

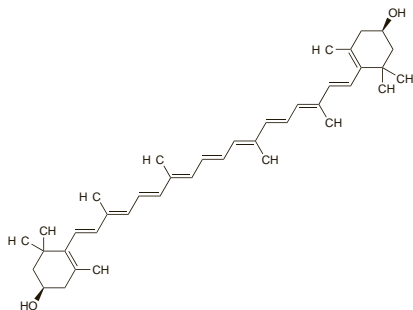
Lievitov; Preparazione H; Siliix C†; Siliix†; **Neth.:** Sperti Preparation H; **Pol.:** Preparacja H†; Vegevit B ; **Port.:** Biogime Fort†; Sperti Preparacao H; **Rus.:** Preparacion H (Пепарейшн Эйч); **S.Afr.:** Preparation H; **Spain:** Preparation H; **Switz.:** A Vogel Capsules polyvitaminees†; 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; Vyvanoids Relief Factor; **Venez.:** Wvampolej†.

Zeaxanthin

Anchovyxanthin; Zeaxanthol. (3R,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.

- 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.
- 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.
- 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; Sinkkisetäatti; Zinc (acétate de) dihydraté; Zinc, acetato de; Zinci Acetas; Zinci acetas dihydricus; Zinkacetat.

$(CH_3COO)_2Zn \cdot 2H_2O = 219.5$.

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. It 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, chloruro 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

$C_{12}H_{10}O_{14}Zn_3 \cdot 3H_2O = 628.4$.

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

Činko Sulfát; Cinko sulfatas; Cink-szulfát; Cynku siarczan; Sinkki-sulfaatti; Siran zinečnatý; Zinc, sulfate de; Zinc, sulfato de; Zinc Sulphate; Zinci sulfas; Zincum Sulphuricum; Zinksulfat.

$ZnSO_4 \cdot 7H_2O = 287.5$.

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 reports¹⁻³ 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

- Porea TJ, *et al.* Zinc-induced anemia and neutropenia in an adolescent. *J Pediatr* 2000; **136**: 688–90.
- Igic PG, *et al.* Toxic effects associated with consumption of zinc. *Mayo Clin Proc* 2002; **77**: 713–16.
- Salzman MB, *et al.* Excessive oral zinc supplementation. *J Pediatr Hematol Oncol* 2002; **24**: 582–4.
- 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 palmo-plantar 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.

- Yanagi T, *et al.* Zinc dental fillings and palmo-plantar 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.

- Hak EB, *et al.* Chromium and zinc contamination of parenteral nutrition 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 homeostasis. 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