust the substance to be examined to pH 6.0 using *dilute hydrochloric acid R* or *dilute sodium hydroxide solution R*. Dilute with *distilled water R* to obtain an aluminium concentration of approximately 5 mg/ml. If the aluminium content of the substance to be examined is lower than 5 mg/ml, adjust to pH 6.0 and dilute with a 9 g/l solution of *sodium chloride R* to obtain an aluminium concentration of about 1 mg/ml. After shaking for at least 30 s, place 25 ml of the preparation in a 25 ml graduated cylinder and allow to stand for 24 h.

It complies with the test if the volume of the clear supernatant is less than 5 ml for the gel with an aluminium content of about 5 mg/ml.

It complies with the test if the volume of the clear supernatant is less than 20 ml for the gel with an aluminium content of about 1 mg/ml.

**Chlorides (2.4.4):** maximum 0.33 per cent.

Dissolve 0.5 g in 10 ml of *dilute nitric acid R* and dilute to 500 ml with *water R*.

**Nitrates:** maximum 100 ppm.

Place 5 g in a test-tube immersed in ice-water, add 0.4 ml of a 100 g/l solution of *potassium chloride R*, 0.1 ml of *diphenylamine solution R* and, dropwise with shaking, 5 ml of *sulphuric acid R*. Transfer the tube to a water-bath at 50 °C. After 15 min, any blue colour in the solution is not more intense than that in a standard prepared at the same time and in the same manner using 5 ml of *nitrate standard solution (100 ppm NO<sub>3</sub>) R*.

**Sulphates (2.4.13):** maximum 0.5 per cent.

Dilute 2 ml of solution S to 20 ml with *water R*.

**Ammonium (2.4.1, Method B):** maximum 50 ppm, determined on 1.0 g.

Prepare the standard using 0.5 ml of *ammonium standard solution (100 ppm NH<sub>4</sub>) R*.

**Arsenic (2.4.2, Method A):** maximum 1 ppm, determined on 1 g.

**Iron (2.4.9):** maximum 15 ppm, determined on 0.67 g.

**Heavy metals (2.4.8):** maximum 20 ppm.

Dissolve 2.0 g in 10 ml of *dilute nitric acid R* and dilute to 20 ml with *water R*. The solution complies with test A. Prepare the reference solution using *lead standard solution (2 ppm Pb) R*.

**Bacterial endotoxins (2.6.14):** less than 5 IU of endotoxin per milligram of aluminium, if intended for use in the manufacture of an adsorbed product without a further appropriate procedure for the removal of bacterial endotoxins.

#### ASSAY

Dissolve 10.00 g in 10 ml of *hydrochloric acid R1*, heating on a water-bath. Cool and dilute to 20 ml with *water R*. To 10 ml of the solution, add *dilute ammonia R1* until a precipitate is obtained. Add the smallest quantity of *dilute hydrochloric acid R* needed to dissolve the precipitate and dilute to 20 ml with *water R*. Carry out the complexometric titration of aluminium (2.5.11). Carry out a blank titration.