There is still no agreement on the most effective oral dose and frequency, and study of this has been complicated by the lack of a suitable oral preparation of phytomenadione.[12,13] Options currently available for oral use include the polyoxyl castor oil and polysorbate-80 containing preparations (unlicensed for oral use) and the colloidal, micelle formulation (licensed for oral use in some countries). These preparations are packaged in glass ampoules, therefore are unsuitable for parents to give at home.

The 1992 recommendations of the British Paediatric Society[8] for oral use of the polyoxyl castor oil formulation suggested a single dose of 500 micrograms on the day of birth. For breast-fed babies, additional doses of 500 micrograms at 7 to 10 days and at 4 to 6 weeks, or 200 micrograms at weekly intervals for 26 weeks, or 50 micrograms daily for 26 weeks, were recommended. Current UK doses[14] for the colloidal preparation in healthy term neonates are 2 mg soon after birth, then 2 mg at 4 to 7 days. Exclusively breast-fed infants should be given a third oral dose of 2 mg one month after birth. Further monthly doses of 2 mg have been recommended while the infant remains exclusively breast-fed. A report[15] of the failure of prophylaxis in 3 breast-fed babies (2 of whom had unidentified cholestatic liver disease) who received 2 doses of this formulation, as recommended in Switzerland, emphasises the importance of the third, and possibly, other, follow-up doses. Plasma vitamin K concentrations in breast-fed infants receiving 3 oral doses of this formulation were at least equal to concentrations in those receiving a single intramuscular dose.[16] A study in Germany, however, found the mixed micellar oral formulation to be no more efficacious than older vitamin K preparations,[17] and a pharmacokinetic study found its absorption to be unreliable in infants with conjugated hyperbilirubinaemia;[18] the authors suggest that even 3 oral doses may not provide sufficient protection against VKDB in infants with latent cholestasis. The most recent advice from the UK Department of Health[14] advocates that all newborn infants should receive vitamin K prophylaxis, both oral and intramuscular routes should be available, and that parents should be involved in the decision on which route is used.

Other oral regimens have been investigated or are in use. In the Netherlands a regimen of 1 mg orally or intramuscularly at birth, followed by 25 micrograms daily or 1 mg weekly by mouth from 1 week to 3 months of age has been found satisfactory.[19,20] In Germany[9,20] and Australia[20] the suggested oral regimen for the polyoxyl castor oil formulation was 1 mg at birth, at 3 to 10 days and at weeks 3 to 6, although some failures have been reported in babies receiving this regimen,[9] and the Australian data confirm it is less effective than a single intramuscular dose.[20] One hospital in the USA has satisfactorily used, for many years, a single 2-mg dose given via nasogastric tube to neonates after birth,[21] although the American Academy of Pediatrics still advocates use of the intramuscular route.[11] In Denmark, a 2-mg dose at birth followed by a weekly dose of 1 mg during the first 3 months of life has effectively prevented any late VKDB in healthy breast-fed babies.[22] In France, for formula-fed neonates at no risk of haemorrhage, 2 mg is given orally at birth, followed by a second dose between day 2 and 7; infants who are breast-fed are given weekly oral doses of 2 mg until cessation of exclusive breast feeding. For neonates at high risk of haemorrhage, however, the first dose is given intramuscularly, or even by slow intravenous injection, according to the clinical state of the infant.[2]

Although phytomenadione crosses the placenta slowly and to a limited extent, it is nevertheless recommended that pregnant women receiving drugs that are vitamin K antagonists (particularly antiepileptics) should receive phytomenadione 10 to 20 mg daily from 36 weeks gestation.[2,23] This is in addition to the requirement that their neonates, who are at high risk of VKDB, receive intramuscular phytomenadione soon after birth. Maternal phytomenadione has been investigated as a means of improving vitamin K status in breast-fed neonates. In 1 study,[24] 5 mg daily for 12 weeks was effective for this purpose.

1. Hathaway WE. Haemostatic disorders in the newborn. In: Bloom AL, Thomas DP, eds. *Haemostasis and thrombosis*. 2nd ed. Edinburgh: Churchill Livingstone, 1987: 554–69.
2. Autret-Leca E, Jonville-Béra A-P. Vitamin K in neonates: how to administer, when and to whom. *Paediatr Drugs* 2001; **3:** 1–8.
3. Tripp JH, McNinch AW. Haemorrhagic disease and vitamin K. *Arch Dis Child* 1987; **62:** 436–7.
4. Brown SG, *et al.* Should intramuscular vitamin K prophylaxis for haemorrhagic disease of the newborn be continued? A decision analysis. *N Z Med J* 1989; **102:** 3–5.
5. Clarkson PM, James AG. Parenteral vitamin K : the effective prophylaxis against haemorrhagic disease for all newborn infants. *N Z Med J* 1990; **103:** 95–6.
6. McNinch AW, Tripp JH. Haemorrhagic disease of the newborn in the British Isles: two year prospective study. *BMJ* 1991; **303:** 1105–9.
7. Von Kries R. Neonatal vitamin K. *BMJ* 1991; **303:** 1083–4.
8. British Paediatric Association. *Vitamin K prophylaxis in infancy*. London, 1992: British Paediatric Association.
9. von Kries R, *et al.* Repeated oral vitamin K prophylaxis in West Germany: acceptance and efficacy. *BMJ* 1995; **310:** 1097–8.
10. American Academy of Pediatrics Vitamin K Ad Hoc Task Force. Controversies concerning vitamin K and the newborn. *Pediatrics* 1993; **91:** 1001–3.
11. American Academy of Pediatrics Committee on Fetus and Newborn. Controversies concerning vitamin K and the newborn. *Pediatrics* 2003; **112:** 191–2.
12. Barton JS, *et al.* Neonatal vitamin K prophylaxis in the British Isles: current practice and trends. *BMJ* 1995; **310:** 632–3.
13. Rennie JM, Kelsall AWR. Vitamin K prophylaxis in the newborn—again. *Arch Dis Child* 1994; **70:** 248–51.
14. Department of Health. *Vitamin K for newborn babies*. London, 1998: Department of Health. Also available at: http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Professionalletters/Chiefmedicalofficerletters/DH_4004993?IdcService=GET_FILE&dID=7634&Rendition=Web (accessed 21/07/08)
15. Baenziger O, *et al.* Oral vitamin K prophylaxis for newborn infants: safe enough? *Lancet* 1996; **348:** 1456.
16. Greer FR, *et al.* A new mixed micellar preparation for oral vitamin K prophylaxis: randomised controlled comparison with an intramuscular formulation in breast fed infants. *Arch Dis Child* 1998; **79:** 300–5.
17. von Kries R, *et al.* Oral mixed micellar vitamin K for prevention of late vitamin K deficiency bleeding. *Arch Dis Child Fetal Neonatal Ed* 2003; **88:** F109–F112.
18. Pereira SP, *et al.* Intestinal absorption of mixed micellar phylloquinone (vitamin K) is unreliable in infants with conjugated hyperbilirubinaemia: implications for oral prophylaxis of vitamin K deficiency bleeding. *Arch Dis Child Fetal Neonatal Ed* 2003; **88:** F113–F118.
19. Cornelissen M, Hirasing R. Vitamin K for neonates. *BMJ* 1994; **309:** 1441–2.
20. Cornelissen M, *et al.* Prevention of vitamin K deficiency bleeding: efficacy of different multiple oral dose schedules of vitamin K. *Eur J Pediatr* 1997; **156:** 126–30.
21. Clark FI, James EJP. Twenty-seven years of experience with oral vitamin K therapy in neonates. *J Pediatr* 1995; **127:** 301–4.
22. Nørgaard Hansen K, Ebbesen F. Neonatal vitamin K prophylaxis in Denmark: three years' experience with oral administration during the first three months of life compared with one oral administration at birth. *Acta Paediatr Scand* 1996; **85:** 1137–9.
23. Delgado-Escueta AV, Janz D. Consensus guidelines: preconception counseling, management, and care of the pregnant woman with epilepsy. *Neurology* 1992; **42** (suppl 5): 149–60.
24. Greer FR, *et al.* Improving the vitamin K status of breastfeeding infants with maternal vitamin K supplements. *Pediatrics* 1997; **99:** 88–92.

Preparations

BP 2008: Menadiol Phosphate Injection; Menadiol Phosphate Tablets; Phytomenadione Injection; Phytomenadione Tablets;
USP 31: Menadiol Sodium Diphosphate Injection; Menadiol Sodium Diphosphate Tablets; Menadione Injection; Phytonadione Injectable Emulsion; Phytonadione Tablets.

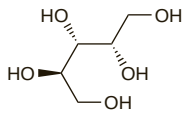
Proprietary Preparations (details are given in Part 3)
Arg.: K1; Konakion; Mestil-Ka; Rupek; ***Austral.:*** K Thrombin†; Konakion; ***Austria:*** Kavitol; Konakion; ***Belg.:*** Konakion; Vitamon K; ***Braz.:*** Kanakion; Kavit; Vikatron; Vita K; ***Chile:*** Auriderm K2; Fitoquinona†; Konakion; ***Cz.:*** Kanavit; ***Denm.:*** Konakion; Menadion; ***Fin.:*** Konakion; ***Ger.:*** Kanavit; Konakion; ***Gr.:*** Konakion; ***Hong Kong:*** Auriderm K2; Konakion; ***Hung.:*** Konakion; ***India:*** Kenadion; ***Indon.:*** Neo-K; ***Irl.:*** Konakion; ***Israel:*** Konakion; ***Ital.:*** Konakion; Vitak; ***Jpn:*** Glakay; Kaytwo; ***Malaysia:*** Konakion; ***Mex.:*** K-50; Konakion; Royken; ***Neth.:*** Konakion; ***Norw.:*** Konakion; ***NZ:*** K-Thrombin; Konakion; ***Philipp.:*** Clotigen; Cycomin; Hema-K; Hemadone; Hemo-K; Konakion; ***Pol.:*** Vitacon; ***Port.:*** Kanakion; ***S.Afr.:*** Konakion; ***Spain:*** Kaergona Hidrosoluble; Konakion; ***Swed.:*** Konakion; ***Switz.:*** Konakion; ***Thai.:*** Glakay; Konakion; KP†; ***Turk.:*** Konakion MM; Libavit K; ***UK:*** Konakion; ***USA:*** Aquamephyton†; Mephyton.

Multi-ingredient: ***Arg.:*** Antidiar†; Estreptocarbocaftiazol; Kacerutin; ***Austral.:*** Chilblain Formula†; ***Chile:*** Hepabil; Katin; Microret K; ***India:*** Cadisper C; CKP; Gynae-CVP; K5 Hair Tincture†; Kalpastic; Siochrome; Styptocid; Styptocip†; ***Indon.:*** Hi-Bone; ***Irl.:*** Bio-Calcium + D + K; ***Mex.:*** Hemosin-K; Microka; Microret K; ***Rus.:*** Vectrum Calcium (Вектрум Кальций); ***Spain:*** Caprofides Hemostatico; Cromoxin K†; ***Thai.:*** Bio-Calcium + D3 + K; Siduol; ***Venez.:*** Dremo-K†.

Xylitol *(BAN)*

E967; Ksilitolis; Ksylitol; Ksylitoli; Xilit; Xilitol; Xylit; *meso*-Xylitol; Xylitolum.

$C_5H_{12}O_5$ = 152.1.
CAS — 87-99-0 (xylitol); 16277-71-7 (D-xylitol).



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn.* Also in *USNF*.

Ph. Eur. 6.2 (Xylitol). A white or almost white crystalline powder or crystals. M.p. 92° to 96°. Very soluble in water; sparingly soluble in alcohol.

USNF 26 (Xylitol). White crystals or crystalline powder. Crystalline xylitol has a melting range between 92° and 96°. It has a sweet taste and produces a cooling sensation in the mouth. Soluble 1 in about 0.65 of water; sparingly soluble in alcohol.

Adverse Effects

Large amounts of xylitol taken orally may cause diarrhoea and flatulence. Hyperoxaluria, which can occur with intravenous infusion, is unlikely after oral use. Hyperuricaemia, changes in liver-function tests, and acidosis (including lactic acidosis) have occurred after intravenous infusion.

Hypersensitivity. A report of oral erosions caused by contact hypersensitivity to xylitol-containing chewing gum.[1]

1. Hanakawa Y, *et al.* Xylitol as a causative agent of oral erosive eczema. *Br J Dermatol* 2005; **152:** 821–2.

Uses and Administration

Xylitol is a polyhydric alcohol (polyol) related to the pentose sugar, xylose (p.2416). It is used as a bulk sweetener in foods and as a sweetener or excipient in pharmaceuticals. Xylitol is also used as a sweetening agent in sugar-free preparations as it is non-cariogenic and is less likely to cause dental caries than sucrose. It is under investigation for the prevention of dental caries and acute otitis media. It was formerly considered as a substitute for glucose in intravenous nutrition but such use has generally been abandoned due to adverse effects.

Dental caries. Chewing-gum containing xylitol appears to have a useful role in the prevention of dental caries (p.180).[1-5]

1. Edgar WM. Sugar substitutes, chewing gum and dental caries—a review. *Br Dent J* 1998; **184:** 29–32.
2. Gales MA, Nguyen T-M. Sorbitol compared with xylitol in prevention of dental caries. *Ann Pharmacother* 2000; **34:** 98–100.
3. Maguire A, Rugg-Gunn AJ. Xylitol and caries prevention—is it a magic bullet? *Br Dent J* 2003; **194:** 429–36.
4. van Loveren C. Sugar alcohols: what is the evidence for caries-preventive and caries-therapeutic effects? *Caries Res* 2004; **38:** 286–93.
5. Burt BA. The use of sorbitol- and xylitol-sweetened chewing gum in caries control. *J Am Dent Assoc* 2006; **137:** 190–6. Correction. *ibid.*; 447.

Otitis media. It has been suggested that xylitol chewing gum[1,2] and xylitol syrup[2,3] may have a preventative effect against acute otitis media (p.182). However, a randomised study[4] found xylitol to be ineffective when given only during an acute respiratory-tract infection.

1. Uhari M, *et al.* Xylitol chewing gum in prevention of acute otitis media: double blind randomised trial. *BMJ* 1996; **313:** 1180–4.
2. Uhari M, *et al.* A novel use of xylitol sugar in preventing acute otitis media. *Pediatrics* 1998; **102:** 879–84.
3. Uhari M, *et al.* Xylitol in preventing acute otitis media. *Vaccine* 2001; **19:** S144–S147.
4. Tapiainen T, *et al.* Xylitol administered only during respiratory infections failed to prevent acute otitis media. Abstract: *Pediatrics* 2002; **109:** 302. Full version: http://pediatrics.aappublications.org/cgi/content/full/109/2/e19 (accessed 08/11/05)

Preparations

Proprietary Preparations (details are given in Part 3)
Canad.: Trident; ***Ger.:*** Xylit; ***Philipp.:*** Xylogel.

Multi-ingredient: ***Arg.:*** Emoform Total; Fluorogel 2001 Chiquitos; Fluorogel 2001 para Dientes Sensibles; Hyper Sensitive; Periobacter; Periodent; Solucion Oral; ***Chile:*** Oralgene; ***Fr.:*** Exova†; ***Ger.:*** Cardioplegin N†; Kalium-Magnesium-Asparaginat†; Saseem; ***Mex.:*** Dentsiblen; Fluoxytil; Periodentyl; Perioxidin; ***Philipp.:*** Xylorinse; ***UK:*** Biotene Oralbalance; BioXtra†; Saliva Natura; Saliva Orthana; ***USA:*** Optimoist.

Dried Yeast

Brewers' Yeast; Cerevisiae Fermentum Siccatum; Faex Siccata; Fermento de Cerveja; Levadura desecada; Levedura Sêca; Levure de Bière; Saccharomyces Siccum; Trockenhefe.

Сушёные Дрожжи

Pharmacopoeias. In *Jpn.*

Profile

Dried yeast consists of unicellular fungi belonging to the family Saccharomycetaceae, dried by a process that avoids decomposition of the vitamins present. The chief species are *Saccharomyces cerevisiae*, *S. carlsbergensis*, and *S. monacensis*. Dried yeast contains thiamine, nicotinic acid, riboflavin, pyridoxine, pantothenic acid, biotin, folic acid, cyanocobalamin, aminobenzoic acid, inositol, and chromium.

Dried yeast is a rich source of vitamins of the B group. It has been used for the prevention and treatment of vitamin B deficiency in doses of 1 to 8 g daily by mouth. Yeast is an ingredient of some preparations for treating haemorrhoids, and some preparations intended to restore normal gastrointestinal flora. Yeast is widely used in brewing.

Antibiotic-associated colitis. Although other organisms, including *Candida* spp., have been implicated in antibiotic-associated diarrhoea, colonisation of the colon with *Clostridium difficile*, a toxin-producing Gram-positive anaerobe, is the most common identifiable cause of antibiotic-associated colitis (p.171) and pseudomembranous colitis. There are reports of benefit with dried yeast in patients with *C. difficile*-associated diarrhoea;[1,2] commercially available brewers' yeast tablets were used, at a dose of 3 tablets three times daily (strength unspecified), in 3 patients refractory to standard treatment,[1] or as adjunctive therapy in 11 patients, using the same dose.[2]

1. Schellenberg D, *et al.* Treatment of Clostridium difficile diarrhoea with brewer's yeast. *Lancet* 1994; **343:** 171–2.
2. Barthram J, *et al.* Further research warranted. *Pharm J* 1997; **259:** 371.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Bioflorin†; Florax†; Ginofloraxt; Levedo; Lomvit†; ***Fr.:*** Microlev†; ***Ger.:*** AgioStop; Furunkulosin†; Hamadin N; Imoflora; Levurinetten N†; Omniflora Akut; Perocur; Santax S; Yomogi; ***India:*** Laviest; ***Ital.:*** Nutrivit†; Zimocel; ***Mex.:*** Levifusa; ***Port.:*** Lio-Levedura†; ***Thai.:*** Brewers Yeast; ***UK:*** Bio-Strath.

Multi-ingredient: ***Arg.:*** Bifena; Karbonetas; ***Austral.:*** ML 20†; Plantiodine Plus†; Preparation H†; ***Austria:*** Levurinetten; Sperti Praparation H; ***Braz.:*** Composto Emagrecedor†; Emagrevit†; Manolio†; ***Canad.:*** Preparation H; ***Chile:*** Sperti Preparation H; ***Cz.:*** Preparation H; ***Fr.:*** Actisoufre; Calciforte; Calciforte Vitamin D ; Carbolevure; D'Contract; Levure Or; Phytophanere; Preparation H; Solacy; Spasmag; ***Ger.:*** Pantovigar N; Sperti Praparation H†; ***Gr.:*** Preparation H; ***India:*** Elfern†; Livogen†; Medithane; Plastules; Softeron-Z; ***Irl.:*** Preparation H; ***Israel:*** Preparation H; ***Ital.:*** Bifilact; Eurogel; Florelax; Lactisporin; Lactivis; Lactolife; Levudin†; Lievitosohn;

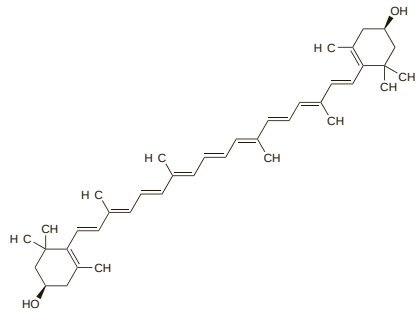
Lievitovit; Preparazione H; Sillix C†; Sillix†; ***Neth.:*** Sperti Preparation H; ***Pol.:*** Preparation H†; Vegevit B ; ***Port.:*** Bioregime Fort†; Sperti Preparacao H; ***Rus.:*** Preparation H (Препарейшн Эйч); ***S.Afr.:*** Preparation H; ***Spain:*** Preparacion H; ***Switz.:*** A Vogel Capsules polyvitamineesf†; Carbolevure; Sperti Preparation H; ***UK:*** Bio-Strath Artichoke Formula; Bio-Strath Valerian Formula; Bio-Strath Willow Formula; Brewers Yeast; Preparation H; Tonic Yeast; Yeast Vite; ***USA:*** Medicone†; Preparation H; Rectagene Medicated Balm; Wyanoids Relief Factor; ***Venez.:*** Wampole†.

Zeaxanthin

Anchovyxanthin; Zeaxanthol. (3*R*,3′*R*)-β,β-Carotene-3,3′-diol.

Зеаксантин

$C_{40}H_{56}O_2$ = 568.9.
CAS — 144-68-3.



Profile

Zeaxanthin is a naturally occurring carotenoid that is promoted as a dietary supplement for age-related macular degeneration (p.785).

◊ References.

1. Mares-Perlman JA, *et al.* The body of evidence to support a protective role for lutein and zeaxanthin in delaying chronic disease: overview. *J Nutr* 2002; **132** (suppl): 518S–524S.
2. Mozaffarieh M, *et al.* The role of the carotenoids, lutein and zeaxanthin, in protecting against age-related macular degeneration: a review based on controversial evidence. *Nutr J* 2003; **2:** 20.
3. Hartmann D, *et al.* Plasma kinetics of zeaxanthin and 3′-dehydro-lutein after multiple oral doses of synthetic zeaxanthin. *Am J Clin Nutr* 2004; **79:** 410–17.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Indon.:*** Eyevit; Matovit Fifty; Nuvision; ***Mex.:*** Snelvit.

Zinc

Cynk; Zincum; Zink.

Zn = 65.38.
CAS — 7440-66-6.

Zinc Acetate

Cink-acetát-dihidrát; Cinko acetatas dihidratas; Cynku octan; E650; Octan zinečnatý dihydrát; Sinkkiasetaatti; Zinc (acétate de) dihydraté; Zinc, acetato de; Zinci Acetas; Zinci acetas dihydricus; Zinkacetat.

$(CH_3CO_2)_2Zn,2H_2O$ = 219.5.
CAS — 557-34-6 (anhydrous zinc acetate); 5970-45-6 (zinc acetate dihydrate).
ATC — A16AX05.
ATC Vet — QA16AX05.

NOTE. Zinc Acetate, Basic is *rINN*.

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

Ph. Eur. 6.2 (Zinc Acetate Dihydrate; Zinc Acetate BP 2008). A white or almost white, crystalline powder or leaflets. Freely soluble in water; soluble in alcohol. A 5% solution in water has a pH of 5.8 to 7.0. Store in nonmetallic containers.

USP 31 (Zinc Acetate). White crystals or granules having a slight acetous odour. Is slightly efflorescent. Soluble 1 in 2.5 of water and 1 in 30 of alcohol; freely soluble in boiling alcohol. pH of a 5% solution in water is between 6.0 and 8.0. Store in airtight containers.

Zinc Chloride

Chlorid zinečnatý; Cink-klorid; Cinko chloridas; Cynku chlorek; Sinkkikloridi; Zinc, chlorure de; Zinc, cloruro de; Zinci chloridum; Zincum Chloratum; Zinkklorid.

$ZnCl_2$ = 136.3.
CAS — 7646-85-7.
ATC — B05XA12.
ATC Vet — QB05XA12.

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

Ph. Eur. 6.2 (Zinc Chloride). A white or almost white, deliquescent, crystalline powder or cast in white or almost white sticks. Very soluble in water; freely soluble in alcohol and in glycerol. An approximately 10% solution in water has a pH of 4.6 to 5.5. Store in nonmetallic containers.

USP 31 (Zinc Chloride). A white or practically white, odourless, crystalline powder, or white or practically white crystalline granules. May also be in porcelain-like masses or moulded into cylinders. It is very deliquescent. Soluble 1 in 0.5 of water, 1 in 1.5 of alcohol, and 1 in 2 of glycerol. Its solution in water or in alcohol is usually slightly turbid, but the turbidity disappears when a small quantity of hydrochloric acid is added. A 10% solution in water is acid to litmus. Store in airtight containers.

Turbidity. Zinc chloride almost always contains some oxychloride which produces a slightly turbid aqueous solution. Turbid solutions, except when intended for ophthalmic use, may be cleared by adding gradually a small amount of dilute hydrochloric acid. Solutions of zinc chloride should be filtered through asbestos or sintered glass, since they dissolve paper and cotton wool.

Zinc Citrate

Zinc Citrate Trihydrate. 2-Hydroxy-1,2,3-propanetricarboxylic acid zinc salt.

Цитрат Цинка

$C_{12}H_{10}O_{14}Zn_3,3H_2O$ = 628.4.
CAS — 546-46-3.

Pharmacopoeias. In *Chin.*

Zinc Gluconate

Zinc, gluconate de; Zinc, gluconato de; Zinci gluconas.

$C_{12}H_{22}O_{14}Zn$ = 455.7.
CAS — 4468-02-4.
ATC — A12CB02.
ATC Vet — QA12CB02.

Pharmacopoeias. In *Chin.* and *US*.

USP 31 (Zinc Gluconate). White or practically white powder or granules. Soluble in water; very slightly soluble in alcohol. pH of a 1% solution in water is between 5.5 and 7.5.

Zinc Sulfate

Çinko Sülfat; Cinko sulfatas; Cink-szulfát; Cynku siarczan; Sinkkisulfaatti; Síran zinečnatý; Zinc, sulfate de; Zinc, sulfato de; Zinc Sulphate; Zinci sulfas; Zincum Sulfuricum; Zinksulfat.

$ZnSO_4,7H_2O$ = 287.5.
CAS — 7733-02-0 (anhydrous zinc sulfate); 7446-20-0 (zinc sulfate heptahydrate).
ATC — A12CB01.
ATC Vet — QA12CB01.

NOTE. 'White vitriol' or 'white copperas' is crude zinc sulfate. ZSU is a code approved by the BP 2008 for use on single unit doses of eye drops containing zinc sulfate where the individual container may be too small to bear all the appropriate labelling information.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *Viet.*
Eur. also includes the monohydrate and the hexahydrate.
US includes the monohydrate and the heptahydrate in one monograph.

Ph. Eur. 6.2 (Zinc Sulphate Heptahydrate; Zinci Sulfas Heptahydricus). Colourless, transparent, crystals or a white or almost white, crystalline powder; efflorescent. Very soluble in water; practically insoluble in alcohol. A 5% solution in water has a pH of 4.4 to 5.6. Store in nonmetallic airtight containers.

Ph. Eur. 6.2 (Zinc Sulphate Hexahydrate; Zinci Sulfas Hexahydricus). Colourless, transparent, crystals or a white or almost white, crystalline powder; efflorescent. Very soluble in water; practically insoluble in alcohol. A 5% solution in water has a pH of 4.4 to 5.6. Store in nonmetallic airtight containers.

Ph. Eur. 6.2 (Zinc Sulphate Monohydrate; Zinci Sulfas Monohydricus). Colourless, transparent, crystals or a white or almost white crystalline powder. Very soluble in water; practically insoluble in alcohol. A 5% solution in water has a pH of 4.4 to 5.6. Store in nonmetallic containers.

USP 31 (Zinc Sulfate). It contains one or seven molecules of water of hydration. Colourless, transparent, prisms, or small needles. May occur as a white, granular, crystalline powder. It is odourless and is efflorescent in dry air. Very soluble in water (heptahydrate); freely soluble in water (monohydrate); practically insoluble in alcohol (monohydrate); insoluble in alcohol (heptahydrate); freely soluble in glycerol (heptahydrate). Its solutions are acid to litmus. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

The most frequent adverse effects of zinc salts (the gluconate and sulfate) given orally are gastrointestinal and include abdominal pain, dyspepsia, nausea, vomiting, diarrhoea, gastric irritation, and gastritis. These are particularly common if zinc salts are taken on an empty stomach, and may be reduced by giving them with meals.

In acute overdosage zinc salts are corrosive, due to the formation of zinc chloride by stomach acid; treatment consists of giving milk or alkali carbonates and activated charcoal. The use of emetics or gastric lavage should be avoided.

Prolonged use of high doses of zinc supplements, orally or parenterally, leads to copper deficiency with associated sideroblastic anaemia and neutropenia; full blood counts and serum cholesterol should be monitored to detect early signs of copper deficiency. Zinc toxicity has occurred after the use of contaminated water in haemodialysis solutions. High serum zinc concentrations may be reduced by using a chelating drug such as sodium calcium edetate (p.1462).

Metal fume fever is an occupational disease associated with inhalation of freshly-oxidised metal fumes, most commonly from zinc, iron or copper. It is characterised by chills, fever, cough, dyspnoea, myalgia, and chest pain, and is generally self-limiting and does not appear to be associated with long-term sequelae.

Effects on the blood. There have been reports[1-3] of anaemia, leucopenia, and neutropenia in patients consuming excessive amounts of zinc supplements for acne. A patient given zinc-containing enteral feeds as well as zinc supplementation was diagnosed with sideroblastic anaemia due to zinc toxicity.[4] All patients were copper-deficient,[1-4] despite supplementation with copper in one case.[4]

1. Porea TJ, *et al.* Zinc-induced anemia and neutropenia in an adolescent. *J Pediatr* 2000; **136:** 688–90.
2. Igic PG, *et al.* Toxic effects associated with consumption of zinc. *Mayo Clin Proc* 2002; **77:** 713–16.
3. Salzman MB, *et al.* Excessive oral zinc supplementation. *J Pediatr Hematol Oncol* 2002; **24:** 582–4.
4. Irving JA, *et al.* Element of caution: a case of reversible cytopenias associated with excessive zinc supplementation. *Can Med Assoc J* 2003; **169:** 129–31.

Hypersensitivity. Report of a patient who developed palmoplantar pustulosis about 1 year after receiving dental fillings containing zinc.[1] Zinc hypersensitivity was confirmed by *in vitro* and patch testing. Complete remission occurred on replacing the dental fillings.

1. Yanagi T, *et al.* Zinc dental fillings and palmoplantar pustulosis. *Lancet* 2005; **366:** 1050.

Parenteral nutrition. Zinc was found to be a common contaminant of various components used for total parenteral nutrition (TPN), and rubber stoppers or glass may have been the source.[1] Levels of zinc found may exceed daily requirements even before the addition of supplementary zinc. The authors suggested it may be important to routinely monitor zinc status in patients receiving long-term TPN, particularly infants and children.

1. 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.

Interactions

The absorption of zinc may be reduced by iron supplements (see also Absorption, under Pharmacokinetics, below) , penicillamine, phosphorus-containing preparations, and tetracyclines. Zinc supplements reduce the absorption of copper, fluoroquinolones (see Antacids and Metal Ions, under Interactions of Ciprofloxacin, p.246), iron, penicillamine, and tetracyclines (p.348).

Pharmacokinetics

Absorption of zinc from the gastrointestinal tract is incomplete, and is reduced in the presence of some dietary constituents such as phytates. Bioavailability of dietary zinc varies widely between different sources, but is about 20 to 30%. Zinc is distributed throughout the body with the highest concentrations found in muscle, bone, skin, eye, and prostatic fluids. It is primarily excreted in the faeces, and regulation of faecal losses is important in zinc homoeostasis. Small amounts are lost in urine and perspiration.

Absorption. Although zinc deficiency (see Deficiency States, under Uses and Administration, below) in some cases may be due to inadequate dietary intake, inhibitors of zinc absorption may also be causative.[1] *Phytates*, which are present in cereals, corn, legumes, and rice, inhibit zinc absorption. The animal *protein* in beef, eggs, and cheese counteracts the inhibitory effect of phytate, whereas the casein in milk decreases zinc absorption. Proteins also often contain other constituents such as inorganic *phosphate* that can negatively affect zinc absorption. Long-term use of *calcium* supplements has no effect on zinc status, but dietary calcium may form insoluble complexes with phytate and zinc, thus decreasing the absorption of zinc. *Iron* can reduce zinc absorption, although the effect is apparent only at a very high