PHARMACOPOEIAL DISCUSSION GROUP
CORRECTION
CODE: E-38
NAME: SODIUM CHLORIDE
(Correction 2 of the sign-off document Rev. 3 signed on 6 November 2013)

Items to be corrected: identifications A and B; Reagents Silver nitrate solution and Potassium pyroantimonate solution added

Harmonised attributes

Attributes	EP	JP	USP
Definition	+	+	+
Identification A	+	+	+
Identification B	+	+	+
Acidity or alkalinity	+	+	+
Bromides	+	+	+
Ferrocyanides	+	+	+
Iodides	+	+	+
Nitrites	+	-	+
Phosphates	+	+	+
Sulphates	+	+	+
Aluminium	+	-	+
Barium	+	+	+
Iron	+	+	+
Magnesium and alkaline-earth metals	+	+	+
Potassium	+	-	+
Loss on drying	+	+	+
Assay	+	+	+

Legend: + will adopt and implement; - will not stipulate

Non-harmonised attributes

Characters/description, Appearance of solution, Arsenic, Bacterial endotoxins, Labelling, Sterility, Storage

Local requirements:

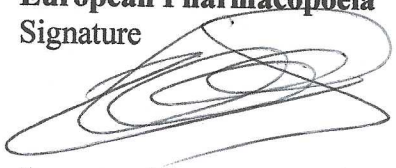
Ph. Eur.	JP	USP
none	Heavy metals	none

Reagents and reference materials

Each pharmacopoeia will adapt the text to take account of local reference substances and spectra and reagent specifications.

CN H.O. Km

European Pharmacopoeia
Signature



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E38 - SODIUM CHLORIDE

NaCl

M_r 58.44

DEFINITION

Sodium chloride contains not less than 99.0 per cent and not more than the equivalent of 100.5 per cent of NaCl, calculated with reference to the dried substance.

IDENTIFICATION

A. Dissolve in 2 mL of *water* a quantity of the substance to be examined equivalent to about 2 mg of chloride (Cl^-). Acidify with *dilute nitric acid* and add 0.4 mL of *silver nitrate solution R1*. Shake and allow to stand. A curdled, white precipitate is formed. Centrifuge and wash the precipitate with three quantities, each of 1 mL, of *water*. Carry out this operation rapidly in subdued light, disregarding the fact that the supernatant solution may not become perfectly clear. Suspend the precipitate in 2 mL of *water* and add 1.5 mL of *ammonia*. The precipitate dissolves easily with the possible exception of a few large particles which dissolve slowly.

B. Dissolve 0.1 g of the substance to be examined in 2 mL of *water*. Add 2 mL of a 150 g/L solution of *potassium carbonate* and heat to boiling. No precipitate is formed. Add 4 mL of *potassium pyroantimonate solution* and heat to boiling. Allow to cool in iced water and if necessary rub the inside of the test-tube with a glass rod. A dense white precipitate is formed.

TESTS

Solution S. Dissolve 20.0 g in *carbon dioxide-free water* prepared from *distilled water* and dilute to 100.0 mL with the same solvent.

Acidity or alkalinity. To 20 mL of solution S add 0.1 mL of *bromothymol blue solution*. 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.

Bromides. To 0.5 mL of solution S add 4.0 mL of *water*, 2.0 mL of *phenol red solution* and 1.0 mL of a 0.1 g/L solution of *chloramine*, prepared immediately before use, and mix immediately. After exactly 2 min, add 0.15 mL of *0.1 M sodium thiosulfate*, mix and dilute to 10.0 mL with *water*. The absorbance of the solution measured at 590 nm, using *water* 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* (100 ppm).

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Ferrocyanides. Dissolve 2.0 g in 6 mL of *water*. Add 0.5 mL of a mixture of 5 mL of a 10 g/L solution of *ferric ammonium sulfate* in a 2.5 g/L solution of *sulfuric acid* and 95 mL of a 10 g/L solution of *ferrous sulfate*. 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*, 2 mL of *0.5 M sulfuric acid*, 25 mL of *iodide-free starch solution* and 25 mL of *water*. After 5 min, examine in daylight. The substance shows no blue colour.

Nitrites. To 10 mL of solution S add 10 mL of *water*. Measure the absorbance of the solution at 354 nm. The absorbance is not greater than 0.01.

Phosphates. Dilute 2 mL of solution S to 100 mL with *water* and add 4 mL of *sulfomolybdic reagent*. Shake and add 0.1 mL of *stannous chloride solution R1*. Prepare a standard in the same manner using 2 mL of *phosphate standard solution (5 ppm PO_4)* and 98 mL of *water*. After 10 min, compare the colours using 20 mL of each solution.
Any colour in the test solution is not more intense than that in the standard (25 ppm).

Sulfates. *All solutions used for this test must be prepared with distilled water.*
Add 3 mL of a 250 g/L solution of *barium chloride* to 4.5 mL of *sulfate standard solution (10 ppm SO_4) R1*. Shake and allow to stand for 1 min. To 2.5 mL of this suspension, add 15 mL of the prescribed solution and 0.5 mL of *acetic acid*. Prepare a standard in the same manner using 15 mL of *sulfate standard solution (10 ppm SO_4) R* instead of the prescribed solution.
After 5 min, any opalescence in the test solution is not more intense than that in the standard.

Prescribed solution: 7.5 mL of solution S diluted to 30 mL with *distilled water*.

Aluminium. If intended for use in the manufacture of peritoneal dialysis solutions, haemodialysis solutions or haemofiltration solutions, it complies with the test for aluminium: maximum 0.2 ppm.
Place the prescribed solution in a separating funnel and shake with 2 quantities, each of 20 mL, and then with one 10 mL quantity of a 5 g/L solution of *hydroxyquinoline* in *chloroform*. Dilute the combined chloroform solutions to 50.0 mL with *chloroform* (test solution).
Prepare a standard in the same manner using the prescribed reference solution.
Prepare a blank in the same manner using the prescribed blank solution.
Measure the intensity of the fluorescence of the test solution (I_1), of the standard (I_2) and of the blank (I_3) using an excitant beam at 392 nm and a secondary filter with a transmission band centred on 518 nm or a monochromator set to transmit at this wavelength.
The fluorescence (I_1-I_3) of the test solution is not greater than that of the standard (I_2-I_3).

Prescribed solution: dissolve 20.0 g in 100 mL of *water* and add 10 mL of *acetate buffer solution pH 6.0*.

Reference solution: a mixture of 2 mL of *aluminium standard solution (2 ppm Al)*, 10 mL of *acetate buffer solution pH 6.0* and 98 mL of *water*.

Blank solution: use a mixture of 10 mL of *acetate buffer solution pH 6.0* and 100 mL of *water*.

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Barium. To 5 mL of solution S add 5 mL of *distilled water* and 2 mL of *dilute sulfuric acid*. 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*.

Iron. To 10 mL of solution S, add 2 mL of a 200 g/L solution of *citric acid* and 0.1 mL of *thioglycollic acid*. Mix, make alkaline with *ammonia* and dilute to 20 mL with *water*. Prepare the standard in the same manner using a mixture of 4 mL of *iron standard solution (1 ppm Fe)* and 6 mL of *water*. After 5 min, any pink colour in the test solution is not more intense than that in the standard (2 ppm).

Magnesium and alkaline earth metals.
To 200 mL of *water* add 0.1 g of *hydroxylamine hydrochloride*, 10 mL of *ammonium chloride buffer solution pH 10.0*, 1 mL of *0.1 M zinc sulfate* and about 0.15 g of *mordant black 11 triturate*. Heat to about 40 °C. Titrate with *0.01 M sodium edetate* until the violet colour changes to full blue. To the solution add 10.0 g of the substance to be examined dissolved in 100 mL of *water*. If the colour of the solution changes to violet, titrate with *0.01 M sodium edetate* until the full blue colour is again obtained.
The volume of *0.01 M sodium edetate* used in the second titration does not exceed 2.5 mL (100 ppm, calculated as Ca).

Potassium. If intended for use in the manufacture of parenteral dosage forms or haemodialysis, haemofiltration or peritoneal dialysis solutions, it contains not more than 500 ppm of K, determined by atomic emission spectrometry.
Test solution. Dissolve 1.00 g of the substance to be examined in *water* and dilute to 100.0 mL with the same solvent.
Reference solutions. Dissolve in *water* 1.144 g of *potassium chloride*, previously dried at 105 ± 2 °C for 3 h, and dilute to 1000.0 mL with the same solvent (600 µg of K per millilitre). Dilute as required.
Measure the emission intensity at 766.5 nm.

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

ASSAY

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

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

REAGENTS

H.O
aq
Ktm

Silver nitrate solution R1
A 42.5 g/L solution of silver nitrate.
Storage: protected from light.

Potassium pyroantimonate solution
Dissolve 2 g of potassium pyroantimonate in 95 mL of hot water. Cool quickly and add a solution containing 2.5 g of potassium hydroxide in 50 mL of water and 1 mL of dilute sodium hydroxide solution. Allow to stand for 24 h, filter and dilute to 150 mL with water.

Stannous chloride solution R
Heat 20 g of tin with 85 mL of hydrochloric acid until no more hydrogen is released. Allow to cool.
Storage: over an excess of tin, protected from air.

Stannous chloride solution R1
Immediately before use, dilute 1 volume of stannous chloride solution R with 10 volumes of dilute hydrochloric acid.

Sulfate standard solution (10 ppm SO_4) R
Immediately before use, dilute with distilled water to 100 times its volume a solution in distilled water containing dipotassium sulfate equivalent to 0.181 g of K_2SO_4 in 100.0 mL.

Sulfate standard solution (10 ppm SO_4) R1
Immediately before use, dilute with ethanol (30 per cent *V/V*) to 100 times its volume a solution containing dipotassium sulfate equivalent to 0.181 g of K_2SO_4 in 100.0 mL of ethanol (30 per cent *V/V*).

Sulfomolybdic reagent
Dissolve with heating 2.5 g of ammonium molybdate in 20 mL of water. Dilute 28 mL of sulfuric acid in 50 mL of water, then cool. Mix the two solutions and dilute to 100 mL with water.
Storage: in a polyethylene container.

Mordant black 11 triturate
Mix 1 g of mordant black 11 with 99 g of sodium chloride.
Test for sensitivity. Dissolve 50 mg in 100 mL of water. The solution is brownish-violet. On addition of 0.3 mL of dilute ammonia the solution turns blue. On the subsequent addition of 0.1 mL of a 10 g/L solution of magnesium sulfate, it turns violet.
Storage: in an airtight container, protected from light.

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