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.

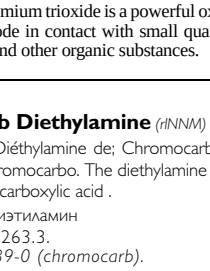
Chromium is an essential trace element as described on p.1934.

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-