Extrapyramidal effects. In a study[1] of 100 hypertensive patients receiving diazoxide, the incidence of extrapyramidal symptoms was 15%.

1. Pohl JEF. Development and management of extrapyramidal symptoms in hypertensive patients treated with diazoxide. *Am Heart J* 1975; **89:** 401–2.

Pancreatitis. Ten patients with severe hypertension and renal failure were treated with diazoxide in a last attempt to avert nephrectomy; 1 patient developed acute pancreatitis and another diabetic ketoacidosis.[1] Both patients recovered from these effects when diazoxide was withdrawn.

1. De Broe M, *et al*. Oral diazoxide for malignant hypertension. *Lancet* 1972; **i:** 1397.

Voice changes. See Effects on the Hair, above.

Treatment of Adverse Effects

Treatment is largely symptomatic. Severe hyperglycaemia may be corrected by giving insulin: less severe hyperglycaemia may respond to oral hypoglycaemics. Hypotension may be managed with intravenous fluids. Severe hypotension may require sympathomimetics. Antiparkinsonian drugs, such as procyclidine, have been given to control extrapyramidal effects while a diuretic may be required for salt and water retention. Diazoxide can be removed from the body by dialysis but recovery is relatively low owing to extensive protein binding.

Precautions

Diazoxide should be used with care in patients with impaired cardiac or cerebral circulation and in patients with aortic coarctation, arteriovenous shunt, heart failure, or other cardiac disorders in which an increase in cardiac output could be detrimental. During prolonged therapy blood-glucose concentrations and blood pressure should be monitored and the blood should be examined regularly for signs of leucopenia and thrombocytopenia; in children, bone and psychological maturation, and growth, should be regularly assessed. Caution is necessary in patients with renal impairment.

If given during labour, diazoxide may cause cessation of uterine contractions and delay delivery unless oxytocin is also given.

Pregnancy. Transplacental transfer of diazoxide was considered[1] to be responsible for an inappropriately low plasma-insulin concentration in an infant whose mother had received a dose of 150 mg daily for 47 days prior to delivery. For reference to alopecia in neonates whose mothers had received diazoxide during pregnancy, see Effects on the Hair under Adverse Effects, above.

For reports of sedation, hypotonia, or apnoea among infants born to mothers given both diazoxide and clomethiazole for the treatment of toxaemia of pregnancy, see Precautions, Pregnancy, in Clomethiazole Edisilate, p.978. Diazoxide is nonetheless one of the drugs that has been used for hypertensive emergencies in pregnancy (see Hypertension, p.1171) and a study found that mini-boluses of diazoxide 15 mg intravenously successfully reduced blood pressure and were well tolerated.[2]

1. Smith MJ, *et al*. Neonatal hyperglycaemia after prolonged maternal treatment with diazoxide. *BMJ* 1982; **284:** 1234.
2. Hennessy A, *et al*. A randomised comparison of hydralazine and mini-bolus diazoxide for hypertensive emergencies in pregnancy: the PIVOT trial. *Aust N Z J Obstet Gynaecol* 2007; **47:** 279–85.

Interactions

The hyperglycaemic, hyperuricaemic, and hypotensive actions of diazoxide may be enhanced by diuretics. Use of diazoxide with other antihypertensives or vasodilators may lead to increased risk of hypotension.

Chlorpromazine. Chlorpromazine was reported[1] to enhance the hyperglycaemic effect of diazoxide in a 2-year-old child.

1. Aynsley-Green A, Illig R. Enhancement by chlorpromazine of hyperglycaemic action of diazoxide. *Lancet* 1975; **ii:** 658–9.

Phenytoin. For the effect of diazoxide on serum-phenytoin concentrations, see Antihypertensives, p.499.

Pharmacokinetics

Diazoxide is readily absorbed from the gastrointestinal tract and more than 90% bound to plasma proteins, although protein binding is decreased in uraemic patients. Its plasma half-life has been estimated to range from about 20 to 45 hours but values of up to 60 hours have been reported. The half-life is reported to be prolonged in renal impairment and shorter for children. The plasma half-life greatly exceeds the duration of vascular activity. Diazoxide is partly metabolised in the liver and is excreted in the urine both unchanged and in the form of metabolites; only small amounts are recovered from the faeces. It crosses the placenta and the blood-brain barrier.

Children. In 4 children with hypoglycaemia the plasma half-life of diazoxide was 9.5 to 24 hours, which is considerably shorter than that in adults.[1]

1. Pruitt AW, *et al*. Disposition of diazoxide in children. *Clin Pharmacol Ther* 1973; **14:** 73–82.

Uses and Administration

Diazoxide increases the concentration of glucose in the plasma; it inhibits the secretion of insulin by the beta cells of the pancreas, and may increase the hepatic output of glucose. When given intravenously, it produces a fall in blood pressure by a vasodilator effect on the arterioles and a reduction in peripheral resistance. Diazoxide is closely related structurally to the thiazide diuretics, but has an antidiuretic action and thus produces fluid and electrolyte retention; it may be given with a diuretic to reduce fluid retention.

Diazoxide is used orally in the management of intractable hypoglycaemia (p.1447) and intravenously in the management of hypertensive crises (p.1171), particularly when first-line drugs such as sodium nitroprusside are ineffective or unsuitable. Diazoxide is not suitable for the chronic treatment of hypertension because of its severe adverse effects.

In **hypoglycaemia**, the initial dose is 3 to 5 mg/kg daily in 2 or 3 divided oral doses, then adjusted according to response. Usual maintenance doses are from 3 to 8 mg/kg daily but total doses of up to 1 g daily have been given to adults with insulinomas (see Carcinoid Tumours and other Secretory Neoplasms, p.643). In neonates the initial dose is 5 mg/kg twice daily; usual maintenance doses range from 3 to 9 mg/kg daily, although up to 21 mg/kg daily may be required. In children from 1 month of age, the initial dose is 1.7 mg/kg three times daily, and the usual maintenance doses are as for neonates; up to 15 mg/kg daily may be required. The hyperglycaemic effect normally begins within 1 hour of a dose and lasts for up to 8 hours. The doses for neonates and children may be given intravenously if necessary.

In **hypertensive crises**, a bolus intravenous injection of 1 to 3 mg/kg is given within 30 seconds, up to a maximum dose of 150 mg, and repeated after 5 to 15 minutes if required.

Reduced doses may be necessary in patients with renal impairment.

Preparations

BP 2008: Diazoxide Injection; Diazoxide Tablets;
USP 31: Diazoxide Capsules; Diazoxide Injection; Diazoxide Oral Suspension.

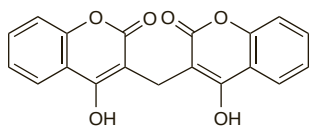
Proprietary Preparations (details are given in Part 3)
Arg.: Proglicem; ***Braz.:*** Tensuril; ***Canad.:*** Hyperstat†; Proglycem; ***Fr.:*** Proglicem; ***Ger.:*** Hypertonalum†; Proglicem; ***Gr.:*** Eudemine; Hyperstat†; Proglycem; ***Ital.:*** Hyperstat†; Proglicem; ***Mex.:*** Hyperstat†; Sefulken; ***Neth.:*** Proglicem; ***Swed.:*** Hyperstat†; ***Switz.:*** Proglicem; ***UK:*** Eudemine; ***USA:*** Hyperstat; Proglycem.

Dicoumarol *(rINN)*

Bishydroxycoumarin; Dicoumarin; Dicoumarolum; Dicumarol *(USAN)*; Dikumarol; Dikumaroli; Melitoxin. 3,3′-Methylenebis(4-hydroxycoumarin).

Дикумарол

$C_{19}H_{12}O_6$ = 336.3.
CAS — 66-76-2.
ATC — B01AA01.
ATC Vet — QB01AA01.



Pharmacopoeias. In *Int.*

Adverse Effects, Treatment, and Precautions

As for Warfarin Sodium, p.1425, although gastrointestinal adverse effects are reported to occur more frequently. The absorption of dicoumarol is affected by food.

Breast feeding. No adverse effects have been seen in breastfeeding infants whose mothers were receiving dicoumarol, and the American Academy of Pediatrics considers[1] that it is therefore usually compatible with breast feeding.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 06/07/04)

Interactions

The interactions associated with oral anticoagulants are discussed in detail under warfarin (p.1427). Specific references to interactions involving dicoumarol can be found under the headings for the following drug groups: analgesics; antiarrhythmics; antibacterials; antidepressants; antidiabetics; antiepileptics; antigout drugs; anxiolytic sedatives; gastrointestinal drugs; lipid regulating drugs; sex hormones; and vitamins.

Pharmacokinetics

Dicoumarol is slowly and erratically absorbed from the gastrointestinal tract and is extensively bound to plasma proteins. It is metabolised in the liver and is excreted in the urine, mainly as metabolites.

Uses and Administration

Dicoumarol is an oral coumarin anticoagulant with actions similar to those of warfarin (p.1432). It has been used in the management of thromboembolic disorders (p.1187). The usual daily maintenance dose, adjusted according to coagulation tests, is 25 to 200 mg.

Because of its unpredictability of response and high incidence of gastrointestinal effects, dicoumarol has been largely replaced by warfarin.

Digitalis Leaf

Digit. Fol.; Digit. Leaf; Digital, hoja de; Digitale Pourprée; Digitale Pourprée, Feuille de; Digitaliksenlehti; Digitalis; Digitalis Folium; Digitalis purpureae folium; Digitalisblad; Feuille de Digitale; Fingerhutblatt; Folha de Dedaleira; Foxglove Leaf; Hoja de Digital; List náprstníku červeného; Piros gyűszűvirághlevél; Rusmenių lapai.

ATC — C01AA03.
ATC Vet — QC01AA03.

NOTE. The term 'digitalis' is often used to describe the entire class of cardiac glycosides.

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Digitalis Leaf). The dried leaf of *Digitalis purpurea*. It contains not less than 0.3% of cardenolic glycosides, expressed as digitoxin, and calculated with reference to the drug dried at 100° to 105°. Protect from light and moisture.
USP 31 (Digitalis). The dried leaf of *Digitalis purpurea* (Scrophulariaceae). The potency is such that, when assayed as directed, 100 mg is equivalent to not less than 1 USP unit. Store in containers that protect it from absorbing moisture.

Profile

Digitalis leaf contains a number of cardiac glycosides with positive inotropic activity, including digitoxin, gitoxin, and gitaloxin. It has the general properties described under digoxin (p.1259) and has been used similarly in the management of heart failure. However, when treatment with a cardiac glycoside is required a single glycoside is preferred to digitalis, and digoxin or digitoxin are most commonly used.

Digitalis is used in herbal medicine.

Homoeopathy. Digitalis leaf has been used in homoeopathic medicines under the following names: Digitalis; Digitalis purpurea; Dig. pur.

Preparations

USP 31: Digitalis Capsules; Digitalis Tablets.

Proprietary Preparations (details are given in Part 3)
Ger.: Digophton†.

Multi-ingredient: ***Austria:*** Augentropfen Stulln; ***Ger.:*** Augentropfen Stulln Mono; Unguentum lymphaticum; ***Switz.:*** Augentonicum; Collypan; ***Venez.:*** Linfoderm.

Digitalis Lanata Leaf

Austrian Digitalis; Austrian Foxglove; Digitalis lanata, hoja de; Digitalis Lanatae Folium; Woolly Foxglove Leaf.

CAS — 17575-20-1 (lanatoside A).

Profile

Digitalis lanata leaf consists of the dried leaves of the woolly foxglove, *Digitalis lanata* (Scrophulariaceae), containing about 1 to 1.4% of a mixture of cardioactive glycosides, including digoxin, digitoxin, acetyldigoxin, acetyldigitoxin, lanatoside A, and deslanoside.

Digitalis lanata leaf is used as a source for the manufacture of digoxin and other glycosides.

◊ There have been reports[1] of toxicity after ingestion of dietary supplements contaminated with digitalis lanata.

1. Slifman NR, *et al.* Contamination of botanical dietary supplements by digitalis lanata. *N Engl J Med* 1998; **339:** 806–11.

Digitoxin *(BAN, rINN)*

Digitaline Cristallisée; Digitoksiini; Digitoksinas; Digitoksyna; Digitoxina; Digitoxine; Digitoxinum; Digitoxoside; Dijitoksin. 3β-[(*O*-2,6-Dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)oxy]-14β-hydroxy-5β-card-20(22)-enolide.

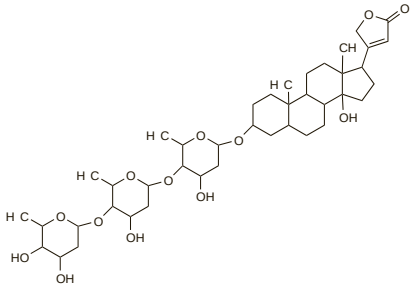
Дигитоксин

$C_{41}H_{64}O_{13}$ = 764.9.

CAS — 71-63-6.

ATC — C01AA04.

ATC Vet — QC01AA04.



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

Ph. Eur. 6.2 (Digitoxin). A white or almost white powder. Practically insoluble in water; slightly soluble in alcohol and in methyl alcohol; freely soluble in a mixture of equal volumes of chloroform and methyl alcohol. Protect from light.

USP 31 (Digitoxin). A cardiotonic glycoside obtained from *Digitalis purpurea*, *Digitalis lanata* (Scrophulariaceae), or other suitable species of *Digitalis*. A white or pale buff-coloured, odourless, microcrystalline powder. Practically insoluble in water; soluble 1 in 150 of alcohol and 1 in 40 of chloroform; very slightly soluble in ether. Store in airtight containers.

Adsorption. Binding to an in-line intravenous filter containing a cellulose ester membrane accounted for a reduction[1] in digitoxin concentration of up to 25% from solutions of digitoxin 200 micrograms in 50 mL of glucose 5% or sodium chloride 0.9%. Pretreatment of the filter with a polymer coating reduced adsorption by about half.[2]

Digitoxin was found to be adsorbed onto glass and plastic in substantial amounts from simple aqueous solutions but not from solutions in 30% alcohol, or in plasma, or urine.[3]

1. Butler LD, *et al*. Effect of inline filtration on the potency of low-dose drugs. *Am J Hosp Pharm* 1980; **37:** 935–41.
2. Kanke M, *et al.* Binding of selected drugs to a "treated" inline filter. *Am J Hosp Pharm* 1983; **40:** 1323–8.
3. Molin L, *et al.* Solubility, partition, and adsorption of digitalis glycosides. *Acta Pharm Suec* 1983: **20:** 129–44.

Adverse Effects, Treatment, and Precautions

As for Digoxin, below. Toxicity may be more prolonged after withdrawal of digitoxin because of the longer half-life.

◊ References.

1. Lely AH, van Enter CHJ. Large-scale digitoxin intoxication. *BMJ* 1970; **3:** 737–40.
2. Gilfrich H-J, *et al.* Treatment of massive digitoxin overdose by charcoal haemoperfusion and cholestyramine. *Lancet* 1978; **i:** 505.
3. Pond S, *et al*. Treatment of digitoxin overdose with oral activated charcoal. *Lancet* 1981; **ii:** 1177–8.
4. Kurowski V, *et al.* Treatment of a patient with severe digitoxin intoxication by Fab fragments of anti-digitalis antibodies. *Intensive Care Med* 1992; **18:** 439–42.
5. Schmitt K, *et al*. Massive digitoxin intoxication treated with digoxin-specific antibodies in a child. *Pediatr Cardiol* 1994; **15:** 48–9.
6. Lehmann G, *et al.* Digitoxin intoxication in a 79-year-old patient: a description of a case and review of the literature. *Int J Cardiol* 2000; **75:** 109–13.
7. Hippius M, *et al.* Adverse drug reaction monitoring—digitoxin overdosage in the elderly. *Int J Clin Pharmacol Ther* 2001; **39:** 336–43.

Interactions

As for Digoxin, below. Since digitoxin is significantly metabolised in the liver it may be affected by drugs that induce microsomal enzymes, including rifampicin (see below) and antiepileptics such as phenobarbital.

Antibacterials. Acute heart failure has been reported in a patient taking digitoxin when treatment with *rifampicin* and isoniazid was started; plasma-digitoxin concentrations fell from a pretreatment steady-state value of 27 nanograms/mL to 10 nanograms/mL. The reduction in the digitoxin concentration was attributed to induction of digitoxin metabolism by rifampicin.[1]

Digitoxin toxicity has been described in 2 patients after addition of *azithromycin* to their therapy.[2]

1. Boman G, *et al*. Acute cardiac failure during treatment with digitoxin—an interaction with rifampicin. *Br J Clin Pharmacol* 1980; **10:** 89–90.
2. Thalhammer F, *et al.* Azithromycin-related toxic effects of digitoxin. *Br J Clin Pharmacol* 1998; **45:** 91–2.

Antineoplastics. A mean overall increase of 109% was seen in digitoxin clearance in 5 patients also given *aminoglutethimide*. The interaction was attributed to the induction of hepatic enzymes by aminoglutethimide.[1]

1. Lønning PE, *et al*. Effect of aminoglutethimide on antipyrine, theophylline, and digitoxin disposition in breast cancer. *Clin Pharmacol Ther* 1984; **36:** 796–802.

Calcium-channel blockers. Steady-state plasma concentrations of digitoxin increased by an average of 35% over 2 to 3 weeks in 8 of 10 patients when *verapamil* 240 mg daily was added to their therapy. Total body clearance and extra-renal clearance of digitoxin were reduced by 27% and 29% respectively although renal excretion was unchanged. Plasma-digitoxin concentrations increased by a mean of 21% in 5 of 10 patients treated with *diltiazem* but were not increased by *nifedipine*.[1]

1. Kuhlman J. Effects of verapamil, diltiazem, and nifedipine on plasma levels and renal excretion of digitoxin. *Clin Pharmacol Ther* 1985; **38:** 667–73.

Diuretics. *Spironolactone* has been reported to decrease the half-life and the urinary elimination of unchanged digitoxin when given for at least 10 days to 8 patients on oral maintenance digitoxin therapy.[1] However, increased digitoxin half-life has been reported[2] in 3 healthy subjects when spironolactone was added to digitoxin therapy. The interaction was judged to be of minor clinical importance.

1. Wirth KE, *et al*. Metabolism of digitoxin in man and its modification by spironolactone. *Eur J Clin Pharmacol* 1976; **9:** 345–54.
2. Carruthers SG, Dujovne CA. Cholestyramine and spironolactone and their combination in digitoxin elimination. *Clin Pharmacol Ther* 1980; **27:** 184–7.

Pharmacokinetics

Digitoxin is readily and completely absorbed from the gastrointestinal tract. Therapeutic plasma concentrations may range from 10 to 35 nanograms/mL but there is considerable interindividual variation. Digitoxin is more than 90% bound to plasma proteins. It is very slowly eliminated from the body and is metabolised in the liver. Most metabolites are inactive; the major active metabolite is digoxin. Enterohepatic recycling occurs and digitoxin is excreted in the urine, mainly as metabolites. It is also excreted in the faeces and this route becomes significant in renal impairment. Digitoxin has an elimination half-life of up to 7 days or more. The half-life is generally unchanged in renal impairment.

The pharmacokinetics of digitoxin may be affected by age and by concurrent diseases (see under Uses and Administration, below).

Uses and Administration

Digitoxin is a cardiac glycoside with positive inotropic activity. It has actions similar to those of digoxin (below) and is used in the management of some cardiac arrhythmias (p.1160) and in heart failure (p.1165).

Digitoxin is the most potent of the digitalis glycosides and is the most cumulative in action. The onset of its action is slower than that of the other cardiac glycosides and it may therefore be less suitable than digoxin for rapid digitalisation; after oral doses its effects may be evident in about 2 hours and its full effects in about 12 hours. Its effects persist for about 3 weeks.

As described under digoxin, dosage should be carefully adjusted to the needs of the individual patient. Steady-state therapeutic plasma concentrations of digitoxin may range from 10 to 35 nanograms/mL; higher values may be associated with toxicity. In adults 1 to 1.5 mg has been given orally in divided doses over 24 hours for rapid digitalisation, while for slow digitalisation an oral dose of 200 micrograms twice daily for 4 days has been given. The usual maintenance dose is 100 to 200 micrograms daily, but 100 micrograms on alternate days may be adequate. Digitoxin may also be given by slow intravenous injection when vomiting or other conditions prevent oral use; maintenance doses of 70 to 100 micrograms daily have been used. It has also been given intramuscularly but injections may be irritant.

Administration in children. Children were found to have a greater volume of distribution of digitoxin than adults and a shorter mean half-life, although individual variation was considerable. The increase in total clearance in children compared with adults was attributed to greater metabolic clearance. Digitalisation doses of 20 micrograms/kg were well tolerated.[1]

1. Larsen A, Storstein L. Digitoxin kinetics and renal excretion in children. *Clin Pharmacol Ther* 1983; **33:** 717–26.

Administration in the elderly. Digitoxin half-life, apparent volume of distribution, and clearance were not found to differ in elderly subjects compared with young adults after intravenous injection in a single-dose study. The long half-life may make once weekly dosing possible in poorly compliant patients.[1]

1. Donovan MA, *et al*. The effect of age on digitoxin pharmacokinetics. *Br J Clin Pharmacol* 1981; **11:** 401–2.

Administration in renal disease. The pharmacokinetics of digitoxin were changed significantly in 5 patients with nephrotic syndrome. The apparent volume of distribution of digitoxin was increased and protein binding decreased. Such patients should be maintained at lower serum-digitoxin concentrations than other patients but will need larger doses because of the shortened serum half-life and the increased renal excretion of digitoxin and its cardioactive metabolites.[1]

1. Storstein L. Studies on digitalis VII: influence of nephrotic syndrome on protein binding, pharmacokinetics, and renal excretion of digitoxin and cardioactive metabolites. *Clin Pharmacol Ther* 1976; **20:** 158–66.

Malignant neoplasms. There has been some interest in the potential anticancer activity of digitoxin and related compounds.

References.

1. Haux J. Digitoxin is a potential anticancer agent for several types of cancer. *Med Hypotheses* 1999; **53:** 543–8.
2. Haux J, *et al*. Digitoxin medication and cancer: case control and internal dose-response studies. *BMC Cancer* 2001; **1:** 11.
3. Johansson S, *et al*. Cytotoxicity of digitoxin and related cardiac glycosides in human tumor cells. *Anticancer Drugs* 2001; **12:** 475–83.
4. López-Lázaro M, *et al*. Digitoxin inhibits the growth of cancer cell lines at concentrations commonly found in cardiac patients. *J Nat Prod* 2005; **68:** 1642–5.
5. López-Lázaro M. Digitoxin as an anticancer agent with selectivity for cancer cells: possible mechanisms involved. *Expert Opin Ther Targets* 2007; **11:** 1043–53.

Preparations

BP 2008: Digitoxin Tablets;
USP 31: Digitoxin Injection; Digitoxin Tablets.

Proprietary Preparations (details are given in Part 3)
Austria: Digimerck; Ditaven†; ***Belg.:*** Digitaline†; ***Braz.:*** Digitaline; ***Ger.:*** Coramedan†; Digimed; Digimerck; Tardigal†; ***Hung.:*** Digimerck; ***Swed.:*** Digitrin†; ***USA:*** Crystodigin.

Digoxin *(BAN, rINN)*

Digoksiini; Digoksin; Digoksinas; Digoksyna; Digoxina; Digoxine; Digoxinum; Digoxosidum. 3β-[(*O*-2,6-Dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)oxy]-12β,14β-dihydroxy-5β-card-20(22)-enolide.

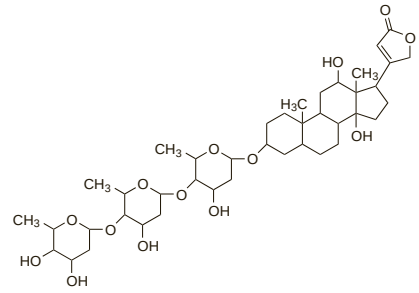
Дигоксин

$C_{41}H_{64}O_{14}$ = 780.9.

CAS — 20830-75-5.

ATC — C01AA05.

ATC Vet — QC01AA05.



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

Ph. Eur. 6.2 (Digoxin). A white or almost white powder or colourless crystals. Practically insoluble in water; slightly soluble in alcohol; freely soluble in a mixture of equal volumes of dichloromethane and methyl alcohol. Protect from light.

USP 31 (Digoxin). A cardiotonic glycoside obtained from the leaves of *Digitalis lanata* (Scrophulariaceae). Clear to white, odourless, crystals, or a white, odourless, crystalline powder. Practically insoluble in water and in ether; slightly soluble in diluted alcohol and in chloroform; freely soluble in pyridine. Store in airtight containers.

Adverse Effects

Digoxin and the other cardiac glycosides commonly produce adverse effects because the margin between the therapeutic and toxic doses is small; plasma concentrations of digoxin in excess of 2 nanograms/mL are considered to be an indication that the patient is at special risk although there is considerable interindividual variation. There have been many fatalities, particularly due to cardiac toxicity.

Nausea, vomiting, and anorexia may be among the earliest symptoms of digoxin toxicity or overdosage; diarrhoea and abdominal pain may occur. Certain neurological effects are also common symptoms of digoxin overdosage and include headache, facial pain, fatigue,