

For discussion of modified formulations of oral rehydration solutions in the treatment of diarrhoea, including the use of cereal-based and low osmolarity preparations, see oral rehydration therapy under Diarrhoea, p.1694.

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- CHOICE Study Group. Multicenter, randomized, double-blind clinical trial to evaluate the efficacy and safety of a reduced osmolarity oral rehydration salts solution in children with acute watery diarrhea. *Pediatrics* 2001; **107**: 613-18.
- Fuchs GJ. A better oral rehydration solution? An important step, but not a leap forward. *BMJ* 2001; **323**: 59-60.
- Anonymous. New oral rehydration solution adopted by WHO and UNICEF. *WHO Drug Inf* 2004; **18**: 138-40.
- Hirschhorn N, et al. Formulation of oral rehydration solution. *Lancet* 2002; **360**: 340-1.
- Cash R, et al. Oral rehydration and hyponatraemia. *Lancet* 1999; **354**: 1733-4.
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- King CK, et al. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. *MMWR* 2003; **52** (RR-16): 1-16. Also available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/r5216a1.htm> (accessed 06/02/06)

**Oral versus intravenous rehydration.** Although intravenous rehydration is advised for patients with the most severe dehydration (see Diarrhoea, p.1694) it is also widely used in some countries in the management of less severe degrees of fluid loss.<sup>1,2</sup> However, a meta-analysis of 16 randomised controlled studies in children with gastroenteritis (5 of which included children with severe dehydration) found that oral or nasogastric rehydration with an appropriate rehydration solution was at least as effective as intravenous rehydration in terms of weight gain and intestinal losses, and was associated with a lower incidence of adverse effects and a reduced length of hospital stay.<sup>3</sup> The authors concluded that there was no evidence to support the ongoing use of intravenous rehydration in most cases of childhood gastroenteritis.

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- Ford-Jones EL, et al. Hospitalization for community-acquired, rotavirus-associated diarrhea: a prospective, longitudinal, population-based study during the seasonal outbreak. *Arch Pediatr Adolesc Med* 2000; **154**: 578-85.
- Fonseca BK, et al. Enteral vs intravenous rehydration therapy for children with gastroenteritis: a meta-analysis of randomized controlled trials. *Arch Pediatr Adolesc Med* 2004; **158**: 483-90.

## Preparations

**BP 2008:** Oral Rehydration Salts;  
**USP 31:** Oral Rehydration Salts;  
**WHO/UNICEF:** Oral Rehydration Salts.

**Proprietary Preparations:** some preparations are listed in Part 3.

## Bicarbonate

Bicarbonato.

**Description.** Bicarbonate is an alkalinising agent given as bicarbonate-containing salts (sodium or potassium bicarbonate) or bicarbonate-producing salts (acetate, citrate, or lactate salts). Allowance should be made for the effect of the cation.

**Incompatibility.** Bicarbonate-producing or bicarbonate-containing solutions have been reported to be incompatible with a wide range of drugs. In many cases this incompatibility is a function of the alkaline nature of the bicarbonate solution. Precipitation of insoluble carbonates may occur, as may production of gaseous carbon dioxide when the bicarbonate ion is reduced by acidic solutions.

## Potassium Bicarbonate

E501; Hydrogenuhlíčan draselný; Kalii Hydrocarbonas; Kalii Hydrogenocarbonas; Kalii hydrogenocarbonas; Kalio-vandenilio karbonatas; Kálium-hidrogén-karbonát; Kaliumváték-karbonát; Kaliumvetykarbonaatti; Monopotassium Carbonate; Potasio, bicarbonato de; Potassium, bicarbonate de; Potassium Hydrogen Carbonate; Potasu wodorowęglan; Potasium Bikarbonat.

$\text{KHCO}_3 = 100.1$ .

CAS — 298-14-6.

ATC — A12BA04.

ATC Vet — QA12BA04.

**Pharmacopoeias.** In *Eur.* (see p.vii) and *US*.

**Ph. Eur. 6.2** (Potassium Hydrogen Carbonate; Potassium Bicarbonate BP 2008). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; practically insoluble in alcohol. When heated in the dry state or in solution, it is gradually converted to potassium carbonate. A freshly prepared 5% solution in water has a pH of not more than 8.6.

**USP 31** (Potassium Bicarbonate). Colourless, odourless, transparent monoclinic prisms or white granular powder. Freely soluble in water; practically insoluble in alcohol. Its solutions are neutral or alkaline to phenolphthalein.

**Equivalence.** Each g of potassium bicarbonate represents about 10 mmol of potassium and of bicarbonate. Potassium bicarbonate 2.56 g is equivalent to about 1 g of potassium.

## Potassium Citrate

Citronan draselný monohydrát; E332; Kalii citras; Kalii Citras Monohydricus; Kalio citratas; Kaliumcitrat; Kaliumsitraatti; Potasio, citrato de; Potassium, citrate de; Potasu cytrynian; Potasium Citrat; Trikálium-citrát; Tripotassium Citrate. Tripotassium 2-hydroxypropane-1,2,3-tricarboxylate monohydrate.

$\text{C}_6\text{H}_5\text{K}_3\text{O}_7\cdot\text{H}_2\text{O} = 324.4$ .

CAS — 866-84-2 (anhydrous potassium citrate); 6100-05-6 (potassium citrate monohydrate).

ATC — A12BA02.

ATC Vet — QA12BA02.

**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), *Int.*, and *US*.

**Ph. Eur. 6.2** (Potassium Citrate). Transparent, hygroscopic crystals or a white or almost white granular powder. Very soluble in water; practically insoluble in alcohol. Store in airtight containers.

**USP 31** (Potassium Citrate). Transparent crystals or a white granular powder. It is odourless and is deliquescent in moist air. Soluble 1 in 1 of water and 1 in 2.5 of glycerol; almost insoluble in alcohol. Store in airtight containers.

**Equivalence.** Each g of potassium citrate (anhydrous) represents about 9.8 mmol of potassium and 3.26 mmol of citrate. Each g of potassium citrate (monohydrate) represents about 9.3 mmol of potassium and 3.08 mmol of citrate. Potassium citrate (monohydrate) 2.77 g is equivalent to about 1 g of potassium.

## Sodium Acetate

E262; Natrii Acetas; Natrii acetat trihydricus; Natrio acetatas trihidricus; Natrium Aceticum; Nátrium-acetát; Natriumacetat trihydrat; Natriumasetaatitrihydraatti; Octan sodný trihydrát; Sodio, acetato de; Sodium (acetate de) trihydraté; Sodu octan.

$\text{CH}_3\text{CO}_2\text{Na}\cdot 3\text{H}_2\text{O} = 136.1$ .

CAS — 127-09-3 (anhydrous sodium acetate); 6131-90-4 (sodium acetate trihydrate).

ATC — B05XA08.

ATC Vet — QB05XA08.

**Pharmacopoeias.** In *Eur.* (see p.vii), *Jpn.*, and *US*.

*US* also allows the anhydrous form.

**Ph. Eur. 6.2** (Sodium Acetate Trihydrate). Colourless crystals. Very soluble in water; soluble in alcohol. A 5% solution in water has a pH of 7.5 to 9.0. Store in airtight containers.

**USP 31** (Sodium Acetate). It contains three molecules of water of hydration or is anhydrous. Colourless, transparent crystals, or a white, granular crystalline powder, or white flakes. It is odourless or has a faint acetous odour. It is efflorescent in warm dry air. Soluble 1 in 0.8 of water, 1 in 0.6 of boiling water, and 1 in 19 of alcohol. pH of a solution in water containing the equivalent of 3% of anhydrous sodium acetate is between 7.5 and 9.2. Store in airtight containers.

**Equivalence.** Each g of sodium acetate (anhydrous) represents about 12.2 mmol of sodium and of acetate. Each g of sodium acetate (trihydrate) represents about 7.3 mmol of sodium and of acetate. Sodium acetate (anhydrous) 3.57 g is equivalent to about 1 g of sodium. Sodium acetate (trihydrate) 5.92 g is equivalent to about 1 g of sodium.

## Sodium Acid Citrate

Disodium Hydrogen Citrate; Disodu wodorocytrynian; E331; Natrium Citricum Acidum; Sodio, citrato ácido de.

$\text{C}_6\text{H}_6\text{Na}_2\text{O}_7\cdot\text{H}_2\text{O} = 263.1$ .

CAS — 144-33-2.

**Pharmacopoeias.** In *Br.*

**BP 2008** (Sodium Acid Citrate). A white, odourless or almost odourless, powder. Freely soluble in water; practically insoluble in alcohol. A 3% solution in water has a pH of 4.9 to 5.2. The BP gives Disodium Hydrogen Citrate as an approved synonym.

**Equivalence.** Each g of sodium acid citrate (sesquihydrate) represents about 7.6 mmol of sodium and 3.8 mmol of citrate. Sodium acid citrate (sesquihydrate) 5.72 g is equivalent to about 1 g of sodium.

## Sodium Bicarbonate

Baking Soda; E500; Hydrogenuhlíčan sodný; Monosodium Carbonate; Natrii Bicarbonas; Natrii hydrogenocarbonas; Natrio-vandenilio karbonatas; Nátrium-hidrogén-karbonát; Natriumváték-karbonát; Natriumvetykarbonaatti; Sal de Vichy; Sodio, hidrogenocarbonato de; Sodium Acid Carbonate; Sodium, bicarbonate de; Sodium Hydrogen Carbonate; Sodu wodorowęglan; Sodyum Bikarbonat.

$\text{NaHCO}_3 = 84.01$ .

CAS — 144-55-8.

ATC — B05CB04; B05XA02.

ATC Vet — QB05CB04; QB05XA02; QG04BQ01.

**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn.*, *US*, and *Viet*.

**Ph. Eur. 6.2** (Sodium Hydrogen Carbonate; Sodium Bicarbonate BP 2008). A white or almost white, crystalline powder. Soluble in water; practically insoluble in alcohol. The pH of a freshly prepared 5% solution in water is not more than 8.6. When heated in the dry state or in solution, it gradually changes into sodium carbonate.

**USP 31** (Sodium Bicarbonate). A white crystalline powder that slowly decomposes in moist air. Soluble 1 in 12 of water; insoluble in alcohol. Its solutions, when freshly prepared with cold water, without shaking, are alkaline to litmus; alkalinity increases on standing, agitation, or heating.

**Equivalence.** Each g of sodium bicarbonate (anhydrous) represents about 11.9 mmol of sodium and of bicarbonate. Sodium bicarbonate 3.65 g is equivalent to about 1 g of sodium.

## Sodium Citrate

Citronan sodný dihydrát; E331; Natrii citras; Natrii Citras Dihydricus; Natrio citratas; Natriumcitrat; Natriumsitraatti; Sodio, citrato de; Sodium, citrate de; Sodu cytrynian; Sodyum Citrat; Trinátrium-citrát; Trisodium Citrate. Trisodium 2-hydroxypropane-1,2,3-tricarboxylate dihydrate.

$\text{C}_6\text{H}_5\text{Na}_3\text{O}_7\cdot 2\text{H}_2\text{O} = 294.1$ .

CAS — 68-04-2 (anhydrous sodium citrate); 6132-04-3 (sodium citrate dihydrate).

ATC — B05CB02.

ATC Vet — QB05CB02.

**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn.*, and *Viet*. *Int.* and *US* specify anhydrous or dihydrate.

**Ph. Eur. 6.2** (Sodium Citrate). A white or almost white, crystalline powder or white or almost white, granular crystals; slightly deliquescent in moist air. Freely soluble in water; practically insoluble in alcohol. Store in airtight containers.

**USP 31** (Sodium Citrate). It is anhydrous or contains two molecules of water of hydration. Colourless crystals, or a white crystalline powder. The hydrous form is soluble 1 in 1.5 of water and 1 in 0.6 of boiling water; insoluble in alcohol. Store in airtight containers.

**Equivalence.** Each g of sodium citrate (anhydrous) represents about 11.6 mmol of sodium and 3.9 mmol of citrate. Each g of sodium citrate (dihydrate) represents about 10.2 mmol of sodium and 3.4 mmol of citrate. Sodium citrate (anhydrous) 3.74 g is equivalent to about 1 g of sodium. Sodium citrate (dihydrate) 4.26 g is equivalent to about 1 g of sodium.

**Storage.** Sterilised solutions when stored may cause separation of particles from glass containers and solutions containing such particles must not be used.

## Sodium Lactate

E325; Lactato de sodio; Natrii lactatis; Natriumlaktaatti; Natrium-laktat; Sodium, lactate de. Sodium 2-hydroxypropionate.

$\text{C}_3\text{H}_5\text{NaO}_3 = 112.1$ .

CAS — 72-17-3.

**Pharmacopoeias.** *Chin.*, *Eur.* (see p.vii), and *US* include preparations of sodium lactate.

**Ph. Eur. 6.2** (Sodium Lactate Solution). It contains a minimum of 50% w/w of sodium lactate and is a mixture of the two enantiomers in about equal proportions. Sodium (S)-Lactate Solution contains a minimum of 50% w/w of sodium lactate, not less than 95% of which is the (S)-enantiomer. The solutions are clear, colourless, slightly syrupy liquids. Miscible with water and with alcohol. pH 6.5 to 9.0.

**USP 31** (Sodium Lactate Solution). It is an aqueous solution containing at least 50% sodium lactate. A clear, colourless or practically colourless, slightly viscous liquid, odourless or having a slight, not unpleasant, odour. Miscible with water. pH between 5.0 and 9.0. Store in airtight containers.

**Equivalence.** Each g of sodium lactate (anhydrous) represents about 8.9 mmol of sodium and of lactate. Sodium lactate (anhydrous) 4.88 g is equivalent to about 1 g of sodium.

## Adverse Effects and Treatment

Excessive use of bicarbonate or bicarbonate-forming compounds may lead to hypokalaemia and metabolic alkalosis, especially in patients with impaired renal function. Symptoms include mood changes, tiredness, slow breathing, muscle weakness, and irregular heartbeat. Muscle hypertonicity, twitching, and tetany may develop, especially in hypocalcaemic patients. Treatment of metabolic alkalosis associated with bicarbonate overdose consists mainly of appropriate correction of fluid and electrolyte balance. Replacement of calcium, chloride, and potassium ions may be of particular importance.

Excessive doses of *sodium salts* may also lead to sodium overloading and hyperosmolality (see Adverse Effects of Sodium, p.1686). Sodium bicarbonate given