ORAL REHYDRATION SALTS

Draft Revision of Published Monograph

Explanatory note

Suggested text for deletion shown in strikethrough.

Suggested text to be added or changed is underlined.

Additional notes provided by Secretariat at end of monograph

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Sales perorales ad rehydratationem - Oral rehydration salts

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

- sodium chloride \( \text{NaCl} \) 2.6g
- trisodium citrate dihydrate \( \text{C}_6\text{H}_5\text{Na}_3\text{O}_7\cdot2\text{H}_2\text{O} \) 2.9g
- potassium chloride \( \text{KCl} \) 1.5g
- anhydrous glucose \( \text{C}_6\text{H}_12\text{O}_6 \) 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 remaining 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, \( \text{NaHCO}_3 \) (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, \( \text{C}_6\text{H}_12\text{O}_6\cdot\text{H}_2\text{O} \), instead of anhydrous glucose.

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

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 C₆H₅O₇⁻³ 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 C₆H₁₂O₆ 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 “General identification tests” as characteristic of sodium (Vol. 1, p. 115).

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 “General identification tests” as characteristic of chlorides (Vol. 1, p. 112).

E. A 5-ml aliquot of the test solution after neutralization yields reaction A described under “General identification tests” as characteristic of citrates (Vol. 1, p. 113).

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 (see p. 47). 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 reconstituted solution following the directions on the label, 7.0-8.8.
Assays

Note. 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 75 ml of solution A to 500 ml with water and determine by flame photometry (see page 23) at a wavelength of 589 nm. Use a standard solution prepared by dissolving sodium chloride R, previously dried to constant mass, 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 100 ml of solution A to 500 ml with water and determine by flame photometry (see page 23) at a wavelength of 767 nm. Use a standard solution prepared by dissolving potassium chloride R, previously dried to constant mass, 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 “Non-aqueous titration”, Method A (Vol. 1, p. 131).

Each ml of perchloric acid (0.1 mol/l) VS is equivalent to 6.303 mg of C₆H₅O₇⁻. Each g of sodium citrate is equivalent to 0.6430 g of C₆H₅O₇⁻.
Glucose. Dissolve about 8 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” (Vol. 1, p. 31) and calculate the quantity, in g, of anhydrous glucose \( C_6H_{12}O_6 \) by multiplying the observed rotation in degrees by 0.9477.

Notes:

The product is a packet containing a sufficient amount of the mixed dry ingredients for preparing a litre of oral rehydration solution; it is not the prepared solution.

Assay

For sodium While for the revised formula the amount of sodium chloride and thus the total amount of sodium in one packet has decreased, the proportion of sodium in the dry mix has slightly increased because of the decrease in the overall weight of ORS in the packet [from 27.9 g to 20.5 g] due to the reduction in the glucose content.

Solution A prepared with 8 g of old formula ORS contained 0.59 g of sodium per 500 ml. Solution A prepared with 8 g of new formula ORS contains 0.665 g of sodium per 500 ml. Therefore to maintain approximately the same concentration of test solution for the assay, it would be necessary to take 3 x 0.59/0.665 ml = 2.66 ml which, rounded down to a convenient figure, would give 2.5 ml. However, in reviewing the monograph, it was noted that there was a discrepancy between the strengths of standard and test solutions. The strength of the standard solution is about 30 x that of the test solution. It is therefore proposed to increase the strength of the test solution by specifying 75 ml of Solution A.

For potassium In reviewing the monograph, it was noted that there was a discrepancy between the strengths of standard and test solutions similar to that in the assay for sodium.

For chloride The volume to be titrated has been reduced to require a lower titration volume.

For glucose The old formula ORS contained 20.0 g of glucose in a total packet weight of 27.9 g while the new formula contains 13.5 g of glucose in a total packet weight of 20.5 g. 7.5 g of old formula ORS contained 5.37 g of glucose. Therefore to take approximately the same amount of glucose for the assay, it is necessary to take 5.37 x 20.5/13.5 g = 8.15 g which, rounded down to a convenient figure, gives 8.0 g.

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