Oral rehydration salts (Sales perorales ad rehydratationem)

Definition. Oral Rehydration Salts (ORS) are dry mixtures of powders containing per packet:

sodium chloride	NaCl	2.6g
trisodium citrate dihydrate	$C_6H_5Na_3O_7,2H_2O$	2.9g
potassium chloride	KCl	1.5g
anhydrous glucose	$C_6H_{12}O_6$	13.5g

Before administration the contents of each packet should be dissolved in 1 litre of water.

Description. A white, crystalline powder; odourless.

Category. Used for the prevention and treatment of dehydration due to diarrhoea, including maintenance therapy.

Storage. Oral Rehydration Salts should be kept in a sealed packet; if a free-flowing powder is required, it should be kept in an airtight packet, preferably made of aluminium laminate.

Labelling. The designation on the packet of Oral Rehydration Salts should state: (1) the total net mass and the mass of the contents of each constituent, both expressed in grams, (2) the required volume of water to reconstitute the solution, (3) directions for the preparation of the solution and its administration, and (4) a warning that any solution that remains unused 24 hours after preparation is to be discarded.

Additional information. In the formulation of Oral Rehydration Salts trisodium citrate dihydrate may be replaced by 2.5 g/l of sodium hydrogen carbonate, $NaHCO_3$ (sodium bicarbonate). However, as the stability of the latter formulation under tropical conditions is very poor, it is recommended only in Oral Rehydration Salts manufactured for immediate use, or where sodium hydrogen carbonate is packaged in separate packets. These formulations would also allow the use of 14.85 g/l of glucose monohydrate, $C_6H_{12}O_6,H_2O$, instead of anhydrous glucose.

The title of the two formulations could be distinguished by: "ORS-citrate" or "OSR-hydrogen carbonate" (bicarbonate).

The title Oral Rehydration Salts (ORS) used without qualification implies that the product is the citrate formulation as defined above.

Oral Rehydration Salts may contain suitable pharmaceutical aids, in minimal quantities, to improve the flow characteristics and/or the flavour.

Requirements

These specifications apply only to ORS-citrate.

One to three single doses may represent a complete treatment; therefore, the contents of each packet should comply with the following requirements.

Oral Rehydration Salts contain not less than **90.0%** and not more than **110.0%** of the equivalent amounts of sodium Na^+, potassium K^+, chlorides Cl^-, citrate $C_6H_5O_7^{3-}$ of the relevant constituents stated on the label, and not less than **90.0%** and not more than **110.0%** of the amount of anhydrous glucose $C_6H_{12}O_6$ stated on the label.

Identity tests

A. Melts when heated; first becomes yellow then brown, swells up and burns, evolving an odour of burnt sugar.

Dissolve the entire contents of one packet in 250 mL of water to prepare the test solution to be used in tests B, C, D, E, and F.

B. The test solution yields reaction A described under 2.1 General identification tests as characteristic of sodium.

C. To 5 mL of the test solution add 4 drops of sodium cobaltinitrite (100 g/l) TS; a yellow-orange precipitate is produced (potassium).

D. A 5-mL aliquot of the test solution yields reaction A described under 2.1 General identification tests as characteristic of chlorides.

E. A 5-mL aliquot of the test solution after neutralization yields reaction A described under 2.1 General identification tests as characteristic of citrates.

F. Add a few drops of the test solution to 5 mL of hot potassio-cupric tartrate TS; a copious red precipitate is

produced (glucose).

Uniformity of mass. Weigh the contents of 20 packets selected at random and determine the average mass. Not more than two of the individual masses deviate from the average mass by more than 5% and none deviates by more than 10%.

Loss on drying. Dry to constant mass at 50 °C; it loses not more than 20 mg/g.

pH value. pH of the solution reconstituted as directed on the label, 7.0-8.8.

Assays

Carry out all the assays on quantities taken from a single packet. If the quantity of one packet is insufficient to carry out all the assays, take another packet for the assay for citrates and for the assay for glucose from the same batch.

Prepare the following solution (= *solution A*) for the assays for sodium, potassium, and chlorides. Dissolve about 8 g of ORS, accurately weighed, in sufficient water to produce 500 mL.

Sodium. Dilute 3 mL of solution A to 500 mL with water and determine by flame photometry as described under 1.8 Atomic spectrometry: emission and absorption at a wavelength of 589 nm. For the preparation of the reference solutions, use a stock standard solution prepared by dissolving sodium chloride R, previously dried to constant mass at 130 °C, in 1000 mL of water to contain 508.4 mg of NaCl (0.2 mg of Na^+ per mL).

Each g of sodium chloride and of trisodium citrate dihydrate is equivalent to 0.3934 g and 0.2345 g of Na^+, respectively.

Potassium. Dilute 3 mL of solution A to 500 mL with water and determine by flame photometry as described under 1.8 Atomic spectrometry: emission and absorption at a wavelength of 767 nm. For the preparation of the reference solutions, use a stock standard solution prepared by dissolving potassium chloride R, previously dried to constant mass at 130 °C, in 1000 mL of water to contain 190.6 mg of KCl (0.1 mg of K^+ per mL).

Each g of potassium chloride is equivalent to 0.5245 g of K^+.

Chlorides. Titrate 20 mL of solution A with silver nitrate (0.1 mol/l) VS, using potassium chromate (100 g/l) TS as indicator.

Each mL of silver nitrate (0.1 mol/l) VS is equivalent to 3.545 mg of Cl^-.

Each g of sodium chloride and of potassium chloride is equivalent to 0.6066 g and 0.4756 g of Cl^-, respectively.

Citrates. Disperse about 2.8 g of ORS, accurately weighed, in 80 mL of glacial acetic acid R1, heat to about 50 °C, cool, dilute to 100 mL with glacial acetic acid R1, and allow to stand for 10 minutes. To 20 mL of the supernatant liquid add 0.25 mL of 1-naphtholbenzein/acetic acid TS and titrate with perchloric acid (0.1 mol/l) VS as described under 2.6 Non-aqueous titration, Method A.

Each mL of perchloric acid (0.1 mol/l) VS is equivalent to 6.303 mg of $C_6H_5O_7^{3-}$. Each g of sodium citrate is equivalent to 0.6430 g of $C_6H_5O_7^{3-}$.

Glucose. Dissolve about 8.0 g of ORS, accurately weighed, in 40 mL of water, add 0.2 mL of ammonia (~100 g/l) TS, and dilute to 50 mL with water. Mix and allow to stand for 30 minutes. Determine the "Optical rotation", using a measurement layer of 100 mm, and calculate the quantity, in g, of anhydrous glucose $C_6H_{12}O_6$ by multiplying the observed rotation in degrees by 0.9477.