(Хилозар-КОМОД); ***S.Afr.:*** Duovisc; Viscoat; ***Singapore:*** Duovisc; Viscoat; ***Switz.:*** Alphastria; Ialugen Plus; Lacrycon; ***Thai.:*** Duovisc; Viscoat; ***Turk.:*** Duovisc; Viscoat; ***UK:*** Atopiclair; Gelclair; Seprafilm; Xclair; Zuidex; ***USA:*** Atopiclair; Deflux; DisCoVisc; Gelclair; Healon Yellow; RadiaPlex Rx; Seprafilm; Viscoat; Zacare Kit; ***Venez.:*** Cepin; Epitheliale AH; Viscoat†.

Hyaluronidase *(BAN, rINN)*

Hialuronidasa; Hialuronidáz; Hialuronidazė; Hiyalüronidaz; Hyaluronidaasi; Hyaluronidas; Hyaluronidasa; Hyaluronidasum.

Гиалуронидаза

CAS — 9001-54-1.
ATC — B06AA03.
ATC Vet — QB06AA03.

NOTE. The name kinetin (p.1603) has also been used as a proprietary name for hyaluronidase.

Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii). *US* includes as an injectable form.

Ph. Eur. 6.2 (Hyaluronidase). An enzyme capable of hydrolysing mucopolysaccharides of the hyaluronic acid type. It is prepared from the testes of mammals by a method that has been shown to reduce contamination by known infectious agents to acceptable limits; a suitable stabilising agent may be added to the purified preparation. A white or yellowish-white, amorphous powder; it contains not less than 300 international units of hyaluronidase activity per mg, calculated with reference to the dried substance. Soluble in water; practically insoluble in alcohol and in acetone. A 0.3% solution in water has a pH of 4.5 to 7.5. Store at 2° to 8° in airtight containers.

Units

The international and USP units are equivalent. One international or USP unit is equivalent to one turbidity-reducing unit or about 3.3 viscosity-reducing units.

Adverse Effects and Precautions

Sensitivity to hyaluronidase occasionally occurs. Because of the danger of spreading infection, the enzyme generally should not be injected into or around an infected area. It has been suggested that the presence of malignancy may similarly be a contra-indication to the use of hyaluronidase. It should not be given by intravenous injection nor should it be used for anaesthetic procedures in cases of unexplained premature labour. Hyaluronidase should not be applied directly to the cornea. It should not be used to reduce the swelling of bites or stings.

Uses and Administration

Hyaluronidase is an enzyme that reversibly depolymerises hyaluronic acid (above), a component of the ground substance or tissue cement surrounding cells, thereby temporarily reducing its viscosity and rendering the tissues more readily permeable to injected fluids.

Hyaluronidase is used to increase the speed of absorption and reduce discomfort due to subcutaneous or intramuscular injection of fluids, to promote resorption of excess fluids and extravasated blood in the tissues, and to increase the effectiveness of local anaesthesia.

In the UK, the usual dose as an adjunct to subcutaneous or intramuscular injection is 1500 units, added directly to the injection. To aid the dispersal of extravasated fluids or blood, the same dose is given in 1 mL of Water for Injections or 0.9% sodium chloride into the affected area. Lower doses of hyaluronidase are used in some countries; in the USA, the usual dose is 150 units.

In hypodermoclysis, hyaluronidase is used to aid the subcutaneous administration of relatively large volumes of fluids, especially in infants and young children, where intravenous injection is difficult. Care should be taken in the treatment of children and the elderly to control the speed and total volume given and to avoid overhydration. Hyaluronidase may be added to the injection fluid or may be injected into the site before the fluid is given. In the UK, 1500 units of hyaluronidase is generally given with each 500 to 1000 mL of fluid for subcutaneous use, but in the USA, 150 units of hyaluronidase is considered adequate for each litre of hypodermoclysis solution.

The diffusion of local anaesthetics is accelerated by the addition of 1500 units (in the USA, 150 units) of hyaluronidase to the anaesthetic solution. It has also been used in ophthalmology as an aid to local anaesthesia at recommended doses of 15 units/mL of local anaesthetic solution. Hyaluronidase has also been used for the treatment of vitreous haemorrhage and diabetic retinopathy.

To improve the resorption of radiopaque agents in subcutaneous urography, hyaluronidase is injected subcutaneously in a dose of 75 units over each scapula followed by injection of the contrast medium at the same site.

Recombinant human hyaluronidase is used for the preparation of oocytes during IVF.

Hyalosidase (GL enzyme) is a highly purified form of hyaluronidase that has been studied.

◊ General references.

1. Watson D. Hyaluronidase. *Br J Anaesth* 1993; **71:** 422–5.

Ophthalmic surgery. In a study[1] involving 150 consecutive patients undergoing surgery for senile cataract, retrobulbar anaesthesia with lidocaine 2% solution plus adrenaline 1:100 000 and hyaluronidase 15 units/mL produced successful anaesthesia in 69 of 75 cases (92%), which was significantly better than 42 of 75 treated with lidocaine plus adrenaline alone. Although poor results have been reported from hyaluronidase and a local anaesthetic without adrenaline to restrict local anaesthetic absorption, the use of the enzyme and adrenaline was recommended as an aid to achieving complete ocular akinesia and anaesthesia in cataract surgery. Hyaluronidase has also been used with a mixture of bupivacaine and lidocaine for peribulbar anaesthesia, but results have been conflicting. In a study[2] in 50 patients, addition of hyaluronidase 25 units/mL of local anaesthetic mixture had no significant effect on time to satisfactory anaesthesia. However, in a second study[3] involving 200 patients, addition of hyaluronidase 50 or 300 units/mL improved the quality of the peribulbar block and, in the case of the higher concentration, also increased the speed of onset.

1. Thomson I. Addition of hyaluronidase to lignocaine with adrenaline for retrobulbar anaesthesia in the surgery of senile cataract. *Br J Ophthalmol* 1988; **72:** 700–2.
2. Prosser DP, *et al*. Re-evaluation of hyaluronidase in peribulbar anaesthesia. *Br J Ophthalmol* 1996; **80:** 827–30.
3. Dempsey GA, *et al*. Hyaluronidase and peribulbar block. *Br J Anaesth* 1997; **78:** 671–4.

Preparations

BP 2008: Hyaluronidase Injection;
USP 31: Hyaluronidase for Injection; Hyaluronidase Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Unidasa; ***Austral.:*** Hyalase; ***Braz.:*** Hyalozima; ***Chile:*** Wydase†; ***Cz.:*** Hyasa†; Hylase; ***Ger.:*** Hylase; ***Gr.:*** Hyalase; ***Hung.:*** Hyase†; ***India:*** Hynidase; ***Israel:*** Hyalase; ***Ital.:*** Jaluran†; ***Neth.:*** Hyason; ***NZ:*** Hyalase; ***S.Afr.:*** Hyalase; ***Turk.:*** Orthovisc; ***UK:*** Hyalase; ***USA:*** Amphadase; Hydase; Hylenex; Vitrase; Wydase†.

Multi-ingredient: ***Arg.:*** Nilflux; ***Austria:*** Lemuval; ***Braz.:*** Oto Xilodase; Postec; Xilodase; ***Ital.:*** Lido-Hyal; ***Pol.:*** Helason; ***Spain:*** Lasonil†; Oto Difusor†; ***Switz.:*** Lido-Hyal.

Hydrangea

Hidrangea; Seven Barks; Smooth Hydrangea; Wild Hydrangea.

Profile

Hydrangea, the root of *Hydrangea arborescens* (Hydrangeaceae), has diuretic and litholytic properties and is used for genitourinary disorders including renal and urinary calculi.

Homoeopathy. Hydrangea has been used in homoeopathic medicines under the following names: Hydrangea arborescens; Hydrang.

Preparations

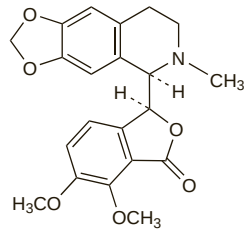
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***UK:*** Antiglan; Backache.

Hydrastine Hydrochloride

Hidrastina, hidrocloruro de; Hydrastyny chlorowodorek. 6,7-Dimethoxy-3-(5,6,7,8-tetrahydro-6-methyl-1,3-dioxolo[4,5-*g*]isoquinolin-5-yl)isobenzofuran-1(3*H*)-one hydrochloride.

$C_{21}H_{21}NO_6$,HCl = 419.9.

CAS — 118-08-1 (hydrastine); 5936-28-7 (hydrastine hydrochloride).



(hydrastine)

Profile

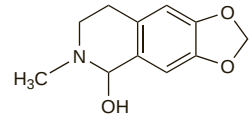
Hydrastine hydrochloride, the hydrochloride of an alkaloid obtained from *Hydrastis canadensis* (Ranunculaceae) (see Hydrastis, below), has been reputed to cause uterine contractions and arrest uterine haemorrhage but it is of doubtful value. It was also formerly used in gastrointestinal disorders. Toxic doses are reported to cause strychnine-like convulsions and relaxation of the gut.

Hydrastinine Hydrochloride

Idrastinina Cloruro. 5,6,7,8-Tetrahydro-6-methyl-1,3-dioxolo[4,5-*g*]isoquinolin-5-ol hydrochloride.

$C_{11}H_{11}NO_2$,HCl = 225.7.

CAS — 6592-85-4 (hydrastinine); 4884-68-8 (hydrastinine hydrochloride).



(hydrastinine)

Profile

Hydrastinine is a derivative of the alkaloid hydrastine (p.2321) and has been used similarly. It has vasoconstrictor properties and has been used as the hydrochloride as an ingredient of topical preparations for minor eye disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austria:*** Dacrin; Haemanal.

Hydrastis

Golden Seal; Goldenseal; Hidraste; Hidrastis; Hydrast.; Hydrastidis Radix; Hydrastis rhizoma; Hydrastisjuuri; Hydrastisrot; Idraste; Kanadinių auksašaknių šakniastiebiai; Vodilkový kořen; Yellow Root.

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.

Ph. Eur. 6.2 (Goldenseal Rhizome; Goldenseal Root BP 2008). The whole or cut, dried rhizome and root of *Hydrastis canadensis* containing not less than 2.5% of hydrastine and not less than 3.0% of berberine, calculated on the dried basis. Protect from light.

USP 31 (Goldenseal). The dried roots and rhizomes of *Hydrastis canadensis* (Ranunculaceae), containing not less than 2.0% of hydrastine and not less than 2.5% of berberine, calculated on the dried basis. Store in airtight containers. Protect from light, moisture, and heat.

Profile

Hydrastis was formerly used to arrest excessive uterine haemorrhage. It is included in some herbal preparations for gastrointestinal disorders and peripheral vascular disorders. The pharmacological activity of hydrastis is attributed primarily to 2 of its constituent alkaloids, berberine (p.2264) and hydrastine (above).

Homoeopathy. Hydrastis has been used in homoeopathic medicines under the following names: Hydrastis canadensis; Hydrdr. can.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Gingivitol N.

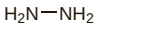
Multi-ingredient: ***Austral.:*** Bilberry Plus; Euphrasia Complex; Herbal Cleanse†; Hydrastis Complex†; Sambucus Complex†; Urapro†; Urinase†; ***Braz.:*** Bromidrastina†; ***Canad.:*** Echinacea Goldenseal Formula†; ***Fr.:*** Climaxol; ***Spain:*** Proctosor†; Solucion Schoum; ***Turk.:*** Ma-Ka-Ta; ***UK:*** Digestive; HRI Golden Seal Digestive; Wind & Dyspepsia Relief.

Hydrazine Sulfate

Hidrazina, sulfato de; Hydrazine Sulphate; Hydrazyny siarczan.

$H_6N_2O_4S$ = 130.1.

CAS — 302-01-2 (hydrazine); 10034-93-2 (hydrazine sulfate).



(hydrazine)

Profile

Hydrazine sulfate is employed in various industrial processes. It is used in the preparation of hydrazine hydrate which is applied after a solution of platinic chloride for corneal tattooing. It has been tried, but with little if any benefit, in the management of cancer-related anorexia and cachexia.

Adverse effects and treatment. References to adverse effects resulting from exposure to hydrazine.[1-5] Pyridoxine has been used in the management of hydrazine intoxication.[6-8]

1. Albert DM, Puliafito CA. Choroidal melanoma: possible exposure to industrial toxins. *N Engl J Med* 1977; **296:** 634–5.
2. Durant PJ, Harris RA. Hydrazine and lupus. *N Engl J Med* 1980; **303:** 584–5.
3. WHO. Hydrazine. *Environmental Health Criteria 68*. Geneva: WHO, 1987. Available at: http://www.inchem.org/documents/ehc/ehc/ehc68.htm (accessed 24/07/08)
4. WHO. Hydrazine health and safety guide. *IPCS Health and Safety Guide 56*. Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/hsg/hsg/hsg056.htm (accessed 24/07/08)
5. Hainer MI, *et al*. Fatal hepatorenal failure associated with hydrazine sulfate. *Ann Intern Med* 2000; **133:** 877–80.
6. Kirklin JK, *et al*. Treatment of hydrazine-induced coma with pyridoxine. *N Engl J Med* 1976; **294:** 938–9.