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.

1. Hahn S, *et al.* Reduced osmolarity oral rehydration solution for treating dehydration caused by acute diarrhoea in children. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 21/06/05).
2. 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.
3. Fuchs GJ. A better oral rehydration solution? An important step, but not a leap forward. *BMJ* 2001; **323:** 59–60.
4. Anonymous. New oral rehydration solution adopted by WHO and UNICEF. *WHO Drug Inf* 2004; **18:** 138–40.
5. Hirschhorn N, *et al.* Formulation of oral rehydration solution. *Lancet* 2002; **360:** 340–1.
6. Cash R, *et al.* Oral rehydration and hyponatraemia. *Lancet* 1999; **354:** 1733–4.
7. Booth I, *et al.* Recommendations for composition of oral rehydration solutions for the children of Europe: report of an ESPGAN working group. *J Pediatr Gastroenterol Nutr* 1992; **14:** 113–15.
8. 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/rr5216a1.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.[1,2] 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.[3] The authors concluded that there was no evidence to support the ongoing use of intravenous rehydration in most cases of childhood gastroenteritis.

1. Elliott EJ, *et al.* Pre-admission management of acute gastroenteritis. *J Paediatr Child Health* 1996; **32:** 18–21.
2. 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.
3. 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; Hydrogenuhličitan draselný; Kalii Hydrocarbonas; Kalii Hydrogenocarbobnas; Kalii hydrogenocarbonas; Kalio-vandenilio karbonatas; Kálium-hidrogén-karbonát; Kaliumvätekarbonat; Kaliumvetykarbonaatti; Monopotassium Carbonate; Potasio, bicarbonato de; Potassium, bicarbonate de; Potassium Hydrogen Carbonate; Potasu wodoroweglan; Potasyum Bikarbonat.

$KHCO_3$ = 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; Potasyum Sitrat; Trikálium-citrát; Tripotassium Citrate. Tripotassium 2-hydroxypropane-1,2,3-tricarboxylate monohydrate.

$C_6H_5K_3O_7,H_2O$ = 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 acetas trihydricus; Natrio acetatas trihidratas; Natrium Aceticum; Nátrium-acetát; Natriumacetat trihydrat; Natriumasetaattitrihydraatti; Octan sodný trihydrát; Sodio, acetato de; Sodium (acétate de) trihydraté; Sodu octan.

$CH_3.CO_2Na,3H_2O$ = 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.

$C_6H_6Na_2O_7,1/H_2O$ = 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; Hydrogenuhličitan sodný; Monosodium Carbonate; Natrii Bicarbonas; Natrii hydrogenocarbonas; Natriovandenilio karbonatas; Nátrium-hidrogén-karbonát; Natriumvätekarbonat; Natriumvetykarbonaatti; Sal de Vichy; Sodio, hidrogenocarbonato de; Sodium Acid Carbonate; Sodium, bicarbonate de; Sodium Hydrogen Carbonate; Sodu wodoroweglan; Sodyum Bikarbonat.

$NaHCO_3$ = 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 Sitrat; Trinátrium-citrát; Trisodium Citrate. Trisodium 2-hydroxypropane-1,2,3-tricarboxylate dihydrate.

$C_6H_5Na_3O_7,2H_2O$ = 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; Natriumlaktat; Sodium, lactate de. Sodium 2-hydroxypropionate.

$C_3H_5NaO_3$ = 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

orally can cause stomach cramps, belching, and flatulence. Extravasation of irritant hypertonic sodium bicarbonate solutions resulting in local tissue necrosis has been reported after intravenous dosage.

Excessive doses of *potassium salts* may lead to hyperkalaemia (see Adverse Effects of Potassium, p.1684). Ingestion of potassium salts can cause gastrointestinal adverse effects, and tablet formulations may cause contact irritation due to high local concentrations of potassium.

Excessive oral doses of *citrate salts* may have a laxative effect.

Effects on the gastrointestinal tract. In addition to minor gastrointestinal effects (see above), spontaneous rupture of the stomach, although an exceedingly rare event, has been reported on several occasions after ingestion of sodium bicarbonate. The bicarbonate was believed to have resulted in the rapid production of enough carbon dioxide to rupture a stomach already distended with food, liquid, or air.[1,2]

1. Mastrangelo MR, Moore EW. Spontaneous rupture of the stomach in a healthy adult man after sodium bicarbonate ingestion. *Ann Intern Med* 1984; **101:** 649.
2. Lazebnik N, *et al*. Spontaneous rupture of the normal stomach after sodium bicarbonate ingestion. *J Clin Gastroenterol* 1986; **8:** 454–6.

Effects on mental state. Sodium lactate infusions have been reported to induce panic attacks, especially in patients with anxiety states, and have been used as a pharmacological model in the evaluation of mechanisms involved in panic disorder.[1] However, the mechanism that underlies panic attacks induced by lactate remains unknown,[1] and it has been suggested[2] that rapid administration of the large sodium load may be involved. There has also been a report[3] of a patient receiving oral lactate (as calcium lactate) who was suffering from panic disorder associated with agoraphobia; when lactate was discontinued, the patient reported a reduction in panic intensity without a decrease in the frequency of attacks.

1. Bourin M, *et al*. Provocative agents in panic disorder. *Therapie* 1995; **50:** 301–6.
2. Peskind ER, *et al*. Sodium lactate and hypertonic sodium chloride induce equivalent panic incidence, panic symptoms, and hypernatremia in panic disorder. *Biol Psychiatry* 1998; **44:** 1007–16.
3. Robinson D, *et al*. Possible oral lactate exacerbation of panic disorder. *Ann Pharmacother* 1995; **29:** 539–40.

Epileptogenic effect. Alkalosis may precipitate seizures; however, absence seizures have also been reported to be associated with sodium bicarbonate administration in a child in whom the serum pH was normal.[1]

1. Reif S, *et al*. Absence seizures associated with bicarbonate therapy and normal serum pH. *JAMA* 1989; **262:** 1328–9.

Precautions

Bicarbonate or bicarbonate-forming compounds should not generally be given to patients with metabolic or respiratory alkalosis, hypocalcaemia, or hypochlorhydria. During treatment of acidosis, frequent monitoring of serum-electrolyte concentrations and acid–base status is essential.

Sodium-containing salts should be given extremely cautiously to patients with heart failure, oedema, renal impairment, hypertension, eclampsia, or aldosteronism (see Sodium, p.1686).

Potassium-containing salts should be given with considerable care to patients with renal or adrenocortical insufficiency, cardiac disease, or other conditions that may predispose to hyperkalaemia (see Potassium, p.1685).

Abuse. High doses of bicarbonate have been taken by athletes to enhance performance in endurance sports by buffering hydrogen ions produced in conjunction with lactic acid.[1] Bicarbonates have also been used to alkalinise the urine and prolong the half-life of basic drugs, notably sympathomimetics and stimulants, thereby avoiding detection; however, such a practice may enhance toxicity.

1. Kennedy M. Drugs and athletes—an update. *Adverse Drug React Bull* 1994; (Dec): 639–42.

Interactions

The effect of oral bicarbonate or bicarbonate-forming compounds in raising intra-gastric pH may reduce or increase the rate and/or extent of absorption of a number of drugs (see also Antacids, p.1692). Alkalinisation of the urine leads to increased renal clearance of acidic drugs such as salicylates, tetracyclines, and barbiturates. Conversely, it prolongs the half-life of basic drugs and may result in toxicity (see also under Abuse, above).

Sodium bicarbonate enhances lithium excretion. The use of *potassium-containing salts* with drugs that increase serum-potassium concentrations such as ACE inhibitors and potassium-sparing diuretics should generally be avoided (p.1685). *Citrate salts* taken orally can enhance the absorption of aluminium from the gastrointestinal tract (see Toxicity, p.1706 under Adverse Effects of Aluminium Hydroxide). Patients with impaired renal function are particularly susceptible to aluminium accumulation and citrate-containing oral preparations, including many effervescent or dispersible tablets, are best avoided by patients with renal failure taking aluminium-containing compounds.

Pharmacokinetics

Oral bicarbonate, such as sodium bicarbonate, neutralises gastric acid with the production of carbon dioxide. Bicarbonate not involved in that reaction is absorbed and in the absence of a deficit of bicarbonate in the plasma, bicarbonate ions are excreted in the urine, which is rendered alkaline, and there is an accompanying diuresis.

Acetates such as potassium acetate and sodium acetate, citrates such as potassium citrate, sodium acid citrate, and sodium citrate, and lactates such as sodium lactate are metabolised, after absorption, to bicarbonate.

Uses and Administration

Bicarbonate-providing salts are alkalinising agents used for a variety of purposes including the correction of metabolic acidosis, alkalinisation of the urine, and as antacids.

When an alkalinising agent is indicated for treating acute or chronic **metabolic acidosis** (p.1667), sodium bicarbonate is usually used. In conditions when acute metabolic acidosis is associated with tissue hypoxia, such as *cardiac arrest* and *lactic acidosis,* the role of such alkalinising agents is controversial (see p.1667, and for guidelines on advanced cardiac life support, p.1156). Sodium lactate has been given as an alternative to sodium bicarbonate in acute metabolic acidosis, but is no longer recommended because of the risk of precipitating lactic acidosis. In *chronic hyperchloraemic acidosis* associated with potassium deficiency, potassium bicarbonate may be preferred to sodium bicarbonate. The citrate salts of potassium or sodium have also been used as alternatives to sodium bicarbonate in treating chronic metabolic acidosis resulting from *renal disorders*. Sodium bicarbonate, lactate and acetate, and potassium acetate are used as bicarbonate sources in *dialysis fluids* (p.1670).

The dose of bicarbonate required for the treatment of acidotic states must be calculated on an individual basis, and is dependent on the acid–base balance and electrolyte status of the patient. In the treatment of chronic acidosis bicarbonate has been given orally and doses providing 57 mmol (4.8 g sodium bicarbonate) or more daily may be required. In severe acidosis, sodium bicarbonate has been given intravenously by continuous infusion usually as a 1.26% (150 mmol/litre) solution or by slow intravenous injection of a stronger (hypertonic) solution of up to 8.4% (1000 mmol/litre) sodium bicarbonate (but see the discussion on metabolic acidosis, p.1667). For the correction of acidosis during advanced cardiac life support procedures, doses of 50 mmol of sodium bicarbonate (50 mL of an 8.4% solution) may be given intravenously to adults. Frequent monitoring of serum-electrolyte concentrations and acid–base status is essential during treatment of acidosis.

Sodium bicarbonate may be used in the management of **hyperkalaemia** (p.1669) to promote the intracellular uptake of potassium and correct associated acidosis, although there is some debate as to its value. Some sources suggest that 50 to 100 mL of an 8.4% solution may be given in severe hyperkalaemia accompanied by acidosis, although more dilute solutions have been used, and care is required, particularly if there is accompanying renal impairment.

Sodium bicarbonate, sodium citrate, and potassium citrate cause **alkalinisation of the urine**. They may therefore be given to relieve discomfort in mild *urinary-tract infections* (p.199) and to prevent the development of uric-acid renal calculi in the initial stages of *uricosuric* therapy for hyperuricaemia in chronic gout (for example, see Precautions for Probenecid, p.558). In both cases, they are given with a liberal fluid intake, usually by mouth, in divided doses of up to about 10 g daily. Sodium bicarbonate may also be used to alkalinise the urine in *acute poisoning* with weakly acidic drugs such as salicylates and phenoxyacetate pesticides; use with a diuretic for 'forced alkaline diuresis' is no longer recommended.

When given orally, sodium bicarbonate and potassium bicarbonate neutralise acid secretions in the gastrointestinal tract and sodium bicarbonate in particular is therefore frequently included in **antacid** preparations (p.1692). To relieve *dyspepsia* doses of about 1 to 5 g of sodium bicarbonate in water have been taken when required. Sodium citrate has been widely used as a 'clear' (non-particulate) antacid, usually with an H_2-antagonist, for the *prophylaxis of acid aspiration* associated with anaesthesia (p.1693). Sodium bicarbonate is also used in various preparations for *double-contrast radiography* where production of gas (carbon dioxide) in the gastrointestinal tract is necessary. Similarly, solutions containing sodium bicarbonate or citrate have been used to treat acute *oesophageal impaction*.

Sodium bicarbonate and sodium or potassium citrate are used as buffering or alkalinising agents in *pharmaceutical formulation*. Sodium or potassium bicarbonate and anhydrous sodium citrate are used in effervescent tablet formulations.

Individual salts also have **other specific uses**. A 5% solution of sodium bicarbonate can be administered as ear drops to soften and remove *ear wax* (see under Docusates, p.1725). Sodium bicarbonate injection has been used to treat *extravasation of anthracycline antineoplastics* (p.640) although as mentioned in Adverse Effects, above, hypertonic solutions may themselves cause necrosis.

Sodium citrate has anti-clotting properties and is used, as sodium acid citrate, with other agents in solutions for the anticoagulation and preservation of blood for *transfusion* purposes. Similarly, sodium citrate 3% irrigation may be useful for the dissolution of *blood clots in the bladder* as an alternative to sodium chloride 0.9%. Enemas containing sodium citrate are given rectally as *osmotic laxatives*. Sodium citrate is also a common ingredient in *cough* mixtures. Eye drops containing sodium citrate 10% have been used in the treatment of chemical *eye burns* (below); they may be used with potassium ascorbate eye drops (see Uses of Vitamin C Substances, p.1984).

Eye disorders. Sodium bicarbonate is used in the management of blepharitis, an inflammation of the margin of the eyelids with various causes. It may be allergic in nature or associated with seborrhoea of the scalp. Infection of the eyelids can produce ulcerative blepharitis, a condition characterised by the formation of yellow crusts which may glue the eyelashes together. Parasites occasionally cause blepharitis. The condition is first treated by cleaning the eyes and eyelids with sodium bicarbonate solution or a suitable bland eye lotion; simple eye ointment or diluted baby shampoo can also be used to soften crusts to aid removal. If an infection is present, antibacterials may be required (p.171). Long-term management consists of daily cleansing of the lid margins with a bland eye lotion.

EYE BURNS. Both heat and chemicals can burn the eye, causing damage to the conjunctiva, cornea, and underlying structures. Burn severity may be influenced by the amount of burning substance that enters the eye and the duration of contact, its temperature and impact force, whether it is a liquid or solid, its pH, and osmolarity.[1,2] Hydrofluoric acid, sulfurous acid, and alkalis readily penetrate the corneal stroma.[2] Immediate irrigation is essential, and a duration of at least 15 to 30 minutes is recommended; it may need to be repeated periodically.

Water or sodium chloride 0.9% solution may be used initially, but because they are hypotonic to the eye there can be an increased uptake of the fluid and diffusion of the burning substance into the deeper layers of the cornea, resulting in oedema. To reduce this risk solutions with higher osmolarities have been suggested, if available, and include balanced salt solution, buffered solutions such as lactated Ringer's solution, and commercial decontamination preparations with amphoteric and chelating properties.[1,2]

For acid and alkali burns ascorbate and citrate eye drops have been tried, and ascorbate given orally, based on suggestions that ascorbate may scavenge free radicals and citrate may reduce the release of free radicals and proteolytic enzymes in burn tissue.[1] However, a retrospective analysis of 121 patients with alkali burns to the eye suggested those with less severe burns (grades 1 and 2) did not benefit from an intensive topical therapy regimen including 10% ascorbate drops and 10% citrate drops;[3] a trend to more rapid healing and better visual outcome were seen in patients with grade 3 burns but in those with the most severe damage (grade 4) the regimen made no difference. In the management of hydrofluoric acid burns of the eye, calcium gluconate has also been used after initial irrigation (see p.2322). Other general treatments that may be required include topical application of anaesthesia, corticosteroids, and antibacterials, treatment for glaucoma, and surgery.[1,2]

1. Schrage NF, *et al.* Eye burns: an emergency and continuing problem. *Burns* 2000; **26:** 689–99.
2. Kuckelkorn R, *et al.* Emergency treatment of chemical and thermal eye burns. *Acta Ophthalmol Scand* 2002; **80:** 4–10.
3. Brodovsky SC, *et al.* Management of alkali burns: an 11-year retrospective review. *Ophthalmology* 2000; **107:** 1829–35.

Osteoporosis. Potassium bicarbonate in an oral dose of 1 to 2 mmol/kg daily improved mineral balance and bone metabolism in a short-term study.[1] However, the authors cautioned against the use of bicarbonate to treat or prevent osteoporosis (p.1084) without further study.[2]

1. Sebastian A, *et al.* Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med* 1994, **330:** 1776–81.
2. Sebastian A, Morris RC. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med* 1994; **331:** 279.

Renal calculi. Citrate forms soluble complexes with calcium, thereby reducing urinary saturation of stone-forming calcium salts. Potassium citrate has a hypocalciuric effect when given orally, probably due to enhanced renal calcium absorption. Urinary calcium excretion is unaffected by sodium citrate, since the alkali-mediated hypocalciuric effect is offset by a sodium-linked calciuresis.[1] Potassium citrate may be beneficial in reducing the rate of stone formation in patients with hypocitraturia[2,3] or hypercalciuria.[4] As mentioned in Uses above, sodium bicarbonate or sodium or potassium citrate may also be used for their alkalinising action, as an adjunct to a liberal fluid intake, to prevent development of uric-acid renal calculi during uricosuric therapy.

Other causes of renal calculi and their treatment are discussed on p.2181.

Urinary alkalinisation with sodium bicarbonate, sodium citrate, or potassium citrate may be useful in the management of cystine stone formation in patients with cystinuria (see under Penicillamine, p.1459).

1. Anonymous. Citrate for calcium nephrolithiasis. *Lancet* 1986; **i:** 955.
2. Pak CYC, Fuller C. Idiopathic hypocitraturic calcium-oxalate nephrolithiasis successfully treated with potassium citrate. *Ann Intern Med* 1986; **104:** 33–7.
3. Tekin A, *et al.* Oral potassium citrate treatment for idiopathic hypocitruria in children with calcium urolithiasis. *J Urol (Baltimore)* 2002; **168:** 2572–4.
4. Pak CYC, *et al.* Prevention of stone formation and bone loss in absorptive hypercalciuria by combined dietary and pharmacological interventions. *J Urol (Baltimore)* 2003; **169:** 465–9.

Preparations

BP 2008: Alginate Raft-forming Oral Suspension; Alkaline Gentian Mixture; Aromatic Magnesium Carbonate Mixture; Compound Magnesium Trisilicate Oral Powder; Compound Sodium Bicarbonate Tablets; Compound Sodium Chloride Mouthwash; Kaolin and Morphine Mixture; Kaolin Mixture; Magnesium Trisilicate Mixture; Potassium Citrate Mixture; Sodium Bicarbonate Ear Drops; Sodium Bicarbonate Eye Lotion; Sodium Bicarbonate Intravenous Infusion; Sodium Bicarbonate Oral Solution; Sodium Citrate Eye Drops; Sodium Citrate Irrigation Solution; Sodium Lactate Intravenous Infusion;
BPC 1968: Effervescent Potassium Tablets;
Ph. Eur.: Anticoagulant Acid-Citrate-Glucose Solutions (ACD); Anticoagulant Citrate-Phosphate-Glucose Solution (CPD);
USP 31: Anticoagulant Citrate Dextrose Solution; Anticoagulant Citrate Phosphate Dextrose Adenine Solution; Anticoagulant Citrate Phosphate Dextrose Solution; Anticoagulant Sodium Citrate Solution; Half-strength Lactated Ringer's and Dextrose Injection; Lactated Ringer's and Dextrose Injection; Lactated Ringer's Injection; Magnesium Carbonate and Sodium Bicarbonate for Oral Suspension; Magnesium Carbonate, Citric Acid, and Potassium Citrate for Oral Solution; Potassium and Sodium Bicarbonates and Citric Acid Effervescent Tablets for Oral Solution; Potassium Bicarbonate and Potassium Chloride Effervescent Tablets for Oral Solution; Potassium Bicarbonate and Potassium Chloride for Effervescent Oral Solution; Potassium Bicarbonate Effervescent Tablets for Oral Solution; Potassium Chloride in Lactated Ringer's and Dextrose Injection; Potassium Chloride, Potassium Bicarbonate, and Potassium Citrate Effervescent Tablets for Oral Solution; Potassium Citrate And Citric Acid Oral Solution; Potassium Citrate Extended-release Tablets; Potassium Gluconate and Potassium Citrate Oral Solution; Potassium Gluconate, Potassium Citrate, and Ammonium Chloride Oral Solution; Sodium Acetate Injection; Sodium Acetate Solution; Sodium Bicarbonate Injection; Sodium Bicarbonate Oral Powder; Sodium Bicarbonate Tablets; Sodium Citrate and Citric Acid Oral Solution; Sodium Lactate Injection; Sodium Lactate Solution; Tricitrates Oral Solution; Trikates Oral Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: LTK250; Urokit; ***Austral.:*** Chlorvescent; Sodibic; Urocit-K; ***Austria:*** Oxalyt; Uralyt-U; ***Belg.:*** Uralyt-U; ***Braz.:*** Acalka†; Citrosodine†; Litocit; ***Canad.:*** Bromo Seltzer; Eno; K-Citra; K-Lyte; Polycitra-K; ***Chile:*** Acalka; Eucerin; Sal De Yasta†; ***Cz.:*** Alkaligen†; Uralyt-U; ***Fr.:*** Elgydium Bicarbonate†; Potensium gelule; ***Ger.:*** Alkala T; Apocit; bicaNorm; Blanel; Kalitrans; Kalium; Kohlensaurebad Bastian; Nephrotrans; Uralyt-U; ***Gr.:*** Citrolithin; ***Hong Kong:*** Urocit-K; ***Hung.:*** Alkaligen; ***India:*** Alkasol; Citralka; Oricitral; ***Irl.:*** Cystopurin; ***Israel:*** Babic; Uralyt-U; ***Ital.:*** Citrosodina; Uralyt-U; ***Jpn:*** Meylon; ***Malaysia:*** Urocit-K; ***Mex.:*** Betsol Z; Bicarnat; Debonal; ***Neth.:*** Citra-Lock; Hospasol; ***Norw.:*** Kajos; ***NZ:*** Citravescent; ***Philipp.:*** Acalka; ***Pol.:*** Citrolyt; Litocid; ***Port.:*** Acalka; Hospasol; Uralyt-U; ***S.Afr.:*** Crystacit; SB Gripe Water; Uralyt-U; ***Singapore:*** Gripe Water†; Urocit-K†; ***Spain:*** Acalka; Hospasol; Plurisalina; ***Swed.:*** Kajos; ***Switz.:*** Nephrotrans; Uralyt-U†; ***Thai.:*** Acalka; Uralyt-U; ***Turk.:*** Anti-Asidoz; Urocid-K; ***UK:*** Boots Gripe Mixture 1 Month Plus; Canesten Oasis; Cymalon Cranberry; Cystitis Relief; Cystocalm; Cystopurin; ***USA:*** Citra pH; K + Care†; K-Lyte; Neut; Urocit-K; ***Venez.:*** Policitra.

Multi-ingredient: numerous preparations are listed in Part 3.

Calcium

Calcio; Kalsiyum; Kalzium.
Ca = 40.078.

Description. Calcium is a cation given as various calcium-containing salts.

Incompatibility. Calcium salts have been reported to be incompatible with a wide range of drugs. Complexes may form resulting in the formation of a precipitate.

Calcium Acetate

Acetate of Lime; Calcii acetas; Calcio, acetato de; Calcium, acétate de; E263; Kalcio acetatas; Kalciumacetat; Kalcium-acetát; Kalsiumasetaatti; Kalsiyum Asetat; Lime Acetate.

$C_4H_6CaO_4$ = 158.2.
CAS — 62-54-4.
ATC — A12AA12.
ATC Vet — QA12AA12.

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Ph. Eur. 6.2 (Calcium Acetate). A white or almost white, hygroscopic powder. Freely soluble in water; slightly soluble in alcohol. A 5% solution in water has a pH of 7.2 to 8.2. Store in airtight containers.
USP 31 (Calcium Acetate). A white, odourless or almost odourless, hygroscopic, crystalline powder. It decomposes to calcium carbonate and acetone when heated to above 160°. Freely soluble in water; slightly soluble in methyl alcohol; practically insoluble in dehydrated alcohol, in acetone, and in benzene. A 5% solution in water has a pH of 6.3 to 9.6. Store in airtight containers.

Equivalence. Each g of calcium acetate (anhydrous) represents about 6.3 mmol of calcium. Calcium acetate (anhydrous) 3.95 g is equivalent to about 1 g of calcium.

Calcium Chloride

Calcii Chloridum; Calcii chloridum dihydricum; Calcio, cloruro de; Calcium Chloratum; Calcium, chlorure de; Chlorid vápenatý; Cloreto de Cálcio; Cloruro de Calcio; E509; Kalcio chloridas; Kalciumklorid; Kalcium-klorid; Kalsiumkloridi; Kalsiyum Klorür; Wapnia chlorek.

$CaCl_2.xH_2O$ = 110.0 (anhydrous); 147.0 (dihydrate).
CAS — 10043-52-4 (anhydrous calcium chloride); 7774-34-7 (calcium chloride hexahydrate); 10035-04-8 (calcium chloride dihydrate).
ATC — A12AA07; B05XA07; G04BA03.
ATC Vet — QA12AA07; QB05XA07; QG04BA03.

Pharmacopoeias. *Chin.*, *Eur.* (see p.vii), *Jpn*, *US*, and *Viet.* include the dihydrate.
Eur. also specifies the hexahydrate.
Ph. Eur. 6.2 (Calcium Chloride Dihydrate; Calcii Chloridum Dihydricum). A white or almost white, hygroscopic, crystalline powder. Freely soluble in water; soluble in alcohol. Store in airtight containers.
Ph. Eur. 6.2 (Calcium Chloride Hexahydrate; Calcii Chloridum Hexahydricum). A white or almost white, crystalline mass or colourless crystals. Very soluble in water; freely soluble in alcohol. F.p. about 29°.
USP 31 (Calcium Chloride). White, hard, odourless fragments or granules. Is deliquescent. Soluble 1 in 0.7 of water, 1 in 0.2 of boiling water, 1 in 4 of alcohol, and 1 in 2 of boiling alcohol. pH of a 5% solution in water is between 4.5 and 9.2. Store in airtight containers.

Equivalence. Each g of calcium chloride (dihydrate) represents about 6.8 mmol of calcium and 13.6 mmol of chloride. Calcium chloride (dihydrate) 3.67 g is equivalent to about 1 g of calcium.

Each g of calcium chloride (hexahydrate) represents about 4.56 mmol of calcium and 9.13 mmol of chloride. Calcium chloride (hexahydrate) 5.47 g is equivalent to about 1 g of calcium.

Calcium Citrate

Calcio, citrato de; Tricalcium Citrate. Tricalcium 2-hydroxypropane-1,2,3-tricarboxylate tetrahydrate.

$C_{12}H_{10}Ca_3O_{14}.4H_2O$ = 570.5.
CAS — 5785-44-4.

Pharmacopoeias. In *US*.
USP 31 (Calcium Citrate). A white, odourless, crystalline powder. Slightly soluble in water; insoluble in alcohol; freely soluble in diluted 3N hydrochloric acid and in diluted 2N nitric acid.

Equivalence. Each g of calcium citrate (tetrahydrate) represents about 5.3 mmol of calcium and 3.5 mmol of citrate. Calcium citrate (tetrahydrate) 4.74 g is equivalent to about 1 g of calcium.

Calcium Glubionate *(USAN, rINN)*

Calcii Glubionas; Calcium Gluconate Lactobionate Monohydrate; Calcium Gluconogalactogluconate Monohydrate; Glubionate de Calcium; Glubionato de calcio. Calcium D-gluconate lactobionate monohydrate.

Кальция Глубионат

$(C_{12}H_{21}O_{12})_2C_6H_{11}O_7)Ca.H_2O$ = 610.5.
CAS — 31959-85-0 (anhydrous calcium glubionate); 12569-38-9 (calcium glubionate monohydrate).
ATC — A12AA02.
ATC Vet — QA12AA02.

Pharmacopoeias. *US* includes Calcium Glubionate Syrup.

Equivalence. Each g of calcium glubionate (monohydrate) represents about 1.6 mmol of calcium. Calcium glubionate (monohydrate) 15.2 g is equivalent to about 1 g of calcium.

Calcium Gluceptate

Calcium Glucoheptonate *(pINN)*; Calcii glucoheptonas; Calcium, glucoheptonate de; Glucoheptonate de Calcium; Glucoheptonato de calcio; Kalcio gliukoheptonatas; Kalciumglukoheptonat; Kalcium-glükoheptonát; Kalcium-glukoheptonát; Kalsiumglukoheptonaatti.

Кальция Глюкогептонат

$C_{14}H_{26}CaO_{16}$ = 490.4.
CAS — 17140-60-2 (anhydrous calcium gluceptate); 29039-00-7 (anhydrous calcium gluceptate).
ATC — A12AA10.
ATC Vet — QA12AA10.

Pharmacopoeias. In *Eur.* (see p.vii). *US* allows anhydrous or with varying amounts of water of hydration.
Ph. Eur. 6.2 (Calcium Glucoheptonate). A mixture in variable proportions of calcium di(D-*glycero*-D-*gulo*-heptonate) and calcium di(D-*glycero*-D-*ido*-heptonate). A white or very slightly yellow, hygroscopic, amorphous powder. Very soluble in water; practically insoluble in alcohol and in acetone. A 10% solution in water has a pH of 6.0 to 8.0. Store in airtight containers.
USP 31 (Calcium Gluceptate). It is anhydrous or contains varying amounts of water of hydration. It consists of the calcium salt of the alpha-epimer of glucoheptonic acid or of a mixture of the alpha and beta epimers of glucoheptonic acid. A white to faintly yellow amorphous powder. It is stable in air, but the hydrous forms may lose part of their water of hydration on standing. Freely soluble in water; insoluble in alcohol and in many other organic solvents. pH of a 10% solution in water is between 6.0 and 8.0.

Equivalence. Each g of calcium gluceptate (anhydrous) represents about 2 mmol of calcium. Calcium gluceptate (anhydrous) 12.2 g is equivalent to about 1 g of calcium.

Calcium Gluconate

Calcii gluconas; Calcii Gluconas Monohydricus; Calcio, gluconato de; Calcium, gluconate de; Calcium Glyconate; E578; Glukonan vápenatý monohydrát; Kalcio gliukonatas; Kalciumglukonat; Kalcium-glükonát; Kalsiumglukonaatti; Wapnia glukonian. Calcium D-gluconate monohydrate.

$C_{12}H_{22}CaO_{14}.H_2O$ = 448.4.
CAS — 299-28-5 (anhydrous calcium gluconate); 18016-24-5 (calcium gluconate monohydrate).
ATC — A12AA03; D11AX03.
ATC Vet — QA12AA03; QD11AX03.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *Viet.* Also in *US* as the anhydrous or the monohydrate form.
Calcium borogluconate is included as an injection in *BP(Vet)*.
Ph. Eur. 6.2 (Calcium Gluconate). A white or almost white, crystalline or granular, powder. Sparingly soluble in water; freely soluble in boiling water.
USP 31 (Calcium Gluconate). It is anhydrous or contains one molecule of water of hydration. White, odourless, crystalline granules or powder. Slowly soluble 1 in 30 of water; soluble 1 in 5 of boiling water; insoluble in alcohol. Its solutions are neutral to litmus.

Equivalence. Each g of calcium gluconate (monohydrate) represents about 2.2 mmol of calcium. Calcium gluconate (monohydrate) 11.2 g is equivalent to about 1 g of calcium.