absorption is a problem, in disaccharide intolerance (without isomaltose intolerance), and in acute and chronic hepatic and renal diseases where protein, mineral, and fluid restriction are often necessary.

Maltodextrin is also employed as a pharmaceutical excipient.

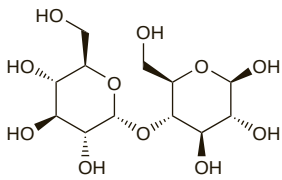
Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Carbohidrato 100; MC Modulo Calorico; ***Austral.:*** Maxijul; ***Braz.:*** Nidex; Oligossac†; ***Canad.:*** Moducal†; ***Chile:*** Modulo Calorico; ***Cz.:*** Fantomalt†; ***Fin.:*** Fantomalt; ***Hong Kong:*** Fiber Basics; ***Ital.:*** Energen; Fantomalt; Maltovis; Nidex; ***NZ:*** Moducal; ***Port.:*** Fantomalt†; Moducal†; ***USA:*** Moducal; ***Venez.:*** Fantomalt.

Multi-ingredient: ***Chile:*** Nutrasweet†; ***Fr.:*** Gumilk; ***Indon.:*** Fantomalt; ***Ital.:*** Giflorex; ***Pol.:*** Fantomalt; ***Venez.:*** Glutapak; Glutapak-R; Hermesetas Gold; Modulo Calorico; Multidex.

Maltose

D-maltose; Maltobiose; Maltosa. 4-*O*-α-D-Glucopyranosyl-β-D-glucopyranose.
$C_{12}H_{22}O_{11}$ = 342.3.
CAS — 69-79-4 (anhydrous maltose); 6363-53-7 (maltose monohydrate).



(anhydrous maltose)

Pharmacopoeias. *Jpn* includes the monohydrate. *USNF* permits the anhydrous and monohydrate forms.
USNF 26 (Maltose). It contains one molecule of water of hydration or is anhydrous. A white, odourless, crystalline powder that has a sweet taste. Freely soluble in water; very soluble in dehydrated alcohol; practically insoluble in ether; slightly soluble in methyl alcohol. pH of a 10% solution in water is between 3.7 and 4.7 (anhydrous form) and between 4.0 and 5.5 (monohydrate form).

Profile

Maltose, a disaccharide composed of two glucose molecules, is less sweet than sucrose. It is obtained from starch by hydrolysis with amylase. Maltose is often present with other sugars in mixtures used as carbohydrate sources. It is also used as a pharmaceutical excipient.

Adverse effects. Hyponatraemia developed after intravenous infusion of normal immunoglobulin in 10% maltose in a patient with acute renal failure after liver transplantation.[1] The effect, which recurred on each of four successive infusions, resembled that of hyperglycaemia and was thought to be due to accumulation of maltose and other osmotically active metabolites in the extracellular fluid.

1. Palevsky PM, *et al.* Maltose-induced hyponatremia. *Ann Intern Med* 1993; **118:** 526–8.

Precautions. Preparations that contain, or are metabolised to, maltose may interfere with the results from glucose tests (p.2314). Overestimation of glucose results may mask hypoglycaemia, resulting in the inappropriate use of insulin.[1,2] The problem may also occur with icodextrin, which produces maltose as a metabolite (see Dialysis, p.1937).

1. Medicines and Healthcare products Regulatory Agency. Medical device alert: ref MDA/2007/058 issued 19 July 2007. Available at: http://www.mhra.gov.uk/PrintPreview/PublicationSP/CON2031807 (accessed 01/07/08)
2. FDA. Important safety information on interference with blood glucose measurement following use of parenteral maltose/parenteral galactose/oral xylose-containing products (issued November 2005). Available at: http://www.fda.gov/cber/safety/maltose110405.htm (accessed 01/07/08)

Preparations

USNF 26: Liquid Glucose.

Proprietary Preparations (details are given in Part 3)
Indon.: Martos; ***Jpn:*** Martos.

Multi-ingredient: ***Fr.:*** Picot†.

Manganese

Mangan; Manganèse; Manganeso; Manganum.
Mn = 54.938045.
CAS — 7439-96-5.

Manganese Chloride

Manganeso, cloruro de.
$MnCl_2.4H_2O$ = 197.9.
CAS — 7773-01-5 (anhydrous manganese chloride); 13446-34-9 (manganese chloride tetrahydrate).

Pharmacopoeias. In *US.*
USP 31 (Manganese Chloride). Large, irregular, pink, odourless, translucent crystals. Soluble in water and in alcohol; insoluble in ether. Store in airtight containers. pH of a 5% solution in water is between 3.5 and 6.0.

Manganese Gluconate

Manganèse, gluconate de; Manganeso, gluconato de; Mangani gluconas. Bis(D-gluconato-O^1,O^2) manganese; Manganese D-gluconate.
$C_{12}H_{22}MnO_{14}$ = 445.2.

Pharmacopoeias. In *Eur.* (see p.vii), which allows either anhydrous or hydrated forms, and in *US*, which allows either anhydrous or the dihydrate.
Ph. Eur. 6.2 (Manganese Gluconate). A white or pale pink, slightly hygroscopic, crystalline powder. Soluble in water; practically insoluble in anhydrous ethanol; insoluble in dichloromethane. Store in non-metallic, airtight containers.
USP 31 (Manganese Gluconate).

Manganese Sulfate

Mangaanisulfaattimonohydraatti; Manganèse (sulfate de) monohydraté; Manganese Sulphate; Manganeso, sulfato de; Mangani Sulfas; Mangani sulfas monohydricum; Mangán(II)-szulfát-monohidrát; Mangano sulfatas; Mangansulfatmonohydrat; Manganu siarczan; Síran manganatý. Manganese (II) sulphate monohydrate.
$MnSO_4.H_2O$ = 169.0.
CAS — 7785-87-7 (anhydrous manganese sulfate); 10034-96-5 (manganese sulfate monohydrate); 10101-68-5 (manganese sulfate tetrahydrate).

Pharmacopoeias. In *Eur.* (see p.vii) and *US. Br.* and *Fr.* also include the tetrahydrate.
BP 2008 (Manganese Sulphate). The tetrahydrate occurs as pale pink, odourless or almost odourless, crystals or crystalline powder. Freely soluble in water; practically insoluble in alcohol.
Ph. Eur. 6.2 (Manganese Sulphate Monohydrate). It occurs as a pale pink, slightly hygroscopic, crystalline powder. Freely soluble in water; practically insoluble in alcohol.
USP 31 (Manganese Sulfate). The monohydrate occurs as pale red, slightly efflorescent crystals, or as a purple, odourless powder. Soluble in water; insoluble in alcohol. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°.

Adverse Effects and Precautions

Acute poisoning due to ingestion of manganese or manganese salts is rare. The main symptoms of chronic poisoning, either from injection or usually inhalation of manganese dust or fumes in air, include extrapyramidal effects which may be followed by progressive deterioration in the CNS. Parenteral manganese should be used cautiously in patients with reduced biliary excretion, especially in cholestatic liver disease. When the duration of total parenteral nutrition is likely to exceed 1 month, serum-manganese concentration and liver function should be checked before starting treatment and regularly during treatment; additives containing manganese should be stopped if serum-manganese concentrations are raised or cholestasis develops.

Accumulation. There are reports of cholestatic liver disease, and possibly changes in the basal ganglia, associated with hypermanganesaemia in children given long-term parenteral nutrition;[1,2] manganese accumulation may be secondary to impaired biliary excretion.[3] Manganese supplementation in such patients requires re-appraisal and whole blood manganese concentrations should be monitored regularly. A low-dose regimen of not more than 1 microgram/kg (0.018 micromoles/kg) daily has been suggested,[2,3] a dose that was also recommended by the American Society for Parenteral and Enteral Nutrition.[4] Hypermanganesaemia and basal ganglia manganese deposition resolved over time in 2 children when the manganese dose in their parenteral nutrition was reduced.[5] Manganese accumulation in the basal ganglia has been seen in patients with liver cirrhosis,[6,7] and may be associated with parkinsonism[7,8] (for reference to the use of aminosalicylic acid in the treatment of manganese-induced parkinsonism, see p.202). Concern has been expressed[9] at the high levels of manganese contained in infant formulas.

1. Reynolds AP, *et al.* Manganese in long term paediatric parenteral nutrition. *Arch Dis Child* 1994; **71:** 527–8.
2. Fell JME, *et al.* Manganese toxicity in children receiving long-term parenteral nutrition. *Lancet* 1996; **347:** 1218–21.
3. Beath SV, *et al.* Manganese toxicity and parenteral nutrition. *Lancet* 1996; **347:** 1773–4. Correction. *ibid.* **348:** 416.
4. Mirtallo J, *et al.* American Society for Parenteral and Enteral Nutrition. Safe practices for parenteral nutrition. *J Parenter Enteral Nutr* 2004; **28:** S39–S70.
5. Kafritsa Y, *et al.* Long term outcome of brain manganese deposition in patients on home parenteral nutrition. *Arch Dis Child* 1998; **79:** 263–5.
6. Krieger D, *et al.* Manganese and chronic hepatic encephalopathy. *Lancet* 1995; **346:** 270–4.
7. Burkhard PR, *et al.* Chronic parkinsonism associated with cirrhosis. *Arch Neurol* 2003; **60:** 521–8.
8. Zatta P, *et al.* The role of metals in neurodegenerative processes: aluminum, manganese, and zinc. *Brain Res Bull* 2003; **62:** 15–28.
9. Hozyasz KK, Ruszczynska A. High manganese levels in milk-based infant formulas. *Neurotoxicology* 2004; **25:** 733.

Pharmacokinetics

Absorption of manganese from the gastrointestinal tract is variable, ranging from 3 to 50%. There is some evidence that the amount absorbed decreases as intake increases, suggesting a homoeostatic response. In the circulation, manganese is bound to transmanganin, a beta-1-globulin. Manganese is stored in the brain, kidneys, pancreas, and liver. It is excreted in bile, and undergoes enterohepatic circulation.

Uses and Administration

Manganese is an essential trace element and small amounts of a salt such as the chloride or sulfate are sometimes added to solutions for total parenteral nutrition. Suggested doses are 275 micrograms (5 micromoles) elemental manganese daily for adults and children over 40 kg, and 1 microgram/kg (0.0182 micromol/kg) daily for infants and children to a maximum of 15 micrograms (see also Accumulation, above).

Manganese compounds or salts that have been used in therapeutics in addition to those mentioned above include manganese amino acid chelate, manganese dioxide, manganese gluconate, and manganese hydrogen citrate.

Human requirements. In the UK neither a reference nutrient intake (RNI) nor an estimated average requirement (EAR) (see p.1925) has been set for manganese although a safe intake for adults was believed to lie above 1.4 mg (26 micromoles) daily.[1] Similarly, in the USA a recommended dietary allowance has not been published, although an adequate intake has been estimated to be 2.3 mg daily for men and 1.8 mg daily for women.[2] A tolerable upper intake level of 11 mg has also been set.[2] WHO has not proposed a safe range of mean population intakes for manganese since neither intakes resulting in deficiency nor threshold toxicity levels have been established.[3] Diets high in unrefined cereals, nuts, leafy vegetables, and tea will be high in manganese.

1. DoH. Dietary reference values for food energy and nutrients for the United Kingdom: report of the panel on dietary reference values of the committee on medical aspects of food policy. *Report on health and social subjects 41.* London: HMSO, 1991.
2. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board. *Dietary Reference Intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc*. Washington DC: National Academy Press, 2001. Also available at: http://www.nap.edu/openbook.php?isbn=0309072794 (accessed 21/07/08)
3. WHO. Manganese. In: *Trace elements in human nutrition and health*. Geneva: WHO, 1996; 163–7.

Preparations

BPC 1973: Compound Ferrous Sulphate Tablets;
USP 31: Manganese Chloride for Oral Solution; Manganese Chloride Injection; Manganese Sulfate Injection.

Proprietary Preparations (details are given in Part 3)
Fr.: Mangaplexe†; ***Mex.:*** MN-Fusin†.

Multi-ingredient: ***Austral.:*** Bio Magnesium; Bioglan Joint Mobility; ***Braz.:*** Eviprostat†; Xantina B12†; Xantinon B12; ***Fr.:*** Cicaplast; Oligoderm; Oligorhine Manganese; ***Ger.:*** Algosteril Trionic†; ***Indon.:*** Eviprostat; Fitbon; Fitbon Plus; ***Irl.:*** Ferrotab†; ***Ital.:*** Sterimar Mn; ***Mex.:*** Actiman; ***Philipp.:*** Ruflex; ***Rus.:*** Tot'Hema (Тотема); ***S.Afr.:*** Ferrous Sulphate Compound; ***Singapore:*** Arthro-Flex; Eviprostat.

Medium-chain Triglycerides

Keskipitkäketjuiset tyydyttyneet triglyseridit; Triacylglyceroly střední nasycené; Triglicéridai, vidutinės grandinės; Trigliceridek, közepes szénláncú zsírsavaké; Triglicéridos de cadena media; Triglycerida saturata media; Triglycerider, medellångkedjiga; Triglycérides à chaîne moyenne.

Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF.*
Ph. Eur. 6.2 (Triglycerides, Medium-chain). They are obtained from the oil extracted from the hard, dried fraction of the endosperm of *Cocos nucifera* or from the dried endosperm of *Elaeis guineensis*. They consist of a mixture of triglycerides of saturated fatty acids, mainly of octanoic acid and of capric acid ($C_{10}H_{20}O_2$ = 172.3). They contain not less than 95% of saturated fatty acids with 8 and 10 carbon atoms. A colourless or slightly yellowish, oily liquid. Practically insoluble in water; miscible with alcohol, with dichloromethane, with petroleum spirit, and with fatty oils. Store in well-filled containers. Protect from light.
USNF 26 (Medium-Chain Triglycerides). They are obtained from the oil extracted from the hard, dried fraction of the endosperm of *Cocos nucifera* or from the dried endosperm of *Elaeis guineensis*. They consist of a mixture of triglycerides of saturated fatty acids, mainly of octanoic acid and of capric acid ($C_{10}H_{20}O_2$ = 172.3). They contain not less than 95% of saturated fatty acids with 8 and 10 carbon atoms. A colourless or slightly yellowish, oily liquid. Practically insoluble in water; miscible with alcohol, with dichloromethane, with petroleum spirit, and with fatty oils. Store in airtight containers at a temperature not exceeding 25°. Protect from light.

Profile

Medium-chain triglycerides are used for enteral and parenteral nutrition (p.1923) in conditions associated with malabsorption of fat, such as cystic fibrosis, enteritis, and steatorrhoea, and after intestinal resection. Medium-chain triglycerides are more readily hydrolysed than long-chain triglycerides and are not dependent