HAEMODIALYSIS SOLUTIONS, CONCENTRATED, WATER FOR DILUTING

Aqua ad dilutionem solutionium concentratarum ad haemodialysim

The following monograph is given for information.

The analytical methods described and the limits proposed are intended to be used for validating the procedure for obtaining the water.

DEFINITION

Water for diluting concentrated haemodialysis solutions is obtained from potable water by distillation, by reverse osmosis, by ion exchange or by any other suitable method. The conditions of preparation, transfer and storage are designed to minimise the risk of chemical and microbial contamination.

When water obtained by one of the methods described above is not available, potable water may be used for home dialysis. Because the chemical composition of potable water varies considerably from one locality to another, consideration must be given to its chemical composition to enable adjustments to be made to the content of ions so that the concentrations in the diluted solution correspond to the intended use.

Attention has also to be paid to the possible presence of residues from water treatment (for example, chloramines) and volatile halogenated hydrocarbons.

For the surveillance of the quality of water for diluting concentrated haemodialysis solutions, the following methods may be used to determine the chemical composition and/or to detect the presence of possible contaminants together with suggested limits to be obtained.

CHARACTERS

Clear, colourless, tasteless liquid.

TESTS

Acidity or alkalinity. To 10 ml of the water to be examined, freshly boiled and cooled in a borosilicate glass flask, add 0.05 ml of methyl red solution R. The solution is not red. To 10 ml of the water to be examined add 0.1 ml of bromothymol blue solution R1. The solution is not blue.

Oxidisable substances. To 100 ml of the water to be examined add 10 ml of dilute sulphuric acid R and 0.1 ml of 0.02 M potassium permanganate and boil for 5 min. The solution remains faintly pink.

Total available chlorine: maximum 0.1 ppm.

In a 125 ml test-tube (A), place successively 5 ml of buffer solution pH 6.5 R, 5 ml of diethylphenylenediamine sulphate solution R and 1 g of potassium iodide R. In a second 125 ml test-tube (B), place successively 5 ml of buffer solution pH 6.5 R and 5 ml of diethylphenylenediamine sulphate solution R. Add as simultaneously as possible to tube A 100 ml of the water to be examined and to tube B a reference solution prepared as follows: to 1 ml of a 10 ng/l solution of potassium iodate R, add 1 g of potassium iodide R and 1 ml of dilute sulphuric acid R; allow to stand for 1 min, add 1 ml of dilute sodium hydroxide solution R and dilute to 100 ml with water R. Any colour in the mixture obtained with the water to be examined is not more intense than that in the mixture obtained with the reference solution.

Chlorides (2.4.4): maximum 50 ppm.

Dilute 1 ml of the water to be examined to 15 ml with water R. The solution complies with the limit test for chlorides.

Fluorides: maximum 0.2 ppm.

Potentiometry (2.2.36, Method I): use as indicator electrode a fluoride-selective solid-membrane electrode and as reference electrode a silver-silver chloride electrode.

Test solution. The water to be examined.

Reference solutions. Dilute 2.0 ml, 4.0 ml and 10.0 ml of fluoride standard solution (1 ppm F) R respectively to 20.0 ml with total-ionic-strength-adjustment buffer R1. Carry out the measurement of each solution.

Nitrates: maximum 2 ppm.

Dilute 2 ml of the water to be examined to 100 ml with nitrate-free water R. Place 5 ml of the dilution in a test-tube immersed in iced water, add 0.4 ml of a 100 g/l solution of potassium chloride R and 0.1 ml of diphenylamine solution R and then, dropwise and with shaking, 5 ml of sulphuric acid R. Transfer the tube to a water-bath at 50 °C. Allow to stand for 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 a mixture of 0.1 ml of nitrate standard solution (2 ppm NO3) R and 4.9 ml of nitrate-free water R.

Sulphates (2.4.13): maximum 50 ppm.

Dilute 3 ml of the water to be examined to 15 ml with distilled water R. The solution complies with the limit test for sulphates.

Aluminium (2.4.17): maximum 10 µg/l.

Prescribed solution. To 400 ml of the water to be examined add 10 ml of acetate buffer solution pH 6.0 R and 100 ml of water 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.

Ammonium: maximum 0.2 ppm.

To 20 ml of the water to be examined in a flat-bottomed and transparent tube, add 1 ml of alkaline potassium tetraiodomercurate solution R. Allow to stand for 5 min. The solution is not more intensely coloured than a standard prepared at the same time and in the same manner using a mixture of 4 ml of ammonium standard solution (1 ppm NH4) R and 16 ml of ammonium-free water R.

Examine the solutions along the vertical axis of the tube.

Calcium: maximum 2 ppm.

Atomic absorption spectrometry (2.2.23, Method I).

Test solution. The water to be examined.

Reference solutions. Prepare reference solutions (1 ppm to 5 ppm) using calcium standard solution (400 ppm Ca) R.

Source: calcium hollow-cathode lamp.

Wavelength: 422.7 nm.

Atomisation devise: oxidising air-acetylene flame.

Magnesium: maximum 2 ppm.

Atomic absorption spectrometry (2.2.23, Method I).

Test solution. Dilute 10 ml of the water to be examined to 100 ml with distilled water R.

Reference solutions. Prepare reference solutions (0.1 ppm to 0.5 ppm) using magnesium standard solution (100 ppm Mg) R.

Source: magnesium hollow-cathode lamp.
Atomic absorption spectrometry (2.2.23, Method I).

**Test solution.** Add 5 ml of nitric acid R per litre of the water to be examined. In a 50 ml borosilicate glass flask, with a ground-glass-stopper, place 20 ml of the water to be examined and add 1 ml of dilute nitric acid R and shake. Add 0.3 ml of bromine water R1. Stopper the flask, shake and heat the stoppered flask at 45 °C for 4 h. Allow to cool. If the solution does not become yellow, add 0.3 ml of bromine water R1 and re-heat at 45 °C for 4 h. Add 0.5 ml of a freshly prepared 10 g/l solution of hydroxylamine hydrochloride R. Shake. Allow to stand for 20 min.

**Reference solutions.** Use freshly prepared reference solutions (0.0005 ppm to 0.002 ppm) obtained by diluting mercury standard solution (1000 ppm Hg) R with a 5 per cent V/V solution of dilute nitric acid R and treat as described for the test solution.

To a volume of solution suitable for the instrument to be used, add stannous chloride solution R2 equal to 1/5 of this volume. Fit immediately the device for the entrainment of the mercury vapour. Wait 20 s and pass through the device a stream of nitrogen R as the carrier gas.

**Source:** mercury hollow-cathode tube or a discharge lamp.

**Wavelength:** 253.7 nm.

**Atomisation device:** flameless system whereby the mercury can be entrained in the form of cold vapour.

**Potassium:** maximum 2 ppm.

Atomic emission spectrometry (2.2.22, Method I).

**Test solution (a).** Dilute 50.0 ml of the water to be examined to 100 ml with distilled water R. Carry out a determination using this solution. If the potassium content is more than 0.75 mg/l, further dilute the water to be examined with distilled water R.

**Test solution (b).** Take 50.0 ml of the water to be examined or, if necessary, the water to be examined diluted as described in the preparation of test solution (a). Add 1.25 ml of potassium standard solution (20 ppm K) R and dilute to 100.0 ml with distilled water R.

**Reference solutions.** Prepare reference solutions (0 ppm; 0.25 ppm; 0.50 ppm; 0.75 ppm; 1 ppm) using potassium standard solution (20 ppm K) R.

**Wavelength:** 766.5 nm.

Calculate the potassium content of the water to be examined in parts per million from the expression:

\[ p \times \frac{n_1 \times 0.5}{n_2 - n_1} \]

- **p** = dilution factor used for the preparation of test solution (a),
- **n_1** = measured value of test solution (a),
- **n_2** = measured value of test solution (b).

**Sodium:** maximum 50 ppm.

Atomic emission spectrometry (2.2.22, Method I).

**Test solution.** The water to be examined. If the sodium content is more than 10 mg/l, dilute with distilled water R to obtain a concentration suitable for the apparatus used.

**Reference solutions.** Prepare reference solutions (0 ppm; 2.5 ppm; 5.0 ppm; 7.5 ppm; 10 ppm) using sodium standard solution (200 ppm Na) R.

**Wavelength:** 589 nm.

**Zinc:** maximum 0.1 ppm.

Atomic absorption spectrometry (2.2.23, Method I): use sampling and analytical equipment free from zinc or not liable to yield zinc under the conditions of use.

**Test solution.** The water to be examined.

**Reference solutions.** Prepare reference solutions (0.05 ppm to 0.15 ppm) using zinc standard solution (100 ppm Zn) R.

**Source:** zinc hollow-cathode lamp.

**Wavelength:** 213.9 nm.

**Atomisation device:** oxidising air-acetylene flame.

**Heavy metals:** maximum 2 ppm.

**Test solution.** Take 50.0 ml of the water to be examined in a glass evaporating dish on a water-bath until the volume is reduced to 20 ml. 12 ml of the solution complies with limit test A. Prepare the standard using lead standard solution (1 ppm Pb) R.

**Microbial contamination.** Total viable aerobic count (2.6.12) not more than 10^5 micro-organisms per millilitre, determined by plate count.

**Bacterial endotoxins (2.6.14):** less than 0.25 IU/ml.

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**HAEMODIALYSIS, SOLUTIONS FOR**

**Solutiones ad haemodialysim**

**DEFINITION**

Solutions for haemodialysis are solutions of electrolytes with a concentration close to the electrolytic composition of plasma. Glucose may be included in the formulation. Because of the large volumes used, haemodialysis solutions are usually prepared by diluting a concentrated solution with water of suitable quality (see the monograph on Haemodialysis solutions concentrated, water for diluting (1167)), using for example an automatic dosing device.

**Concentrated solutions for haemodialysis**

Concentrated haemodialysis solutions are prepared and stored using materials and methods designed to produce solutions having as low a degree of microbial contamination as possible. In certain circumstances, it may be necessary to use sterile solutions.

During dilution and use, precautions are taken to avoid microbial contamination. Diluted solutions are to be used immediately after preparation.

Concentrated solutions for haemodialysis are supplied in:
- rigid, semi-rigid or flexible plastic containers,
- glass containers.

Three types of concentrated solutions are used:

1. **Concentrated solutions with acetate or lactate**

Several formulations of concentrated solutions are used. The concentrations of the components in the solutions are such that after dilution to the stated volume the concentrations of the components per litre are usually in the following ranges: