immediately before going to bed. It should be avoided in patients who have difficulty swallowing.

◊ References.

1. Henry DA, *et al*. Glucomannan and risk of oesophageal obstruction. *BMJ* 1986; **292:** 591–2.
2. Renard E, *et al*. Noninsulin-dependent diabetes and glucose intolerance: effect of glucomannan fibre on blood glucose and serum insulin. *Sem Hop Paris* 1991; **67:** 153–7.
3. Vuksan V, *et al*. Beneficial effects of viscous dietary fiber from konjac-mannan in subjects with the insulin resistance syndrome: results of a controlled metabolic trial. *Diabetes Care* 2000; **23:** 9–14.
4. Staiano A, *et al*. Effect of the dietary fiber glucomannan on chronic constipation in neurologically impaired children. *J Pediatr* 2000; **136:** 41–5.
5. Loening-Baucke V, *et al*. Fiber (glucomannan) is beneficial in the treatment of childhood constipation. Abstract: *Pediatrics* 2004; **113:** 259. Full version: http://pediatrics.org/cgi/content/full/113/3/e259 (accessed 23/05/06)
6. Keithley J, Swanson B. Glucomannan and obesity: a critical review. *Altern Ther Health Med* 2005; **11:** 30–4.
7. Vanderbeek PB, *et al*. Esophageal obstruction from a hygroscopic pharmacobezoar containing glucomannan. *Clin Toxicol* 2007; **45:** 80–2.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Modekal†; ***Chile:*** Redicres Rapido†; ***Fr.:*** Muraligne†; ***Ger.:*** bioNorm mit Konjak†; ***India:*** Dietmann; ***Ital.:*** Dicoplus; Dietoman; NormaLine; ***Mex.:*** Dietoman; Esbeltex; Naturalfit†; ***Port.:*** Bioregime†; Florilax†.

Multi-ingredient: ***Arg.:*** KLB6 Fruit Diet; ***Chile:*** Delgadol Fibra; ***Fr.:*** Filigel; ***Ital.:*** Agioslim; Ecamannan; Glucoman; Lactomannan; ***Port.:*** Bioregime Fort†; Bioregime SlimKit†; Excess†.

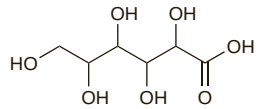
Gluconic Acid

Dextronic Acid; E574; Glycogenic Acid; Maltonic Acid; Pentahydroxycaproic Acid. D-Gluconic acid.

Глюконовая Кислота

$C_6H_{12}O_7$ = 196.2.

CAS — 526-95-4.



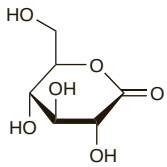
Gluconolactone

E575; Glucono delta-lactone; Glucono-delta-lactone; 1,5-Gluconolactone; D-Glucono-1,5-lactone. D-Gluconic acid δ-lactone.

Глюконолактон

$C_6H_{10}O_6$ = 178.1.

CAS — 90-80-2.



Pharmacopoeias. In *US*.

USP 31 (Gluconolactone). A fine, white, practically odourless, crystalline powder. Freely soluble in water; sparingly soluble in alcohol; insoluble in ether.

Profile

Gluconolactone is hydrolysed to gluconic acid, a polyhydroxy acid. It has similar properties to the alpha hydroxy acids glycolic acid (p.1598) and mandelic acid (p.296) and has been used in skin disorders and for urinary catheter care. Gluconolactone and gluconic acid are also used as food additives.

◊ References.

1. Grimes PE, *et al*. The use of polyhydroxy acids (PHAs) in photoaged skin. *Cutis* 2004; **73** (suppl 2): 3–13.

Preparations

Proprietary Preparations (details are given in Part 3)

Ital.: Neostrata.

Multi-ingredient: ***Arg.:*** Neoceuticals Crema Despigmentante de Dia†; Neoceuticals Gel de Limpieza Facial; Neostrata; ***Austral.:*** Neostrata; ***Canad.:*** Neostrata; ***Chile:*** Neostrata; ***Fr.:*** Ruboderm Plus; ***UK:*** Uriflex R; Uro-Tainer Solution R; ***USA:*** Renacidin.

Glucosamine *(USAN, rINN)*

Chitosamine; Glucosamina; Glucosaminum; NSC-758. 2-Amino-2-deoxy-β-D-glucopyranose.

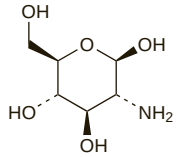
Глюкозамин

$C_6H_{13}NO_5$ = 179.2.

CAS — 3416-24-8.

ATC — M01AX05.

ATC Vet — QM01AX05.



Glucosamine Hydrochloride *(rINNM)*

Chitosamine Hydrochloride; Glucosamine, Chlorhydrate de; Glucosamini Hydrochloridum; Glukozaminy chlorowodorek; Hidrocloruro de glucosamina.

Глюкозамина Гидрохлорид

$C_6H_{13}NO_5$.HCl = 215.6.

CAS — 66-84-2.

Pharmacopoeias. In *US*.

USP 31 (Glucosamine Hydrochloride). A 2% solution in water has a pH of 3.0 to 5.0. Store in airtight containers. Protect from light.

Glucosamine Sulfate Potassium Chloride

$(C_6H_{14}NO_5)_2SO_4$,2KCl = 605.5.

Pharmacopoeias. In *US*.

USP 31 (Glucosamine Sulfate Potassium Chloride). A 2% solution in water has a pH of 3.0 to 5.0. Store in airtight containers. Protect from light.

Glucosamine Sulfate Sodium Chloride

$(C_6H_{14}NO_5)_2SO_4$,2NaCl = 573.3.

Pharmacopoeias. In *US*.

USP 31 (Glucosamine Sulfate Sodium Chloride). A 2% solution in water has a pH of 3.0 to 5.0. Store in airtight containers. Protect from light.

Profile

Glucosamine is a natural substance found in chitin, mucoproteins, and mucopolysaccharides. It is involved in the manufacture of glycosaminoglycan, which forms cartilage tissue in the body; glucosamine is also present in tendons and ligaments. Glucosamine must be synthesised by the body but the ability to do this declines with age. Glucosamine and its salts have therefore been advocated in the treatment of rheumatic disorders including osteoarthritis. Glucosamine may be isolated from chitin or prepared synthetically; glucosamine sulfate and hydriodide, have also been used.

Effects on glucose metabolism. Glucosamine has a role in glucose metabolism, increasing insulin resistance in skeletal muscle,[1,2] which has raised concerns about its safety profile in diabetic patients.[3] However, alteration of glycaemic homoeostasis was not found in a 3-year randomised controlled study in patients without diabetes.[4] A review[5] of the literature found limited data on diabetic patients taking glucosamine supplements, and recommended close monitoring of blood glucose levels in this group until more data are available.

1. Adams ME. Hype about glucosamine. *Lancet* 1999; **354:** 353–4.
2. Chan NN, *et al*. Drug-related hyperglycemia. *JAMA* 2002; **287:** 714–15.
3. Chan NN, *et al*. Glucosamine sulphate and osteoarthritis. *Lancet* 2001; **357:** 1618–9.
4. Reginster JY, *et al*. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. *Lancet* 2001; **357:** 251–6.
5. Stumpf JL, Lin SW. Effect of glucosamine on glucose control. *Ann Pharmacother* 2006; **40:** 694–8.

Osteoarthritis. Glucosamine and its salts are widely available as licensed products or so-called 'health supplements' used for the management of osteoarthritis (p.11); they may be combined with other substances supposed to be of benefit, including chondroitin (p.2280), vitamins, and various herbs. Meta-analyses[1,2] of randomised placebo-controlled studies concluded that while there was some evidence for efficacy of glucosamine and chondroitin in the treatment of osteoarthritis, methodological flaws and publication bias had led to exaggeration of its potential benefit,[1] and that further studies are needed to fully characterise their disease-modifying properties.[2] A systematic review[3] of the use of glucosamine for osteoarthritis that included later controlled studies concluded that glucosamine is as safe as placebo but there was little evidence of improvement in pain or function. A further randomised controlled study[4] in 222 patients with hip osteoarthritis found no benefit after treatment with glucosamine for 2 years compared with placebo, and a meta-analysis[5] of controlled studies of chondroitin for osteoarthritis of the knee or hip concluded that chondroitin had minimal or no benefit. Further research is needed to confirm whether there are differences in efficacy between glucosamine salts, preparations, or routes, and when used with other agents (e.g. chondroitin) or in different patient subgroups.[3] A large multicentre double-blind study[6] in 1583 patients with symptomatic knee osteoarthritis to compare glucosamine and chondroitin, either alone or in combination, found no clear evidence of benefit in pain reduction compared with placebo or celecoxib, although there was a tendency to more positive results in a subset of patients with moderate to severe knee pain.

1. McAlindon TE, *et al*. Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis. *JAMA* 2000; **283:** 1469–75.
2. Richy F, *et al*. Structural and symptomatic efficacy of glucosamine and chondroitin in knee osteoarthritis: a comprehensive meta-analysis. *Arch Intern Med* 2003; **163:** 1514–22.
3. Towheed TE, *et al*. Glucosamine therapy for treating osteoarthritis. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2005 (accessed 14/05/08).
4. Rozendaal RM, *et al*. Effect of glucosamine sulfate on hip osteoarthritis: a randomized trial. *Ann Intern Med* 2008; **148:** 268–77.
5. Reichenbach S, *et al*. Meta-analysis: chondroitin for osteoarthritis of the knee or hip. *Ann Intern Med* 2007; **146:** 580–90.
6. Clegg DO, *et al*. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med* 2006; **354:** 795–808.

Skin reactions. The Australian Adverse Drug Reactions Advisory Committee (ADRAC)[1] has received 51 reports of allergic skin reactions with glucosamine, including erythematous rash, angioedema, urticaria, rash, and pruritus. It was noted that some preparations contain glucosamine sourced from seafood and therefore people with an allergy to shellfish may be at greater risk for hypersensitivity reactions.

1. Adverse Drug Reactions Advisory Committee (ADRAC). Skin reactions with glucosamine. *Aust Adverse Drug React Bull* 2005; **24:** 23. Also available at: http://www.tga.gov.au/adr/aadrb/aadr0512.pdf (accessed 14/05/08)

Preparations

USP 31: Glucosamine and Chondroitin Sulfate Sodium Tablets; Glucosamine and Methylsulfonylmethane Tablets; Glucosamine Tablets; Glucosamine, Chondroitin Sulfate Sodium, and Methylsulfonylmethane Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Adaxil; Artrilase; Asoglutan; Baliartrin; Belmalen Plus; Findol; Gluco Arrumalon; Glucocartiflex; Mecanyl; Ostatac; Pertinar; Vartalon Complemento; Vartalon K; ***Austral.:*** GenFlex; ***Braz.:*** Dinaflex; Glucoreumin; Injeflex; ***Chile:*** Artridol; Bioflex; Dinaflex; Reufin; Viartril†; ***Cz.:*** Dona; Flexove; Gool; Mediflex; Voltadyn; ***Denm.:*** Ledamin; Ledflex†; ***Fin.:*** Arthryl; G-Lenk; Glucadol; Movere; ***Fr.:*** Oscart; ***Ger.:*** Dona 200-S; ***Gr.:*** Anarthril; Donarot; Glucosamil; Glusamon; Nerita; Recosine; Viartril; ***Hong Kong:*** Arthritil; Cartril-S; Chitaq; Doctor's Choice for Joints; Donna; F-Vial; MarinEx; Viartril S; Vidatril; Vitoport; Vocarxil; ***Hung.:*** Dona; Gool; ***Indon.:*** Jointfit Cream; Mediflex; Reflexor; ***Irl.:*** Arthrimel; Dona; ***Ital.:*** Dona; Viartril S†; ***Malaysia:*** Artronil; Cartril-S; Cosamine; Donna; Procosa; Viartril S; ***Mex.:*** Artriman; Faximin; Vartalon; Viartril†; ***Neth.:*** Cartimin; Glucadol; ***Norw.:*** Gluxine; Movere; ***Philipp.:*** Viartril S; ***Pol.:*** Arthryl; ***Port.:*** Arthramina; Glucomed; Glucosine; Glufan; Viartril S; ***Singapore:*** ArthriCare; Artril; Artronil; Gluco-S†; Glutilage; Kudona†; Viartril S; Vital; ***Spain:*** Cartisorb; Ceremir; Coderol; Glufan; Hespercorbin; Obifax†; Xicil; ***Swed.:*** Artrox; Glucomed; Glucosine; ***Thai.:*** Artronil; Athril; Flexsa; Gluco-S; Glucosa; Glusa; Glusamine; Viartril S; ***UK:*** Alateris; Flexeze; Joint-e-Licious; ***Venez.:*** Vartalon; Viartril S.

Multi-ingredient: ***Arg.:*** Artrilase Complex; Artrocaptin; Asotrex; Baliartrin Duo; Car-ti buron flex; Cartiflex Forte; Ecosamina; Etinox; Finartrit; Findol Plus; Gluco Arrumalon Duo; Glucobefol; Glucotrin VL; Mecanyl Duo; Nectar G; Sigmaflex; Vartalon Duo; ***Austral.:*** Bioglan Joint Mobility; GenFlex 3; GenFlex Plus; OsteoEze Bone & Joint Care; ***Braz.:*** Artrolive; Condroflex; ***Canad.:*** Glucosamine Joint & Muscle Cream with MSM†; ***Chile:*** Artridol Duo; Condrosamina†; Dinaflex Duo; Eniflex†; Euroflex; Flexure; Hiperflex; Osteo Bi-Flex; ***Hong Kong:*** Arthritil Plus; Procosamine†; ***India:*** Cosantin†; Kondro; Osteocip; Osteoflex; ***Indon.:*** Aptivium Optimum Joint Formula; Artriox; Artritin; Bonic; Cartin Plus; Chondro-PA; Fitbon; Fitbon Plus; Flexor; Fripos; Joint Care; Jointfit; Maxitrin; Naturica Artro; Naturica Artro Plus; OA; OA Forte; OA Plus; Osamin; Oste; Ostela; Osteoflam; Osteokom; Osteokom Forte; Osteonic; Osteor; Osteor Plus; Osteor-C; Osvion Plus; Rheumatin; Rheumatin Forte; Triflexor; Triostee; Viopor; Viopor-M; Viostin Com; Viostin Com DS; Vosteon; ***Ital.:*** Cartago; Fitogenase; Joint Support; Osteoclar; Reumilase SD; ***Mex.:*** Actiman; Artiflex; Vartalon Compositum; ***Philipp.:*** Flexxbon; Ruflex; ***Port.:*** Synchrocell; Synchrorose; Synchrovit; ***Rus.:*** Artra (Артра); Theraflex (Терафлекс); ***S.Afr.:*** ProFLEX; ProFLEX 750; ***Singapore:*** Arthro-Flex; Articolase (w/glucosamine); Artril C; Cartipro; Flexeze†; Glucocal; Glutilage Plus; Seven Seas JointCare; Seven Seas JointCare Max; ***UK:*** Arheumacare; BackOsamine; Flexeze; GlucOsamax; Healtheries Musseltone & Glucosamine; Joint Action; Jointace; JointCare Max; ***USA:*** Dorofen; ***Venez.:*** Artrosamin; Flexurat.

Glucose Oxidase

Corylophyline; β-D-Glucopyranose aerodehydrogenase; Glucosa oxidasa; Microcide; Notatin; P-FAD.

CAS — 9001-37-0.

Profile

Glucose oxidase is an enzyme obtained from certain fungi, which catalyses the oxidation of glucose to gluconic acid, with the concomitant production of hydrogen peroxide. It is used for its preservative properties as an additive in certain foods, sometimes with catalase (p.2278). It is also used in fertility tests and tests of diabetic control. It has been used as an ingredient of toothpastes for its supposed benefits in the prophylaxis of dental caries.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Bromelin†; Expectoral†; ***Singapore:*** Biotene; ***UK:*** Biotene Dry Mouth; Biotene Oralbalance; ***USA:*** Biotene with Calcium.

Glucose Tests

Glucosa, pruebas de.

Profile

Several tests are available so that patients with diabetes mellitus (p.431) can monitor their disease. Tests can be employed to detect the presence of glucose in the urine and some of the preparations are used to detect several substances in the urine. These tests are easy to carry out but are not considered reliable enough for insulin-dependent patients who should ideally check their blood-glucose concentrations using one of the available blood tests. Diabetic clinics often measure the degree of haemoglobin glycosylation as an indicator of mean blood-glucose control over a period of weeks or months.

Urine tests generally use either the copper-reduction method or the glucose-oxidase method and both produce a colour change in the presence of glucose. Blood tests generally use the glucose-oxidase method; they may be read visually or by means of a meter. A meter gives the more precise reading. Patients should be properly trained in the use of these tests and in the interpretation of the results; they should be aware that concomitant drug therapy might affect the result.

Precautions. Preparations that contain, or are metabolised to, maltose (p.1956), galactose (p.1481), or xylose (p.2416) may interfere with the results from glucose tests based on dehydrogenase pyrroloquinolinequinone (GDH-PQQ) monitoring systems as these are non-specific for glucose. Overestimation of glucose results may mask hypoglycaemia, resulting in the inappropriate use of insulin.[1,2]

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

Preparations

USP 31: Glucose Enzymatic Test Strip.

Proprietary Preparations (details are given in Part 3)

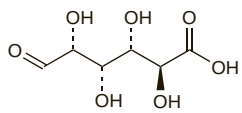
Arg.: Accu-Chek; Accutrend Glucosa; Ascensia; Betachek; Dextrostix; Diabur-Test 5000†; Diastix; Elite; Glucostix; Glucotide†; Glucotrend†; Glukotest†; Haemo-Glukotest 20-800†; One Touch; Precision Plus; Prestige†; Sure Step; ***Austral.:*** Accu-Chek; Accutrend Glucose; Advantage†; Ascensia; Betachek†; BM-Test BG; BM-Test Glycemie 20-800; Clinistix; Clinitest; Diabur-Test 5000; Diascreen Glucose†; Diastix; Esprit; ExacTech†; Glucoflex-R†; Glucometer†; Glucostix; Medi-Test Glucose; MediSense Sof-Tact†; Omnitest†; Optium†; Precision Plus†; Tes-Tape†; ***Braz.:*** Accu-Chek; Accutrend; Glico-Fita; Haemo-Glukotest; ***Canad.:*** Accu-Chek†; Accutrend GC†; Advantage; Ascensia Elite; Chemstrip uG; Clinistix; Clinitest; Diastix; One Touch; Sof-Tact; ***Chile:*** Accu-Chek; Accutrend Glucosa; Ascencia; Glukotest†; ***Fr.:*** Accu-Chek; Ascensia; BM-Test Glycemie†; Clinistix; Clinitest†; Euroflash; Glucomen; Glucotide†; Glucotrend†; Medisense; One Touch; ***India:*** Diastix; ***Irl.:*** Accu-Chek; BM-Accutest; BM-Test 1-44†; Clinistix; Clinitest; Combina Glucose; Diabur-Test 5000; Diastix; Freestyle; Glucomen; Glucometer Elite; Glucostix; Glucotide; Hypoguard†; Medisense†; One Touch; PocketScan; ***Ital.:*** Accu-Chek; Accutrend Glucose†; Ascensia; Clinistix; Clinitest; Diabur-Test 5000; Diastix; Euroflash; EZ Smart; Freestyle Papillon; Glucocard; Glucofilm†; Glucometer†; Glucosan†; Glucostix†; Glucotrend†; Glukurtest†; Haemoglukotest 20-800†; One Touch; Uni-Check; ***Mex.:*** Accu-Chek; Accutrend Glucose; Clinitest; Dextrostix; Diabur-Test 5000; Diastix; Gluco-Cinta†; Glucostix†; Glucotide†; Haemo-Glukotest 20-800; ***NZ:*** Accu-Chek Advantage; Accutrend Glucose†; BM-Test 1-44†; Clinistix; Clinitest; Diabur-5000; Diastix; Glucocard†; Glucometer Elite†; Glucometer Esprit†; Glucostix†; Precision Plus†; ***Port.:*** Clinistix; Elite†; Euroflash†; Glucocard; Glucodisk; Glucostix; Glucotouch†; One Touch; ***UK:*** Ascensia Glucodisc; BM-Accutest; BM-Test 1-44; Breeze 2; Clinistix; Clinitest; Diabur-Test 5000; Diastix; ExacTech; Freestyle; Glucomen; Glucostix†; Glucotide†; Hypoguard Supreme Plus; Medi-Test Glucose; Medi-Test Glycaemie C†; Medisense; Optium Plus; ***USA:*** Accu-Chek Advantage; Chemstrip bG; Chemstrip uG; Choice DM; Clinistix; Clinitest; Diascan; Diastix; First Choice; Glucofilm; Glucostix; One Touch.

Glucuronic Acid

D-Glucuronic acid.

$C_6H_{10}O_7$ = 194.1.

CAS — 576-37-4 (D,L-glucuronic acid); 6556-12-3 (D-glucuronic acid); 3789-97-7 (glucuronamide); 3574-23-0 (D-glucuronamide); 61914-43-0 (D-glucuronamide); 63-29-6 (glucurolactone); 32449-92-6 (glucurolactone); 14984-34-0 (sodium glucuronate).



(D-glucuronic acid)

Profile

Glucuronic acid is one of the components of hyaluronic acid (p.2320) and also has an important role in the metabolism of many endogenous substances, drugs, and toxins. It has been used topically as a potential precursor of hyaluronic acid, and has also been used as a nutritional supplement. Glucuronamide, glucurolactone (glucuronic acid lactone), diolamine glucuronate, and other glucuronates have also been used as supplements.

Preparations

Proprietary Preparations (details are given in Part 3)

Hong Kong: Guronsan†.

Multi-ingredient: ***Belg.:*** Guronsan; ***Chile:*** Neostrata†; ***Fr.:*** Detoxalgine†; Guronsan; ***Hong Kong:*** Jetepar; ***Ital.:*** Ietepar†; ***Malaysia:*** Jetepar; ***Philipp.:*** Jetepar; ***Port.:*** Guronsan; Synchrocell; Synchrovit; ***Singapore:*** Jetepar; ***Spain:*** Guronsan.

Gluten

Profile

Gluten is a mixture of 2 proteins, gliadin and glutenin, and is present in wheat flour and to a lesser extent in barley and rye. Gliadin is a prolamine, one of the 2 chief groups of plant proteins, and glutenin belongs to the other main group termed glutelins.

Gluten is of medicinal and pharmaceutical interest in that patients with coeliac disease (p.1922) are sensitive to the protein fraction of gluten contained in the normal diet. Treatment consists of the use of gluten-free diets; gluten-free foods are available.

A gluten-free diet may also be beneficial in patients with dermatitis herpetiformis (p.1578).

Glycerol *(rINN)*

E422; Glicerin; Glicerol; Glicerolis; Gliserin; Gliserol; Glisin; Glycerin; Glycerine; Glycérol; Glycerolum; Glyseroli. Propane-1,2,3-triol.

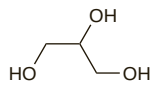
Глицерол

$C_3H_8O_3$ = 92.09.

CAS — 56-81-5.

ATC — A06AG04; A06AX01.

ATC Vet — QA06AG04; QA06AX01; QA16QA03.



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

Eur. and *Int.* also include Glycerol (85 per cent).

Ph. Eur. 6.2 (Glycerol). A clear, colourless or almost colourless, very hygroscopic, syrupy liquid, unctuous to the touch. Miscible with water and with alcohol; slightly soluble in acetone; practically insoluble in fixed oils and in essential oils. Store in airtight containers.

USP 31 (Glycerin). A clear, colourless, hygroscopic, syrupy liquid. Has not more than a slight characteristic odour, which is neither harsh nor disagreeable. Miscible with water and with alcohol; insoluble in chloroform, in ether, and in fixed and volatile oils. Its solutions are neutral to litmus. Store in airtight containers.

Incompatibility. Strong oxidising agents form explosive mixtures with glycerol. Black discoloration has been reported with glycerol and bismuth subnitrate or zinc oxide when exposed to light.

Adverse Effects and Precautions

The adverse effects of glycerol are primarily due to its dehydrating action.

When taken orally glycerol may cause headache, nausea, and vomiting; diarrhoea, thirst, dizziness, and mental confusion may occur less frequently. Cardiac arrhythmias have been reported.

Glycerol increases plasma osmolality resulting in the withdrawal of water from the extravascular spaces. The consequent expansion of extracellular fluid, especially if sudden, can lead to circulatory overload, pulmonary oedema, and heart failure; glycerol must therefore be used with caution in patients at risk, such as those with hypervolaemia, cardiac failure, or renal disease. Severe dehydration can occur and glycerol should be used cautiously in dehydrated patients. Patients with diabetes mellitus may additionally develop hyperglycaemia and glycosuria after metabolism of glycerol. Nonketotic hyperosmolar hyperglycaemic coma is rare, but fatalities have been reported.

Haemolysis, haemoglobinuria, and acute renal failure have also been associated with glycerol when given intravenously (see Raised Intracranial Pressure, below).

Glycerol can cause irritation when given topically or rectally. A local anaesthetic may be used before application of glycerol to the cornea to reduce the likelihood of a painful response.

For incompatibilities with glycerol, including the risk of explosive mixtures, see above.

Effects on the cardiovascular system. A 73-year-old man, free of cardiac complaints but who had previously had an acute myocardial infarction, developed severe pulmonary oedema after use of glycerol orally for elevated intra-ocular pressure.[1] The necessity for detailed cardiac evaluation before the use of oral glycerol was emphasised.

1. Almog Y, *et al.* Pulmonary edema as a complication of oral glycerol administration. *Ann Ophthalmol* 1986; **18:** 38–9.

Effects on the ears. A 56-year-old man given 100 mL of glycerol and 100 mL of sodium chloride 0.9% as part of a test for Ménière's disease developed temporary hearing loss in the non-involved ear. Two previous reports of deterioration in hearing associated with the glycerol test were reviewed by the author.[1]

1. Mattox DE, Goode RL. Temporary loss of hearing after a glycerin test. *Arch Otolaryngol* 1978; **104:** 359–61.

Effects on the eyes. Caution in applying glycerol to the cornea has been recommended. Studies in *animals*[1] and in man[2] have indicated that the topical application of glycerol to the eye can damage the endothelial cells of the cornea.

1. Sherrard ES. The corneal endothelium in vivo: its response to mild trauma. *Exp Eye Res* 1976; **22:** 347–57.
2. Goldberg MH, *et al.* The effects of topically applied glycerin on the human corneal endothelium. *Cornea* 1982; **1:** 39–44.

Hyperosmolar nonketotic coma. Hyperosmolar nonketotic coma has been associated with the oral use of glycerol[1] and deaths have occurred.[2] The most susceptible patients are maturity-onset elderly diabetics with acute or chronic disease predisposing to fluid deprivation, and in these patients oral glycerol may be best avoided.[1] If glycerol is used in patients with predisposing conditions, adequate measures should be taken to recognise the development of hyperosmolar nonketotic hyperglycaemia and prevent dehydration.[1,2]

1. Oakley DE, Ellis PP. Glycerol and hyperosmolar nonketotic coma. *Am J Ophthalmol* 1976; **81:** 469–72.
2. Sears ES. Nonketotic hyperosmolar hyperglycemia during glycerol therapy for cerebral edema. *Neurology* 1976; **26:** 89–94.

Pharmacokinetics

Glycerol is readily absorbed from the gastrointestinal tract and undergoes extensive metabolism, mainly in the liver; it may be used in the synthesis of lipids, metabolised to glucose or glycogen, or oxidised to carbon dioxide and water. It may also be excreted in the urine unchanged.

◊ References.

1. Nahata MC, *et al.* Variations in glycerol kinetics in Reye's syndrome. *Clin Pharmacol Ther* 1981; **29:** 782–7.
2. Heinemeyer G. Clinical pharmacokinetic considerations in the treatment of increased intracranial pressure. *Clin Pharmacokinet* 1987; **13:** 1–25.

Uses and Administration

Glycerol is an osmotic dehydrating agent with hygroscopic and lubricating properties. When given orally or parenterally, glycerol increases the plasma osmolality, resulting in the movement of water by osmosis from the extravascular spaces into the plasma.

Glycerol is given by mouth for the short-term reduction of vitreous volume and intra-ocular pressure before and after ophthalmic surgery, and as an adjunct in the management of acute glaucoma (p.1873). Its onset of action is rapid, with a maximal reduction in intra-ocular pressure occurring about 1 to 1⁄ hours after a dose; the duration of action is about 5 hours. The usual initial dose of glycerol is 1 to 1.8 g/kg given as a 50% solution. There can be problems of palatability when glycerol solutions are given orally; chilling or flavouring the solutions may help.

Glycerol may be applied topically to reduce corneal oedema, but as the effect is only transient its use is largely limited to an adjunct in eye examination and diagnosis. Glycerol eye drops can be painful on instillation and use of a local anaesthetic beforehand has been recommended.

Glycerol has also been given orally or intravenously to reduce intracranial pressure (see below).

Glycerol may be used rectally as suppositories or a solution in single doses to promote faecal evacuation in the management of constipation (p.1693). It usually acts within 15 to 30 minutes. Glycerol is commonly classified as an osmotic laxative but may act additionally or alternatively through its local irritant effects; it may also have lubricating and faecal softening actions.

Glycerol is used as a demulcent in cough preparations (p.1547).

Glycerol has many applications in pharmaceutical formulation; these include its use as a vehicle and solvent, as a sweetening agent, as a preservative in some liquid medications, as a plasticiser in tablet film-coating, and as a tonicity adjuster. It is often included in topical preparations such as eye drops, creams, and lotions as a lubricant and also for its moisturising properties since, when absorbed, its hygroscopic action can enhance moisture retention. Ear drops for the removal of ear wax often contain glycerol as a lubricating and softening agent.

Glycerol is also used as a cryoprotectant in cryopreservation.

Diagnosis of Ménière's disease. Glycerol has been used[1] in the diagnosis of Ménière's disease (p.564) to distinguish potentially reversible cochlear dysfunction from the relatively irreversible pathology of advanced disease, or to predict the results of endolymphatic sac surgery. Glycerol is given by mouth to