Bromides: maximum 100 ppm.

To 0.5 ml of solution S add 4.0 ml of *water R*, 2.0 ml of *phenol red solution R2* and 1.0 ml of a 0.1 g/l solution of *chloramine R* and mix immediately. After exactly 2 min, add 0.15 ml of *0.1 M sodium thiosulphate*, mix and dilute to 10.0 ml with *water R*. The absorbance (*2.2.25*) of the solution measured at 590 nm, using *water R* as the compensation liquid, is not greater than that of a standard prepared at the same time and in the same manner, using 5.0 ml of a 3.0 mg/l solution of *potassium bromide R*.

Ferrocyanides. Dissolve 2.0 g in 6 ml of *water R*. Add 0.5 ml of a mixture of 5 ml of a 10 g/l solution of *ferric ammonium sulphate R* in a 2.5 g/l solution of *sulphuric acid R* and 95 ml of a 10 g/l solution of *ferrous sulphate R*. No blue colour develops within 10 min.

Iodides. Moisten 5 g by the dropwise addition of a freshly prepared mixture of 0.15 ml of *sodium nitrite solution R*, 2 ml of *0.5 M sulphuric acid*, 25 ml of *iodide-free starch solution R* and 25 ml of *water R*. After 5 min, examine in daylight. The mixture shows no blue colour.

Nitrites. To 10 ml of solution S add 10 ml of *water R*. The absorbance (*2.2.25*) is not greater than 0.01 at 354 nm.

Phosphates (*2.4.11*): maximum 25 ppm.

Dilute 2 ml of solution S to 100 ml with *water R*.

Sulphates (*2.4.13*): maximum 200 ppm.

Dilute 7.5 ml of solution S to 30 ml with *distilled water R*.

Aluminium (*2.4.17*): maximum 0.2 ppm, if intended for use in the manufacture of peritoneal dialysis solutions, haemodialysis solutions or haemofiltration solutions.

Prescribed solution. Dissolve 20.0 g in 100 ml of *water R* and add 10 ml of *acetate buffer solution pH 6.0 R*.

Reference solution. Mix 2 ml of *aluminium standard solution (2 ppm Al) R*, 10 ml of *acetate buffer solution pH 6.0 R* and 98 ml of *water R*.

Blank solution. Mix 10 ml of *acetate buffer solution pH 6.0 R* and 100 ml of *water R*.

Arsenic (*2.4.2, Method A*): maximum 1 ppm, determined on 5 ml of solution S.

Barium. To 5 ml of solution S add 5 ml of *distilled water R* and 2 ml of *dilute sulphuric acid R*. After 2 h, any opalescence in the solution is not more intense than that in a mixture of 5 ml of solution S and 7 ml of *distilled water R*.

Iron (*2.4.9*): maximum 2 ppm, determined on solution S.

Prepare the standard using a mixture of 4 ml of *iron standard solution (1 ppm Fe) R* and 6 ml of *water R*.

Magnesium and alkaline-earth metals (*2.4.7*): maximum 100 ppm, calculated as Ca and determined on 10.0 g.

Use 150 mg of *mordant black 11 triturate R*. The volume of *0.01 M sodium edetate* used is not more than 2.5 ml.

Potassium: maximum 5.00×10^2 ppm, if intended for use in the manufacture of parenteral dosage forms or haemodialysis, haemofiltration or peritoneal dialysis solutions.

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

Test solution. Dissolve 1.00 g in *water R* and dilute to 100.0 ml with the same solvent.

Reference solutions. Dissolve 1.144 g of *potassium chloride R*, previously dried at 100-105 °C for 3 h, in *water R* and dilute to 1000.0 ml with the same solvent (600 µg of K per millilitre). Dilute as required.

Wavelength: 766.5 nm.

Heavy metals (*2.4.8*): maximum 5 ppm.

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

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 2 h.

Bacterial endotoxins (*2.6.14*): less than 5 IU/g, if intended for use in the manufacture of parenteral dosage forms without a further appropriate procedure for removal of bacterial endotoxins.

ASSAY

Dissolve 50.0 mg in *water R* and dilute to 50 ml with the same solvent. Titrate with *0.1 M silver nitrate* determining the end-point potentiometrically (*2.2.20*).

1 ml of *0.1 M silver nitrate* is equivalent to 5.844 mg of NaCl.

LABELLING

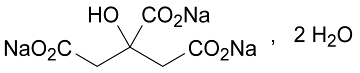
The label states:

- where applicable, that the substance is suitable for use in the manufacture of parenteral dosage forms,
- where applicable, that the substance is suitable for use in the manufacture of peritoneal dialysis solutions, haemodialysis solutions or haemofiltration solutions.

01/2008:0412
corrected 6.0

SODIUM CITRATE

Natrii citras



$C_6H_5Na_3O_7,2H_2O$ M_r 294.1
[6132-04-3]

DEFINITION

Trisodium 2-hydroxypropane-1,2,3-tricarboxylate dihydrate.

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

CHARACTERS

Appearance: white or almost white, crystalline powder or white or almost white, granular crystals, slightly deliquescent in moist air.

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

IDENTIFICATION

A. To 1 ml of solution S (see Tests) add 4 ml of *water R*. The solution gives the reaction of citrates (*2.3.1*).

B. 1 ml of solution S gives reaction (a) of sodium (*2.3.1*).

TESTS

Solution S. Dissolve 10.0 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*).

Acidity or alkalinity. To 10 ml of solution S add 0.1 ml of *phenolphthalein solution R*. Not more than 0.2 ml of *0.1 M hydrochloric acid* or *0.1 M sodium hydroxide* is required to change the colour of the indicator.

Readily carbonisable substances. To 0.20 g of the powdered substance to be examined add 10 ml of *sulphuric acid R* and heat in a water-bath at 90 ± 1 °C for 60 min. Cool rapidly. The solution is not more intensely coloured than reference solution Y_2 or GY_2 (*2.2.2, Method II*).

Chlorides (*2.4.4*): maximum 50 ppm.

Dilute 10 ml of solution S to 15 ml with *water R*.

Oxalates: maximum 300 ppm.

Dissolve 0.50 g in 4 ml of *water R*, add 3 ml of *hydrochloric acid R* and 1 g of *zinc R* in granules and heat on a water-bath for 1 min. Allow to stand for 2 min, decant the liquid into a test-tube containing 0.25 ml of a 10 g/l solution of *phenylhydrazine hydrochloride R* and heat to boiling. Cool rapidly, transfer to a graduated cylinder and add an equal volume of *hydrochloric acid R* and 0.25 ml of *potassium ferricyanide solution R*. Shake and allow to stand for 30 min. Any pink colour in the solution is not more intense than that in a standard prepared at the same time in the same manner using 4 ml of a 50 mg/l solution of *oxalic acid R*.

Sulphates (*2.4.13*): maximum 150 ppm.

To 10 ml of solution S add 2 ml of *hydrochloric acid R1* and dilute to 15 ml with *distilled water R*.

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*.

Water (*2.5.12*): 11.0 per cent to 13.0 per cent, determined on 0.300 g. After adding the substance to be examined, stir for 15 min before titrating.

Pyrogens (*2.6.8*). If intended for use in the manufacture of large-volume parenteral dosage forms, the competent authority may require that it comply with the test for pyrogens. Inject per kilogram of the rabbit's mass 10 ml of a freshly prepared solution in *water for injections R* containing per millilitre 10.0 mg of the substance to be examined and 7.5 mg of pyrogen-free *calcium chloride R*.

ASSAY

Dissolve 0.150 g in 20 ml of *anhydrous acetic acid R*, heating to about 50 °C. Allow to cool. Titrate with *0.1 M perchloric acid*, using 0.25 ml of *naphtholbenzein solution R* as indicator until a green colour is obtained.

1 ml of *0.1 M perchloric acid* is equivalent to 8.602 mg of $C_6H_5Na_3O_7$.

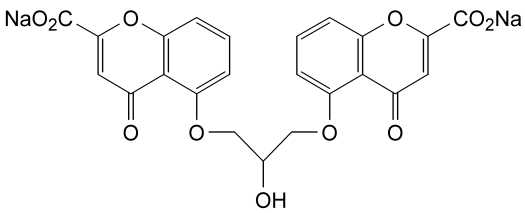
STORAGE

In an airtight container.

01/2008:0562
corrected 6.0

SODIUM CROMOGLICATE

Natrii cromoglicas



$C_{23}H_{14}Na_2O_{11}$ M_r 512.3
[15826-37-6]

DEFINITION

Sodium cromoglicate contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of disodium 5,5′-[(2-hydroxypropane-1,3-diyl)bis(oxy)]bis(4-oxo-4*H*-1-benzopyran-2-carboxylate, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder, hygroscopic, soluble in water, practically insoluble in alcohol.

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. Dissolve 10.0 mg in *phosphate buffer solution pH 7.4 R* and dilute to 100.0 ml with the same solvent. Dilute 10.0 ml of this solution to 100.0 ml with the same solvent. Examined between 230 nm and 350 nm (*2.2.25*), the solution shows two absorption maxima, at 239 nm and 327 nm. The ratio of the absorbance at the maximum at 327 nm to that at the maximum at 239 nm is 0.25 to 0.30.

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *sodium cromoglicate CRS*. Examine the substances prepared as discs.

C. Dissolve about 5 mg in 0.5 ml of *methanol R*. Add 3 ml of a solution in *methanol R* containing 5 g/l of *aminopyrazolone R* and 1 per cent *V/V* of *hydrochloric acid R*. Allow to stand for 5 min. The solution shows an intense yellow colour.

D. It gives reaction (a) of sodium (*2.3.1*).

TESTS

Solution S. Dissolve 0.5 g in *carbon dioxide-free water R* and dilute to 25 ml with the same solvent.

Appearance of solution. Solution S is not more opalescent than reference suspension II (*2.2.1*) and not more intensely coloured than reference solution BY_5 (*2.2.2, Method II*).

Acidity or alkalinity. To 10 ml of solution S add 0.1 ml of *phenolphthalein solution R*. The solution is colourless. Add 0.2 ml of *0.01 M sodium hydroxide*. The solution is pink. Add 0.4 ml of *0.01 M hydrochloric acid*. The solution is colourless. Add 0.25 ml of *methyl red solution R*. The solution is red.

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel* GF_{254} *R* as the coating substance.

Test solution. Dissolve 0.2 g of the substance to be examined in a mixture of 1 volume of *acetone R*, 4 volumes of *tetrahydrofuran R* and 6 volumes of *water R* and dilute to 10 ml with the same mixture of solvents.

Reference solution. Dissolve 10 mg of *1,3-bis(2-acetyl-3-hydroxyphenoxy)-2-propanol CRS* in *chloroform R* and dilute to 100 ml with the same solvent.

Apply separately to the plate 5 µl of each solution. Develop over a path of 10 cm using a mixture of 5 volumes of *glacial acetic acid R*, 50 volumes of *ethyl acetate R* and 50 volumes of *toluene R*. Allow the plate to dry in air and examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with the test solution, apart from the principal spot (which remains at the starting point), is not more intense than the spot in the chromatogram obtained with the reference solution (0.5 per cent).

Oxalate. Dissolve 0.10 g in 20 ml of *water R*, add 5.0 ml of *iron salicylate solution R* and dilute to 50.0 ml with *water R*. Determine the absorbance (*2.2.25*) at 480 nm. The