appearance of neurological symptoms is currently being studied with some encouraging results.7 There is some evidence to suggest that the childhood form may have an immunological component, but results using immunosuppressants or immunoglobu-lins have been reported to be disappointing.⁵ Bone marrow transplants may improve symptoms but should only be tried in those with mild cerebral involvement.1 Lovastatin can also reduce plasma concentrations of very-long-chain fatty acids.8

- 1. van Geel BM, et al. X linked adrenoleukodystrophy: clinical presentation, diagnosis, and therapy. J Neurol Neurosurg Psychiatry 1997; 63: 4–14.
- Moser HW, et al. Adrenoleukodystrophy: new approaches to a neurodegenerative disease. JAMA 2005; 294: 3131–4.
- 3. Aubourg P, et al. A two-year trial of oleic and erucic acids ("Lorenzo's oil") as treatment for adrenomyeloneuropathy. N Engl J Med 1993; **329:** 745–52.
- 4. Kaplan PW, et al. Visual evoked potentials in adrenoleukodystrophy: a trial with glycerol trioleate and Lorenzo oil. *Ann Neu-*rol 1993: **34:** 169–74.
- 5. Rizzo WB. Lorenzo's oil—hope and disappointment. N Engl JMed 1993; 329: 801-2.
- van geel BM, et al. Progression of abnormalities in adrenomy-eloneuropathy and neurologically asymptomatic X-linked adre-noleukodystrophy despite treatment with "Lorenzo's oil". J Neurol Neurosurg Psychiatry 1999; 67: 290-9.
- Moser HW, et al. Follow-up of 89 asymptomatic patients with adrenoleukodystrophy treated with Lorenzo's oil. Arch Neurol 2005; 62: 1073–80.
- 8. Pai GS, et al. Lovastatin therapy for X-linked adrenoleukodystrophy: clinical and biochemical observations on 12 patients. Mol Genet Metab 2000; 69: 312–22.

Adverse effects. Thrombocytopenia has been reported in patients receiving Lorenzo's oil, although patients are often asymptomatic.1 It is possible that giant platelets which retain most of their function are produced and that these are not counted by automatic counting procedures giving a false impression of thrombocytopenia.2

Lymphocytopenia with an increased incidence of infection has also been reported in few patients.3

- 1. Zinkham WH, et al. Lorenzo's oil and thrombocytopenia in patients with adrenoleukodystrophy. N Engl J Med 1993; 328:
- Stöckler S, et al. Giant platelets in erucic acid therapy for adre-noleukodystrophy. Lancet 1993; 341: 1414–15.
- Unkrig CJ, et al. Lorenzo's oil and lymphocytopenia. N Engl J Med 1994; 330: 577.

Preparations

Proprietary Preparations (details are given in Part 3) Ital.: GTO Oil

Lovage Root

Gelsvių šaknys; Korzeń lubczyka; Lestyángyökér; Levistici radix; Levístico; Libečkový kořen; Libstickerot; Liebstöckelwurzel; Liperinjuuri; Livèche (racine de); Livèche, racine de.

Pharmacopoeias. In Eur. (see p.vii).

Ph. Eur. 6.2 (Lovage Root). The whole or cut, dried rhizome and root of Levisticum officinale. The whole drug contains not less than 0.4% v/w of essential oil and the cut drug not less than 0.3% v/w of essential oil, calculated with reference to the dried drug. Protect from light.

Profile

Lovage root is used in herbal medicine for gastrointestinal and urinary-tract disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: Austria: Ehrenhofer-Salbe; Cz.: Zaludecni Cajova Smes; **Ger.:** Canephron; Nephroselect M; Presselin Nieren-Blasen K 3†, **Rus.:** Canephron N (Канефрон Н); **Switz.:** Tisane pour les reins et la ves-

Luprostiol (BAN, rINN)

Luprostioli; Luprostiolum. $(\pm)-(Z)-7-\{(1S,2R,3R,5S)-2-[(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(3-(2S)-2)-(2S)-3-(2S)-2-(2S)-3-(2S)-3-(2S)-3-(2S)-3-(2S)-3-(2S)-3-(2S)-3-(2S)-3-(2S)-3-$ Chlorophenoxy)-2-hydroxypropylthio]-3,5-dihydroxycyclopentyl}hept-5-enoic acid.

Лупростиол

 $C_{21}H_{29}CIO_6S = 445.0.$ CAS - 67110-79-6.

ATC Vet - QG02AD91.

Luprostiol is a synthetic analogue of dinoprost (prostaglandin F2). It is used as a luteolytic in veterinary medicine.

Lupulus

Apyniu spurgai; Chmelová šištice; Hop Strobile; Hopfenzapfen; Hops: Houblon: Houblon, cône de: Humalankukka: Humlekotte: Humulus; Komlótoboz; Lupuli flos; Lupuli Strobulus; Lúpulo; Strobili Lupuli: Szyszka chmielu.

Pharmacopoeias. In Eur. (see p.vii).

Ph. Eur. 6.2 (Hop Strobile). The dried, generally whole, female inflorescences (strobiles) of the hop plant Humulus lupulus. It has a characteristic aromatic odour. Protect from light.

Lupulus has been used as a bitter, and supplies the characteristic flavour of beers. It is used in herbal and folk medicine as a seda-

Homoeopathy. Lupulus has been used in homoeopathic medicines under the following names: Humulus lupulus; Lupulinum; Humulus lupulus e glandulis; Lupul.

Preparations

Proprietary Preparations (details are given in Part 3)

Ger.: Lactidorm†; Rus.: Novo-Passit (Ново-Пассит); Switz.: Klosterfrau

Multi-ingredient: Arg.: Calmtabs†; Austral.: Extralife Sleep-Care; Humulus Compound; Natural Deep Sleep; Pacifenity†; Passifora Complex†; Passionflower Plus; Prosed-X†; ReDormin; Relaxaplex†; Austria: Baldracin; Baldrian ArlA; Hova; Montana; Nervenruh; Nerventee St Severin; Sedadom; Wechseltee St Severin; Braz.: Remilev; Canad.: Herbal Nerve; Herbal Sleep Well†; Relax and Sleep; Chille: Valupas; Cz.: Baldracin; Detsky Caj s Hermankem; Fytokliman Planta; Hova; Klosterfrau Beruhigungs Forte†; Nov-Passit; Sanason; Schlaf-Nerventee Nf.; Species Nervinae Planta; Valofyt Neo; Visinal†; Fr.: Nostress; Notabac; Ger: Alluna Nacht; Ardevsedon Awedom dur Baldrian-Dispert Nacht; Baldrian-Pan Nathd. Forter; Novo-rassir; Sanason; Scriai-Nerventee N;; Species Nervinae Planta; Valotý Neo; Visinal; Fir. Nostres; Notabac; Ger.: Alluna Nacht; Ardeysedon; Avedorm duo; Baldrian-Dispert Nacht; Baldriparan N Stark; Biosedon†; Boxocalm; Cefasedativ†; Dormeasan; Dormoverlan; Gutnacht†; Hicoton†; Ilja Rogoff; JuDorm†; Kneipp Gute Nacht; Kytta-Sedativum; Leukona-Beruhigungsbad†; Lomasleep†; Luvased; Moradorm S; Nervendragees†; Nervenkapseln; Nervinfant N†; Nervoregin forte†; Nervoregin phyto; Pascosedon; Phytogran†; Presselin Nerven K I N†; Schlaf- und Nerventee; Seda-Plantina†; Sedacur; Sedaselect D; Sedasyk†, Selon; Sensinerv forte†; Somnuvis S†; Stomasal Med†; Valdispert comp†; Valenana mild†; Valverde Baldrian Hopfen bei Einschlafstorungen und zur Beruhigung†; Vivinox Day, Hung.; Hova; ReDormin; Sedacur; Israel; Nerven-Dragees; Ital.: Calmason; Ermenoias; Melissa (Specie Composta)†; Nex.: Nei; Nervinetas; Pol.: Calmina; Hova; Kalms; Klimax†; Lekosen; Lumewal; Nervendragees; Nervinolum; Nervonix; Nervosoi; Nervobonisoi; Passispasmin; Passispasmoi; Sedomis; Tablekti Uspokajiajace; Vallup; Vallused; Rus.: Doppelherz Vitlaotonik (Доплемгерц Виталотоник); Passifit (Пассифит); Sanason (Санасон); SAfr.: Avena Sativa Comp; Switz.: Baldriparan; Dicalm†; Dormeasan; Dragees pour le coeur et les nerfs; Dragees pour le sommeli; Dragees sedatives 5.Afr.: Avena sativa Comp.; Witz.: Baldnparan; Dicamr; Domeasan; Drages pour le sommeli: Dragees sedatives
Dr Welti; Hova; Hyperiforce comp; Nervinetten; Phytomed Nervo†; Phytomed Somni†; ReDomin; Relaxo; Soporin; Tisane calmante pour les enfants; Tisane pour le sommeil et les nerfs; Valverde Coeur; Valverde Sommeil; Zeller Sommeil; WK: Anased; Avena Sativa Comp; Gerard House Serenity; Gerard House Somnus; HRI Calm Life; HRI Night; Kalms; Kalms; Calms; Calmarden Newerbard North Calmarden Newerbard North Country (victor) Sleep; Ńatrasleep; Newrelax; Nodoff; Nytol Herbal; Quiet Days; Quiet Life; Quiet Nite: Quiet Tyme: Relax B : Slumber: Sominex Herbal: Stressless: Quiet Nite; Quiet Tyme; Relax B ; Slumber; Sominex Herbal; Stressless; Unwind Herbal Nytol; Valerina Night-Time; Ymea; **Venez.:** Insocaps; Lupassin; Nervinetas.

Lycopene

F160(d).

CAS - 502-65-8.

Pharmacopoeias. In US which also includes Tomato Extract Containing Lycopene.

USP 31 (Lycopene). A mixture of geometrical isomers of lycopene. Store in airtight containers under an inert gas at a temperature of 8° to 15°. Protect from light.

Profile

Lycopene is a carotenoid responsible for the red colour of tomatoes and some other fruits including rose fruit (p.2381). It is used as a colouring agent and antoxidant. Much interest has been expressed in the antoxidant properties of lycopene for the potential prevention of diseases such as cardiovascular disease and some cancers, particularly of the prostate gland. Lycopene is also an ingredient of some skin preparations.

♦ References.

 Everson KM, McQueen CE. Lycopene for prevention and treatment of prostate cancer. Am J Health-Syst Pharm 2004; 61: 1562-6

Preparations

Proprietary Preparations (details are given in Part 3) Arg.: Licopenox.

Multi-ingredient: Arg.: Natubrown; Braz.: Licovit; Fr.: Phytolongbronze; Phytosolaire; Hong Kong: Palmetto Plus†; India: Lycored; Indon.: Legres; Legreskin; Lycoc; Optimax; Stacare; Philipp.: Nutrotal; Singapore: Palmetto Plus

Lysergide (BAN, rINN)

Lisergida; Lisérgido; LSD; LSD-25; Lysergic Acid Diethylamide; Lysergidum. (+)-NN-Diethyl-D-lysergamide; (6aR,9R)-NN-Diethyl-4,6,6a,7,8,9-hexahydro-7-methylindolo[4,3-fg]quinoline-9carboxamide.

Лизергид $C_{20}H_{25}N_3O = 323.4.$ CAS — 50-37-3.

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of lysergide: 25; 25s; 100s; A; Acid; Acid tabs; Acido; Aeon flux; Alice; Al-

phabet; Angel tears; Angry paper; Animal; Barrels; Bart Simpson; Battery acid; Beast; Beavis & Butthead; Bells; Bevis & Butthead; Big D; Big daddy; Bird head; Birdhead; Black acid; Black star; Black sunshine; Black tabs; Blackbird; Blaze; Blotter; Blotter acid; Blotter cube; Blotters; Blue acid; Blue barrels; Blue chairs; Blue cheers; Blue fly; Blue heaven; Blue heavens; Blue microdot; Blue mist; Blue moons; Blue star; Blue tabs; Blue vials; Boomers; Brown bombers; Brown dots; Buvard; Cal-Blue vials; Boomers; Brown bombers; Brown dots; Buvard; Cai-ffornia sunshine; Cap; Caps; Casper the ghost; Caviar; Cheap basing; Cheers; Chief; Chinese dragons; Cid-drip the entertainer; Chocolate chips; Church; Cid; Class; Coffee; Colors; Comic book; Conductor; Contact lens; Crackers; Crystal; Crystal tea; Cube; Cupcakes; D; Deeda; Dental floss; Diablo; Dinosaurs; Domes; Dose; Doses; Dosure; Dots; Double dome; Dragon; DSL; El Cid; Electric Kool Aid; Ellis Day; Elvis; Eye Candy; Felix; Felix the Cat; Fields; Flash; Flashers; Flat blues; Flats; Flying triangle; Frogs; Fry; Gel; Gel caps; Gelatine squares; Geltab; Ghost; God's flesh; Golden dragon; Golf balls; Goofy's; Gooney birds; Grape parfait; Green double domes; Green single dome; Green single domes; Green wedge; Grey shields; Groovy lemon; Hats; Hawaiian sunshine; Hawk; Haze; Head light; Head lights; Headlights; Heaven; Heavenly; Heavenly blue; Illusions; Infinity; Instant zen; Jesus Christ acid; Kaliedescope; Keys to the kingdom; L; LAD; Lake Shore Drive; Laogor; Lason daga; Lason sa daga; Lavender; LBJ; Leary's; Lenos; Lens; Lids; Lime acid; Little smoke; Live, Spit and Die; Logor; Loony Toons; LSD; LSD-25; Lucy; Lucy in the sky with diamonds; Magic Tickets; Mellow yellow; Mickey's; Microdot; Microdots; Midnight Quinn; Mighty Quinn; Mikes; Mind blow; Mind detergent; Mist; Mister Natural; Monstre rouge; Monstre vert; Monterey Purple; Moons; Mother of God; Newspapers; One way; Oneway; Optical illusions; Orange ba; Orange barrels; Orange cubes; Orange haze; Orange micro; Orange sunshine; Orange wedges; Owsley; Owsley's acid; Owsley's blue dot; Ozzie's stuff; Pane; Paper; Paper acid; Peace; Peace tablets; Peaks; Pearly gates; Pellets; Pepa; Phoenix; Pills; Pink blotters; Pink panther; Pink robots; Pink wedge; Pink wedges; Pink witche; Pink witches; Pizza; Potato; Pure love; Purple barrels; Purple dome; Purple dots; Purple flats; Purple gel tabs; Purple haze; Purple hearts; Purple mikes; Purple ozoline; Purple wedge; Pyramid; Pyramids; Rain Drops; Rainbow; Recycle; Red lips; Rips; Royal blues; Roz-rox; Russian sickles; Sacrament; Sandoz; Serenity; Sheets; Shields; Sherman; Sid; Smears; Smiley; Snowmen; South parks; Specks; Square dancing tickets; Squirrel; Stamp; Stanley's stuff; Star; Strawberries; Strawberry; Strawberry fields; Sugar, Sugar cubes; Sugar lumps; Sunrise; Sunshine; Sunshine Acid; Superman; Syd; T; Tab; Tabs; Tail lights; Teddy bears; The Ghost; The Hawk; Ticket; Tickets; Ticket to ride; Timothy Leary; Timothy Leary Ticket; Trip; Trippers; Trips; Twenty-five; Uncle Sid; Uncle Sidney; Valley dolls; Vodka acid; Volcano 5; Vulcoes; Wafer; Waffles; Watercolors; Wedding bells; Wedge; Wedges; White dust; White lightning; White Owsley's; Window glass; Window pane; Woodstock; Yellow; Yellow dimples; Yellow sunshine; Yellows; Ying Yang; Zen; Zig Zag

Profile

Lysergide was formerly used therapeutically but is now encountered as a drug of abuse for its hallucinogenic and psychedelic properties

There is considerable variation in individual reaction to lysergide. Disorders of visual perception are among the first and most constant reactions to lysergide. Subjects may be hypersensitive to sound. Extreme alterations of mood, depression, distortion of body image, depersonalisation, disorders of thought and time sense, and synaesthesia may be experienced. Anxiety, often amounting to panic, may occur (a 'bad trip'). Duration of effects may last for up to 12 hours after ingestion, although hallucinations can sometimes last up to 48 hours and psychoses for up to 4 days. The effects of lysergide may recur months after ingestion

of lysergide; the recurrence or 'flashback' may be spontaneous or induced by alcohol, other drugs, stress, or fatigue.

The subjective effects of lysergide may be preceded or accompanied by somatic effects that are mainly sympathomimetic in nature and include mydriasis, tremor, hyperreflexia, hyperthermia, piloerection, muscle weakness, and ataxia. There may be nausea and vomiting and increased heart rate and blood pressure. Derangement of blood clotting mechanisms has been described. In addition, respiratory arrest, convulsions, and coma may result from overdoses. There is no evidence of fatal reactions to lysergide in man, although accidental deaths, suicides, and homicides have occurred during lysergide intoxication.

Tolerance develops to the behavioural effects of lysergide after several days and may be lost over a similar period. There is crosstolerance between lysergide, mescaline, and psilocybine and psilocin, but not to amfetamine or to cannabis.

Physical dependence on lysergide does not seem to occur.

Mace Oil

Macis, aceite de.

NOTE. Mace has also been used as a name for solutions of chloroacetophenone (p.2280), a tear gas.

Profile

Mace oil is a volatile oil obtained by distillation from mace, the arillus of the seed of Myristica fragrans (Myristicaceae).

Nutmeg (p.2355) is the dried kernel of the seed of M. fragrans. Mace is used as a flavour and carminative similarly to nutmeg. It has also been used with herbal substances and other volatile agents in preparations for musculoskeletal and respiratory-tract disorders. As with nutmeg, large doses of mace may cause epileptiform convulsions and hallucinations.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: Austria: China-Eisenwein; Cz.: Dr Theiss Schweden bitter; Original Schwedenbitter; Rus.: Himcolin (Химколин).

Macrogols

Macrogola; Macrogoles; Macrogoller; Makrogoler; Makrogoliai; Makrogolit; Makrogolok; Makrogoly; PEGs; Polietilen Glikoller; Polyethylene Glycols; Polyoxyethylene Glycols.

CH₂(OH)(CH₂OCH₂)_mCH₂OH. Alternatively some authorities use the general formula $H(OCH_2CH_2)_nOH$ when the number assigned to n for a specified macrogol is I more than that of m in the first formula.

CAS — 25322-68-3 (macrogols); 37361-15-2 (macrogol 300).

ATC - A06AD15. ATC Vet - QA06AD15.

Nomenclature. Macrogol is BAN and rINN. The name is followed by a figure which corresponds approximately to its average molecular weight.

Pharmacopoeias. Macrogols of various molecular weights are included in many pharmacopoeias.

Eur. (see p.vii) has a general monograph describing macrogol 300, 400, 600, 1000, 1500, 3000, 3350, 4000, 6000, 8000. 20 000, and 35 000. USNF has a general monograph describing Polyethylene Glycol which requires that it be labelled with the average nominal molecular weight as part of the official title.

Ph. Eur. 6.2 (Macrogols). Mixtures of polymers with the general formula $H(OCH_2CH_2)_nOH$, where n represents the average number of oxyethylene groups. The type of macrogol is defined by a number that indicates the average relative molecular mass. A suitable stabiliser may be added.

Macrogol 300, 400, and 600 are clear, viscous, colourless or almost colourless, hygroscopic liquids. Miscible with water; very soluble in alcohol, in acetone, and in dichloromethane.

Macrogol 1000 is a white or almost white, hygroscopic solid with a waxy or paraffin-like appearance. Very soluble in water; freely soluble in alcohol and in dichloromethane.

Macrogol 1500 is a white or almost white solid with a waxy or paraffin-like appearance. Very soluble in water and in dichloromethane; freely soluble in alcohol.

Macrogol 3000 and 3350 are white or almost white solids with a waxy or paraffin-like appearance. Very soluble in water and in dichloromethane; very slightly soluble in alcohol.

Macrogol 4000, 6000, and 8000 are white or almost white solids with a waxy or paraffin-like appearance. Very soluble in water and in dichloromethane; practically insoluble in alcohol.

Macrogol 20 000 and 35 000 are white or almost white solids with a waxy or paraffin-like appearance. Very soluble in water; practically insoluble in alcohol; soluble in dichloromethane.

All macrogols are practically insoluble in fatty oils and in mineral oils. All macrogols should be stored in airtight containers.

USNF 26 (Polyethylene Glycol). Addition polymers of ethylene oxide and water, represented by the formula H(OCH₂CH₂)_nOH, in which n represents the average number of oxyethylene groups. They may contain a suitable antoxidant. Each macrogol is usually designated by a number that corresponds approximately to its average molecular weight. As the average molecular weight increases, the water solubility, hygroscopicity, and solubility in organic solvents decrease, while the viscosity increases

Liquid grades occur as clear to slightly hazy, colourless or practically colourless, slightly hygroscopic, viscous liquids, having a slight, characteristic odour. Solid grades occur as practically odourless, white, waxy, plastic material having a consistency similar to beeswax, or as creamy-white flakes, beads, or powders. Liquid grades are miscible with water; solid grades are freely soluble in water; all grades are soluble in alcohol, in acetone, in chloroform, in ethoxyethanol, in ethyl acetate, and in toluene; all grades are insoluble in ether and in hexane. The pH of a 5% solution of a macrogol in water is between 4.5 and 7.5. Store in airtight containers.

Incompatibility. Macrogols can demonstrate oxidising activity leading to incompatibilities. The activity of bacitracin or benzylpenicillin may be reduced in a macrogol base. Some plastics are softened by macrogols.

Adverse Effects and Precautions

Macrogols appear to have relatively low toxicity, although any toxicity appears to be greatest with the macrogols of low molecular weight. They may cause stinging when used topically, especially on mucous membranes, and have been associated with hypersensitivity reactions such as urticaria. Hyperosmolality, metabolic acidosis, and renal failure have been reported after topical application of macrogols to burn patients. Topical preparations with a macrogol base should therefore be used with caution in patients with renal impairment and/or large areas of raw surfaces, burns, or open wounds.

Patients undergoing bowel cleansing with mixtures of macrogols (3350 or 4000) and electrolytes commonly experience local gastrointestinal discomfort, bloating, and nausea. Abdominal cramps, vomiting, and anal irritation may also occur and there have been rare reports of possible hypersensitivity reactions. These colonic layage solutions are contra-indicated in gastrointestinal obstruction or perforation, ileus, gastric retention, peptic ulcer disease, and toxic megacolon; caution is advisable in patients with ulcerative colitis. Since aspiration may be a problem, they should be used with caution in patients with an impaired gag reflex, reflux oesophagitis, or diminished levels of consciousness. They should be given with caution to diabetic patients. Drugs taken within one hour of starting colonic lavage with an oral macrogol and electrolyte mixture may be flushed from the gastrointestinal tract unabsorbed.

Effects on fluid and electrolyte homoeostasis. A syndrome of elevated total serum calcium (with a concomitant decrease in ionised calcium), hyperosmolality, metabolic acidosis, and renal failure has been observed in animals1 and in burn patients² after the topical application of preparations with a macrogol base. The FDA has recommended that topical preparations containing macrogols should be used with caution in burn patients with known or suspected renal impairment, as macrogols absorbed through denuded skin and not excreted normally by a compromised kidney could lead to symptoms of progressive renal impairment.3

The use of macrogol and electrolyte solutions for bowel preparation has also been associated with sodium and water retention, resulting in exacerbation of heart failure in a patient with diabetic gastroparesis,4 and with the development of pulmonary oedema possibly due to aspiration in a child without cardiac or renal dis-

- 1. Herold DA, et al. Toxicity of topical polyethylene glycol. Toxi-
- col Appl Pharmacol 1982; **65**: 329–35.

 2. Bruns DE, et al. Polyethylene glycol intoxication in burn patients. Burns 1982; 9: 49-52.
- 3. Anonymous. Topical PEG in burn ointments. FDA Drug Bull 1982; **12:** 25–6.

 4. Granberry MC, *et al.* Exacerbation of congestive heart failure
- after administration of polyethylene glycol-electrolyte lavage solution. *Ann Pharmacother* 1995; **29:** 1232–5.
- Paap CM, Ehrlich R. Acute pulmonary edema after polyethylene glycol intestinal lavage in a child. *Ann Pharmacother* 1993; 27: 1044–7.

Effects on the kidneys. Macrogol 400, which was present in a lorazepam injection, could have contributed to renal damage suggestive of acute tubular necrosis in a patient who received large doses (averaging lorazepam 95 mg daily) for 43 days. 1 The cumulative dose of macrogol 400 during this period was about 220 mL.

1. Laine GA, et al. Polyethylene glycol nephrotoxicity secondary to prolonged high-dose intravenous lorazepam. Ann Pharmacother 1995; 29: 1110-14.

Hypersensitivity. Hypersensitivity to macrogols is uncommon but both immediate urticarial reactions and delayed allergic contact dermatitis have been reported following the topical application of preparations with a macrogol vehicle or base.1 An anaphylactic reaction has been associated with the ingestion of macrogols in a multivitamin tablet.² The manufacturers of preparations containing macrogols and electrolytes for bowel cleansing have reported isolated instances of skin reactions and rhinorrhoea.

- 1. Fisher AA, Immediate and delayed allergic contact reactions to
- polyethylene glycol. Contact Dematitis 1978; 4: 135–8.

 2. Kwee YN, Dolovich J. Anaphylaxis to polyethylene glycol (PEG) in a multivitamin tablet. J Allergy Clin Immunol 1982; 69:

Overdosage. Ingestion of 2 litres of a colonic lavage solution containing macrogol 400 instead of macrogol 4000 resulted in a patient developing severe metabolic acidosis due to systemic absorption of the macrogol and rapidly becoming comatose.1 The patient was successfully treated with intravenous bicarbonate and dialysis.

1. Bélaïche J, et al. Coma acidosique après préparation colique par du polyèthylène glycol. Gastroenterol Clin Biol 1983; **7:** 426–7.

Pharmacokinetics

Liquid macrogols may be absorbed when taken by mouth but macrogols of high molecular weight, such as macrogol 3350, are not significantly absorbed from the gastrointestinal tract. There is evidence of absorption of macrogols when applied to damaged skin. Macrogols entering the systemic circulation are predominantly excreted unchanged in the urine; low-molecular-weight macrogols may be partly metabolised.

◊ References.

 DiPiro JT, et al. Absorption of polyethylene glycol after administration of a PEG-electrolyte lavage solution. Clin Pharm 1986; **5:** 153–5.

Uses and Administration

Macrogols are relatively stable, non-toxic compounds which have a range of properties depending on their molecular weight. They are widely used in pharmaceutical manufacturing as watersoluble bases for topical preparations and suppositories, as solvents and vehicles, and as solubilising agents, tablet binders, plasticisers in film coating, and tablet lubricants. They have also been reported to have antibacterial properties. Macrogols of high molecular weight such as macrogol 4000 have been used as inert markers in studies on intestinal absorption and excretion.

A mixture of macrogol 3350 or 4000 with electrolytes is used for bowel preparation before colonoscopy, radiological procedures, or surgery. These preparations have been formulated so that the osmotic activity of the macrogol and concentrations of the electrolytes result in a minimum net effect on the fluid and electrolyte balance. Reconstituted aqueous solutions of different preparations contain about 59 g or 100 g or 105 g of the macrogol per litre. The method of administration depends on the preparation. Adults are given 200 to 300 mL of the reconstituted aqueous solution, which they have to swallow rapidly, and this is repeated every 10 to 15 minutes until the rectal effluent is clear, or until a total of 3 to 4 litres of the solution has been consumed. Alternatively, 2 litres of reconstituted solution is taken in the evening preceding the clinical procedure, or divided as 1 litre in the evening and 1 litre in the early morning of the day of the procedure. A dose for children is 25 mL/kg per hour. Bowel evacuation usually begins about 1 hour after starting dosage and is complete in about 4 hours. Patients should fast for at least 2 or 3 hours before drinking the solution. Additional flavouring ingredients, sugar, or other sweeteners should not be added to the solution. If distension or pain occur, dosage should be temporarily stopped or the interval between drinks extended. For use by nasogastric tube, a rate of 20 to 30 mL per minute has been used. Similar preparations are used in patients 12 years of age and over for the treatment of chronic constipation in a usual dose of 125 mL of a solution containing 105 g of the macrogol per litre, up to three times daily. The maximum course is 2 weeks, which may be repeated if necessary. For children with chronic constipation, the usual initial daily dose for those aged 2 to 6 years is 62.5 mL, and for those aged 7 to 11 years, 125 mL. Thereafter, the dose should be increased or decreased as necessary to produce regular soft stools; the usual maximum dose is 250 mL dai-

In the management of faecal impaction, 8 doses of 125 mL of solution should be consumed within 6 hours for a maximum of 3 days. Patients with impaired cardiovascular function should take no more than 2 doses in any one hour. Children aged 5 to 11 years may be treated for faecal impaction in an escalating dose until disimpaction occurs up to a maximum of 7 days; the total daily dose should be divided and consumed within a 12-hour period. Four doses of 62.5 mL of solution are given initially on the first day, increasing steadily to a maximum of 12 doses daily on days 5 to 7. Doses for prevention of recurrence of faecal impaction in children are as for children's doses for chronic constipation (see above). The BNFC recommends that children aged 1 to 5 years with faecal impaction may be given two doses of 62.5 mL of solution on the first day, then four doses daily for 2 days, then 6 doses daily for 2 days, and finally 8 doses daily on days 6 and 7. Conjugation of drugs and therapeutic proteins with macrogols (pegylation) has been tried in an attempt to improve their pharmacokinetic profiles and to reduce their adverse effects. Pegylation may also reduce the immunogenicity of therapeutic proteins. Examples of pegylated proteins include pegademase (p.2364), pegaspargase (p.682), and peginterferon alfa (p.888).

Drug delivery systems. References to the use of macrogols in delivery systems for drugs and proteins.

- Reddy KR. Controlled-release, pegylation, liposomal formula-tions: new mechanisms in the delivery of injectable drugs. Ann Pharmacother 2000; **34:** 915–23.

 2. Harris JM, *et al.* Pegylation: a novel process for modifying phar-
- macokinetics. Clin Pharmacokinet 2001; 40: 539-51

Phenol poisoning. Washing with liquid macrogols has been recommended in the emergency treatment of skin contamination with phenol, see p.1656.