intake was believed to be above 25 micrograms daily for adults.[1] Similarly, in the USA a recommended dietary allowance has not been published but the adequate intake was estimated to be 35 micrograms daily for young men and 25 micrograms daily for young women.[2] WHO considers that the minimum population mean intake likely to meet normal needs for chromium might be about 33 micrograms daily, and that supplementation of this element should not exceed 250 micrograms daily until more is known.[3]

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. Chromium. In: *Trace elements in human nutrition and health*. Geneva: WHO, 1996: 155–60.

Supplementation. Although a daily chromium intake of 200 nanograms/kg has been suggested in children given total parenteral nutrition (TPN), a study in 15 children[1] given long-term parenteral nutrition found that supplementation at about this level was associated with serum-chromium concentrations 4 to 42 times higher than the mean value in 15 children not receiving TPN. Raised serum-chromium concentrations were associated with a decrease in glomerular filtration rate; one year after stopping chromium supplementation, which reduced intake to 50 nanograms/kg daily (as contaminants of water and TPN solutions), chromium concentrations, although lower, were still higher than controls and renal function had not altered. The authors subsequently ceased chromium supplementation in both children and adults, since chromium contamination of TPN solutions appeared adequate to prevent deficiency, although it was acknowledged that signs of chromium deficiency might take some years to appear. Chromium contamination in various preparations used in paediatric parenteral nutrition has been studied.[2]

1. Moukarzel AA, *et al*. Excessive chromium intake in children receiving total parenteral nutrition. *Lancet* 1992; **339:** 385–8.
2. Hak EB, *et al*. Chromium and zinc contamination of parenteral nutrient solution components commonly used in infants and children. *Am J Health-Syst Pharm* 1998; **55:** 150–4.

Preparations

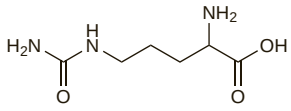
USP 31: Chromic Chloride Injection; Chromium Picolinate Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: NH4 Silhouette; Ripped Max; Sigmar Lipo; Tonekin; ***Austral.:*** Chrome; ***Chile:*** Edul K-200; ***Fr.:*** Chromasvelt; ***Ital.:*** Croben; ***Mex.:*** Cromifusin†; Ifa Slim†; ***USA:*** Chroma-Pak.

Multi-ingredient: ***Arg.:*** Centellacrom; Cholesterol Reducing Plan†; Garcinia Cambogia Compuesta; Herbaccion Diet; IP-6; Metabolic; Novosual†; Tonekin Plus†; Top Life Diet†; ***Austral.:*** Bioglan 3B Beer Belly Buster; Citri Slim+Trim; Digestaid; Pro-Shape†; ***Indon.:*** Biocholes; Kitoles; Vitaslim; ***Mex.:*** Lipo Slim N†; Slim-D; ***Philipp.:*** Liposorb; Nutrafit.

Citrulline

N^5-(Aminocarbonyl)-L-ornithine; N^δ-Carbamylornithine; Citrulina; L-citrulline; NSC-27425. α-Amino-δ-ureidovaleric acid.
$C_6H_{13}N_3O_3$ = 175.2.
CAS — 372-75-8.



Profile

Citrulline is a non-essential amino acid that is involved in the urea cycle. Citrulline and citrulline malate are used as dietary supplements.

Hyperammonaemia. Citrulline has been given as an alternative to arginine in the management of hyperammonaemia (p.1929) due to **urea cycle disorders**.

Lysinuric protein intolerance is another condition associated with hyperammonaemia and similar neurological sequelae. In this condition there is no deficiency of urea-cycle enzymes but a deficiency of urea-cycle substrate, such as ornithine, which results in reduced synthesis of citrulline. Patients are treated with dietary protein restriction and citrulline supplementation, which improves protein tolerance and nutrition but only slightly ameliorates growth retardation. Osteoporosis may be severe in children with this disorder.[1] A child presenting with osteopenia and diagnosed with lysinuric protein intolerance was given large oral doses of citrulline (up to 5.7 g daily). Aside from a substantial increase in protein tolerance, a striking acceleration in linear growth and bone mass was reported.[2] Lysine deficiency may be implicated in growth retardation,[1] but lysine supplementation may precipitate diarrhoea and malabsorption.[2] Six patients with lysinuric protein intolerance and receiving oral citrulline were supplemented with oral lysine. Larger lysine doses of 0.55 mmol/kg and 1.1 mmol/kg given consecutively, caused profuse diarrhoea, but smaller doses of 0.05 mmol/kg, given three times daily (up to a maximum dose of 2.5 mmol) were well tolerated. Plasma lysine concentrations were normalised with no adverse effects on the urea cycle.[1]

1. Lukkarinen M, *et al*. Oral supplementation corrects plasma lysine concentrations in lysinuric protein intolerance. *Metabolism* 2003; **52:** 935–8.
2. Carpenter TO, *et al*. Lysinuric protein intolerance presenting as childhood osteoporosis: clinical and skeletal response to citrulline therapy. *N Engl J Med* 1985; **312:** 290–4.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Stimol; ***Indon.:*** Stimol; ***Port.:*** Dynergum; ***Rus.:*** Stimol (Стимол); ***Spain:*** Stimol; ***Switz.:*** Biostimol.

Multi-ingredient: ***Braz.:*** Ornihepat†; Ornitargin; ***Fr.:*** Epuram†; ***Ger.:*** Polilevo N†; ***Ital.:*** Ipoazotal Complex; Ipoazotal†; Polilevo†.

Cod-liver Oil *(BAN)*

Aceite de hígado de bacalao; Baliık yağı; Cod Liver Oil; Csukamájolaj; Foie de morue, huile de; Huile de Foie de Morue; Iecoris aselli oleum; Kalanmaksaöljy; Lebertran; Menkių kepenų taukai; Ol. Morrh.; Óleo de Bacalhau; Oleum Jecoris Aselli; Oleum Morrhuae; Olio di Fegato di Merluzzo; Rybí olej; Torskleverolja.

Тресковый Печёночный Жир
CAS — 8001-69-2.

Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Jpn,* and *US.*
Ph. Eur. 6.2 (Cod-liver Oil (Type A) and Cod-liver Oil (Type B)). Purified fatty oils obtained from the fresh livers of *Gadus morhua* and other species of Gadidae, solid substances being removed by cooling and filtering. The oils contain not less than 600 units (180 micrograms) and not more than 2500 units (750 micrograms) of vitamin A per g and not less than 60 units (1.5 micrograms) and not more than 250 units (6.25 micrograms) of vitamin D_3 (colecalciferol) per g. Authorised antoxidants in concentrations not exceeding those prescribed by the competent authority may be added.
Clear yellowish viscous liquids. Practically insoluble in water; slightly soluble in alcohol; miscible with petroleum spirit. Store in well-filled airtight containers. Store under an inert gas if no antoxidant is added. Protect from light.
USP 31 (Cod Liver Oil). The partially destearinated fixed oil obtained from the fresh livers of *Gadus morrhua* and other species of Gadidae. It contains not less than 600 units (180 micrograms) and not more than 2500 units (750 micrograms) of vitamin A per g and not less than 60 units (1.5 micrograms) and not more than 250 units (6.25 micrograms) of vitamin D per g. It may be flavoured by the addition of not more than 1% of a suitable flavour or a mixture of flavours. A suitable antoxidant may be added.
A thin, oily liquid, having a characteristic, slightly fishy but not rancid odour. Slightly soluble in alcohol; freely soluble in carbon disulfide, in chloroform, in ether, and in ethyl acetate. Store in airtight containers. It may be bottled or packaged in containers from which air has been expelled by the production of a vacuum or by an inert gas.

Profile

Cod-liver oil is a rich source of vitamin D (p.1986) and a good source of vitamin A (p.1971). It also contains several essential fatty acids.

Cod-liver oil dressings or ointment have been advocated to accelerate healing in burns, ulcers, pressure sores, and superficial wounds, but controlled observations have failed to substantiate claims of their value.

Preparations

USP 31: Cod Liver Oil Capsules.

Proprietary Preparations (details are given in Part 3)
Austral.: Hypol†; ***Austria:*** Adecaps; Vitapan; ***Ger.:*** Gelovital; Unguentolan; ***Hong Kong:*** Scott's Emulsion; ***India:*** Seaking†; ***Ital.:*** Dermovitamina; ***Pol.:*** Letin-Tran; Masc Tranowa; Naturkaps Tran; Tran; ***Spain:*** Aceite Geve Concentrado; ***Switz.:*** Morrhulan; ***Turk.:*** Seven Seas Pulse; ***Venez.:*** North Sea†; Scott Tradicional; Supercod.

Multi-ingredient: ***Arg.:*** Abanta; Atomoderma A-D; Atomoderma Plus; Eryteal; Hipoglos con Hidrocortisona; Klorane Bebe Eryteal; ***Austral.:*** Covitol; Desitin Nappy Rash Ointment; Hypol; ***Austria:*** Dermilon; Dermowund; Desitin; Leukichtan; Mirfulan; Nuri-Kapseln; Pudan-Lebertran-Zinksalbe; Vulpuran; ***Belg.:*** Mitosyl; Newderm†; Polyseptol; ***Braz.:*** Blumen†; Calciumvit Infantil†; Hiposan; Oxizinco; Topiglos; ***Canad.:*** Desitin; ***Chile:*** Cikavit; Deltisan; Dulinas†; Neneglos; Pediaderm†; Vatanal; ***Cz.:*** Desitin†; ***Fr.:*** Eryteal†; Halivite†; Magalite; ***Ger.:*** Dermilon; Desitin; Leukona-Wundsalbe†; Mirfulan; Mirfulan Spray N; Mitosyl N; Zinksalbe; ***Gr.:*** Fissan-Pate†; Fissan†; ***Hong Kong:*** Desitin; Scott's Emulsion Orange; ***India:*** Seaking Plus†; ***Indon.:*** Co-Q-10; Scott's Emulsion; ***Irl.:*** Caldease; Morhulin; ***Israel:*** Desitin; Rekasitin; Zincod; ***Ital.:*** Fosfarsile Junior; Neo-Ustiol; Steril Zeta; Trofo 5; ***Mex.:*** Bacnutri; Capent; Desitin; Emulsion de Scott; Glossderm; Sutin†; ***Norw.:*** Aselli; ***Pol.:*** Dehalid†; Rectosec; Tran z Olejem Wiesiolkowym†; Tranvit; ***Port.:*** Mitosyl; ***S.Afr.:*** Achromide; Daromide; SB Universal Ointment; Ung Vernleigh; ***Singapore:*** Seven Seas JointCare High Strength; ***Spain:*** Avril; ***Switz.:*** Keroderm†; Leucen; Radix†; Unguentolan; Vita-Hexin; ***UK:*** Arheumacare; Clogar; JointCare Max; M & M; Morhulin; ***USA:*** A and D Medicated; Caldesene; Clocream; Desitin; Diaper Rash; Dyprotex; ***Venez.:*** Wampole†.

Copper

Cobre; Cuivre; Cuprum; Koppar; Kupari; Kupfer; Miedź.
Cu = 63.546.
CAS — 7440-50-8.

Pharmacopoeias. *Eur.* (see p.vii) includes Copper for Homoeopathic Preparations.
Ph. Eur. 6.2 (Copper for Homoeopathic Preparations; Cuprum ad Praeparationes Homoeopathicae). A reddish-brown powder. Practically insoluble in water and in alcohol; soluble in hydrochloric acid and in nitric acid.

Calcium Copperedetate

Cuproedetato cálcico. Calcium [ethylenediaminetetra-acetato{4–}-*N,N′,O,O′*]copper (II) dihydrate.
$C_{10}H_{12}CaCuN_2O_8,2H_2O$ = 427.9.
CAS — 66317-91-7 (anhydrous calcium copperedetate).

Pharmacopoeias. In *BP(Vet).*
BP(Vet) 2008 (Calcium Copperedetate). A blue crystalline powder. It contains 9.1 to 9.7% of Ca and 14.4 to 15.3% of Cu. Freely soluble in water, the solution gradually precipitating the tetrahydrate; practically insoluble in alcohol.

Copper Chloride

Cobre, cloruro de; Cupric Chloride; Miedzi chlorek.
$CuCl_2,2H_2O$ = 170.5.
CAS — 7447-39-4 (anhydrous copper chloride); 10125-13-0 (copper chloride dihydrate).

Pharmacopoeias. In *US.*
USP 31 (Cupric Chloride). Bluish-green, deliquescent crystals. Freely soluble in water; soluble in alcohol; slightly soluble in ether. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°.

Copper Gluconate

Cobre, gluconato de. Copper D-gluconate (1:2); Bis(D-gluconato-O^1,O^2) copper.
$C_{12}H_{22}CuO_{14}$ = 453.8.
CAS — 527-09-3.

Pharmacopoeias. In *US.*

Copper Sulfate

Cobre, sulfato de; Copper Sulph.; Copper Sulphate; Cuivre (Sulfate de); Cuivre, sulfate de; Cupri sulfas; Cupri Sulphas; Cupric Sulfate; Kopparsulfat; Kuparisulfaatti; Kupfersulfat; Miedzi(II) siarczan; Réz(II)-szulfát; Síran měďnatý; Sulfato de Cobre; Vario sulfatas. Copper (II) sulphate pentahydrate.
$CuSO_4,5H_2O$ = 249.7.
CAS — 7758-98-7 (anhydrous copper sulfate); 7758-99-8 (copper sulfate pentahydrate).
ATC — V03AB20.
ATC Vet — QV03AB20.

NOTE. Crude copper sulfate is sometimes known as 'blue copperas', 'blue stone', and 'blue vitriol'.

Pharmacopoeias. In *Eur.* (see p.vii), *US,* and *Viet.*
Eur. and *Viet.* also include anhydrous copper sulfate.
Ph. Eur. 6.2 (Copper Sulphate Pentahydrate). A blue crystalline powder or transparent blue crystals. Freely soluble in water; practically insoluble in alcohol; soluble in methyl alcohol.
Ph. Eur. 6.2 (Copper Sulphate, Anhydrous). A greenish-grey, very hygroscopic, powder. Freely soluble in water; practically insoluble in alcohol; slightly soluble in methyl alcohol. Store in airtight containers.
USP 31 (Cupric Sulfate). Deep blue, triclinic crystals, or blue, crystalline granules or powder. It effloresces slowly in dry air. Soluble 1 in 3 of water, 1 in 0.5 of boiling water, 1 in 500 of alcohol, and 1 in 3 of glycerol. Its solutions are acid to litmus. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°.

Adverse Effects and Treatment

Adverse effects from copper have tended to arise after absorption of the metal from cooking utensils and during dialysis. Ingestion of copper from cooking utensils is associated mainly with hepatotoxicity. Dialysis procedures may supply copper through the water supply or from parts of the equipment and when this happens patients may suffer haemolysis and other haematological reactions, kidney involvement, and hepatotoxicity; the toxicity is generally a result of poor equipment maintenance.

Adverse effects attributed to copper have been reported in women with copper-containing intra-uterine devices. There have been isolated case reports of various effects such as allergy and endometrial changes. However, it is difficult to separate those adverse effects that are due to the device from those due solely to the copper.

The symptoms of Wilson's disease (hepatolenticular degeneration) (see p.1459) are due to an accumulation of copper in various parts of the body.

Copper salts if ingested can produce severe gastrointestinal effects and there may be systemic absorption of copper leading to the effects discussed above. The use of sprays of copper salts in agriculture has been associated with lung changes. Treatment of copper poisoning is symptomatic and may involve the use of a chelating agent to remove any absorbed metal. Dialysis has been tried.

Effects on the liver. Cirrhosis and acute liver failure have been attributed to chronic excessive copper supplement ingestion.[1] Supplementation with 10 mg daily of copper (around the safe upper limit) for 2 months has been reported to be associated with transient mild increases in serum aminotransferase values.[2]

1. O'Donohue J, *et al*. Micronodular cirrhosis and acute liver failure due to chronic copper self-intoxication. *Eur J Gastroenterol Hepatol* 1993; **5:** 561–2.
2. Araya M, *et al*. Supplementing copper at the upper level of the adult dietary recommended intake induces detectable but transient changes in healthy adults. *J Nutr* 2005; **135:** 2367–71.

Interactions

Large doses of zinc supplements may inhibit the gastrointestinal absorption of copper.

Uses and Administration

Copper is an essential trace element although severe copper deficiency, which is associated with anaemia, neutropenia, and bone demineralisation, is rare in humans. Copper sulfate is added to parenteral feeds as a source of copper in the prophylaxis and treatment of deficiency states. Doses that have been used for prophylaxis range from 0.5 to 1.5 mg (7.9 to 23.6 micromoles) of copper daily although up to 3 mg daily has been suggested in established deficiency; infants have received 20 micrograms/kg (0.3 micromol/kg) of copper daily. The dose should be governed by the serum-copper concentration, which in healthy adults ranges between 0.7 and 1.6 micrograms/mL (0.01 to 0.025 micromol/mL).

Copper sulfate and other soluble salts of copper have an astringent action on mucous surfaces and in strong solutions they are corrosive. Copper nitrate has been used in preparations for the removal of warts. The uses of copper acetate are discussed on p.2287.

Copper has a contraceptive effect (p.2070) when present in the uterus, and is added to some intra-uterine contraceptive devices; such devices are considered to be effective and safe for several years after insertion, and may be the most effective method for emergency contraception (p.2071). Copper is also reported to have an antimicrobial action.

Copper sulfate has been used to prevent the growth of algae in reservoirs, ponds, and swimming pools and as a molluscicide in the control of fresh-water snails that act as intermediate hosts in the life-cycle of the parasites causing schistosomiasis.

Reagents containing copper sulfate are used in tests for reducing sugars.

In veterinary medicine calcium copperedetate, copper methionate, copper oxide, and cuproxoline are used for the prevention and treatment of copper deficiency.

Copper bracelets are worn as a folk remedy for rheumatic disorders: there is no good evidence to justify such a practice.

Homoeopathy. Copper has been used in homoeopathic medicines under the following names: Cuprum metallicum; Cuprum; Cuprum met.; Cup. met.

Copper sulfate has been used in homoeopathic medicines under the following names: Cuprum sulfuricum; Cuprum sulphuricum; Cup. s.

◊ General references.

1. Wang T, Guo Z. Copper in medicine: homeostasis, chelation therapy and antitumor drug design. *Curr Med Chem* 2006; **13:** 525–37.

Deficiency states. Acquired copper deficiency is very rare and the small number of cases have usually involved patients on total parenteral nutrition or long-term enteral nutrition.[1] Copper deficiency may also be due to malnutrition,[2] malabsorption, or secondary to excessive zinc consumption.[3,4] Clinical manifestations of deficiency include hypocupraemia, hypoceruloplasminaemia, neutropenia, anaemia, osteoporosis, and fracture of the long bones.[2] However, cases may present with neurological signs resembling the subacute combined degeneration normally associated with vitamin B_{12} deficiency.[3,4] Effects on blood may be absent, and zinc concentrations normal;[3] however, hyperzincaemia may be seen even in the absence of exogenous zinc consumption.[4]

Menkes' disease is an X-linked genetic disorder associated with a defect in copper transport, which almost invariably results in death due to progressive cerebral degeneration by the age of 3 years.[5,6] Clinical features include skeletal abnormalities, severe mental retardation, thrombosis, hypothermia, arterial abnormalities, and characteristic facial features.[7] Early parenteral treatment with copper-histidine complex may be of benefit in such children.[5-8] Optimal response to copper therapy appears to occur only in patients who are identified in the newborn period and who have some residual copper-transport activity. More than 3 years of copper replacement therapy may not be necessary or desirable.[6]

1. Masugi J, *et al*. Copper deficiency anemia and prolonged enteral feeding. *Ann Intern Med* 1994; **121:** 386.
2. Cordano A. Clinical manifestations of nutritional copper deficiency in infants and children. *Am J Clin Nutr* 1998; **67** (suppl): 1012S–1016S.
3. Kumar N, *et al*. Copper deficiency myelopathy produces a picture like subacute combined degeneration. *Neurology* 2004; **63:** 33–9.
4. Kumar N. Copper deficiency myelopathy (human swayback). *Mayo Clin Proc* 2006; **81:** 1371–84.
5. Sarkar B, *et al*. Copper-histidine therapy for Menkes' disease. *J Pediatr* 1993; **123:** 828–30.
6. Kaler SG, *et al*. Neonatal diagnosis and treatment of Menkes disease. *N Engl J Med* 2008; **358:** 605–14.
7. Kirodian BG, *et al*. Treatment of Menkes disease with parenteral copper histidine. *Indian Pediatr* 2002; **39:** 183–5.
8. Cox DW. Disorders of copper transport. *Br Med Bull* 1999; **55:** 544–55.

Human requirements. In the UK dietary reference values (see p.1925) have been published for copper.[1] Although an estimated average requirement (EAR) could not be derived a reference nutrient intake (RNI) of 1.2 mg (19 micromoles) daily was set for adults; RNIs of lower values were also specified for infants and children.[1] The Expert Group on Vitamins and Minerals[2] have established a safe upper level (SUL) for copper of 160 micrograms/kg daily.

In the USA the recommended dietary allowance (RDA) for copper is 900 micrograms daily in adults, and the tolerable upper intake level is 10 mg daily.[3]

WHO has estimated a minimum population mean intake of 1.2 mg daily for women and 1.3 mg daily for men, and safe upper limits of population mean intakes of 10 mg daily for women and 12 mg daily for men;[4] values are also estimated for infants and children.

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. Expert Group on Vitamins and Minerals. Safe Upper Levels for vitamins and minerals (May 2003). Available at: http://www.food.gov.uk/multimedia/pdfs/vitmin2003.pdf (accessed 10/11/05)
3. 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)
4. WHO. Copper. In: *Trace elements in human nutrition and health.* Geneva: WHO, 1996: 123–43.

Schistosomiasis. Although most control programmes for schistosomiasis (p.138) use niclosamide as a molluscicide, and copper salts have largely been abandoned for snail control, WHO noted in 1993 that copper sulfate was still used for this purpose in Egypt.[1]

1. WHO. The control of schistosomiasis: second report of the WHO expert committee. *WHO Tech Rep Ser 830* 1993. Available at: http://libdoc.who.int/trs/WHO_TRS_830.pdf (accessed 21/07/08)

Preparations

BPC 1973: Compound Ferrous Sulphate Tablets;
USP 31: Cupric Chloride Injection; Cupric Sulfate Injection.

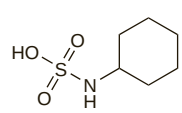
Proprietary Preparations (details are given in Part 3)
Austral.: Multiload; ***Braz.:*** Multiload; ***Canad.:*** Gyne-T†; ***Chile:*** Diuprotect; Multiload; Safety T; ***Denm.:*** Multiload; ***Fr.:*** Gynelle 375; Ionarthrol†; Metacuprol; Multiload; TT 380; UT 380; ***Ger.:*** femena; Multiload; ***Hong Kong:*** Flexi-T; Multiload; ***Indon.:*** Copper-T; ***Israel:*** Anticon; Mona-Lisa; Multiload; ***Ital.:*** Gravigard; Gynefix; Multiload; No-Gravid; Telo Cypro†; UT 380; ***Malaysia:*** Multiload; ***Mex.:*** Cuprifusin†; Multiload†; ***Neth.:*** Multiload†; ***NZ:*** Multiload; ***Port.:*** Multiload†; ***S.Afr.:*** Cuprocept CCL†; Dalcept†; Multiload†; Tricept†; ***Singapore:*** Multiload; Sof-T†; ***Switz.:*** Multiload; ***Thai.:*** Multiload; ***Turk.:*** Multiload; ***UK:*** Flexi-T; Gynefix; Multiload; ***USA:*** Paragard T380A; ***Venez.:*** Multiload.

Multi-ingredient: ***Arg.:*** Dermalibour; Nova-T; ***Austral.:*** APR Cream†; Ascoxal; ***Braz.:*** Belagin; Micotox†; Sulfato Ferroso Composto; Sulfatofer†; ***Canad.:*** Nova-T; ***Chile:*** Agua Sulfatada Picrica; Cicalfate; Nova-T†; Sebium H2O; ***Fin.:*** Ascoxal†; ***Fr.:*** Atoderm moussant; Cicalfate; Cicaplast; Cu-Zn; Decramp; Dermalibour; Dermo-Sulfuryl; Dermocuivre; Eryase; Nova-T; Oligoderm; Oligorhine; Oligorhine Manganese; Purif-Ac Emulsion; Purif-Ac Gel; Ramet Dalibour; Ramet Pain; Ruboderm Plus; Septalibour†; ***Ger.:*** Nova-T; Solco-Derman; ***Hong Kong:*** Aderma Dermalibour†; Cool Mint Listerine; Nova-T; Solcoderm; ***India:*** Hepatoglobine; ***Indon.:*** Nova-T; ***Irl.:*** Ferrotab†; ***Israel:*** Nova-T; ***Ital.:*** Cuprosodio; Cuprosodio Plus; Emmenoiasi; Inflamase; Nova-T; Rinogutt Atlantic; Sterimar Cu; ***Malaysia:*** Nova-T; Solcoderm†; ***Mex.:*** Ascoxal; Dalidome; Daribur; Nova-T; ***Neth.:*** Nova-T†; ***Norw.:*** Ascoxal†; ***NZ:*** Nova-T; ***Rus.:*** Solcoderm (Солкодерм); ***S.Afr.:*** Ferrous Sulphate Compound; Lotio Pruni Comp cum Cupro; Muscle Rub; Nova-T; ***Singapore:*** Nova-T; ***Swed.:*** Ascoxal†; ***Switz.:*** Nova-T; Solcoderm; ***Thai.:*** Nova-T†; ***Turk.:*** Nova-T; ***UK:*** Foresight Iron Formula; Nova-T; ***USA:*** ORA5; ***Venez.:*** Cianofer; Cobalfer; Fercobre†; Folifer B-12; Hepafol con B-12; Nova-T.

Cyclamic Acid *(BAN, USAN)*

Ciclámico, ácido; Cyclam. Acid; E952; Hexamic Acid. *N*-Cyclohexylsulphamic acid.

$C_6H_{13}NO_3S$ = 179.2.
CAS — 100-88-9.



Calcium Cyclamate

Calc. Cyclam.; Calcium Cyclohexanesulfamate; Ciclamato de calcio; Cyclamate Calcium; E952. Calcium *N*-cyclohexylsulphamate dihydrate.

$C_{12}H_{24}CaN_2O_6S_2.2H_2O$ = 432.6.
CAS — 139-06-0 (anhydrous calcium cyclamate); 5897-16-5 (calcium cyclamate dihydrate).

Potassium Cyclamate

Cyclamate potassium; HSDB 1239; Monopotassium cyclohexanesulfamate; potassium cyclohexanesulfamate. Potassium *N*-cyclohexysulphamate.

$C_6H_{12}NO_3SK$ = 217.3.
CAS — 7758-04-5.

Sodium Cyclamate *(BAN, rINN)*

Ciclamato de sodio; Cyclamate de Sodium; Cyclamate Sodium; E952; Natrii cyclamas; Natrio ciklamatas; Nátrium-ciklamát; Natriumcyklamat; Natrium-cyklamát; Natriumsyklamaatti; Siklamat Sodyum; Sod. Cyclam.; Sodium, cyclamate de; Sodium Cyclohexanesulphamate. Sodium *N*-cyclohexylsulphamate.

Натрия Цикламат

$C_6H_{12}NNaO_3S$ = 201.2.
CAS — 139-05-9.

Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii).
Ph. Eur. 6.2 (Sodium Cyclamate). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; slightly soluble in alcohol. A 10% solution in water has a pH of 5.5 to 7.5.

Profile

Cyclamic acid and its salts are intense sweetening agents. In dilute solutions (up to about 0.17%) sodium cyclamate is about 30 times as sweet as sucrose but this factor decreases at higher concentrations. When the concentration approaches 0.5%, a bitter taste becomes noticeable. It is stable to heat.

The use of cyclamates as artificial sweeteners in food, soft drinks, and artificial sweetening tablets was at one time prohibited in Great Britain and some other countries because of concern about the metabolite cyclohexylamine. However, after reappraisal their use is now allowed.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Kaldil Diet; ***Braz.:*** Sucaryl; ***Canad.:*** Sucaryl†; ***Turk.:*** Tadalin.

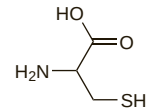
Multi-ingredient: ***Arg.:*** Rondo; Sucaryl; ***Austral.:*** Sucaryl; ***Braz.:*** Finn Cristal; ***Chile:*** Sucaryl†; Sukar-Sin; ***Fr.:*** Sucaryl; ***Israel:*** Sucrin; ***Ital.:*** Diet Sucaryl; ***NZ:*** Sucaryl; ***Port.:*** Dulceril†; ***Rus.:*** Zuckli (Цюкли); ***Turk.:*** Dolce; Dulcaryl.

Cysteine *(rINN)*

C; Cisteína; Cys; Cystéine; L-Cysteine; Cysteinum; E920; L-Cysteina. L-2-Amino-3-mercaptopropionic acid.

Цистеин

$C_3H_7NO_2S$ = 121.2.
CAS — 52-90-4.



Pharmacopoeias. In *Ger.*

Cysteine Hydrochloride *(rINNM)*

Cisteino hidrochloridas monohidratas; Cisztein-hidroklorid-monohidrát; Cys Hydrochloride; Cystéine, Chlorhydrate de; Cystéine (chlorhydrate de) monohydraté; L-Cysteine Hydrochloride Monohydrate; Cystein-hydrochlorid monohydrát; Cysteinhydrokloridmonohydrat; Cysteini Hydrochloridum; Cysteini hydrochloridum monohydricum; Hidrocloruro de cisteína; Kysteiinihydrokloridimonohydraatti; L-Cysteiny chlorowodorek. L-2-Amino-3-mercaptopropionic acid hydrochloride monohydrate.

Цистеина Гидрохлорид

$C_3H_7NO_2S,HCl,H_2O$ = 175.6.
CAS — 52-89-1 (anhydrous L-cysteine hydrochloride); 7048-04-6 (L-cysteine hydrochloride monohydrate).

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.
Ph. Eur. 6.2 (Cysteine Hydrochloride Monohydrate; Cysteine Hydrochloride BP 2008). A white or almost white crystalline powder or colourless crystals. Freely soluble in water; slightly soluble in alcohol. Protect from light.
USP 31 (Cysteine Hydrochloride). White crystals or crystalline powder. Soluble in water, in alcohol, and in acetone.

Profile

Cysteine is a non-essential amino acid. Cysteine and cysteine hydrochloride are used as dietary supplements.