Homoeopathy. Chamomile has been used in homoeopathic medicines under the following names: Chamomilla; Cham.

◊ Reviews.

1. Berry M. The chamomiles. *Pharm J* 1995; **254:** 191–3.

Hypersensitivity. References.

1. Van Ketel WG. Allergy to Matricaria chamomilla. *Contact Dermatitis* 1987; **16:** 50–1.
2. McGeorge BC, Steele MC. Allergic contact dermatitis of the nipple from Roman chamomile ointment. *Contact Dermatitis* 1991; **24:** 139–40.
3. Rodriguez-Serna M, *et al.* Allergic and systemic contact dermatitis from Matricaria chamomilla tea. *Contact Dermatitis* 1998; **39:** 192–3.
4. Jensen-Jarolim E, *et al.* Fatal outcome of anaphylaxis to camomile-containing enema during labor: a case study. *J Allergy Clin Immunol* 1998; **102:** 1041–2.
5. Giordano-Labadie F, *et al.* Allergic contact dermatitis from camomile used in phytotherapy. *Contact Dermatitis* 2000; **42:** 247.
6. Foti C, *et al.* Contact urticaria from Matricaria chamomilla. *Contact Dermatitis* 2000; **42:** 360–1.
7. de la Torre Morín F, *et al.* Clinical cross-reactivity between Artemisia vulgaris and Matricaria chamomilla (chamomile). *J Investig Allergol Clin Immunol* 2001; **11:** 118–22.
8. Paulsen E, *et al.* Cosmetics and herbal remedies with Compositae plant extracts — are they tolerated by Compositae-allergic patients? *Contact Dermatitis* 2008; **58:** 15–23.

Preparations

Ph. Eur.: Matricaria Liquid Extract.

Proprietary Preparations (details are given in Part 3)
Austria: Kamillosan; ***Belg.:*** Babygencal; Kamillosan; ***Braz.:*** Ad-Muc; Kamillosan; ***Chile:*** Kamillosan†; ***Cz.:*** APS Balneum†; Hermankovy; Kamillosan; Rumancek Pravy†; ***Fr.:*** Cefamig; ***Ger.:*** Azulon; Chamo S†; Eukamillat†; Galenat Kamill N†; Kamillan supra; Kamille N†; Kamille†; Kamillen-Bad N Ritsert; Kamillen†; Kamillenbad Intradermi; Kamillencreme N†; Kamillenextract†; Kamillin; Kamilloderm†; Kamillopur; Kamillosan; Markalakt†; Matmille; PC 30 N; Soledum med†; ***Hong Kong:*** Camoderm; ***India:*** Kamillosan; ***Indon.:*** Kamillosan; ***Irl.:*** Kamillosan; ***Ital.:*** Ceru Spray; Milla; ***Mex.:*** Balsamo Nordin; Kamillosan; ***NZ:*** Kamillosan†; ***Pol.:*** Azulan; Azuseptol; ***Port.:*** Kamilosan; ***Rus.:*** Romasulan (Ромазулан); ***S.Afr.:*** Ashton & Parsons Infants Powders; ***Singapore:*** Camoderm†; ***Switz.:*** Kamillen-Bad†; Kamillex; Kamillin Medipharm; Kamillofluid; Kamillosan; ***UK:*** Ashton & Parsons Infants Powders; Kamillosan; ***Venez.:*** Kamillen.

Multi-ingredient: numerous preparations are listed in Part 3.

Chaparral

Profile

Chaparral is derived from the creosote bush, *Larrea tridentata* (Zygophyllaceae). It has been included in various herbal preparations but such use has been associated with severe hepatotoxicity. Recommendations that products containing chaparral should not be consumed have been made in several countries.

Masoprocol (p.742) is an antineoplastic isolated from the creosote bush.

Hepatotoxicity. References.

1. Gordon DW, *et al.* Chaparral ingestion: the broadening spectrum of liver injury caused by herbal medications. *JAMA* 1995; **273:** 489–90.
2. Batchelor WB, *et al.* Chaparral-induced hepatic injury. *Am J Gastroenterol* 1995; **90:** 831–3.
3. Sheikh NM, *et al.* Chaparral-associated hepatotoxicity. *Arch Intern Med* 1997; **157:** 913–19.
4. Kauma H, *et al.* Toxic acute hepatitis and hepatic fibrosis after consumption of chaparral tablets. *Scand J Gastroenterol* 2004; **39:** 1168–71.

Preparations

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

Chenodeoxycholic Acid *(BAN, rINN)*

Acide chénodésoxycholique; Ácido quenodeoxicólico; Acidum chenodeoxycholicum; CDCA; Chenic Acid; Chenodeoksicholio rūgštis; Chenodiol *(USAN)*; Kenodeoksikolik Asit; Kenodeoksikoolihappo; Kenodeoxicholsyra; Kenodezoxikólsav; Kyselina chenodeoxycholová. 3α,7α-Dihydroxy-5β-cholan-24-oic acid.

Хенодезоксиколевая Кислота

$C_{24}H_{40}O_4$ = 392.6.
CAS — 474-25-9.
ATC — A05AA01.
ATC Vet — QA05AA01.

Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn.*
Ph. Eur. 6.2 (Chenodeoxycholic Acid). A white or almost white powder. Very slightly soluble in water; freely soluble in alcohol; soluble in acetone; slightly soluble in dichloromethane.

Adverse Effects and Precautions

As for Ursodeoxycholic Acid, p.2408. Diarrhoea may occur more frequently than with ursodeoxycholic acid. A transient rise in liver-function test values and hypercholesterolaemia (low-density lipoprotein) have been reported with chenodeoxycholic acid.

Chenodeoxycholic acid is embryotoxic in some *animals*.

Interactions

As for Ursodeoxycholic Acid, p.2408.

Pharmacokinetics

Chenodeoxycholic acid is absorbed from the gastrointestinal tract and undergoes first-pass metabolism and enterohepatic recycling. It is partly conjugated in the liver before being excreted into the bile and, under the influence of intestinal bacteria, the free and conjugated forms undergo 7α-dehydroxylation to lithocholic acid. Some lithocholic acid is excreted directly in the faeces and the rest absorbed, mainly to be conjugated and sulfated by the liver before excretion in the faeces. Chenodeoxycholic acid also undergoes epimerisation to ursodeoxycholic acid.

◊ References.

1. Crosignani A, *et al.* Clinical pharmacokinetics of therapeutic bile acids. *Clin Pharmacokinet* 1996; **30:** 333–58.

Uses and Administration

Chenodeoxycholic acid is a naturally occurring bile acid (p.2266). When given orally it reduces hepatic synthesis of cholesterol and provides additional bile salts to the pool available for solubilisation of cholesterol and lipids. It has been used for the dissolution of cholesterol-rich gallstones (p.2409) in patients with a functioning gallbladder, in usual doses of about 15 mg/kg daily. The daily dose may be divided unequally and the larger dose given before bedtime to counteract the increase in biliary cholesterol concentrations seen overnight. Treatment may need to be given for up to 2 years, depending on the size of the stone. It should be continued for about 3 months after radiological disappearance of the stones. Chenodeoxycholic acid is also used in reduced doses with ursodeoxycholic acid.

Chenodeoxycholic acid has been used as a dietary supplement in neonates and children with inborn errors of bile acid synthesis: it has been used in the treatment of cerebrotendinous xanthomatosis; with cholesterol in the Smith-Lemli-Opitz syndrome; and with cholic acid for bile acid synthesis defects.

Preparations

Proprietary Preparations (details are given in Part 3)

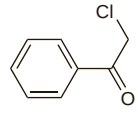
Austria: Chenofalk†; ***Belg.:*** Chenofalk†; ***Ger.:*** Chenofalk; ***Hong Kong:*** Chenofalk†; ***Hung.:*** Chenofalk†; ***Indon.:*** Chenofalk; ***Israel:*** Chenofalk; Soluston†; ***Mex.:*** Chenofalk†; Sulobil; ***Neth.:*** Chenofalk; ***Port.:*** Chebil†; Xeby†; ***Spain:*** Quenobilan; Quenocol†; ***Turk.:*** Chenofalk.

Multi-ingredient: ***Austria:*** Lithofalk†; ***Ger.:*** Lithofalk; Urso Mix†; ***Gr.:*** Lithiofalk†; ***Ital.:*** Bilenor.

Chloroacetophenone

ω-Chloroacetophenone; 1-Chloroacetophenone; Cloroacetofenona; CN; CN Gas; Phenacyl Chloride. 2-Chloroacetophenone.

C_8H_7ClO = 154.6.
CAS — 532-27-4.



NOTE. The name mace is applied to solutions of chloroacetophenone.

Profile

Chloroacetophenone is a lachrymatory which is irritant to the skin and eyes. It has been used in a riot-control gas; it is described as a tear gas.

◊ References.

1. Hu H, *et al.* Tear gas—harassing agent or toxic chemical weapon? *JAMA* 1989; **262:** 660–3.
2. Treudler R, *et al.* Occupational contact dermatitis due to 2-chloracetophenone tear gas. *Br J Dermatol* 1999; **140:** 531–4.
3. Blain PG. Tear gases and irritant incapacitants. 1-chloroacetophenone, 2-chlorobenzylidene malononitrile and dibenz[b,f]-1,4-oxazepine. *Toxicol Rev* 2003; **22:** 103–10.

Chloroplatinic Acid

Cloroplatínico, ácido; Kloroplatinasyra; Kwas chloroplatynowy. Hexachloroplatinic acid hexahydrate.

$H_2PtCl_6,6H_2O$ = 517.9.
CAS — 16941-12-1 (anhydrous chloroplatinic acid); 18497-13-7 (chloroplatinic acid hexahydrate).

Profile

Aqueous solutions of platinic chloride ($PtCl_4$ = 336.9) are used in corneal tattooing solutions.

Chondroitin Sulfate Sodium

Chondroitin 4-Sulfate (chondroitin sulfate A); Chondroitin Sulphate Sodium; Chondroïtine, sulfate sodique de; Chondroitini natrii sulfas; Chondroitin-sulfát sodná sůl; Chondroityny sodu siarczan; CSA (chondroitin sulfate A); Sodium Chondroitin Sulfate; Sodyum Kondroitin Sülfat.

$(C_{14}H_{19}NO_{14}SNa_2)_n$.
CAS — 9007-28-7 (chondroitin sulfate); 9082-07-9 (chondroitin sulfate sodium); 24967-93-9 (chondroitin sulfate A); 39455-18-0 (chondroitin sulfate A sodium); 25322-46-7 (chondroitin sulfate C); 12678-07-8 (chondroitin sulfate C sodium).
ATC — M01AX25.
ATC Vet — QM01AX25.

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Ph. Eur. 6.2 (Chondroitin Sulphate Sodium). A natural copolymer based mainly on the two disaccharides obtained from cartilage of both terrestrial and marine origins. Depending on the animal species of origin, it shows different proportions of 4-sulfate and 6-sulfate groups. A white or almost white, hygroscopic powder. Freely soluble in water; practically insoluble in alcohol and in acetone. A 5% solution in water has a pH of 5.5 to 7.5. Store in airtight containers. Protect from light.
USP 31 (Chondroitin Sulfate Sodium). The sodium salt of the sulfated linear glycosaminoglycan obtained from bovine, porcine, or avian cartilages of healthy and domestic animals used for food by humans. It consists mostly of the sodium salt of the sulfate ester of *N*-acetylchondrosamine (2-acetamido-2-deoxy-β-D-galactopyranose) and D-glucuronic acid copolymer. These hexoses are alternately linked β-1,4 and β-1,3 in the polymer. Chondrosamine moieties in the prevalent glycosaminoglycan are monosulfated primarily on position 4 and less so on position 6. Chondroitin sulfate sodium is extremely hygroscopic once dried. Store in airtight containers.

Profile

Chondroitin sulfate is an acid mucopolysaccharide that is a constituent of most cartilaginous tissues. It is used as the sodium salt, chondroitin sodium sulfate. It is given orally in reactive arthritides (see under Spondyloarthropathies, p.13), such as gonococcal arthritis, and is sometimes given with glucosamine (p.2313) for its supposed chondroprotective action in bone, joint, and connective tissue disorders. It is also used for its visco-elastic properties as an adjunct to ocular surgical procedures, including cataract extraction and intra-ocular lens implantation, and has been used for the relief of dry eye. A medium containing chondroitin sulfate A has been used to preserve corneas for transplantation. Chondroitin sulfate sodium has also been used as a means of replacing the glycosaminoglycan layer in the bladder in the treatment of interstitial cystitis (p.2179). Chondroitin sulfate A and C are components of the heparinoid danaparoid (p.1255).

Osteoarthritis. For references to the use of chondroitin in the treatment of osteoarthritis, including doubts about its value, see under Glucosamine, p.2313.

Preparations

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

Proprietary Preparations (details are given in Part 3)
Arg.: Bioflogil; Condroitina†; Condrosulf†; Dunason; Liquiprin; Lubrictin; Norfisar†; Prof; Structum; ***Austria:*** Condrosulf; ***Belg.:*** Lacrypos; ***Braz.:*** Dunason; ***Canad.:*** Uracyst; ***Chile:*** Condro Sorb†; Condrosulf; ***Cz.:*** Condral; Condrosulf; ***Fr.:*** Chondrosulf; Lacrypos; Structum; ***Ger.:*** Uropol-S; ***Hung.:*** Condrosulf; ***Indon.:*** Viostin S; ***Malaysia:*** Chondril; ***Mex.:*** Condrosulf; Dunason; Maxus; Structum; ***Pol.:*** Condral; Recalcin; ***Port.:*** Condrosulf; Ossin; ***Rus.:*** Chondroitine-Akos (Хондроитин-Акос); Chondrolon (Хондролон)†; Structum (Структум); ***Spain:*** Condro San; Condrodin†; Condrosulf; ***Switz.:*** Condrosulf; Structum.

Multi-ingredient: ***Arg.:*** Artrilase Complex; Artrocaptin; Asotrex; Baliartrin Duo; Cartiflex Forte; Ecosamina; Etinox; Finartrit; Findol Plus; Gluco Arrumalon Duo; Glucotrin VL; Lacrimax; Maxus; Mecanyl Duo; Optilac; Sigmaflex; Vartalon Duo; Viscoat; ***Austral.:*** Duovisc; GenFlex 3; GenFlex Plus; Viscoat; ***Braz.:*** Artrolive; Condroflex; ***Canad.:*** Uracyst Test Kit; ***Chile:*** Artridol Duo; Condrosamina†; Dinaflex Duo; Euroflex; Flexure; Hiperflex; Osteo Bi-Flex; ***Fr.:*** Viscoat; ***Ger.:*** Duovisc; Integra†; Viscoat; ***Hong Kong:*** Arthritil Plus; Duovisc†; Viscoat†; ***Hung.:*** Viscoat†; ***India:*** Cosantin†; Kondro; Osteocip; Osteoflex; ***Indon.:*** Aptivium Optimum Joint Formula; Artriox; Artritin; Bonic; Cartin Plus; Chondro-PA; 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; Reumilase SD; Viscoat; ***Malaysia:*** Duovisc; Viscoat; ***Mex.:*** Actiman; Artiflex; Vartalon Compositum; ***NZ:*** Viscoat; ***Philipp.:*** Flexxbon; Viscoat; ***Rus.:*** Artra (Артра); Chondroitine-Akos (Хондроитин-Акос); Chondroxide (Хондроксид); Theraflex (Терафлекс); ***S.Afr.:*** Duovisc; Viscoat; ***Singapore:*** Artril C; Duovisc; Flexeze†; Glutilage Plus; Seven Seas JointCare; Viscoat; ***Thai.:*** Duovisc; Viscoat; ***Turk.:*** Duovisc; Viscoat; ***UK:*** Flexeze; GlucOsamax; Joint Action; Jointace; ***USA:*** DisCoVisc; Viscoat; ***Venez.:*** Artrosamin; Viscoat†.

Chrome Alum

Chromium Potassium Sulfate; Chromium Potassium Sulphate; Cromo, alumbre de.

$KCr(SO_4)_2,12H_2O$ = 499.4.
CAS — 10141-00-1 (anhydrous chrome alum); 7788-99-0 (chromium potassium sulfate dodecahydrate).

Profile
Chrome alum is used in leather tanning, as a mordant in dyeing, and for hardening gelatin in photographic materials. It has been used as a sclerosant in medicine.

Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Arg.:*** Skleremo†; ***Braz.:*** Varikromo†; ***Fr.:*** Scleremo.

Chromium Trioxide
Anhídrido Crómico; Chromic Acid; Chromic Anhydride; Chromu(VI) tlenek; Cromo, trióxido de.
CrO_3 = 99.99.
CAS — 1333-82-0.

Profile
Chromium trioxide and other chromium compounds are used in industry. Solutions of chromium trioxide are corrosive, acting by oxidation. Repeated contact with chromium and its salts may cause eczematous dermatitis, particularly in hypersensitive persons and can also cause deep perforating ulcers known as 'chrome holes'. If inhaled, chromic dusts cause rhinitis and painless ulcers which may perforate the nasal septum; inhalation may cause severe lung damage and inflammation of the eyes. There may also be involvement of the CNS and there is an increased risk of lung cancer. Hexavalent chromium compounds are more dangerous than di- or trivalent compounds.

Acute symptoms of poisoning from the ingestion of chromium salts include intense thirst, dizziness, abdominal pain with vomiting and diarrhoea, hepatic injury, anuria or oliguria, and peripheral vascular collapse. Kidney damage may lead to fatal uraemia.

Treatment is symptomatic and supportive. Protective measures should be taken when handling or working with chromium and its salts.

Chromium trioxide was formerly used as a caustic and astringent.

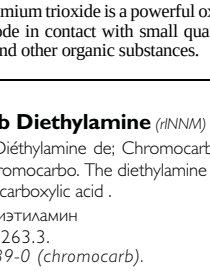
Chromium is an essential trace element as described on p.1934.

Adverse effects. General references[1-4] to chromium toxicity including reports of poisoning with ammonium dichromate,[5] chromium tripicolinate,[6] chromium trioxide,[7] potassium dichromate,[8-10] and sodium dichromate.[11]

1. WHO. Chromium. *Environmental Health Criteria 61*. Geneva: WHO, 1988. Available at: http://www.inchem.org/documents/ehc/ehc/ehc61.htm (accessed 30/07/08)
2. Health and Safety Executive. The toxicity of chromium and inorganic chromium compounds. *Toxicity Review 21*. London: HMSO, 1989.
3. Barceloux DG. Chromium. *J Toxicol Clin Toxicol* 1999; **37:** 173–94.
4. Dayan AD, Paine AJ. Mechanisms of chromium toxicity, carcinogenicity and allergenicity: review of the literature from 1985 to 2000. *Hum Exp Toxicol* 2001; **20:** 439–51.
5. Meert KL, *et al.* Acute ammonium dichromate poisoning. *Ann Emerg Med* 1994; **24:** 748–50.
6. Cerulli J, *et al.* Chromium picolinate toxicity. *Ann Pharmacother* 1998; **32:** 428–31.
7. Matey P, *et al.* Chromic acid burns: early aggressive excision is the best method to prevent systemic toxicity. *J Burn Care Rehabil* 2000; **21:** 241–5.
8. Michie CA, *et al.* Poisoning with a traditional remedy containing potassium dichromate. *Hum Exp Toxicol* 1991; **10:** 129–31.
9. Stift A, *et al.* Liver transplantation for potassium dichromate poisoning. *N Engl J Med* 1998; **338:** 766–7.
10. Kolacinski Z, *et al.* Acute potassium dichromate poisoning: a toxicokinetic case study. *J Toxicol Clin Toxicol* 1999; **37:** 785–91.
11. Ellis EN, *et al.* Effects of hemodialysis and dimercaprol in acute dichromate poisoning. *J Toxicol Clin Toxicol* 1982; **19:** 249–58.

Handling. Chromium trioxide is a powerful oxidising agent and is liable to explode in contact with small quantities of alcohol, ether, glycerol, and other organic substances.

Chromocarb Diethylamine *(rINNM)*
Chromocarbe, Diéthylamine de; Chromocarbi Diethylaminum; Dietilamina de cromocarbo. The diethylamine salt of 4-oxo-4*H*-1-benzopyran-2-carboxylic acid .
Хромокарба Диэтиламин
$C_{14}H_{17}O_4N$ = 263.3.
CAS — 4940-39-0 (chromocarb).



(chromocarb)

Profile
Chromocarb diethylamine is used to reduce capillary haemorrhage (including conjunctival haemorrhage) associated with various disorders, and for venous insufficiency. It is given by mouth in doses of 0.6 to 1.2 g daily in divided doses. It is also used as eye drops; 1 or 2 drops of a 10% solution have been instilled up to 6 times daily.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Angioftal†; ***Fr.:*** Angiophtal†; Campel; ***Ital.:*** Fludarene; ***Port.:*** Fradilen; ***Spain:*** Activadone.

Chrysoidine Hydrochloride Citrate
Crisoidina, hidrocloruro del citrato de. 4-Phenylazobenzene-1,3-diamine hydrochloride citrate; Azobenzene-2,4-diamine hydrochloride citrate.
$C_{12}H_{12}N_4,HCl,C_6H_8O_7$ = 440.8.
CAS — 532-82-1 (chrysoidine hydrochloride); 5909-04-6 (chrysoidine hydrochloride citrate).

Profile
Chrysoidine hydrochloride citrate has been used as a dye but has been associated with tumours of the bladder.

Carcinogenicity. The development of tumours of the urinary bladder in anglers was possibly associated with the use of chrysoidine hydrochloride (chrysoidine Y; CI Basic Orange 2; Colour Index No. 11270) for colouring the maggots used as bait.[1-3]

1. Searle CE, Teale J. Chrysoidine-dyed bait: a possible carcinogenic hazard to anglers? *Lancet* 1982; **i:** 564.
2. Sole GM. Maggots dyed with chrysoidine: a possible risk to anglers. *BMJ* 1984; **289:** 1043–4.
3. Massey JA, *et al.* Maggots dyed with chrysoidine. *BMJ* 1984; **289:** 1451–2.

Chymopapain *(BAN, USAN, rINN)*
BAX-1526; Chymopapaïne; Chymopapainum; Kymopapaiini; Kymopapain; NSC-107079; Quimopapaína; Quimopapaina.
Химопапаин
CAS — 9001-09-6.
ATC — M09AB01.
ATC Vet — QM09AB01.

Description. Chymopapain is a proteolytic enzyme isolated from the latex of papaya (*Carica papaya*), differing from papain in electrophoretic mobility, solubility, and substrate specificity. Molecular weight about 27 000.

Units
One nanokatal (nKat) is defined as the amount of chymopapain which produces 1 nanomole of *p*-nitroaniline per second from DL-benzoylarginine-*p*-nitroanilide substrate at pH 6.4 and 37°.

In some countries CTE units have been used, defined as the amount of chymopapain that produces a hydrolysate from acid-denatured haemoglobin at pH 4.0 in one minute with an optical density at 275 nm equivalent to that of a tyrosine solution 0.0001%.

Adverse Effects
The most important adverse effect of chymopapain is anaphylaxis, which can occur in up to about 1% of patients. It has resulted in fatalities and restricts use to a single treatment session per patient. Typical symptoms include angioedema, hypotension, laryngeal oedema and bronchospasm, shock, and cardiac arrest. Allergic skin reactions may also occur. Other reported reactions include headache, nausea and vomiting, paralytic ileus, urinary retention, thrombophlebitis, paraesthesias, foot-drop, and discitis. Severe muscle spasm and an increase in back pain are common. Paraplegia, acute transverse myelitis, and intracerebral and subarachnoid haemorrhage have occurred.

Incidence of adverse effects. A 1984 postmarketing surveillance study on a US chymopapain preparation for intradiscal injection (*Chymodiactin*) involved data from 29 075 patients (representing about 50% of the total number of vials sold).[1] Anaphylactic reactions were confirmed in 194 patients (0.67%), 2 of whom died. The incidence was higher in women than in men. In 52 cases the reaction occurred after the test dose. Serious neurological reactions reported were: cerebral haemorrhage (6 cases, 3 fatal; autopsy revealed that they had underlying cerebrovascular abnormalities); paraplegia (11 cases, 5 of which may have been due to incorrect needle placement); transverse myelitis with paraplegia (2 cases, after 2 and 3 weeks, with subsequent recovery); and seizures (2 cases on injection and 1 several days after the procedure). Twenty-two patients had discitis with severe back pain and spasm. In 9 cases bacteria could be cultured, and 1 patient subsequently developed fatal *Staphylococcus aureus* meningitis.

Another review[2] of serious reactions associated with chymopapain between 1982 and 1991 (including data from the earlier postmarketing study) involved 121 reports among about 135 000 patients. They included fatal anaphylaxis (7), infections (24), haemorrhage (32), and neurological reactions (32).

Both reviews concluded that careful attention to proper patient selection and correct techniques of intradiscal needle placement are the most important factors in avoiding adverse effects with chymopapain.

1. Agre K, *et al.* Chymodiactin postmarketing surveillance: demographic and adverse experience data in 29075 patients. *Spine* 1984; **9:** 479–85.
2. Nordby EJ, *et al.* Safety of chemonucleolysis: adverse effects reported in the United States, 1982–1991. *Clin Orthop* 1993; **293:** 122–34.

Precautions
Chymopapain should not be used in those patients with a known sensitivity to papaya proteins or in patients with progressive paralysis, or tumours of the spinal cord, or lesions of the cauda equina. Severe spondylolisthesis is also a contra-indication. It should not be given to patients with heart failure, coronary artery disease, or respiratory failure who may be at increased risk if anaphylaxis occurs, nor to patients receiving beta blockers.

Care is required in administering chymopapain to ensure that the injection is into the disc and not intrathecal. However, discography is not recommended since the use of contrast media may exacerbate neurotoxicity and may inactivate the enzyme.

The risk of allergic reactions associated with chymopapain is so high that no patient should ever receive it more than once. Tests to identify those most at risk and pretreatment with antihistamines (H_1 and H_2) and corticosteroids may be used, but facilities for the emergency management of anaphylactic reactions should always be to hand when giving patients chymopapain. The risk of anaphylaxis is higher in women.

Injection of more than one disc is associated with an increased frequency of neurological reactions; therefore, such injection should only be carried out following confirmation of definite further disc involvement.

Uses and Administration
Chymopapain is used as an injection into the intervertebral disc in the treatment of sciatic pain and other symptoms secondary to herniation of intervertebral discs of the lumbar spine (chemonucleolysis).

Chymopapain injection should preferably be given under local, rather than general, anaesthesia. The dose for a single intervertebral disc is 2 to 4 nanokatals, with a maximum dose per patient of 8 nanokatals.

Chemonucleolysis. Dissolution of the disc by injection of chymopapain or other enzymes (chemonucleolysis) has been used as an effective alternative to surgery in patients with lumbar disc herniation (see Low Back Pain, p.7). However, concerns about its safety have led to a decline in its use, and discectomy is often preferred.

References.

1. Nordby EJ, *et al.* Chemonucleolysis. *Spine* 1996; **21:** 1102–5.
2. Brown MD. Update on chemonucleolysis. *Spine* 1996; **21** (24 suppl): 62S–68S.
3. Poynton AR, *et al.* Chymopapain chemonucleolysis: a review of 105 cases. *J R Coll Surg Edinb* 1998; **43:** 407–9.
4. Wittenberg RH, *et al.* Five-year results from chemonucleolysis with chymopapain or collagenase: a prospective randomized study. *Spine* 2001; **26:** 1835–41.

Preparations
Proprietary Preparations (details are given in Part 3)
Austral.: Chymodiactin; ***Spain:*** Chymodiactin†.

Chymotrypsin *(BAN, rINN)*
Chimotripsinas; α-Chymotrypsin; Chymotrypsine; Chymotrypsinum; Kimotripszin; Kymotrypsiini; Kymotrypsin; Quimotripsina.
Химотрипсин
CAS — 9004-07-3.
ATC — B06AA04; S01KX01.
ATC Vet — QB06AA04; QS01KX01.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.
Ph. Eur. 6.2 (Chymotrypsin). A proteolytic enzyme obtained by the activation of chymotrypsinogen extracted from the pancreas of beef. It contains not less than 5 microkatals in each mg. A white or almost white, crystalline or amorphous powder; the amorphous form is hygroscopic. Sparingly soluble in water. A 1% solution in water has a pH of 3.0 to 5.0. Solutions have a maximum stability at pH 3 and a maximum activity at about pH 8. Store at 2° to 8° in airtight containers. Protect from light.
USP 31 (Chymotrypsin). A proteolytic enzyme crystallised from an extract of the pancreas gland of the ox, *Bos taurus* (Bovidae). It contains not less than 1000 USP units in each mg, calculated on the dried basis. A white to yellowish-white, crystalline or amorphous, odourless powder. An amount equivalent to 100 000 USP units is soluble in 10 mL of water and in 10 mL of sodium chloride 0.9%. Store in airtight containers at a temperature not exceeding 40°.

Units
Various methods have been used to assay the potency of chymotrypsin. Ph. Eur. 6.2 expresses activity in terms of microkatals while USP 31 expresses in terms of USP units. Other units that may be encountered are FIP units, Armour units, and Denver (or Wallace or Wampole) units.

Uses and Administration
Chymotrypsin is a proteolytic enzyme that has been used in ophthalmology for the dissection of the zonule of the lens, thus facil-