5. Gradin M, *et al*. Pain reduction at venipuncture in newborns: oral glucose compared with local anesthetic cream. *Pediatrics* 2002; **110:** 1053–7.
6. Rabago D, *et al*. A systematic review of prolotherapy for chronic musculoskeletal pain. *Clin J Sport Med* 2005; **15:** 376–80.
7. Dagenais S, *et al*. Prolotherapy injections for chronic low-back pain. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2007 (accessed 23/06/08).
8. Topol GA, *et al*. Efficacy of dextrose prolotherapy in elite male kicking-sport athletes with chronic groin pain. *Arch Phys Med Rehabil* 2005; **86:** 697–702.

Preparations

BP 2008: Glucose Intravenous Infusion; Glucose Irrigation Solution; Potassium Chloride and Glucose Intravenous Infusion; Potassium Chloride, Sodium Chloride and Glucose Intravenous Infusion; Sodium Chloride and Glucose Intravenous Infusion;
Ph. Eur.: Anticoagulant Acid-Citrate-Glucose Solutions (ACD); Anticoagulant Citrate-Phosphate-Glucose Solution (CPD);
USNF 26: Dextrose Excipient; Liquid Glucose;
USP 31: Alcohol in Dextrose Injection; Anticoagulant Citrate Dextrose Solution; Anticoagulant Citrate Phosphate Dextrose Adenine Solution; Anticoagulant Citrate Phosphate Dextrose Solution; Dextrose and Sodium Chloride Injection; Dextrose Injection; Half-strength Lactated Ringer's and Dextrose Injection; Lactated Ringer's and Dextrose Injection; Multiple Electrolytes and Dextrose Injection Type 1; Multiple Electrolytes and Dextrose Injection Type 2; Multiple Electrolytes and Dextrose Injection Type 3; Multiple Electrolytes and Dextrose Injection Type 4; Potassium Chloride in Dextrose and Sodium Chloride Injection; Potassium Chloride in Dextrose Injection; Potassium Chloride in Lactated Ringer's and Dextrose Injection; Ringer's and Dextrose Injection; Sodium Chloride and Dextrose Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Glucolin; Glucotem; Kissimin; Nutrosa; ***Austral.:*** Insta-Glucose†; ***Austria:*** Glucosteril; ***Canad.:*** Glucodex†; ***Cz.:*** Ardeanutrisol G; Spofagnost†; ***Fin.:*** Glucosteril; ***Ger.:*** Glucosteril; ***Hung.:*** Isodex; ***Indon.:*** Otsu-D5; Wida D5 and D10; ***Ital.:*** Energen; ***Pol.:*** Maltan; ***Port.:*** Glucosada; Glucosado; Glucosteril; ***Rus.:*** Glucosteril (Глюкостерил); ***Spain:*** Apir Glucosado; Biberon; Flebobag Glucosa; Fleboflex Glucosa; Fleboplast Glucosa; Freeflex Glucosa; Glucosmon; Meinvenil Glucosa; Plast Apyr Glucosado; Suero Glucosado Isotonico; ***UK:*** GlucoGel; ***USA:*** Dex4 Glucose; Glutose; Insulin Reaction.

Multi-ingredient: ***Arg.:*** High Energy; Sucaryl; Suimel; ***Austral.:*** BSS Plus; Dexsal; Emetrol†; No Doz Plus; Nyal Chesty Cough†; Vig†; ***Austria:*** BSS Plus; Gluco-Salzlosung; ***Braz.:*** Dramin B-6 DL; Glicofisiologica†; ***Canad.:*** BSS Plus; Sclerodex; ***Fr.:*** BSS Plus; Coramine Glucose; Notabac; ***Ger.:*** BSS Plus; Kochsalz mit Glucose; ***Hong Kong:*** BSS Plus†; ***Hung.:*** BSS Plus; ***India:*** Toniazol†; ***Irl.:*** Venos Expectorant; Venos Honey & Lemon; ***Israel:*** BSS Plus; Peptical; ***Ital.:*** Alcalosio; Apergan; Fosfarsile Forte; ***Malaysia:*** BSS Plus; ***Mex.:*** Combinacion PI†; ***Norw.:*** Salidex; ***Pol.:*** Glucardiamid; ***Port.:*** Glucosalino; ***Rus.:*** Gluconeodesum (Глюконеодез); ***S.Afr.:*** BSS Plus; ***Singapore:*** BSS Plus; ***Spain:*** Acetuber; Apir Glucosalino; Flebobag Glucosalina; Fleboplast Glucosalina; Freeflex Glucosalina; Glucopotasico; Glucosalina; Glucosalino; Meinvenil Glucosalina; Plast Apyr Glucosalino; Suero Glucosalino; ***Switz.:*** BSS Plus†; Glucosalin; Glucosaline; Gly-Coramin; ***Thai.:*** BSS Plus; Euro-Collins; Gluco-Calcium; ***UK:*** Buttercup Infant Cough Syrup; Buttercup Syrup (Blackcurrant flavour); Buttercup Syrup (Honey and Lemon flavour); Lockets Medicated Linctus; PEP; Venos Cough Mixture; Venos Expectorant; Venos Honey & Lemon; ***USA:*** BSS Plus; Emetrol; Formula EM; Nausetrol; ***Venez.:*** BSS Plus†; Dextro-Sal†; Glucofisiologica†.

Glutamic Acid *(USAN, rINN)*

Acide glutamique; Ácido glutámico; Acidum glutamicum; E; E620; Glu; L-Glutamic Acid; Glutamiinihappo; Glutaminic Acid; Glutaminsav; Glutaminsyra; Glutamo rūgštis; Kwas glutaminowy; Kyselina glutamová. L-(+)-2-Aminoglutaric acid.

Глутаминовая Кислота

$C_5H_9NO_4$ = 147.1.

CAS — 56-86-0.

Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii).
Ph. Eur. 6.2 (Glutamic Acid). A white or almost white, crystalline powder or colourless crystals. Freely soluble in boiling water; slightly soluble in cold water; practically insoluble in alcohol, in acetic acid, and in acetone. Protect from light.

Glutamic Acid Hydrochloride *(rINNM)*

Acide Glutamique, Chlorhydrate de; Acidum Glutamicum Hydrochloridum; Aciglumin; Glu Hydrochloride; Hidrocloruro del ácido glutámico. L-(+)-2-Aminoglutaric acid hydrochloride.

Глутаминовой Кислоты Гидрохлорид

$C_5H_9NO_4$,HCl = 183.6.

CAS — 138-15-8.

ATC — A09AB01.

ATC Vet — QA09AB01.

Pharmacopoeias. In *Ger.*

Glutamine *(USAN, rINN)*

Gln; Glutamina; L-Glutamine; Glutaminum; Levoglutamida; Lévoglutamide; Levoglutamide; Levoglutamidum; Q. L-Glutamic acid 5-amide; L-(+)-2-Aminoglutaramic acid.

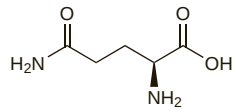
Левоглутамид

$C_5H_{10}N_2O_3$ = 146.1.

CAS — 56-85-9.

ATC — A16AA03.

ATC Vet — QA16AA03.



Pharmacopoeias. In *Ger.* and *US.*
USP 31 (Glutamine). White crystals or crystalline powder. Soluble in water; practically insoluble in alcohol and in ether. Store at a mean temperature not exceeding 25°.

Profile

Glutamic acid is a non-essential amino acid which is degraded readily in the body to form glutamine (levoglutamide). Glutamic acid and glutamine are used as dietary supplements. The dipeptides *N*(2)-L-alanyl-L-glutamine (Ala-Gln) and glycyl-L-glutamine (Gly-Gln) are used similarly.

Glutamic acid hydrochloride, which releases hydrochloric acid in the stomach, has been used in the symptomatic treatment of achlorhydria or hypochlorhydria in usual oral doses of 250 to 750 mg with meals.

A glutamine-based oral suspension is under investigation for the treatment of oral mucositis.

Antineoplastic toxicity. Vincristine neurotoxicity has been reduced by the use of oral glutamic acid (see Administration Error, p.787).

Oral supplementation with glutamine may also have a role in alleviating the diarrhoea associated with irinotecan (see Effects on the Gastrointestinal System, p.737).

A glutamine-based oral suspension is under investigation for the treatment of oral mucositis associated with cancer chemotherapy (p.640). In breast cancer patients with moderate to severe oral mucositis glutamine reduced both the incidence and severity of the mucositis.[1] A literature review[2] reported variable results with glutamine supplementation for chemotherapy-induced mucositis, but stated that higher doses may be beneficial.

Oral glutamine was found to be of no benefit in alleviating myalgias or arthralgias associated with paclitaxel therapy.[3]

1. Peterson DE, *et al.* Randomized, placebo-controlled trial of Saforis for prevention and treatment of oral mucositis in breast cancer patients receiving anthracycline-based chemotherapy. *Cancer* 2007; **109:** 322–31.
2. Savarese DMF, *et al*. Prevention of chemotherapy and radiation toxicity with glutamine. *Cancer Treat Rev* 2003; **29:** 501–13.
3. Jacobson SD, *et al*. Glutamine does not prevent paclitaxel-associated myalgias and arthralgias. *J Support Oncol* 2003; **1:** 274–8.

Parenteral and enteral nutrition. Evidence that glutamine is involved in the regulation of muscle protein synthesis, maintenance of gut mucosal barrier function, and possibly enhanced immunological response has led to studies of supplementation with glutamine or more stable peptide derivatives in parenteral and enteral nutrition regimens for patients with injury and infection.[1] Although non-essential under normal circumstances, many consider glutamine to be a conditionally essential amino acid in patients with catabolic disease.[2,3]

Supplementation of parenteral nutrition regimens with glutamine has been shown to reduce clinical infection in patients who have undergone bone marrow transplantation[4] or who have suffered multiple trauma.[5] Improved survival has been reported among intensive-care patients given parenteral feeds supplemented with glutamine,[6,7] although a larger study found it difficult to demonstrate benefit.[8] A systematic review,[9] including these studies, inferred that seriously ill patients, with gastrointestinal failure and receiving parenteral nutrition, should receive glutamine supplements for at least 6 days and at a dose of greater than 200 mg/kg daily, in order to derive maximum benefit. Low plasma glutamine concentration upon admission to an intensive-care unit was considered to be an independent risk factor for mortality, and it has been suggested that plasma concentrations be used as an indicator for glutamine supplementation.[10]

In patients undergoing major uncomplicated surgery on the lower gastrointestinal tract, a significantly better postoperative nitrogen balance was achieved in those whose total parenteral nutrition regimen had been supplemented with about 20 g daily of glutamine coupled with alanine (L-alanyl-L-glutamine) (equivalent to about 12 g daily of glutamine) when compared with a control group.[11] Others[12] have shown that supplementation of total parenteral nutrition solutions with a glutamine dipeptide (glycyl-L-glutamine), in quantities equivalent to 230 mg/kg of glutamine daily, prevented the increased intestinal permeability and atrophic changes in the intestinal mucosa associated with unsupplemented solutions. Supplementation of total parenteral nutrition with α-ketoglutarate or a dipeptide, ornithine-α-ketoglutarate, reduced muscle protein depletion in one study,[13] suggesting that this may be a more physiological way of providing glutamine. Although recognising that clinical benefit in terms of infectious complications remained to be established, a review[14] of the use of ornithine-α-ketoglutarate stated that supplementation in the elderly improved clinical outcome in chronic malnutrition, by increasing appetite and body-weight gain and improving healing.

1. Sacks GS. Glutamine supplementation in catabolic patients. *Ann Pharmacother* 1999; **33:** 348–54.
2. Kelly D, Wischmeyer PE. Role of -glutamine in critical illness: new insights. *Curr Opin Clin Nutr Metab Care* 2003; **6:** 217–22.
3. Melis GC, *et al*. Glutamine: recent developments in research on the clinical significance of glutamine. *Curr Opin Clin Nutr Metab Care* 2004; **7:** 59–70.
4. Ziegler TR, *et al*. Clinical and metabolic efficacy of glutamine-supplemented parenteral nutrition after bone marrow transplantation: a randomized, double-blind, controlled study. *Ann Intern Med* 1992; **116:** 821–8.
5. Houdijk APJ, *et al*. Randomised trial of glutamine-enriched enteral nutrition on infectious morbidity in patients with multiple trauma. *Lancet* 1998; **352:** 772–6.
6. Griffiths RD, *et al*. Six-month outcome of critically ill patients given glutamine-supplemented parenteral nutrition. *Nutrition* 1997; **13:** 295–302.
7. Goeters C, *et al*. Parenteral L-alanyl-L-glutamine improves 6-month outcome in critically ill patients. *Crit Care Med* 2002; **30:** 2032–7.
8. Powell-Tuck J, *et al*. A double blind, randomised, controlled trial of glutamine supplementation in parenteral nutrition. *Gut* 1999; **45:** 82–8.
9. Novak F, *et al*. Glutamine supplementation in serious illness: a systematic review of the evidence. *Crit Care Med* 2002; **30:** 2022–9.
10. Wernerman J. Glutamine and acute illness. *Crit Care* 2003; **9:** 279–85.
11. Stehle P, *et al*. Effect of parenteral glutamine peptide supplements on muscle glutamine loss and nitrogen balance after major surgery. *Lancet* 1989; **i:** 231–3.
12. van der Hulst RRWJ, *et al*. Glutamine and the preservation of gut integrity. *Lancet* 1993; **334:** 1363–5.
13. Wernerman J, *et al.* α-Ketoglutarate and postoperative muscle catabolism. *Lancet* 1990; **335:** 701–3.
14. Blonde-Cynober F, *et al*. Use of ornithine α-ketoglutarate in clinical nutrition of elderly patients. *Nutrition* 2003; **19:** 73–5.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Dipeptiven; ***Austria:*** Dipeptiven; Neuroglutamin; ***Chile:*** Dipeptiven; ***Cz.:*** Dipeptiven; ***Denm.:*** Dipeptiven; ***Fin.:*** Dipeptiven; Hypochylin; ***Fr.:*** Dipeptiven; ***Ger.:*** Dipeptamin; Glutamin; Gluti-Agil mono; Pepsaletten N; ***Gr.:*** Dipeptiven; ***Hung.:*** Dipeptiven; ***Indon.:*** Dipeptiven; ***Irl.:*** Adamin-G; ***Ital.:*** Dipeptiven; Glutacerebro†; Glutaven; Memoril†; ***Malaysia:*** Dipeptiven; ***Mex.:*** Dipeptiven; ***Neth.:*** Dipeptiven; ***Norw.:*** Dipeptiven; ***Pol.:*** Dipeptiven; ***Port.:*** Cebrotex†; Dipeptiven; ***Rus.:*** Dipeptiven (Дипептивен); ***Spain:*** Dipeptiven; ***Swed.:*** Dipeptiven; Hypochylin; ***Switz.:*** Dipeptiven; ***Thai.:*** Dipeptiven; ***Turk.:*** Dipeptiven; ***UK:*** Dipeptiven.

Multi-ingredient: ***Arg.:*** Normoprost Compuesto; ***Austral.:*** Aspartatol; Bioglan Digestive Zyme; Liv-Detox†; Prozyme†; ***Austria:*** Aslavital; ***Braz.:*** Taludon†; ***Chile:*** Glutacyl Vitaminado; Hexalectol; ***Fr.:*** Phakan†; Vita-Dermacide; YSE Glutamique; ***Ger.:*** Glutarsin E†; Vitasprint B †; ***Hong Kong:*** Dipeptiven; Esafosfina Glutammica; ***Hung.:*** Glutarsin E; ***Indon.:*** Proseval; Stamino; ***Ital.:*** Acutil Fosforo; Briogen†; Esaglut†; Fosfo Plus; Glutamin Fosforo; Memovit B12; Vitasprint Complex†; Vitasprint†; ***Philipp.:*** Glutaphos; Spasmo-Canulase; ***Port.:*** Cebrotex Forte; Espasmo Canulase; Phakan†; Relavit Fosforo; ***Rus.:*** Eltacin (Элтацин); ***S.Afr.:*** Dipeptiven; Lentogesic; Spasmo-Canulase; ***Spain:*** Agudil; Gastroglutal†; Nucleserina; Tebetane Compuesto; ***Switz.:*** Phakolen†; Spasmo-Canulase; Vitasprint Complex; ***Venez.:*** Glutapak; Glutapak-R.

Glycine *(rINN)*

Acidum Aminoaceticum; Aminoacetic Acid; Aminoättiksyra; Aminoetikkahappo; E640 (glycine or glycine sodium); G; Glicin; Glicina; Glicinas; Glicyna; Gly; Glycin; Glycinum; Glycocoll; Glysiini; Sucre de Gélatine.

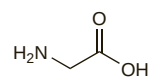
Глицин

$C_2H_5NO_2$ = 75.07.

CAS — 56-40-6.

ATC — B05CX03.

ATC Vet — QB05CX03.



Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Jpn*, and *US.*
Ph. Eur. 6.2 (Glycine). A white or almost white crystalline powder. It exhibits polymorphism. Freely soluble in water; very slightly soluble in alcohol. A 5% solution in water has a pH of 5.9 to 6.4.
USP 31 (Glycine). A white, odourless crystalline powder. Soluble 1 in 4 of water at 25°, 1 in 2.6 at 50°, 1 in 1.9 at 75°, and 1 in 1.5 at 100°; soluble 1 in 1254 of alcohol; very slightly soluble in ether. Its solutions are acid to litmus.

Adverse Effects and Precautions

Systemic absorption of glycine irrigation solutions can lead to disturbances of fluid and electrolyte balance and cardiovascular and pulmonary disorders (see below).

Glycine irrigation should be used cautiously in patients with hepatic impairment since any absorption and consequent metabolism may cause hyperammonaemia. The possible effects on fluid and electrolyte balance warrant cautious use in patients with cardiopulmonary or renal dysfunction; glycine irrigation is contraindicated in anuric patients.

Systemic absorption. Absorption of glycine irrigation solution during surgical procedures can cause disturbances of the circulatory and nervous systems.[1-3] Often seen after transurethral resection of the prostate, these symptoms and signs have been referred to as the transurethral resection syndrome,[1] although they have also been described after other urological or gynaecological surgical procedures.[4,5] Hyponatraemia and glycine toxicity are thought to be responsible for the clinical manifestations.[1,2,5]

Symptoms and signs include chest pains, hypertension, hypotension, bradycardia, anuria, dyspnoea, nausea, vomiting, restlessness, confusion, apprehension, irritability, headache, and seizures.[1,3-5] Chills, diarrhoea, and abdominal pain have also been reported,[1] as have visual disturbances and blindness.[3,6] Myocardial infarction,[7,8] coma, and death may occur.[5,7]

Absorption may occur rapidly, through the intravascular route, or, more rarely, slowly via extravascular absorption.[1,2,4] Extravasation should be suspected when abdominal pain and swelling are apparent.[4,9] Ethanol has been added to the irrigation fluid, and ethanol breath tests performed regularly during procedures in order to detect and monitor absorption.[1,2,4,9] However, the syndrome has still occurred despite monitoring;[9] awareness of the pattern of ethanol changes and clinical symptoms associated with extravascular as well as intravascular absorption are considered essential.[4,9]

1. Olsson J, *et al.* Symptoms of the transurethral resection syndrome using glycine as the irrigant. *J Urol (Baltimore)* 1995; **154:** 123–8.
2. Tauzin-Fin P. Complication des liquides d'irrigation à base de glycocolle: le syndrome de résorption. *Therapie* 2002; **57:** 48–54.
3. Radziwill AJ, *et al.* Visual disturbances and transurethral resection of the prostate: the TURP syndrome. *Eur Neurol* 1997; **38:** 7–9.
4. Hahn RG. Transurethral resection syndrome after transurethral resection of bladder tumours. *Can J Anaesth* 1995; **42:** 69–72.
5. Siddiqui MA, *et al.* Glycine irrigant absorption syndrome following cystoscopy. *Clin Nephrol* 1996; **45:** 365–6.
6. Karci A, Erkin Y. Transient blindness following hysteroscopy. *J Int Med Res* 2003; **31:** 152–5.
7. Byard RW, *et al.* Glycine toxicity and unexpected intra-operative death. *J Forensic Sci* 2001; **46:** 1244–6.
8. Hahn RG, Persson P-G. Acute myocardial infarction after prostatectomy. *Lancet* 1996; **347:** 335.
9. Hahn RG. Life-threatening transurethral resection syndrome despite monitoring of fluid absorption with ethanol. *Eur J Anaesthesiol* 1995; **12:** 431–3.

Uses and Administration

Glycine is a non-essential aliphatic amino acid. It is used as a dietary supplement.

Glycine is sometimes used with antacids in the treatment of gastric hyperacidity. It is also used as an ingredient of some aspirin preparations with the object of reducing gastric irritation.

Sterile solutions of glycine 1.5% in water, which are hypotonic and non-conductive, are used as urogenital irrigation solutions during certain surgical procedures, particularly transurethral resection of the prostate.

Glycine hydrochloride has also been used.

Preparations

BP 2008: Glycine Irrigation Solution;
USP 31: Glycine Irrigation.

Proprietary Preparations (details are given in Part 3)
Fr.: Derm Hydralin; Gyn-Hydralin; ***Hong Kong:*** Gyn-Hydralin; ***Mex.:*** Glisuret†.

Multi-ingredient: ***Arg.:*** Normoprost Compuesto; ***Austral.:*** Cal Alkyline; ***Austria:*** Centramin; ***Braz.:*** B-Vesil; ***Chile:*** Dolotol 12; ***Fr.:*** Cristopal†; Derm'Intim; Item Alphazole; Phakan†; Pruriced; ***India:*** Cotaryl; ***Ital.:*** Detoxicon; Digestivo Antonetto; ***Mex.:*** Segel†; ***Port.:*** Phakan†; ***Rus.:*** Eltacin (Элтацин); ***Spain:*** Sanieb†; Tebetane Compuesto; ***Switz.:*** DAM Antacidum; Phakolen†.

Used as an adjunct in: ***Austral.:*** Cardiprin; Disprin Direct; ***Cz.:*** Godasal; ***Ger.:*** Godamed; Praecineural; ***Hong Kong:*** Cardiprin; Glyprin; ***Indon.:*** Contrexyn; Inzana; Minigrip; ***Israel:*** Lysoprin†; ***Ital.:*** Aspiglicina; Geyfritz†; ***Malaysia:*** Cardiprin; Glyprin; ***NZ:*** Cardiprin†; ***Pol.:*** Alka-Prim; Asprocol; ***Singapore:*** Cardiprin; Glyprin; ***Thai.:*** Caparin; Cardiprin.

Halibut-liver Oil

Aceite de hígado de fletán; Aceite de Higado de Hipogloso; Heilbuttleberöl; Ol. Hippogloss.; Oleum Hippoglossi; Oleum Jecoris Hippoglossi.

Палтусовый Печёночный Жир

CAS — 8001-46-5.

Pharmacopoeias. In *Br.*
BP 2008 (Halibut-liver Oil). The fixed oil extracted from the fresh or suitably preserved liver of the halibut species belonging to the genus *Hippoglossus*. It contains not less than 30 000 units of vitamin A activity per g. Wt per mL 0.915 to 0.925 g. A pale to golden yellow liquid with a fishy, but not rancid, odour and taste. Practically insoluble in alcohol; miscible with chloroform, with ether and with petroleum spirit. Store in well-filled containers. Protect from light.

Profile

Halibut-liver oil is used as a means of giving vitamins A (p.1971) and D (p.1986); the proportion of vitamin A to vitamin D is usually greater in halibut-liver oil than in cod-liver oil (p.1935). It is usually given in capsules.

Preparations

BP 2008: Halibut-liver Oil Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: Pancutan Base; ***Canad.:*** Nutrol A; ***Switz.:*** Halibut.

Multi-ingredient: ***Arg.:*** Eryteal; Klorane Bebe Eryteal; Pancutan; ***Austria:*** Nuri-Kapseln; Vitawund; ***Chile:*** Hipoglos; Mintaglos; Nistaglos; ***Fr.:*** Eryteal†; Preparation H; ***Port.:*** Halibut; ***Switz.:*** A Vogel Capsules polyvitamineses†.

Hetaflur *(BAN, USAN, rINN)*

Cetylamine Hydrofluoride; GA-242; Hétaflur; Hetaflurum; SKF-2208. Hexadecylamine hydrofluoride.

Гетафлур

$C_{16}H_{35}N,HF$ = 261.5.
CAS — 3151-59-5.

Profile

Hetaflur is used as a source of fluoride (see Sodium Fluoride, p.1962) in the prevention of dental caries.

Preparations

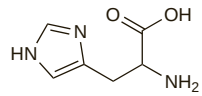
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Israel:*** Elmex†.

Histidine *(USAN, rINN)*

H; His; Histidiini; Histidin; Histidina; Histidinas; L-Histidine; Histidinum; Hisztidin; NSC-137773. L-2-Amino-3-(1*H*-imidazol-4-yl)propionic acid.

Гистидин

$C_6H_9N_3O_2$ = 155.2.
CAS — 71-00-1.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.
Ph. Eur. 6.2 (Histidine). Colourless crystals or a white or almost white crystalline powder. Soluble in water; very slightly soluble in alcohol. Protect from light.
USP 31 (Histidine). White, odourless crystals. Soluble in water; very slightly soluble in alcohol; insoluble in ether. pH of a 2% solution in water is between 7.0 and 8.5.

Histidine Hydrochloride

Histidiinihydrokloridimonohydraatti; Histidina, hidrocloruro; Histidine (chlorhydrate d') monohydraté; Histidine Monohydrochloride; Histidin-hydrochlorid monohydrát; Histidinhydrokloridmonohydrat; Histidini hydrochloridum monohydricum; Histidinium Chloride; Histidino hidrochloridas monohidratas; Histydyny monochlorowodorek; Hisztidin-hidroklorid-monohidrát. L-Histidine hydrochloride monohydrate.

$C_6H_9N_3O_2,HCl,H_2O$ = 209.6.
CAS — 645-35-2 (anhydrous histidine hydrochloride).

Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii).
Ph. Eur. 6.2 (Histidine Hydrochloride Monohydrate). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; slightly soluble in alcohol. A 5% solution in water has a pH of 3.0 to 5.0. Protect from light.

Profile

Histidine is a basic amino acid that is essential for infant growth and which may be essential for some other groups, such as patients with uraemia. Histidine and histidine hydrochloride are used as dietary supplements.

Honey

Clarified Honey; Gereinigter Honig; Honung; Hunaja; Madu; Med; Medus; Mel; Mel Depuratum; Mel Despumatum; Miel; Miel Blanc; Miel purificada; Purified Honey; Strained Honey.

Мёд

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn*. Also in *USNF*.
Ph. Eur. 6.2 (Honey; Mel). It is produced by bees (*Apis mellifera*) from the nectar of plants or from secretions of living parts of plants, which the bees collect, transform by combining with specific substances of their own, deposit, dehydrate, store, and leave in the honey comb to ripen and mature. If the bee has been exposed to treatment to prevent or cure diseases or to any substance intended for preventing, destroying, or controlling any pest, unwanted species of plants or animals, appropriate steps are taken to ensure that the levels of residues are as low as possible. It is an almost white to dark brown, viscous liquid which may be partly crystalline.
USNF 26 (Purified Honey). It is obtained by purification of honey from the comb of the bee, *A. mellifera* and all subspecies of *A. mellifera*. The honey is extracted by centrifugation, pressure, or other suitable procedures. Specific gravity 1.400 and 1.435 at 20°. Store in airtight containers. It is not intended for infants under one year of age unless it is free from *Clostridium* spp.

Profile

Honey, which contains about 70 to 80% of glucose and fructose, is used as a demulcent and sweetening agent, especially in linctuses and cough mixtures (p.1547). Preparations containing honey are used in the management of skin ulcers, wounds, and burns.

Contamination. Honey has been identified as a source of *Clostridium botulinum* spores and thus recommendations have been made that honey should not be given to infants under 1 year because of the risk of causing infant botulism.[1,2]

Honey produced from certain species of *Rhododendron* plants has been found to contain grayanotoxins. Grayanotoxin I is responsible for honey poisoning, manifest as bradycardia, cardiac arrhythmias, hypotension, gastrointestinal disturbances, dizziness, loss of consciousness, blurred vision, chills, cyanosis, sweating, and salivation.[3,4] Convulsions have also been reported.[4]

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2. Tanzi MG, Gabay MP. Association between honey consumption and infant botulism. *Pharmacotherapy* 2002; **22:** 1479–83.
3. Özhan H, *et al.* Cardiac emergencies caused by honey ingestion; a single centre experience. *Emerg Med J* 2004; **21:** 742–4.
4. Dilber E, *et al.* A case of mad honey poisoning presenting with convulsion: intoxication instead of alternative therapy. *Turk J Med Sci* 2002; **32:** 361–2.

Wounds. Anecdotal reports and traditional usage dating back to ancient Egypt suggest that honey may be of some value as a wound dressing (p.1585). Its antibacterial properties are attributed both to high osmolality and the liberation of hydrogen peroxide, but may vary with the source:[1-4] in Europe, some of the best activity has been seen with lime-flower honey.[2] Sterilised manuka honey (p.2337) was reported to heal a leg ulcer infected with meticillin-resistant *Staphylococcus aureus*,[5] although a randomised open-label study found no evidence that dressings impregnated with manuka honey improved the healing of venous leg ulcers at 12 weeks compared with usual care.[6] In a preliminary study, honey obtained from the tea plant (see Xanthine-containing Beverages, p.2415) significantly reduced the incidence of grade 3 and 4 radiation-induced oral mucositis.[7]

A group from India[8] has reported that the properties of honey offer a potentially simple and cheap means of preserving skin grafts in developing countries, with 100% uptake of reconstituted grafts stored for up to 6 weeks and 80% uptake of those stored for 7 to 12 weeks. In comparison with sulfadiazine silver, occlusive honey dressings were also found to be more effective for the treatment of superficial partial thickness thermal burns.[9]

However, concern has been expressed since honey may contain not only chemical contaminants but clostridial spores (see also above), and it has been suggested[2] that to be medically acceptable, honey must be sterile, residue-free, and of measured antibacterial activity.

Sugar has been used similarly to honey in treating wounds (see p.1970).

1. Greenwood D. Honey for superficial wounds and ulcers. *Lancet* 1993; **341:** 90–1.
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4. Booth S. Are honey and sugar paste alternatives to topical antiseptics? *J Wound Care* 2004; **13:** 31–3.
5. Natarajan S, *et al.* Healing of an MRSA-colonized, hydroxyurea-induced leg ulcer with honey. *J Dermatol Treat* 2001; **12:** 33–6.
6. Jull A, *et al.* Honey as Adjuvant Leg Ulcer Therapy trial collaborators. Randomized clinical trial of honey-impregnated dressings for venous leg ulcers. *Br J Surg* 2008; **95:** 175–82.
7. Biswal BM, *et al.* Topical application of honey in the management of radiation mucositis: a preliminary study. *Support Care Cancer* 2003; **11:** 242–8.
8. Subrahmanyam M. Storage of skin grafts in honey. *Lancet* 1993; **341:** 63–4.
9. Subrahmanyam M. A prospective randomised clinical and histological study of superficial burn wound healing with honey and silver sulfadiazine. *Burns* 1998; **24:** 157–61.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Antibacterial Honey Barrier; ***Ital.:*** Oramil; ***Neth.:*** Melrosum; ***UK:*** Medihoney Antibacterial Wound Gel; Mesitran.

Multi-ingredient: ***Arg.:*** Expectosan Hierbas y Miel; ***Austral.:*** Logicin Natural Lozenges†; ***Braz.:*** Calmatoss†; Elixir de Inhamet†; Expectomel; Melagriao; Melxi†; Peitoral Martel†; ***Canad.:*** Mielocol; ***Chile:*** Fray Ro-